

Medical Faculty
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Annual Report 2017



CONTENTS

Foreword	5
Historical	
A brief history of the Faculty	6
Strategy and Numbers	
Research strategy	10
The Medical Faculty in numbers	11
Key people and Institutions	
Organigramm	12
Key people	13
Structural development.....	14
Teaching	
Human Medicine	16
Teaching at the School of Dental Medicine.....	18
Reintroduction of a Master program in Pharmacy.....	20
Master Program in Biomedical Sciences.....	21
Master Program in Biomedical Engineering	22
CAS, DAS and MAS Degree Programs.....	24
Promotion of young academics	
PhD education	28
Grants	30
Mentoring 4 Women	31
Centers and Platforms	
ARTORG Center for Biomedical Engineering Research	32
Department for BioMedical Research (DBMR).....	34
Microscopy Imaging Center (MIC).....	36
Swiss Institute for Translational and Entrepreneurial Medicine (sitem-insel)	38
University Neurocenter.....	40
Institutes at the University of Bern	
Institute of Anatomy.....	42
Institute of Biochemistry and Molecular Medicine (IBMM)	44
Institute for the History of Medicine	46
Institute of Pharmacology	48
Institute of Physiology.....	50
Institute of Social and Preventive Medicine.....	52
Institute for Surgical Technology and Biomechanics.....	54
Theodor Kocher Institute	56
Institute for Infectious Diseases	58
Institute of Pathology.....	60
Institute of Forensic Medicine.....	62
Institute of Primary Health Care (BIHAM).....	64
Institute of Complementary Medicine	66
Institute of Medical Education.....	68
Institute of Dental Medicine.....	70

Clinics at the University Hospital, Inselspital

Department of General Internal Medicine	72
Department of Anaesthesiology and Pain Medicine.....	74
Department of Angiology	76
Department of Ophthalmology	78
Department of Dermatology	80
Department of Diabetes, Endocrinology, Nutritional Medicine and Metabolism (UDEM)	82
Department of Obstetrics and Gynecology.....	84
Department of Geriatrics.....	86
Department of Hematology and Central Hematology Laboratory	88
Department of Cardiovascular Surgery	90
Department of ENT, Head and Neck Surgery	92
Department of Infectious Diseases	94
Department of Intensive Care Medicine	96
Department of Cardiology	98
Department of Pediatric Surgery	100
Department of Pediatrics	102
Department of Medical Oncology	104
Department of Nephrology and Hypertension	106
Department of Neurosurgery	108
Department of Neurology	110
Department of Nuclear Medicine	112
Department of Orthopedic Surgery and Traumatology	114
Department of Osteoporosis	116
Department for Plastic and Hand Surgery.....	118
Department for Pulmonary Medicine.....	120
Department of Radiation Oncology	122
Department of Immunology, RIA.....	124
Department of Cranio-Maxillofacial Surgery.....	126
Department of Thoracic Surgery.....	128
Department of Urology.....	130
Department for Visceral Surgery and Medicine.....	132
Department of Emergency Medicine	134
Department of Diagnostic and Interventional Neuroradiology.....	136
Department of Diagnostic, Interventional and Pediatric Radiology (DIPR)	138
Department of Magnetic Resonance Spectroscopy and Methodology.....	140
Department of Clinical Chemistry.....	142

Universitäre Psychiatrische Dienste Bern (UPD)

University Hospital of Old Age Psychiatry and Psychotherapy (APP).....	144
University Hospital of Child and Adolescent Psychiatry and Psychotherapy (KJP)	146
University Hospital of Psychiatry and Psychotherapy (PP).....	148

FOREWORD

The University of Bern was founded in 1834 and has from the beginning included a Medical Faculty. In the last 183 years, many personalities formed and developed our Faculty, including Theodor Kocher, who was awarded the Nobel Prize in 1909 for his work on the thyroid gland. Theodor Kocher was the first surgeon and the first Swiss medical doctor to have received the Prize. Today the Medical Faculty is one of the five complete Medical Faculties in Switzerland offering a full program of study in Medicine and Dental Medicine. In addition, Master studies in Biomedicine and Biomedical Engineering have been established. Our faculty is ranked among the top 100 medical institutions world-wide.

High-quality undergraduate teaching and close student - faculty contact remain central to our philosophy. The popularity of our teaching is reflected by the number of medical students enrolled which has increased continuously in the last decade and is the highest in Switzerland (with over 240 students beginning the first year). From September 2018, we will accommodate an additional 100 students in the first year of study, the total first year medical class then numbering approximately 340. In 2017, we have worked hard to optimally plan the new content of our teaching programs, as well as resources and logistics, which needed to be adapted to the increased numbers of students. We are happy to say that we will continue offering a problem-oriented study program, which demands a high proportion of well-trained teaching staff. In addition, the Medical Faculty, together with its University Hospitals (Inselspital and UPD) offers medical resident programs in each field which are continuously being improved and require close collaboration between the different clinics.

The Medical Faculty of Bern provides excellent opportunities for high quality research. Together with the Board of Directors of the Inselspital, our research strategy was updated in 2017. Basic research is carried out in the pre-clinical institutions (Anatomy, Physiology, Biochemistry and Molecular Medicine, Pharmacology, Pathology, Infectious Diseases). Additional basic research is facilitated by the Department of Biomedical Research (DBMR), which offers all clinics of the Inselspital and UPD excellent opportunities, infrastructure and technical support for their work. Clinical research, including large international trials, is performed with the support of

the Clinical Trial Unit (CTU) working closely with the Institute of Social and Preventive Medicine (ISPM) and the Institute of Primary Health Care (BIHAM). To promote patient-oriented clinical research, an innovative MD-PhD program in Clinical Sciences was started in 2017. Our Faculty gives strong support to the promotion of young researchers and to gender equality. We offer intramural grant opportunities for clinical (e.g. CTU grants) and experimental researchers.

Translational research programs in the fields of biomedical engineering were greatly energized by the creation of the unique Center for Artificial Organs (ARTORG) in 2008. Accordingly, research in biomedical engineering enjoys excellent conditions. Furthermore, it is planned that some research groups in this field will be re-located in the Swiss Institute for Translational and Entrepreneurial Medicine (SITEM) which is currently under construction on the Inselspital Campus in close proximity to all the clinics of the University Hospital. The move is planned for Spring 2019. Another strategic step to strengthen Translational Medicine was the decision to build up a Center for Precision Medicine. Together with other local platforms (e.g. the unique Bern Liquid Biobank, which was inaugurated in 2017), this Center will give Bern a strong position within the Swiss Personalized Health Network (SPHN) initiative. It is planned that Precision Medicine be integrated in the daily medical practice of our clinics. The aim is to make the Inselspital one of the leading University Hospitals in the world in consequence of this important translational focus.

We hope that you will enjoy reading this report, which was prepared to promote familiarity with all the knowledge and collaborations within and outside our University. We take this opportunity to thank all our employees and partners for their outstanding commitment which has made 2017 a very successful year for the Medical Faculty of Bern.

Hans-Uwe Simon
Dean
(on behalf of the Board of the Medical Faculty)

A BRIEF HISTORY OF THE FACULTY

Precursors

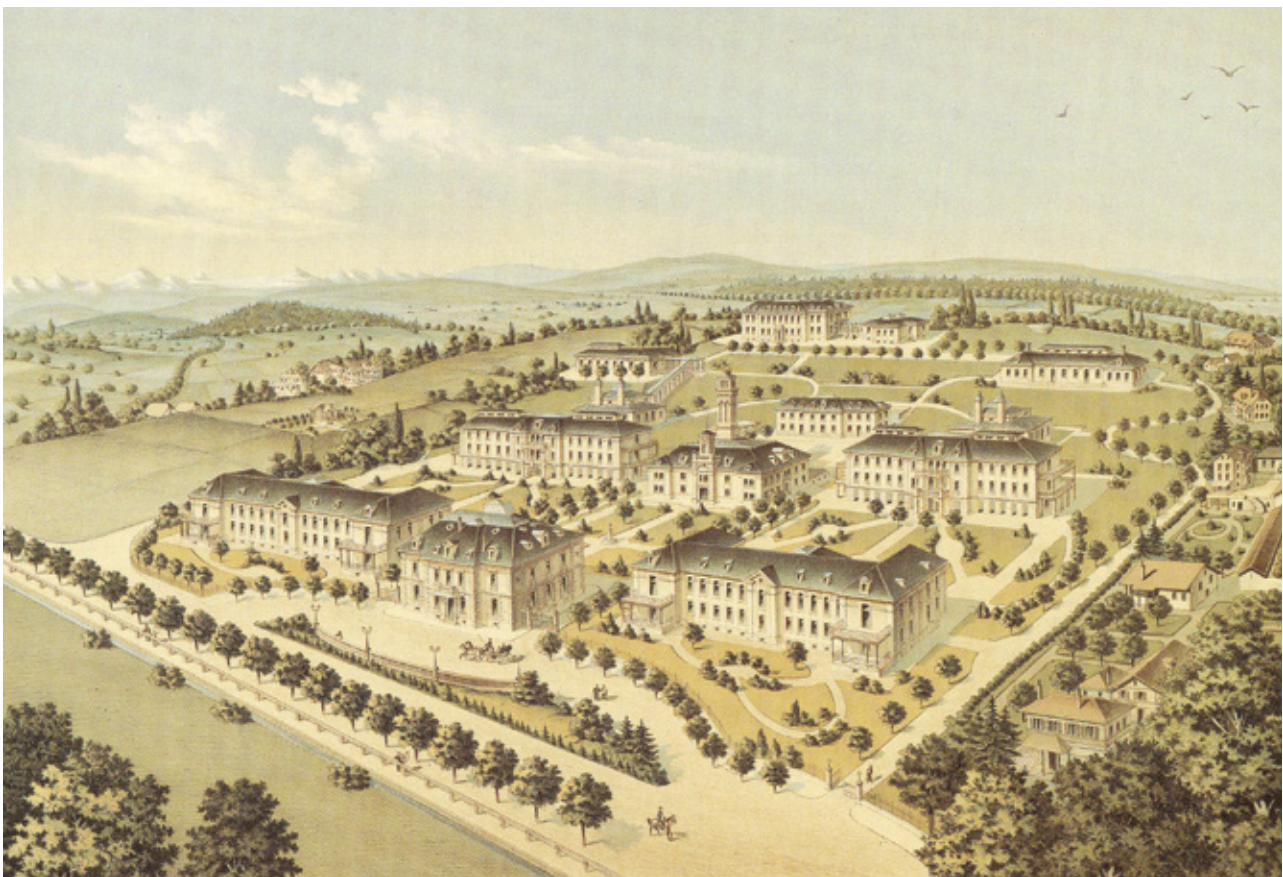
A medical faculty, called *facultas medica* or *collegium medicum*, existed already in the 16th century, long before the foundation of the University. This was, however, not a research or teaching institution but an appointed body of physicians and surgeons providing medical care and expertise for the city and State of Bern. A first proper but still very humble educational institution, the Medical Institute (Medizinisches Institut), was established in 1797 as a private initiative of local physicians, surgeons and apothecaries. In 1805, it was transformed into the Medical Faculty of the newly established Academy which in its turn was the precursor of the University, founded in 1834.

19th century

In the early 19th century, Switzerland was academically still a developing country. Thanks to the reigning liberal attitude the State and the University of Bern were willing to attract the best scholars from Germany, the leading nation in research at that time. The whole first group of full medical professors and 65% of all those appointed in the 19th century were Germans. Gabriel Gustav Valentin (1810-1883) is a

good example. Originating from Breslau, he was a very promising young scholar who had just detected together with his teacher Jan Evangelista Purkyně the mechanisms of the ciliated epithelium. At the early age of 26, he was appointed as full professor of physiology and comparative anatomy, becoming thus the first Jewish professor at a German-language university. During his many years in Bern, he published extensively and established himself as a leading authority in cytology.

Some of Valentin's German colleagues stayed in Bern only for a few years, e.g. Theodor Langhans (1839-1915), discoverer of the Langhans giant cells or Ludwig Lichtheim (1845-1928), one of the founders of modern neurology. They helped, however, to strengthen Bern's reputation and to attract further eminent and internationally acclaimed scientists. Among those we may mention Hugo Kronecker (1839-1914), a master of physiological methods with an extensive professional network and pupils all over the world. Another important figure was Alexander Tschirch (1856-1939), the undisputed authority on pharmacognosy, recipient of six honorary doctoral degrees and honorary memberships of 40 academic



The newly built University Hospital, 1884.

societies. And finally, there was Josef Jadassohn (1863-1936), whose name is connected with a series of dermatoses and anomalies and who transformed Bern into an international center of dermatology.

Theodor Kocher, Nobel laureate

The most prominent figure of the early period was, however, Theodor Kocher (1841-1917), a Swiss. As professor and head of the surgical clinic he shaped the Medical Faculty and was the figurehead of the University for 45 years. He performed detailed clinical-pathological observations and physiological experiments in order to establish a more solid basis of surgery. In his highly influential surgical handbook – translated into several languages – he presented a ‘system of safe surgery’ based on slow operating techniques and painstaking haemostasis (using ‘Kocher clamps’). He had a particular impact on the emerging American medicine, especially through the dozens of surgeons who visited him each year. According to his manifold innovations and his high standing, he was elected first president of the International Society of Surgery in 1903 and was awarded the 1909 Nobel Prize in Medicine for his contributions to the physiology, pathology, and surgery of the thyroid.

Medical technology

Kocher was not only the key figure to establish the Medical Faculty as an internationally renowned institution, he started also Bern’s tradition of excellence in medical technology. He designed a whole series of surgical instruments, produced by Schaerer Inc., which served as models for generations. His successor, Fritz de Quervain (1868-1940) continued the collaboration with Schaerer and constructed together with the industrial company the world’s first fully adjustable operation table in 1912. Hermann Sahli (1856-1933), head of the medical clinic, developed a series of analytical devices to measure pulse, blood pressure etc. which allowed general practitioners to keep up with the increasing demands of modern medicine. His hemometer, a simple instrument used for colorimetric measurement of hemoglobin, was copied and used for decades in medical practices all over the world. Since the 1880s, there was also close collaboration between University and industry in the area of ophthalmology. It gained a new level of importance with Prof. Hans Goldmann (1899-1991) and Haag-Streit Inc. who developed split lamps, perimeters and tonometers which set new international standards.



Theodor Kocher operating in front of an international audience, 1912 (William Halsted, among others).

A BRIEF HISTORY OF THE FACULTY

Of even greater consequence was the work of Maurice E. Müller (1918-2009). Together with a group of young surgical colleagues and engineers he developed new materials and techniques for internal plate fixation of fractures (osteosynthesis) and hip prosthesis.



Müller practising osteosynthesis, 1960.

Establishing new standards in a globalized medical world meant not only a medical but also an economic success. Müller's inventions led to the establishment of several foundations and the creation of various companies (Mathys, Synthes, Straumann; Protek, later Sulzer, then Zimmer). In recognition of his international impact, Müller was named "Orthopaedic Surgeon of the 20th Century" by the International Society of Orthopaedic Surgery and Traumatology. Müller generously founded the University's Institute for Biomechanics, today's Institute for Surgical Technology and Biomechanics. The ISTB, the ARTORG Center for Biomedical Engineering Research and other institutions continue our tradition of developing internationally acclaimed new medical technologies.

Increasing demands

The history of the Medical Faculty is, of course, deeply intertwined with the history of the local hospital, the Inselspital, a charitable foundation dating back to 1354. Some clinical teaching at the hospital was already offered in the premodern period and required little regulations. With the foundation of the University in 1834, however, the hospital had to assume new duties. Besides the traditional care of poor people, it now had to provide beds and patients

for teaching and research and increasingly serve as a medical center for the whole region – obligations the foundation could carry out only with the support of the Canton of Bern. From 1834 to today, a series of contracts lays down the financial and organizational details of this cooperation.

In reaction to the growing demands, in 1884 – not least thanks to the efforts of Kocher – a new hospital was built on a site outside the city walls. Increasing specialization and need of infrastructure led soon to new institutes, clinics and thus new buildings on the hospital site as well as in the nearby city district. Around 1900, the still modest student numbers rose considerably. This was not, however, due to local interest but to women who were not allowed to study at most universities but accepted by the liberal Universities of Bern, Zurich, Lausanne and Geneva. Between 1864 and 1914, more than 7'000 women from foreign countries, mainly Russia, pursued a medical course in Switzerland (1'600 in Bern), more than in the rest of Europe combined. It took several decades until another sharp increase in student numbers occurred in the 1960s thanks to the generation of the baby boomers. This increase was coupled with large investments in infrastructure, medical research and technology. After some 20 years of consolidation a new sharp rise of student numbers started around 2000 which is mainly due to an increased demand for locally trained medical doctors and new master programs in biomedicine.



Students (mainly Russian women) in the dissection hall, 1907.

Deans of the Medical Faculty

1834–1835	Hugo Mohl	1936–1938	Paul Casparis
1835–1838	Hermann Askan Demme	1938–1940	Jakob Klaesi
1838–1843	Wilhelm Philipp Friedrich Vogt	1940–1941	Hans Bluntschli
1843–1847	Gabriel Gustav Valentin	1941–1943	Alexander von Muralt
1847–1849	Friedrich Miescher	1943–1945	Eduard Glanzmann
1849–1852	Friedrich Wilhelm Theile	1945–1947	Hans Goldmann
1852–1857	Wilhelm Rau	1947–1949	Joseph Dettling
1857–1860	Wilhelm Philipp Friedrich Vogt	1949–1951	Curt Hallauer
1860–1861	Wilhelm Rau	1951–1953	Karl Lenggenhager
1861–1865	Gabriel Gustav Valentin	1953–1955	Bernhard Walthard
1865–1867	Daniel Jonquière	1955–1957	Walther Wilbrandt
1867–1869	Christoph Theodor Aeby	1957–1959	Erich Hintzsche
1869–1871	Karl Emmert	1959–1961	Walter Neuweiler
1871–1874	Georg Albert Lücke / Henri Dor	1961–1963	Hugo Aebi
1874–1876	August Breisky / Th. Kocher	1963–1965	Adolf Zuppinger
1876–1878	Heinrich Irenäus. Quincke	1965–1967	Franz Escher
1878–1880	Theodor Langhans	1967–1969	Johann Kuske
1880–1882	Ernst Pflüger	1969–1971	Eugen Läuppi
1882–1884	Ludwig Lichtheim	1971–1973	André Schroeder
1884–1886	Marcellus Wilhelm von Nencki	1973–1978	Jürg Hodler
1886–1888	Hugo Kronecker	1978–1981	Beat Roos
1888–1890	Rudolf Demme	1981–1983	Herbert A. Fleisch
1890–1892	Ernst Pflüger	1983–1985	Harald Reuter
1892–1894	Hans Strasser	1985–1987	Rudolf Berchtold
1894–1896	Hermann Sahli	1987–1989	Max Hess
1896–1898	Alexander Tschirch	1989–1991	Georg Eisner
1898–1900	Theodor Kocher	1991–1993	Alfred H. Geering
1900–1902	Arthur Carl Wilhelm Heffter	1993–1995	Hans-Rudolf Lüscher
1902–1904	Theodor Langhans	1995–1997	Bernhard H. Lauterburg
1904–1906	Josef Jadassohn	1997–1999	Kurt Schopfer / H.-R. Lüscher
1906–1908	August Siegrist	1999–2004	Emilio Bossi
1908–1910	Wilhelm Kolle	2004–2008	Martin Täuber
1910–1911	Emil Bürgi	2008–2016	Peter Eggli
1911–1912	Leon Asher	2016–today	Hans-Uwe Simon
1912–1914	Hans Strasser		
1914–1916	Hans Guggisberg		
1916–1918	Leon Asher		
1918–1920	Carl Wegelin		
1920–1921	Fritz de Quervain		
1921–1923	Georg Sobernheim		
1923–1924	Fritz de Quervain		
1924–1926	Friedrich Lüscher		
1926–1928	Emil Bürgi		
1928–1930	Hans Guggisberg		
1930–1932	Carl Wegelin		
1932–1934	Walther Frey		
1934–1936	Emil Bürgi		

RESEARCH STRATEGY

The Medical Faculty of the University of Bern has developed a joint research strategy for the period 2017 – 2021 together with the University Hospital (Inselspital) and Psychiatric Services of the University of Bern (UPD). This strategy includes the vision of strengthening Bern as a city with a strong medical school and intensive research activities, and of encouraging interactions with companies developing medical products. A network of strong basic and clinical research projects is to be developed, with the goal of transferring knowledge and technology for medical use. For instance, it has been decided that our Faculty will actively support the Swiss Institute for Translational and Entrepreneurial Medicine (SITEM), the site for which is currently under construction on the Inselspital Campus in close proximity to all University Hospital clinics. In the following, we will briefly describe the content of our research strategy.

Financial support

Our academic institutions can obtain financial support in three ways:

- All institutions receive basic support for their development
- Additional support is provided according to institutional performance based on an annual evaluation of all institutions
- Excellent individual researchers performing highly competitive research can expect additional support

Support of young researchers

The support of young academics has the highest priority and takes place at each level of support. We have programs aiming to prepare our undergraduate students for an academic career. The development of more and higher qualified clinician-scientists represents our central goal. To achieve this, we have established a new graduate program, our Graduate School for Health Sciences, in which doctoral degrees in Clinical Sciences can be earned. Importantly, this program grants young researchers who are engaged in clinical service 50% protected research time over a period of 4 years. Among other important issues, we promote gender-equal opportunity. In particular, our goal is to encourage the training of more female scientists. Other important goals are the early

scientific independence of our young academics and their competitive acquisition of research grants from external resources.

Research foci

The Medical Faculty of the University of Bern promotes synergies and translational medicine, in consequence supporting the creation and consolidation of centers sharing common research topics and technologies. The use of common methodological platforms is vital to encourage exchange of knowledge between different teams and to be able to finance the changing infrastructures needed for competitive research. The following functional research units of the Medical Faculty represent open platforms providing infrastructure and technical competence which can be used by all researchers against payment of fees:

- Clinical trial unit (CTU)
- Department for Biomedical Research (DBMR)
- ARTORG Center for Biomedical Engineering Research
- Experimental Animal Center (EAC), including a Clean Mouse Facility (CMF)
- Microscopy Imaging Center (MIC)
- (Future) Center for Precision Medicine

Thematic foci have been defined according to scientific performance. Here, we intend to use synergistic activities in accordance with the following strategic foci of the University Hospital and the UPD:

- University Center for Heart and Vascular Diseases
- University Neurocenter
- University Cancer Center Inselspital

This research strategy was confirmed by majority vote of all Faculty members in May 2017.

THE MEDICAL FACULTY IN NUMBERS

1'748 students in **2** Bachelorprograms and **4** Masterprograms,
164 students in **19** CAS / DAS / MAS programs

259 Final Master Degrees, thereof **180** in Medicine, **30** in Dental Medicine,
16 MSc in Biomedical Sciences, **33** MSc in Biomedical Engineering

313 Doctorate Degrees, thereof **194** Dr. med., **34** Dr. med. dent.,
76 from the Graduate School for Cellular and Biomedical Sciences and
9 from the Graduate School for Health Sciences

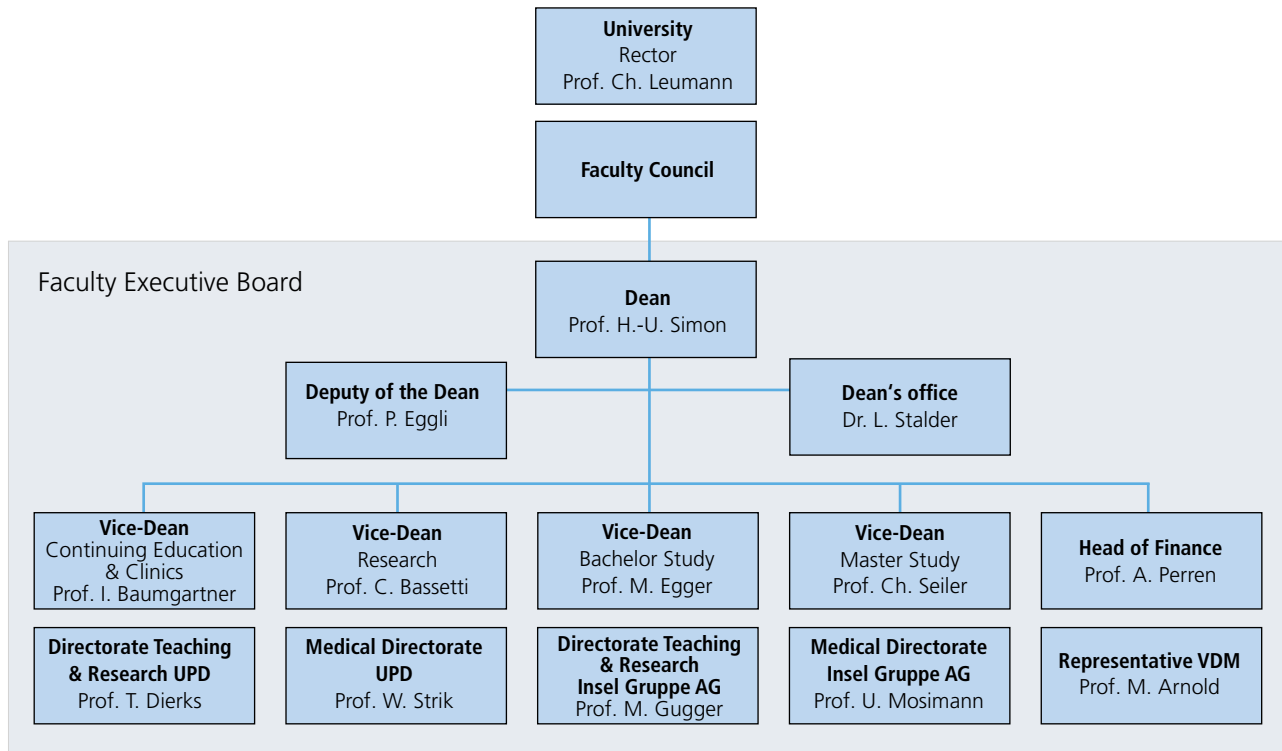
99 Full Professors, **17** Assistant Professors,
118 Associate Professors and **360** Lecturers

1 Faculty, **3** organisations, **38** clinics, **17** institutes

176'393'930 Mio Budget,
additionally **25'606'235** Mio from the Swiss National Science Foundation and
65'056'738 Mio third party funds for research

2'067 Original Articles published, **46'497** times cited
(articles from years 2014 – 2015),
130'307 hours of teaching

ORGANIGRAM



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Prof. Ch. Leumann



Dean
Prof. H.-U. Simon



Deputy of the Dean
Prof. P. Eggli



Dean's office
Dr. L. Stalder



Vice-Dean
Continuing
Education & Clinics
Prof. I. Baumgartner



Vice-Dean
Research
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Bachelor Study
Prof. M. Egger



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Representative VDM
Prof. M. Arnold

KEY PEOPLE

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- Prof. Philippe Zysset
- PD Dr. Matthias Widmer
- Prof. Thomas Müller

Students' representative

- Noemi Fischer
- Nils Maria Kallen

Consultative member

- Dr. Lukas Stalder

Administration

- Therese Sifeddine

STRUCTURAL DEVELOPMENT

Area Muesmatt

The Preclinical Institutes will have to move to the campus of the University Hospital because the Institutes of Exact Sciences will be taking over the Muesmatt area. This switch is being driven partly by the planned extension of the central train station. The planning for the first Center for Teaching and Research has already begun (panel 07). It is planned for the Preclinical Institutes and should create synergies between, e.g. Anatomy, Physiology, ARTORG and ISTB. A feasibility study has shown that the available space should be sufficient for the needs of teaching and research (especially a large lecture hall for 400 people).

«The Preclinical Institutes will have to move to the campus of the University Hospital. The planning of the first Center for Teaching and Research has already begun.»

Installation of laboratories in the building Murtenstrasse 40/42

The Department of Biomedical Research (DBMR) has been obliged to give up a substantial part of its laboratory space due to the demolition of the Haller / Ludwig House, Pavilion 52 and the conversion of the 6th floor of the Institute of Pathology. In the first basement of the Murtenstrasse 40/42 building, the University Hospital has, therefore, installed new, modern laboratories that have been occupied by the DBMR since February 2016.

New laboratory building Murtenstrasse 24 for the Department of Biomedical Research (DBMR) and the Institute of Legal Medicine (IRM)

After the clear "Yes" of the Bernese voters in February 2016 to the financing of a new building, Murtenstrasse 24, construction work began in the summer of 2016. The resulting building will have five upper, one attic and five basement floors. The flexibly usable upper floors will provide modern research and training space for the DBMR and the IRM. In the 1st to 3rd basements, additional usable space will be created for the institutes. The car-parking garage in the 4th and 5th basement will be accessed via the existing entrance to the University Hospital parking. Because of the heavy groundwater inflow encountered during excavation, a construction delay of up to one year will result. DBMR and IRM are now expected to move into the new building by the end of 2021.

University Hospital: Theodor-Kocher-Haus

The new building located at the Friedbühlstrasse is the first building to be built as part of the "Masterplan Inselspital". This building, which was inaugurated as the Theodor-Kocher-Haus with the participation of Federal Councilor Schneider-Ammann and Cantonal Councilor Schnegg will be used initially as a temporary location for the Clinic for Obstetrics and Gynecology during their re-construction period. Afterward, following slight modifications and expansion, it will house the Organ and Tumor center. The expansion for this definitive use will include five additional floors. The laying of the cornerstone took place on December 6, 2016, in a festive setting.



1st stage: Use by the Clinic for Obstetrics and Gynecology (Summer 2018) on the left and 2nd stage: Subsequent expansion for the Organ and Tumor Center on the right. Copyright: nightnurse images gmbh

University Hospital: New building for the Heart and Vascular Center

The new building on panel 12 provides space for the Swiss Cardiovascular Center and other specialist clinics. With the new building, clinics will be brought closer together promising an optimization of interdisciplinary treatment concepts. For example, in the new Building 12, cardiologists and cardiac surgeons will treat heart attacks on one floor together.

«With the new building, clinics will be brought closer together promising an optimization of interdisciplinary treatment concepts.»



sitem-insel

In April 2017, the Swiss School for Translation and Entrepreneurship in Medicine commenced operations under the leadership of Prof. U. Huynh-Do with a multidisciplinary kick-off symposium and with Module 1 (Introduction to Research and Development). The 11 first graduates of the Master of Advanced Studies are all experienced researchers with at least 5-6 years of experience in research and development in the fields of diagnostics, medical devices and molecules. The professorship for the Swiss School was also advertised in Spring 2017 and the Symposium took place in mid-September 2017.

A building for the Swiss School for Translation and Entrepreneurship in Medicine is under construction and should be ready for occupancy in 2019. Room assignments are currently in progress. Furthermore, a new center for diabetes research (Diabetes Center Bern) will be built. This new center at the interface of research, development and industry further strengthens the medical focus of Canton Bern.

HUMAN MEDICINE

FACTS 2017

Bachelor of Medicine

Study places human medicine	220
Study places dental medicine	35
Students (including repeaters) human medicine	237
Students (including repeaters) dental medicine	45
Starters bachelor program human medicine 2014	219
Ending with bachelor degree human medicine 2017	202
Drop out in the bachelor program	3%

Mobility	Incoming students bachelor	0
	Outgoing students bachelor	3

Master of Medicine

Study places human medicine 2017	250
Starter master program human medicine 2017	243
Starter master program human medicine 2014	184
Ending with master degree human medicine 2017	179
Drop out in the master program during 2014-2017	3%

Mobility	Incoming students master (electives)	150
	Outgoing students master (electives)	60

Federal Exams

Multiple choice exam, candidates 2017	179
Multiple choice exam, passing 2017 (100%)	179
Clinical skills exam, candidates 2017	179
Clinical skills exam, passing 2017 (99.4%)	178

For more than 200 years, physicians and medical doctors have been trained at the Medical Faculty in Bern. It is currently the second largest institution for the training of medical professionals in Switzerland. Every year the Governing Council of the Bern Canton determines the maximum capacity for the degree programme in human medicine based on the staffing, physical and financial resources of the University of Bern and accommodating quality and safety requirements. Currently there are 220 training places for human medicine and by August 2018, the student numbers will be increased by 100 to 320.

In 2007, the curriculum was changed to the Bologna system, which subdivided the training into Bachelors and Masters-degree programmes. The Bern curriculum for human medicine is characterised by a comprehensive and balanced training concept and is one of the best training programmes in Switzerland. A unique feature is the high practical relevance and the patient-orientated training. The content of the training is based on the Swiss Learning Objectives Catalogue (SCLO), which forms the basis of the

Federal examinations. The principle of research-led teaching, which is supported in the Medical Faculty, ensures a close relationship and incorporation of current research findings in teaching.

Another unique feature of medical education in Bern is that the Bachelor degree in human medicine follows the methodical, didactic learning and teaching approach of problem-based learning (PBL). Using PBL, student education is based on a modern concept that focuses not on memorising facts but rather on the application of acquired knowledge. Using medically relevant case studies, the required natural science and basic medical knowledge is incorporated into thematic units. PBL is based on distinct but complementary training methods, which include lectures, specialist internships, training in clinical skills, elective internships in clinical practice and research, internships in primary care, electronic learning media, fora and weekly feedback events, as well as the continuous review of student progress in formative and summative evaluations. The Bern Masters programme offers a subject-specific and practice-oriented study model with a high emphasis on bedside learning in the Teaching Hospitals. Special emphasis is placed on communication training. The Inselspital Bern, a University hospital focussing primarily on treatment, offers comprehensive training in more than 50 disciplines. Integrated also within the Masters curriculum is a scientific thesis and a mandatory internship in General Practice. The „Bern Family Doctor internship“ is groundbreaking in Switzerland and German-speaking countries.

The modern didactic concepts used in the Bachelors and Masters programmes allow students to successfully complete the human medicine degree programme at the Faculty of Medicine Bern and pass the Federal examination (based on the MedBG Art. 6); Bern graduates taking the Swiss Federal Licensing Examinations achieve very good results compared to the national average, and these graduates enter further training as “ready to practice” and well organised. The Bern curriculum is received very positively abroad and Bern graduates compare well internationally and are in demand.

The broad-based generation and implementation of the curriculum ensures the implementation of the training objectives (SCLO) and the self-evaluation of the teaching. This guarantees that all groups involved in the curriculum participate in the decision-making

process for the development of the human medicine study program.

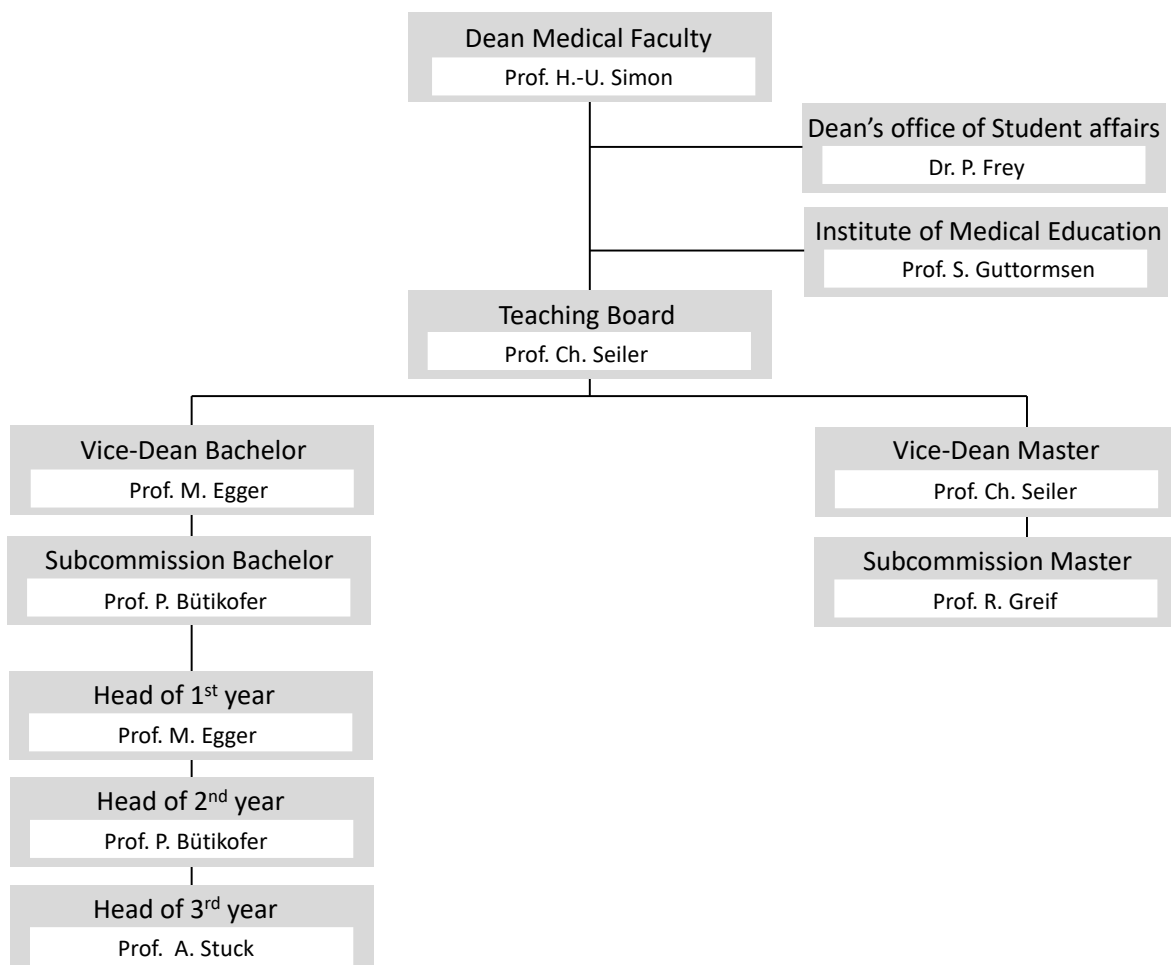
The teaching staff is qualified to meet the requirements of the study program. Potential problems may arise through the prioritisation of research, the “biologisation” of staff (as it increasingly is recruited more from natural sciences than from medicine), or if some staff withdraw from teaching. Deficits exist - these concern the need to strengthen teaching at the Inselspital Bern and mechanisms to encourage individual appreciation of the value of engagement with teaching as well as regard for academic teaching. The new teaching capacity plan framed by the performance requirements of the Inselspital Bern should improve the current unsatisfactory involvement in teaching.

In terms of infrastructure there are also deficits. The Faculty of Medicine has minimal influence to improve

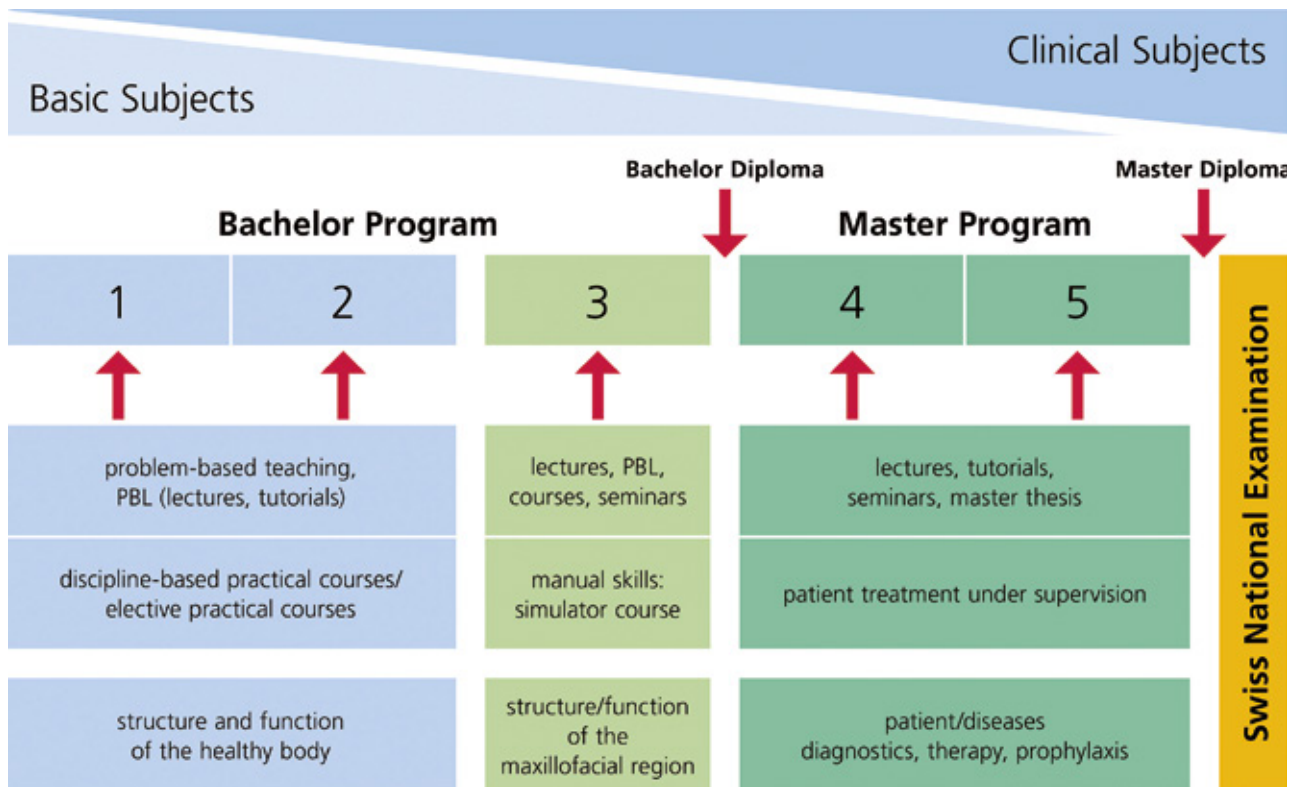
the situation. Thus, the listening room/auditory space is likely to remain unsatisfactory, but from autumn 2018 there will be additional and sufficient seminar and examination rooms available for small group tutorials in the ‘Renferhaus’, as well as an additional learning centre for students.

Future requirements such as increased study place capacity can be accommodated with the current Bern curriculum, but will require infrastructure development when the number of study places is raising. Altogether we conclude that the Bern Human Medicine curriculum is successful and well positioned. Challenges in a continued developing curriculum within the national frameworks and structures, and within our university that aim to adapt to new requirements flexibly, are approached in a constructive way. Both, the Medical Faculty and the University, keep up the quality of this curriculum with its longstanding tradition.

Committees for undergraduate medical education



TEACHING AT THE SCHOOL OF DENTAL MEDICINE



The **zmk bern (ZMK Bern)** is one of the few schools of dental medicine in the world offering a fully integrated interdisciplinary synoptic program.

The course of studies in dental medicine is based on the detailed national curriculum for dental medicine. Evidence-based treatment concepts ensure the high quality of dental care in Switzerland. Both Bachelor and the Master programs in Dental Medicine at the University of Bern were accredited in December 2011 by the Rectors' Conference of the Swiss Universities based on the proposal by the Swiss Center of Accreditation and Quality Assurance in Higher Education. In 2017, the process for the next accreditation was started.

At the end of the Master program, candidates are tested on their ability to correctly and independently perform interdisciplinary treatment on patients as well as for their theoretical and analytical competence. Furthermore, they have to present up a Master thesis that may consist of

- an academic discussion of a topic relevant to dentistry
- an extended case study involving at least one case and relevant literature (evidence-based)

- a report of academic research (e.g. clinical trial protocol), or
- a fully elaborated e-learning case.



Swiss national examination in dental medicine

Upon completion of the Master degree, candidates have to take the Swiss National Examination in dental medicine. Since 2011, the examination has been based on a multiple-choice test conducted simultaneously nationwide. The qualifications required by the national syllabus ensure a national standard of high quality.

In 2017, all of the 30 candidates successfully passed the Master exam as well as the Swiss National Examination in dental medicine.

The number of students and the male/female ratio are listed in the table below.

After the Master degree is awarded and the Swiss National Examination in dental medicine passed, the young dentists are qualified to treat patients independently in private practice.

Number of students 2017 (year 3-5)

	female	male	total
Spring 2017	54 (52.94%)	48 (47.06%)	102
Fall 2017	56 (54.37%)	47 (45.63%)	103



REINTRODUCTION OF A MASTER PROGRAM IN PHARMACY

Since the closure of the Pharmaceutical Institute of the Faculty of Medicine of the University of Bern in the 1990s, the Natural Science Faculty of the University of Bern hosts the first two years of the Bachelor program in Pharmaceutical Sciences. Afterwards, most of the students change for the 3rd year of the Bachelor and the Master degrees to Basel. A Bachelor and Master in Pharmaceutical Sciences is also offered at the ETH Zurich and the University of Geneva.

The job description of pharmacists is undergoing a profound change. With the partial revision of the the Medical Profession law (MedBG) as of January 1st, 2016, pharmacists will be given new responsibilities for the diagnosis and treatment of common diseases. With the report of the Federal Council on the postulate Humbel (October 2016), the policy strengthens a repositioning of pharmacies in primary health care. In order to optimally train the next generation of pharmacists for their new skills and role in primary health care, all universities are currently reforming their degree programs in Pharmaceutical Sciences. Therefore, the seamless transfer of Bernese students to other universities will no longer be possible in the future. In addition, there is already an increasingly severe shortage of pharmacists due to an insufficient training capacity.

«With the partial revision of the Medical Profession law (MedBG) as of January 1st, 2016, pharmacists will be given new responsibilities for the diagnosis and treatment of common diseases.»

Against the background of these developments, the Canton of Bern and the University have decided to offer again a full-time program in Pharmaceutical Sciences in Bern. The study course is planned as a cooperation between the Natural Science Faculty and the Medical Faculty. It comprises a solid scientific education in the Bachelor's degree program "Pharmaceutical Sciences" at the Natural Science Faculty, followed by a strongly practice- and patient-oriented training in the Master's program

"Pharmacy" at the Medical Faculty, which also prepares participants for the federal examination as a Pharmacist.

For the instruction in the clinical competences required in accordance with the newly revised MedBG, the Medical Faculty can turn to the expertise of the Institute for Medical Teaching (IML) as well as the Institute of General Practice and Primary Care (BIHAM). Particular attention will also be paid, in close cooperation with BIHAM, to the aspect of better interprofessional cooperation between pharmacists and other service providers in primary health care. This interdisciplinary and cooperative approach including two faculties is unique in Switzerland so far.

«It comprises a solid scientific education in the Bachelor's degree program "Pharmaceutical Sciences" at the Natural Science Faculty, followed by a strongly practice- and patient-oriented training in the Master's program "Pharmacy" at the Medical Faculty.»

In October 2017, the University approved the re-introduction of the Bachelor and the Master programs in Pharmaceutical Sciences. The time schedule with the start of the third year of the Bachelor's program in the Fall semester 2019 is ambitious. A particular challenge is the establishment and appointment of the Professorship in Galenics, including the necessary infrastructure for research and internships. Detailed planning is currently taking place for the Master's program, which will be offered for about 50 students for the first time in Fall semester 2020.

MASTER PROGRAM IN BIOMEDICAL SCIENCES

In Switzerland there is a chronic shortage of biomedical science professionals which affects industry and universities equally and which is being mostly compensated by immigration of qualified persons from other European countries. In order to counteract this, various new educational programs in the fields of biomedicine and the life sciences have emerged throughout Switzerland over the last few years. Among these endeavors, the Master program in Biomedical Sciences at the Medical Faculty of the University of Bern plays a central role. It started 12 years ago as a cooperation between the Universities of Fribourg (Bachelor) and Bern (the consecutive Master).

As the oldest full-time program in Biomedical Sciences in Switzerland, our program follows the principle that education must take place exactly at the interface between medicine and the natural sciences. Therefore, the first year is mainly focused on natural sciences. The second year comprises the basics of human anatomy, biochemistry and physiology. In most of these classes, the students participate alongside students of human medicine. The years three (the last year of the undergraduate degree) and four (the first year of Master study which is conducted in English) are tightly coordinated between the two universities, focusing on the development of current research methods and a 'tour' of pathophysiology and clinically relevant features of all organ systems. Physicians, basic scientists and teachers from the pharmaceutical research industry teach these classes. In accordance with this study content, graduates of the Master curriculum have a broad knowledge of current issues in human biomedicine and have comprehensive skills in modern research methods.

«As the oldest full-time program in Biomedical Sciences in Switzerland, our program follows the principle that education must take place exactly at the interface between medicine and the natural sciences.»

As might be expected from this broad portfolio, graduates with a 'Master in Biomedical Sciences' are sought-after candidates for positions as PhD students at universities or for positions within the pharmaceutical research industry. The breadth of training will also accommodate future research areas in medicine such as Artificial Intelligence and Personalized Medicine. Since the award of the first master's diploma in 2011, 156 students have completed their studies in Biomedical Sciences, with the three best graduates receiving a generous prize from CSL Behring each year. Since 2013, an alumni organization, which is very active, furthers educational events and advises students on career planning issues (<http://biomedicalsciences.ch/>).



MASTER PROGRAM IN BIOMEDICAL ENGINEERING

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Julia
Spyra
Study
Coordinator



Prof. Mauricio
Reyes
Master Thesis
Coordinator

Introduction

In 2016, we celebrated the 10th anniversary and are very glad to report on the continuing excellent health of our master's program in Biomedical Engineering. In the academic year 2016/17, 43 regular and 6 exchange students were admitted and 35 biomedical engineers graduated from our program. Hallmarks of our program remain the proximity to the local hospital network, the research oriented towards clinical applications, the internationality with all mandatory courses in English, the compatibility of the study calendar with a part-time job, and the accessibility to bachelor students from universities as well as universities of applied sciences.

Curriculum

The full-time study program offered in cooperation with the Bern University of Applied Sciences takes 4 and can be extended to a maximum of 6 semesters. To support regular part-time work, mandatory courses take place on only 3 days per week.

Preparation Courses

Our program's interdisciplinary nature mirrors our students' diverse backgrounds. Especially students with a non-engineering background, e.g. in medicine, biosciences or related fields, may not fulfil all course prerequisites. Therefore, preparation courses in MATLAB, C++ Programming, Electrical Engineering,



Robotic cochlear implantation, Inselspital Bern (© ARTORG Center, 2017).

and Mathematics were introduced to bridge the knowledge gaps. An additional one is planned in Mechanical Engineering.

Basic Modules

The basic modules Human Medicine, Applied Mathematics, and Biomedical Engineering provide students with the basic knowledge and tools to master the more complex subject matters of the specialized courses.

Major Modules as Specialization

While all basic modules are mandatory, the choice between the major modules Biomechanical Systems, Electronic Implants, or Image-Guided Therapy constitutes the first opportunity for specialization. The overall concept gives rise to a high degree of diversity and flexibility. It allows for numerous course combinations, thus making choices with regard to personal preferences and professional prospects possible.

Module Complementary Skills

Apart from the rapid development of technology itself, today's biomedical engineers are increasingly challenged by complementary issues like ethical aspects, project planning, quality assurance and product safety, legal regulations and intellectual property rights, as well as marketing aspects. Language competence in English is of paramount importance both in an industrial and academic environment. In the module Complementary Skills students select courses like Innovation Management, Regulator Affairs and Patents, Ethics in Biomedical Engineering, Scientific Writing in Biomedical Engineering, Introduction to Epidemiology and Health Technology Assessment.

Master's Thesis

The last semester is dedicated to a master's thesis project on an individually suited topic in an academic research group at the University of Bern or the Bern University of Applied Sciences or, for particular cases, in an industrial R & D department.



The Biomedical Engineering Day 2017 attracted almost 300 students, researchers, alumni, and company representatives.

CAS, DAS AND MAS DEGREE PROGRAMS

HUMAN MEDICINE

The Medical Faculty of the University of Bern presents several CAS, DAS and MAS-titles in various areas of Human Medicine:

www.medizin.unibe.ch/dienstleistungen/rechtssammlung/weiterbildung/index_ger.html
www.zuw.unibe.ch

Clinical Research (CAS)

The Certificate of Advanced Studies in Clinical Research is coordinated by the Institute of Social and Preventive Medicine. The main goal is to learn how to plan and conduct clinical research projects and how to communicate their results.

www.cas-clinicalresearch.ch

Clinical Nutrition (CAS)

The Certificate of Advanced Studies in Clinical Nutrition is a cooperation between the « Gesellschaft für Klinische Ernährung der Schweiz » (GESKES) and the Medical Faculty. The main goal is the promotion of evidence-based knowledge and training in Clinical Nutrition for physicians, nutritionists, nurses, pharmacists and nutritional scientists. The teaching programme is presented in the form of lectures, practical sessions, case studies, self-directed learning, seminars and workshops.

www.geskes.ch/

Translational Nephrology (CAS / DAS)

The continuous education program Translational Nephrology provides extensive insights into the basics of nephrology by studying the physiology and pathophysiology of kidney function in health and disease. The program is intended for national and international graduates with a natural- and medical science background who are interested in basic- and clinical- renal research.

www.nephrologie.unibe.ch/

Hepatology (CAS / DAS)

Liver diseases are frequent and complex. If the patients fail to receive the correct therapy, they are at risk to develop severe complications. In this CAS/DAS, one learns by working in an excellent liver unit embedded in a multidisciplinary clinic about diagnosis, management and treatment of patients affected by liver disease.

www.unibe.ch/unibe/portal/content/e152701/e332574/e344598/e623092/wb_rgl_hepatologie_ger.pdf



Spiritual Care

The Certificate of Advanced Studies in Spiritual Care is a cooperation between the Theological Faculty, the Faculty of Human Sciences and the Medical Faculty. The main goal is a reflected and professional handling of spiritual topics.

www.theol.unibe.ch/weiterbildung/cas_spiritual_care/index_ger.html

Translation and Entrepreneurship in Medicine (CAS / DAS / MAS)

These continuous education programs are coordinated by the Swiss Institute for Translational and Entrepreneurial Medicine in Bern (sitem-insel). The sitem-insel School aims to promote researchers and train executives in the fields of translational medicine and biomedical entrepreneurship. Participants are expected to acquire the necessary skills to initiate and implement the translation process from the stage of development in industry or basic science institutions into clinical applications with the ultimate purpose of commercialization. Participants should have a MS or higher degree in life sciences, medicine, biomedical engineering or equivalent. For the MAS they should in addition submit a proposal for a translational medicine project on which they will work during the MAS.

www.sitem-insel.ch/wprs/wp-content/uploads/2014/10/Brosch_sitem-insel_school_3.6MB.pdf

Continuing education programs in exercise therapy in sports and medicine (CAS/DAS)

The continuing education programs in exercise and sports therapy provides extra-occupational, practice-oriented and theory-supported further education for movement and sports therapy of disease, including cardiovascular disease, diabetes, and cancer.

The programs are aimed at graduates with a bachelor's and / or master's / licentiate's degree in sports and physical education, a bachelor's degree in health sciences and technology, as well as dipl. Gymnastic and sports teachers I / II, dipl. Physiotherapist, dipl. Physical education teacher FH. Offered are the Diploma or Certificate of Advanced Studies Swiss Exercise Therapy in Sports and Medicine (DAS / CAS SwissETSM Unibe) and the specific Certificate of Advanced Studies Swiss Cardiovascular and Diabetes Therapy (CAS SwissCDT Unibe). www.sportmedizin.insel.ch/uni-bern-module

Exercise and sports therapy in orthopedics, rheumatology and traumatology (CAS ORT)

The further education in movement and sports therapy for orthopedics, traumatology and rheumatology provides theoretical and practical basis for movement therapy interventions in patients with orthopedic, rheumatological and traumatological disorders for inpatient and outpatient rehabilitation as well as for secondary prophylaxis.

www.svg.ch/files/Broschuere_ORT_2018_2019.pdf

Exercise and sports therapy for mental illness (CAS PSY)

The CAS movement and sports therapy for the treatment of mental illness provides a theoretical and practical basis for movement and sport therapy interventions in patients with mental illness for inpatient and outpatient rehabilitation as well as for secondary prophylaxis.

www.svg.ch/files/Broschuere_CAS_PsyErk_2018_2019.pdf

Interprofessional Specialized Palliative Care (CAS)

The main goal of this advanced training course is to present specialist palliative care knowledge to physicians, nurses and other health professionals. Students receive further education as specialists allowing them to play a leading or supporting role in specialized palliative care teams.

www.palliativzentrum.insel.ch/de/lehre/weiterbildung/cas-interprofessionelle-spezialisierte-palliative-care/

Leadership of Healthcare Organisations (CAS)

This Certificate of Advanced Studies is coordinated by the Institute of Social and Preventive Medicine. It conveys leadership competence-oriented towards health care organizations and focuses on appropriate forms of the integration of medicine and management.

www.cas-leadership.ch/

Public Health (CAS / DAS / MAS)

This program is hosted by the medical faculties of the universities of Basel, Zürich and Bern. The main goal is to provide key skills to future Public-Health-Professionals.

www.public-health-edu.ch/mas

CAS, DAS AND MAS DEGREE PROGRAMS

Master of Medical Education (MAS)

The Master of Medical Education program in Bern is based on a systematic and evidence-based approach. The main goal is to acquire the required skills in order to meet future challenges in medical teaching. www.iml.unibe.ch/angebote/lehre/master-of-medical-education-mme

Managing Medicine in Health Care Organisations (CAS)

This Certificate of Advanced Studies is coordinated by the Institute of Social and Preventive Medicine. The CAS provides management competence for health care organizations and an understanding of organized health care against the background of the rapid changes in medicine.

DENTISTRY

The Medical Faculty of the University of Bern presents six MAS-titles in various areas of Dentistry: www.zmk.unibe.ch/weiterbildung/weiterbildung/master_of_advanced_studies/index_ger.html

Master of Advanced Studies in Implant Dentistry (MAS IMP)

A 3-year, full-time program (180 ECTS), which combines all surgical and prosthodontic aspects of implant dentistry. The postgraduate students usually spend one year in the Department of Oral Surgery and two years in the Department of Reconstructive Dentistry and Gerodontology.

Master of Advanced Studies in Orthodontics and Dentofacial Orthopedics (MAS ORTHO)

A 4-year, full-time program (240 ECTS), which aims to provide dentists with a solid evidence-based academic education and broad, high-level clinical training in order to become specialists in Orthodontics and Dentofacial Orthopedics.



Master of Advanced Studies in Cariology, Endodontology and Pediatric Dentistry (MAS REST)

A 3-year, full-time program (180 ECTS), which teaches postgraduate students theoretically and clinically in evidence-based cariology and restorative dentistry, endodontology as well as pediatric dentistry. The structured curriculum consists of weekly lectures and seminars as well as daily clinical training supervised by experienced instructors.

Master of Advanced Studies in Oral and Implant Surgery (MAS ORALSURG and IMPSURG)

A 3-year, full-time program (180 ECTS), which provides a thorough and comprehensive clinical and theoretical training in all aspects of oral surgery as well as the surgical aspects of implant dentistry. The postgraduate students follow a strict curriculum with a gradually increasing level of difficulty and challenge according to SAC-classifications.

Master of Advanced Studies in Periodontology and Implant Dentistry (MAS PER and IMP)

A 3-year, full-time program (180 ECTS) aiming to provide dentists with a broad high-level clinical training in periodontology and implant dentistry as well as a solid evidence-based academic education in order to become specialists in Periodontology.

Master of Advanced Studies in Reconstructive and Implant Dentistry (MAS REC and IMP)

A 3-year, full-time program (180 ECTS), which integrates advanced clinical and theoretical training in reconstructive dentistry/ dental implant therapy and its associated disciplines within a strict and structured curriculum. The MAS REC and IMP Unibe provides the basis with which a dentist can become a Swiss federal specialist in Reconstructive Dentistry SSO.

PHD EDUCATION

The Medical Faculty is associated with two graduate schools offering structured doctoral programs:

- the Graduate School for Cellular and Biomedical Sciences (GCB); <http://www.gcb.unibe.ch/>
- the Graduate School for Health Sciences (GHS); <http://www.ghs.unibe.ch/>

In addition to the Faculty of Medicine, the GCB is also supported by the Faculty of Science and the Vetsuisse Faculty, while the Faculty of Human Sciences participates together with the Medical Faculty in the GHS.

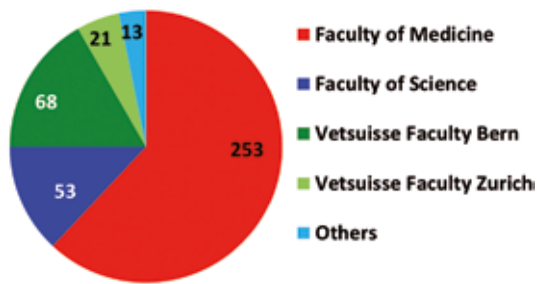
Both graduate schools offer research-oriented curricula with a wide choice of courses and special workshops tailored to the individual interests and

needs of PhD candidates. The focus is on the individual thesis projects where the candidates get the best possible support from an expert supervisory committee in their respective research area. In addition, emphasis is put on high-quality training in research methods and study design, which is ensured by the provision of appropriate courses. The PhD programs direct the candidates towards independent scientific work and enable them to assume scientific responsibility.

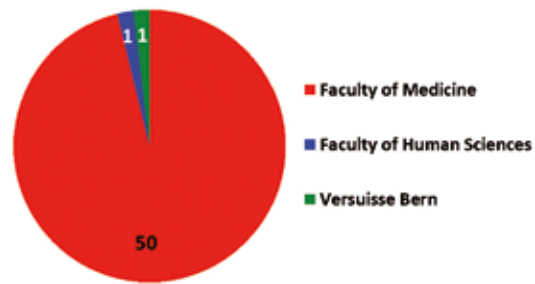
MD-PhD fellowships

The MD-PhD-studies are supported by competing scholarships of the SNSF and SAMW. In 2017, two out of eleven national fellowships were awarded to candidates from the University of Bern.

Number of participants as of 31.12.2017



408 total within then GCB
Others: 8 from IRB Bellinzona; 3 from Biotechnology Institute Thurgau; Kreuzlingen; 1 AO Research Davos; 1 RMS Foundation Bettlach



52 total within then GHS

Number of PhD degrees in 2017

Type of Degree	F	M	Total
MD,PhD	5	4	9
DVM,PhD	6	2	8
PhD in Biomedical Engineering	2	12	14
PhD in Biomedical Sciences	21	14	35
PhD in Immunology	6	3	9
PhD in Neuroscience	2	1	3
PhD of Science in Biochem. & Mol.Biol.	7	8	15
PhD of Science in Cell Biology	2	1	3
Total	51	45	96

96 in total - 74 were acquired at the Faculty of Medicine.
Prize for best PhD degree:
Cristina Leoni, IRB Bellinzona.

Speciality area; PhD in Health Sciences	F	M	Total
Epidemiology and Biostatistics	1		1
Epidemiology	3	1	4
Public Health	1	1	2
Physiotherapy	1		1
Neurosciences	2		2
Total	8	2	10

10 in total - 9 were acquired at the Faculty of Medicine

GRADUATE SCHOOL FOR CELLULAR AND BIOMEDICAL SCIENCES

Focus

Training in experimental research with state of the art methods in molecular life sciences, biomedical sciences and biomedical engineering. Research areas include cell biology, biochemistry, molecular biology, immunology, genetics, biomedical sciences, epidemiology as well as tissue engineering and computer-assisted surgery.

Requirements

Master's degree in molecular life sciences, biomedicine, medicine, biomedical engineering or a related field depending on the project.

Program structure

Five expert committees

- Biological Systems
- Biomedical Sciences
- Cell Biology
- Molecular Biology/Biochemistry
- Biomedical Engineering

Thesis committee

Each candidate is supported by a thesis committee consisting of supervisor, co-advisor and a member of an expert committee as mentor.

Intermediate assessment

During the mid-term evaluation after 18-24 months, the doctoral candidates present their research data in the form of a seminar and determine what is still necessary for the successful completion of their doctoral studies.

Awarded PhD titles

- PhD of Science in Cell Biology
- PhD of Science in Biochemistry & Molecular Biology
- PhD in Biomedical Sciences
- PhD in Immunology
- PhD in Neuroscience
- PhD in Biomedical Engineering

Curricula for medical doctors

MD-PhD program

The focus is on basic sciences, but the PhD candidates can spend 20% of their time in the clinic. Graduates receive one of the following titles:

- MD,PhD (Doctor of Medicine and Philosophy)
- DDS,PhD (Doctor of Dentistry and Philosophy)
- DVM,PhD (Doctor of Veterinary Medicine and Philosophy)

GRADUATE SCHOOL FOR HEALTH SCIENCES

Focus

Studies of social, psychological, physiological and environmental factors that determine the health of individuals and populations, as well as the effects of these factors on physical and mental health. Both basic and applied research deals with topics from the fields of epidemiology, social medicine, psychology, neurosciences and clinical sciences.

Requirements

Master's degree in psychology, medicine, biomedicine, epidemiology, geography, sport science or other fields depending on the respective research project.

Program structure

Three expert committees

- Epidemiology, Health Promotion, Medical Education, Social Sciences.
- Neurosciences
- NEW since 2017: Clinical Sciences

Thesis committee

Each candidate is supported by a supervisor and a co-referee.

Intermediate assessment

During the mid-term evaluation after 18-24 months, the doctoral candidates present their research data in the form of a seminar and determine what is still necessary for the successful completion of their doctoral studies

Awarded PhD titles

- PhD in Health Sciences (specialist area)

Curricula for medical doctors

PhD in Clinical Sciences; 50:50 model

Patient-oriented research and clinical career. The PhD candidates work 50% in research and 50% in the clinic. Graduates receive the title:
PhD in Health Sciences

GRANTS

Graduate School in Health Science (GHS)

Health Sciences, Cognitive Neurosciences, Clinical Sciences

Career stage: young MD's (open to other health professionals, psychologist, biologists, engineers)

Duration: 3 - 5 years

Number of calls/year: for Clinical Sciences: 1x per year, otherwise continuously

Funding source: Medical Faculty

Graduate School for Cellular and Biomedical Sciences (GCB)

Career stage: biologists, engineers, MedVet, MD's

Duration: 3-4 years

Number of calls/year: continuously

Funding source: Medical Faculty

CTU Grants

Career stage: MD's before Habilitation

Duration: 1.5 years

Number of calls/year: 2x per year

Funding source: University Hospital

Uni Bern Initiator Grant

Career stage: postdocs and young PI

Number of calls/year: 2x per year

Funding source: University

Additional Information: open to all disciplines; support for proposals for third-party funded career schemes (SNF mobility fellowships, Ambizione, SNSF-professorship; EU Marie-Curie-S. fellowships, ERC grants, etc)

Numerous Foundations

Career stage: during BSc or MSc

Duration: 1-5 years

Number of calls/year: 1x per year

Funding source: Foundations

Additional Information: open for students registered at University of Bern in academic years 2 - 6

Travel Grants

Career stage: during BSc or MSc

Duration: 1-6 years

Number of calls/year: continuously

Funding source: Dean's office

Additional Information: open for students registered at University of Bern in academic years 1 - 6

Internships at the Albert Schweitzer Hospital in Lambarene

Career stage: during MSc

Duration: 0.5 year

Number of calls/year: 2x per year

Funding source: Dean's office

Additional Information: open for students registered at University of Bern in academic years 5-6

MENTORING 4 WOMEN

For the past 6 years, women who wish to actively plan and promote their academic career in the Medical Faculty have been successfully supported with a Mentoring Program.

«M4W program participants gain comprehensive access to an outstanding network.»

Within the Mentoring 4 Women Program, which was founded in 2012, mentees are accompanied in a one-to-one relationship by an academic professional mentor from the Medical Faculty for two years. The mentees work out an individual career plan with clear goals. Thereby, they benefit from the experience of their mentor, who among other things also provides them with important contacts for setting up a professional network. In addition, the mentees receive valuable tips on time management, the successful acquisition of third-party funding as well as the publication of research articles. Furthermore, they are also actively supported in achieving other goals

such as work-life balance. Mentors have committed themselves to actively promote young women interested in an academic career as a physician. Both parties benefit from a regular exchange. There are other established mentoring programs at the University of Bern in other faculties. The M4W program works closely and in a network with the equal opportunities department of the University of Bern. As a result, M4W program participants gain comprehensive access to an outstanding network. The M4W program is funded by the Federal Program for Equal Opportunities and the Medical Faculty of the University of Bern.

«Mentors have committed themselves to actively promote young women interested in an academic career as a physician.»



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IGT



Prof. Olivier
Guenat
OOC



PD Dr. Stavroula
Mouggiakakou
DTR



SNF Prof. Laura
Marchal-Crespo
GER



Prof. Tobias
Nef
GER



Prof. Dominik
Obrist
CVE



Prof. Raphael
Sznitman
OTL



Dr. Wilhelm
Wimmer
HRL

Research Partners

- Department of Angiology (Iris Baumgartner)
- Department of Cardiology (Stephan Windecker)
- Department of Cardiovascular Surgery (Thierry Carrel)
- Department of Diagnostic and Interventional Neuroradiology (Jan Gralla)
- Department of Diagnostic, Interventional and Paediatric Radiology (Johannes Heverhagen)
- Department of Intensive Care Medicine (Stephan Jakob, Jukka Takala)
- Department of Nephrology and Hypertension (Bruno Vogt)
- Department of Neurology (René Müri, Claudio Bassetti)
- Department of Neurosurgery (Andreas Raabe)
- Department of Ophthalmology (Sebastian Wolf)
- Department of Otolaryngology, Head and Neck Surgery (Marco Caversaccio)
- Department of Pneumology (Thomas Geiser)
- Department of Thoracic Surgery (Ralf Schmid)
- Department of Visceral Medicine and Transplantation Surgery (Guido Beldi, Daniel Candinas)
- University Clinic of Diabetes, Endocrinology, Nutritional Medicine & Metabolism (Christoph Stettler)
- University Hospital of Old Age Psychiatry and Psychotherapy (Stefan Klöppel)

Structure Profile

The ARTORG Center has seven research teams:

- Organs-on-Chip Technologies (Olivier Guenat)
- Diabetes Technology (Stavroula Mouggiakakou)
- Hearing Research Laboratory (Wilhelm Wimmer)
- Image Guided Therapies (Stefan Weber)
- Gerontechnology and Rehabilitation (Laura Marchal-Crespo, Tobias Nef)
- Cardiovascular Engineering (Dominik Obrist)
- Ophthalmic Technology Laboratory (Raphael Sznitman)

Technical specialties in microfluidics, fluid mechanics, rapid prototyping, image processing, robotics and artificial intelligence are applied to resolve unmet clinical challenges in neurology, respiratory, ENT, ophthalmology, hepatobiliary, metabolic and cardiovascular medicine.

Research Profile

The ARTORG Center is the biomedical engineering research hub of the University of Bern. A multidisciplinary team of clinicians, engineers, life scientists, allied health professionals, social and management scientists, commercial partners and patient stakeholders work together. Medical translation research that addresses unmet clinical needs in seven major disease areas transforms basic research findings in imaging,

modelling, materials and engineering into better treatments for patients.

- Biomimicry Organ-On-Chip platform of lung alveoli that replicates tissue architecture and respiratory motion
- Novel robotic training strategies to improve neuro-rehabilitation of brain injured patients
- Bionic cardiovascular devices designed to for improved hemodynamics and electrophysiological performance
- Artificial-Intelligence assistance for high-speed and precision ophthalmic diagnostic technology
- Image-guided surgical robotics and energy therapies to supersede unguided, manual surgery
- Diagnose, protect from and restore hearing loss with objective methods and disruptive patient-specific device designs
- Artificial-Intelligence for diabetes patient empowerment
- Virtual reality tools and tele-rehabilitation technology for brain injured patients

Teaching Profile

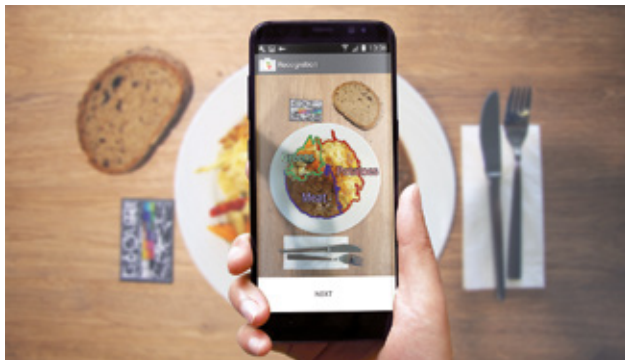
The ARTORG Center participates in the Master's degree studies program in Biomedical Engineering (BME) that accepts non-consecutive candidates from life-sciences, medicine, business and engineering disciplines. BME Masters students are taught by University of Bern faculty and external faculty from the Bern Biomedical Engineering Network, including the Bern University of Applied Sciences, and each carry out an independent research project. The ARTORG postgraduate program currently has 45 PhD students on full-time research projects. Students also hold membership in the Graduate School for Cellular and Biomedical Sciences. Students receive support from supervisors and post-doctoral colleagues and are encouraged to present and publish their work during their research studies. As members of the Medical Faculty their research is at the interface between technical and medical disciplines.

Highlights 2017

The Organs-on-Chip Technologies Group was nominated at the Swiss Medtech Award 2017 for the project Lung Fibrosis-on-Chip realized in the frame of a CTI project with the ARTORG start-up AlveoliX AG, the Department of Pneumology of the University Hospital of Bern and Creaholic SA.

The Diabetes Technology group in collaboration with UDEM (Prof. Dr. med. Christoph Stettler) has launched the world's first Diabetes-smartphone trial on computer vision based carbohydrate estimation (GoCarb). The method increases

the accuracy of self-directed carbohydrate estimation by diabetic patients and may allow a better glucose control, more precise treatment and enhanced quality of life.



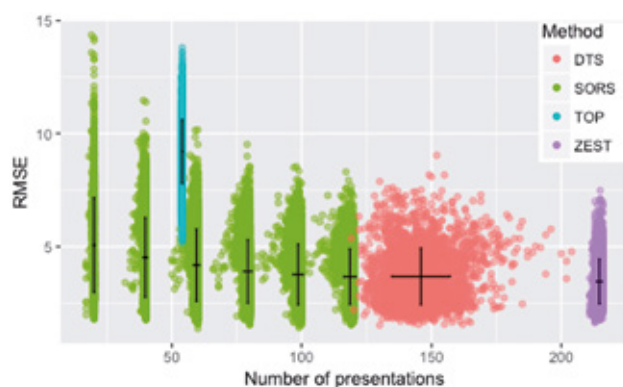
GoCarb in action.

Prof Laura Marchal-Crespo is an internationally renowned expert in robot-assisted motor learning. Her work focusses on developing and testing innovative training regimes for existing therapeutic robots. She joined the ARTORG's Gerontechnology and Rehabilitation Group this year as the newly appointed Swiss National Science Foundation Professor.



Developing new control strategies for upper limb rehabilitation robots.

Work in the Ophthalmic Technology Group has developed a collaborative project on Artificial Intelligence tools for diagnostic screening with the Department of Ophthalmology.



Acquired visual fields of glaucoma patients using our approach (green) and existing methods for different amounts of time. This corresponds to a 120% acquisition speedup over current standards of care without significant accuracy reductions. This effectively opens the door for both faster acquisition times and measuring wider fields of view, both of which will be explored in an upcoming clinical study within the Department of Ophthalmology, University Hospital Bern.

The Image guided therapy group and the team of the ENT department (Prof. Dr. med. Marco Caversaccio) continued the world's first clinical trial of robotic cochlear implantation platform to perform robotic cochlear implantations in 5 further patients in 2017. The work was published in the recently established Science Robotics journal.

The Cardiovascular Engineering Group launched a commercial collaboration with CorFlow Therapeutics AG for the joint development of a novel endovascular technology for the treatment of microvascular obstructions after heart attack. Supported by the William Demant Foundation the Hearing Research Laboratory is participating in a research collaboration with the The National Institute for Health Research Nottingham Biomedical Research Centre University of Nottingham, U.K. on objective tinnitus diagnosis.

Selected Competitive Grants

- Hasler Foundation, A Cyber-Human System to Optimize Medication in Parkinson Patients, CHF 520'000, Tobias Nef
- CTI, Lung-on-Chip System for Preclinical Study, CHF 654'000, Olivier Guenat
- CTI, Automated assistive system for intravitreal injections, CHF 388'512, Raphael Sznitman
- CTI, Development and non-clinical verification of a diagnostic and therapeutic approach for microvascular obstructions in heart attack patients, CHF 820'000, Dominik Obrist
- PASC, HPC-PREDICT – High-Performance Computing for the Prognosis of Adverse Aortic Events, CHF 510'000, Dominik Obrist
- SNF, Towards a complete approach for robotic cochlea implantation - Complementing steps of robotic inner ear access and electrode array insertion, CHF 910'000, Stefan Weber
- SNF/CTI BRIDGE, Towards intelligent, sensor-enhanced, robotic neurosurgery, CHF 2'000'000, Stefan Weber, Andreas Raabe and CSEM

Selected Publications

- P. Urwyler, R. Stucki, L. Rampa, R. Muri, U. P. Mosimann, and T. Nef, "Cognitive impairment categorized in community-dwelling older adults with and without dementia using in-home sensors that recognise activities of daily living.," *Sci. Rep.*, vol. 7, p. 42084, Feb. 2017. doi: 10.1038/srep42084
- L. Bally et al., "Carbohydrate Estimation Supported by the GoCARB System in Individuals With Type 1 Diabetes: A Randomized Prospective Pilot Study.," *Diabetes care*, vol. 40, no. 2. United States, pp. e6–e7, Feb. 2017. doi: 10.2337/dc16-2173
- Y. Mermoud, M. Felder, J. D. Stucki, A. O. Stucki, and O. T. Guenat, "Microimpedance tomography system to monitor cell activity and membrane movements in a breathing lung-on-chip," *Sensors Actuators B Chem.*, vol. 255, pp. 3647–3653, Feb. 2018. doi: 10.1016/j.snb.2017.09.192
- S. Frey, A. Haine, R. Kammer, H. von Tengg-Kobligk, D. Obrist, and I. Baumgartner, "Hemodynamic Characterization of Peripheral Arterio-venous Malformations.," *Ann. Biomed. Eng.*, vol. 45, no. 6, pp. 1449–1461, Jun. 2017. doi:10.1007/s10439-017-1821-9, 2017
- S. Weber et al., "Instrument flight to the inner ear," *Sci. Robot.*, vol. 2, no. 4, p. eaal4916, Mar. 2017. doi: 10.1126/scirobotics.aal4916

Department for BioMedical Research (DBMR)

University of Bern
Bern, Switzerland



Prof. Mark Rubin
Director DBMR



Prof. Robert Rieben
Directorate
Coordinator
Murtenstrasse
40/50,
Augenklinik



Prof. Willy Hofstetter
Directorate
Coordinator
M.E. Müller-Haus,
Pathologie



PD Dr. Manfred Heller
Coordinator
Kinderklinik



Prof. Peter Vermathen
Coordinator
Erlachstrasse 9A



PD Dr. Monique Vogel
Coordinator
Sahli-Haus 1+2

Structure Profile

The role of the Department for BioMedical Research DBMR is to provide its 45 research groups with optimal infrastructure and scientific support. The vast majority (40) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainders (5) are internal DBMR groups, who are involved in the scientific support and coordination of equipment and infrastructure on a daily basis. Equally important, the DBMR is responsible for operating Technology and Animal Core Facilities. It also hosts the Clinical Trials Unit (CTU) Bern. Furthermore, the groups of the department are supported by central services responsible for administration, informatics, technical support and bioinformatics.

Research Partners

As research partners, we have the DBMR Research Groups:

- Anaesthesiology
- Angiology
- Audiology
- Bone Biology & Orthopaedic Research
- Cardiology
- Cardiovascular Research
- Cardiovascular Surgery
- Clinical Radiopharmacy
- Cranio-Maxillofacial Surgery
- Dermatology, Endocrinology / Diabetology (Adults)
- Endocrinology / Diabetology / Metabolism (Paediatrics)
- Endocrinology of the Breast
- Endometriosis and Gynaecological Oncology
- Endometrium & Ovary
- Experimental Haemostasis
- Experimental Radiology
- Gastroenterology / Mucosal Immunology
- Hand Surgery
- Hematology (Adults)
- Hematology / Oncology (Paediatrics)
- Hepatology
- Human Genetics
- Intensive Care Medicine
- Magnetic Resonance Spectroscopy and Methodology (AMSM)
- Molecular Biology
- Nephrology and Hypertension
- Neurology
- Neurosurgery
- Oncology / Haematology (Adults)

- Ophthalmology
- Orthopaedic Surgery
- Osteoporosis
- Pediatric Surgery
- Plastic Surgery
- Precision Oncology
- Prenatal Medicine
- Protein and Cell Biology
- Pulmonary Medicine (Adults)
- Pulmonary Medicine (Paediatrics)
- Radiation Oncology
- Rheumatology
- Thoracic Surgery
- Tumor-Immunology
- Urology
- Visceral and Transplantation Surgery

Research Profile

The Department for BioMedical Research DBMR is a research department of the Faculty of Medicine of the University of Bern with the mission to provide the researchers of the Inselspital (Bern University Hospital, www.insel.ch) with the best possible environment and infrastructures. Our aim is to bridge laboratory-based and biomedical patient-oriented clinical research.

Teaching Profile

Most of the research groups of the department are hosting masters, PhD, MD-PhD-students, and post-doctoral fellows who are integrated in the research projects of the individual groups. PhD-students are generally enrolled in the graduate school of cellular and biomedical sciences of the University of Bern. The Department organizes progress reports, seminars, and conferences that can be credited by the PhD-students. Furthermore, all group leaders of the department participate in teaching activities.

Highlights 2017

In May 2017, Prof. Mark Rubin was appointed as Director of the Department of Clinical Research DCR, as well as leader of the newly created Precision Oncology group.

In August, the group Ion Channels and Channelopathies left DCR and moved to the IBMM.

In September 2017, the department changed its name to Department for BioMedical Research.

Selected Competitive Grants

- «Swiss Oncology and Cancer Immunology Breakthrough Platform» (SOCIBP) under the leadership of Mark Rubin is supported by the SPHN and the focal topic of «Personalized Health and Related Technologies» (PHRT) of the ETH sector with a total of 4.9 million francs (36 months)
- ERC Advanced: Development of healthy host-microbial mutualism in early life (EUR 2.5 Mio., A. Macpherson)
- ERC Consolidator: Connectivity Correlate of Molecular Pathology in Neurodegeneration (EUR 2 Mio., S. Saxena)
- ERC Consolidator: All optical deconstruction of thalamic control of sleep-wake states (CHF 1'610'000; A. Adamantidis)

Selected Publications

- Abdelhafez MM, Shaw J, Sutter D, Schnider J, Banz Y, Jenni HJ, Voegelin E, Constantinescu MA, Rieben R. Effect of C1-INH on ischemia/reperfusion injury in a porcine limb ex vivo perfusion model. *Molecular Immunology* 2017, 88:116-124. DOI 10.1016/j.molimm.2017.06.021
- Zhang S, Wotzkow C, Bongoni AK, Shaw-Boden J, Siegrist M, Taddeo A, Blank F, Hofstetter W, Rieben R. Role of the plasma cascade systems in ischemia/reperfusion injury of bone. *Bone* 2017, 97:278-286
- Pauli C, Hopkins BD, Prandi D, Shaw R, Fedrizzi T, Sboner A, Sailer V, Augello M, Puca L, Rosati R, McNary TJ, Churakova Y, Cheung C, Triscott J, Pisapia D, Rao R, Mosquera JM, Robinson B, Faltas BM, Emerling BE, Gadi VK, Bernard B, Elemento O, Beltran H, Demichelis F, Kemp CJ, Grandori C, Cantley LC, Rubin MA. Personalized In Vitro and In Vivo Cancer Models to Guide Precision Medicine. *Cancer discovery*. 2017; 7(5):462-477. NIHMSID: NIHMS849941
- Blattner M, Liu D, Robinson BD, Huang D, Poliakov A, Gao D, Nataraj S, Deonaraine LD, Augello MA, Sailer V, Ponnala L, Ittmann M, Chinnaiyan AM, Sboner A, Chen Y, Rubin MA, Barbieri CE. SPOP Mutation Drives Prostate Tumorigenesis In Vivo through Coordinate Regulation of PI3K/mTOR and AR Signaling. *Cancer Cell*. 2017; 31(3):436-451. NIHMSID: NIHMS851730
- Faltas BM, Prandi D, Tagawa ST, Molina AM, Nanus DM, Sternberg C, Rosenberg J, Mosquera JM, Robinson B, Elemento O, Sboner A, Beltran H, Demichelis F, Rubin MA. Clonal evolution of chemotherapy-resistant urothelial carcinoma. *Nature Genetics*. 2016; 48(12):1490-1499. NIHMSID: NIHMS873163
- Beltran H, Prandi D, Mosquera JM, Benelli M, Puca L, Cyrta J, Marotz C, Giannopoulou E, Chakravarthi BV, Varambally S, Tomlins SA, Nanus DM, Tagawa ST, Van Allen EM, Elemento O, Sboner A, Garraway LA, Rubin MA, Demichelis F. Divergent clonal evolution of castration-resistant neuroendocrine prostate cancer. *Nature medicine*. 2016; 22(3):298-305. NIHMSID: NIHMS751180
- Blom RAM, Amacker M, van Dijk RM, Moser C, Stumbles PA, Blank F, von Garnier C. Pulmonary Delivery of Virosome-Bound Antigen Enhances Antigen-Specific CD4+ T Cell Proliferation Compared to Liposome-Bound or Soluble Antigen. *Front Immunol*. 2017 Apr 7;8:359. PMID: 28439267

- Blom RAM, Amacker M, Moser C, van Dijk RM, Bonetti R, Seydoux E, Hall SRR, von Garnier C, Blank F. Virosome-bound antigen enhances DC-dependent specific CD4+ T cell stimulation, inducing a Th1 and Treg profile in vitro. *Nanomedicine*. 2017 Jul;13(5):1725-1737. PMID: 28214610
- Ruef N, Dolder S, Aeberli D, Seitz M, Balani D, Hofstetter W. Granulocyte-macrophage colony-stimulating factor-dependent CD11c-positive cells differentiate into active osteoclasts. *Bone*. 2017 97:267-277
- Schaller B, Saulacic N, Beck S, Imwinkelried T, Liu EWY, Nakahara K, Hofstetter W, Iizuka T. Osteosynthesis of partial rib osteotomy in a miniature pig model using human standard-sized magnesium plate/screw systems: Effect of cyclic deformation on implant integrity and bone healing. *J Craniomaxillofac Surg*. 2017 45(6):862-871
- Nasher F, Heller M, Hathaway LJ. (2018) Streptococcus pneumoniae Proteins AmiA, AliA, and AliB Bind Peptides Found in Ribosomal Proteins of Other Bacterial Species. *Frontiers in Microbiol*. 8:2688. doi: 10.3389/fmicb.2017.02688
- Meneses N, Taboada H, Dunn MF, Vargas MD, Buchs N, Heller M, Encarnación S. (2017) The naringenin-induced exoproteome of *Rhizobium etli* CE3. *Arch Microbiol*. 199(5):737-755. doi: 10.1007/s00203-017-1351-8. PMID: 28255691
- Brügger V, Duman M, Bochud M, Mürger E, Heller M, Ruff S, Jacob C. (2017) Delaying Histone Deacetylase Response to Injury Accelerates Conversion into Repair Schwann Cells and Nerve Regeneration. *Nature Commun*. 8:14272. doi: 10.1038/ncomms14272. PMID: 28139683

Microscopy Imaging Center (MIC)

c/o Theodor Kocher Institute
Freiestrasse 1, 3012 Bern



Prof. Britta Engelhardt
President
Representative of the Medical Faculty



Prof. Michael Stoffel
Representative of the Vetsuisse Faculty



Prof. Volker Heussler
Representative of the Faculty of Science



PD Dr. Ruth Lyck
Coordinator

Structure Profile

The MIC was founded in 2005 and has since developed into the University of Bern's center of excellence for high-end microscopy in the life sciences. Experts in microscopy from a total of 14 institutes from the Medical Faculty, the Faculty of Science and the Vetsuisse Faculty of the University of Bern and from the University of Fribourg have joined forces to provide central access to numerous high-end microscopes and imaging systems for all university members. In 2017 the directive panel, which is the MIC Commission, consisted of 27 representatives from the participating institutes. The steering panel of the MIC is the MIC Board formed by the MIC chair, the representatives from the participating faculties and the MIC coordinator. Currently MIC manages 50 instruments among which are 36 light microscopes, 8 electron microscopes, 3 mesoscopes, 2 atomic force microscopy systems and a microCT, which have been used in 2017 by more than 290 active users. Highly qualified scientists, who provide expertise and support, oversee the equipment of the MIC. The MIC is furthermore instrumental in identifying new technologies to be implemented at the University of Bern and thus in supporting strategical novel acquisitions for example through R'Equip programs.

Research Partners

- Swiss BioImaging - Swiss Microscopy and Imaging Core Facility Network, www.swissbioimaging.org
- German BioImaging (GerBI) - German national network of microscopists and imaging specialists, www.germanbioimaging.org
- Euro-BioImaging - The European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences (Euro-BioImaging, EuBI or EuBI ERIC), www.eurobioimaging.eu
- European Light Microscopy Initiative (ELMI) - Communication network between European scientists working in the field of light microscopy and the manufacturers of their equipment, www.embl.org/elmi/
- Neubias - The Network of European BioImage Analysts, COST Action CA15124, eubias.org/neubias/
- Science IT Support, SciTS, www.scits.unibe.ch, PD Dr. Sigve Haug, Mathematical Institute, University of Bern
- Prof. Paolo Favaro, Institute of Computer Science, University of Bern
- Prof. Raphael Sznitman, ARTORG Center - Ophthalmic Technology Lab, University of Bern
- Dr. Akitaka Ariga, Laboratory for High Energy Physics (LHEP), University of Bern

Research Profile

The MIC brings together researchers from various life science areas. They provide expert knowledge in microscopy to make the discipline «Microscopy» accessible to the researcher's community of the University of Bern at an uppermost expert level. The expertise ranges from live imaging of whole organisms to organs, cells and subcellular dynamics. High-throughput setups are available to screen large cohorts of living or fixed samples. The MIC portfolio offers imaging from 2D to 4D and from the mesoscopic scale to the ultra-structural level. Electron microscopy allows resolution up to the nanometer scale in transmission or scanning mode and can be combined with serial block face sectioning. Atomic force microscopy allows for the analysis of surfaces of materials or organism with micrometer to nanometer resolution. For details of the full range of MIC activities and services, please visit the MIC homepage at www.mic.unibe.ch.

Teaching Profile

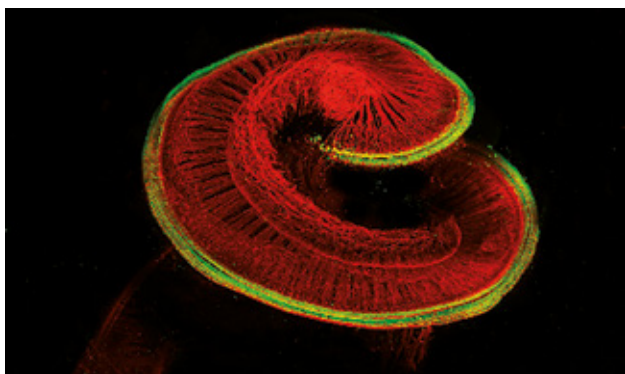
MIC sustains a wide range of teaching activities. In 2017, the lecture series on Advanced Microscopy was attended by 72 students at the master and PhD level. MIC workshops are offered by MIC experts on selected microscopy techniques. MIC trainings cover a multitude of topics, ranging from basic wide field microscopy to confocal microscopy and from software handling to writing own scripts for automated image acquisition or analysis. A swissuniversity-funded PhD program, named Cutting Edge Microscopy (CEM), has started in January 2017. The MIC organizes a yearly summer school and other teaching events for the 20 students of the CEM PhD program.

Highlights 2017

On April 5, 2017, the MIC organized a Mini Symposium on 'Image analysis in microscopy'. It was the first event of this kind, aiming to bring together researchers from the Universities of Bern and Fribourg interested in image processing as well as experts from outside. Presentations dealt with the application of state-of-the-art image processing methods and software. This mini-symposium was very well attended and lively discussions reflected the importance of the topic. Based on requests from several participants, the MIC has organized workshops on ilastik, KNIME and FIJI macros in the following months.

The MIC Research Day took place in the afternoon of June 28, 2017, at the Vetsuisse Faculty, University of Bern. The MIC Research Day is designed to provide a platform for

exchange between scientists of the University of Bern and the University of Fribourg who rely on microscopy in their life science research.



Cochlea of the rat. Sensory hair cells are stained in green, the neurons of the auditory nerve, known as spiral ganglion neurons, are shown in red. Michael Perny, Marta Rocchio, Inner Ear Research Laboratory, DBMR, University of Bern.

On June 28, 2017, the students of the CEM PhD program attended the Kick-Off meeting jointly organized by the MIC and the CEM administration at Schloss Bümpliz. An interactive atmosphere and lively discussions characterized the Kick-Off meeting.

On September 5, 2017, the MIC members met at Schloss Bümpliz for the MIC Retreat. We discussed the "Vision 2025" for future development of the MIC. A common tenor was the call for the MIC to be a SNF-recognized core facility. All MIC members agreed on the difficulties in covering maintenance costs of microscopes. Overall, this event was perfectly suited for discussions in a relaxed atmosphere and for having a common look at the MICs' future.

On September 16, 2017, the University of Bern celebrated the Nacht der Forschung. The MIC contributed various short talks about the benefit and fascination of high-quality microscopy. An exhibition of historic microscopes and of microscopic images decorated the seminar room and thus added to the enjoyable atmosphere of the presentations. In parallel, the visitors had the opportunity to build a simple microscope with their mobile phone camera, using a glass bead and a holder. We also set up three binocular microscopes and a specimen preparation station. In addition, histological samples from the medicine basic education



Left: Microscopy for the public. PhD student Nora Ruef demonstrates microscopy to a school girl. ©Manu Friederich, University of Bern. Right: Migration of a fibroblast. Montage of subsequent steps into one image. ©Olivier Pertz, Institute of Cell Biology.

were available for close scrutiny. Specimen preparation and inspection through the microscope was highly attractive especially for children.

On September 14, 2017, representatives of the Swiss Microscopy Core Facilities gathered in Fribourg at a meeting that was co-organized by members of the University of Fribourg and the Swiss Integrative Center for Human Health (SICHH). The main topic of this event was the management of research data. This perfectly organized event enhanced the networking between the Swiss Microscopy Core Facilities.

On December 8, 2017, the traditional MIC Symposium took place in the Langhans Auditorium of the Institute of Pathology, University of Bern. This year, a record of 150 participants from the University of Bern, whole Switzerland, Italy and Germany met to discuss recent advances and challenges in the area of big data in light and electron microscopy.



MIC Symposium 2017. Snapshots.

Selected Competitive Grants

- SNF R'Equip 2017: A spinning disk microscope with equipment for high-content throughput and live-cell microscopy. Professor Olivier Pertz, Institute of Cell Biology, University of Bern

Selected Publications

- Burda PC, Caldelari R, Heussler VT: Manipulation of the Host Cell Membrane during Plasmodium Liver Stage Egress. *MBio* 2017, 8(2)
- Thiel A, Mogel H, Bruggisser J, Baumann A, Wyder M, Stoffel MH, Summerfield A, Posthaus H: Effect of Clostridium perfringens beta-Toxin on Platelets. *Toxins (Basel)* 2017, 9(10)
- Guichard P, Hamel V, Le Guennec M, Banterle N, Iacovache I, Nemcikova V, Fluckiger I, Goldie KN, Stahlberg H, Levy D et al: Cell-free reconstitution reveals centriole cartwheel assembly mechanisms. *Nature communications* 2017, 8:14813
- Ackerknecht M, Gollmer K, Germann P, Ficht X, Abe J, Fukui Y, Swoger J, Ripoll J, Sharpe J, Stein JV: Antigen Availability and DOCK2-Driven Motility Govern CD4(+) T Cell Interactions with Dendritic Cells In Vivo. *J Immunol* 2017, 199(2):520-530
- Lyck R, Lecuyer MA, Abadier M, Wyss CB, Matti C, Rosito M, Enzmann G, Zeis T, Michel L, Garcia Martin AB et al: ALCAM (CD166) is involved in extravasation of monocytes rather than T cells across the blood-brain barrier. *J Cereb Blood Flow Metab* 2017, 37(8):2894-2909

Swiss Institute for Translational and Entrepreneurial Medicine (sitem-insel)

Freiburgstrasse 3 (building under construction)
3010 Bern



Prof. em. Felix Frey
CEO



Prof. Rudolf Blankart
Director Promoting Agencies

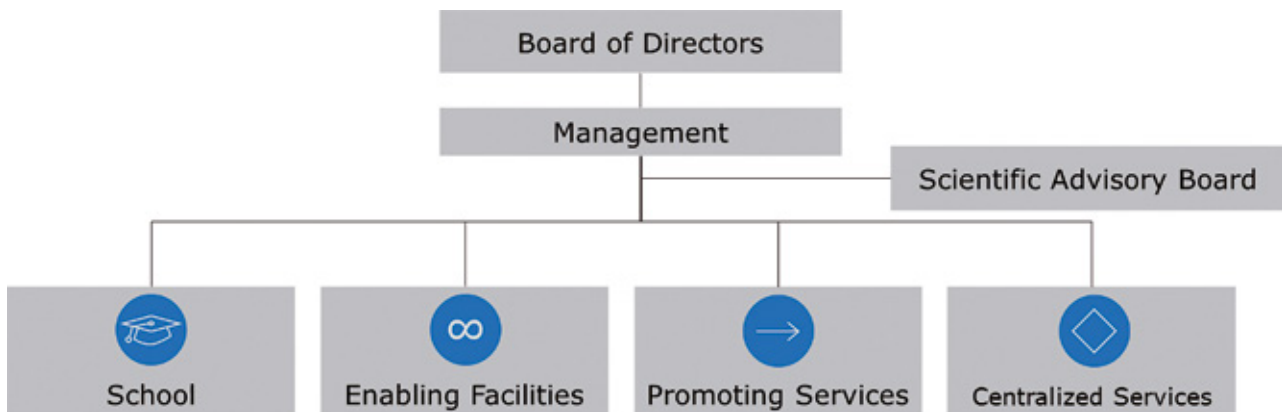


Dr. Christian Rosser
Director Centralised Services



Prof. Uyen Huynh-Do
Director School ad interim

Structure Profile



Research Partners

- Clinical Anatomy, KARL STORZ SE & Co, Tuttlingen, Germany
- Dental Translational Research Center, Institut Straumann AG, Basel, Switzerland
- Experimental Radiology, Siemens Healthineers AG, Zurich, Switzerland
- Diabetes Research Center, Willy Michel/Ypsomed Holding AG, Solothurn, Switzerland
- Metabolomics, Waters Limited, Canada
- Protein Research Center, CSL Behring AG, Bern, Switzerland
- Center of Competence for Public Management, University of Bern, Bern, Switzerland
- Berner Fachhochschule, Bern, Switzerland
- Hamburg Center for Health Economics, Universität Hamburg, Hamburg, Germany
- Centre for Research on Health and Social Care Management, University of Bocconi, Milano, Italy

Research Profile

The sitem-insel was created to establish, operate, and develop a National Centre of Excellence for Translational Medicine and Entrepreneurship. sitem-insel is organized as a non-profit oriented public private partnership. sitem-insel seeks to professionalize the essential interaction between scientists conducting basic research in the private sector and universities, clinicians, regulatory bodies, and investors.

The mission of sitem-insel is to create and foster an enhanced environment for translational medicine in Switzerland. The sitem-insel strategy rests on three pillars:

- The sitem-insel School offers university-level continuing professional development courses taught by university and private-sector lecturers.
- The sitem-insel Enabling Facilities provide infrastructure to foster cooperation between industrial partners, basic scientists and clinicians on InseleCampus with the ultimate goal to bring novel diagnostic and therapeutic products towards clinical application.
- The sitem-insel Promoting Services aim to optimize the administrative-regulatory effort along the route from invention to commercialization.



Teaching Profile

Collaboration with the University of Bern

In addition to lectures and seminars in the field "Medicine and Industry" and "Regulatory Affairs and Health Technology Assessment", the directors of sitem-insel are

currently supervising and advising three PhD students and several master theses from the Center of Competence for Public Management, University of Bern. The doctoral studies are in the fields of regulatory affairs, health care management and strategy building for public private partnership organizations.

sitem-insel School

The sitem-insel School, which aims to promote young researchers and train executives in the fields of translational medicine and biomedical entrepreneurship, started in April 2017 with eleven master students. Lecturers and supervisors of the school are representatives from research and development-oriented private companies, scientists from universities, clinicians, collaborators from regulatory agencies, and financial experts. The program is certified by the University of Bern and participants may obtain the degrees of «Master of Advanced Studies» (MAS), «Diploma of Advanced Studies» (DAS) or «Certificate of Advanced Studies» (CAS).

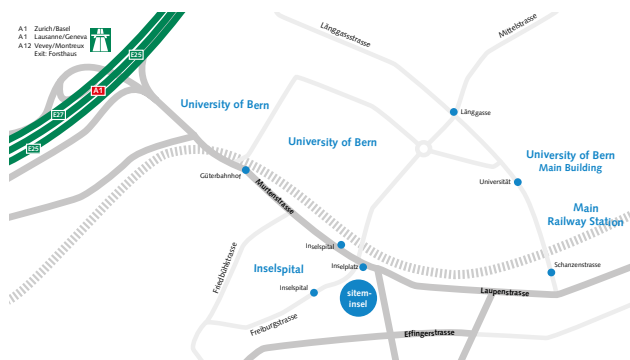
Highlights 2017

Subsidies and Shareholders

In 2016, sitem-insel was being approved by the Swiss Confederation (Bund) to be of national importance and is therefore receiving 25 Mio CHF of each, the Swiss Confederation and the Canton of Bern for the years 2017 to 2020. The shareholders of sitem-insel are from the private sector (Chefärztevereinigung des Inselspitals, CSL Behring AG, Grosse Apotheke Dr. Bichsel AG, Zur Rose Group AG, Catfil AG) as well as the public sector (University of Bern, Berner Fachhochschule, Bretscherfonds and Inselstiftung) and the share capital amounts to approximately 12 Mio. CHF as of December 2017.

New Building on the Inselhospital Campus

sitem-insel will be located at the entrance of the Inselcampus (s. map). Construction work started in early 2017. In June 2017 the foundation stone was laid together with Federal Council Member Johann N. Schneider-Ammann and Christoph Ammann, Member of the Government for the Canton of Bern.



Private Foundation for Diabetes Research Center established

Willy Michel, Chairman of the Board at the Ypsomed Group, will provide the sum of 50 Mio. CHF from private means for the Diabetes Centre Berne (DCB), which will be established in the sitem-insel building. The DCB addresses unsolved problem areas in the treatment of diabetes mellitus and will cooperate closely with the University Clinic for Diabetology, Endocrinology, Nutritional Medicine & Metabolism (UDEM) of the Insel group (www.diabetescenterberne.com).

Selected Competitive Grants

- HORIZON 2020 (H2020-SC1-2017): Pushing the boundaries of Cost and Outcome analysis of Medical Technologies (COMED)

Selected Publications

- Huynh-Do, U., Anderle, P. 2017. Educating Scientists in Translational and Entrepreneurial Medicine: Unmet Needs and Challenges. *Technology Transfer and Entrepreneurship*, 4(2): 126-131
- Sachweh, A., von Kodolitsch, Y., Kölbl, T., Larena-Avellaneda, A., Wipperfurth, S., Bernhardt, A. M., Girdauskas, E., Detter, C., Reichenspurner, H., Blankart, C. R., & Debus, E. S. 2017. I-SWOT as instrument to individually optimize therapy of thoracoabdominal aortic aneurysms. *Gefässchirurgie*, 22(1): 8-16
- Hatz, M. H. M., Schreyögg, J., Torbica, A., Boriani, G., & Blankart, C. R. B. 2017. Adoption Decisions for Medical Devices in the Field of Cardiology: Results from a European Survey. *Health Economics*, 26: 124-144
- Varabyova, Y., Blankart, C. R., Greer, A. L., & Schreyögg, J. 2017. The determinants of medical technology adoption in different decisional systems: A systematic literature review. *Health Policy*, 121(3): 230-242
- Rosser, C. 2017. Weber and His Bequest for Public Administration in Europe. In: ONGARO, Edoardo and Sandra Van Thiel (Eds.). *The Palgrave Handbook of Public Administration and Management in Europe*. Basingstoke: Palgrave Macmillan: 1011-1029

University Neurocenter

University of Bern
Switzerland



Prof.
Claudio Bassetti
(speaker)
Neurology



Prof.
Andreas Raabe
Neurosurgery



Prof.
Jan Gralla
Neuroradiology



Prof.
Maja Steinlin
Neuropediatrics



Prof.
Werner Strik
Psychiatry



Rosmarie Wyss



Barbara Weiss-
Zurschmiede



Michela
Mordasini



Heidi
Baumgartner



Beat Burri

Structure Profile

The Neurocenter of Bern was founded in 2012. With 180 beds (except Psychiatry), over 1'400 collaborators, more than 75'000 ambulatory and more than 8'000 stationary patients, and over 3'500 operations and interventions each year it is the largest of its kind in Switzerland.

Research Partners

- Alzheimer Research Center, Karolinska Institute, Stockholm, Sweden
- Department of Neurology, University of California Los Angeles (UCLA), USA
- Department of Pediatric Neurology, Royals Children Hospital, Murdoch Research Institute, Melbourne Australia
- Department of Pulmonology, University Hospital, Bern
- Faculty of Psychology, University of Bern
- Institute for Artificial Organs (ARTORG), University of Bern
- Institute for Research in Biomedicine, Università della Svizzera italiana, Bellinzona
- Institute for Surgical Technology and Biomechanics, University of Bern
- Swiss Center for Electronics and Microtechnology, Neuchâtel

Research Profile

Research areas with strong transdisciplinary approaches/interactions within the Neurocenter include the following:

- stroke* (4 out of 5 departments), including complex neurovascular diseases
- sleep-wake-epilepsy*, including epilepsy surgery (4/5)
- movement disorders, including functional neurosurgery for Parkinson's disease, neurological and psychiatric disorders (5/5)
- neurorehabilitation including computer-assisted systems and robotics (4/5)
- neuroimmunology* (3/5)
- neurodegeneration*/dementia (3/5)

- intraoperative imaging, neuromonitoring, augmented reality, navigation associated developments, targeted procedures and 3D printing and simulation techniques (2/5)
- systems neuroscience and psychopathology (3/5)

*in these areas clinical/human and experimental/animal approaches are used

The research groups of the Neurocenter use the following common research platforms:

- neuro-clinical trial unit (in collaboration with the CTU Bern)
- human neurophysiological laboratories
- human neuroimaging facilities (including the neurointerventional lab)
- animal research facilities (ZEN, center for experimental neurology)
- technological facilities (ARTORG center)
- support center for advanced neuroimaging (SCAN)



Teaching Profile

The following pre- and postgraduate events are jointly organized by different departments of the Neurocenter each year (download program [here](#)):

- clinical neuroscience Bern (CNB) meeting and science slam (organizers: U. Fischer, T. Nef)
- stroke meeting, European Stroke Winter School, brain-heart symposium (M. Arnold, U. Fischer, J. Gralla, J. Beck)
- BENESCO seminars, Bernese sleep-wake days, Winter and Summer Sleep Schools (C. Bassetti, M. Gugger, K. Schindler, A. Adamantidis, C. Nissen)
- neuro-emergencies symposium (W. Z'Graggen, U. Fischer)

Following an initiative of the Neurocenter a new PhD in Clinical Sciences was launched in October 2017 (www.ghs.unibe.ch).

Highlights 2017

In 2017, 29 SNF (18 in the Neurology Department) projects were running and more than 250 original publications were published in the Neurocenter.

This year two ERC consolidator grants were awarded to A. Adamantidis and S. Saxena (both at the Neurology Department).

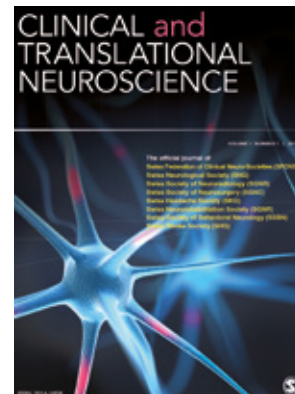


Prof. Smita Saxena
Connectivity Correlate of Molecular Pathology in Neurodegeneration: Investigating the role of dysfunctional neuronal circuits in governing selective neuronal vulnerability and promoting pathological degeneration of vulnerable neurons in neurodegenerative diseases.



Prof. Antoine Adamantidis
All-optical deconstruction of thalamic control of sleep-wake states: Investigation of the role of the thalamus as a hub that integrates sleep-wake inputs of both subcortical and cortical origin into stable sleep-wake states in mice. The project will provide a mechanistic perspective on sub-cortical, thalamo-cortical and cortical control of brain oscillations during sleep-wake states, and their functions in cognition and consciousness in the rodent brain.

A new international journal (Clinical and Translational Neuroscience, journals.sagepub.com/home/ctn) was launched by 8 Swiss clinical neuro-societies. The editorial office of CTN is in Bern and its editorial board includes four members of the Neurocenter: C. Bassetti (Editor-in-Chief), A. Adamantidis, A. Chan and A. Raabe.



Selected Competitive Grants

Only the largest grant obtained in 2017 of each department of the Neurocenter is listed:

- Neurology: SNF Sinergia: Sleep as a model to understand and manipulate cortical activity in order to promote neuroplasticity and functional recovery after stroke (CHF 1'830'000; PI: C. Bassetti)
- Neurosurgery: BRIDGE Project 20B2-1-176498 /1: Towards intelligent sensor enhanced robotic neurosurgery (CHF 2'000'000; PI: A. Raabe, S. Weber)
- Neuroradiology: "Stroke treatment goes personalized (Stray Cats)" (CHF 474'000; PI: J. Gralla)
- Neuropediatrics: Onset-Study, Jacobs Foundation (CHF 150'000; PI: R. Everts and C. Roebers)

Selected Publications

- Bargiotas P, Eugster L, Oberholzer M, Debove I, Lachenmayer L, Mathis J, Pollo C, Schüpbach WMM, Bassetti CL. Sleep-wake functions and quality of life in patients with subthalamic deep brain stimulation for Parkinson's disease. PLoS One 2017; 12: e=190027
- Kornfeld S, Yuan R, Biswal BB, Grunt S, Kamal S, Delgado Rodríguez JA, Regényi M, Wiest R, Weisstanner C, Kiefer C, Steinlin M, Everts R. Resting-state connectivity and executive functions after pediatric arterial ischemic stroke. Neuroimage Clin. 2017; 17:359-367
- Reitmeir R, Eyding J, Oertel MF, Wiest R, Gralla J, Fischer U, Giquel PY, Weber S, Raabe A, Mattle HP, Z'Graggen WJ, Beck J. Is ultrasound perfusion imaging capable of detecting mismatch? A proof-of-concept study in acute stroke patients. J Cereb Blood Flow Metab 2017; 37:1517-1526
- Strik W, Stegmayer K, Walther S, Dierks T. Systems Neuroscience of Psychosis: Mapping Schizophrenia Symptoms to Brain Systems. Neuropsychobiology 2017 (in press)
- Zubler F, Steimer A, Kurmann R, Bandarabadi M, Novy J, Gast H, Oddo M, Schindler K, Rossetti AO. EEG synchronization measures are early outcome predictors in comatose patients after cardiac arrest. Clin Neurophysiol 2017; 128 (4): 635-642

Institute of Anatomy

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Prof. Annette Draeger
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Prof. Nadia Mercader Huber
Co-Director



Prof. Benoît Zuber
Co-Director



PD Dr. Stefan Tschanz
Central Services
Leader



PD Dr. Asparouh Iliev



Prof. Marianne Geiser



PD Dr. Gudrun Herrmann



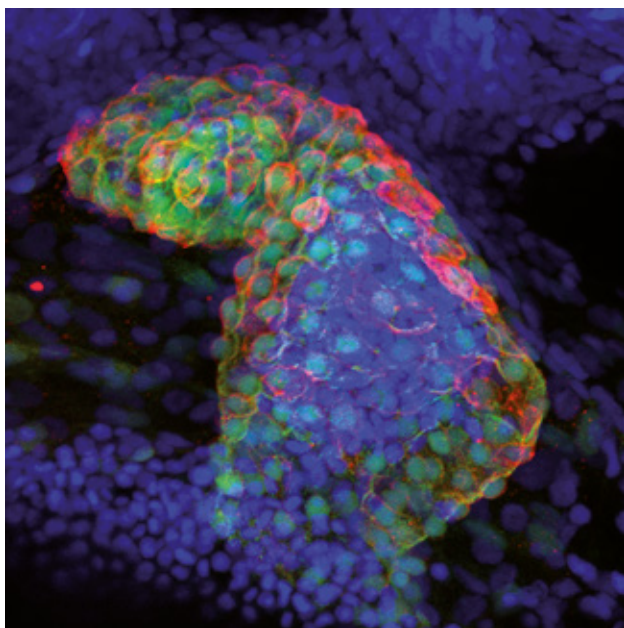
Prof. Johannes Schittny

Research Partners

- Prof. Michael Stoffel, Dept. of Veterinary Anatomy University of Bern, Bern, Switzerland
- Prof. Martin Frenz, Inst. of Applied Physics, University of Bern, Bern, Switzerland
- Prof. José Antonio Enrique, Centro Nacional de Investigaciones Cardiovasculares CNIC, Madrid, Spain
- Prof. Julien Vermet, IGBMC, Strasbourg, France
- Prof. Gisou van der Goot, EPFL, Lausanne, Switzerland
- Prof. Abbas Ourmazd, University of Wisconsin-Milwaukee, USA
- Prof. Sibylle Schneider-Schaulies, Institute of Virology and Immunobiology, University of Würzburg, Germany

Research Profile

The Institute's research interests cover a variety of topics ranging from basic to applied science: cardiovascular development, repair and regeneration, fine structural



Embryonic zebrafish heart imaged with a confocal microscope. Green channels shows *tbx5a*:GFP, red channel anti-Myosin Heavy Chain immunostainings.

investigation of neuronal synapses, research on the effect of bacterial toxins and the prevention of antimicrobial resistance, pulmonary development and function of ciliae in the respiratory tract, as well as dangers of occupational exposure to inhaled particles. One of the Institute's expertise is imaging. We image tissues and organs at the macroscopic, microscopic and ultrastructural level using micro-CT, Synchrotron Radiation based X-ray Tomographic Microscopy, in vivo Confocal and Light Sheet Microscopy, cryo-Electron Microscopy and Serial Block Face Scanning Electron Microscopy. The Institute is part of the Microscopy Imaging Center (MIC) of the University. Our research models include cell culture, zebrafish, mice and patient samples. The Institutes also offers a Swiss-wide unique service in micro-morphological analysis of primary ciliary dyskinesia.

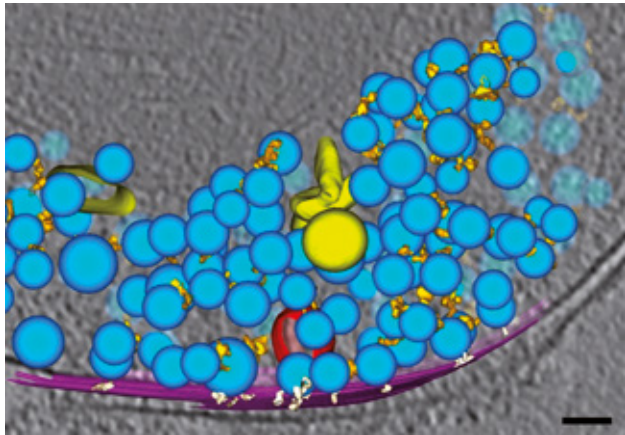
Teaching Profile

The Institute of Anatomy is responsible for the comprehensive teaching of preclinical medical students (human, dentistry and veterinary medicine) and students of related paramedical fields (Biomedical Sciences, Bioengineering, Physiotherapy, Osteopathy) in subjects such as Gross Anatomy, Histology, Embryology and Cell Biology. 5 Master theses, 8 MD theses, and 2 PhD theses were completed in 2017 at the Institute. In addition, postgraduate education and advanced surgical training is provided for medical graduates specializing in a large variety of surgical fields.

Highlights 2017

After an SNF Professorship at the Institute of Anatomy, Benoît Zuber has succeeded to Peter Eggli and was promoted to associate professor (extraordarius) in February 2017. He leads the Department of Microscopic Anatomy and Structural Biology. The Zuber group investigates synaptic vesicle exocytosis using a structural biology approach, namely time-resolved cryo-electron microscopy (cryo-EM), which provides molecular resolution. This year they have resolved changes occurring in the presynaptic cytomatrix milliseconds after the onset of an action potential. These results provide insight in the mechanism synaptic vesicles get primed for exocytosis. The Zuber lab is also specialized in protein structure determination by single particle cryo-EM

and investigates thereby the mechanism of membrane insertion and pore formation of bacterial pore forming toxins (Iacovache et al, Nat Commun 2016). The Zuber group has introduced serial block face scanning electron microscopy, a new methodology that enables the 3-dimensional ultrastructural investigation of very large tissue samples. The group participates in a number of local, national, and international collaborations and develops methodological and technological improvements (Odrizola et al., bioRxiv 2017). In addition, Zuber's department provides services in sample preparation for electron microscopy and imaging in the frame of the Microscopy Imaging Center (MIC).



Synapse as visualized by cryo-EM.

Selected Competitive Grants

- ERC Starting grant (337703)
- European Industrial Doctorate Program (H2020-MSCA-ITN-2016)
- SNF Professorship Extension (163761)
- Gebert-Rüf Foundation SNF SCOPES (152454)

Selected Publications

- Lovric G, Vogiatzis Oikonomidis I, Mokso R, Stampanoni M, Roth-Kleiner M, Schittny JC. Automated computer-assisted quantitative analysis of intact murine lungs at the alveolar scale. *PLoS One*. 2017 Sep 21;12(9):e0183979
- Saad L, Hlushchuk R, Barré S, Gianni-Barrera R, Haberthür D, Banfi A, Djonov V.: Correlative Imaging of the Murine Hind Limb Vasculature and Muscle Tissue by MicroCT and Light Microscopy. *Sci Rep*. 2017; 7:41842
- Odrizola, A., J. Llodrá, J. Radecke, C. Ruegsegger, S. Tschanz, S. Saxena, S. Rohr, and B. Zuber. 2017. High contrast staining for serial block face scanning electron microscopy without uranyl acetate. *bioRxiv*
- Maurer J, Hupp S, Bischoff C, Foertsch C, Mitchell TJ, Chakraborty T, Iliev AI. Distinct Neurotoxicity Profile of Listeriolysin O from *Listeria monocytogenes*. *Toxins*. 2017 Jan 13;9(1). pii: E34
- Geiser M, Jeannet N, Fierz M, Burtscher H. Evaluating Adverse Effects of Inhaled Nanoparticles by Realistic In Vitro Technology. *Nanomaterials*. 2017 Feb 22;7(2). pii: E49

Institute of Biochemistry and Molecular Medicine (IBMM)

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Managing Director
Head NCCR
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Prof. Christiane Albrecht



Prof. Michael Altmann



Prof. Peter Bütikofer
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Prof. Charles Roch-Philippe



Prof. Dimitrios Fotiadis
Co-Director



Prof. Jürg Gertsch
Co-Director



Prof. Matthias Hediger



Dr. Martin Lochner



Prof. Christine Peinelt

Research Partners

- Departments of Chemistry and Biochemistry, Biomedical Research, Nephrology and Hypertension, Inselspital, Institutes of Physiology, Pathology, Urology, University of Bern, Bern, Switzerland
- Department of Biosystems Science and Engineering, ETH Zurich, Zurich, Switzerland
- Swiss Institute of Bioinformatics, University of Geneva, Geneva, Switzerland
- School of Medicine, University of Nottingham, Nottingham, UK
- Department of Pharmacology, University of Cambridge, Cambridge, UK
- School of Life Sciences, University of Warwick, Coventry UK
- Max-Planck- Institute, Munich, Germany
- Laboratory of Molecular Electron Microscopy, The Rockefeller University, New York, USA
- PeterMac Institute, Melbourne, Australia
- NIH, NIAAA, Rockville, USA

Research Profile

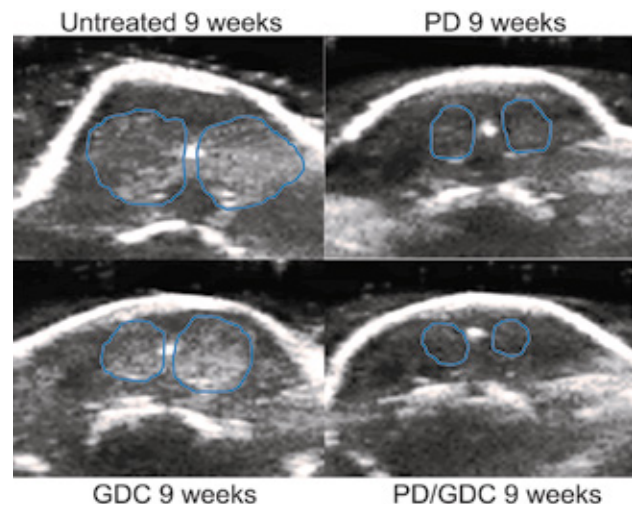
The research activities at the Institute of Biochemistry and Molecular Medicine (IBMM) focus on the structure, function, and pharmacology of membrane proteins such as transporters, ion channels, and membrane receptors. A strong emphasis is put on the roles of these membrane proteins in human diseases such as cancer, neurological and cardiac disorders, pre-eclampsia and pathogen infections. Currently, more than 100 scientists, of whom many are Ph.D. students and postdoctoral fellows, belong to one of the ten groups of the IBMM. Furthermore, the IBMM hosts most of the Bernese groups of the Swiss National Science Foundation-funded National Center of Competence in Research (NCCR) TransCure that was established in 2010 at the University of Bern. The NCCR TransCure brings together more than 90 scientists with expertise in membrane transport physiology, structural biology, and medicinal chemistry. These three disciplines are also represented at the IBMM.

Teaching Profile

The institute provides basic and specialized teaching at both pregraduate and postgraduate levels in the Faculties of Medicine and Natural Sciences and in the VetSuisse faculty. It is also involved in the GCB graduate school. The teaching activities at the IBMM are at the interface of the natural and medical sciences. In addition, several members of the IBMM are actively involved in the reorganization of the curriculum for Medical Students and the new Pharmacy curriculum at the University of Bern.

Highlights 2017

Combined MEK and PI3'-kinase inhibition reveals synergy in targeting thyroid cancer in vitro and in vivo
Anaplastic thyroid carcinoma (ATC) is one of the deadliest malignancies in human with a poor prognosis (median survival < 6 months). Unlike most differentiated thyroid carcinomas, ATC is refractory to chemotherapy and the combination of surgery and radioactive iodine. We have developed in the lab an ATC mouse model using clinically

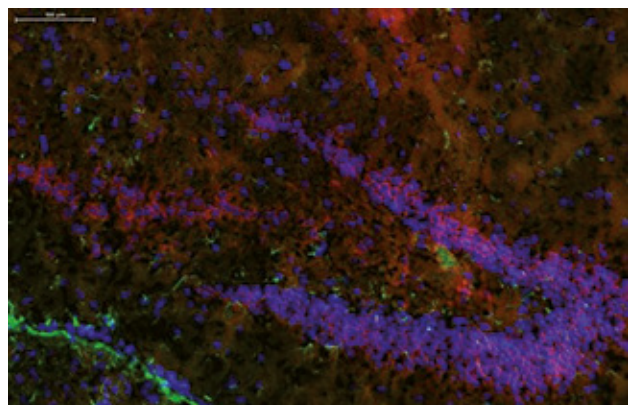


Thyroid ultrasound after MAPK inhibitor (PD), PI3K inhibitor (GDC) or combo.

relevant mutations. We demonstrated that combined inhibition of the MAPK and PI3K pathways synergized in terms of proliferation and apoptosis induction in human cell lines. In addition, the combination treatment led to an enhanced tumor shrinkage with a reduction in tumor-specific markers, advocating for tissue re-differentiation in our mouse model. This translation study shows a proof of principle that ATC patients could benefit from this drug combination targeting both signaling pathways. (Oncotarget. 2017, 8, 24604-24620).

Chemical probes to potently and selectively inhibit endocannabinoid cellular reuptake

The extracellular effects of the endocannabinoids anandamide and 2-arachidonoyl glycerol are terminated by enzymatic hydrolysis after crossing cellular membranes by facilitated diffusion. The lack of potent and selective inhibitors for endocannabinoid transport has prevented the molecular characterization of this process, thus hindering its biochemical investigation and pharmacological exploitation. We report the design, chemical synthesis, and biological profiling of natural product-derived N-substituted 2,4-dodecadienamides as selective endocannabinoid uptake inhibitors. The highly potent (IC₅₀ = 10 nM) inhibitor WOBE437 exerted pronounced cannabinoid receptor-dependent anxiolytic, antiinflammatory, and analgesic effects in mice by increasing endocannabinoid levels. A tailored diazirine-containing photoaffinity probe (RX-055) irreversibly blocked membrane transport of both endocannabinoids, providing mechanistic insights into this complex process. This study describes suitable inhibitors to target endocannabinoid membrane trafficking and uncovers a novel endocannabinoid pharmacology with implications for drug discovery. (PNAS, 2017, 114, E5006-E5015).

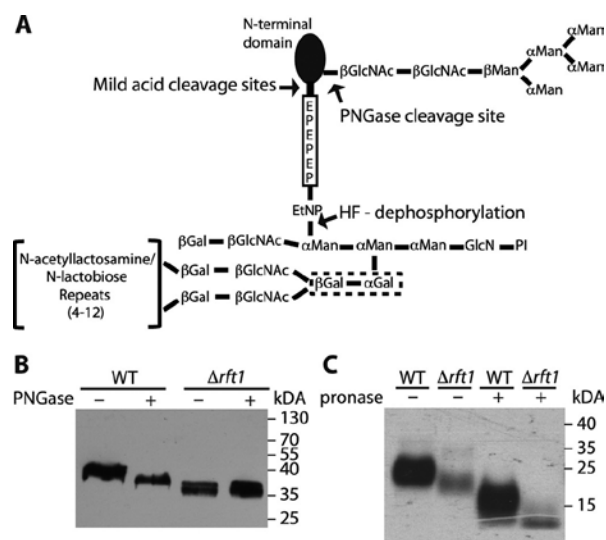


Expression of endocannabinoid system in the dentate gyrus of the hippocampus.

RFT1 Protein Affects Glycosylphosphatidylinositol (GPI) Anchor Glycosylation

The membrane protein RFT1 is essential for normal protein N-glycosylation, but its precise function is not known. In contrast to the situation in yeast, RFT1 is not essential for growth of the parasitic protozoan *Trypanosoma brucei*. We found that the lack of *T. brucei* RFT1 (TbRFT1) not only affects protein N-glycosylation but also glycosylphosphatidylinositol (GPI) anchor side chain modification. The major GPI-anchored proteins of *T. brucei* parasites were shown have truncated GPI anchor side chains in TbRFT1 null parasites compared to wild-type cells. Interestingly, GPI underglycosylation was not the result of decreased or defective formation of the GPI precursors in the endoplasmic

reticulum, but rather due to modifications that are expected to occur in the Golgi. Our results implicate RFT1 in a wider range of glycosylation processes than previously appreciated. (JBC, 2017, 292, 1103-1111)



Schematic representation of procyclin glycosylation (A) and analysis of GPI-anchored proteins in TbRFT1 null cells (B,C). Procyclins from TbRft1 null (*rft1*) parasites migrate with a lower molecular mass than procyclins from wild-type (WT) cells.

Selected Competitive Grants

- Swiss National Science Foundation (NCCR TransCure (leading house), NCCR Molecular Systems Engineering, SNSF project grants No. 31003A_173155, 310030_165741, 31003A_162581, 31003A_176175, 31003A_146722, 31003A_149958, 31003A_156376, SNSF Sinergia grants: CR33I3_156233, CRSII3_160782
- Swiss Heart Foundation
- CTI Grant Feasibility Study
- MS Foundation
- Lindenhof Foundation Bern
- Swiss Cancer League

Selected Publications

- Petra Gottier, Amaia Gonzalez-Salgado, Anant Menon, Yuk-Chien Liu, Alvaro Acosta-Serrano, Bütikofer Peter: RFT1 Protein Affects Glycosylphosphatidylinositol (GPI) Anchor Glycosylation. *J Biol Chem.* 2017, 292(3):1103-1111
- Oussama EIMokh, Dorothee Ruffieux-Daidié, Matthias A. Roelli, Amandine Stooss, Wayne A. Phillips, Jürg Gertsch, Matthias S. Dettmer, Roch-Philippe Charles: Combined MEK and PI3'-kinase inhibition reveals synergy in targeting thyroid cancer in vitro and in vivo. *Oncotarget.* 2017, 8(15):24604-24620
- David Kalbermatter, Po-Lin Chiu, Jean-Marc Jeckelmann, Zöhre Ucuruma, Thomas Walz, Dimitrios Fotiadis: Electron crystallography reveals that substrate release from the PTS IIC glucose transporter is coupled to a subtle conformational change. *J Struct Biol.* 2017, 199(1):39-45
- Vanessa Petrucci, Andrea Chicca, Sandra Glasmacher, Janos Paloczi, Zongxian Cao, Pal Pacher, Jürg Gertsch. Pepcan-12 (RVD-hemopressin) is a CB2 receptor positive allosteric modulator constitutively secreted by adrenals and in liver upon tissue damage. *Sci Rep.* 2017, 7(1):9560
- Corneille Edgar Ontsouka, Xiao Huang, Eldar Aliyev, Christiane Albrecht: In Vitro Characterization and Endocrine Regulation of Cholesterol and Phospholipid Transport in the Mammary Gland. *Mol Cell Endocrinol.* 2017, 439:35-45

Institute for the History of Medicine

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PD Dr. Martina
King



Dr. Pascal
Germann



Stefan
Hächler
head of archive



Dr. Dorothe
Zimmermann
head of collection



Bruno
Müller
head of library

Research partners

- Institute of History, University of Bern
- Institute of Germanic Languages and Literatures, University of Bern
- School of Liberal Arts, Indiana University
- Center for African Studies, University of Florida
- Department of History, University of Montréal
- Institute for History and Ethics of Medicine, University of Cologne
- Institute for History and Ethics of Medicine, University of Heidelberg
- Institute of History, University of Zurich
- Institute of Biomedical Ethics and History of Medicine, University of Zurich
- Institute for the History of Medicine and Health, University of Lausanne

Research Profile

The Institute for the History of Medicine, founded in 1963, is a small institution with a single professorship and a single research assistant position. In addition, a number of researchers are employed in externally funded projects. We have a long tradition of research on Albrecht von Haller, the Republic of Letters and the production of knowledge in the 18th century. Another broad focus is the theory and practice of Western medicine from the 18th to the 20th century. There is also a general interest in all studies related to the local history of medicine and health. A further area of expertise is the history of pharmacy. We are particularly keen to develop research projects based on unexplored archival material allowing for new medicohistorical perspectives. A central source for current and future projects is our own expanding archive. The institute owns also a rich library of 100,000 volumes and maintains a collection of 10,000 medical objects. Our collections are accessible to the general public and are important resources for research and teaching.

Teaching profile

Members of the institute teach history of medicine, theory of medicine and medical humanities within the teaching programs for students of medicine. We are also teaching medical students at the Universities of Basel and Fribourg. In addition, we offer seminars to history students at the Philosophical Faculty of our University.

Highlights 2017

Medical practice and international networks. Albert Schweitzer's Hospital in Lambarene, 1913-1965

In this SNSF project we provide a first thorough historical

study of Schweitzer's hospital, using a praxeological approach based on an exceptionally rich and hitherto unstudied corpus of archival material. In 2017, Tizian Zumthurn finished his PhD thesis which highlights – among others – the often improvised nature of biomedicine practiced at the hospital.



Prof. Steinke and Dr. Mabika with archival material from the Albert Schweitzer Hospital.

Health and welfare after the boom: a history of the quality of life concept, 1965-2000

In 2017, Dr. Pascal Germann developed this new SNSF Project which will fund his scholarships at Johns Hopkins and other Universities. It investigates the social, political, and epistemic conditions under which the quality of life concept gained acceptance and wielded influence.

Online-edition of Albrecht von Haller's book reviews and letters: expertise and communication in the emerging scientific community

This is a project developed together with the Institute of History and the Institute of Germanic Languages and Literatures at our University. It is funded through the new SNSF program Edition projects in the humanities. In 2017, thanks to the funding of the Burgergemeinde of Bern and the Rector's Office of the University, a fundamental transformation of the database Haller into a new digital platform has been undertaken in order to start the edition project next year.

From ergot to LSD. Materiality, local and global knowledge in the agricultural, industrial and scientific production of psychotropic substances

This is a SNSF project based partly on the papers of Albert Hofmann in our Institute. In 2017, Dr. Beat Bächli made full use of his research in the Harvard Herbaria Archives and studied especially the transformation of mexican magic mushrooms into psychotropic substances of the western industrial society.

Clinical trials in psychopharmacology

In the last few years, public reports have shed critical light on the clinical trials in the early years of psychopharmacology in Switzerland. In 2017, Dr. Urs Germann has analysed the context and the practices at the University Psychiatric Clinic in Basel and has written a preliminary report on behalf of the institution. He works also on a similar report for the University Hospital of Psychiatry Zurich.

Narrative medicine teaching

In 2017, PD Dr. Dr. Martina King developed and implemented a new compulsory course of narrative medicine for 4th year students of medicine. It explains the character and structure of various kinds of medical records and helps the students to understand how note taking constructs narratives and realities.

Archives

In 2017, we have finished the process of preparation and digitization and transferred the archive of the Swiss Academy of Medical Sciences to our Institute (approx. 2,000 files). Similar preparatory work on the archives of the Swiss Medical Association (FMH) has been undertaken. The institute will thus preserve the archives of two of the most important Swiss medical institutions.

Medical Museum Bern

On behalf of the Inselspital Foundation and with support from the Rector's Office, the Medical Faculty and external foundations, the Institute is preparing the opening of the Medical Museum Bern in late 2018.

Competitive Grants

- Swiss National Science Foundation (grants No. 100011_149880; 100011_159614; 10FE15_157963; PZZHP1_174862)

Selected Publications

- Pascal Germann: "Nature's laboratories of human genetics": Alpine isolates, hereditary diseases and medical genetic fieldwork, 1920–1970, in: Heike Petermann et al. (eds.): History of human genetics: important discoveries and global perspectives (Springer International Publishing, 2017), 145-166
- Urs Germann: Plausible Geschichten. Zur narrativen Qualität gerichtspsychiatrischer Gutachten um 1900, in: Volker Hess, Alexa Geisthövel (eds.): Medizinische Gutachten. Geschichte einer neuzeitlichen Praxis (Göttingen: Wallstein, 2017), 318-339
- Urs Germann: Medikamentenprüfungen an der Psychiatrischen Universitätsklinik Basel. Pilotstudie mit Vorschlägen für das weitere Vorgehen. Bericht zuhanden der Universitären Psychiatrischen Kliniken Basel (Bern 2017), 77p
- Martina King: Im Labor der Abstraktion: Mikrobiologismen in der literarischen und bildkünstlerischen Moderne um und nach 1900, Kulturpoetik 17/1 (2017), 42-62
- Hines Mabika: Medicaliser l'Afrique. Enjeux, stratégies et processus d'introduction de la médecine occidentale au Gabon (XIXe-Xxe siècle) (Paris: L'Harmattan, 2017), 299p



Albert Hofmann with mushrooms and colleagues, 1958.

Institute of Pharmacology

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Prof. Andrea
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Deputy Director



Prof. Thomas
Kaufmann



SNF Prof. Georgia
Konstantinidou



Prof. Stephan
von Gunten



Prof. Shida
Yousefi



Prof. Uwe
Zangemeister-Wittke

Research Partners

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- Institute of Experimental Immunology, Laboratory of Neuroinflammation, University of Zurich, Zurich, Switzerland
- Department of Pharmacology, Toxicology and Clinical Pharmacy, Institute of Pharmacy, University of Tübingen, Germany
- Institute of General Pharmacology, University of Frankfurt/Main, Frankfurt/Main, Germany
- Department of Medicine, University of Toronto and Centre for Innovation, Canadian Blood Services, Toronto, Ontario, Canada
- Department of Immunology, Stefan Angelov Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria
- Center of Laboratory Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Department of Dermatology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Institute of Nutritional Science, Nestlé Research Center, Lausanne, Switzerland
- Swiss EoE Research Group, Olten, Switzerland

Research Profile

The Institute of Pharmacology was founded in 1885. Seven research groups are involved in the investigation of pathophysiological processes that contribute to inflammation and tumor diseases with the aim of discovering new drug targets. Several diseases serve as models to study such processes. The interdisciplinary approach includes different fields, including immunology, cell biology, molecular biology and pathology. Besides the pathogenic aspects of our research, we have developed several *in vitro* and *in vivo* test systems to determine potential effects of a given drug on the immune system. The spectrum of research ranges from fundamental research to clinical trials in which the efficacy of new drugs in humans is tested. The research requires a network of physician-scientists from many different clinics. For example, several groups are interested in the role of apoptosis and autophagy in inflammatory diseases and cancer. In particular, they investigate pathogenic mechanisms of the following diseases: Atopic dermatitis, hypereosinophilic syndromes, eosinophilic esophagitis, sepsis, as well as malignant melanoma and lymphomas. We receive clinical samples for our research and are involved in several clinical drug studies.

Teaching Profile

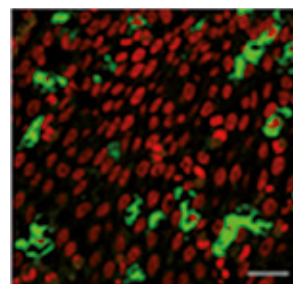
The institute participates in University teaching programs for students of medicine, dental medicine, biomedicine and biology. We also teach students of medicine and biomedicine of the University of Fribourg.

Highlights 2017

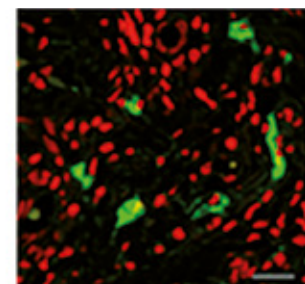
Evidence of an abnormal epithelial barrier in active, untreated and corticosteroid-treated eosinophilic esophagitis (EoE)

Eosinophilic esophagitis (EoE) is a chronic disease characterized by symptoms related to esophageal dysfunction and an eosinophil-predominant inflammation. This study aimed to investigate whether the recently observed sensitization to *Candida albicans* in patients with EoE is owing to pre-existing disease and its underlying abnormal epithelial barrier or, alternatively, is linked to corticosteroid (CS) therapy. Our study provides evidence that EoE is associated with an abnormal epithelial barrier and postulates that CS therapy, by reducing innate immune mechanisms, may promote *Candida albicans* colonization and likely subsequent sensitization.

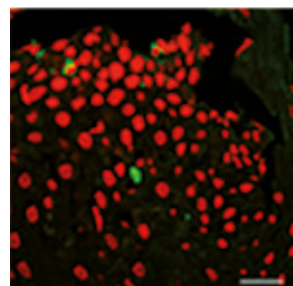
EoE naive



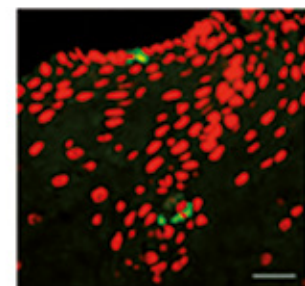
EoE on steroids



EoE off steroids



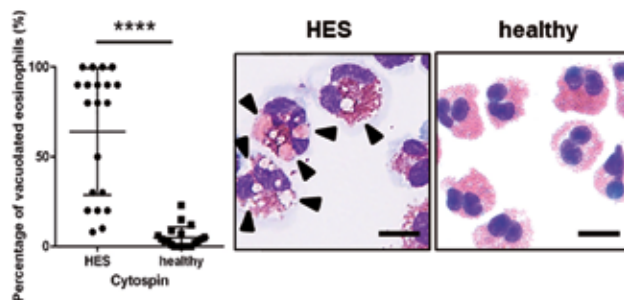
Controls



Representative images of immunofluorescence staining show the eosinophilic inflammation (eosinophils are stained in green) in the indicated subgroups of patients. Scale bars, 10 μ m.

Adhesion-induced eosinophil cytolysis requires the receptor-interacting protein kinase 3 (RIPK3)-mixed lineage kinase-like (MLKL) signaling pathway, which is counterregulated by autophagy

Eosinophils are a subset of granulocytes that can be involved in the pathogenesis of different diseases, including allergy. Their effector functions are closely linked to their cytotoxic granule proteins. Release takes place through several different mechanisms, one of which is cytolysis, which is associated with release of intact granules, so-called clusters of free eosinophil granules. The mechanism underlying this activation-induced form of cell death in eosinophils has remained unclear. We report that adhesion-induced eosinophil cytolysis takes place through RIPK3-MLKL-dependent necroptosis, which can be counter-regulated by autophagy.



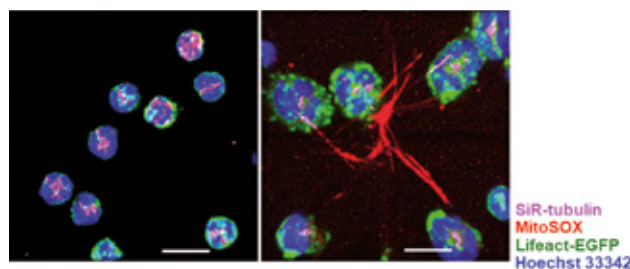
Cytoplasmic vacuolization is observed in blood eosinophils as an early sign of cytolysis. Morphological analysis of blood eosinophils demonstrated a relatively higher frequency of cytoplasmic vacuolization in eosinophils from hypereosinophilic syndrome (HES) patients as compared to healthy donors. Values are means \pm SEM. ****, $p < 0.0001$. Representative original data are also shown (arrowheads point to vacuoles). Scale bars, 10 μ m.

ROS and glutathionylation balance cytoskeletal dynamics in neutrophil extracellular trap (NET) formation

In this study, we demonstrate that ROS-induced actin and tubulin glutathionylation controls cell cytoskeleton dynamics and neutrophil extracellular trap (NET) formation. Physiological activation of neutrophils leads to moderate reactive oxygen species (ROS) production, and cell cytoskeleton glutathionylation. ROS-induced actin and tubulin glutathionylation is tightly regulated by glutaredoxin 1 (Grx1). Disruption of Grx1 or deficient ROS production (CGD patients) unbalances cell cytoskeleton rearrangements and leads to a dysfunctional innate immune response in neutrophils.

Low ROS

Physiological ROS level



Confocal microscopy images demonstrate extracellular NET formation (DNA scaffold is seen in red) as well as actin polymerization (green) and visualization of tubulin (purple). Scale bars, 10 μ m.

Selected Competitive Grants

- Swiss National Science Foundation (grant No. 310030-166473; 310030-153346; 31003A_173215; 31003A_149387; 310030_162552; 310030-146215; 310030E-132762; 310030A-138201)
- Swiss Cancer League (KFS-3703-08-2015; KFS-3248-08-2013)
- HORIZON 2020 (Marie Skłodowska-Curie Action): MEL-PLEX

Selected Publications

- Schneider C, Wicki S, Graeter S, Timcheva T, Keller C, Quast I, Leontyev D, Djoumerska-Alexieva I, Käsermann F, Jakob S, Dimitrova P, Branch D, Cummings R, Lünemann J, Kaufmann T, Simon HU, von Gunten S: IVIG regulates the survival of human but not mouse neutrophils. *Sci. Rep.* 7 (2017), 1296. doi: 10.1038/s41598-017-01404-0
- Schwalm S, Beyer S, Frey H, Hacen R, Grammatikos G, Thomas D, Geisslinger G, Schaefer L, Huwiler A*, Pfeilschifter J* (*shared last authorship): Sphingosine Kinase-2 Deficiency Ameliorates Kidney Fibrosis by Up-Regulating Smad7 in a Mouse Model of Unilateral Ureteral Obstruction. *Am. J. Pathol.* 187 (2017), 2413-2429. doi: 10.1016/j.ajpath.2017.06.017. Epub 2017 Aug 12
- Stojkov D, Amini P, Oberson K, Sokollik C, Duppenhaler A, Simon HU, Yousefi S. ROS and glutathionylation balance cytoskeletal dynamics in neutrophil extracellular trap formation. *J Cell Biol.* 2017 Dec 4;216(12):4073-4090. doi: 10.1083/jcb.201611168. Epub 2017 Nov 17
- Radonjic-Hoesli S, Wang X, de Graauw E, Stoeckle C, Styp-Rekowska B, Hlushchuk R, Simon D, Spaeth PJ, Yousefi S, Simon HU. Adhesion-induced eosinophil cytolysis requires the receptor-interacting protein kinase 3 (RIPK3)-mixed lineage kinase-like (MLKL) signaling pathway, which is counterregulated by autophagy. *J Allergy Clin Immunol.* 2017 Dec;140(6):1632-1642. doi: 10.1016/j.jaci.2017.01.044. Epub 2017 Apr 12
- Reinhart R, Rohner L, Wicki S, Fux M, Kaufmann T. BH3 mimetics efficiently induce apoptosis in mouse basophils and mast cells. *Cell Death Differ.* 2018 Jan;25(1):204-216. doi: 10.1038/cdd.2017.154. Epub 2017 Sep 29

Institute of Physiology

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Prof. Thomas Nevia
Managing Director



Prof. Walter Senn
Codirector



Prof. Stephan Rohr
Codirector



Prof. Ernst Niggli
Codirector



Prof. Marcel Egger



Prof. Stéphane Cioocchi (SNF)



Prof. Jan Kucera



Prof. Jürg Streit

Research Partners

- Humboldt University, NeuroCure Cluster of Excellence, Berlin, Germany
- Brain Research Institute, University of Zürich, Zürich
- Brain Mind Institute, EPFL, Lausanne
- Department of Pharmacy and Drug Science, University of Bari Aldo Moro, Bari, Italy
- Soft Transducers Laboratory, EPFL Neuchâtel
- Microsystems Laboratory, EPFL, Lausanne
- Department of Neuroscience, Mount Sinai School of Medicine, New York, USA
- Center for Arrhythmia Research, University of Michigan, Ann Arbor, USA

Research Profile

The Department of Physiology performs basic preclinical research in cardiac- and neurophysiology. The five groups in cardiac physiology investigate pathological conditions that lead to heart failure and arrhythmias. They use electrophysiological and imaging techniques as well as computer simulations to elucidate the mechanisms of excitation-contraction coupling on the subcellular, cellular and organ level. In particular, two-photon uncaging combined with confocal microscopy is used to investigate the calcium dynamics in cardiomyocytes. Finally, the role of myofibroblasts in cardiac arrhythmogenesis is investigated using novel imaging techniques and optogenetic tools.

Six groups conduct research in neurophysiology. The common theme is to understand neuronal network dynamics in the brain in health and disease. Strategies to cure retina degeneration are devised as well as developing new treatment strategies for chronic pain or spinal cord regeneration. The formation of emotional memories, anxiety and depression are studied from single cells to neuronal networks with electrophysiological, two-photon imaging, optogenetics and behavioural approaches. A strong computational neuroscience group develops new theories about learning, memory and cognition.

Teaching Profile

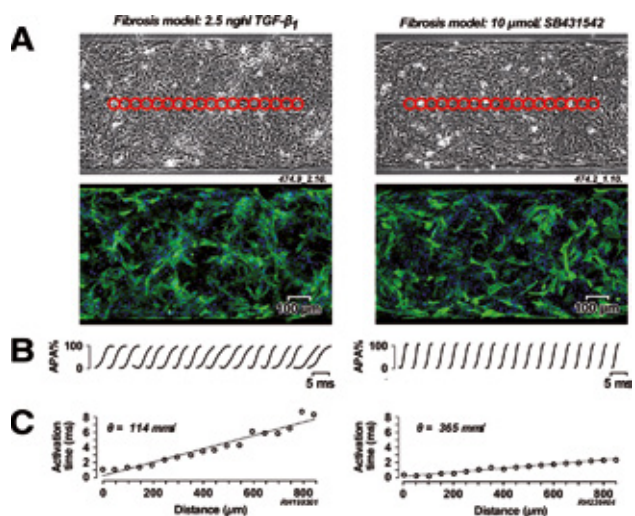
The Department of Physiology is predominantly engaged in the education of students of human and dental medicine (Bachelor, years 1 to 3). The Department is responsible for the entire field of physiology, covering all lectures and practical courses. We are also involved in interdisciplinary small group teaching in the framework of the problem based learning program (PBL) and we supervise medical as well as natural science master and PhD theses. Lecturers of our institute participate in the training of students in veterinary

medicine and pharmacy (Course in Basic Physiology, in German language). A similar course is also offered in English for the "Master in Biomedical Engineering" (BME) program. Our institute coordinates the master program in Biomedical Sciences (BMSc). We also contribute to the BeNeFri program in Neuroscience and to the Lecture Series on Advanced Microscopy organized by the Microscopy Imaging Center (MIC) of the University of Bern.

Highlights 2017

Salvarani et al. (2017) *TGF- β_1 (Transforming Growth Factor- β_1) Plays a Pivotal Role in Cardiac Myofibroblast Arrhythmogenicity*. *Circ Arrhythm Electrophysiol*, 10:e004567

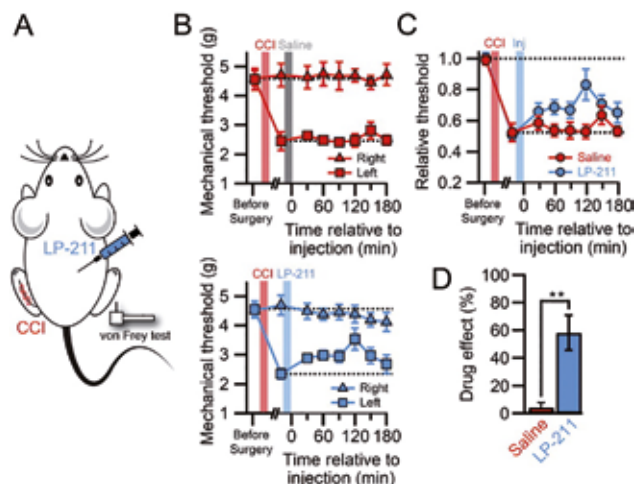
Myofibroblasts, the cells held responsible for excess deposition of extracellular matrix proteins during fibrotic remodeling of the heart, are capable of establishing heterocellular gap junctional contacts with cardiomyocytes ensuing electrotonic communication between these cells and resulting in ectopic electrical activations and a massive slowing of conduction in cardiac tissue, which, in combination, lead to reentrant activity, the most frequent cause of sudden cardiac death. In the present study, we found that the arrhythmogenic effect of cardiac myofibroblasts



(A) Phase contrast (upper) and immunofluorescence images (lower) of strands of cardiomyocyte strands coated with myofibroblasts (green) that were exposed to TGF- β_1 (left) or a blocker of TGF- β_1 receptors, SB431542 (right). (B) Optically recorded action potential upstrokes during impulse propagation from left to right. (C) The plots of activation time vs. distance indicate presence of very slow conduction in TGF- β_1 treated preparations (left) and normal conduction velocities when TGF- β_1 signaling was blocked with SB431542 (right).

on coupled cardiomyocytes is dependent in an all-or-none fashion on the presence of TGF- β_1 signaling leading to an arrhythmogenic remodeling of the ion channel repertoire of myofibroblasts and increases the strength of heterocellular gap coupling to cardiomyocytes. Thus TGF- β_1 may serve as a biomarker for hearts at risk for arrhythmias and pharmacological targeting of TGF- β_1 signaling may have a therapeutic benefit.

Santello et al. (2017) The brain-penetrant 5-HT7 receptor agonist LP-211 reduces the sensory and affective components of neuropathic pain. *Neurobiol Dis*, 106:214-221
Neuropathic pain is a debilitating pathological condition of high clinical relevance. Changes in neuronal excitability in the anterior cingulate cortex (ACC) play a central role in the negative emotional and affective aspects of chronic pain. We evaluated the effects of LP-211, a new serotonin receptor type 7 (5-HT₇R) agonist that crosses the blood-brain barrier, on ACC neurons in a mouse model of neuropathic pain. We could show that systemic treatment with this 5-HT₇R agonist leads to modulation of the ACC, which dampens sensory and affective aspects of chronic pain. Serotonergic neuromodulation in the brain might therefore present a new treatment strategy for neuropathic pain.

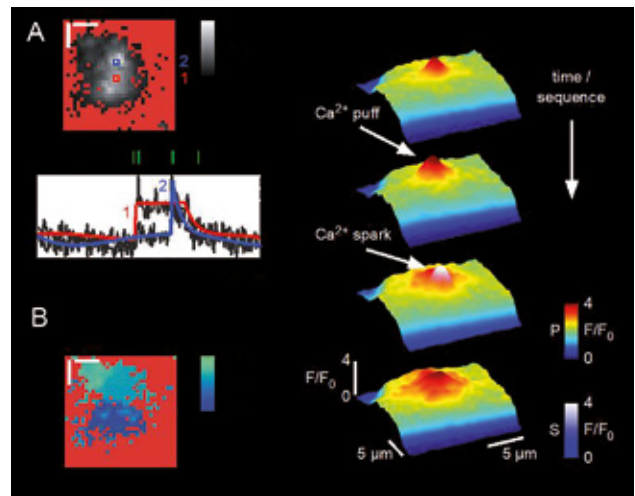


Systemic LP-211 administration is analgesic for neuropathic pain. (A) Experimental design for the i.p. injection of LP-211 or saline in CCI animals. (B) Time course of the mechanical withdrawal threshold of mice subjected to CCI surgery and then tested after saline (upper graph) or LP-211 injection (lower graph). (C) Withdrawal threshold of the injured paw normalized to the non-injured paw in saline (red) and LP-211 (blue) treated groups. D. Bar graph showing the drug effect of saline and LP-211 treated animals suggesting an analgesic effect of LP-211.

Wullschleger et al. (2017) Functional local crosstalk of inositol 1,4,5- trisphosphate receptor- and ryanodine receptor- dependent Ca²⁺ release in atrial cardiomyocytes. *Cardiovascular Res.*, 113: 542–552

In the heart, the leading mechanism of intracellular Ca²⁺ release is Ca²⁺-induced Ca²⁺ release (CICR) via sarcoplasmic reticulum (SR) release channels (ryanodine receptors, RyRs), which is a prerequisite for muscle contraction. A second mechanism, Ca²⁺ release through channels sensitive to the intracellular second messenger inositol-1,4,5-trisphosphate (InsP₃) has been described (IP₃ICR) that might be associated with several cardiac pathologies. We identified and characterized functional local crosstalk between cardiac Ca²⁺ release mechanisms identifying a bidirectional interaction

between RyRs and InsP₃Rs. In this way, local interaction of both SR-Ca²⁺ release channels may contribute to the shaping of global Ca²⁺ transients and thereby to contractility in cardiac myocytes.



(A) Local IP₃ICR with subsequently triggered Ca²⁺ sparks (CICR). The x-y-region of interest (ROI) shows an IP₃ICR event with an adjacent Ca²⁺ spark. The corresponding time courses of fluorescence are given. Below, red: Ca²⁺ puff, blue: Ca²⁺ spark, green marks (l) correspond to the surface plots shown in B. (B) Time-coded mapping of a ROI. The Ca²⁺ puff (dark blue area) occurred 584 ms after starting the sequence of interest. The Ca²⁺ spark (green area) followed after another 210 ms. Surface plot series of a Ca²⁺ puff triggering a Ca²⁺ spark.

Selected Competitive Grants

- ERC Consolidator Grant: Dissection of a cortical microcircuit for the processing of pain affect. (T. Nevia)
- ERC Starting Grant: Neuronal circuits for emotions in the ventral CA1 hippocampus. (S. Ciocchi)
- SNF Lead Agency Grant: Prospective coding with pyramidal neurons. (W. Senn)
- SNF Project Grant: Cardiac calcium signaling in health and disease: role of SR Ca²⁺ release and ryanodine receptor release channels (RyRs). (E. Niggli)
- SNF Project Grant: Structural and functional evidence for electrotonic coupling between stromal and parenchymal cells in the heart. (S. Rohr)

Selected Publications

- Salvarani N, Maguy A, De Simone SA, Miragoli M, Jousset F, Rohr S (2017) TGF- β_1 (Transforming Growth Factor- β_1) Plays a Pivotal Role in Cardiac Myofibroblast Arrhythmogenicity. *Circ Arrhythm Electrophysiol*, 10:e004567
- Santello M, Bisco A, Nevia NE, Lacivita E, Leopoldo M, Nevia T (2017) The brain-penetrant 5-HT7 receptor agonist LP-211 reduces the sensory and affective components of neuropathic pain. *Neurobiol Dis*, 106:214-221
- Van Wyk M, Hulliger EC, Girod L, Ebner A, Kleinlogel S (2017) Present molecular limitations of ON-bipolar cell targeted gene therapy. *Front Neurosci*, 11:161
- Wanz AL, Lobmaier JS, Mast FW, Senn W (2017) Spatial But Not Oculomotor Information Biases Perceptual Memory: Evidence From Face Perception and Cognitive Modeling. *Cognitive Science*, 41:1533–1554, 2017
- Wullschleger M, Blanch J, Egger M (2017) Functional local crosstalk of inositol 1,4,5-trisphosphate receptor- and ryanodine receptor-dependent Ca²⁺ release in atrial cardiomyocytes. *Cardiovasc Res*, 113: 542-552

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PD Dr. Christian Althaus



PD Dr. Julia Bohlius



Prof. Matthias Egger



Prof. Claudia Kuehni



Prof. Nicola Low



Prof. Stefan Reichenbach



Prof. Georgia Salanti



Dr. Adrian Spoerri



PD Dr. Ben Spycher



Brigitte Wanner



Prof. Marcel Zwahlen

Project Websites

- Esther Switzerland - Network for the Promotion of Institutional Health Partnerships
- leDEA-SA - International epidemiologic Databases to Evaluate AIDS
- MIWOCA - Migrant Women's Health Care Needs for Chronic Illness Services in Switzerland
- The Leicestershire & Rutland Cohort Studies
- STROBE - Strengthening the Reporting of Observational Studies in Epidemiology
- SCCR - Swiss Childhood Cancer Registry
- SHCS - Swiss HIV Cohort Study
- SNC - Swiss National Cohort
- SwissRDL - Medical Registries and Data Linkage
- TB-Network - Molecular and clinical epidemiology of tuberculosis in Switzerland

Research Profile

The Institute of Social and Preventive Medicine (ISPM) at the University of Bern carries out interdisciplinary research in the fields of social and behavioural health, clinical epidemiology and biostatistics, and international and environmental health with the aim of contributing to the promotion of health and prevention of disease and advancing and disseminating knowledge of health and disease in populations.

Teaching Profile

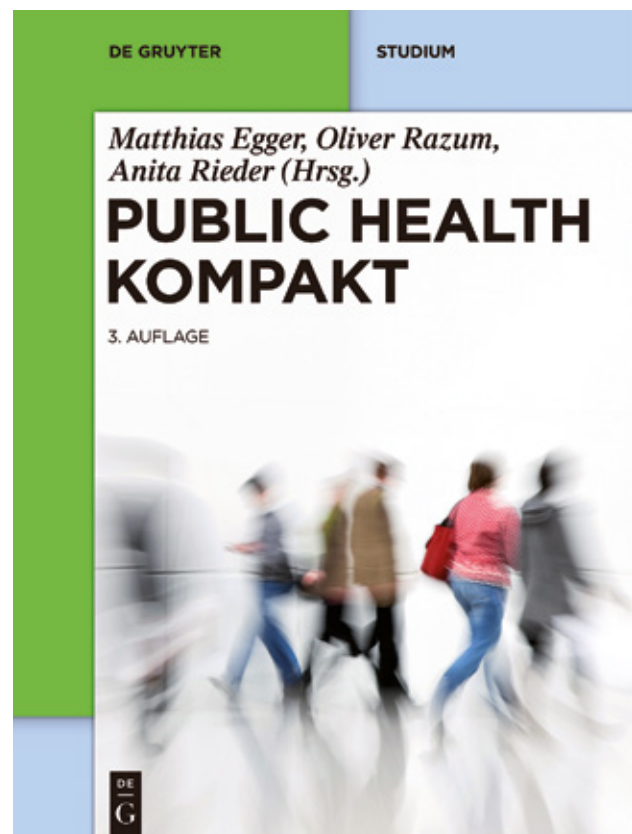
The institute participates in University teaching programs for students of medicine, biomedicine and biomedical engineering. We also teach students of biomedicine of the University of Fribourg. The institute is also teaching in PhD and post-graduate courses of the Swiss School of Public Health.

Highlights 2017

New version of Public Health Kompakt

The third edition of Public Health: A Compact Introduction to Social and Preventive Medicine (otherwise known as Public Health Kompakt) appeared in December 2017. The 525 page textbook provides basic information about public health, including prevention, health promotion, epidemiology, biostatistics, and healthcare systems. The new edition

has been updated and expanded to address issues such as the global approach to public health; migration and refugees; work and health; the aging of the population; and the "Life Course Approach to Health".



ISPM Claudia Kuehni to be first recipient of Ewald Weibel Prize for lung research

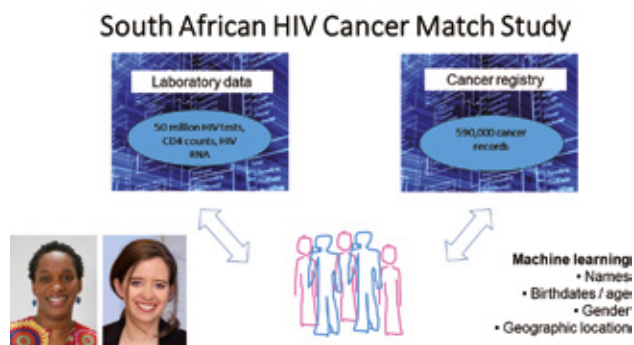
The Ewald Weibel Prize for lung research in Switzerland was awarded for the first time in 2017. The award was created in recognition of Ewald Rudolf Weibel, Professor Emeritus and former Director of the Anatomical Institute. The recipient is Claudia Kuehni of the University of Bern's Institute of Social and Preventive Medicine.

Kuehni received the prize in recognition of her “outstanding epidemiological and clinical work on lung disease in children,” particularly in the fields of lung development, childhood asthma, and primary ciliary dyskinesia, as well as for her contribution to the development of neonatal screenings for cystic fibrosis.



The South African HIV Cancer Match Study

The study uses machine-learning techniques to create a National Cohort of HIV-positive children in adults in South Africa based on routinely collected laboratory data. In a first step, more than 50 million laboratory records for HIV tests, CD4 and HIV RNA measurements are de-duplicated to create a cohort of 4 to 10 million individuals. In a second step, this cohort is linked to the National Cancer Registry in South Africa, to identify individuals who were diagnosed with cancer. South Africa has one of the highest HIV prevalences in the world and detailed epidemiological data are urgently needed to understand and monitor the cancer epidemic in this population. The study is done in collaboration with the National Cancer Registry in Johannesburg, South Africa, and the Institute of Social and Preventive Medicine, University of Bern, and funded by the US National Institutes of Health and the Swiss National Science Foundation.



Dr. Mazvita Sengayi (National Cancer Registry, Johannesburg) and PD Dr. Julia Bohlius (Institute of Social and Preventive Medicine, University of Bern) lead the South African HIV Cancer Match Study.

Tuberculosis mortality and living conditions in Bern, Switzerland, 1856-1950

ISPM research assistant Kathrin Zürcher received a special CHF 1,000 prize in March 2017 from the Swiss Foundation for Tuberculosis Research (swissTB) for her historical article looking at correlations between the tuberculosis mortality

rate and living conditions in the Swiss capital between 1856 and 1950. TB mortality in Bern, Switzerland, decreased 10-fold between 1856 and 1950, from 330 per 100,000 to 33 per 100,000. A number of factors are believed to have contributed to the massive decline.

The article, published in February 2016 by PLoS One, was based on historical documents from the city of Bern archives. Zürcher and co-authors found that more people living in an apartment, fewer windows, and less direct sunlight were associated with a higher mortality rate.

Selected Competitive Grants

- SNF (406940-145149, 320030-153442, 33CS30-148415, 323630-158120, 325130-160171, 32473B-160115, 32003B-160320, 32003B-162820, IZ07Z0-160909, 324730-163452, 32473B-160153, 320030-166656, 320030-170069, 320030-176233)
- Krebsforschung (KFS-3533-08-2014, KFS-3862-02-2016, KFS-4012-08-2016, KFS-4157-02-2017, KFS-4156-02-2017)
- EU: IMI Get Real (<http://www.imi-getreal.eu/>)
- NIH:leDEA-SA (since 2005)

Selected Publications

- Henao-Restrepo AM, Camacho A, Longini IM, Watson CH, Edmunds WJ, Egger M, Carroll MW, Dean NE, Diatta I, Doumbia M, Draguez B, Duraffour S, Enwere G, Grais R, Gunther S, Gsell PS, Hossmann S, Watle SV, Konde MK, Keita S, Kone S, Kuisma E, Levine MM, Mandal S, Mauget T, Norheim G, Riveros X, Soumah A, Trelle S, Vicari AS, Rottingen JA, Kiemy MP. Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ca Suffit!). *Lancet* 2017;389:505-518
- Krauer F, Riesen M, Reveiz L, Oladapo OT, Martinez-Vega R, Porgo TV, Haefliger A, Broutet NJ, Low N, Group WHOZCW. Zika Virus Infection as a Cause of Congenital Brain Abnormalities and Guillain-Barre Syndrome: Systematic Review. *PLoS Med* 2017;14:e1002203
- Leucht S, Leucht C, Huhn M, Chaimani A, Mavridis D, Helfer B, Samara M, Rabaioli M, Bacher S, Cipriani A, Geddes JR, Salanti G, Davis JM. Sixty Years of Placebo-Controlled Antipsychotic Drug Trials in Acute Schizophrenia: Systematic Review, Bayesian Meta-Analysis, and Meta-Regression of Efficacy Predictors. *Am J Psychiatry* 2017;174:927-942
- Solomkin J, Gastmeier P, Bischoff P, Latif A, Berenholtz S, Egger M, Allegranzi B. WHO Guidelines to prevent surgical site infections-Authors' reply. *Lancet Infect Dis* 2017;17:262-264
- Schindler M, Belle FN, Grotzer MA, von der Weid NX, Kuehni CE, Swiss Paediatric Oncology G. Childhood cancer survival in Switzerland (1976-2013): Time-trends and predictors. *Int J Cancer* 2017;140:62-74
- Panczak R, Luta X, Maessen M, Stuck AE, Berlin C, Schmidlin K, Reich O, von Wyl V, Goodman DC, Egger M, Zwahlen M, Clough-Gorr KM. Regional Variation of Cost of Care in the Last 12 Months of Life in Switzerland: Small-area Analysis Using Insurance Claims Data. *Med Care* 2017;55:155-163

Institute for Surgical Technology and Biomechanics

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Prof. Lutz
Nolte
Director



Prof. Philippe
Zysset
Deputy Director



Prof. Philippe
Büchler



Prof. Benjamin
Gantenbein



Prof. Mauricio
Reyes



Prof. Guoyan
Zheng

Research Partners

- Department of Orthopaedics and Traumatology, University Hospital of Bern, Bern, Switzerland
- Department of Neuroradiology, University Hospital of Bern, Bern, Switzerland
- Department of Orthopaedics and Traumatology, Lausanne University Hospital, Lausanne, Switzerland
- Institute for Biomechanics, Swiss Federal Institute of Technology Zürich, Zürich, Switzerland
- Laboratory for Mechanics of Materials, Swiss Federal Laboratories for Materials Science and Technology (EMPA), Thun, Switzerland
- Computer-Aided Medical Procedures & Augmented Reality, Technical University München, München, Germany
- Department of Orthopaedic Surgery, Surgical Science and Research Centre for Regenerative Medicine Tokai University School of Medicine, Isehara, Kanagawa, Japan
- Imaging-based Computational Biomedicine Lab, Nara Institute of Science and Technology, Nara, Japan
- Beckman Research Institute, City of Hope, California, USA
- Centre for Advanced Orthopaedic Studies, Harvard Medical School, Boston, USA

Research Profile

The ISTB emerged from the Maurice E. Müller Institute for Biomechanics founded in 1981. Five research groups contribute to the development of novel diagnostic and surgical technologies with an emphasis on the musculoskeletal system. Basic and applied research are conducted for the prevention or treatment of disease, working from the cell to organs. The focus is on developing solutions that address particular clinical problems or unmet clinical needs.

Tissue and organ mechano-biology aims at understanding cellular response to biomechanical stimuli and how cellular communities develop in 3D tissue and organ cultures. Medical image analysis employs image-based models to quantify and support the decision-making process of clinicians for diseases of the central nervous system. Computational bioengineering exploits modern simulation tools such as finite element analysis to resolve practical and fundamental clinical questions. Information processing in medical interventions involves pre-operative planning, intra-operative treatment and post-operative control of challenging surgeries such as peri-acetabular osteotomy or femoro-acetabular impingement treatment. Musculoskeletal biomechanics focuses on multi-scale structure-function relationships of bone tissue from the extra-cellular matrix to the organ level.

Together with ARTORG, the ISTB also manages a core facility in the form of a machine shop supporting construction and production of various parts for experimental set-ups in biomedical engineering.

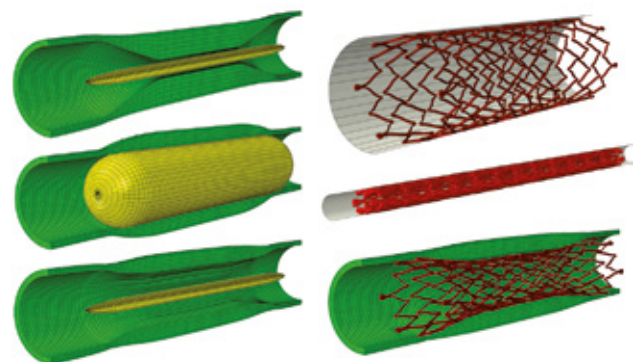
Teaching Profile

The institute coordinates the master program for biomedical engineering in cooperation with the Bernese university of applied sciences. Within this program, the researchers of ISTB contribute substantially to the basic modules as well as to the specialization modules in biomechanical systems and image guided therapy. Supervision of master and doctoral theses represents an important part of the teaching activity.

Highlights 2017

Finite element analysis of peripheral arterial disease

Oversizing of the stents in the peripheral arterial tract is commonly performed to ensure strong wall apposition and increased luminal gain. However, the effects of oversizing on the mechanical behaviour of diseased peripheral artery remains unclear. We developed finite element analyses of the revascularization of pathologic arteries having different plaque types. We found that balloon angioplasty heavily affects the outcome of endovascular therapy. In addition, stent oversizing produces only marginal lumen gain for a significant increase in arterial stresses. Moreover, for arteries with heavily calcified plaques, oversizing should be avoided as it leads to stresses close to the failure limit.



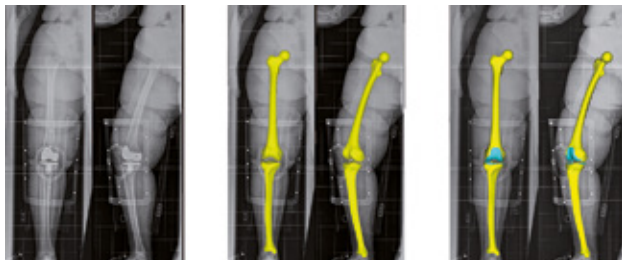
Human and machine intelligence for accurate and robust MRI-based brain lesion quantification

A novel technique for estimating uncertainty from automated MRI brain tumor segmentation was developed, enabling a streamline and time-effective monitoring of computer-generated results. The approach was combined with a novel

brain tumor segmentation technique, which was evaluated as part of the international Brain Tumor Segmentation (BRATS) Challenge, ranking among best approaches. By combining this information with novel time-effective human-machine interfaces, high-throughput quantification analysis of neuroimaging data can be analysed within the clinical workflow.

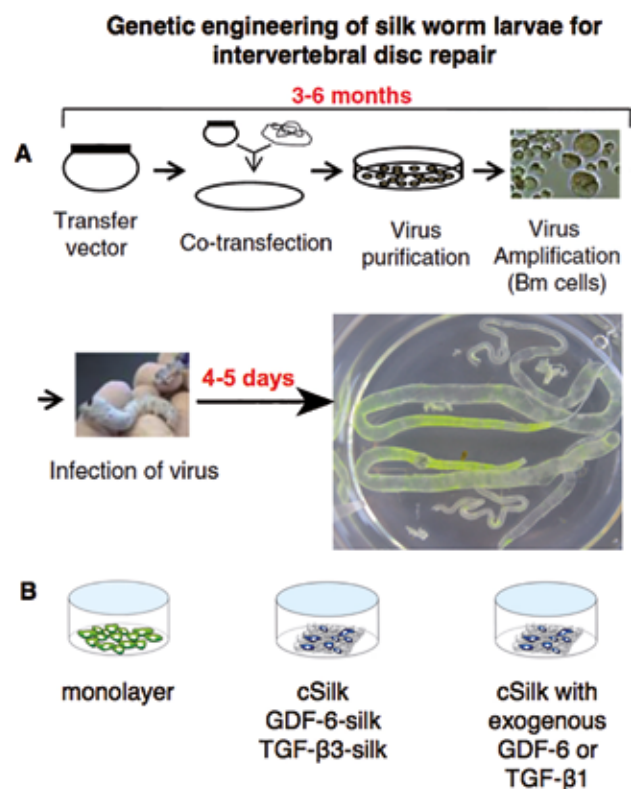
A novel technology for 3D planning and treatment evaluation of total knee arthroplasty (TKA) using 2D X-ray radiographs

We developed a novel solution to derive 3D models of musculoskeletal structures from 2D X-ray images. We then created a software to use the derived 3D models for 3D planning and treatment evaluation of TKA. Validated on 43 patients from two different clinical centres, in over 70% cases the new technology derived the same implant size as CT-based ground truth and average angular errors were all smaller than 1.5°. The 2D-3D reconstruction-based solution is a novel, accurate and cost-effective technology for planning and treatment evolution of TKA.



Silk Engineering and “Fishing” of Tissue-specific Progenitor cells for the Intervertebral Disc

The TOM group successfully completed and reported novel results of a tissue engineering study using a combined biomaterials approach using genetically-engineered silk and



fibrin hydrogel for intervertebral disc repair in organ culture (DOI: 10.1002/jor.23778). Further, the group reported on the identification of tissue-specific progenitor cells positive for the endothelial marker angiopoietin receptor-1 of the intervertebral disc in a bovine animal model (DOI: 10.1186/s13287-016-0337-9). These progenitor cell population could be targeted as a cell source for regenerative therapy. Finally, molecular investigations are ongoing to improve non-unions in spinal fusion.

Finite element analysis based on HR-pQCT for the assessment of wrist strength

A fast patient-specific estimation of wrist strength was developed using homogenized finite element (hFE) analysis based on high-resolution peripheral computed tomography (HR-pQCT). Fresh frozen forearms were scanned by HR-pQCT and tested under compression up to failure. A software was created to process the HR-pQCT images and generate an FE model of the wrist. The strength calculated from the hFE analyses correlated strongly with the experimental one ($r^2=0.96$) and showed a reproducibility below 2.2%. The hFE method represents a fast and accurate diagnostic tool to identify individuals at risk of wrist fracture.

Selected Competitive Grants

- Swiss National Science Foundation (grant no 200021_165510; 320030_173130; 205321_157207; 205321_163224; 205321_169607; 320030L_163363)
- CTI (grant no 18193.1 PFLS-LS; 27450.1 PFLS-LS; T-2017-023)
- Swiss Cancer League (grant no KFS-3979-08-2016)
- HansJörg Wyss Medical
- Horizon 2020 - Marie Skłodowska-Curie Global Fellowship (grant no 753878, GlimS)

Selected Publications

- Gökgöl Can, Diehm Nicolas, Büchler Philippe: Numerical Modeling of Nitinol Stent Oversizing in Arteries with Clinically Relevant Levels of Peripheral Arterial Disease: The Influence of Plaque Type on the Outcomes of Endovascular Therapy. *Ann. Biomed. Eng.* (2017), 45(6):1420-1433
- Frauchiger Daniela, Heeb Silvan, May Rahel, Wöltje Michael, Benneker Lorin, Gantenbein Benjamin: Differentiation of MSC and annulus fibrosus cells on genetically-engineered silk fleece-membrane-composites enriched for GDF-6 or TGF-β3. *J. Orthop. Res.* (2017), in press
- Meier Raphael, Porz Nicole, Knecht Urs peter, Loosli Tina, Schucht Philippe, Beck Jurgen, Slotboom Johannes, Wiest Roland, and Reyes Mauricio: Automatic estimation of extent of resection and residual tumor volume of patients with glioblastoma. *J. Neurosurg.* (2017), 127(4):798-806
- Weimin Yu, Moritz Tannast, Guoyan Zheng: Non-rigid free-form 2D-3D registration using a B-spline-based statistical deformation model. *Pattern Recognit.* (2017), 63:689 – 699
- Hosseini Hadi, Dünki Andreas, Fabech Jonas, Stauber Martin, Vilayphiou Nicolas, Pretterklieber Michael, Pahr Dieter, Van Rietbergen Bert and Zysset Philippe: Fast estimation of Colle’s fracture load of the distal radius by non-linear finite element analysis based on high resolution peripheral computed tomography. *Bone* (2017), 97:65-75

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**Research Group Leader and Head of the Transgenic Mouse and Cryoconservation Unit

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- Institute for Research in Biomedicine, Bellinzona, Switzerland
- Department of Pathology and Immunology, University Hospital Geneva, Geneva, Switzerland
- Centre de Physiopathologie de Toulouse-Purpan, INSERM UMR1043, Toulouse, France
- Center for Genome Research, Barcelona, Spain
- Kennedy Institute of Rheumatology, University of Oxford, UK
- Integrated Cardio Metabolic Centre, Karolinska Institutet, Huddinge, Sweden
- Centre de Recherche, Laboratoire de la barrière hémato-encéphalique, Université d'Artois, Lens, France
- Department of Biomedical Engineering, University of Rochester Medical Center, NY, USA

Research Profile

Founding of the TKI in 1950 was made possible by a donation of the Bernese Nobel laureate Theodor Kocher in 1912. Current research at the TKI is dedicated to investigate cellular and molecular mechanisms involved in inflammation. A special focus hereby lies on immune cell migration during immune surveillance and inflammation employing cutting-edge 3D *in vitro* and *in vivo* live cell imaging methodologies and targeted transgenic models. Ongoing research projects address for example how and where activated immune cells enter the immune privileged central nervous system (CNS) during neuroinflammatory diseases such as multiple sclerosis and stroke, or how immune cell subsets interact within the lymph node to mount an immune response or how tumor cells cross the blood-brain barrier forming brain metastases. Additional projects on the role of innate immunity in inflammation complement this portfolio. Knowledge on the migration strategies employed by different immune cell subsets will allow to improve immunomodulatory therapies for numerous diseases. Research competence at the TKI allows for the coordination of the Microscopy Imaging Center (MIC, www.mic.unibe.ch) and the heading of the Mouse Cryoconservation and Mouse Transgenic and Genetic

Engineering Facility, a member of the transgenesis platform of the Swiss Animal Facilities Network (SAFN).

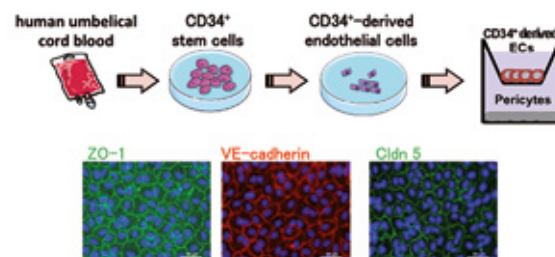
Teaching Profile

The TKI is involved in local, national and international teaching efforts. The institute offers a large portfolio of lectures and practical classes in immunology, microscopy, vascular cell biology, transgenic mouse technologies, inflammation and high end *in vitro* and *in vivo* live cell imaging for bachelor, master and graduate students in the Medical, Science and Vetsuisse Faculties. The institute is furthermore involved in teaching of students of medicine and biomedicine of the University of Fribourg. The TKI hosts the two interfaculty Graduate Schools (Graduate School for Cellular and Biomedical Sciences (www.gcb.unibe.ch) & Graduate School for Health Sciences (www.ghs.unibe.ch)). In addition, coordination of the Swissuniversities supported PhD programs "Cell Migration" and "Cutting Edge Microscopy" are localized at the TKI. Britta Engelhardt is coordinator of the Horizon2020 funded international PhD student training program BtRAIN (www.btrain-2020.eu).

Highlights 2017

*Modelling the multi-step migration of human T-cell subsets across *in vitro* models of the human blood-brain barrier and blood-cerebrospinal fluid barrier*

Molecular mechanisms mediating T-cell migration into the CNS in multiple sclerosis (MS) have largely been studied in animal models, which do not mimic the full picture of

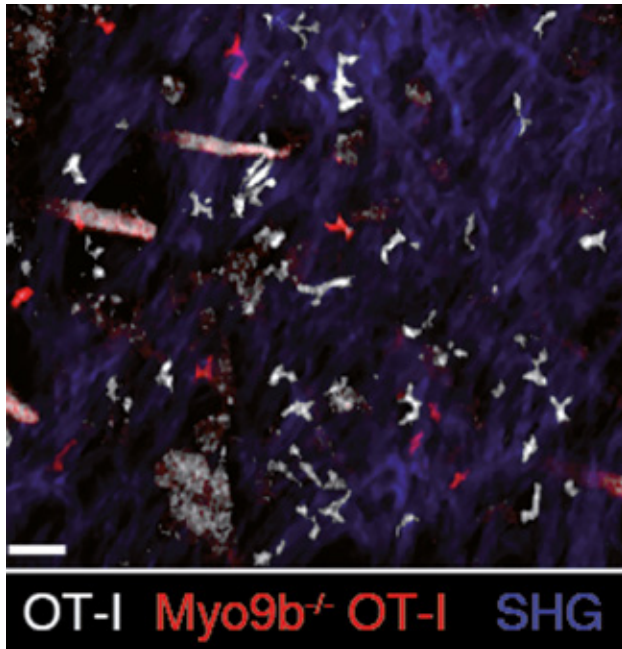


Human *in vitro* models of the BBB and BCSFB. CD34⁺ stem cells are sorted from umbilical cord blood and *in vitro* differentiated into endothelial cells (ECs). CD34⁺ derived ECs are then co-cultured with bovine pericytes to acquire BBB characteristics. Immunofluorescence stainings show junctional localization of ZO-1, claudin-3 and VE-cadherin by the brain like ECs.

MS neuropathology. In a collaborative approach, we have established novel *in vitro* models of the human blood-brain barrier (BBB) and blood-cerebrospinal fluid barrier (BCSFB), allowing us to side by side compare the cellular and molecular mechanisms involved in the migration of human CD4⁺ T cell-subsets across these two brain barriers. We have furthermore established a novel nanomembrane based microfluidic device with unique optical characteristics and a very small scale, now allowing to study the extravasation of rare patient derived T-cell subsets across the BBB under physiological flow *in vitro*.

The Rho regulator Myo9b enables non-lymphoid tissue seeding of protective CD8⁺ T cells

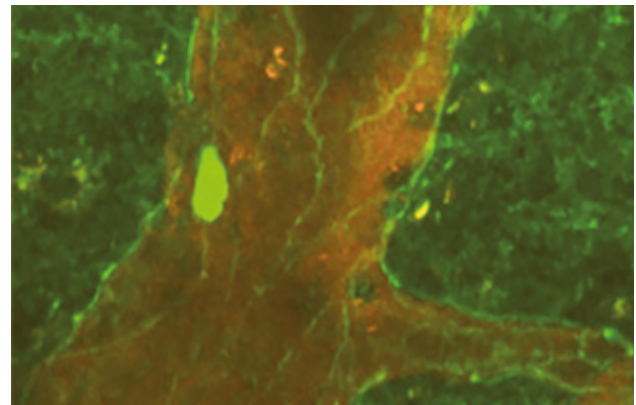
Tissue-resident memory T cells (T_{RM}) populate barrier organs such as skin, but their behavior in these exposed organs is not well understood. Using intravital imaging of cellular motility and interactions in LNs and skin, we noted that TCR-transgenic OT-I CD8⁺ T cells deficient in the actomyosin regulator Myo9b were defective in their ability to cross the basement membrane separating dermis from epidermis. This results in blunted capacity of Myo9b-deficient T_{RM} to protect the host from a local viral infection.



Intravital imaging image of dsRed-expressing OT-I (white) and GFP-expressing Myo9b-deficient OT-I T cells (red) in skin on day 30 post viral infection. SHG, second harmonic generation indicating collagen. Scale bar, 30 μm.

Two-Photon imaging of T-cell interactions with the cervical spinal cord microvasculature during neuroinflammation in vivo.

Two-photon intravital microscopy (2P-IVM) has been established as a powerful tool to study cell-cell interactions in the animal model of multiple sclerosis, experimental autoimmune encephalomyelitis (EAE). We established a novel spinal cord window preparation allowing to use 2P-IVM to image the post-arrest multistep T-cell extravasation across the cervical spinal cord microvessels. The technology will allow to study the cellular pathway of T-cell diapedesis across the BBB by establishing visualization of endothelial junctions in this vascular bed.



Visualizing junctions of the blood-brain barrier endothelium in VE-cadherin-GFP knock-in mice with experimental autoimmune encephalomyelitis (EAE). An autoaggressive CD4⁺ T cell (green) can be seen crawling along the junction of the spinal cord microvessel. Endothelial junctions are visible as green lines in VE-cadherin-GFP knock-in mice. Contrast enhancement of the blood vessels was achieved by injection of Texas Red-dextran (MW = 70,000).

Selected Competitive Grants

- Swiss National Science Foundation (31003A_17013, CRSII3_154483, 31003A_172994, 16CRSII5_170969, CR23I3_156234, 310030_173137)
- European Union: (FP7 MCA-ITN 607962nEUROinflammation; H2020-MSCA-ITN-2015 675619)
- State Secretary for Education, Research and Innovation (Eurostars Project E!9059 SIAGEN-MS)
- Swiss Multiple Sclerosis Society
- Swiss Cancer League (KFS-3524-08-2014)

Selected Publications

(*corresponding author if not senior author)

- Ackerknecht, M, Gollmer K, Germann P, Ficht X, Abe J, Fukui Y, Swoger J, Ripoll J, Sharpe J, Stein JV. 2017. Antigen availability and DOCK2-driven motility govern CD4⁺ T cell interactions with dendritic cells in vivo. *J Immunol.* Jul 15;199(2):520-530
- Haghayegh Jahromi N, Tardent H, Enzmann G, Deutsch U, Kawakami N, Bittner S, Vestweber D, Zipp F, Stein JV, Engelhardt B. 2017. A Novel Cervical Spinal Cord Window Preparation Allows for Two-Photon Imaging of T-Cell Interactions with the Cervical Spinal Cord Microvasculature during Experimental Autoimmune Encephalomyelitis. *Front Immunol.* 2017 Apr 11; 8:406. doi: 10.3389/fimmu.2017.00406. eCollection 2017
- Moore TL, Hauser D, Gruber T, Rothen-Rutishauser B, Lattuada M, Petri-Fink A, Lyck R. Cellular Shuttles: Monocytes/Macrophages Exhibit Transendothelial Transport of Nanoparticles under Physiological Flow. *ACS Appl Mater Interfaces* 2017, 9 (22): 18501-18511
- Lyck R*, Lécuyer MA, Abadier M, Wyss C, Matti C, Rosito M, Enzmann G, Zeis T, Michel L, Garcia A, Sallusto F, Gosselet F, Deutsch U, Weiner JA, Schaeren-Wiemers N, Prat A, Engelhardt B. 2017. ALCAM (CD166) is involved in extravasation of monocytes rather than T cells across the blood-brain barrier. *J Cereb Blood Flow Metab.* 37(8):2894-2909
- Uster S, Matos Coelho F, Aeberli D, V Stein J, Hofstetter W, Engelhardt B*, Seitz M. 2017. TNF-α blockade mediates bone protection in antigen - induced arthritis by reducing osteoclast precursor supply. *Bone* 107:56-65

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- Environmental Microbiology Laboratory, EPFL, Lausanne, Switzerland
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- Institutes of Veterinary Bacteriology, of Virology and Immunology, and of Parasitology, Department of Infectious Diseases and Pathobiology, Vetsuisse Faculty, University of Bern
- Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, South Africa
- Cluster for Regenerative Neuroscience, Department for Biomedical Research, University of Bern

Research Profile

The Institute for Infectious Diseases (IFIK) is the only University Institute in Switzerland that covers the entire spectrum of microbiology, including virology, bacteriology, mycology, parasitology, molecular diagnostic and infection serology integrated in comprehensive diagnostic services, research, and education. The IFIK provides diagnostic services recognized by Swissmedic and accredited according ISO/IEC 17025, (STS 0363) for patient care in public hospitals including the Insel group, the largest hospital group in Switzerland. The IFIK is home to the Swiss National Reference Centre for Pneumococci and to the Swiss National Centre for Antibiotic Resistance (anresis.ch) mandated by the Federal Office of Public Health.

The 3 major research focuses at the IFIK are antimicrobial resistance, infections of the central nervous system, and host-microbiome interactions in infections of the intestine and airways.

The IFIK has put a focus on the development of novel highly parallel sequencing technologies for microbiome research and future diagnostic applications. As part of this initiative the IFIK offers next-generation sequencing (nanopore sequencing) as a research and diagnostics service.

Specific research topics of the IFIK include:

- Characterization of novel and emerging antimicrobial resistance genes along with their mobile genetic elements (e.g., plasmids)
- Antibiotic resistance detection by novel and rapid molecular methods
- One-Health approach to study origins and spread of multidrug-resistant Gram-negative bacteria among humans, animals, environment and food chain
- Pathophysiology and therapy of central nervous infections and related neurofunctional sequelae.
- Role of microbiota in gut and airway infection
- Bacteria-bacteria communication: *S. pneumoniae* sensing of co-colonizing bacteria
- Streptococcal infection biology and biofilm formation
- Synthetic biology for next-generation intestinal microbial therapy and preventive medicine

Teaching Profile

The IFIK provides a broad spectrum of teaching programs for students of human medicine, dental medicine, pharmacology, biomedical sciences and biology. The IFIK accepts applications for master and MD and PhD doctoral theses and research postdoc fellowships. Our Institute is actively engaged in the FAMH postgraduate training in Clinical Microbiology. This 4 year training is open to medical doctors (MD), to biologists with a PhD in science as well as to Doctors of pharmacy. During this 4-year training program candidates will rotate through the different diagnostic laboratories of IFIK.

IFIK is part of the HONOURS consortium, an EU-financed Marie Skłodowska-Curie Action training network on host switching pathogens, infectious outbreaks and zoonosis. The objective is to train early stage researchers in all aspects of infectious outbreaks. The consortium consists of 10 high profile universities, research institutions and companies

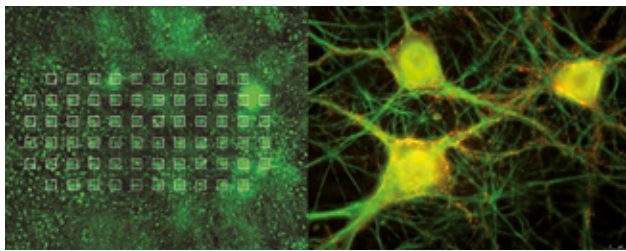
located in Belgium, Germany, the Netherlands, Spain, Switzerland and the United Kingdom.

Highlights 2017

Three IFIK research groups, were awarded with the first Interfaculty Research Cooperation (IRC) grants of the University of Bern for the projects “One Health: Cascading and Microbiome-Dependent Effects on Multitrophic Health” and “Decoding Sleep: From Neurons to Health & Mind” respectively.

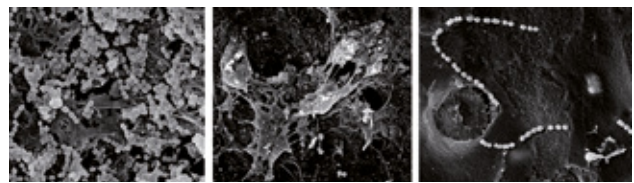
Together with the Departments of Intensive Care and Infectious Diseases of the University Hospital of Bern, the IFIK is involved in the project “Personalized Swiss Sepsis Study (PSSS)” by the new Swiss Personalized Health Network (SPHN) initiative. The objective of this project is personalised diagnosis and treatment in the case of life-threatening sepsis. Further research highlights from the IFIK include:

- Development of an *in-vitro* stem cell-based bioassay grown on micro-electrode arrays enabling the live recording of the biological activity of *Clostridium botulinum* neurotoxins. This novel neuron-on-electrode-chip may help replace animal testing for neurotoxin detection and provides a physiological relevant platform for drug-screening of neuroactive compounds.



Cultivated neurons in green on a multi-electrode array forming a functional network (left panel). Each electrode is outlined and highlighted by a white square. A magnification showing a neuronal culture (right panel). Visible in green are neurons. The yellow and red dots show the localization of the SV2 receptor that is used by the botulinum neurotoxins for the uptake into the neurons.

- First demonstration of direct RNA sequencing from patient stool samples of complete RNA *Enterovirus* genome via nanopore sequencing.
- Development of a rapid real-time PCR to directly detect colistin resistance in the stool samples.
- Development of a complete resistome analysis pipeline for multidrug resistant bacterial strains from sample processing, sequencing, to bioinformatic analyses for the rapid diagnosis and informed therapy of multiresistant bacterial infection.
- IFIK researchers reveal the interplay between pneumococcal conjugate vaccines and nasopharyngeal microbiota using next-generation sequencing.
- Demonstration that cocktails of bacteriophages can be implemented against MDR bacteria.
- IFIK researchers are collaborating with South African researchers to study pneumococci from meningitis patients.
- Identification of a bacterial peptide recognition mechanism in *Streptococcus pneumoniae* that detects and reacts to co-colonizing bacterial species of the nasopharynx.
- A bedside-to-bench approach reveals that adjunctive gentamicin treatment, postulated to synergize with penicillin, against group B *Streptococcus* is clinically not relevant. This work can help reduce polypharmacy issues in antibiotic therapy.



Scanning electron microscopy of Group B *Streptococcus* biofilm (left panel). Penicillin alone reduces biofilm (middle panel). The combination of penicillin plus local high-dose gentamicin retransforms bacteria from biofilm to planktonic phase (right panel). (images: C. Ruppen, IFIK)

Selected Competitive Grants

- Interfaculty Research Cooperations: One Health: Cascading and Microbiome-Dependent Effects on Multitrophic Health (CHF 1'073'000 A. Ramette, S. Hapfelmeier)
- European Union Horizon 2020 Grant agreement No 721367. Marie Skłodowska-Curie Action (MSCA) training network on host switching pathogens, infectious outbreaks and zoonosis (HONOURS) (Total: CHF 3 740 000; IFIK: CHF 260 000, S. Leib)
- SNF Swiss-South Africa Joint Research Programme grant 170844: Virulence of pneumococcal serotypes in human meningitis (CHF 349'900, S. Leib, L. Hathaway)
- SNF 169791: In-vivo study of protective intestinal long-term colonization with microbiota-syntrophic strains of *Salmonella typhimurium* and *Citrobacter rodentium* (CHF 370'000, S. Hapfelmeier)
- SNF Sinergia; 160780; Viral Plasticity Underlying Tropism And Pathogenesis/ Innate Immune Evasion Of Emerging Viruses (CHF 1'846'550.- to the consortium of Vetsuisse Faculty and IFIK, University of Bern, Spiez Laboratory and Faculté de Biologie et Médecine Université de Lausanne)

Selected Publications

- Donà V, Bernasconi OJ, Pires J, Collaud A, Overesch G, Ramette A, Perreten V, Endimiani A. Heterogeneous Genetic Location of *mcr-1* in Colistin-Resistant *Escherichia coli* Isolates from Humans and Retail Chicken Meat in Switzerland: Emergence of *mcr-1*-Carrying IncK2 Plasmids. *Antimicrob Agents Chemother.* 2017 Oct 24;61(11)
- Influence of the pneumococcal conjugate vaccines on the temporal variation of pneumococcal carriage and the nasal microbiota in healthy infants: a longitudinal analysis of a case-control study. Mika M, Maurer J, Korten I, Allemann A, Aebi S, Brugger SD, Qi W, Frey U, Latzin P, Hilty M. *Microbiome.* 2017 Jul 24;5(1):85
- Buschor, S., Cuenca, M., Uster, S. S., Schären, O. P., Balmer, M. L., Terrazos, M. A., Schürch CM, Hapfelmeier S. (2017). Innate immunity restricts *Citrobacter rodentium* A/E pathogenesis initiation to an early window of opportunity. *PLoS Pathogens*, 13(6), e1006476. <http://doi.org/10.1371/journal.ppat.1006476>
- Jenkinson SP, Grandgirard D, Heidemann M, Tschertler A, Avondet MA, Leib SL. Embryonic Stem Cell-Derived Neurons Grown on Multi-Electrode Arrays as a Novel In vitro Bioassay for the Detection of *Clostridium botulinum* Neurotoxins. *Front Pharmacol.* 2017 Feb 23;8:73. doi: 10.3389/fphar.2017.00073. eCollection 2017. PubMed PMID: 28280466; PubMed Central PMCID: PMC5322221
- Sendi P, El Hay MA, Brandt CM, Spellerberg B. Group B *Streptococcal* Toxic Shock Syndrome and *covR/S* Mutations Revisited. *Emerg Infect Dis.* 2017 Jan;23(1):150-152

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- Radboud University, Nijmegen, Netherlands
- ARTORG Center for Biomedical Engineering Research, University of Bern, Switzerland
- Institute of Pathology, University Hospital Basel, Basel, Switzerland
- Helmholtz Zentrum Neuherberg, Germany
- Australian pancreatic genome initiative (APGI) Garvan Institute, Sydney, Australia
- Department of Neurology, School of Medicine, Stanford University, CA, USA
- Department of Immunology and Microbiology, The Scripps Research Institute, La Jolla, CA, USA
- Institute of Medical Microbiology, University Hospital Essen, University Duisburg-Essen, Essen, Germany
- Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, USA

Research Profile

In addition to its diagnostic service, the Institute of Pathology is active in clinical, translational and basic science. Pathologists and researchers focus on the areas of tumor immunology, inflammation, autophagy as well as on prognostic/predictive biomarkers and molecular pathogenesis of various tumor types. In the Division of Experimental Pathology at present seven independent research groups address questions related to the etiopathogenesis of neoplastic or inflammatory disorders, but also to the identification of novel biomarkers in inflammatory disorders and to the development of vaccination strategies against solid tumors. The research of clinical pathologists contributes to WHO classifications, clinical guidelines and improved histopathological diagnostics. Furthermore, the Translational Research Unit (TRU) manages services of the Tissue Bank Bern (TBB) and supports tissue-based research by providing histology, tissue visualization, tissue microarraying and digital pathology expertise.

Teaching Profile

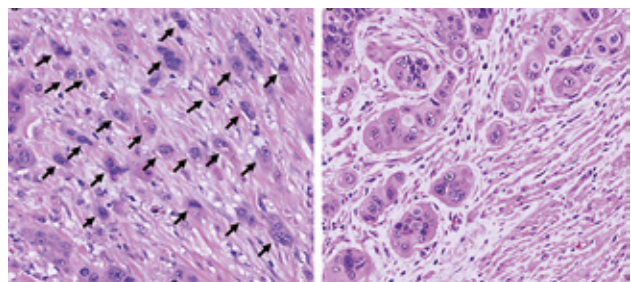
The Institute of Pathology is active in teaching across different faculties and departments at the University of Bern, including the disciplines of Medicine, Cell Biology, Biomedical Sciences, and Bioinformatics, and participates with standard lectures, Problem Based Learning tutorials and workshops. The Institute hosts 10-15 new Medical Master students per year as well as numerous MSc (Cell Biology), and PhD

students under the umbrella of the Graduate School of Cellular and Biomedical Sciences, University of Bern.

Highlights 2017

Tumor Budding

Tumor budding (BD) is a histological feature defined by the presence of single cells or small tumor cell clusters detached from the invasion front in colorectal cancer. Our hypothesis is that these cells undergo partial epithelial-mesenchymal transition (EMT) and show characteristics of stemness. Despite strong evidence for the importance of this feature, its integration into routine diagnostics was still missing, the reason being the lack of consensus regarding clinical scenarios, scoring and reporting of this feature. In 2016, the International Tumour Budding Consensus Conference (ITBCC) took place in Bern, Switzerland and gathered worldwide experts to discuss this topic. Agreement on an evidence-based, standardized method for BD for routine practice was achieved. In addition to guidelines published this year, BD is now included as an additional prognostic factor in the UICC's TNM classification and in the latest CAP guidelines.

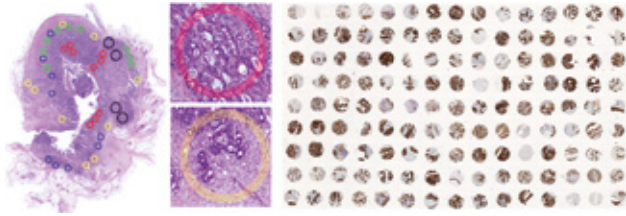


Example of (left) tumor budding and (right) poorly differentiated clusters defined as five tumor cells or more (Lugli et al. Mod Pathol, 2017).

Digital Pathology

The Translational Research Unit (TRU) is developing digital pathology on four fronts. Since the establishment of the next-generation Tissue Microarray (ngTMA[®]) platform in 2012, approx. 12'000 patients are included onto tissue microarrays. Tissue cores come from annotated digital scans that allow researchers to select histological areas for further downstream analysis. Moreover, TRU has collaborated on more than 20 image analysis projects and has trained medical and biology students to use digital algorithms. TRU is running its first neural network classifier project with the aim of future diagnostic application. Following a public call for

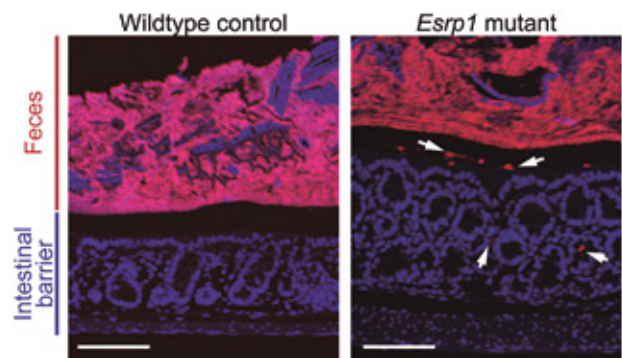
tender, a research database to manage patient cohorts and digital scans, including ngTMAs has been selected and will serve as a central repository for research results. In addition, diagnostic scanner and image management systems are being tested for future implementation. Already now, our diagnostic slide sharing experience has begun, with experts from around the world accessing scans for second opinions.



Digital scan annotated with a tool allowing precise histological areas to be selected for capture and construction of ngTMA[®].

Experimental Pathology: The ESRP1-GPR137 axis contributes to intestinal pathogenesis

The intestinal lining – a one cell-thick barrier – is often disrupted during intestinal diseases, causing gut leakiness. Intestinal epithelial cells make up the lining of the intestine and the normal activity of these cells is disturbed during inflammatory diseases. In the intestine, the protein ESRP1 is only found in epithelial cells, but its function in the epithelial barrier was unclear. We now showed that attenuated ESRP1 activity in mutant mice worsen the course of intestinal diseases. Patients with inflammatory bowel diseases or intestinal cancer show reduced ESRP1 activity, and therefore also of GPR137, which is directly controlled by ESRP1. Reduced functions of GPR137 weaken the intestinal barrier. Hence, ESRP1 or GPR137 activity positively correlates with the survival of patients with intestinal cancer.



Bacteria (white arrows) penetrate the leaky intestinal barrier of *Esp1* mutant mice. Scale bars: 100 μ m.

Selected Competitive Grants

- Swiss National Science Foundation (grant No. 310030_170084, CRSII3_154414, 33CS30_148422, 310030_152872, 314730_163086, PA00P3_136468, 320030_176083, 31003A_173219, 31003A_175656)
- Peter Hans Hofschneider - Stiftung für Experimentelle Biomedizin
- Free Novation (Novartis)
- Swiss Cancer Research/Swiss Cancer League (KLS-3408-02-2014, KFS-3409-02-2014, KFS 4162-02-2017-R, KLS-4227-08-2017)

Selected Publications

- Lugli A, et al. Recommendations for reporting tumor budding in colorectal cancer based on the International Tumor Budding Consensus Conference (ITBCC) 2016. *Mod Pathol.* 2017 Sep;30(9):1299-1311
- Mager LF, et al. The ESRP1-GPR137 axis contributes to intestinal pathogenesis. *Elife.* 2017 Oct 4;6
- Keller CW, et al. The autophagy machinery restrains iNKT cell activation through CD1D1 internalization. *Autophagy.* 2017 Jun 3;13(6):1025-1036
- Haimovici A, et al. PU.1 supports TRAIL-induced cell death by inhibiting NF- κ B-mediated cell survival and inducing DR5 expression. *Cell Death Differ.* 2017 May;24(5):866-877
- Hussain M, et al. Basophil-derived interleukin-4 promotes epicutaneous antigen sensitization concomitant with the development of food allergy. *Journal of Allergy and Clinical Immunology,* 2017 Apr 5. S0091-6749(17)30566-3

Institute of Forensic Medicine

Bühlstrasse 20
3012 Bern



Prof. Christian Jackowski
Director



Prof. Wolfgang Weinmann
Deputy Director
Forensic Toxicology and Chemistry



Dr. Sandra Lösch
Physical Anthropology



PD Dr. Christian Schyma
Forensic Medicine and Imaging



Dr. Silvia Utz
Forensic Molecular Biology



Prof. Michael Liebreuz
Forensic Psychiatric Services



Matthieu Glardon
Forensic Physics and Ballistics



PD Dr. Dr. iur. Antoine Roggo
Medical Law



Dr. Matthias Pfäffli
Traffic Medicine

Research Partners

- Institute of Legal Medicine, University of Bonn, Germany
- Institute of Legal Medicine, University of Schleswig-Holstein Kiel, Kiel, Germany
- Center for Medical Image Science and Visualization, CMIV, Linköping University, Linköping, Sweden
- Department of Diagnostic, Interventional and Pediatric Radiology, Hospital and University of Bern Inselspital, Switzerland
- Institute of Forensic Medicine, University Medical Center Freiburg, Germany
- Department of Chemistry and Biochemistry, University of Bern, Switzerland
- Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital, University of Zürich, Switzerland
- Department of Prehistory, Institute of Archaeological Sciences, University of Bern, Switzerland
- Laboratory of Soil Biodiversity, University of Neuchâtel, Neuchâtel, Switzerland
- Netherlands Forensic Institute, Den Haag, The Netherlands

Research Profile

The Institute of Forensic Medicine consists of eight departments. Each department conducts research projects within the context of forensic sciences. The department of Forensic Medicine and Imaging, the department of Forensic Toxicology and Chemistry and the department of Physical Anthropology received external fundings. The Institute of Forensic Medicine in Bern is world leading in forensic physics and ballistics, forensic imaging and alcohol consumption markers. Furthermore, forensic psychiatric projects, forensic genetics projects and traffic medicine projects have been successfully performed.

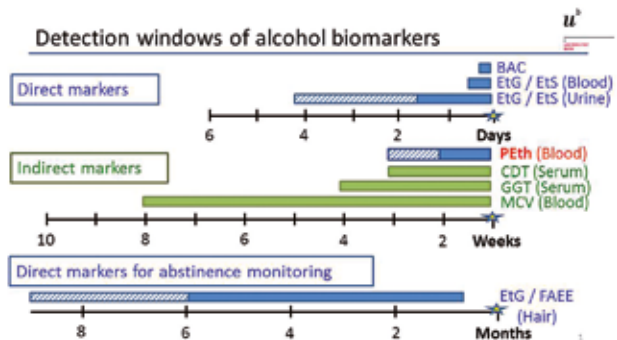
Teaching Profile

On behalf of the University of Bern, the Institute of Forensic Medicine in Bern (IRM) is responsible for the training and continuing education of students of medicine and jurisprudence, medical personnel and the institutions of the administration of justice and the police.

Highlights 2017

Evaluation of the direct alcohol biomarker phosphatidyl ethanol (PEth) for driving aptitude assessment

The use of phosphatidyl ethanol (PEth) in blood as a marker for alcohol abstinence has been validated in comparison to ethyl glucuronide in hair (hEtG), which is usually used in Switzerland for abstinence monitoring in driving aptitude assessment. In comparison to other alcohol markers (CDT, MCV, γ GT) PEth shows higher sensitivity and specificity for detection of excessive and – due to lowering the mass spectrometric detection limit – also for detection of moderate alcohol consumption. Even single consumption of alcohol up to 0.8 g/kg blood alcohol concentration yielded a positive PEth finding for at least 3 days after drinking.



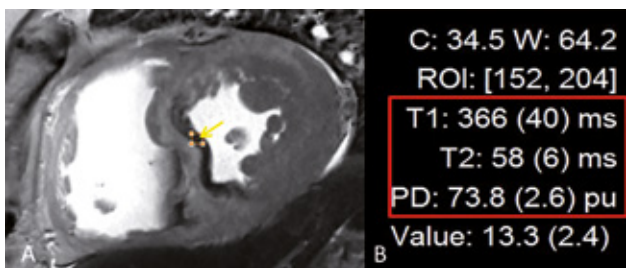
Mind the gap – A qualitative study about knowledge acquisition of judges and legal experts

Medical knowledge is important for the law profession, as it can often determine rulings, therefore impacting individuals and society. Legal experts indicated that insufficient scientific literacy skills were taught during law school, even though they often have to deal with medical information in their profession. Medical knowledge learning is informal and often stems from queries using the internet. To reach legal professionals, it has to be presented in a way comprehensible to the layman and in legal or in interdisciplinary journals.



Temperature corrected post-mortem 3T MR quantification of histopathological early acute and chronic myocardial infarction: a feasibility study

Quantitative MRI sequences allow for quantification of tissue parameters called T1 and T2 relaxation times and proton density. These parameters can be quantified by placing measuring fields in conspicuous regions in MR images (A). Dedicated software gives specific quantitative values for the measured region (B). In this post-mortem study a quantification sequence was used for examination of 60 hearts. It could be shown that based on quantitative values MRI heart examinations are feasible for diagnosis of different age stages of myocardial infarction.

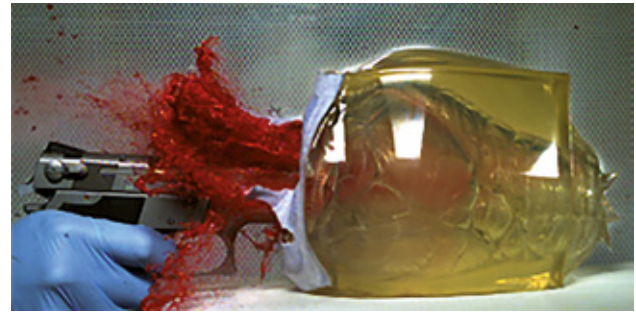


Postmortem cardiac MRI – chronic septal infarction (black) and according measurements of T1, T2 and proton density.

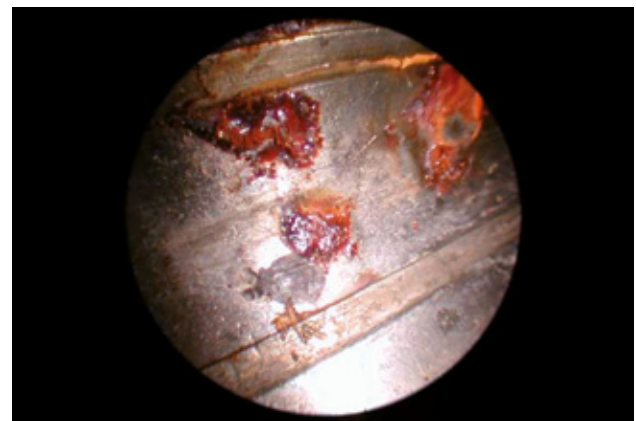
The Point-Blank Shot – from the shot to the stain: an interdisciplinary forensic analysis (SNF project 310030E-147628 / 1)

After contact shots to the head biological traces could be detected inside firearm barrels. More than 100 suicide cases by firearms in the Canton of Bern were investigated revealing a great heterogeneity of biological staining inside barrels. A systematic experimental study was conducted to analyse the influencing factors using sophisticated ballistic

target models, high speed video, video-endoscopy and DNA-quantification. Whereas the distance was the most important factor, muzzle gas pressure and the temporary cavity played only a secondary role.



Experimental contact shot on ballistic gelatine – reproduction of back spatter traces.



Endoscopic view into a barrel – biological traces due to back spatter.

Selected Competitive Grants

- Swiss National Science Foundation (grant No. CR3113L_157024; CR1313_149583; CR1311_166559; 310030E-147628/1)
- Gebert RUF Stiftung (grant No. GRS-075/14)

Selected Publications

- Canela C, Buadze A, Dube A, Eich D, Liebrezn M (2017). Skills and compensation strategies in adult ADHD - A qualitative study. PLoS One. 12(9)
- Furrer L, Jackowski C, Pfäffli M (2017). Cocaine testing in fitness-to-drive assessments: comparison between hair analysis, urinalysis and self-reports. Alcohol Drug Addict 2017; 30(2):103-112
- Schyma C, Bauer K, Brünig J, Schwendener N, Müller R (2017). Visualization of the powder pocket and its influence on staining in firearm barrels in experimental contact shots. Int J Legal Med 131(1):167-172
- Siegenthaler L, Sprenger F, Kneubuehl BP, Jackowski C (2017). Impact energy of everyday items used for assault. International Journal of Legal Medicine (in print)
- Somers J, Cooper C, Alterauge A, Löscher S (2017). A Medieval/Early Modern Alpine Population from Zweisimmen, Switzerland: A Comparative Study of Anthropology and Palaeopathology. International Journal of Osteoarchaeology, 27(6):958-972

Institute of Primary Health Care (BIHAM)

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Director



PD Dr. Arnaud Chiolero
Deputy Director



Prof. Reto Auer
Head of Research



Dr. Bruno da Costa
Head of Methodology and Biostatistics



Dr. Cinzia del Giovane
Head of Methodology and Biostatistics



Dr. Martin Feller
Research Coordination



Dr. Roman Hari
Head of Teaching



Dr. Sven Streit
Head of Career Development

Research Partners

- Division of General Internal Medicine, Inselspital, University of Bern, Switzerland
- Department of Cardiology, Inselspital, University of Bern, Switzerland
- Department of Neurology, Inselspital, University of Bern, Switzerland
- Institute of Social and Preventive Medicine (ISPM) & Clinical Trial Unit (CTU), University of Bern, Switzerland
- Department of Primary Care and Public Health, Leiden University Medical Center, The Netherlands
- Departments of Medicine and of Epidemiology and Biostatistics, UCSF, CA, USA
- Department of Epidemiology, McGill University, Montreal, Canada
- Applied Health Research Centre, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Canada
- Policlinique Médicale Universitaire (PMU), University of Lausanne, Switzerland
- Institute of Social and Preventive Medicine (IUMSP), Lausanne University, Switzerland

Research Profile

The Institute of Primary Health Care of the University of Bern (BIHAM) trains and fosters the next generation of primary care physicians and carries out research in primary health care, epidemiology and public health. It offers an interdisciplinary environment with excellent methodological support and access to a large network of practicing primary care physicians. Research projects are conducted notably about multimorbidity, overdiagnosis, deprescription, screening, smoking, hypertension and prevention, with grants from the Swiss National Science Foundation (SNSF) and European Union. Systematic reviews are also conducted. In 2017, three PhD students have joined the team of researchers.

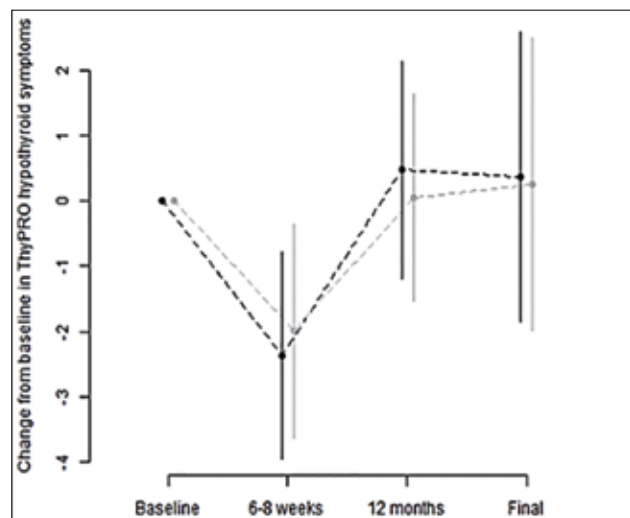
Teaching in Primary Care

Medical students spend 27 days in private practice within our clerkships "Berner Hausarztpraktika". By 2017/2018, a major reform of the clerkships was implemented, leading to a better distribution of the training days over 5 years, an optimization of educational focus every year and a sustainable operability with 100 additional students. In parallel, primary care teaching is done through lectures, workshops on clinical skills and primary care-specific subjects, and by leading interdisciplinary collaborations for education in communication and diagnostic ultrasound.

Research Highlights 2017

No benefit of thyroid hormone replacement therapy in sub-clinical hypothyroidism, NEJM 2017

Subclinical hypothyroidism affects 10% of older adults. It has been associated with unspecific but common symptoms, such as tiredness, and is often treated with thyroid hormone replacement therapy, despite weak evidence of benefits. In the largest multicenter randomized controlled trial, we found no benefit of thyroid hormone replacement therapy in elderly with subclinical hypothyroidism. These results may spare millions of elderly the necessity of taking a daily therapy.

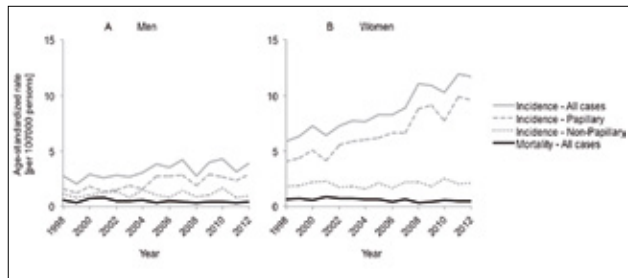


Change in ThyPRO Hypothyroid symptom score used to assess symptoms for thyroid disease.

Heating cigarettes produce smoke, JAMA Int Med 2017

Philip Morris International (PMI) recently launched IQOS, a cigarette holder that heats a cigarette at 330 ° C. The producer claims that IQOS does not produce smoke. This claim could help circumvent smoking bans in closed public spaces. We compared the content of the aerosol generated by IQOS with that of a conventional cigarette. Volatile organic compounds, polycyclic aromatic hydrocarbons and carbon monoxide were present in the aerosol of IQOS, which shows IQOS releases smoke. Products like IQOS should be subject to the same smoking bans as conventional cigarettes.

Growing overdiagnosis of thyroid cancer, PLoS One 2017
Overdiagnosis of thyroid cancer has been found in several countries. We compared secular trends in surgical intervention rate for thyroid cancer with the incidence and mortality of thyroid cancer in Switzerland. We conducted a population-based temporal trend study from 1998 to 2012. We observed a large increase in the incidence of thyroid cancer, limited to papillary and early stage tumors, with a three- to four-fold parallel increase in thyroidectomy. The mortality slightly decreased. These findings suggest that a substantial and growing part of thyroid cancers are overdiagnosed and overtreated.



Age-standardized incidence and age-standardized mortality rates for thyroid cancer in Switzerland, 1998-2012 (PLoS One 2017;12(6):e0179387).

Variation in the treatment of hypertension among the oldest-old, BMC Geriatr 2017

We assessed decision to start antihypertensive treatment in patients aged more than 80 years among general practitioners (GPs) across 29 countries. Among more than 2500 GPs in Europe, Brazil, Israel and New Zealand, considerable variation was found in the decision to start treatment (Figure 3). In 83% of the countries, frailty decreased the decision to start antihypertensive treatment. Hypertension trials among the oldest-old should include frail patients.



Percentages of general practitioners who decided to start antihypertensive treatment in all cases of oldest-old patients (BMC Geriatr 2017; 17(1):93).

Selected Competitive Grants

- OPERAM trial on multimorbidity and polypharmacy – EU's Horizon 2020 (grant agreement 634238)
- Thyroid & neuropsychiatry – SNSF (320030_172676)
- OPTICA trial polypharmacy by GPs– SNSF (NFP74;407440_167465)
- Electronic cigarette trial – SNSF (IICT 33IC30_173552)
- Colon screening trial – SNSF (NFP74; 407440_167519)

Selected Publications

- Stott DJ, Rodondi N, et al; TRUST Study Group. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. *N Engl J Med* 2017;376(26):2534-2544
- Jegerlehner S, Bulliard JL, Aujesky D, Rodondi N, Germann S, Konzelmann I, Chiolerio A; NICER Working Group. Overdiagnosis and overtreatment of thyroid cancer: A population-based temporal trend study. *PLoS One* 2017;12(6):e0179387
- Auer R, et al. Heat-Not-Burn Tobacco Cigarettes: Smoke by Any Other Name. *JAMA Intern Med* 2017;177(7):1050-52
- Streit S, Verschuur M, Rodondi N, et al. Variation in GP decisions on antihypertensive treatment in oldest-old and frail individuals across 29 countries. *BMC Geriatr* 2017; 17(1):93
- da Costa BR, et al. Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. *Lancet* 2017;390(10090):e21-e33

Institute of Complementary Medicine

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Fabrikstrasse 8, 3012 Bern



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Wolf
Managing
Director



Dr. Martin
Frei-Erb



Dr. Johannes
Fleckenstein



Prof. Lorenz
Fischer

Research Partners

- Canton Hospital Fribourg (HFR), Fribourg, Switzerland
- Paracelsus-Spital Richterswil, Switzerland
- Department of Electrical Engineering ESAT, STADIUS KU Leuven, Leuven, Belgium
- Medical University of Vienna, Department of Medicine I, Clinical Division of Oncology, Vienna, Austria
- Central Council of Homeopathy Research (CCRH), Ministry of AYUSH, Government of India, India
- Division of Pediatric Hematology/Oncology, University Children's Hospital Bern, Inselspital, Bern, Switzerland
- Pain Centre, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Bern University of Applied Sciences, Health, Physiotherapy, Switzerland
- Department of Gynecologic Endocrinology and Reproductive Medicine, University Clinic of Obstetrics and Gynecology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Department of Sports Medicine, Goethe-University of Frankfurt, Germany

Research Profile

Group Fischer: The main research topic in Neural Therapy continues to be the clinical presentation and neurophysiology of sympathetically maintained pain and inflammation. We work on new mechanisms of action (positive feedback loops) and carry out clinical studies. Extensive studies (efficacy, costs) are ready for publication.

Group Fleckenstein: The integration of acupuncture in clinical routine is the main research objective in Traditional Chinese Medicine (TCM) and acupuncture. We perform clinical studies to evaluate the add-on effect of TCM/acupuncture to guideline treatments (e.g. menopause, SNF-project) and work on mechanism of action (e.g. peripheral neurophysiology). We are experienced partners in the methodological planning of acupuncture studies (including control procedures).

Group Frei-Erb: The group of homeopathy deals with Swiss GPs job satisfaction, use of complementary medicine in patients with cancer or organ/blood stem cell transplant, a systematic review of controlled clinical studies extended by gray literature and follow-up of individual treatment in children with ADD/ADHD or cancer.

Group Wolf: Research in integrative and anthroposophically extended medicine comprises patient centered translational and clinical research. One of the main research topics is investigating effects of colored light on human physiology. Other research topics include several clinical trials, in collaboration with e.g. the Inselspital, on effects of medication and non-medication therapies in the field of integrative medicine.

Teaching Profile

The institute participates with lectures and courses in the curricula for medical students at the University of Bern. Additionally, lectures on homeopathy are given for pharmacology students at ETH Zurich, lectures on neural therapy at the University of Zurich and lectures on TCM/acupuncture at the University of Basel.

Two medical doctoral theses and five master theses were successfully completed.

Lorenz Fischer's book on neural therapy is the official textbook for neural therapy training in Switzerland, Germany, Spain, South America etc. Johannes Fleckenstein is a lecturer for Swiss and German Medical Acupuncture Societies.

Highlights 2017

Group Fischer

Last year's work on the stellate ganglion published in "Autonomic Neuroscience" generated worldwide response. Another 2017 highlight was the request for cooperation in the research on the autonomic nervous system and inflammation from an important research partner.

Group Fleckenstein

At the Multidisciplinary Expert Meeting of Psychiatric, Psychotherapeutic, and Psychosomatic Medicine at the University of Bern, Agnes Schitter won the 2017 poster award for her research on the impact of Water Shiatsu in the rehabilitation of polytrauma.

Group Frei-Erb

Antibiotics Awareness Week 13. – 17 November 2017: In a workshop we discussed with GPs a newly developed tool for describing individual homeopathic treatment for uncomplicated acute cystitis in women to reduce the prescription of antibiotics. It was appraised as feasible tool in daily practice.

Based on the contributions from the participants of the workshop our group will work to optimize this tool and conduct a testing phase in GPs practices.

Group Wolf

At the yearly conference of the International Society of Oxygen Transport to Tissue (ISOTT) in Halle, Germany, Felix Scholkmann, PhD received the prestigious Melvin Knisely Award for outstanding young investigators. Prof. Wolf was chosen as President-elect of the International Society for Complementary Medicine Research ISCMR.

Selected Competitive Grants

- Swiss Cancer League (KFS-4259-08-2017)
- Software AG Foundation (BA-P11425, P12117)

Selected Publications

- Metz AJ, Klein SD, Scholkmann F, Wolf U. Continuous coloured light altered human brain haemodynamics and oxygenation assessed by systemic physiology augmented functional near-infrared spectroscopy. *Sci Rep.* 2017 Aug 30;7(1):10027. doi: 10.1038/s41598-017-09970-z
- Scholkmann F, Hafner T, Metz AJ, Wolf M, Wolf U. Effect of short-term colored-light exposure on cerebral hemodynamics and oxygenation, and systemic physiological activity. *Neurophotonics.* 2017 Nov 20. doi: 10.1117/1.NPh.4.4.045005
- Marszalek G, Torchetti L, Barth J, Wolf U, Frei-Erb M. Einstellung von Ärzten gegenüber Komplementärmedizin in einer ländlichen Region der Schweiz: Ergebnisse einer Umfrage. *Complement Med Res.* 2017;24(5):310-316. doi:10.1159/000480332
- Eisenhardt S, Fleckenstein J. Traditional Chinese medicine valuably augments therapeutic options in the treatment of climacteric syndrome. *Arch Gynecol Obstet.* 2016 Jul;294(1):193-200. doi: 10.1007/s00404-016-4078-x
- Fischer L. Physical and neurobiological principles in: Liem T., Van den Heede P. (Eds): *Foundations of morphodynamics in osteopathy*, Handspring, Edinburgh 2017

Institute of Medical Education

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Guttormsen
Director



PD Dr. Sören
Huwendiek
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Dr. Philippe
Zimmermann
Department Head



Dr. Sandra
Trachsel
Department Head



Dr. Kai
Schnabel
Department Head

Research Partners

- Federal Office of Public Health
- Medical Faculty Zürich
- Medical Faculty Lausanne
- Medical Faculty Geneva
- Bern University Hospital (Inselspital)
- University Hospital Zürich
- LMU München, Klinikum der Universität München, Germany
- Charité Universitätsmedizin Berlin, Germany
- Medical Faculty Würzburg, Germany
- Maastricht University, The Netherlands

Research Profile

Interdisciplinary research in Medical Education and related fields, both quantitative, qualitative and mixed method research.

Formative Assessment: workplace-based assessment, feed forward, multisource feedback, Virtual Patients.

Summative assessment: involvement of children in high stakes objective structured clinical examination (OSCE); scoring and pass-fail decision in multiple choice exams: assessment of communication skills in OSCE; assessment of clinical reasoning; development of innovative assessment formats.

Teaching: Understanding and improving various teaching formats: Interprofessional teaching; Peer Teaching, Communication training.

E-Learning: Research on the impact of cognitive load for learning in multimedia applications, use of social media in online learning environments, early on-line learning of communication skills.



IML released new software packages supporting written and practical assessments (Picture: MCQ on tablets).

Human-Computer Interaction: new technologies in educational settings, digital transformation/education, mobile educational technologies, interface design of educational applications.



Practical exam (OSCE) with children as 'standardised patients' in the 5th year exam.

Teaching Profile

Undergraduate training at the Medical Faculty in Bern: PBL, Clinical skills trainings (coordination for faculty; trainings in internal medicine, pediatrics etc.), communication trainings (years 4 – 6), interprofessional trainings (venipuncture, confidentiality, elective workshop), Peer-Teaching (ECG, venipuncture), eLearning.

Postgraduate training: Program leadership (S. Trachsel, S. Guttormsen) and teaching in the international MAS Master of Medical Education (MME) of the University of Bern. Postgraduate teaching activities of IML includes also the Master of Medical education in Germany (K. Schnabel); Harvard Macy Institute Program for Leading Innovation in Healthcare and Education at Harvard Medical School (S. Huwendiek); invited workshops; Faculty development, Clinical Teaching and Feedback trainings, Courses and trainings for exam authors, Communication trainings.

Highlights 2017

Awards for educational projects

- SAMW Award: Interprofessionality 2017: B. Brem (IML), Claudia Schlegel (Berner Bildungszentrum Pflege) und Noemi Schaffner (BFH). Project: Interprofessionelles Lernen mit interprofessionellen Peer Tutoren.
- Award of the association for medical education of the German speaking countries (GMA) for the most innovative project idea: "Improving the education of medical

students by curriculum development with entrustable professional activities: a trinational pilot project": S. Pinilla, K. Dimitriadis, A Hofhansl, A Anvari-Pirsch, Ch. Berendonk, S. Huwendiek.

SPSim 2017 Conference was organised by the Institute for Medical Education (S. Guttormsen conference Chair). SPSim is an international and interprofessional conference on the use of simulations and standardized patients in healthcare education organized by four partner institutions: BFH, HESAV, BZ Pflege and the IML in Bern. <http://www.with-simulation.ch/previous-conferences/>

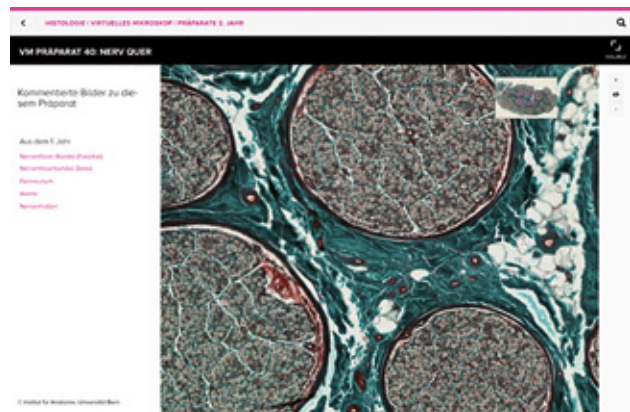
Successful implementation of a *peer-teaching course for ECG Training* in the 6th year of under-graduate medical education in cooperation with U. Woermann and J. Fuhrer, head of rhythmology and electrophysiology at the University Hospital.

Mandated from the national exam commission for the federal licencing exam, the IML organised for the first time a *national two-day workshop for the development and revision of Multiple Choice-questions* for the federal exam in human medicine. The workshop resulted in a good output of high qualitative exam questions (T. Schurter, B. König, J. Meng, C. Delmas, M. Liechti, F. Wagner, B. Zurbuchen, P. Jucker, M. Dahinden, R. Laubscher, E. van Gessel, R. Bonvin, P. Bednarski, B. Hug, R. Kropf)

Development and production of more than 600 moulages together with the Dep. of Dermatology for the federal licensing exam with support of 3D printing technologies: M. Germano. S. Wüst, D. Bauer, K. Schnabel

PROFILES: A new national framework of learning objectives for undergraduate education in human medicine was finalised. Two IML Co-Workers were part of the national developing team: P. Jucker-Kupper as general secretary and Ch. Berendonk as member of the working group.

Modernization of the e-Learning tool MorphoMed (R. Beck, U. Woermann with external experts): The online learning program for Anatomy, Histology and Pathology was completely redesigned and published in September 2017. Feedback from students and faculty was very positive. <https://elearning.medizin.unibe.ch/>



'MorphoMed', New design and architecture.

The engagements of children as standardised patients in an objective structured clinical examination (OSCE) was successfully implemented in Bern for the second time: S. Feller, R. Krings, K. Schnabel, S. Wüst, M. Steinlin, F. Merz, S. Huwendiek. The involvement of the children as standardized patients was highly appreciated by the students and examiners.

Selected Competitive Grants

- SNF / NFP 74: «Spiritual Care in Chronic Pain. Interdisciplinary Research for Interprofessional Practice in Medicine and Nursing» (S. Guttormsen co applicant, S. Peng Keller, main applicant)
- Federal Office of Public Health: "Bildung und Berufsausübung: Evaluationsinstrumente" in the frame of the funding program "Interprofessionalität": S. Huwendiek, S. Guttormsen, C. Bachmann, A. Lörwald, J. Meng-Hentschel, F. Neubauer, F. Wagner, B. Zurbuchen
- Universität Bern / Förderung innovative Lehre: From student to team member: An inverted classroom concept integrates students in interprofessionell team simulation trainings; Sauter, Thomas (Insel*), K. Schnabel, D. Bauer, W. Hautz*, A. Exadaktylos*
- Federal Office of Public Health (FOPH): Improving the assessment of communication competencies in the Swiss Federal Licensing Examination in Human Medicine. Basel: Biller Silke; Bern: Huwendiek S. & Schnabel K., Bachmann C., Berendonk C., Feller S., Glauser C., Lörwald A., Woermann U. Geneva: Junod Perron. J. Lausanne: Bonvin R., Monti M.; Zürich: Breckwoldt J., Jünger E., Kropf R.
- FOPH / National exam commission: Development and testing of Hybrid simulations for the federal licensing exam: Schnabel.K., Bauer, D. (IML), Bonvin, R. (LA), Schirlo, Ch., Breckwoldt, J. (ZH)

Selected Publications

- Schmitz, F. M., Schnabel, K., Stricker, D., Fischer, M. R., & Guttormsen, S. (2017). Learning communication from erroneous video-based examples: A double blind randomised controlled trial. *PEC, Patient Education and Counseling*. <http://dx.doi.org/10.1016/j.pec.2017.01.016>
- Huwendiek, S., Reichert, F., Duncker, C.; de Leng, Bas A., van der Vleuten, C. P. M., Muijtjens, A. M. M., Bosse, H-M., Haag, M., Hoffmann, Gg. F., Tönshoff, B., Dolmans, D. (2017): Electronic assessment of clinical reasoning in clerkships: A mixed-methods comparison of long-menu key-feature problems with context-rich single best answer questions. *Medical Teacher*, 39(5), pp. 476-485
- Lahner M-L., Lörwald, A. C., Bauer, D., Nouns, Z. M., Krebs, R., Guttormsen, S. Fischer, M. R. Huwendiek, S. (2017): Multiple True-False Items: A comparison of scoring algorithms", *Advances in Health Sciences Education*, in print, <https://doi.org/10.1007/s10459-017-9805-y>
- Sonntag U, Peters H, Schnabel KP*, Breckwoldt J* (2017): 10 years of didactic training for novices in medical education at Charité, *GMS J Med Educ*. 2017; 34(4):Doc39 *shared last-authorship
- Lörwald A. C, Lahner, F. M. Greif, R., Berendonk, Ch., Norcini, J., Huwendiek, S. (2017): Factors influencing the educational impact of Mini-CEX and DOPS: A qualitative synthesis, *Medical Teacher*, Online first, DOI: 10.1080/0142159X.2017.1408901

Institute of Dental Medicine

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Prof. Anton Sculean
Executive Director
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Prof. Daniel Buser
Director of the Clinic of Surgery and Stomatology



Prof. Hendrik Meyer-Lückel
Director of the Clinic of Preventive, Restorative, and Pediatric Dentistry



Prof. emeritus Adrian Lussi
Former Director of the Clinic of Preventive, Restorative, and Pediatric Dentistry



Prof. Christos Katsaros
Director of the Clinic of Orthodontics and Dentofacial Orthopaedics



Prof. Urs Brägger
Director of the Clinic of Reconstructive Dentistry and Gerodontology



Prof. Martin Schimmel
Head of the Division of Gerodontology

Research Partners

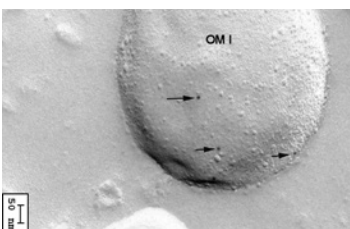
- Clinic of Rheumatology, Clinical Immunology and Allergology, University of Bern
- Institute of Microbiology, Faculty of Biotechnology, Biophysics and Biochemistry, Jagiellonian University, Krakow, Poland
- Department of Periodontology, Faculty of Odontology, Malmö University, Malmö, Sweden
- Various industry partners, e.g. Straumann, Basel, Switzerland, Geistlich Pharma AG, Wolhusen, Switzerland

Research Profile

The School of Dental Medicine was founded in 1921 and consists of 5 clinics and 1 division. The main research focus is translational and clinical, encompassing the most important areas in dentistry. Main research streams are the investigation of etiology and pathogenesis of caries and periodontitis as well as tooth erosion. Other research fields include the investigation of saliva and of mechanisms involved in periodontal and bone wound healing, osseointegration of dental implants and cleft-lip and palate and craniofacial disorders, oral function in elders as well as the investigation of dental materials. The research facilities comprise the laboratory of oral microbiology, oral molecular biology, oral cell biology, oral histology, cariology and dental erosion and dental materials. The research involves a strong network of basic researchers and clinicians from the various clinics from the School of Dental Medicine, medical hospital and numerous international centers.

Highlights in Research

P. gingivalis glutaminyl cyclase (QC) is expressed in vivo
Human glutaminyl cyclases (QC and isoQC) are thought to play an important role in maintaining inflammatory conditions. Meanwhile also a glutaminyl cyclase synthesized by *Porphyromonas gingivalis* (PgQC) was discovered and expression of PgQC was visualized by means of freeze

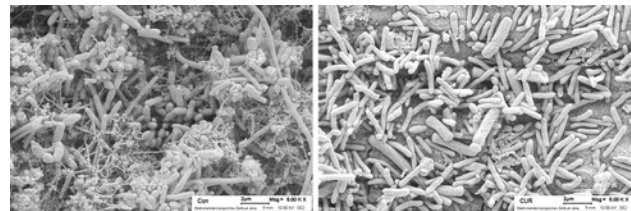


Visualization of bacterial glutaminyl cyclase (->) in *Porphyromonas gingivalis* ATCC 33277 after 24 h of anaerobic incubation and freeze fracturing SEMs. OM I: outer membrane inner layer.

fractioning SEMs. The protein seems to be located mainly in peri-plasmatic space. In eight of 13 *P. gingivalis* positive biofilm samples obtained from patients with periodontitis, PgQC expression was detected. PgQC might be a potential target in periodontal antimicrobial therapy.

Activity of Er:YAG laser on biofilm ablation from dental surfaces

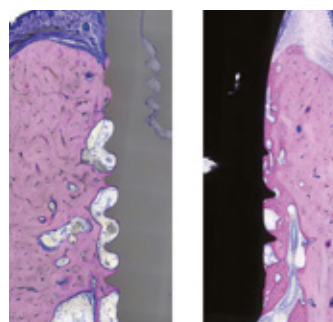
Bacterial biofilms play a major role in the etiology of periodontal and peri-implant diseases. Biofilms formed on dentine or titanium surfaces were placed into artificially-created pockets and removed with various modalities. On titanium-surfaces the use of Er:YAG resulted in superior biofilm removal and higher attachment of osteoblast-like cells.



In vitro 12-species biofilm without (Con) and after applying mechanical therapy by means of a curette (CUR).

Bone response to functionally loaded, two-piece zirconia implants

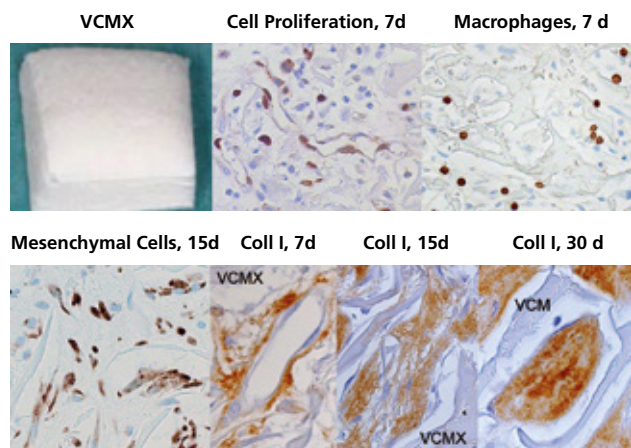
Titanium is still the material of choice for dental implants to replace missing teeth. Concerns about hypersensitivity as well as particle and ion release of titanium have paved the way for alternative biomaterials like zirconia. In this preclinical study two-piece sandblasted and acid-etched zirconia and titanium dental implants were placed in healed tooth extraction sites in canine mandibles. The results demonstrated a comparable bone integration of two-piece zirconia and titanium implants.



Representative micrographs showing osseointegration of dental implants. Zirconia on the left, titanium on the right.

A novel volume-stable collagen matrix supports cell proliferation, fibroblast and blood vessel invasion, and collagen deposition

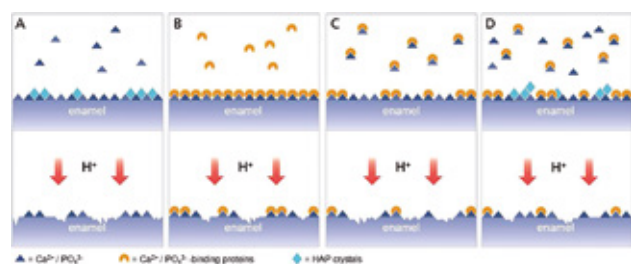
Lack of sufficient soft tissue width and thickness can compromise function, esthetics or even survival of teeth and implants. This study aimed to investigate the tissue response to a volume-stable porcine collagen matrix (VCMX) by means of immunohistochemistry 4h, 4, 7, 15, 30 and 90d after installation in a canine, buccal soft tissue pouch model. These results show a high biocompatibility and excellent tissue integration of this novel biomaterial, supporting its clinical use for soft tissue augmentation.



Representative images of the biomaterial before implantation (VCMX). Immunohistochemistry with antibodies against PCNA (cell proliferation), macrophages, vimentin (mesenchymal cells), and collagen type I.

Erosion and saliva research

A recent translational research project by the erosion and saliva research group has shown that the right proportion of proteins and mineral ions in saliva are critical for the formation of the salivary pellicle – a protective barrier formed on the surface of the tooth. Both proteins and the mineral ions have a positive effect on their own, but also interact.



Model of salivary protection of the tooth surface (enamel) from acid attack. (A) Artificial saliva only with the mineral ions component. (B) Dialysed saliva only with the protein component. (C) Saliva with both components: protein and a low mineral ion concentration. (D) Saliva with both components: protein and a high mineral ion concentration (Baumann T, et al. *Sci Rep.* 2017;7:12999).

Teaching Profile

The School of Dental Medicine is providing undergraduate and postgraduate teaching. The undergraduate dental curriculum is based on the Bologna reform leading to the Bachelor and Master Degree in Dentistry. The undergraduate teaching at the School of Dental Medicine is provided for a total of about 100 students/year in the 3rd, 4th and 5th year consisting of theoretical (e.g. lectures and seminars) and practical (e.g. laboratory and clinical work) parts. The

postgraduate teaching encompasses 3-4 year postgraduate programs leading to speciality and / or MAS degrees in Preventive Dentistry and Cariology, Periodontology, Oral Surgery, Reconstructive Dentistry and Orthodontics & Dentofacial Orthopedics..

Highlights 2017

- Top ranking for the School of Dental Medicine (rank N° 22 according to QS World University Rankings by Subject 2017, and rank n°17 according to the Shanghai Rankings's Global Ranking of Academic Subjects 2017). Most importantly, the School of Dental Medicine ranked second in terms of H-Index and citation per paper according to QS World University Rankings 2017 and was ranked n° 1 among all German speaking dental schools.
- Open Door's Day on April 1st 2017. More than 1500 guests and visitors had the opportunity to have insight in the clinical and research facilities of the School of Dental Medicine
- Researcher's Night on September 16. Within the frame of the research performed at the University of Bern, the School of Dental Medicine presented various translational research projects performed in the research laboratories and clinical facilities.
- Prof. Christos Katsaros, President of the European Orthodontic Society (EOS) organized in June 2017 the 93rd EOS Congress in Montreux with more than 2100 participants.
- Prof. emeritus Adrian Lussi was awarded Teacher of the Year in recognition of his didactic skills and his marked efforts for the dental students at the School of Dental Medicine.

Selected Competitive Grants

- FP7-HEALTH-F3-2012-306029 TRIGGER (finished April 2017)
- Osteology, 13-101 project, The role of subepithelial connective tissue graft or a collagen based matrix on determining epithelial differentiation around teeth and dental implants. A preclinical study

Selected Publications

- Wittneben JG, Gavric J, Belser UC, Bornstein MM, Joda T, Chappuis V, Sailer I, Brägger U. Esthetic and Clinical Performance of Implant-Supported All-Ceramic Crowns Made with Prefabricated or CAD/CAM Zirconia Abutments: A Randomized, Multicenter Clinical Trial. *J Dent Res.* 2017 Feb;96(2):163-170
- Kouskoura T, Katsaros C, von Gunten S. The Potential Use of Pharmacological Agents to Modulate Orthodontic Tooth Movement (OTM). *Front Physiol.* 2017 Feb 8;8: 67
- Chappuis V, Cavusoglu Y, Buser D, von Arx T: Lateral ridge augmentation using autogenous block grafts and guided bone regeneration: A 10-year prospective case series study. *Clin Implant Dent Relat Res.* 19:85-96, 2017
- Flury S, Peutzfeldt A, Schmidlin PR, Lussi A. Exposed Dentin: Influence of Cleaning Procedures and Simulated Pulpal Pressure on Bond Strength of a Universal Adhesive System. *PLoS One.* 2017 Jan 12;12(1):e0169680
- Eick S, Meier I, Spoerlé F, Bender P, Aoki A, Izumi Y, Salvi GE, Sculean A. In Vitro-Activity of Er:YAG Laser in Comparison with other Treatment Modalities on Biofilm Ablation from Implant and Tooth Surfaces. *PLoS One.* 2017 Jan 26;12(1):e0171086. doi: 10.1371/journal.pone.0171086

Department of General Internal Medicine

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Poliklinik



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Chefarzt und
Leiter Klinische
Pharmakologie

Research Partners

- Department of Medicine, University of Pittsburgh, Pennsylvania, USA
- Institute of Primary Health Care (BIHAM)
- Geriatric Medicine, Cliniques universitaires Saint-Luc, Brussels, Université catholique de Louvain, Belgium
- Department of Geriatric Medicine and Expertise Centre Pharmacotherapy in Old Persons (EPHOR), University Medical Centre Utrecht, Netherlands
- Department of Medicine (Geriatrics), University College Cork, Cork, Ireland
- Clinical Trial Unit, Bern university, Bern, Switzerland
- Division of General Internal Medicine, Brigham and Women's Hospital, Boston, MA, USA
- Division of Clinical Pharmacology & Toxicology, University Hospital Basel, Switzerland
- European Drug Emergencies Network (Euro-DEN), European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), Lisbon, Portugal

Research Profile

The research at the Department of General Internal Medicine is exclusively patient-oriented clinical research. The main research expertise are:

- Venous thromboembolism
- Patient multimorbidity, polypharmacy, and complexity
- subclinical hypothyroidism
- Hospital readmission
- Overdiagnosis
- Pain therapy
- Personalized drug therapy and drug safety

Teaching Profile

The department is very engaged in the teaching of medical students of the Bern university medical school. The department covers teaching both at bedside and ex cathedra, from Bachelor to master students. Clinical Skills Training, OSCE Exams are also part of the teaching activity. Finally, we offer internships to a large number of medical students. Moreover, the department is engaged in the teaching of the dental students at the Bern University.

Highlights 2017

Thyroid Hormone Therapy provided no apparent benefits in older persons with subclinical hypothyroidism

The use of levothyroxine to treat subclinical hypothyroidism is controversial. We conducted a double-blind, randomized, placebo-controlled, parallel-group trial involving 737 adults who were at least 65 years of age and who had persisting subclinical hypothyroidism. We found no differences in the mean change at 1 year in the Hypothyroid Symptoms score (0.2 ± 15.3 in the placebo group and 0.2 ± 14.4 in the levothyroxine group; between-group difference, 0.0; 95% confidence interval, -2.0 to 2.1); between-group difference, 0.4; 95% CI, -2.1 to 2.9).

Usefulness of D-Dimer Testing in Predicting Recurrence in Elderly Patients with Unprovoked Venous Thromboembolism

Whether post-anticoagulation D-dimer levels are useful in predicting recurrence in elderly patients with unprovoked venous thromboembolism is unknown. We followed up 157 patients aged ≥ 65 years with acute symptomatic, unprovoked venous thromboembolism in a prospective, multicenter cohort study. There was no statistically significant association between quantitative or dichotomized D-dimer levels and venous thromboembolism recurrence. The area under the receiver operating characteristic curve for predicting recurrent venous thromboembolism was moderate (0.66; 95% confidence interval [CI], 0.51-0.82). D-dimer testing alone may not be useful in identifying elderly patients with unprovoked venous thromboembolism who are at low risk of recurrent venous thromboembolism and in whom anticoagulants may be safely stopped.

Association of Stress Biomarkers With 30-Day Unplanned Readmission and Death

The theory that posthospitalization stress might increase the risk of postdischarge complications has never been investigated. We prospectively included 346 patients aged ≥ 50 years admitted to the department of general internal medicine at a large community hospital. Forty patients (11.6%) had a 30-day unplanned readmission or death. High serum copeptin and cortisol levels were associated with an increase

in the odds of unplanned readmission or death (odds ratios [95% confidence interval] 2.69 [1.29-5.64] and 3.43 [1.36, 8.65], respectively). High serum levels of copeptin and cortisol at discharge were independently associated with 30-day unplanned readmission or death, supporting a possible negative effect of hospitalization stress during the postdischarge period.

Selected Competitive Grants

- HORIZON 2020
- Swiss National Science Foundation (Grant No. 320030_172676; 31003A_160206)
- Swiss National Science Foundation Professorship (PP00P3_170656)
- SGAIM Foundation

Selected Publications

- Stott DJ, Rodondi N, et al; TRUST Study Group. Thyroid Hormone Therapy for Older Adults with Subclinical Hypothyroidism. *N Engl J Med* 2017;376(26):2534-2544
- Baumgartner C, da Costa BR, Collet TH, Feller M, Floriani C, Bauer DC, Cappola AR, Heckbert SR, Ceresini G, Gussekloo J, den Elzen WPJ, Peeters RP, Luben R, Völzke H, Dörr M, Walsh JP, Bremner A, Iacoviello M, Macfarlane P, Heeringa J, Stott DJ, Westendorp RGJ, Khaw KT, Magnani JW, Aujesky D, Rodondi N; Thyroid Studies Collaboration. Thyroid Function Within the Normal Range, Subclinical Hypothyroidism, and the Risk of Atrial Fibrillation. *Circulation*. 2017 Nov 28;136(22):2100-2116
- Faller N, Limacher A, Méan M, Righini M, Aschwanden M, Beer JH, Frauchiger B, Osterwalder J, Kucher N, Lämmle B, Cornuz J, Angelillo-Scherrer A, Matter CM, Husmann M, Banyai M, Staub D, Mazzolai L, Hugli O, Rodondi N, Aujesky D. Predictors and Causes of Long-Term Mortality in Elderly Patients with Acute Venous Thromboembolism: A Prospective Cohort Study. *Am J Med*. 2017 Feb;130(2):198-206
- Duthaler U, Berger B, Erb S, Battegay M, Letang E, Gaugler S, Krähenbühl S, Haschke M. Automated high throughput analysis of antiretroviral drugs in dried blood spots. *J Mass Spectrom*. 2017 Aug;52(8):534-542
- Burke RE, Schnipper JL, Williams MV, Robinson EJ, Vasilevskis EE, Kripalani S, Metlay JP, Fletcher GS, Auerbach AD, Donzé JD. The HOSPITAL Score Predicts Potentially Preventable 30-Day Readmissions in Conditions Targeted by the Hospital Readmissions Reduction Program. *Med Care*. 2017 Mar;55(3):285-290

Department of Anaesthesiology and Pain Medicine

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Nurses



Dr. Markus
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Research

Research Partners

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- Prof. Martin Fiedler and Prof. Carlo Lagriadère, Inselspital, Bern University Hospital, Bern, Switzerland
- Prof. Michel Struys, Groningen University Medical Center, Groningen, Netherlands
- Prof. George Thalmann and Prof. Fiona Burkhard, Inselspital, Bern University Hospital, Bern, Switzerland

Research Profile

Given the very definition of anaesthesiology as a field of collaborative perioperative medicine, it's no surprise that our scientific investigations cover a wide range of topics, including projects in airway management, cardiac anaesthesia, genetics and molecular biology, pain medicine, pharmacology, respiratory physiology, and anaesthesia in urologic patients. Overall, we aim at defining the best practices for personalized perioperative patient care, with basic science as our foundation and translational medicine as our vision for the future.

Our goal is to significantly contribute to precision medicine in anaesthesiology and perioperative care, both nationally and internationally. As a first step, we were very pleased to learn that we will be supported for a project with the Bern University Hospital's biobank. In this project we will address the clinically relevant and pressing need to define biomarkers, which will in turn help us to provide enhanced perioperative care in cardiac anaesthesia. In teaming up with our surgical partners, we are in a unique position to match this data to clinical outcome, including long-term follow-up. We expect this to be a long-term project, thereby enabling scientists at the Bern University Hospital to both generate competitive scientific data and improve patient care. As devoted acute care physicians and scientists, we support the Inselspital's vision of becoming the leading Swiss University Hospital.

Our research division supports a professional data management system which was significantly developed in 2017. Under the guidance of PD Dr. Andreas Vogt, the data team helps our principal investigators not only to acquire clinical data from patients treated, but also to comply with cantonal, federal and international standards and laws. This is of utmost importance given the ever-increasing obligations deriving from research in human subjects.

Teaching Profile

In our department, we successfully train about 70 residents in anaesthesiology and pain medicine each year, as well as offering courses and symposia for certified anaesthesiologists. Many medical master's and doctoral theses are successfully completed under the guidance of our principal investigators.

Additionally, we train anaesthesia nurses, lab technicians and research assistants. We aim to teach our staff the fundamentals of anaesthesiology as well as introducing them to cutting-edge innovations. A range of lessons can be learned from current clinical and basic science literature.

Further, each University of Bern medical student spends a week with our teams in one of the operating rooms, with on-the-spot training being accompanied by teaching lectures and simulation. In our faculty development program, we teach colleagues from the Inselspital as well as from other Swiss institutions "the art of lecturing" and offer courses in medical teaching and scientific writing, all open to respective professionals.

A well-cited article that we published in the peer-reviewed journal "Anesthesia & Analgesia" examined the question of whether responsible leaders are "selecting, training, and supporting the best" when we recruit staff and students to the fields of anaesthesiology and acute care medicine. Given global trends and recent evidence from human resource sciences, we believe we are selecting, training, and supporting the best at our department.

Highlights of 2017

Together with more than 100 other "TRICS-3 Investigators", Prof. Dr. Balthasar Eberle MD and research nurse Monika Stucki contributed to the international multicenter trial "Restrictive or Liberal Red-Cell Transfusion for Cardiac Surgery", published in the renowned New England Journal of Medicine. Additionally, a group led by PD Dr. Patrick Wüthrich, MD, published a randomized clinical trial in "Anaesthesiology". Those are just two of our recent publications.

We are proud of the many presentations, talks, and posters given by our researchers at both national and international conferences, and of our staff's contributions to more than 50 peer-reviewed and PubMed-listed publications and numerous book chapters.

Our department is fortunate to be able to recruit students and residents to work with us as junior scientists, and to have the opportunity to support their enthusiasm with our passion for science.

Finally, although personal accomplishments are of great importance both for individuals and the department, we believe that our success is based not only on individual achievements but also on our staff's ability to work as a team.

Selected Competitive Grants

- Mach-Gaensslen Foundation, Unterägeri, Switzerland
- Bernische Krebsliga, Bern, Switzerland
- Swiss National Science Foundation (SNSF), Bern, Switzerland
- Nestlé Foundation, Lausanne, Switzerland
- Schweizerische Gesellschaft für Anästhesiologie und Reanimation

Selected Publications

- Erdoes G, Kietaihl C, Boehme S, Ullrich R, Markstaller K, Eberle B, Klein KU. Cerebral Gaseous Microemboli are Detectable During Continuous Venovenous Hemodialysis in Critically Ill Patients: An Observational Pilot Study. *J Neurosurg Anesthesiol.* 2017
- Vasireddy R, Roth C, Mathis J, Goette J, Jacomet M, Vogt A. K-band Doppler radar for contact-less overnight sleep marker assessment: a pilot validation study. *J Clin Monit Comput.* 2017
- Furrer MA, Fellmann A, Schneider MP, Thalmann GN, Burkhard FC, Wuethrich PY. Impact of Packed Red Blood Cells and Fresh Frozen Plasma Given During Radical Cystectomy and Urinary Diversion on Cancer-related Outcome and Survival: An Observational Cohort Study. *Eur Urol Focus.* 2017
- Pedersen TH, Gysin J, Wegmann A, Osswald M, Ott SR, Theiler L, Greif R. A randomised, controlled trial evaluating a low cost, 3D-printed bronchoscopy simulator. *Anaesthesia.* 2017
- Luedi MM, Singh SK, Mosley JC, Hatami M, Gumin J, Sulman EP, Lang FF, Stueber F, Zinn PO, Colen RR. A Dexamethasone-regulated Gene Signature Is Prognostic for Poor Survival in Glioblastoma Patients. *J Neurosurg Anesthesiol.* 2017

Department of Angiology

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Schindewolf



PD Dr. Sebastian
Sixt

Research Partners

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- Clinical Trials Unit Bern, Department of Clinical Research, University of Bern, Bern, Switzerland
- Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria
- University Hospital Bern, Department of Visceral Surgery and Medicine, Bern, Switzerland
- University Hospital Bern, Department of Vascular Surgery, Bern, Switzerland
- University Hospital Bern, Department of General Internal Medicine, Bern, Switzerland
- University Hospital Basel, Department of Angiology, Basel, Switzerland
- University Hospital Zurich, Department of Angiology, Zurich, Switzerland
- University Hospital Frankfurt, Department of Hemostaseology, Frankfurt, Germany
- University Hospital Lübeck, Department of Dermatology, Lübeck, Germany
- University Hospital Mainz, Department of Cardiology/ Angiology, Mainz, Germany

Research Profile

The Division of Angiology is dedicated to a multitude of research projects to advance the field of vascular medicine. The spectrum of research ranges from fundamental research to clinical trials that comprise analysis, classification and computational hemodynamic modeling of congenital vascular malformations, stereotactic MRI-based imaging guidance techniques, risk factor analysis and risk factor modulating therapies in peripheral artery disease, endovascular treatment of peripheral artery disease, drug therapy and endovascular management of venous thromboembolism, and contrast-enhanced ultrasound imaging techniques for outcome prediction in atherosclerotic disease.

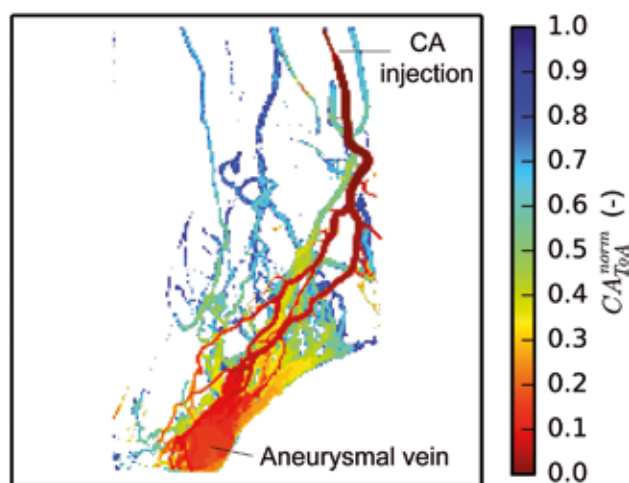
Teaching Profile

The Division of Angiology participates in University teaching programs for students of medicine and sports-/ physiotherapists. Further activities are regular student lectures and courses (clinical skills), weekly DHGE lectures, and weekly internal education in the field of vascular medicine.

Highlights 2017

Hemodynamic Characterization of Peripheral Arterio-venous Malformations (pAVMs)

In collaboration with ARTORG Center for Biomedical Engineering Research, University of Bern, Switzerland, a set of computational methods and prototype pAVM models were introduced that allow determining the hemodynamic consequences of different shunt morphologies on surrounding vascular components. The analysis of contrast agent (CA) transport through different malformation types revealed a set of diagnostic parameters (CA time of arrival, CAtoA) that show great potential in allowing an automated classification and characterization of peripheral arterio-venous malformations (pAVMs).



Use of Fondaparinux Off-Label or Approved Anticoagulants

for Management of Heparin-Induced Thrombocytopenia
Heparin-induced thrombocytopenia (HIT) is a life-threatening prothrombotic adverse drug reaction. It is caused by an antibody formation triggering complex of heparin and the positively charged, tetrameric platelet factor 4 (PF4) and leads to platelet activation and aggregation. Due to venous and arterial thromboses, the mortality rate is up to 30%. Switching to a nonheparin anticoagulant (argatroban, danaparoid, lepirudin) is mandatory for patients with strongly suspected HIT. In this multi-centre registry study we demonstrate that off-label anticoagulation with the synthetic

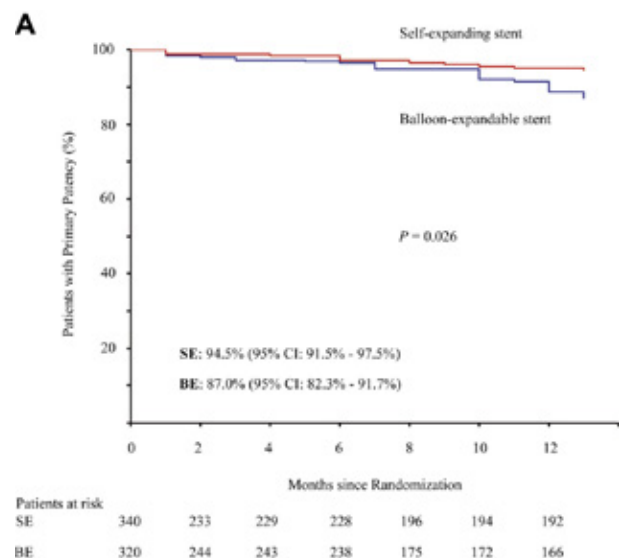
anti-factor Xa-inhibitor fondaparinux is effective to prevent venous and arterial thromboembolic complications, and safe with regard to bleeding complications when compared with the approved anticoagulants.

TABLE 7 Complications of First-Line Alternative Anticoagulation per Treatment Day*

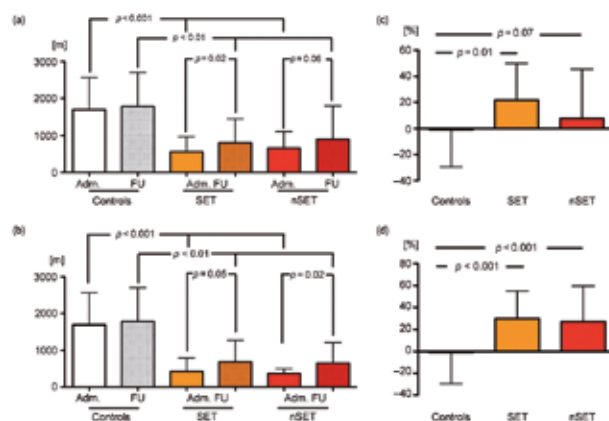
	Argatroban	Danaparoid	Fondaparinux
Treatment duration, days	7.5 (1.0-191.0)	8.0 (1.0-61.0)	4.0 (1.0-118.0)
Bleedings			
Bleeding complications	6.5	6.6	4.8†
Bleeding risk per treatment day	0.87	0.83	1.2
Thromboembolic events, arterial and venous			
Thromboembolic complications	8.7	8.2	0
Thrombosis risk per treatment day	1.16	1.03	<1.0

Values are median (range) or %. *Lepirudin was not analyzed due to the small first-line treatment group of only 4 patients. †Contains 1 bleeding event in a 92-year-old female patient with a minor nonclinically relevant bleeding from a rectal angiodysplasia with no drop in hemoglobin levels that occurred 17 days after single exposure with 1 × 5 mg of subcutaneously administered fondaparinux. No medical intervention was necessary.

Self-Expanding Versus Balloon-Expandable Stents for Iliac Artery Occlusive Disease: The Randomized ICE Trial
 Iliac artery lesions are increasingly treated endovascular. Most commonly, stents are implanted. However, no treatment recommendation on balloon-expandable stents (BE) versus self-expanding stents (SE) has been issued to date. In our randomized study we assigned 1:1 either to BE or to SE. In our follow up we found a twelve-month incidence of restenosis of 6.1% after SE and 14.9% after BE (P=0.006). Kaplan-Meier estimate of primary patency was 94.5% and 87.0%, respectively (P=0.026).



Supervised exercise training in peripheral arterial disease increases vascular shear stress and profunda femoral artery diameter



Exercise training (ET) is known to promote arteriogenesis in peripheral arterial disease (PAD) patients. It remains unclear whether supervised ET (SET) promotes arteriogenesis more efficiently than non-SET (nSET). Walking distance increased in both SET and nSET patients. However, individual changes in walking distance were higher for SET patients (p=0.01) than nSET patients (p=0.07). Our results indicate that SET promotes arteriogenesis more efficiently than nSET.

Selected Publications

- Schindewolf M, Steindl J, Beyer-Westendorf J et al. Use of Fondaparinux Off-Label or Approved Anticoagulants for Management of Heparin-Induced Thrombocytopenia. *Journal of the American College of Cardiology* 2017;70:2636-2648
- Dopheide JF, Rubrech J, Trumpp A et al. Supervised exercise training in peripheral arterial disease increases vascular shear stress and profunda femoral artery diameter. *European journal of preventive cardiology* 2017;24:178-191
- Krankenberg H, Zeller T, Ingwersen M et al. Self-Expanding Versus Balloon-Expandable Stents for Iliac Artery Occlusive Disease: The Randomized ICE Trial. *JACC Cardiovascular interventions* 2017;10:1694-1704
- Frey S, Haine A, Kammer R et al. Hemodynamic Characterization of Peripheral Arterio-venous Malformations. *Annals of biomedical engineering* 2017;45:1449-1461

Department of Ophthalmology

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Prof. Beatrice Früh
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Prof. Mathias Abegg
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Prof. Volker Enzmann
Research Laboratories

Research Partners

- ARTORG, University of Bern, Bern, Switzerland
- Dept. of Biology, University of Fribourg, Switzerland
- Dept. of Anatomy, University of Bern, Switzerland
- Schepens Eye Research Institute/Massachusetts Eye and Ear, Boston, MA, USA;
- Department of Ophthalmology, Harvard Medical School, Boston, MA, USA.
- Dept. of Ophthalmology and Visual Sciences, University of Louisville, Louisville, KY, USA
- Hôpital Ophtalmique Jules-Gonin, Université de Lausanne, Switzerland
- Lab for Retinal Cell Biology, Department of Ophthalmology, University of Zurich, Switzerland
- Augenklinik, Universitätsspital Basel, Switzerland
- Department of Ophthalmology, University Hospital Regensburg, Regensburg, Germany

Research Profile

The Department of Ophthalmology was founded in 1834 and is involved in clinical and basic research in the field of visual sciences and ophthalmology. Several clinical research groups are involved in the investigation of the pathophysiology and treatment of vitreoretinal diseases, glaucoma, neuro-ophthalmologic disorders and external disease. Clinical research includes phase I-IV studies as well as the development of new imaging modalities for retinal diseases. The Bern Photographic Reading Center (BPRC) is an internationally renowned center for coordination and independent evaluation of images obtained in clinical multicenter trials. Research projects in cooperation with the ophthalmic technology group at the ARTORG-Center explore new deep-learning approaches for image evaluation. The research groups involved in basic research use state-of-the-art molecular, cellular and imaging techniques for in vitro, cell culture, ex vivo and in vivo studies. Research projects in Experimental Ophthalmology focus on the potential of stem cells and progenitor cells in restoring visual function, in ocular immunology and the influence of the microbiome on inflammatory eye diseases, as well as on new avenues to treat them. The ophthalmogenetics group continuously strives to identify new phenotype-genotype correlations in inherited eye diseases by molecular diagnostic and to understand their impact on eye development.

Teaching Profile

The Dept. Ophthalmology participates in University teaching programs for students of medicine, biomedicine, neuroscience and biology.

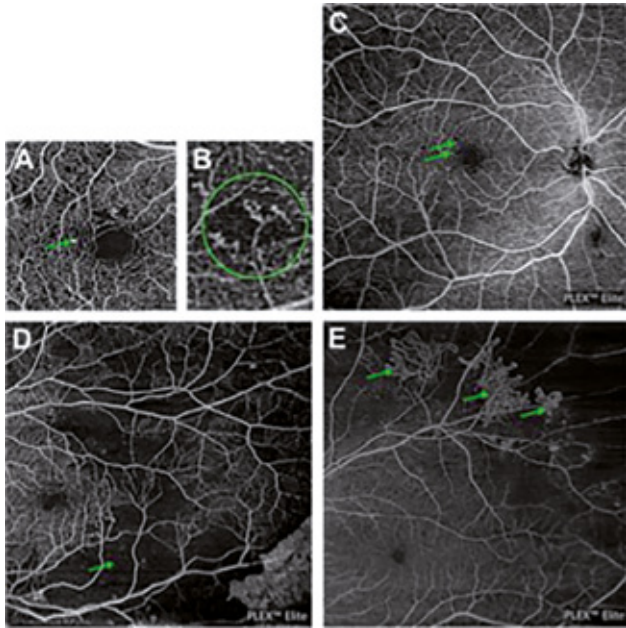
Highlights 2017

Association of the Intestinal Microbiome with the Development of Neovascular Age-Related Macular Degeneration

Age-related macular degeneration (AMD) is the most frequent cause of blindness in the elderly. There is evidence that nutrition, inflammation and genetic risk factors play an important role in the development of AMD. Recent studies suggest that the composition of the intestinal microbiome is associated with metabolic diseases through modulation of inflammation and host metabolism. To investigate whether compositional and functional alterations of the intestinal microbiome are associated with AMD, we sequenced the gut metagenomes of patients with AMD and controls. The genera *Anaerotruncus* and *Oscillibacter* as well as *Ruminococcus torques* and *Eubacterium ventriosum* were relatively enriched in patients with AMD, whereas *Bacteroides eggerthii* was enriched in controls. Patient's intestinal microbiomes were enriched in genes of the L-alanine fermentation, glutamate degradation and arginine biosynthesis pathways and decreased in genes of the fatty acid elongation pathway. These findings suggest that modifications in the intestinal microbiome are associated with AMD, inferring that this common sight threatening disease may be targeted by microbiome-altering interventions.

Vascular Abnormalities In Diabetic Retinopathy Assessed With Swept-Source Optical Coherence Tomography Angiography Widefield Imaging

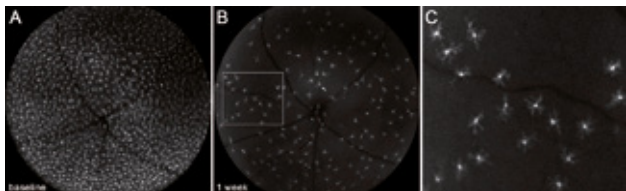
Comparison of Swept-Source Optical Coherence Tomography Angiography (SS-OCTA) widefield imaging in the detection of diabetic vascular abnormalities versus ETDRS based color fundus photograph severity grading, reveals a higher detection rate of IRMAs on SS-OCTA.



Vascular abnormalities of diabetic retinopathy in swept source optical coherence tomography angiography flow images. A Microaneurysm(s) (green arrow). B Small areas of capillary reduced perfusion with adjacent intraretinal microvascular abnormality (IRMA; green circle) C Microaneurysms (green arrows). D Areas of capillary non-perfusion (green arrow). E Neovascularization in the vitreo-retinal interface (green arrows).

Dramatic Effect of Oral CSF-1R Kinase Inhibitor on Retinal Microglia Revealed by In Vivo Scanning Laser Ophthalmoscopy

We reported sound evidence that the small molecule pharmaceutical PLX5622, a highly selective CSF-1R kinase inhibitor, crosses the blood–retina barrier and suppresses microglia activity. Members of this class of drug are in advanced clinical development stages and may represent a novel approach to modulate ocular inflammatory processes.



Ultra-widefield blue light fundus autofluorescence images at baseline (A) and after 1 week of CSF-1R kinase inhibitor treatment (B) from a representative animal. The area outlined in (B) is magnified in (C) to highlight the ramified processes typical for quiescent retinal microglia.

Selected Competitive Grants

- A pragmatic, randomized, non-inferiority trial comparing the effectiveness of Botulinum toxin-based treatment with conventional strabismus surgery in acquired esotropia SNF 331C30_173533
- Computer Assisted Selective Retina Therapy with Optical Coherence Tomography Laser Dosimetry Control. SNF 325230_163306

Selected Publications

- Schaal KB, Munk MR, Wyssmueller I, Berger LE, Zinkernagel MS, Wolf S. Vascular Abnormalities in Diabetic Retinopathy Assessed with Swept-Source Optical Coherence Tomography Angiography Widefield Imaging. *Retina*. 2017
- Dysli C, Wolf S, Berezin MY, Sauer L, Hammer M, Zinkernagel MS. Fluorescence lifetime imaging ophthalmoscopy. *Progress in retinal and eye research*. 2017;60:120-43
- Zinkernagel MS, Zysset-Burri DC, Keller I, Berger LE, Leichtle AB, Largiader CR, Fiedler GM, Wolf S. Association of the Intestinal Microbiome with the Development of Neovascular Age-Related Macular Degeneration. *Scientific reports*. 2017;7:40826
- Ebnetter A, Waldmeier D, Zysset-Burri DC, Wolf S, Zinkernagel MS. Comparison of two individualized treatment regimens with ranibizumab for diabetic macular edema. *Graefes' archive for clinical and experimental ophthalmology*. 2017;255(3):549-55
- Kokona D, Schneider N, Giannakaki-Zimmermann H, Jovanovic J, Ebnetter A, Zinkernagel M. Noninvasive Quantification of Retinal Microglia Using Widefield Autofluorescence Imaging. *Investigative ophthalmology & visual science*. 2017;58(4):2160-5

Department of Dermatology

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Prof. Christoph Schlapbach



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Prof. Robert Hunger



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Research Partners

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- Prof. A. Lanzavecchia, Institute for Research in Biomedicine, Bellinzona
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Research profile

Our Department performs basic and translational research focused on the mechanisms of inflammatory and autoimmune skin diseases as well as on the regulation of cell-cell adhesion and of cytoarchitecture. Specifically, our objectives are:

- To characterise the nature of T-helper 9 cells and their role in various diseases: atopic eczema, psoriasis, hidradenitis suppurativa and drug reactions
- To study the autoimmune response and the molecular events leading to skin blistering in pemphigus and bullous pemphigoid
- To assess the mechanisms of the interaction of plakin family members with various intermediate filaments in epithelia and striated muscle cells
- To understand how stem cells contribute to homeostasis of the skin
- To carry out clinical trials with different targeted therapies for atopic dermatitis and psoriasis

Teaching Profile

Our Department participates in various pre-graduate teaching programmes in both the Medical Faculty and the Faculty of Science. Furthermore, the Department has a close

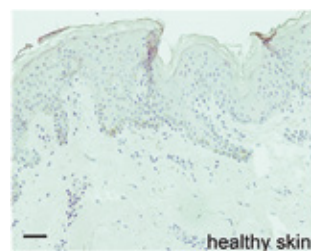
exchange with the Regional Dermatology Training Centre in Tanzania. The objective of the Centre is to promote the care of skin disease in sub-Saharan Africa as well as to provide training for young physicians. We regularly host one to three African specialists for training in dermatopathology.

Highlights 2017

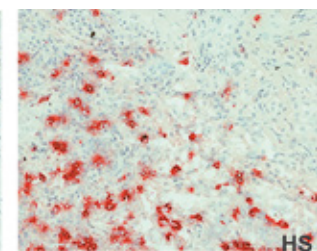
Interleukin-32 is highly expressed in cutaneous lesions of hidradenitis suppurativa

Hidradenitis suppurativa (HS) is a potential devastating chronic inflammatory skin disease. The underlying pathogenic mechanisms are poorly understood. Previous studies indicate that various pro-inflammatory cytokines like TNF- α , IL-12, IL-17, IL-23 are involved in the inflammatory reaction of HS. We have investigated tissue expression and serum levels of IL-32, a pro-inflammatory cytokine in HS patients. Our results demonstrate that IL-32 is upregulated in HS patients when compared with various controls. IL-32 was expressed by natural killer cells, T cells, macrophages and dendritic cells in the dermis. IL-32 mRNA levels in lesional HS skin correlate positively with interferon- γ and IL-17A and negatively with IL-13. IL-32 may thus represent a new therapeutic target in HS.

healthy skin

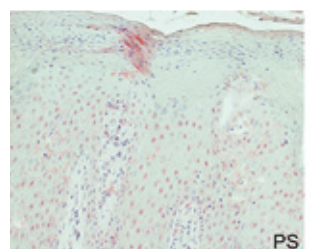


hs

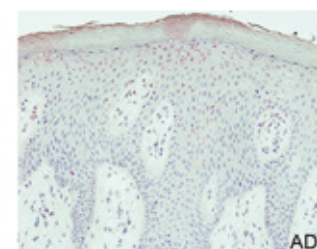


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Psoriasis



Atopic dermatitis



Immunohistochemical staining for IL-32.

Evidence of a role for eosinophils in blister formation in bullous pemphigoid

Bullous pemphigoid (BP) is an autoimmune bullous disease of the skin characterised by sub-epidermal blister formation due to autoantibodies to hemidesmosomal antigens. Our studies have provided evidence that IL-5-activated eosinophils directly contribute to BP blister formation in the presence of BP autoantibodies. Dermal-epidermal separation induced by eosinophils is dependent on adhesion and Fcγ receptor activation, requires elevated ROS production and degranulation, and involves eosinophil extracellular trap formation.

Selected Competitive Grants

- SNF Pemphigus-from pathogenesis to therapeutics (Pegasus): Epitope spreading in pemphigus (CHF 212'463; L. Borradori)
- SNF Sinergia: A One health approach to unravel novel genes and molecular pathways in dermatology (CHF: 2'493'769; E. J Müller, co-applicant)
- Swiss Personalised Health Network (SPHN) Board: Identification of biomarkers and therapeutic targets in inflammatory disease immunotherapy by high-dimensional single cell analysis and cluster proteomics (total: CHF 1'283'000, Ch. Schlapbach, co-applicant)
- Peter Hans Hofschneider Stiftungsprofessur für molekulare Medizin (Prof. Ch. Schlapbach)

Selected Publications

- Yan KX, Huang Q, Fang X, Zhang ZH, Han L, Gadaldi K, Kang KF, Zheng ZZ, Xu JH, Yawalkar N. IgE and FcεRI are highly expressed on innate cells in psoriasis. *Br J Dermatol.* 2016, 175:122-33
- Seyed Jafari SM, Shafighi M, Beltraminelli H, Geiser T, Hunger RE, Gazdhar A. Improvement of Flap Necrosis in a Rat Random Skin Flap Model by In Vivo Electroporation-Mediated HGF Gene Transfer. *Plast Reconstr Surg.* 2017, 139:1116e-1127e
- de Graauw E, Sitaru C, Horn M, Borradori L, Yousefi S, Simon HU, Simon D. Evidence for a role of eosinophils in blister formation in bullous pemphigoid. *Allergy* 2017;72:1105-1113
- Simon D, Page B, Vogel M, Bussmann C, Blanchard C, Straumann A, Simon HU. Evidence of an abnormal epithelial barrier in active, untreated and corticosteroid-treated eosinophilic esophagitis. *Allergy.* 2018;73:239-247
- Vinay K, Cazzaniga S, Amber KT, Feldmeyer L, Naldi L, Borradori L. Rituximab as first line adjuvant in pemphigus: retrospective analysis of the long-term outcomes in a single center. *J Am Acad Dermatol.* 2017 Nov 13. pii: S0190-9622(17)32689-0

Department of Diabetes, Endocrinology, Nutritional Medicine and Metabolism (UDEM)

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PD Dr. Stavroula Mouggiakakou



Dr. Roman Trepp

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- Department of Internal Medicine, Medical University of Graz, Austria
- Department of Management, Technology, and Economics, ETH Zurich
- Department of Biology, Institute of Molecular Systems Biology, ETH Zurich
- Lab of Digital Epidemiology, EPFL Campus Biotech
- Center of Laboratory Medicine, Inselspital Bern
- University Clinic for Nuclear Medicine, Inselspital Bern
- Institute of Social and Preventive Medicine (ISPM) University of Bern
- ARTORG Center for Biomedical Engineering Research, Diabetes Technology, University of Bern
- Division of Diabetes, Endocrinology and Gastroenterology, University of Manchester, UK

Research Profile

Our research groups cover the field of diabetes, endocrinology, nutrition, and metabolism. Within the framework of the recently founded Diabetes Center Bern, an important scope is the development, investigation and implication of novel technological approaches in the field (insulin pumps, glucose sensors, and artificial pancreas systems, hybrid and/or closed-loop systems) together with international collaborators and industrial partners. This is complemented by the development of alternative technical approaches to prevent diabetes and/or improve control (i.e. software applications coupled with interactive modules, deep machine learning, etc). In collaboration with our group at ARTORG and our nutritional researchers, algorithmic studies take advantage of novel computer vision technology to develop alternative ways to improve nutritional aspects (automated quantification of dietary content). Additional emphasis lies on epidemiological studies (primary prevention but also prevention of diabetic sequelae and cardiovascular complications). Additionally, our nutritional research encompasses malnutrition and nutrient supplements and a novel group led by a tenured track professor will aim at combining technological developments and novel –omics technologies in this area. Endocrine research focuses on neuroendocrine tumors, thyroid, parathyroid, and pituitary disease. Finally, metabolic research encompasses the investigation of various disease models, covering the range from type 1 diabetes to inborn errors of metabolism.

Teaching Profile

Our University clinic participates in University teaching programs for students of medicine, dental medicine, and biomedicine, additionally, we teach Master- students in Biomedical Engineering.

Highlights 2017

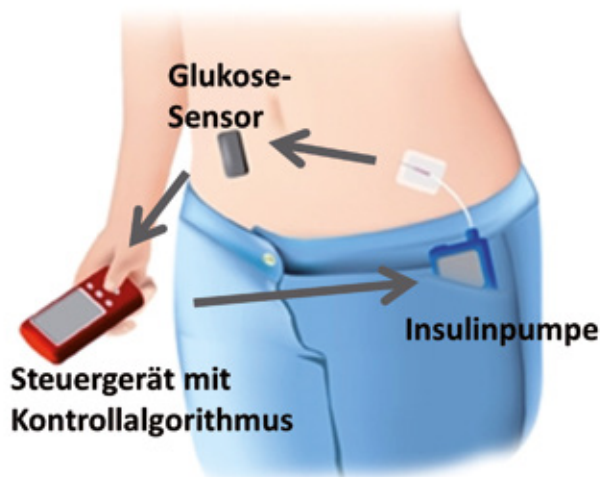
Foundation of the Diabetes Center Bern (DCB)

In summer 2017, the foundation of the novel DCB was announced thanks to a generous funding (50 million Swiss Francs) granted by Willi Michel, chairman of the board of directors of the Ypsomed Holding AG and the Ypsomed Group. The DCB is embedded within the Swiss Institute for Translational and Entrepreneurial Medicine (sitem-insel) and will be a public-private partnership initiative between UDEM and industrial partners (e.g. Ypsomed, but also novel start-up companies). The DCB aims to investigate modern diabetes-related treatment strategies, to translate promising approaches into applicable medical products, and finally to enable commercialization.

Artificial Pancreas in different Types of Diabetes mellitus

Closed-loop systems – synonymously denoted as artificial pancreas - are composed of an insulin pump, continuous glucose monitoring and a control algorithm that autonomously adjusts insulin delivery in response to real-time sensor glucose levels. In a recent study, the feasibility and effectiveness of day-and-night hybrid closed-loop insulin delivery under free-living conditions in well-controlled type 1 diabetic (T1D) adults was investigated. This pivotal study provided evidence that unsupervised day-and-night hybrid closed-loop insulin delivery was safe, well-tolerated and improved glycemic control in adult T1D patients. In a second, ongoing study we investigate the capability of fully closed-loop insulin delivery to reduce hyperglycemia in inpatient type 2 diabetic (T2D) patients. Inpatient hyperglycemia is an unmet risk-factor for increased morbidity, mortality, and length of stay and healthcare expenditures. Using a novel Model Predictive Control (MPC) algorithm developed by our research partners from the University of Cambridge, this system predicts and corrects impending glucose excursions under consideration of recent meal intakes and active insulin doses. Results from the first 100 patients have been presented at the Annual Meeting of the Swiss Endocrine Society and show a significantly increased time in target glycemia, lower glucose variations, while no increased risk of hypoglycemia was detected. The utilization of fully closed-loop

insulin delivery could, therefore, substantially improve inpatient hyperglycemia and facilitate management of T2D in hospitals, particularly shortening length of stay.



Artificial Intelligence and Computer Vision for Dietary Assessment

Together with our research group at ARTORG we introduced the first fully operative system for automatic estimation of carbohydrate content of meals using computer vision based on commercially available smartphones. In a pivotal clinical study with T1DM patients we not only demonstrated feasibility but also showed a significantly improved postprandial glycaemic control. While the current system is able to quantify carbohydrates, next generation systems will focus on additional nutrients (eg protein and fat), thereby broadening the scope towards type 2 diabetes, obesity, and general dieting.

Selected Competitive Grants

- JDRF, National Institute for Health Research Cambridge Biomedical Research Centre, Wellcome Strategic Award (100574/Z/12/Z)
- Swiss National Science Foundation (P1BEP3_165297)
- European Union Seventh Framework Programme (FP7-PEOPLE-2011-IAPP) grant agreement no. 286408
- MyTreat - 18172.1 PFLS-LS

Selected Publications

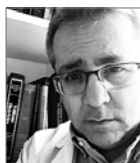
- Bally L, et al: Day-and-night glycaemic control with closed-loop insulin delivery versus conventional insulin pump therapy in free-living adults with well controlled type 1 diabetes: an open-label, randomised, crossover study. *Lancet Diabetes Endocrinol.* 2017 Apr; 5(4): 261–270. doi: 10.1016/S2213-8587(17)30001-3
- Bally L, et al: Carbohydrate Estimation Supported by the GoCARB System in Individuals With Type 1 Diabetes: A Randomized Prospective Pilot Study. *Diabetes Care.* 2017 Feb;40(2):e6-e7. doi: 10.2337/dc16-2173
- Bally L, et al: Metabolic Effects of Glucose-Fructose Co-Ingestion Compared to Glucose Alone during Exercise in Type 1 Diabetes. *Nutrients.* 2017 Feb 21;9(2). pii: E164. doi: 10.3390/nu9020164
- Aeberhard C, et al: Effect of preoperative immunonutrition on postoperative short-term outcomes of patients with head and neck squamous cell carcinoma. *Head Neck-J Sci Spec.* In Press
- Aubry E, et al: Are Patients Affected by Mitochondrial Disorders at Nutritional Risk? *Nutrition.* In Press

Department of Obstetrics and Gynecology

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Group Leader



PD Dr. Martin Müller
Group Leader



PD Dr. Marc Baumann
Group Leader



PD Dr. Andreina Schoeberlein
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Research Laboratory
Prenatal Medicine
Group Leader

Research Partners

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- Departments of Cardiology and Rheumatology, University of Bern, Switzerland
- Department of Pediatrics and Neonatology, Maastricht University, Maastricht NL
- Department of Neurosurgery and of Cellular and Molecular Physiology, Yale University, New Haven, CT, USA
- Obstetrics, Gynecology and Reproductive Sciences, Yale Medical School, Yale University, New Haven, CT, USA
- Biolncept, LLC, Cherry Hill NJ, USA
- Cryosave Inc., Pfäffikon, Switzerland

Research Profile

The Division Obstetrics and Feto-Maternal Medicine of the Department of Obstetrics and Gynecology has strong research focus in following fields of research:

- Stem cells and Neuroregeneration
- Preeclampsia
- Further clinical research fields including preterm birth, induction of labor, postpartum hemorrhage, prenatal diagnosis

Stem cells and Neuroregeneration

The mechanisms leading to injury and neuroregeneration and the potential of human umbilical cord tissue-derived stem cells (UC-MSC) for neuroregeneration are investigated. We assess the administration of MSC and exosomes derived from UC-MSC in in vitro and in vivo perinatal neuroregeneration models, with emphasis on the regulatory functions of their miRNAs cargo. Another research focus is on the development of a therapy based on preimplantation factor, which plays an important role in the embryonic development. Noninvasive routes of application protocols (e.g. intranasal) have been successfully evaluated.

Preeclampsia

We study the molecular mechanisms of preeclampsia and investigate the role of specific placental transport mechanisms in preeclampsia and test possible therapeutic approaches. We focus on the glucose and uric acid transport, since both play an essential role in preeclampsia. The mechanisms leading to the so called "fetal programming" are of special interest, since this leads to an increased incidence of cardiovascular and metabolic diseases after an intrauterine preeclampsia exposition.

Metabolic and cardiovascular complications during pregnancy and long term outcome

Increasing maternal age, the epidemics in obesity and other metabolic disorders, as well as a growing number of pregnancies conceived after assisted reproductive technology in recent years have had a significant impact on the prevalence of pregnancies complicated by preeclampsia, placental insufficiency, gestational diabetes, and prematurity. Our research focuses on diagnostic aspects, accurate risk stratification tools and novel prevention and treatment approaches. Moreover, studies on the cardiovascular function during pregnancy and postpartum will help us to better understand which women are at those increased risks and if adequate life style instructions and follow up will help at long term.

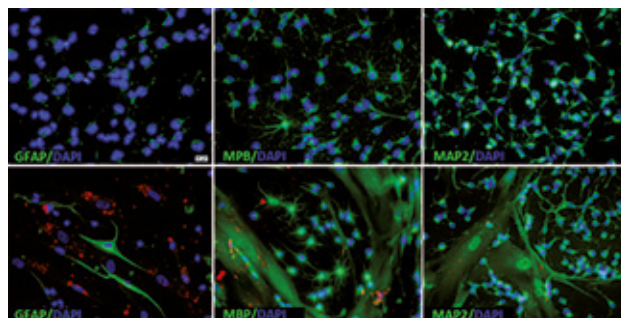
Teaching Profile

The Department is involved in clinical and preclinical teaching in medicine, biomedicine and biology at undergraduate, masters and MD or PhD levels. Our PhD students follow the training program of the Graduate School for Cellular and Biomedical Sciences. Postgraduate teaching activities includes resident and fellowship training programs.

Highlights 2017

Umbilical cord tissue mesenchymal stem cells trigger oligodendroglial differentiation in neural progenitor cells

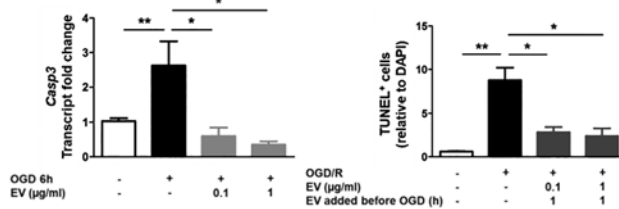
Our aim was to elucidate the possible mechanism, including cell-to-cell contact, through which differentiation in neural progenitor cells (NPC) is triggered after exposure to UC-MSC. The effect of UC-MSC on the expression of neuroglial markers in NPC was assessed in co-culture (CC), conditioned medium (CM) or transwell co-culture experiments. Their secretomes were studied by mass spectrometry. NPC showed an increased expression of glial markers after CC with UC-MSC or exposure to UC-MSC-CM. CC had a more prominent effect on the expression of glial markers



compared to CM or transwell co-cultures. A possible role in enhancing this maturation was attributed to the laminin $\alpha 2$ -subunit. Cell-to-cell contact between UC-MSC and NPC is decisive to induce oligodendrogenesis on NPC, while trophic factor secretion is sufficient to promote astrogensis.

Umbilical cord mesenchymal stem cells prevent HI-mediated programmed cell death

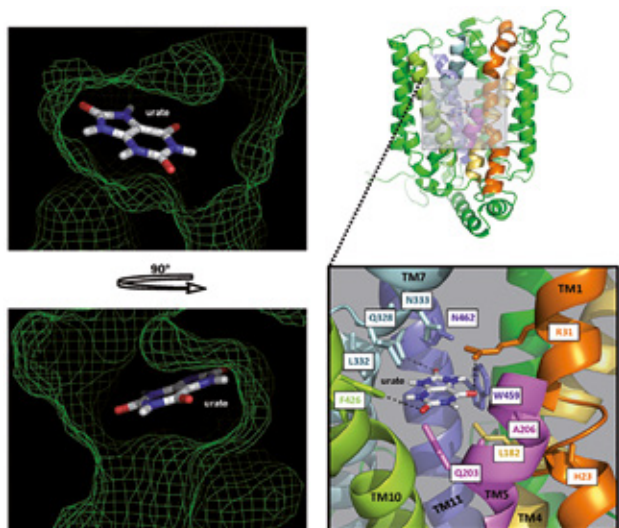
Hypoxic-ischemic (HI) insult in the perinatal phase induces apoptosis, which initiates neurodegeneration. In an in vitro model of oxygen-glucose-deprivation/reoxygenation (OGD/R) mimicking HI injury in the mouse neuroblastoma cell line neuro2a (N2a), we showed that OGD/R significantly increased DNA fragmentation and Caspase 3 (Casp3) transcription.



Apoptosis triggered by oxygen-glucose-deprivation/reoxygenation was reversed (left) or prevented (right) by UC-MSC exosomes in neuronal cells. The expression levels of the microRNAs (miR) let-7a and let-7e, known regulators of Casp3, were inversely correlated to Casp3. Their antiapoptotic effect seems to be mediated by the transfer of EV-derived let-7-5p miR.

Properties and role of Glucose transporter 9 in preeclampsia

Glucose transporter 9 (GLUT9/SLC2A9) is the major regulator of uric acid homeostasis in humans. Hyperuricemia due to impaired regulation by GLUT9 in pregnancy is closely associated with preeclampsia. We unveiled that uric acid transport mediated by the GLUT9a but not the GLUT9b splice variant is chloride-dependent. Using molecular dynamic studies, we identified two positively charged residues H23 and R31 in the N-terminal domain of hGLUT9a which can explain the observed functional differences. The N-terminal domain of GLUT9a interacts with small negatively charged ions like iodine, which might have a clinical implication in hyperuremia-associated diseases, specifically during pregnancy.



Selected Competitive Grants

- Swiss National Science Foundation (grant No. 149958)
- National Institute of Health, Small Business Technology Transfer (STTR) Program
- Gottfried and Julia Bangerter-Rhyner Foundation
- Cryo-Save AG, Pfäffikon SZ, Switzerland

Selected Publications

- Lüscher BP, Marini C, Joerger-Messerli MS, Huang X, Hediger MA, Albrecht C, Baumann MU, Surbek DV. Placental glucose transporter (GLUT)-1 is down-regulated in preeclampsia. *Placenta*. 2017 Jul;55:94-99
- Martin Mueller, Byron Oppliger, Marianne Joerger-Messerli, Ursula Reinhart, Eytan Barnea, Michael Pidas, Boris W Kramer, Daniel V Surbek, Andreina Schoeberlein. Wharton's jelly mesenchymal stem cells protect the immature brain in rats by modulating cell fate. *Stem Cells Dev*, 2017; 26:239-248
- Byron Oppliger, Marianne Joerger-Messerli, Cedric Simillion, Martin Mueller, Daniel V Surbek, Andreina Schoeberlein. Mesenchymal Stem Cells from Umbilical Cord Wharton's Jelly Trigger Oligodendroglial Differentiation in Neural Progenitor Cells through Cell-to-Cell Contact. *Cytotherapy*, 2017; 19:829-838
- Nicoletta Di Simone, Fiorella Di Nicuolo, Riccardo Marana, Rossella Castellani R, Francesco Ria, Manuela Veglia, Giovanni Scambia, Daniel Surbek, Eytan Barnea, Martin Mueller. Synthetic Preimplantation Factor (PIF) prevents fetal loss by modulating LPS induced inflammatory response. *PLoS One*. 2017;12(7): e0180642
- Mosimann B, Amylidi-Mohr S, Höland K, Surbek D, Risch L, Raio L. Importance of Timing First-Trimester Placental Growth Factor and Use of Serial First-Trimester Placental Growth Factor Measurements in Screening for Preeclampsia. *Fetal Diagn Ther*. 2017;42(2):111-116
- Endrich O, Rimle C, Zwahlen M, Triep K, Raio L, Nelle M. Asphyxia in the Newborn: Evaluating the Accuracy of ICD Coding, Clinical Diagnosis and Reimbursement: Observational Study at a Swiss Tertiary Care Center on Routinely Collected Health Data from 2012-2015. *PLoS One*. 2017 Jan 24;12(1):e0170691

Department of Geriatrics

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Prof. Andreas
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Clinical Director

Research Partners

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- Department of Orthopedics and Traumatology, University of Bern, Bern, Switzerland
- Department of Geriatrics, University of Basel, University Hospital Basel, Basel, Switzerland
- Geriatrics, University of Geneva, University Hospital Geneva, Geneva, Switzerland
- Department of Geriatrics, University of Lausanne, University Hospital Lausanne, Lausanne, Switzerland
- Department of Geriatrics, University of Zurich, University Hospital Zurich, Zurich, Switzerland
- National Institute of Gerontology and Geriatrics, Ana Aslan, Bucharest, Romania
- Department of Geriatrics and Medicine, University of Florence, Florence, Italy
- Rehabilitation Center Kliniken Valens, Valens, Switzerland

Research Profile

The Department of Geriatrics of the University of Bern was founded in 2004. The research is closely related to the clinical activities of the Geriatrics Department, with inpatient units for acute geriatrics (Spital Tiefenau), for inpatient rehabilitation (Spital Belp) and for ambulatory and co-management geriatric services (Inselspital). The main research domains involve:

- geriatric assessment in hospitalized older patients
- emergency care in older patients
- health risk assessment in healthy older people
- frailty and risk assessment in older patients
- rehabilitation in older patients

For this purpose, the Department of Geriatrics of the University of Bern collaborates closely with the Institute of Social and Preventive Medicine at the University of Bern, and conducts research projects in collaboration with clinical partners in other clinical disciplines and geriatric departments nationally and internationally.

Teaching Profile

Teaching geriatrics is one of the key missions of the Department of Geriatrics of the University of Bern. The main focus is teaching of medical students, students in medical dentistry, and postgraduate teaching of residents in internal and geriatric medicine.

Highlights 2017

Geriatric assessment in patients undergoing transcatheter aortic valve implantation

This prospective cohort comprised 330 consecutive TAVI patients ≥ 70 years who had a pre-intervention assessment of frailty. In this study we found that the assessment of frailty significantly enhances prediction of one-year mortality after TAVI compared to conventional cardiac risk scores. Based on the experience with this cohort, Geriatrics Bern is one of the key contributors to international guidelines defining the role of geriatric assessment in TAVI patients.

Regional variation of cost of care in the last 12 months of life in Switzerland

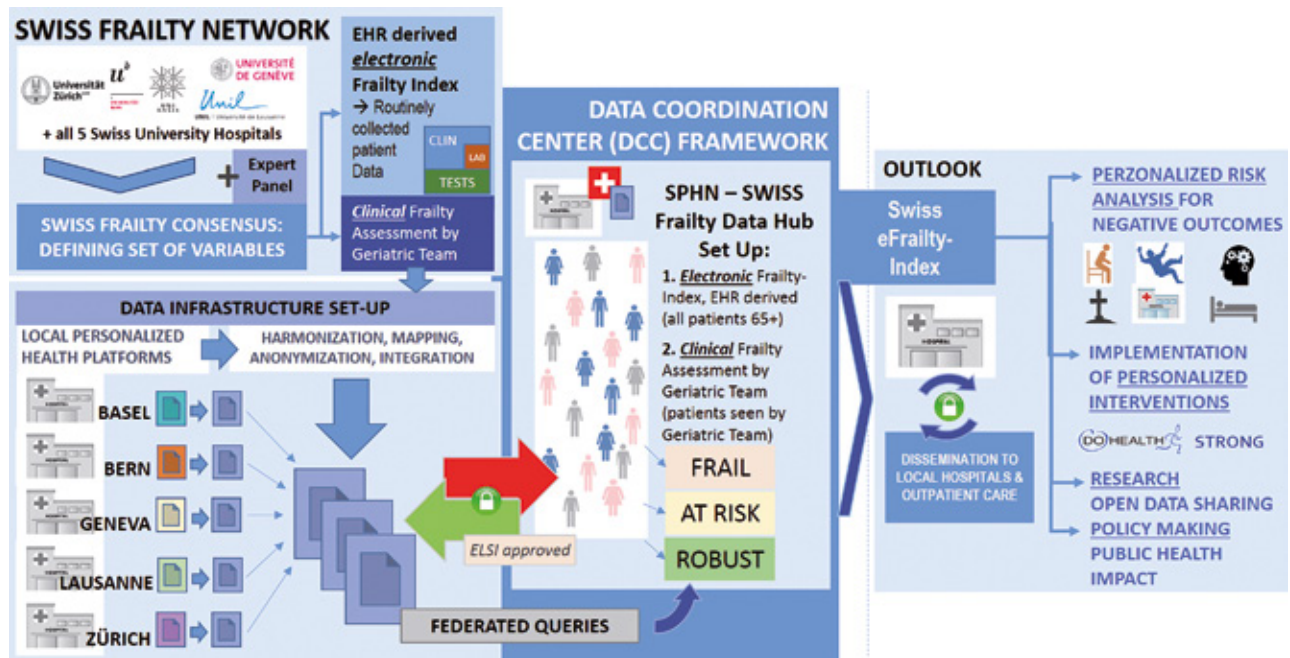
Health care spending increases sharply at the end of life. Little is known about variation of cost of end of life care between regions and the drivers of such variation. In this epidemiological study based on a large health insurance database, we found previously unknown large regional variation of cost of care during the last year of life for older women. A potential driver for this difference is a lack of consensus on post-acute care in Switzerland, a finding with major health policy implications.

Interventions to increase physical activity (PA) among older community-dwelling adults

In this randomized controlled study, we tested an updated version of health risk assessment for older persons (HRA-0), a tool developed by Geriatrics Bern in an international collaboration, in a cohort of older persons in Bucharest, Romania. We found major improvements in levels of physical activity, further evidence to support implementation of this tool in regional or national community-based programs.

Swiss Frailty Network and Repository (SFN+R)

To date, frailty is under-diagnosed in clinical care of older adults due to lack of consensus on core outcome sets. The Department of Geriatrics Bern, in collaboration with the four other University Geriatric Departments in Switzerland was successful in obtaining funds for one of seven driver projects of the Swiss Personalized Health Network. The Figure summarizes the key concept of this repository. The plan is to find a consensus on how to measure frailty, not only for patients hospitalized in the geriatric departments, but for all older patients admitted to University hospitals in Switzerland. With this approach it will be possible to add measures of frailty to personalized databases. The ultimate goals of this



project include: (1) to establish acute care treatment guidelines for senior patients at risk of or with established frailty and (2) to prevent negative frailty-related outcomes.

Selected Competitive Grants

- Swiss Personalized Health Network: Swiss Frailty Network and Repository 2018 to 2020 (Co-Investigator: CHF 1.785 Mio)

Selected Publications

- Schoenenberger AW, Moser A, Bertschi B, Wenaweser P, Windecker S, Carrel D, Stuck AE, Stortecky S. Improvement of risk prediction after transcatheter aortic valve implantation (TAVI) by combining frailty with conventional risk scores. *J Am Coll Cardiol Intv*, in press
- Ungar A, Mannarino G, van der Velde N, Baan J, Thibodeau MP, Masson JB, Santoro G, van Mourik M, Jansen S, Deutsch C, Bramlage P, Kurucova J, Thoenes M, Maggi S, Schoenenberger AW. Comprehensive geriatric assessment in patients undergoing transcatheter aortic valve implantation – results from the CGA-TAVI multicentre registry. *BMC Cardiovascular Disorders* 2018. doi.org/10.1186/s12872-017-0740-x
- Herghelegiu AM, Moser A, Prada GI, Born S, Wilhelm M, Stuck AE. Effects of health risk assessment and counselling on physical activity in older people: A pragmatic randomised trial. *PLoS One*. 2017;12:e0181371. doi: 10.1371/journal.pone.0181371. eCollection 2017
- Panczak R, Luta X, Maessen M, Stuck AE, Berlin C, Schmidlin K, Reich O, von Wyl V, Goodman DC, Egger M, Zwahlen M, Clough-Gorr KM. Regional Variation of cost of care in the last 12 months of life in Switzerland small-area analysis using insurance claims data. *Med Care* 2017;55: 155–163
- Oesch P, Kool J, Fernandez-Luque L, Brox E, Evertsen G, Civit A, Hilfiker R, Bachmann S. Exergames versus self-regulated exercises with instruction leaflets to improve adherence during geriatric rehabilitation: a randomized controlled trial. *BMC Geriatr*. 2017;17:77

Department of Hematology and Central Hematology Laboratory

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PD Dr. Nicolas Bonadies



Dr. med. & phil. nat. Michael Nagler

Research Partners

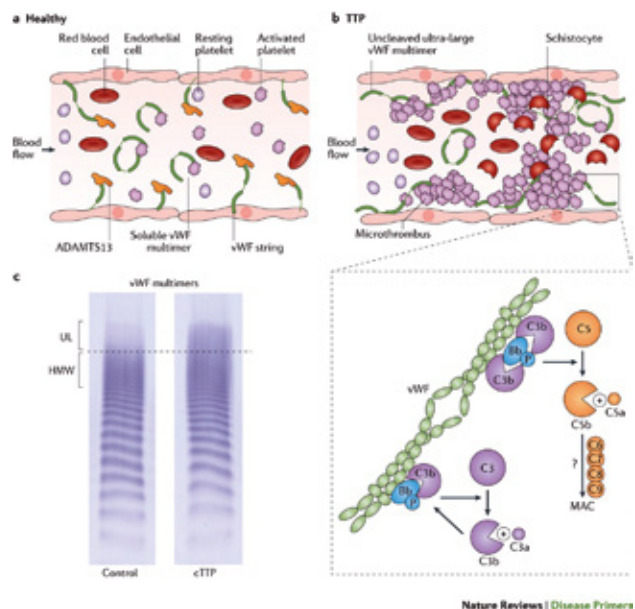
- Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland
- Contributors to the hereditary TTP registry (www.ttpregistry.net)
- Clinical Genetics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute and National Health Institute, Bethesda, USA
- Institute of Research in Immunology and Cancer, University of Montreal, Montréal, Canada
- Division of Hematology/Oncology, Boston Children's Hospital and Department of Pediatric Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, USA
- Severe Aplastic Anemia Working Party of the European Society for Blood and Bone Marrow Transplantation
- NICER Working Group
- Working Party Hemostasis of the Swiss Society of Haematology, Switzerland

Research Profile

The Department of Hematology and Central Hematology Laboratory was founded in 1965. Eight research groups are involved in the investigation of epidemiological and pathophysiological processes as well as diagnosis, prognosis and therapeutic approaches of blood-related disorders. Five of these groups are also affiliated to the Department for BioMedical Research of the University of Bern. The research spectrum comprises fundamental, translational and clinical research.

Current areas of laboratory research programs include mouse models of hematophysiology and hematopathology with their translation to human hematological disorders (Anne Angelillo-Scherrer), hematopoiesis and molecular genetics (Gabriela Baerlocher & Elisabeth Oppliger Leibundgut), hemostasis (Johanna Kremer Hovinga), inflammation and hematopoiesis (Ramanjaneyulu Allam) and precision medicine for patients with myeloid malignancies (Nicolas Bonadies).

Additional research topics are telomere biology, telomere biology in bone marrow failure syndromes and telomerase inhibition in myeloproliferative neoplasms (Gabriela Baerlocher), targeted diagnostics in hematological malignancies (Vera Ulrike Bacher), late effects after hematopoietic stem cell transplantation and cancer treatments and bone marrow failure (Alicia Rovó), thrombotic microangiopathies and Von Willebrand disease (Johanna A. Kremer Hovinga Strebel) and diagnosis, prognosis, monitoring and treatment in patients with hemostatic disorders (Michael Nagler).



Pathophysiology of thrombotic thrombocytopenic purpura. Kremer Hovinga, J. A. et al. (2017) Thrombotic thrombocytopenic purpura Nat. Rev. Dis. Primers doi:10.1038/nrdp.2017.20.

Part of the research requires access to patients registries, biobanks or cohorts to collect epidemiological data, improve and standardize diagnosis and treatment and monitor outcomes. Examples are the International hereditary thrombotic thrombocytopenic (TTP) registry (currently ~200

participants, of which ~125 are confirmed patients), the Swiss myelodysplastic syndrome (MDS) registry/biobank and The Swiss cohort of elderly patients with venous thromboembolism (SWITCO65+). Finally, part of the research occurs in the context of national and international working groups, like the Working Party Hemostasis of the Swiss Society of Hematology, the NICER Working Group, the Severe Aplastic Anemia Working Party of the European Society for Blood and Bone Marrow Transplantation and The Cardiovascular Disease and Associated Risk Factors Working Group from the National Institutes of Health Hematopoietic Cell Transplantation Late Effects Initiative.

Teaching Profile

The department participates in University teaching programs for students of medicine, dental medicine and biomedical sciences.

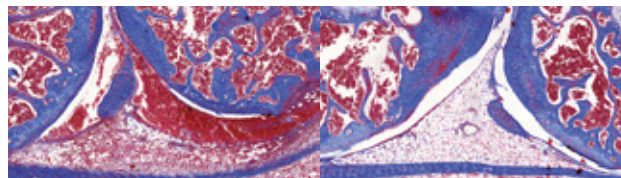
Highlights 2017

Improvement of relative survival in elderly patients with acute myeloid leukemia emerging from population-based cancer registries in Switzerland between 2001 and 2013
Acute myeloid leukemia (AML) is a hematological malignancy with increasing incidence in the elderly. We performed a population-based, observational analysis of AML cases reported to the Cantonal Cancer Registries in Switzerland. Data was aggregated by the National Institute for Epidemiology and Cancer Registration and stratified for the time periods 2001-2007 and 2008-2013. Overall, 2351 new AML cases were registered with a stable age-standardized incidence rate. This indicates that our observed raise of annual AML cases (+10.9%) is mainly related to demographic ageing and not to an increase of age-specific risks. The fraction of non-classifiable AML cases decreased over time but remained high in elderly patients, suggesting less accurate diagnostics and reporting with increasing age. 5yrs relative survival (RS) correlated with AML risk class and age, but improved only modestly overall (19.2% to 23.3%). Interestingly, we identified a significant improvement of RS in patients aged 65-74yrs (5yrs: 5.2% to 13.5%; $p < 0.001$). As surrogate for changes in management, we found an increase of allogeneic hematopoietic stem cell transplantations (1.4 to 7%) and clinical trial activities (25 to 29%) for elderly AML patients during the observation period. Thus, recent progress in management of elderly AML patients results in an improvement of survival on a population-based level in Switzerland. Therefore therapeutic nihilism is not justifiable.

Targeting anticoagulant protein S to improve hemostasis in hemophilia

Improved treatments are needed for hemophilia A and B, bleeding disorders affecting 400,000 people worldwide. We investigated whether targeting protein S (PS) could promote hemostasis in hemophilia by re-balancing coagulation. PS is an anticoagulant acting as cofactor for activated protein C and tissue factor pathway inhibitor (TFPI) making PS a key regulator of thrombin generation. Here, we report that targeting PS rebalances coagulation in hemophilia. PS gene targeting in hemophilic mice protected them against bleeding, especially when intra-articular. Mechanistically, these mice displayed increased thrombin generation, resistance to activated protein C and TFPI, and improved fibrin network. Blocking PS in plasma of hemophilia patients normalized *in vitro* thrombin generation. Both PS and TFPI were detected

in hemophilic mice joints. PS and TFPI expression was stronger in joints of hemophilia A than hemophilia B patients when receiving on demand therapy. In contrast, PS and TFPI expression was decreased in hemophilia A patients receiving prophylaxis with coagulation factor concentrates, and comparable to osteoarthritis patients. These results establish PS inhibition as both controller of coagulation and potential therapeutic target in hemophilia. The murine PS silencing RNA approach that we successfully used in hemophilic mice might constitute a new therapeutic concept for hemophilic patients.



Microscopic evaluation of the knee intra-articular space of an injured leg in F8/Pros1^{+/-} mice (hemophilia A mice) previously treated with murine protein S silencing RNA (mPS siRNA - right) or control siRNA (Ctrl siRNA - left). Arrows indicate red blood cells extravasation.

Selected Competitive Grants

- Swiss National Science Foundation (grant No. PP00P3_157486/1, 310030_153436, 314730_173127, 314730_173127), Swiss Cancer Research (Health Services Research grant, HSR-4085-11-2016)

Selected Publications

- Kremer Hovinga JA, Coppo P, Lämmle B, Moake JL, Miyata T, Vanhoorelbeke K. Thrombotic thrombocytopenic purpura. *Nat Rev Dis Primers* (2017), 3:17020
- Rovó A, Kulasekararaj A, Medinger M, Chevalier P, Ribera JM, Peffault de Latour R, Knol C, Iacobelli S, Kanfer E, Benedetto B, Maury S, Quarello P, Kob MBC, Schouten H, Blau IW, Tichelli A, Hill A, Risitano A, Passweg J, Marsh J, Dreger P, Dufour C. Association of aplastic anemia and lymphoma: a report from the Severe Aplastic Anemia Working Party of the European Society of Blood and Bone Marrow Transplantation. *Br. J. Haematol.* (2017), in press
- Schnegg-Kaufmann A, Feller A, Baldomero H, Rovó A, Manz MG, Gregor M, Efthymiou A, Bargetzi M, Hess U, Spertini O, Chalandon Y, Passweg JR, Stussi G, Arndt V, Bonadies N, and the NICER Working Group. Improvement of relative survival in elderly patients with acute myeloid leukaemia emerging from population-based cancer registries in Switzerland between 2001-2013. *Cancer Epidemiol.* (2017), 52:55-62
- Prince R, Bologna L, Manetti M, Melchiorre D, Rosa I, Dewarrat N, Suardi S, Amini P, Fernández JA, Burnier B, Quarroz C, Reina Caro MD, Matsumura Y, Kremer Hovinga JA, Griffin JH, Simon HU, Ibba-Manneschi L, Saller F, Calzavarini S, Angelillo-Scherrer A. Targeting anticoagulant protein S to improve hemostasis in hemophilia. *Blood* (2017), in press
- Studt JD, Alberio L, Angelillo-Scherrer A, Asmis LM, Fontana P, Korte W, Mendez A, Schmid P, Stricker H, Tsakiris DA, Wuillemin WA, and Nagler M. Accuracy and consistency of anti-Xa activity measurement for determination of rivaroxaban plasma levels. *J. Thromb. Haemost.* (2017), 15:1576-1583

Department of Cardiovascular Surgery

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Prof. Jürg Schmidli



Prof. Lars Englberger



Prof. Dominik Obrist



Prof. Alexander Kadner



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PD Dr. Florian Schönhoff



PD Dr. Henriette Most

Research Partners

- Microsystems Laboratory, EPFL, Lausanne
- Department of Biomedicine, University of Basel and University Hospital Basel
- Laboratoire de Signalisation et Physiopathologie Cardiovasculaire, UMR-S 1180, INSERM, Université Paris-Sud, Université Paris-Saclay, Châtenay-Malabry, France
- Molecular & Translational Cardiology, Department of Internal Medicine III, Heidelberg University Hospital, Heidelberg University, Germany
- Integrated Actuators Laboratory - Zentrum für künstliche Muskeln. EPFL Lausanne, Microcity Neuchâtel
- Fachhochschule für Ingenieurwissenschaft, Biel

Research Profile

With research activities in fundamental, technical, engineering and clinical domains, the Department of Cardiovascular Surgery is well positioned to make important contributions in the cardiovascular field. The close collaborations between clinicians and scientists foster translational approaches and provides a particular enriching research and educational environment. One key objective of our pre-clinical research concerns the development of strategies to optimize cardiac graft quality with donation after circulatory death. With specifically designed research models, we have identified clinically applicable approaches to limit graft damage and aid in the evaluation of graft suitability for transplantation.

With respect to clinical research, the Department of Cardiovascular Surgery has long been a center of excellence in Europe with a special expertise in diseases of the aorta. More than 450 thoracic, abdominal and thoraco-abdominal procedures are performed yearly, making it by far the largest center in Switzerland. Patients are referred from all over Switzerland and abroad. Research is an integral part of our effort to deliver optimal patient care. With the large, interdisciplinary, Marfan clinics, we are at the forefront of bench-to bedside developments and are actively investigating various aortic aneurysm etiologies.

Teaching Profile

Members of the Department of Cardiovascular surgery participate in University teaching at multiple levels. We provide clinical training and course lectures for both undergraduate and graduate students. In addition, we supervise and mentor students completing their Master's degrees, MD Dissertations, or PhD degrees.

Highlights 2017

Clinical research

One main focus in aortic medicine was the in-depth analysis of acute aortic syndromes. The term "acute aortic syndrome" is used to refer to patients presenting with aortic dissection, intramural hematoma and penetrating aortic ulcer. Although a large number of patients is affected, the prognosis of intramural aortic hematoma beyond the first year of diagnosis remained largely unknown. Patients with intramural hematoma followed at our institution over the past 12 years demonstrated surprisingly low rates of long-term aortic complications, whereas all-cause mortality was substantial and interventions after the first year were rarely necessary.

In another study, we analyzed data from a large patient cohort undergoing surgery on the aortic arch. In a collaborative effort comprising 37 large, aortic centers in 12 countries, we investigated different techniques of aortic arch replacement. As the large number of patients allowed for extensive propensity score matching we were able to identify procedural risk factors for stroke and mortality. International registries maintained by the International Aortic Arch Study group are important tools to gather information on these highly invasive aortic procedures help clarify indications.

We collaborated in a successful Horizon 2020 (The European Union Framework Programme for Research and Innovation) grant proposal entitled "Paraplegia Prevention in Aortic Aneurysm Repair by Thoracoabdominal Staging with 'Minimally Invasive Segmental Artery Coil-Embolization': A Randomized Controlled Multicentre Trial". This trial aims to reduce the incidence of spinal cord injury through staged occlusion of segmental arteries, thereby stimulating the growth of collateral arterial networks and enhancing blood supply to the spinal cord. The trial is anticipated to start in March 2018.

Experimental research

Heart transplantation remains the gold standard for improving quality of life and survival in patients with advanced heart failure, but graft supply is insufficient to meet the need for all patients. Donation after circulatory death (DCD) could improve donor heart availability; however, the inevitable period of warm ischemia prior to graft procurement raises concern about graft damage. We recently reported that high levels of fatty acids immediately prior to global warm ischemia, as would be expected in DCD, lead to a

50% reduction in contractile graft recovery compared to no-fat conditions. Thus, the effects of pre-ischemic fat levels should be addressed in all clinical situations involving cardiac ischemia.

Construction of 3D-heart-models through rapid prototyping
Cardiac malformations can present with complex anatomy and high variability. In order to accurately plan and perform interventional and surgical treatments of congenital heart disease, a profound understanding of the spatial relationships of cardiac structures is required. In collaboration with the ARTORG Centre for Biomedical Engineering Research, we are developing 3D modeling techniques to plan surgical interventions, represent complex anatomical structures, illustrate surgical methods for education of students and surgeons and develop personalized implants. Within this proposed work, a collection of high-quality virtual and physical models, of hearts with CHD is to be developed and made publicly available. The collection, which will be constructed from state-of-the-art, multimodal cardiac imaging, will aim to provide physicians with representative, tangible and interactive models that can supplement traditional teaching techniques. By improving the quality and public accessibility of heart models, it is believed that training and education quality will consequently be increased.



Construction of 3D-heart-models through rapid prototyping.

Selected Competitive Grants

- A collaborative platform for artificial muscles (together with EPFL, Nanocity), Siemens Stiftung CHF 12 Mio.
- Prevention of paraplegia in thoraco-abdominal aneurysmsPAPA-ARTiS, EU Horizon 2020 EUR 250'000
- Mycotic aortic aneurysms and aortic graft infections, INSEL Gruppe grant 2016-2018: CHF 75'000
- A publicly available collection of virtual and physical 3D models of congenital heart defects for surgical planning and training, Schweizerische Herzstiftung, CHF 96'000

Selected Publications

- Bockeria L, Svanidze OI, Kim A, Shatalov K, Makarenko V, Cox M, Carrel T (2017). Total cavopulmonary connection with a new bioabsorbable vascular graft: First clinical experience. *J Thorac Cardiovasc Surg*, 153(6): 1542-1550
- Franzone A, Pilgrim T, Arnold N, Heg D, Langhammer B, Piccolo R, Roost E, Praz F, Räber L, Valgimigli M, Wenaweser P, Jüni P, Carrel T, Windecker S, Stortecky S (2017). Rates and predictors of hospital readmission after transcatheter aortic valve implantation. *Eur Heart J*, 38(28): 2211-2217
- Jahren SE, Winkler B, Heinisch PP, Wirz J, Carrel T, Obrist D (2017). Aortic root stiffness affects the kinematics of bio-prosthetic aortic valves. *Interactive Cardiovasc Thorac Surg*, 24(2): 173-180
- Niederberger P, Farine E, Arnold MR, Wyss RK, Sanz-Garcia MN, Méndez CN, Gahl B, Fiedler GM, Carrel T, Tevaearai H, Longnus S (2017). High pre-ischemic fatty acid levels decrease cardiac recovery in an isolated rat heart model of donation after circulatory death. *Metabolism*, 71:107-117
- Perlman G, Praz F, Puri R, Ofek H, Ye J, Philippon F, Carrel T, Pibarot P, Attinger A, Htun NM, Dvir D, Moss R, Campelo-Parada F, Bédard E, Reineke D, Moschovitis A, Lauck S, Blanke P, Leipsic J, Windecker S (2017). Transcatheter Tricuspid Valve Repair With a New Transcatheter Coaptation System for the Treatment of Severe Tricuspid Regurgitation: 1-Year Clinical and Echocardiographic Results. *JACC. Cardiovascular Interventions*, 10(19):1994-2003
- Weiss S, Tobler EL, von Tengg-Kobligk H, Makaloski V, Becker D, Carrel T, Schmidli J, Wyss T (2017). Self Made Xeno-pericardial Aortic Tubes to Treat Native and Aortic Graft Infections. *Eur J Vasc Endovasc Surg*, 54(5): 646-652

Department of ENT, Head and Neck Surgery

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Director and
Chairman



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Audiology



Prof. Eberhard Seifert
Head of Phoniatriy



Prof. Dominique Vibert
Head of
Neurootology



PD Dr. Roland Giger
Deputy Director



PD Dr. Georgios Mantokoudis
Head of
Cochlea-Implants



Dr. Wilhelm Wimmer
Head of Hearing
Research
Laboratory

Research Partners

- ARTORG Center, ISTB, University of Bern, Switzerland
- Department for BioMedical Research (DBMR)
- Neuroradiology, Nephrology, Radiology, Vascular surgery University Hospital, Bern, Switzerland
- Department of Otorhinolaryngology, University Hospital of Zurich, Switzerland
- Nottingham Hearing Biomedical Research Unit, University of Nottingham, UK
- CAScination AG, Bern, Switzerland
- MED-EL GmbH, Innsbruck, Austria
- Cochlear AG, Basel, Switzerland
- Cendres+Métaux SA, Biel/Bienne, Switzerland
- Bernafon/Oticon A/S, Smørum, Denmark
- Sonova AG, Stäfa, Switzerland

Research Profile

The Department of ENT, Head and Neck Surgery is developing and integrating new technologies that aim to improve patient care. Projects at our center encompass areas such as oncology in ENT or vestibular loss, but major emphasis lies in projects centered around the ear, hearing and the treatment of hearing loss. In a collaborative effort with the Hearing Research Laboratory at the ARTORG Center, our research activities aim to provide innovative technology to help hearing impaired patients and to assist clinicians in the diagnosis and treatment of hearing pathologies. The range of projects includes cochlear implantation, tinnitus, spatial hearing and hearing through bone conduction and involves preclinical studies, anatomical studies, and the conduction of clinical trials with patients.

Teaching Profile

Besides training of young ENT surgeons on a daily basis and in internal courses, a number of university courses are taught by the members of our department:

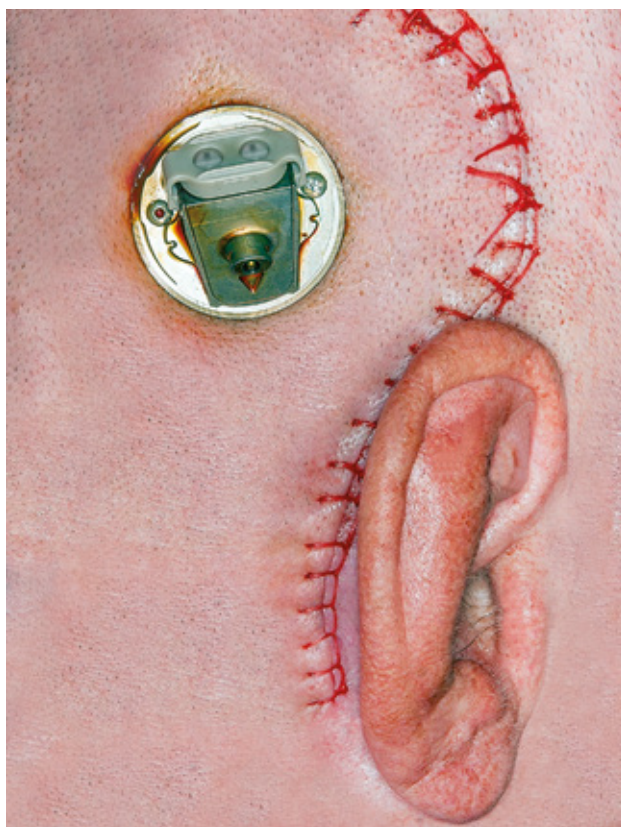
- Courses (lectures) in ENT for medical students
- Course (lectures) in biomedical acoustics
- Clinical skills in ENT for medical students
- Course (lectures) on ENT for dentists
- Course (lectures) on Phoniatriy for speech therapists (University of Fribourg)
- Course (lectures) on speech fluency disorders for speech therapists (University of Fribourg)
- Course (lectures) on audiology for speech therapists (University of Fribourg)

Highlights 2017

Worldwide Leading Role for Clinical Integration of Innovative Technology developed at the University and University Hospital, Bern, Switzerland

The Department of ENT, Head and Neck Surgery is taking the responsibilities required to develop and evaluate new disruptive clinical technologies. Our modern infrastructure and well-trained employees enable a safe and efficient clinical integration of complex workflows.

In our operating rooms, two technologies are undergoing the world wide's first clinical evaluations: the **Bone-Anchored Port (BAP)** and **Robotic Cochlear Implantation (RCI)**. BAP is a long-term vascular port for hemodialysis that is implanted in the temporal bone. To date, 4 patients underwent BAP surgery in our department. RCI is a minimally invasive technology that enables a patient-specific surgical access to the inner ear for cochlear implantation. As one of

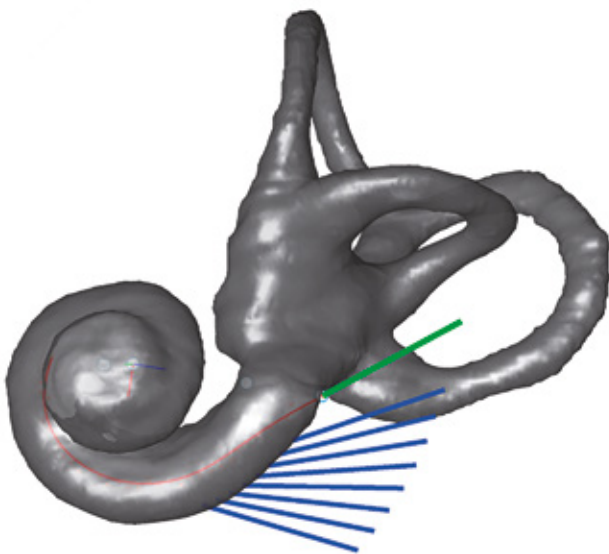


Bone-Anchored Port (BAP) surgery.



Robotic Cochlear Implantation.

the early adopters of computer-assisted procedures, our department together with the ARTORG Center were the main driving forces to advance the development of BAP and RCI. In the last year, 6 patients were successfully implanted using the RCI method.



Computation of optimal insertion trajectories for patient-specific cochlear implantation.

Novel Approaches in Experimental Audiology

To enable a more realistic but reproducible testing of patients with hearing disorders, we investigate new methods for sound field audiometry. The aim is to generate dynamic sound environments for the simulation of everyday life situations. Patients can be tested before and after their treatment and different treatment options can be compared. Figure 3 shows a set-up (in development) for the testing of sound localization and speech understanding in diffuse, uncorrelated noise. Another ongoing project focuses on cochlear implants, i.e. devices for persons with profound hearing loss, which stimulate the inner ear electrically. Our aim is to understand the electrical current spread during stimulation in cochlear implants and to improve speech recognition in noisy conditions.



Multi speaker set up for sound field audiometry.

Improved Tinnitus Diagnosis

Tinnitus is the perception of sound in the absence of an external acoustic stimulus. Severe forms of tinnitus can substantially impair quality of life. Although often originating from inner ear damage, most types of tinnitus are maintained in their chronic form by abnormal neuronal activity. Objective tinnitus assessment could be enabled by identification of neuronal correlates in Electroencephalography (EEG). Our research project aims to gain new insights into the behavior of tinnitus and to potentially improve clinical tinnitus assessment and classification by statistical approaches and computational modelling.

Selected Competitive Grants

- Eurostars-2, EU Horizon 2020 and Eureka (E! 11597 RCI)
- Commission for Technology and Innovation CTI (26132.1 PFSATW-ES)
- CTU-Forschungs-Grant 2017

Selected Publications

- Caversaccio M, Gavaghan K, Wimmer W, Williamson T, Ansò J, Mantokoudis G, Gerber N, Rathgeb C, Feldmann A, Wagner F, Scheidegger O, Kompis M, Weisstanner C, Zoka-Assadi M, Roesler K, Anschuetz L, Huth M, Weber S. Robotic cochlear implantation: surgical procedure and first clinical experience. *Acta Otolaryngol* 137(4):447-454 (2017)
- Kompis M, Wimmer W, Caversaccio W. Long term benefit of bone anchored hearing systems in single sided deafness. *Acta Otolaryngol* 137: 398-402 (2017)
- Mantokoudis G, Koller R, Guignard J, Caversaccio M, Kompis M, Senn P. Influence of Telecommunication Modality, Internet Transmission Quality, and Accessories on Speech Perception in Cochlear Implant Users. *J Med Internet Res* 24;19(4):e135. (2017)
- Perny M, Solyga M, Grandgirard D, Roccio M, Leib SL, Senn P. Streptococcus pneumoniae-induced ototoxicity in organ of Corti explant cultures. *Hear Res* 2017;350:100-109
- Wimmer W, Kompis M, Stieger C, Caversaccio M, Weder S: Directional microphone contralateral routing of signals in cochlear implant users: a within-subjects comparison. *Ear Hear* 38(3):368-373 (2017)

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Research Partners

- Institute for Infectious Diseases, University of Bern, Bern, Switzerland
- Swiss Centre for Antibiotic resistance, Anresis
- Swiss HIV Cohort Study
- Institute for Social and Preventive Medicine, University of Bern, Bern, Switzerland
- leDEA, International Epidemiology Databases to Evaluate AIDS, National Institute of Health, Bethesda, USA
- Swissnoso, Nationales Zentrum für Infektionsprävention
- Swiss Transplant Cohort Study
- Funginos, Fungal Infections Network of Switzerland
- EUROSIDA
- Swiss Tropical and Public Health Institute, Basel, Switzerland
- Liver Center, Dpt. Visceral Surgery and Medicine, Inselspital, Bern, Switzerland
- Kirby Institute, Sydney, Australia

Research Profile

Being part of the Bern University Hospital our research focuses on clinical aspects and epidemiology of infectious diseases. Lab facilities are in the partner Institute for Infectious Diseases (IFIK). We conduct collaborative research involving the entire spectrum of infectious diseases with our clinical partners within the Insel Group.

HIV infection is one of our main areas of research. We lead many research projects within the framework of the Swiss HIV Cohort Study and international collaborations. Main focuses are HIV/ Hepatitis co-infections, both in the European and the African context, opportunistic infections, HIV-infection in pregnancy and migration and HIV. Locally and in international collaborations, we investigate incidence, course and treatment of infectious diseases in people who inject drugs, fungal infections and antimicrobial drug resistance.

The infection prevention unit has a focus on healthcare-associated infections and conducts research partnering with a number of clinical specialties of the Insel Group and

collaborates with IFIK and the external surveillance systems Anresis and Swissnoso. Study designs range from qualitative research to clinical trials on to large data analyses. Together with our partner IFIK we are active in clinical and microbiological research on bacterial resistance.

Teaching Profile

The department is in charge of the teaching program Infectious Diseases for students in medicine, mainly in the master study part, but also participates in the bachelor part. We are actively involved in clinical skills training and problem based learning modules. Medical students can spend practical months in our department in the Wahlstudienjahr. We are involved in teaching programs of Dental Medicine and Biomedicine and Biology.

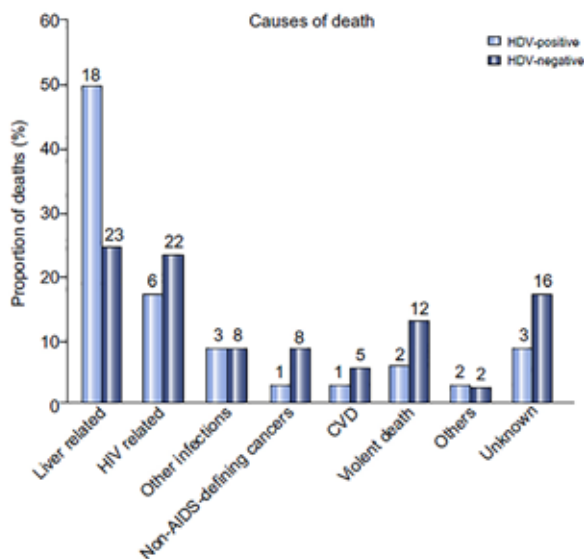
Our department is accredited for postgraduate education for medical specialisation in Infectious Diseases and Tropical Medicine.

Highlights 2017

Burden of hepatitis delta virus (HDV) and Hepatitis C in HIV-infected populations

In the SHCS, we showed that HDV infection, which affects 10% of individuals with chronic hepatitis B infection, was a strong risk factor for HCC, liver-related death and overall mortality (Figure, Béguelin et al. J Hepatol 17). Tenofovir-containing antiretroviral therapy, which is highly potent in suppressing HBV, did not have a significant impact on HDV viral load (Béguelin et al. Clin Infect Dis 17). In light of these results, it was important to assess the prevalence of active HDV infection in HIV cohorts in sub-Saharan Africa, a region severely affected by the HBV epidemic. We found only two patients (3%) with anti-HDV antibodies in Zambia, and no patient from an HIV/HBV-coinfection cohort in Tanzania had a replicating HDV infection (Vinikoor et al. Clin Infect Dis 17, Winter et al. Int J Infect Dis 16). In the fields of HCV infection, we recently described the rapidly changing trends in treatment uptake and efficacy and impact on liver fibrosis (Béguelin et al, Liver International 2017). Two related

mathematical modelling studies demonstrated the role of risk behavior and treatment-as-prevention to curb the HCV epidemic in HIV-infected individuals [Salazar et al, J Viral Hepatitis 2017, Hepatology 2016].



Outbreak investigation

In 2016, the infection prevention unit was commissioned by the FOPH to organize a nationwide outbreak investigation when it became clear that multiple cantons had seen cases of *Burkholderia cepacia* complex infection, an environmental bacteria prone to cause outbreaks. The recently published article displays nicely how a cosmetic product used in many hospitals was identified to be the source of the outbreak and that it had been contaminated at the production site (Sommerstein et al, Eurosurveillance 2017).

Optimising perioperative prophylaxis

In a collaboration with cardiac surgery, the introduction of a dual perioperative antibiotic prophylaxis targeting a common cause of sternal wound infections, coagulase-negative staphylococci, was shown to have a significant impact on the infection rate (Reineke et al, Eur J Cardiothor Surg 2017).

Selected Competitive Grants

- SNF 324730-146143: Understanding and Predicting the Hepatitis C Epidemic in HIV-infected Patients, A. Rauch
- SNF 324730_149792: Opportunistic Infections in the Era of combination ART: Collaborative Analysis of European HIV Cohort Studies; H. Furrer
- SNF Marie Heim Vögtlin PMPDP3_171259: Clinical Impact and Evolution of AmpC Producers under Selective Pressure of Different Antimicrobials: a Molecular Analysis to Predict Risk Factors for Cephalosporin Resistance and to Evaluate the Best Antibiotic Treatment Strategy, B. Babouee Flury
- SNF Ambizione-PROSPER fellowship PZ00P3_154730/PZ00P3_177118: HIV and viral hepatitis co-infection: informing management strategies through dedicated cohort studies in sub-Saharan Africa and Switzerland, G Wandeler
- SNF #148522 Swiss HIV Cohort Study and Swiss Mother and Child HIV Cohort Study. A. Rauch and H. Furrer co-applicants

Selected Publications

- Béguelin C, Moradpour D, Sahli R, Suter-Riniker F, Lüthi A, Cavassini M, Günthard HF, Battegay M, Bernasconi E, Schmid P, Calmy A, Braun DL, Furrer H, Rauch A, Wandeler G; Swiss HIV Cohort Study. Hepatitis delta-associated mortality in HIV/HBV-coinfected patients. *J Hepatol*. 2017;66(2):297-303
- Vinikoor MJ, Sinkala E, Chilengi R, Mulenga L, Chi BH, Zyambo Z, Hoffmann CJ, Saag MS, Davies MA, Egger M, Wandeler G. Impact of antiretroviral therapy on liver fibrosis among HIV-infected adults with and without HBV coinfection in Zambia. *Clin Infect Dis*. 2017 May 15;64(10):1343-1349
- Veit O, Domingo C, Niedrig M, Staehelin C, Sonderegger B, Delphine H, Stoeckle M, Calmy A, Schiffer V, Bernasconi E, Flury D, Hatz C, Zwahlen M, Furrer H; Swiss HIV Cohort Study. Long-term immune response to yellow fever vaccination in HIV-infected individuals depends on HIV-RNA suppression status: Implications for vaccination schedule. *Clin Infect Dis*. 2017 Nov 11, ahead of print
- Buetti N, Atkinson A, Marschall J, Kronenberg A. Incidence of bloodstream infections: a nationwide surveillance of acute care hospitals in Switzerland 2008-2014, *BMJ Open* 2017;7(3):e013665
- Lo Priore E, Fliedner M, Heverhagen J, Novak U, Marschall J. The role of a surveillance programme for introducing peripherally inserted central catheters: a 2-year observational study in an academic hospital. *Swiss Med Wkly* 2017;147:w14441

Department of Intensive Care Medicine

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Sandra Pfister Clinic Manager	Matthias Theis Nursing Manager	Brigitte Hämmerli Head of IIMC Nursing Deputy Nursing Manager	Prof. Jukka Takala Director and Chief Physician	Prof. Stephan Jakob Chief Physician IIMC Head of Research	Felix Zürcher Head of Logistics
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Research Partners

- Center for Research in Intensive Care (CRIC), Copenhagen, Denmark, Prof. Dr. M. Moller, Prof. Dr. A. Perner
- ANZIC Clinical Trials Group, Australia and New Zealand
- Helsinki University Hospital, Helsinki, Finland, Prof. V. Pettilä
- Universitätsspital Basel, Basel, Schweiz, PD. Dr. M. Siegemund
- ETH Zürich, EPFL Lausanne, Switzerland
- Medical University of Graz, Vienna, Austria, Prof. Dr. K. Amrein
- Charité University Medicine Berlin, and Goettingen University, Germany, Prof. Dr. W. Doehner and Prof. Dr. Dr. von Haehling, Cachexia Research Groups
- Charité Center of Excellence for Cardiac Arrest, Berlin, Germany, Prof Dr. C. Storm

Research Profile

Key objective of our research group is to advance the pathophysiological understanding of critical illness and associated (multiple) organ failure. Numerous clinical trials including international multicenter trials are currently performed. Experimental research projects include animal models particularly on the pathophysiology of circulatory and pulmonary function. Such experimental research is performed in the Experimental Surgery Unit (ESI) of the Department for BioMedical Research (DBMR) of the University of Bern. Additional research objective embrace other projects to increase clinical treatment quality and organizational aspects of intensive care medicine.

Teaching Profile

The department provides training for the full spectrum of training for Intensive Care Medicine. This includes training to qualify as a specialist, training for medical students, advanced training for specialist nurses to qualify as certified experts in intensive nursing (NDS HF), and training for individuals to become professional healthcare assistants. A broad spectrum of educational methods including simulator-based training are performed. Echocardiography, Sonography and ECMO training is provided for intensive care medicine professionals.

Selected Competitive Grants

- Silico prediction of phage-bacteria infection models (Prof. Y.-A. Que), Swiss National Fonds (SNF, 915T CHF)
- Comet-AKI trial (supported by the "NEXT" grant, European Society of Intensive Care, ESICM; 40T CHF, Co-Applicant Prof. Dr. J. C. Schefold)
- Hypertonic Saline for Fluid Resuscitation after Cardiac Surgery (HERACLES trial) Dr. C. Pfortmueller (Swiss Heart Foundation, Novartis, B. Braun 147 TCHF)
- SPHN Swiss personalized Health Network (Prof. Dr. S. Jakob, Co-Recipient, 2.3 Mio CHF)

Selected Publications

- Bloch A, Tomaschett C, Jakob SM, Schwinghammer A, Schmid T. Compression sonography for non-invasive measurement of lower leg compartment pressure in an animal model. *Injury*. 2017
- Bloch A, Glas M, Kohler A, Baumann U, Jakob SM. Non-Invasive Assessment of Intra-Abdominal Pressure Using

Ultrasound Guided Tonometry – a Proof-of-Concept Study.
Shock. Published Ahead of Print

- Synergistic Interaction Between Phage Therapy and Antibiotics Clears *Pseudomonas Aeruginosa* Infection in Endocarditis and Reduces Virulence. Oechslin F, Piccardi P, Mancini S, Gabard J, Moreillon P, Entenza JM, Resch G, Que YA. *J Infect Dis.* 2017 Mar 1;215(5):703-712
- Schefold JC, Berger D, Zürcher P, Lensch M, Perren A, Jakob SM, Parviainen I, Takala J. Dysphagia in Mechanically Ventilated ICU Patients (DYnAMICS): A Prospective Observational Trial. *Crit Care Med.* 2017 Dec;45(12):2061-2069
- Moller PW, Winkler B, Hurni S, Heinisch PP, Bloch A, Sondergaard S, Jakob SM, Takala J, Berger D. Right atrial pressure and venous return during cardiopulmonary bypass. *Am J Physiol Heart Circ Physiol.* 2017 Aug 1;313(2):H408-H420

Department of Cardiology

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Prof. Thomas Pilgrim



Prof. Lorenz Räber



Prof. Marco Valgimigli



Prof. Stephan Windecker

Research Partners

- Clinical Trials Unit, University of Bern
- Departments of Cardiology at the University Hospitals Zurich, Basel, Fribourg, Lausanne and Geneva

Research Profile

The Department of Cardiology at Bern University Hospital has a broad range of clinical research activities that encompass investigation of devices for the minimal-invasive, percutaneous treatment of coronary artery disease and valvular heart disease, pharmacological studies on antithrombotic drugs to prevent thromboembolism and lipid-modifying drugs for cardiovascular risk reduction. The teams are involved in large scale, multicenter, international, randomized clinical trials as well as in first-in-man human studies using novel innovative products. The research group has well established national and international partnerships.

Teaching Profile

The Department of Cardiology participates in University teaching programs for medicine students.

Highlights 2017

Cardiovascular manifestations commonly arise from atherosclerotic plaque rupture that produces platelet activation, thrombus formation and reduction of blood flow to the heart or brain. Antithrombotic therapy is central to prevent blood clot formation and constitutes an essential component of therapy in the field of cardiology. Recently, we developed a simple five-item risk score, which provides a standardized tool for the prediction of out-of-hospital bleeding while on dual antiplatelet therapy, see Figure 1 (www.precisedaptscore.com). As an important aspect for any treatment strategy is the long-term potential for harm, ongoing trials are focusing on different duration and composition of antithrombotic therapies among patients at high-risk of bleeding, among patients with atrial fibrillation requiring concomitant antiplatelet and anticoagulant therapy, and among patients undergoing transcatheter aortic valve replacement for aortic stenosis.

Since the first successful use of a balloon catheter in 1977, researchers worldwide have been searching for the ideal stent for treatment of constricted coronary vessels. Great hopes were placed on scaffolds made of lactic acid which completely dissolve within three to four years. Yet, studies show that very late thrombosis occurs more frequently after implantation of bioresorbable scaffold than with conventional drug-eluting stents. Using catheter imaging technique (optical coherence tomography), the mechanisms underlying

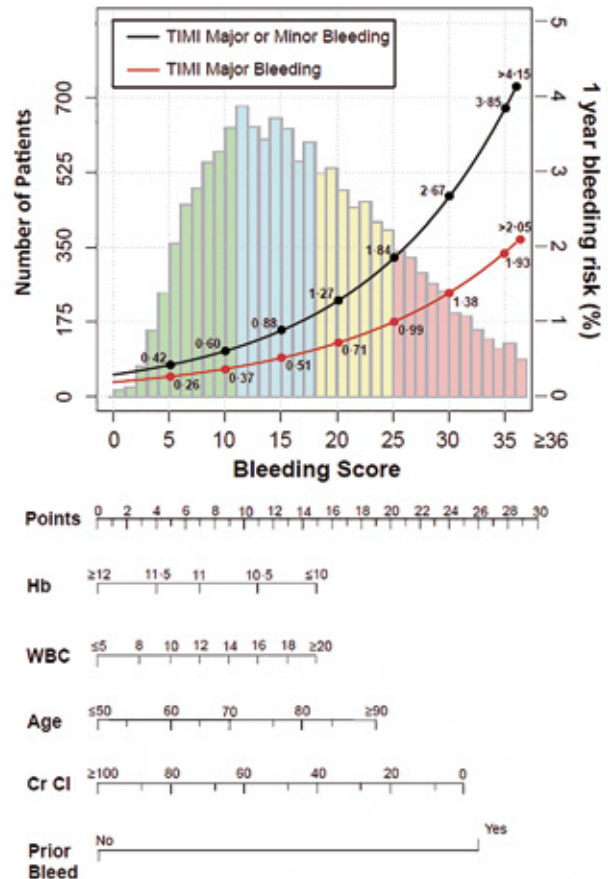


Fig. 1: Prediction of out-of-hospital bleeding while on dual antiplatelet therapy (Lancet 2017).

these complications could be elucidated. Scaffold discontinuity, which suggests an unfavorable resorption-related process, followed by malapposition and neoatherosclerosis were identified as the leading mechanism leading to very late scaffold thrombosis.

Transcatheter Aortic Valve Replacement (TAVR) represents an alternative treatment strategy for patients with severe aortic valve stenosis at increased risk for surgical aortic valve replacement. Refinements in device technology, improved imaging and streamlining of the procedure resulted in a decline in peri-procedural complications, and prepared the ground for the expansion of TAVR to intermediate and low risk patients. In a meta-analysis of randomized trials, we showed a survival benefit of TAVR as compared to surgical aortic valve replacement throughout two years of follow-up. Our group compares different strategies for the treatment of valvular heart disease, investigate the importance of cardiac

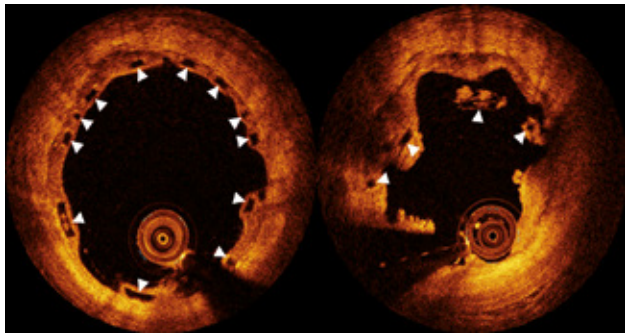


Figure 2: Ten months after implantation, imaging with optical coherence tomography confirms the correct position of the bioresorbable scaffold (left). Yet, six months later, the scaffold struts had collapsed (image right). This lead to blood clot formation and heart attack.

comorbidities on clinical outcomes, and studies newer generation devices for the treatment of aortic stenosis. Transcatheter mitral valve repair remains challenging in complex anatomical situations. We analyzed the procedural and 30-day results of the first-in-man study of a new system, the Edwards PASCAL system. The results indicated a high rate of technical success and reduction of mitral regurgitation severity.

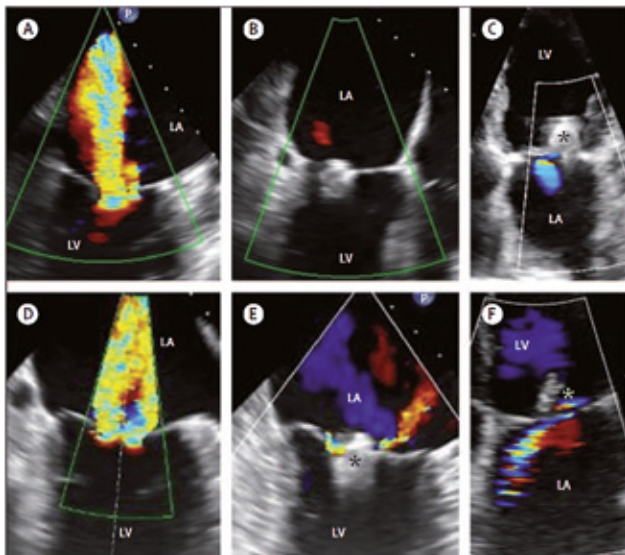


Figure 3: Procedural and 30 day echocardiogram results after implantation. Echocardiogram images before the procedure (A), immediately after the procedure (B), and 30 days after implantation (C) of one PASCAL device in a patient with severe functional mitral regurgitation and short posterior leaflet (6 mm). LA=left atrium. LV=left ventricle. Asterisks (*) show the spacer (Lancet, 2017).

Selected Competitive Grants

- Swiss National Science Foundation (Grant No 32003B_163059 "REVEAL in TAVI"; 33IC30_166855 "SERVE IICT")
- European Union FP7 Program, "CULPRIT SHOCK"
- Dr Anna Lam, Grant der Schweizerischen Herzrhythmus Stiftung

Selected Publications

- Costa F, van Klaveren D, James S, Heg D, Räber L, Feres F, Pilgrim T, Hong MK, Kim HS, Colombo A, Steg PG, Zanchin T, Palmerini T, Wallentin L, Bhatt DL, Stone GW, Windecker S, Steyerberg EW, Valgimigli M, PRECISE-DAPT Study Investigators: Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials., *Lancet*. 2017 Mar 11;389(10073):1025-1034
- Yamaji K, Ueki Y, Souteyrand G, Daemen J, Wiebe J, Nef H, Adriaenssens T, Loh JP, Lattuca B, Wykrzykowska JJ, Gomez-Lara J, Timmers L, Motreff P, Hoppmann P, Abdel-Wahab M, Byrne RA, Meincke F, Boeder N, Honton B, O'Sullivan CJ, Ielasi A, Delarche N, Christ G, Lee JKT, Lee M, Amabile N, Karagiannis A, Windecker S, Räber L.: Mechanisms of Very Late Bioresorbable Scaffold Thrombosis: The INVEST Registry., *J Am Coll Cardiol*. 2017 Nov 7;70(19):2330-2344
- Franzone A, Pilgrim T, Arnold N, Heg D, Langhammer B, Piccolo R, Roost E, Praz F, Räber L, Valgimigli M, Wenaweser P, Jüni P, Carrel T, Windecker S, Stortecky S.: Rates and predictors of hospital readmission after transcatheter aortic valve implantation. *Eur Heart J*. 2017 Jul 21;38(28):2211-2217
- Praz F, Spargias K, Chrissoheris M, Büllsfeld L, Nickenig G, Deuschi F, Schueler R, Fam NP, Moss R, Makar M, Boone R, Edwards J, Moschovitis A, Kar S, Webb J, Schäfer U, Feldman T, Windecker S: Compassionate use of the PASCAL transcatheter mitral valve repair system for patients with severe mitral regurgitation: a multicentre, prospective, observational, first-in-man study. *Lancet*. 2017 Aug 19;390(10096):773-780

Department of Pediatric Surgery

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Prof. Steffen
Berger



PD Dr. Elizaveta
Faslser-Kan



PD Dr. Thoralf
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Dr. Kai
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PD Dr. Ulf
Kessler

Research Partners

- Division of cytogenetics (University of Bern)
- Zahnmedizinische Kliniken (University of Bern)
- Pharma center (University of Basel)
- Department of Biomedicine (University of Basel)
- School of Pharmacy (University of Kent, UK)
- Department of human genetics and USA computation Institute (Univ. of Chicago, USA)
- Children's Hospital (Harvard Medical School, Boston, USA)
- Group Prof. von Gunten, Institute of Pharmacology (University of Bern)

Research Profile

- Oncobiology (laboratory research in childhood malignancies). Study of the expression of Tim-3 and Gal-9 molecules and their roles in leukemia and in pediatric solid tumors: PD Dr. E. Faslser-Kan
- Necrotizing enterocolitis of the newborn (Hosting of the Swiss national NEC registry): Prof. S. Berger, PD Dr. U. Kessler, Dr. M. Kordasc
- Pathophysiology of appendicitis: PD Dr. U. Kessler
- Health related quality of life after pediatric extremity fractures (clinical research and follow up studies): PD Dr. T. Liebs
- Clinical outcome research and development of new operative strategies in pediatric hip surgery: Dr. K. Ziebarth

Teaching Profile

The Department for Pediatric Surgery participates in University teaching programs for students of medicine (bed-side teaching, practical year, surgical rotation for students). The research laboratory participates in PhD programs and education of biology students and research technicians.

Highlights 2017

Research laboratory

Our research laboratory is equipped with all cell culture facilities and a Cell-IQ V2 MLF phase contrast and multi label fluorescence cell imaging and analysis system which is shared with the Institute of Pathology of the University of Bern. This system allows for long term automatized cell imaging studies.

Research visit of PD Dr. Faslser-Kan to Boston Children's Hospital in 2017.

Intensified collaboration with Prof. Sumbayev, School of Pharmacy (University of Kent, UK), resulting in several publications 2015-2017. This research collaboration focusses

on factors of the immune response and factors affecting disease progression in acute myeloid leukemia.

NEC Group

The national registry database was set up and passed ethical board review for all of the nine participating neonatal institutions in Switzerland. Until now 170 patients have been entered to the retrospective section of this registry. We expect to enter about 50 new patients annually from Switzerland. Although necrotizing enterocolitis (NEC) of the neonate is one of the major research topics in pediatric surgery, such a specific registry has not been developed before. Our group is in contact with international projects, e.g. the American NEC Society to establish a research network in this field. We are especially interested in the effects of associated cardiac disease on the development and outcome of NEC in neonates.

Orthopedic group

We initiated a project to assess the health-related quality of life (HRQL) in patients who have sustained an extremity fracture during childhood or adolescence by the use of patient reported outcome measures. Herefore we developed scores to validate the assessment of HRQL. By these instruments, all frequent pediatric fractures of the long bones and their respective treatment will be analyzed as to their long term effects on quality of life. After response from more than 2'500 patients, we identified demographic, clinical and radiological risk factors that are associated with the clinical outcome. Other interests of our research groups are the clinical outcomes after surgical treatment of paediatric hip and knee diseases, including slipped capital femoral epiphysis and ruptured anterior cruciate ligaments.

Selected Competitive Grants

- Batzebär grants PD Dr. Faslser-Kan, PD Dr. Liebs
- AO foundation grant Dr. Ziebarth, Dr. Slongo

Selected Publications

- Barteneva NS, Baiken Y, Faslser-Kan E, Alibek K, Wang S, Maltsev N, Ponomarev E, Sautbayeva Z, Kauanova S, Moore A, Beglinger Ch, Vorobjev IA. Extracellular vesicles in gastrointestinal cancer in conjunction with microbiota: on the border of kingdoms. 2017, BBA Reviews on Cancer, vol. 1868, p. 372-393
- Gonsalves Silva I, Yasinska I, Sakhnevych S, Fiedler W, Wellbrock J, Bardelli M, Varani L, Hussain R, Siligardi G, Ceccone G, Berger SM, Ushkarjov Yu, Gibbs BF, *Faslser-Kan E, and Sumbayev V*. The molecular galectin-9 secretory pathway involved in the immune escape of human acute

myeloid leukemia cells. 2017 Ebiomedicine, vol . 22, p. 44-57. *joint-corresponding authors

- Kessler U Mosbahi S, Walker B, Hau EM, Cotton M, Peiry B, Berger S, Egger B. Conservative treatment versus surgery for uncomplicated appendicitis in children: a systematic review and meta-analysis. Arch Dis Child. 2017 Dec;102(12):1118-1124. Epub 2017 Aug 17
- Ziebarth K, Milosevic M, Lerch TD, Steppacher SD, Slongo T, Siebenrock KA. High Survivorship and Little Osteoarthritis at 10-year Followup in SCFE Patients Treated With a Modified Dunn Procedure. Clin Orthop Relat Res. 2017 Apr;475(4):1212-1228
- Tannast M, Jost LM, Lerch TD, Schmaranzer F, Ziebarth K, Siebenrock KA: The modified Dunn procedure for slipped capital femoral epiphysis: the Bernese experience. J Child Orthop. 2017 Apr;11(2):138-146

Department of Pediatrics

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Prof. Christoph
Aebi
Director



Prof. Christa
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Endocrinology



Prof. Maja
Steinlin
Neurology



Prof. Sabina
Gallati
Genetics



Prof. Philipp
Latzin
Pulmonology

Department Profile

The Department of Pediatrics is one of the largest clinics within the Medical Faculty of the University of Bern and one of the most diverse, comprising all medical specialties (apart from cardiology). There are one Director and Ordinarius (Prof. Christoph Aebi, pediatric Infectiology) and four Extraordinaria (core units: Endocrinology, Neurology, Genetics and Pulmonology), whose activities are presented. The Department is also strongly involved in teaching at the medical faculty. Most students receive their teaching in Pediatrics at our Children's Hospital Inselspital. For the first time in Switzerland and worldwide within the top ten, Pediatrics in Bern offers OSCE examinations with children as actors.

Division of Pediatric Infectious Diseases

Research topics

Main research projects were clinical studies in the field of severe bacterial infections and diagnostics of infections in children. The Swiss Pediatric Sepsis Study was conducted 2011-2016 in 10 Swiss pediatric centers (lead by the University Children's Hospital Bern). It is one of the largest prospective clinical studies on bacterial sepsis in children worldwide and has led to successful collaborations with other research consortia on sepsis in Europe.

Highlight of the year

As a result of the successful European collaboration on sepsis Bern is part of the H2020 financed PERFORM study, led by Imperial College London, on the optimization of infection diagnostics in children with fever; patient recruitment starting this year.

Selected references

- Epidemiology of blood culture-proven bacterial sepsis in children in Switzerland: a population-based cohort study. Agyeman P, Schlapbach LJ, Giannoni E, ... Kuehni CE, Aebi C, Berger C, for the Swiss Pediatric Sepsis Study. *The Lancet Child Adolesc Health.* 2017; 1:124-33
- Cerebrospinal fluid CXCL13 as a diagnostic marker of neuroborreliosis in children: a retrospective case-control study. Remy MM, Schöbi N, Kottanattu L, Pfister S, Duppenhaller A, Suter-Riniker F. *J Neuroinflammation.* 2017 Aug 31;14(1):173. doi: 10.1186/s12974-017-0948-9

Division of Pediatric Endocrinology, Diabetology and Metabolism

Research topics

Main research projects were wet-lab based in fields of molecular endocrinology and metabolism. Rare human disorders in these fields, including growth hormone deficiency, disorders of steroid hormones and sexual development (DSD), as well as mitochondrial disorders have been studied. In addition, translational studies on steroid metabolomics in disorders premature adrenarche, PCOS and congenital adrenal hyperplasia were pursued. Finally, clinical studies based on patient registries in topics of obesity and DSD were conducted.

Highlight of the year

Under the lead of Bern, the Swiss DSD Cohort Study was launched nation-wide with connections to international i-dsd research.

Selected references

- Combined transcriptome and metabolome analyses of metformin effects reveal novel links between metabolic networks in steroidogenic systems. Udhane SS, Legeza B, Marti N, Hertig D, Diserens G, Nuoffer JM, Vermathen P, Flück CE. *Sci Rep.* 2017 Aug 17;7(1):8652
- CYP17A1 inhibitor abiraterone, an anti-prostate cancer drug, also inhibits the 21-hydroxylase activity of CYP21A2. Malikova J, Brixius-Anderko S, Udhane SS, Parween S, Dick B, Bernhardt R, Pandey AV. *J Steroid Biochem Mol Biol.* 2017 Nov;174:192-200

Division of Neuropaediatrics, Development and Rehabilitation

Research topics

Main research topic was stroke in childhood. Neuropaediatrics Bern has the lead in the population-based Swiss Neuropaediatric Stroke Registry (SNPSR) since 2000, being the base for many research analyses. In the HERO (hemispheric reorganization after stroke) study, reorganization after stroke during childhood is studied by connectivity MRI and magnetic stimulation. Further, the NEMO (neonates and memory) study follows children from neonatal birth until teen age considering long term cognitive functioning and development of the brain. This study expanded to the ONSET study, examining effects of brain lesions at different time points during childhood.

Highlights of the year

Thanks to an international collaboration lead by Bern, the PASTA study, the first randomized treatment trial in acute childhood stroke was designed and published. The Brainfit study, comparing effects of cognitive training versus sport activities in oncological children has started.

Selected references

- Cortical morphometry and cognition in very preterm and term-born children at early school age. Mürner-Lavanchy I, Rummel C, Steinlin M, Everts R. *Early Hum Dev.* 2017 Nov 24;116:53-63
- Resting-state connectivity and executive functions after pediatric arterial ischemic stroke. Kornfeld S, ... Steinlin M, Everts R. *Neuroimage Clin.* 2017 Oct 17;17:359-367

Division of Human Genetics

Research topics

Main research focus was development of a lung disease gene panel based on high-throughput sequencing and allowing a correct diagnosis as well as genotype–phenotype association studies in patients with CF-like but CFTR mutation negative disorders. On the other hand the focus was on the characterization of mitochondrial disorders leading to the identification of novel genes (e.g. SDHD, ECHS1) involved in these devastating rare diseases. In addition, genotype-phenotype associations in patients with CF diagnosed by newborn screening are studied.

Highlight of the year

Under the lead of Bern (University Clinic of Ophthalmology and Division of Human Genetics), the buildup of a Swiss registry for patients affected by Retinitis pigmentosa was launched.

Selected references

- SDHA mutation with dominant transmission results in complex II deficiency with ocular, cardiac, and neurologic involvement. Courage C, Jackson CB, Hahn D, Euro L, Nuoffer JM, Gallati S, Schaller A. *Am J Med Genet A.* 2017 Jan;173(1):225-230
- Characterization of two novel intronic OPA1 mutations resulting in aberrant pre-mRNA splicing. Bolognini R, Gerth-Kahlert C, Abegg M, Bartholdi D, Mathis N, Sturm V, Gallati S, Schaller A. *BMC Med Genet.* 2017 Feb 28;18(1):22

Division of Pediatric Pulmonology and Allergy

Research topics

Main research focus was variability of lung function by sensitive measurement techniques, e.g. multiple breath wash-out, and novel functional lung MRI imaging techniques. In addition, two large cohort studies are led by the Children's Hospital Bern (BILD; Bern-Basel infant lung development and SCILD; Swiss cystic fibrosis infant lung development cohort). In these cohorts infants are followed from birth throughout childhood to assess longitudinally lung growth and morbidity.

Highlights of the year

Kathryn Ramsey, PhD was awarded an Ambizione Research Fellowship to follow up children of the SCILD cohort. Dr. Sophie Yammine, PhD was awarded the Pfizer Prize for her discovery of independent development paradigm of gas exchanging pulmonary alveoli.

Selected references

- Elevated lung clearance index in infants with cystic fibrosis shortly after birth. Kieninger E, Yammine S, Korten I, ... Casaulta C, Latzin P; and the SCILD; and BILD study groups. *Eur Respir J.* 2017 Nov 9;50(5)
- Respiratory viruses in healthy infants and infants with cystic fibrosis: a prospective cohort study. Korten I, Kieninger E, ... Casaulta C, Latzin P; SCILD and BILD study groups. *Thorax.* 2017 Aug 4

Department of Medical Oncology

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PD Dr. Urban
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PD Dr. Julian
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PD Dr. Carsten
Riether

Research Partners

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- Department of Urology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Department of Biomedicine, University of Basel, Basel, Switzerland
- Institute of Pathology, University of Basel, Basel, Switzerland
- Institute of Pathology, University of Bern, Bern, Switzerland
- Institute of Oncology Research, Bellinzona, Switzerland
- GENCODE project, Hinxton, United Kingdom
- International Cancer Genome Consortium (ICGC), CHUV, Lausanne, Switzerland

Research Profile

The Department of Medical Oncology is comprised of research groups involved in basic and translational research as well as a clinical trial unit in which more than 160 patients are treated per year in interventional phase I to phase III studies. We try to better understand cancer through a combination of experimental and bioinformatic approaches with a focus on long non-coding RNAs (lncRNAs). An important focus of our research is in translational hemato-oncology. We analyze molecular and cellular mechanisms how different components of the bone marrow micro-environment such as immune cells and stromal cells affect disease-initiating and -maintaining leukemia stem cells and protect them from immune-mediated elimination. The main focus of the clinical studies in hemato-oncology is to improve treatment protocols for autologous stem cell transplantation. Several investigator-initiated studies assessing the outcome of patients after autologous stem cell transplantation, the mobilization procedure and the high-dose chemotherapy schemes are currently ongoing. The main research interest of the lymphoma research group is to analyze the role of autophagy in disease development and to understand a hereditary form of lymphoma. In a second more clinical and translational research focus, we are interested in the immunotherapy of cancer.

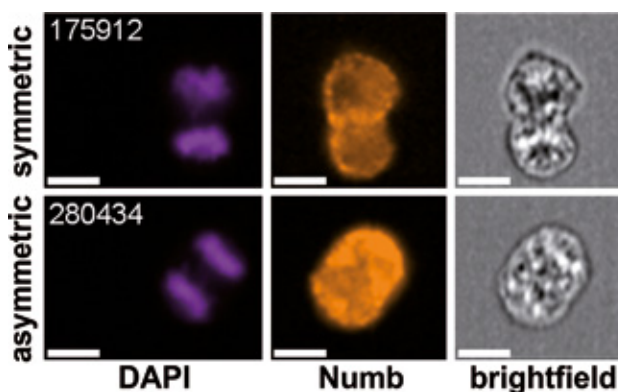
Teaching Profile

The Department of Medical Oncology participates in the lectures for students of medicine (4th to 6th year), biomedicine and biology. We also teach students of biomedicine of the University of Fribourg. In addition, we train students in clinical skills and in the field of oncology (4th to 6th year).

Highlights 2017

CD27 signaling expands leukemia stem cells

We could recently demonstrate that CD70/CD27 signaling in acute myeloid leukemia (AML) cells activates stem cell gene expression programs, including the Wnt pathway, and promotes symmetric cell division and proliferation. Soluble CD27, reflecting the extent of CD70/CD27 interactions in vivo, was significantly elevated in the sera of newly diagnosed AML patients and is a strong independent negative prognostic biomarker for overall survival. Blockade of CD70/CD27 signaling reduced AML stem/progenitor cell numbers and prolonged survival in AML patient-derived xenograft models. Based on this translational study, a clinical phase I/II trial was initiated at the Inselspital assessing safety and efficacy of a human anti-CD70 antibody in combination with the hypomethylating agent Vidaza for the treatment of AML patients (NCT03030612).



Symmetric and asymmetric division in AML cells assessed by the distribution of the cell fate determinant Numb.

A new method accelerates the mapping of genes in the 'Dark Matter' of our DNA

Recent studies have revealed tens of thousands of new genes in our genome, called "long non-coding RNAs" (lncRNAs). The functions of the vast majority remain unknown, but several hundred have so far been linked to cancer. Biomedical studies of lncRNAs depend on accurate maps, or annotations, of their genes. But present maps are highly incomplete, and depend on slow and inaccurate methods. As part of the international GENCODE consortium, we have developed a new approach, "Capture Long Seq" (CLS), which targets lncRNA genes and sequences them using long-read PacBio technology. The result is lncRNA annotation of highest quality, produced rapidly and economically. Therefore

CLS promises to radically improve maps of lncRNAs, leading eventually to identification of new therapeutic targets.

NSAID treatment with meloxicam enhances peripheral autologous stem cell mobilization in myeloma patients.

Chemotherapy with G-CSF is used to mobilize peripheral stem cells in multiple myeloma (MM) patients before autologous stem cell transplantation. Preclinical studies suggested that the nonsteroidal anti-inflammatory drug meloxicam enhances the mobilization of CD34+ cells. We prospectively compared two cohorts of MM patients in first remission mobilized with G-CSF and chemotherapy. The second cohort additionally received oral meloxicam. Meloxicam was well tolerated and associated with similar hematologic engraftment after transplantation and equal survival rates. However, the meloxicam group had higher CD34+ cell levels on day 8 of the mobilization procedure ($p=0.007$), and fewer patients needed more than one collection day ($p=0.04$). This resulted in reduced administrations of the rescue compound plerixafor ($p=0.03$) and thus significantly less costs.

Selected Competitive Grants

- Swiss National Science Foundation (grant no. 31003A_169956; 310030_170170)
- Swiss Cancer League (KLS-3346-02-2014; KFS-3815-02-2016; KLS-3790-02-2016)
- Sinergia grant (2017-2021)

Selected Publications

- Riether, C., Schurch, C. M., Bührer, E. D., Hinterbrandner, M., Huguenin, A. L., Hoepner, S., Zlobec, I., Pabst, T., Radpour, R. & Ochsenbein, A. F. CD70/CD27 signaling promotes blast stemness and is a viable therapeutic target in acute myeloid leukemia. *J Exp Med* 214, 359-380, doi:10.1084/jem.20152008 (2017)
- Al Sayed MF, Ruckstuhl CA, Hilmenyuk T, Claus C, Bourquin JP, Bornhauser BC, Radpour R, Riether C, Ochsenbein AF. CD70 reverse signaling enhances NK cell function and immunosurveillance in CD27-expressing B-cell malignancies. *Blood* 2017 Jul 20;130(3):297-309. doi: 10.1182/blood-2016-12-756585. Epub 2017 May 11
- Julien Lagarde, Barbara Uszczyńska-Ratajczak, Silvia Carbonell, Carrie Davis, Thomas R Gingeras, Adam Frankish, Jennifer Harrow, Roderic Guigo, Rory Johnson. High-throughput annotation of full-length long noncoding RNAs with Capture Long-Read Sequencing. *Nature Genetics* (In Press)
- Gilli S, Novak U, Taleghani BM, Baerlocher GM, Leibundgut K, Banz Y, Zander T, Betticher D, Egger T, Rauch D, Pabst T. BeEAM conditioning with bendamustine-replacing BCNU before autologous transplantation is safe and effective in lymphoma patients. *Ann Hematol.* 2017;96:421-429
- Gössi F, Spahn M, Zweifel M, Panagiotis S, Mischo A, Stenner F, Hess U, Berthold D, Bargetzi M, Schardt J, Pabst T. Comparison of three or fewer high-dose chemotherapy cycles as salvage treatment in germ cell tumors in first relapse. *Bone Marrow Transplant.* 2017;52:334-336

Department of Nephrology and Hypertension

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Prof. Bruno Vogt
Clinic Director



Prof. Dominik Uehlinger
Deputy Clinic Director



Prof. Uyen Huynh-Do



Prof. Daniel Fuster



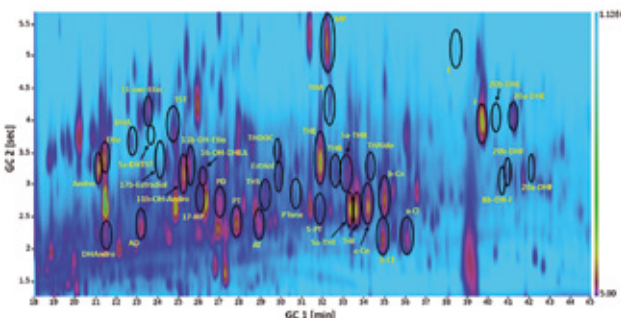
PD Dr. Geneviève Escher

Research Partners

- Prof. Olivier Bonny and PD Dr. Menno Pruijm, CHUV, Lausanne
- Prof. Murielle Bochud, IUMSP, Lausanne
- Prof. Alain Doucet, Collège de France, Paris
- Prof. Tobias Huber, Hamburg-Eppendorf, Germany
- Prof. Brian Walker, University of Edinburgh, UK
- Prof. Zoltan Takats, Imperial College London, UK
- Prof. Claudio Ponticelli, Istituto Clinico Humanitas IRCCS, Italy
- Prof. Francesco Scolari, Universtità degli studi di Brescia, Italy
- Dr Ali Gharavi, Columbia University Medical Center, New York, USA
- Prof. Orson Moe, UT Southwestern, Dallas, TX

Research Profile

The department of Nephrology and Hypertension is the centre for patients with kidney diseases and hypertension in the canton of Bern. Six different research groups are involved in the investigation of pathophysiological mechanisms contributing to renal function loss upon hypoxia, chronic allograft failure after kidney transplantation, formation of kidney stones and development of renal fibrosis. Our interdisciplinary approach includes different cell culture models, molecular biology, gas chromatography and mass spectrometry, magnetic resonance imaging, animal experimentation with several transgenic mice and rat models, and clinical studies. We are currently improving the analyses of steroids, oxysterols, bile acids and vitamin D metabolites in urine and plasma by gas chromatography and mass spectrometry, and two dimensional gas chromatography Time of Flight Mass Spectrometry, to better identify specific patterns for endocrine diseases. Additionally patients are recruited for our kidney biobank which contains renal biopsies, plasma, serum, 24h urine, genomic DNA and peripheral



Total ion chromatograms of a human 24 h urine sample.

blood mononuclear cells. Combined with renal imaging, this valuable samples collection of well characterized patients represents an ideal research platform to explore disease markers and their links to the progression of renal disease. Using these different tools, diagnostic's improvement and implement of novel therapeutic approaches could enhance the patients' well-being.

Teaching Profile

The department participates in University teaching programs for students of medicine and biomedicine in Bern. It also supervises bachelor and master students for their thesis.

Highlights 2017

Steroid metabolome as new diagnostic tool for an endocrine disorder

One main research field of our clinic focuses on the analysis of the steroid hormone metabolome in healthy subjects and its diagnostic performance in human disorders. Some common endocrine disorders affect directly the steroid hormone metabolism with vast metabolic consequences, however their diagnosis still face major challenges. As a result of a very fruitful cooperation between our clinic as a member of the Swiss Kidney Project on Genes in Hypertension (SKIPOGH) and the Division of Pediatric Endocrinology and Diabetology of the Inselspital Bern, a diagnostic test was developed on the basis of urinary steroid hormone metabolites. The test predicts for the first time one important exponent of these disorders with high accuracy. An associated publication is under review in a high impact peer reviewed journal. For pending patent matters we are not yet able to publish more detailed information for this highlight.

Bone anchored port - a novel vascular access for hemodialysis

The population of patients on renal replacement therapy is getting older with an increasing number of comorbidities. While arteriovenous fistulas remain the preferred vascular access for dialysis, less patients qualify for this type of access. The "bone anchored port" (BAP) is a novel vascular access for renal replacement therapy that has been developed by researchers of the Departments of Nephrology and Hypertension, Otorhinolaryngology, Cardiovascular Surgery and ArtOrg, in collaboration with Cendres+Métaux, Bienne. The project has been funded by three KTI grants. A first study on the use of the BAP in chronic hemodialysis patients is currently conducted. Four BAPs have been implanted at the Inselspital and are successfully used for dialysis so far. The study is designed as a multicenter study and will

be expanded to other dialysis centers in Switzerland and Germany once sufficient local experience is available.



Patient with bone anchor port getting ready for the dialysis.

www.nostone.ch

In 2015 the SNSF launched the first call for Investigator Initiated Clinical Trials (IICT). One of these first round funded IICTs is the NOSTONE trial. NOSTONE is a multicenter, randomized, placebo-controlled, double-blind trial with the aim to assess the efficacy of standard and low dose of hydrochlorothiazide (HCT) in the recurrence prevention of calcium-containing kidney stones. HCT 12.5 mg, 25 mg, 50 mg or placebo will be given once daily for 36 months to patients who had at least 2 kidney stones in the past 10 years. The primary outcome will be incidence of stone recurrence, a composite of symptomatic or radiologic recurrence. At 12 sites throughout Switzerland, 416 patients will be recruited (see map). End of January 2018, 168 patients were enrolled. The trial will end in Mai 2021.



NOSTONE study sites.

Selected Competitive Grants

- Thiazides in the recurrence prevention of calcareous nephrolithiasis (SNF, Prof. Daniel Fuster)
- Mechanisms of thiazide-induced glucose intolerance (SNF, Prof. Daniel Fuster)
- NCCR Transcure (SNF, Prof. Daniel Fuster)
- Role of the TWEAK/Fn14 axis in Calcineurin Inhibitor Toxicity (CNT) of the Kidney (SNF, Dr Daniel Sidler)
- Red blood cell survival in patients with renal failure - assessment and therapy modelling implications (SNF, Prof. Dominik Uehlinger)
- NCCR Kidney.CH (SNF, Prof. Huynh-Do Uyen)
- STCS (SNF, Prof. Huynh-Do Uyen)
- IKKP2 (FP7 Cofund, Prof. Huynh-Do Uyen)

Selected Publications

- Sidler D, Wu P, Herro R, Claus M, Wolf D, Kawakami Y, Kawakami T, Burkly L, Croft M. TWEAK mediates inflammation in experimental atopic dermatitis and psoriasis. *Nat Commun.* 2017 May 22;8:15395. doi: 10.1038/ncomms15395
- Pathare G, Dhayat N, Mohebbi N, Wagner CA, Cheval L, Neuhaus TJ, Fuster DG. Acute regulated expression of pen-drin in human urinary exosomes. *Pflugers Arch.* 2017 Aug 12. doi: 10.1007/s00424-017-2049-0. [Epub ahead of print]
- Dhayat NA, Gradwell MW, Pathare G, Anderegg M, Schneider L, Luethi D, Mattmann C, Moe OW, Vogt B, Fuster DG. Furosemide/Fludrocortisone Test and Clinical Parameters to Diagnose Incomplete Distal Renal Tubular Acidosis in Kidney Stone Formers. *Clin J Am Soc Nephrol.* 2017 Sep 7;12(9):1507-1517. doi: 10.2215/CJN.01320217. Epub 2017 Aug 3
- Bochud M, Jenny-Burri J, Pruijm M, Ponte B, Guessous I, Ehret G, Petrovic D, Dudler V, Haldimann M, Escher G, Dick B, Mohaupt M, Paccaud F, Burnier M, Pèchère-Bertschi A, Martin PY, Vogt B, Ackermann D. Urinary cadmium excretion is associated with increased synthesis of cortico- and sex steroids in a population study. *J Clin Endocrinol Metab.* 2017 Oct 25. (Epub ahead of print)
- Mistry HD, Kurlak LO, Mansour YT, Zurkinden L, Mohaupt MG, Escher G. Increased maternal and fetal cholesterol efflux capacity and placental CYP27A1 expression in preeclampsia. *J Lipid Res.* 2017 Jun;58(6):1186-1195. doi: 10.1194/jlr.M071985. Epub 2017 Apr 10

Department of Neurosurgery

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Raabe



Prof. Jürgen
Beck



Prof. Claudio
Pollo



Prof. Philippe
Schucht



Prof. Hans-Rudolf
Widmer



Prof. Werner
Z'Graggen

Research Partners

- Institute for Artificial Organs, University of Bern
- University Department of Neurology, Inselspital, Bern
- University Department of Diagnostic and Interventional Neuroradiology
- Swiss Center for Electronics and Microtechnology, Neuchatel
- Department of Neurobiology Research, University of Southern Denmark, Odense C, Denmark
- Division of Pharmacology and Toxicology, Vetsuisse Faculty, University of Bern
- Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London, UK
- Institute for Exact Sciences, University of Bern
- Mathematical Oncology Laboratory, Universidad de Castilla-La Mancha
- Swiss Federal Institute of Technology Lausanne (EPFL)

Research Profile

Our department has both clinical and experimental research areas. Our clinical research commitment is driven by the need to improve and refine neurosurgical operations. Focusing on this area, we examine and test how to translate increasingly frequent emerging new technologies into neurosurgical practice. Development of new and innovative technologies or modification of procedures to improve safety and success of neurosurgical operations include intraoperative imaging, neuromonitoring, augmented reality, navigation associated developments, targeted procedures and 3D printing, and simulation techniques. Another focus in collaboration with the Neurocenter Clinical Trial Unit are clinical studies or trials to investigate different managements or treatments. We also investigate in several projects of diagnosis and treatment of cerebral ischemia and hemorrhage. In our laboratory of regenerative experimental medicine we aim at the development and improvement of therapeutic strategies for Parkinson's disease. In this context cell replacement therapy is one major focus since many years. At present we investigate the potential of antagonizing Nogo-A on graft function based on the outcome of our *in vitro* studies. In addition, in another attempt we investigate the regenerative and neuroprotective potential of soluble factors secreted by circulating endothelial precursor-stem cells termed Endothelial Progenitor Cells.

Teaching Profile

The Department of Neurosurgery participates in university teaching programs for students of medicine. We organize workshops for medical students and have 3 dozen medical students on in-house rotations per year. We organize a series of both national and international courses on specialized topics of neurosurgery. The research laboratory is co-organizer of the lecture series "Disease and Repair in the CNS" for master students of the gcb Bern. Hans Rudolf Widmer serves as mentor and co-advisor for PhD students of the gcb Bern. Supervision of master and doctoral students of the medical faculty.

Highlights 2017

Our **neuromonitoring** group has continued to investigate the use of continuous mapping in motor eloquent brain tumors and examined the benefit of using this technique in vestibular schwannoma and skull base surgery. Other research areas were transcranial stimulation, language mapping, spinal cord mapping and other techniques.

Intracerebral hemorrhage remains a major unresolved problem. Our SNF founded SWITCH trial investigates a new form of surgical treatment that does, for the first time, not harm the brain. The Inselspital leads and coordinates this trial and has succeeded to recruit now 59 patients in 7 European countries.

Spontaneous intracranial hypotension (SIH) is a disabling form of headache in otherwise healthy young patients. Since years we focus on this disease and we finally founded the first interdisciplinary SIH-board. Our research revealed a spinal cause that can be treated and we were able to operate the largest patient series in Europe.

Developments like **directional leads**, analysis of cerebral electrophysiological signals and new image modalities improve our understanding on the physiopathology of brain diseases and provide new insights in brain and spine neuromodulation therapies. This research is performed in collaboration with different groups within the Neurozentrum, the EPFL and Oxford University.

Diagnosis and treatment of cerebral ischemia

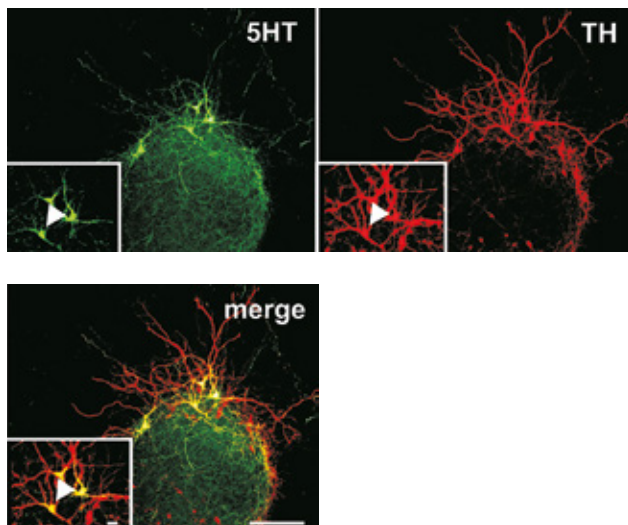
The neurointensive group focused on methods for detection of hypoperfused brain areas during the vasospasm phase after subarachnoid hemorrhage using ultrasound and CT perfusion imaging. Other research areas were monitoring of ventricular width and changes of intracranial pressure with ultrasound and development of a method for CT-guided ventricular drain placement.

Novel concepts to visualize tumor boundaries during surgery

The Horao project reached its first milestone and successfully concluded a crowd funding campaign. In spring 2018 a prize based competition will be launched in search of non-invasive technologies that will help to improve brain tumor surgery in real time.

A subpopulation of dopaminergic neurons co-expresses serotonin in ventral mesencephalic cultures but not after intrastriatal transplantation in a rat model of Parkinson's disease

Cell replacement therapy is a promising avenue in the treatment of Parkinson's disease. The main source of donor tissue is the human fetal midbrain which consists of a mixed neuronal population with potential impact for clinical trials. We report that a significant sub-population of dopaminergic neurons in fetal tissues co-expresses serotonin. The representative microphotographs show double immunofluorescence stainings for serotonin (5HT) and the dopaminergic marker tyrosine hydroxylase (TH) in cultured neurospheres. Scale bars: 100µm and 20µm (inserts).



Selected Competitive Grants

- BRIDGE Project 20B2-1_176498 / 1: Towards intelligent sensor enhanced robotic neurosurgery
- Novartis Foundation, Basel (grant No. 16C195), Neutralization of Nogo-A for Improvement of cell replacement Strategies in Parkinsons disease
- RESURGE – Randomized controlled comparative phase II trial on surgery for glioblastoma recurrence, Schweizer Nationalfonds
- Implantable Autonomous Wireless Bio-Electronics for High-Resolution Monitoring and Detection of Epilepsy in-vivo, Schweizer Nationalfonds
- Electrophysiological recordings to optimize deep brain stimulation for Parkinson's disease: Parkinson Schweiz

Selected Publications

- Di Santo S, Seiler S, Ducray AD, Meyer M and Widmer HR (2017). A subpopulation of dopaminergic midbrain neurons co-expresses serotonin in cultures of rat and human origin but not after transplantation in an animal model of Parkinson's disease. *Cell Transpl.* 26(4): 679 - 691
- Seiler S, Di Santo S, Andereggen L and Widmer HR (2017). Antagonization of the Nogo-receptor 1 enhances dopaminergic fiber outgrowth of transplants in a rat model of Parkinson's disease. *Front. Cell. Neurosci.* 11:151. doi: 10.3389/fncel.2017.00151
- Reitmeir R, Eyding J, Oertel MF, Wiest R, Gralla J, Fischer U, Giquel PY, Weber S, Raabe A, Mattle HP, Z'Graggen WJ, Beck J (2017). Is ultrasound perfusion imaging capable of detecting mismatch? A proof-of-concept study in acute stroke patients. *J Cereb Blood Flow Metab* 2017;37:1517-1526
- Raabe C, Fichtner J, Beck J, Gralla J, Raabe A. Revisiting the rules for freehand ventriculostomy: a virtual reality analysis. *J Neurosurg.* 2017 May 19:1-8. doi: 10.3171/2016.11.JNS161765
- Beck J, Fung C, Ulrich CT, Fiechter M, Fichtner J, Mattle HP, Mono ML, Meier N, Mordasini P, Z'Graggen WJ, Gralla J, Raabe A. Cerebrospinal fluid outflow resistance as a diagnostic marker of spontaneous cerebrospinal fluid leakage. *J Neurosurg Spine.* 2017 Aug;27(2):227-234

Department of Neurology

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Director
Ordinarius



Prof. Andrew Chan
Deputy
Director



Prof. Antoine Adamantidis
Extraordinarius
ERC*



Prof. Urs Fischer
Extraordinarius



Prof. René Müri



Prof. Marcel Arnold



Prof. Kaspar Schindler



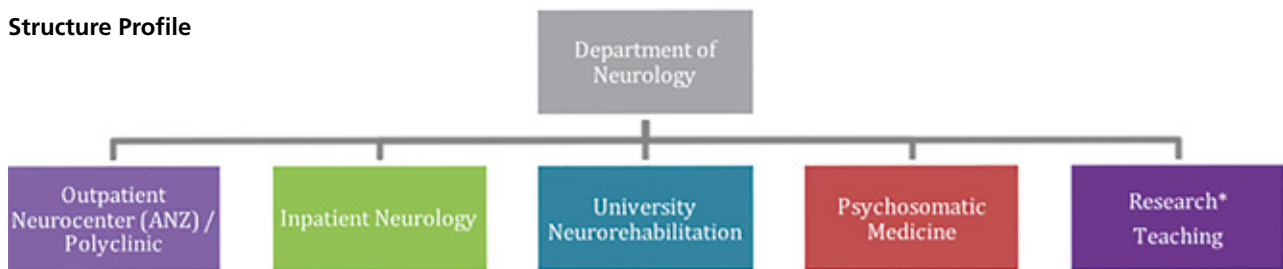
Prof. Smita Saxena
ERC*



Prof. Selma Aybek
SNF

* consolidator grants received in 2017

Structure Profile



Research Partners

- Department of Diagnostic and Interventional Neuroradiology, University Hospital, Bern
- Department of Neurosurgery, University Hospital, Bern
- Department of Pulmonology, University Hospital, Bern
- Gerontechnology and Rehabilitation Group, ARTORG Center, University of Bern, Bern
- Department of Psychology, University of Bern, Bern
- Institute for Research in Biomedicine, Università della Svizzera italiana, Bellinzona
- Department of Neurology, McGill University, Montreal, Canada
- Department of Neurology, University Hospital, Leyden, Netherlands
- Institute of Physiology, Università degli Studi, Milano, Italy
- Center for Integrative Genomics, University of Lausanne, Lausanne
- Department of Neurology, University Hospital Helsinki, Finland

Research Profile

The Department of Neurology in Bern is with 133 beds and over 100 academic collaborators the largest in Switzerland with the biggest number of patients in highly specialized medicine areas (epilepsy surgery, stroke, deep brain stimulation).

Approaches available

- Clinical trials coordinated by Neuro-CTU and CTU Bern
- Neurophysiological studies in the sleep-wake epilepsy

(SWEZ), neurovascular, neuromuscular, visuo-perceptual, and vestibular centers

- Experimental studies in the ZEN (center of experimental neurology) with state of the art molecular / neurophysiological methods and animal models of stroke, narcolepsy, EAE and ALS

Research topics

- Sleep-wake physiology: sleep circuits, wake circuits, function of sleep oscillations
- Sleep-wake disorders: narcolepsy, stroke and other brain disorders, parasomnias, RLS
- Epilepsy: ictogenesis, seizure dynamics, intracranial EEG, time series analysis
- Stroke: large randomised controlled trials in acute stroke and secondary prevention, observational and translational studies, biomarkers, neuroimaging
- Neuroimmunology: immunotherapy: mechanisms of action, protective autoimmunity, steroid resistance, translational research approaches
- Neurorehabilitation: non-invasive brain stimulation in brain recovery and plasticity, computer-assisted neurorehabilitation systems, and robotics
- Movements disorders / neurodegeneration: deep brain stimulation, neuroimaging studies, cerebellar ataxia, motoneuronal diseases, gene therapy, drug targets

Teaching Profile

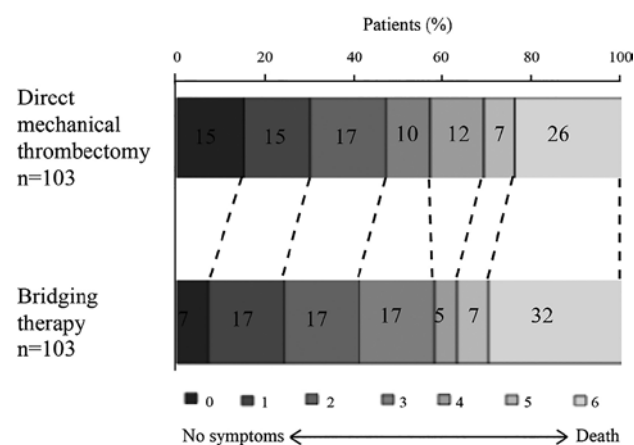
Undergraduate teaching is provided for students of medicine, dental medicine, biomedicine and biology.

Training in neurology: with over 50 positions, we are the largest residency program in the country. Fellowships are offered in stroke, epilepsy, sleep, movement disorders, neuroimmunology, neurorehabilitation, and general neurology. Our postgraduate training curriculum can be downloaded [here](#). The new PhD in Clinical Sciences started in October 2017.

Highlights 2017

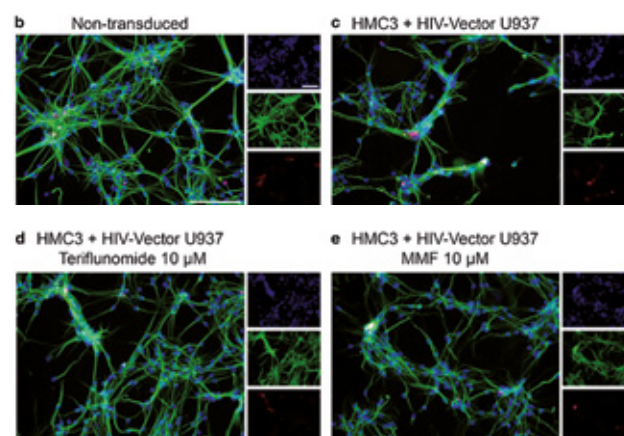
A new experimental research focus on neurodegeneration, e.g. motor neuron disease / spinocerebellar ataxia, (coordination: S. Saxena) in the ZEN and a new clinical research focus on functional neurological disorders (coordination: S. Aybek) were established. In 2017, two ERC consolidator grants started in our department and there were a total of 18 SNF grants running (4 obtained in 2017). We further obtained a SNF grant for a MD-PhD. We published total of 60 original publications, including the following 3 papers:

- Bellwald S, et al. Direct mechanical intervention versus bridging therapy in stroke patients eligible for intravenous thrombolysis: a pooled analysis of two registries. *Stroke*, in press. Our matched pair analysis found no difference in outcome in patients with an acute ischaemic stroke treated with and without intravenous thrombolysis prior to mechanical thrombectomy. Based on these findings we designed the large multicenter randomised controlled trial SWIFT DIRECT (patient recruitment start October 2017, Co-PIs U. Fischer and J. Gralla).



- Steimer A, et al. Predictive modeling of EEG time series for evaluating surgery targets in epilepsy patients. *Hum Brain Mapp.* 2017 May;38(5):2509-2531. Predictive modeling of intracranially recorded electroencephalographic signals (iEEG) was used to delineate epileptogenic brain tissue in patients suffering from pharmacoresistant epilepsy. This sophisticated and modern mathematical method allowed to correctly predict seizure control after surgery depending on the areas of resection in individual patients and thus represents a novel tool for personalized and quantified diagnostics.
- Ambrosius B, et al. Teriflunomide and monomethylfumarate target HIV-induced neuroinflammation and neurotoxicity. *J Neuroinflammation.* 2017 Mar 11;14(1):51. Effects of teriflunomide and monomethylfumarate on HIV related monocyte/microglia activation and neurotoxicity have been studied. Treatment with both drugs downregulates

cytokine secretion and therefore reduces cell death in co-cultured human fetal neurons. Thus modulation of the immune system may target neurotoxicity in HIV infected persons.



In 2017, A. Adamantidis and C. Gutierrez received the 2017 Pfizer-Prize in neurosciences / diseases of the neurosystem.

Selected Competitive Grants

Listed below are selected grants with only the most endowed grant per PI included:

- SNF Sinergia: Sleep as a model to understand and manipulate cortical activity in order to promote neuroplasticity and functional recovery after stroke. (CHF 1'830'000; C. Bassetti)
- ERC consolidator: Connectivity Correlate of Molecular Pathology in Neurodegeneration. (CHF 1'680'000; S. Saxena)
- ERC consolidator: All optical deconstruction of thalamic control of sleep-wake states. (CHF 1'610'000; A. Adamantidis)
- SNF project funding: Safety of Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with Non-valvular atrial fibrillation (ELAN safety). CHF 680'000
- SNF project funding: Creativity after focal brain lesions – a matter of paradoxical facilitation? (CHF 500'000; R. Müri)

Selected Publications

- Pace M, Adamantidis A, Facchin L, Bassetti C. Role of REM Sleep, Melanin Concentrating Hormone and Orexin/Hypocretin Systems in the Sleep Deprivation Pre-Ischemia. *PLoS One.* 2017 Jan 6;12(1):e0168430
- Meichtry JR, Cazzoli D, Chaves S, von Arx S, Pflugshaupt T, Kalla R, Bassetti CL, Gutbrod K, Müri RM. Pure optic ataxia and visual hemianopia - extending the dual visual hypothesis. *J Neuropsychol.* 2017 Mar 4. doi: 10.1111/jnp.12119
- Bellwald S, Weber R, Dobrocky T, Nordmeyer H, Jung S, Hadisurya J, Mordasini P, Mono ML, Stracke P, Sarikaya H, Bernasconi C, Kerger K, Arnold M, Chapot R, Gralla J, Fischer U. Direct mechanical intervention versus bridging therapy in stroke patients eligible for intravenous thrombolysis: a pooled analysis of two registries. *Stroke*, in press
- Steimer A, Müller M, Schindler K. Predictive modeling of EEG time series for evaluating surgery targets in epilepsy patients. *Hum Brain Mapp.* 2017 May;38(5):2509-2531
- Ambrosius B, Faissner S, Guse K, von Lehe M, Grunwald T, Gold R, Grewe B, Chan A. Teriflunomide and monomethylfumarate target HIV-induced neuroinflammation and neurotoxicity. *J Neuroinflammation.* 2017 Mar 11;14(1):51

Department of Nuclear Medicine

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Research Partners

- Paul Scherrer Institute, PSI, Villigen, Switzerland
- German Cancer Research Center, DKFZ, Heidelberg, Germany
- Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital, Bern University Hospital, Switzerland
- Department of Radiation Oncology, Inselspital Bern, University Hospital, University of Bern, Bern, Switzerland
- Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital, Bern, Switzerland

Research Profile

The Imaging Laboratory of the Department of Nuclear Medicine, under the responsibility of Dr. Bernd Klaeser, Dr. Thilo Weitzel and Prof. Dr. Thomas Krause pursues a complex of projects dedicated to quantitative Positron Emission Tomography (PET), including integrated quality control and normalization of quantitative image data, e.g. in the context of multi-centre trials. Based on such prerequisites, the team including Dr. George Prenosil works on PET derived feature extraction, classification and automated assessment of image data.

In a clinical research context, Dr. Bernd Klaeser addresses dedicated high-resolution, interventional and organ-specific PET/CT techniques, with a current focus on head and neck and vasculitis imaging. Further research topics in the field of Medical Physics held by Dr. Markus Fürstner and Dr. Michael Hentschel, follow the objective of improved dosimetry and safety of radionuclide therapies.

As the Head of Clinical Radiopharmacy at the University Hospital Bern, Switzerland, Dr. Martin A. Walter's work is dedicated to combining radiolabeling of biologically relevant molecules with high-throughput techniques such as microfluidics to deepen our understanding of tumor biology and bring precision medicine platforms into clinical practice.

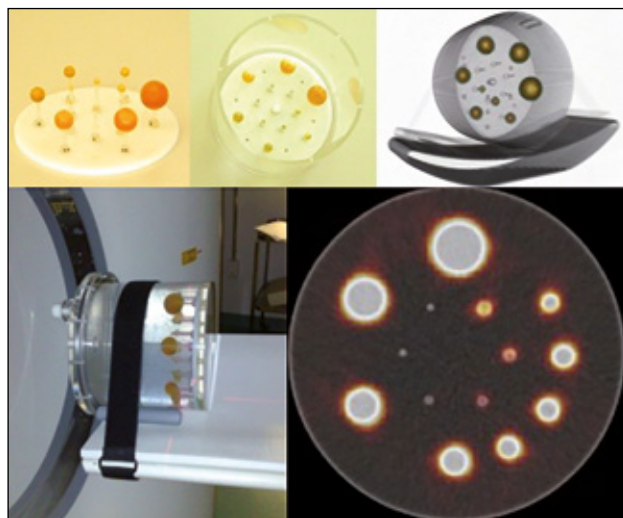
Teaching Profile

The department participates in University teaching programs for students of medicine and biomedical sciences. Further we are involved in the education of medical technical radiology assistants.

Highlights 2017

Transconvolution based equalization of positron energy effects for the use of 68Ge/68Ga phantoms in determining 18F PET recovery

Transconvolution is a comprehensive method for cross calibration in quantitative PET imaging, developed by the Imaging Laboratory of the Department of Nuclear Medicine. Phantom measurements constitute an essential element to characterize comparability between different PET/CT systems, e.g., within multi-centre clinical trials, and are most reliably performed with long-lived solid state 68Ge/68Ga phantoms, while F18-labelled radiopharmaceuticals are used for most clinical studies. In this project, we developed a new method that conveys 18F measurements into 68Ge measurements or vice versa.

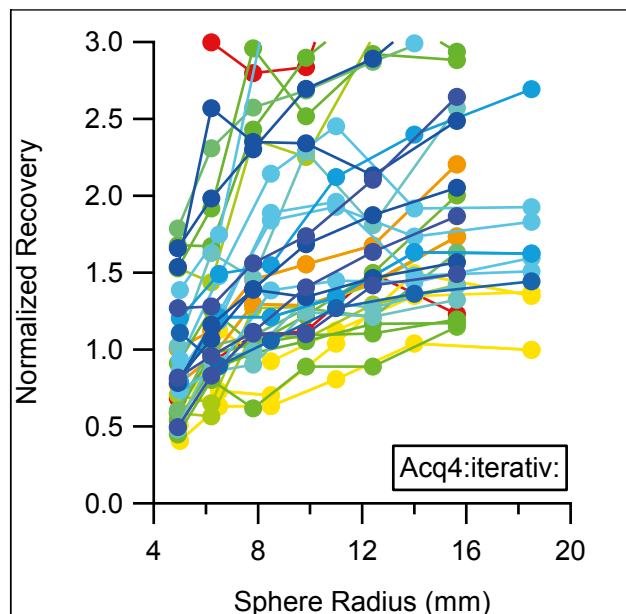


Measurements with 68Ge/68Ga solid state phantoms.

SGNM/SSMN Swiss PET/CT Survey

On behalf of the Swiss Society of Nuclear Medicine, the Imaging Laboratory conducted a nationwide study accomplishing an overview about the variability of PET/CT systems in Switzerland, and especially in variability and comparability in quantitative PET/CT measurements. Based on an analysis of more than 500 PET image datasets current sources of quantitative variability of PET measurements were identified. Quantitative PET imaging in a multi-centre setting requires

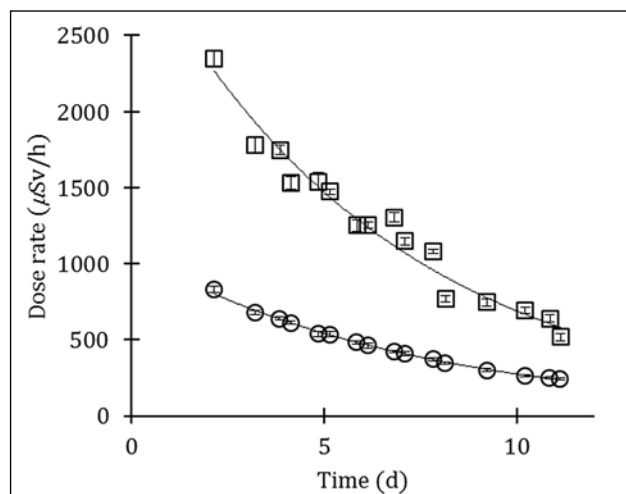
standardization or matching of multiple such parameters as general site setup, cross-calibration of systems, standardization of acquisition parameters, as well as normalization of specific imaging systems characteristics and exposure.



Distribution of phantom activity recovery from different PET systems.

Determination of individual thyroid clearance effective half-life with a common handheld electronic dosimeter

Radioiodine is a standard treatment of hyperthyroidism. Prescribed radiation doses in the thyroid gland should be planned individually to avoid overdosing and to minimize radiation burden to non-target organs. Clinically applied semi-individual approaches for dose calculation relying on disease-specific mean effective radioiodine half-lives remain inaccurate in a substantial proportion of patients. In this study, we described and validated a simple method for individual radioiodine thyroid half-life determination with an handheld electronic dosimeter complementing current stationary uptake counter measurements, intending to improve the accuracy of radioiodine treatment planning.



Handheld electronic dosimeter thyroid dose rates measurements after radioiodine application, for different setups.

Selected Competitive Grants

- Swiss National Science Foundation
- Bernese Cancer League
- Braun Foundation
- Foundation Claude & Giuliana
- Helmut Horten Foundation

Selected Publications

- Poeppel TD, Handkiewicz-Junak D, Andreeff M, Becherer A, Bockisch A, Fricke E, Geworski L, Heinzel A, Krause BJ, Krause T, Mitterhauser M, Sonnenschein W, Bodei L, Delgado-Bolton RC, Gabriel M. EANM guideline for radionuclide therapy with radium-223 of metastatic castration-resistant prostate cancer. *Eur J Nucl Med Mol Imaging*. 2017 Dec 12. doi: 10.1007/s00259-017-3900-4
- Fürstner M, Hentschel M, Spanjol PM, Prenosil GA, Weidner S, Krause T, Klaeser B. Technical Note: Determination of individual thyroid clearance effective half-life with a common handheld electronic dosimeter. *Med Phys*. 2017 Apr;44(4):1558-1562. doi: 10.1002/mp.12161
- Prenosil GA, Hentschel M, Fürstner M, Krause T, Weitzel T, Klaeser B. Technical Note: Transconvolution based equalization of positron energy effects for the use of (68) Ge/(68) Ga phantoms in determining (18) F PET recovery. *Med Phys*. 2017 Jul;44(7):3761-3766. doi: 10.1002/mp.12330
- Umlauf M, Radojewski P, Spanjol PM, Dumont R, Marincek N, Kollar A, Brunner P, Beyersmann J, Müller-Brand J, Maecke HR, Laimer M, Walter MA. Diabetes Mellitus and Its Effects on All-Cause Mortality After Radiopeptide Therapy for Neuroendocrine Tumors. *J Nucl Med*. 2017 Jan;58(1):97-102. doi: 10.2967/jnumed.116.180687
- Brunner P, Jörg AC, Glatz K, Bubendorf L, Radojewski P, Umlauf M, Marincek N, Spanjol PM, Krause T, Dumont RA, Maecke HR, Müller-Brand J, Briel M, Schmitt A, Perren A, Walter MA. The prognostic and predictive value ofsstr(2)-immunohistochemistry andsstr(2)-targeted imaging in neuroendocrine tumors. *Eur J Nucl Med Mol Imaging*. 2017 Mar;44(3):468-475. doi: 10.1007/s00259-016-3486-2

Department of Orthopedic Surgery and Traumatology

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Chairman



Prof. Matthias Zumstein
Vice Chairman,
Head Shoulder,
Elbow and
Sports



Prof. Lorin M. Benneker
Head Spine
Surgery



Prof. Moritz Tannast
Research Leader
Hip Surgery



PD Dr. Frank M. Klenke
Head Knee
Surgery and
Tumor Surgery



PD Dr. Fabian Krause
Head Foot &
Ankle Surgery



PD Dr. Johannes D. Bastian
Geronto-
Orthopedics



Dr. Sven Hoppe
Translational
Medicine &
Spine Research

Research Partners

- Institute for Surgical Technology and Biomechanics, University of Bern, Bern, Switzerland
- Musculoskeletal Research Unit, Vetsuisse Faculty, University of Zürich, Zürich, Switzerland
- Department of Small Animals, Division of Diagnostic Imaging, Vetsuisse Faculty, University of Zürich, Zürich, Switzerland
- AO Research Institute, Davos, Switzerland
- RMS Foundation, Bettlach, Switzerland
- SUVA, Luzern, Switzerland
- Institute for Forensic Medicine, University of Bern, Bern, Switzerland
- Institute for Topographic and Clinical Anatomy, University of Bern, Switzerland
- Institute of Pathology, University of Bern, Bern, Switzerland

Research Profile

The Department of Orthopedic Surgery consists of 6 research groups. In each specific field, we perform clinical as well as pre-clinical and basic research. Hip research focus on the development of osteoarthritis of the and pre-arthritis deformities like femoroacetabular impingement. 3D MRI is used to simulate pre-arthritis deformities and access early stages of chondral lesions. In a sheep model, different impingement morphologies and its treatment can be simulated. Spine research is focused on disc degeneration models and tissue-engineered disc regeneration and the treatment of osteoporotic fractures. The main focus of knee research is the regenerative treatment of the anterior cruciate ligament. Prosthetic infections and anti-infectious implants are also research topics. The shoulder and elbow team is working on statistical shape modeling of shoulder morphology, rotator cuff regeneration incl. stem cells and the investigation of surgical techniques and implants. Arthrosis of the ankle joint, innovative treatment of ankle fractures and AMIC plastic in osteochondral lesions is the main focus in foot and ankle research. Orthogeriatrics investigates the impact of orthogeriatric pathways and rehabilitations protocols on the clinical outcome in geriatric patients. Translational medicine is the latest research field which will come to focus during the next years.

Teaching Profile

The Department participates in University teaching programs for students of medicine, physiotherapy, nursing and sports. Moreover, we are active in advanced training for general

practitioners and emergency physicians as well as for orthopedic surgeons. The Department is certified teaching facility of the AO Foundation, the largest community of musculoskeletal disorders, and constantly hosts several fellows in all sub-disciplines.

Highlights 2017

Femoral osteochondroplasty can be performed effectively without the risk of avascular necrosis or femoral neck fractures in an experimental ovine FAI model

Schmaranzer F, Arendt L, Lerch TD, Steppacher SD, Nuss K, Wolfer N, Dawson HE, von Rechenberg B, Kircher PR, Tannast M.

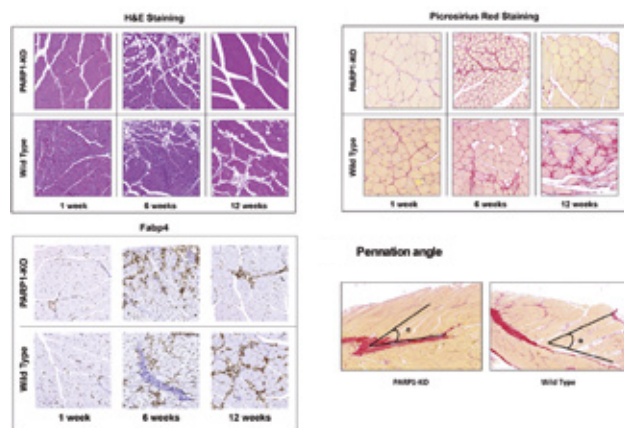
To establish a safe induction of cam-type femoroacetabular impingement (FAI) in sheep, one should be able to perform a femoral osteochondroplasty safely. In this experimental, controlled, prospective study nine sheep underwent unilateral FAI induction through an intertrochanteric, varus osteotomy and femoral osteochondroplasty. Radiographs, computed tomography (CT) scans and MRI and Histology were acquired. No signs for AVN or for femoral neck fractures



were detected. Mean alpha angles and femoral neck diameters decreased significantly ($p < 0.001$) superiorly by at least 30° respectively 4 mm after the offset creation. We conclude that femoral osteochondroplasty can be performed effectively and without the risk of AVN or femoral neck fractures in this ovine model.

Neer Award 2016: Reduced Muscle Degeneration and Decreased Fatty Infiltration after Rotator Cuff Tear in a Poly(Adp-Ribose) Polymerase 1 (Parp-1) Knock-out Mouse Model

Kuenzler MB, Nuss K, Karol A, Schär MO, Hottiger M, Raniga S, Kenkel D, von Rechenberg B, Zumstein MA. Disturbed muscular architecture, atrophy, and fatty infiltration remain irreversible in chronic rotator cuff tears even after repair. Poly (adenosine 5'-diphosphate-ribose) polymerase 1 (PARP-1) is a key regulator of inflammation, apoptosis, muscle atrophy, muscle regeneration, and adipocyte development. We could show that the absence of PARP-1 leads to a reduction in muscular architectural damage, early inflammation, apoptosis, atrophy, and fatty infiltration after combined tenotomy and neurectomy of the rotator cuff muscle.



Ankle joint pressure changes in high tibial and distal femoral osteotomies

Krause F, Barandun A, Klammer G, Zderic I, Gueorguiev B, Schmid T.

Varus and valgus malalignment of the knee was simulated in human cadaver full-length legs. Testing included four measurements: baseline malalignment, 5° and 10° re-aligning osteotomy, and control baseline malalignment. For HTO, testing was rerun with the subtalar joint fixed. In order to represent half body weight, a 300 N force was applied onto the femoral head. Intra-articular sensors captured ankle pressure. We could show that the re-alignment of coronal plane knee deformities by HTO and DFO altered ankle pressure characteristics. When the subtalar joint was fixed in the varus position, migration of centre of force after HTO was more significant than when the subtalar joint was fixed in valgus.

Selected Competitive Grants

- Krause, Kurze: Prospektiv, randomisierte Multi-Center Studie zum Vergleich von Schmerz, Funktion und Rückkehr zur Arbeit bei konservativ vs. operativ versorgten stabilen lateralen Malleolarfrakturen, SUVA: 131.000 CHF
- Hoppe, Bennker: 10 years results after vertebroplasty of vertebral compression fractures, Lindenhofstiftung: 65.000 CHF
- Zumstein: Unterschiede der dreidimensionalen Scapula-Morphologie bei Patienten mit glenohumeraler Osteoarthritis und einer gesunder Kontrollgruppe Deutsche Arthrose-Hilfe e.V. : 10.000 Euro
- Einfluss des Subtalgelenkes auf die Wirksamkeit von Kalkaneus vs. supramalleolären Korrekturosteotomien SFAS: 10'000 CHF

Selected Publications

- Femoral osteochondroplasty can be performed effectively without the risk of avascular necrosis or femoral neck fractures in an experimental ovine FAI model. Schmaranzer F, Arendt L, Lerch TD, Steppacher SD, Nuss K, Wolfer N, Dawson HE, von Rechenberg B, Kircher PR, Tannast M. Osteoarthritis Cartilage. 2017 Oct 20. pii: S1063-4584(17)31260-8. doi: 10.1016/j.joca.2017.10.009
- Neer Award 2016: Reduced Muscle Degeneration and Decreased Fatty Infiltration after Rotator Cuff Tear in a Poly(Adp-Ribose) Polymerase 1 (Parp-1) Knock-out Mouse Model. Kuenzler, M. B., K. Nuss, A. Karol, M. O. Schar, M. Hottiger, S. Raniga, D. Kenkel, B. von Rechenberg and M. A. Zumstein. J Shoulder Elbow Surg, (2017)
- Ankle joint pressure changes in high tibial and distal femoral osteotomies. Krause F, Barandun A, Klammer G, Zderic I, Gueorguiev B, Schmid T. Bone Joint J. 99:59-65, 2017
- Percutaneous screw fixation of the iliosacral joint: A case-based preoperative planning approach reduces operating time and radiation exposure. Ecker TM, Jost J, Cullmann JL, Zech WD, Djonov V, Keel MJB, Benneker LM, Bastian JD. Injury. 2017 Aug;48(8):1825-1830. doi: 10.1016/j.injury.2017.06.016. Epub 2017 Jun 20
- Short Posterior Stabilization in Combination With Cement Augmentation for the Treatment of Thoracolumbar Fractures and the Effects of Implant Removal. Hoppe S, Aghayev E, Ahmad S, Keel MJB, Ecker TM, Deml M, Benneker LM. Global Spine J. 2017 Jun;7(4):317-324. doi: 10.1177/2192568217699185. Epub 2017 Apr 7

Department of Osteoporosis

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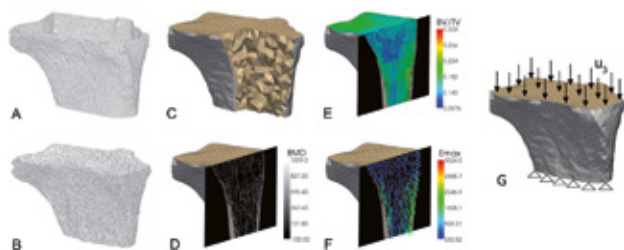
Prof. Kurt
Lippuner
Chairman and
Head

Research Partners

- AO Research Institute Davos, AO Foundation, Davos, Switzerland
- Department of Orthopaedic Surgery, Bern University Hospital, University of Bern, Bern, Switzerland
- ETH Zurich, Institute for Biomechanics, 8093 Zurich
- Free University of Amsterdam (ACTA), Amsterdam, the Netherlands
- Institute of Surgical Technology and Biomechanics, University of Bern, Bern, Switzerland
- Radboud University Medical Center, Nijmegen, the Netherlands
- Swiss Paraplegic Centre, Clinical Trial Unit, Nottwil, Switzerland
- University Hospitals of Geneva, Service of Bone Diseases, Department of Rehabilitation and Geriatrics, Geneva, Switzerland
- University of Lausanne, Bone and Joint Department, Lausanne, Switzerland
- Zhejiang Chinese Medical University, Hangzhou, China

Research Profile

The research activities of the Department of Osteoporosis cover a broad range of aspects within the field of metabolic bone diseases including clinical and translational projects. Research areas comprise the epidemiology and socio-economic burden of osteoporotic fractures, the refinement of fracture risk prediction through novel general (e.g. FRAX®-Score) and local osteoporotic diagnostics including the establishment of bone strength prediction via finite element analysis using high-resolution peripheral quantitative CT (HR-pQCT) at the forearm and distal tibia (collaborative project with ISTB, Univ. Bern). In a clinical project (granted by



Framework for the generation of a FE model from HR-pQCT data. Separation of cortical (A) and trabecular bone (B); Mesh (C) with image-based cortical thickness (D); Image-based material properties of each element with bone volume fraction (E) and trabecular anisotropy (F); (G) Boundary conditions. (Images adapted from Varga P1, Dall'Ara E, Pahr DH, Pretterklieber M, Zysset PK, Biomech Model Mechanobiol. 2011, 10(4):431-44).

the SNSF) under the joined leadership of the ETH Zurich and our clinic, HR-pQCT technology combined with biochemical markers of bone turnover are used to follow the micro-structural changes during fracture healing in healthy and osteoporotic humans.

Projects on targeted stimulation of bone anabolism through local therapeutic intervention at high risk topographic sites (spine and hip) represent the current therapeutic research focus of our experimental/ translational research group (see highlights). Last but not least, our department has been internationally acknowledged and awarded for many years as a research site for clinical phase II and III trials relating to the pharmacological treatment of primary and secondary osteoporosis in men and women.

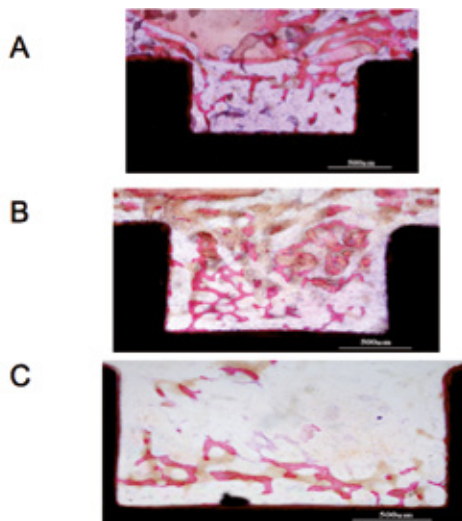
Teaching Profile

Undergraduate teaching (osteoporosis lectures in the context of geriatrics as well as lectures on calcium phosphate metabolism), and practical courses on pharmaceutical medicine are given to students of human medicine. For students of biomedical engineering a module of the course Biomechanics Labs (responsible coordinator: Prof. Ph. Zysset, ISTB, Univ. Bern) with practical teaching on measurement technologies in Biomechanical Engineering is held. The department of osteoporosis is a postgraduate training site for residencies in General Internal Medicine, Endocrinology (Lab), and Pharmaceutical Medicine (the sole residency program of that speciality at the University Hospital in Bern).

Highlights 2017

A novel experimental implant that permits the quantitative grading of surface-property effects on osseointegration in an osteoporotic bone environment

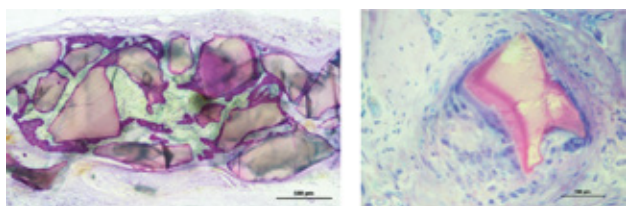
Experimental investigation of local osteogenic treatment in patients needing dental or orthopaedic implants in an osteoporotic environment requires adequate experimental implants permitting quantitative grading of implant osseointegration over time. Such a novel experimental implant, a single large-chamber implant model, was designed and tested. Implants of various sizes were inserted into the edentulous maxillae of adult goats with a physiologically osteoporotic masticatory apparatus. A discriminative quantitative grading of osseointegration was shown to be possible when using such a large-chamber model. The biological potential of novel functionalized implant surfaces to potentiate and expedite osseointegration under adverse (e.g. osteoporotic) conditions is currently under research. Hunziker et al., Intl. J. Oral Maxillofacial Surg., in press.



Implants of various sizes were inserted into the edentulous maxillae of adult goats with a physiologically osteoporotic masticatory apparatus. A: small size, B: middle size, C: large size.

Hyaluronic Acid promotes BMP-2 - induced osteogenesis in a collagen carrier

Novel future treatment principles of osteoporosis relate to the local anabolic therapy of osteoporotic predilection sites such as the spine and the hip by using tissue engineering principles for bone tissue. Bone morphogenetic protein (BMP-2) is a well known strongly osteogenic drug that potentially can be used for such purposes. It is currently in clinical use for the treatment of spinal fusions and non-unions. However, its use is associated with serious unwanted effects such as ectopic ossifications and neurological symptoms. These effects seem associated with the high dosage schedule applied. We hypothesized that a combination use of BMP-2 with hyaluronan (HA) is able to significantly promote the osteogenesis potential of BMP-2, allowing for use at lower dosage levels with the potential to suppress unwanted side effects. This hypothesis was tested by simulating the clinical application mode of using BMP-2 together with an absorbable collagen sponge as carrier (ACS). In vivo-testing was performed using a well-established subcutaneous assay for ectopic ossification induction in rats. The total volume of newly formed bone tissue was significantly higher at an optimal dose of BMP-2 of 10 microgram in the combined application with HA/ACS. At this BMP-2 dosage level the new bone tissue formed was approximately 100% larger than bone volumes obtained at lower or higher BMP-dosage levels obtained in the absence of HA. We conclude that HA added to the BMP/ACS carrier constructs is able to promote osteogenesis on a dose-dependent basis. Huang et al., *Polymers*, 9:17, 2017.



Overview of sponge material in situ (left) and high magnification of sponge material, illustrating cellular reactions and formation of new bone tissue (right).

Selected Competitive Grants

- SNF 320030L_170205 (D-A-CH): Local remodelling and mechanoregulation of bone fracture healing in healthy, aged, and osteoporotic humans. Collaborative Project with ETH Zurich, Medical University Innsbruck, University Hospital Ulm. 2017-2020; 372'000 CHF
- SNF no 165510 Micro-Meso Scale Transition of Bone Strength. 2016-2019; 381000 CHF)
- China Scholarship Council, Scholarship for Dr. Hairong Huang. (2014 - 2017; 110000 CHF)

Selected Publications

- Hunziker EB, Jovanovic J, Horner A, Keel MJ, Lippuner K, Shintani N. Optimisation of BMP-2 dosage for the osseointegration of porous titanium implants in an ovine model. *N. Eur Cell Mater*. 2016 Nov 18;32:241-256
- Hunziker, EB, Habegger, M, Rudolf, S, Liu, Y, Gu, Z, Lippuner, K, Shintani, N, Enggist, L. A novel experimental dental implant permits the quantitative grading of surface-property effects on osseointegration. *Int J Oral Maxillofacial Surg*, 2017, in press
- Huang H, Wismeijer D, Hunziker EB, Wu G. The Acute Inflammatory Response to Absorbed Collagen Sponge Is Not Enhanced by BMP-2. *Int J Mol Sci*. 2017 Feb 25;18(3)
- Bone HG, Wagman RB, Brandi ML, Brown JP, Chapurlat R, Cummings SR, Czerwiński E, Fahrleitner-Pammer A, Kendler DL, Lippuner K, Reginster JY, Roux C, Malouf J, Bradley MN, Daizadeh NS, Wang A, Dakin P, Pannaciuoli N, Dempster DW, Papapoulos S. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomised FREEDOM trial and open-label extension. *Lancet Diabetes Endocrinol*. 2017 Jul;5(7):513-523
- Popp AW, Senn R, Curkovic I, Senn C, Buffat H, Popp PF, Lippuner K. Factors associated with acute-phase response of bisphosphonate-naive or pretreated women with osteoporosis receiving an intravenous first dose of zoledronate or ibandronate. *Osteoporos Int*. 2017 Jun;28(6):1995-2002

Department for Plastic and Hand Surgery

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Prof. Mihai
Constantinescu



Prof. Esther
Vögelin

Research Partners

- Cardiovascular Research Group, Department for BioMedical Research, University of Bern
- Department of Pharmaceutical Technology, Institute of Pharmacy, University of Jena, Germany
- Department of Plastic Surgery and Hand Surgery, University Hospital Zurich, University of Zurich, Switzerland
- Institut de Recherche Expérimentale et Clinique (IREC), Université catholique de Louvain, Brussels, Belgium
- Institute for Stem Cell Biology and Regenerative Medicine (inStem), Bangalore, India
- Institute of Anatomy, University of Bern, Bern, Switzerland
- Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences, ETH Zurich, Switzerland.
- Institute of Pathology, University of Bern, Switzerland
- Swiss Federal Laboratories for Materials Science and Technology, St Gallen, Switzerland.
- University Institute of Clinical Chemistry, Inselspital, Bern University Hospital, University of Bern, Switzerland

Research Profile

The University Clinic for Plastic and Hand Surgery at the Inselspital Bern has existed since 1979. The clinic is conducting clinical and basic research in the fields of Plastic, Reconstructive and Aesthetic Surgery, under the direction of Prof. Mihai Constantinescu, and Hand Surgery and Surgery of the Peripheral Nerve, under the direction of Prof. Esther Vögelin. The Plastic Surgery clinical research focuses on the implementation of 3D models of aesthetic tissue reconstruction and innovative strategies for the diagnosis and treatment of critical ischemic tissue and malignant skin tumors. Hand surgery research is oriented to develop new treatment modalities for hand injuries by application of new drugs and evaluation of innovative modalities for repair of peripheral-nerve injuries. The clinic is also conducting several basic research projects in the field of vascularized composite allotransplantation. In this field, the interests of the group focus on the use of site-specific immunosuppression to reduce off-target systemic toxicity and increase compliance, and to characterize the role of the lymphatic system in allograft rejection. Moreover, the group is investigating the possibility of using tissue-engineering and innovative nanoparticle-based modalities for the treatment of nerve injuries and surgical complications.

Teaching Profile

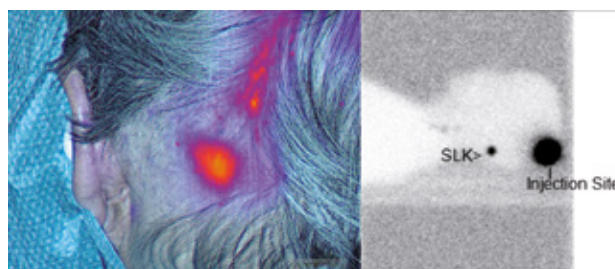
The clinic participates in University teaching programs for students of Medicine, Biomedical Science and Molecular Life Science. Moreover, we are involved in outreach activities for

education of young students, such as the Swiss Youth in Science program and the mentoring of Matura Projects of the Swiss Academy of Science. We also offer a microsurgery course for the training of all the medical specialties.

Highlights 2017

A diagnostic sensitivity study to analyse the ability of intradermally administered indocyanine green (ICG) and near infrared fluorescence imaging (NIRFI) to transcutaneously identify sentinel lymph nodes (SLNs) in malignant melanoma - a clinical, prospective, single-arm, single-blinded, single-centre Phase II study

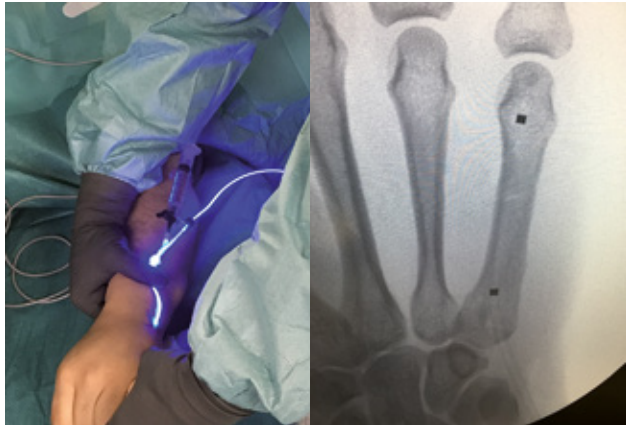
The treatment of Malignant Melanoma (an aggressive skin cancer whose incidence in Switzerland is the highest among all European countries) employs standardly a SLN biopsy. The gold standard technique to identify SLN is based on the use of the radioisotope technetium -99m. There is evidence that using less invasive and less costly methods like ICG based near infrared imaging is possibly equally as effective. Using a new state-of-the-art imaging device that employs 3D imaging techniques to increase the depth of transcutaneous scanning the clinic for Plastic Surgery aims to prospectively evaluate the sensitivity of the ICG imaging technique in comparison to radioisotope based lymphoscintigraphy. We hope that we can thus change the SLN biopsy technique leading ultimately to improved quality of life for the melanoma patient. An example of perioperative visualization of an occipital SLN with the ICG near infrared imaging device and traditional Tc99m lymphoscintigraphy is presented below.



Treatment of metacarpal fractures by means of a photodynamic polymer (IlluminOss™). A monocentric, retrospective, observational study

Displaced fractures are best treated surgically either by bouquet pinning or plate osteosynthesis. Bouquet pinning spares the soft tissue envelope but implant related complications such as pin tract infection, intraarticular migration of the wire and arrosion of the ECU tendon are encountered necessitating early implant removal. On the other hand, plate osteosynthesis achieves high primary stability.

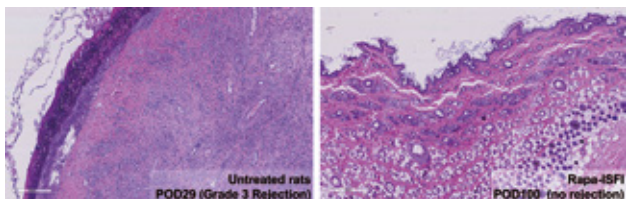
However, high rate of joint stiffness as a result of adhesions in the extensor mechanism may require early implant removal and tenolysis. The clinic for Hand Surgery aims to evaluate the effectiveness of an intramedullary photodynamic polymer (IlluminOss™) for stabilizing dislocated metacarpals, comparing this innovative approach with the established osteosynthesis techniques. After reduction of the fracture, the implant is introduced into the bone and then cured by light. The evaluation is based on archived electronic patient data gathered during surgery and consultations at 6 weeks, 3 months and 6 months postoperatively at the Department of Hand Surgery Inselspital Bern from patients with dislocated fifth-metacarpal fractures.



Left: Light curing of polymer at a wavelength of 436 nm. Right: Fifth-metacarpal after reduction with implant.

Site-specific immunosuppression in hand transplantation

Vascularized composite allotransplantation (VCA), such as hand-transplantation, has the potential to restore esthetic and function in patients who have suffered severe injuries. However, adverse effects of chronic high-dose immunosuppression regimens strongly limit the access to procedures in the clinic. Thus, our research focuses on the development of new therapies aimed at delivering the drug directly into the allograft with the aim to reduce toxicity as well as to improve therapeutic outcomes. Recently, we demonstrated that intra-graft delivery of tacrolimus promotes VCA survival by increasing tissue drug availability and promoting the establishment of transient chimerism and thus long-term graft acceptance. More recently, we developed an in situ forming implant loaded with rapamycin (Rapa-ISFI) demonstrating long-term acceptance of VCA by promotion of immunoregulatory mechanisms, such as chimerism and donor-specific Treg induction. Representative histological pictures of untreated rats rejecting their grafts and of Rapa-ISFI treated rats 100 days after transplantation is shown.



Selected Competitive Grants

- Swiss National Science Foundation (grants: 156773, 169231)
- US Department of Defense, Reconstructive Transplant Research Program - Award W81XWH 17-1-0686
- American Foundation for Surgery of the Hand (AFSH), Basic Science Grant - Award 1404
- Bernische Krebsliga
- Schweizerischen Gesellschaft für Handchirurgie: Forschungspreis

Selected Publications

- Damian Sutter, Dzhuliya V. Dzhonova, Jean-Christophe Prost, Cedric Bovet, Yara Banz, Jean-Christophe Leroux, Robert Rieben, Esther Vögelin, Jan A. Plock, Paola Luciani, Adriano Taddeo, Jonas T. Schnider. Delivery of Rapamycin Using In Situ Forming Implants Promotes Immunoregulation and Vascularized Composite Allograft Survival. Submitted (2017)
- Radu Olariu, Julie Denoyelle, Franck M. Leclère, Dzhuliya V. Dzhonova, Thusitha Gajanayake, Yara Banz, Michael Hayoz, Mihai Constantinescu, Robert Rieben, Esther Vögelin, Adriano Taddeo. Intra-graft injection of tacrolimus promotes survival of vascularized composite allotransplantation. *Journal of Surgical Research*, vol. 218, pp. 49–57, 2017
- Mai M. Abdelhafez, Jane Shaw, Damian Sutter, Jonas T. Schnider, Yara Banz, Hansjörg Jenni, Esther Vögelin, Mihai A. Constantinescu, Robert Rieben. Effect of C1-INH on ischemia/reperfusion injury in a porcine limb ex vivo perfusion model. *Molecular Immunology*, vol. 88, p.p. 116-124, Aug. 2017
- Jerome Duisit, Louis Maistriaux, Adriano Taddeo, Giuseppe Orlando, Virginie Joris, Emmanuel Coche, Catherine Behets, Jan Lerut, Chantal Dessy, Giulio Cossu, Esther Vögelin, Robert Rieben, Pierre Gianello, and Benoît Lengelé. *Bioengineering a Human Face Graft: The Matrix of Identity*. *Ann. Surg.*, p. 1, Jul. 2017
- Zacharia Mbaidjol, David Kiermeir, Annemarie Schönfeld, Jörg Arnoldi, Martin Frenz, Mihai A. Constantinescu. Endoluminal laser-assisted vascular anastomosis—an in vivo study in a pig model. *Lasers in Medical Science*, Vol. 32, pp 1343–1348, August 2017

Department for Pulmonary Medicine

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Prof. Thomas Geiser



Prof. Christophe von Garnier



PD Dr. Sebastian Ott



Dr. Manuela Funke



Dr. Anne-Kathrin Brill



Dr. Amiq Gazdhar



PD Dr. Fabian Blank

Research Partners

- Prof. Guenat, Organ-on-chip, ARTORG Center, University of Bern, Bern, Switzerland
- Prof. Lars Knudsen, Institute of Functional and Applied Anatomy, Hannover Medical School, German Center for Lung Research, Hannover, Germany
- PD Dr. Kathrin Hostettler, Pulmonary Division, Basel University Hospital, Basel, Switzerland
- Prof. Phil Stumbles, Murdoch University, Western Australia
- Sleep-Wake-Epilepsy Center, Bern University Hospital, Inselspital, Bern, Switzerland
- Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom
- Prof. Bruno Crestani, Pulmonary Division, Hôpital Bichat, Paris, France
- Pulmonary Medicine, MGH, Harvard, Boston, USA
- University Institute of Clinical Chemistry, University of Bern, Bern, Switzerland
- Dr. Alexander Eggel, Rheumatology, Immunology and Allergology Division, Bern University Hospital, Inselspital, Bern, Switzerland

Research Profile

Our research focus concentrates on lung injury, inflammation, immunity and regeneration.

Above all, our fundamental research groups pay particular attention to the regulation of pulmonary immune responses by designing liposomes and virosomes that are administered to the respiratory tract (Ch. von Garnier/F. Blank). The potentials of such bio-mimetic particles are tested in models of asthma and chronic obstructive pulmonary disease (COPD) to redirect skewed mucosal immune responses. We also examine the potential of stem cells to regenerate lung tissue after injury and fibrosis. (Th. Geiser/A. Gazdhar). We are interested in pathomechanistic studies of lung fibrosis and new treatment approaches (M. Funke). Finally, we participate in the development of novel in vitro technology (lung-on-chip) in collaboration with Prof. Olivier Guenat. Clinical study focuses are sleep medicine and interstitial lung diseases. In sleep medicine and non-invasive ventilation we are involved in several clinical studies on sleep disordered breathing and stroke, cardiac conditions and treatment options for respiratory failure (S.R. Ott/A.-K. Brill). In interstitial lung diseases we conduct investigator initiated clinical studies to treat patients with idiopathic pulmonary fibrosis. We also conduct cohort studies with biobanking for new biomarker discovery for patients with idiopathic interstitial pneumonias (M. Funke).

Teaching Profile

The Department of Pulmonary Medicine provides training in respiratory medicine for students in medicine, biomedicine, dentistry, sport sciences and biomedical research. We teach physiotherapists at the Bern University of applied sciences and the Swiss neurophysiologists in respiratory medicine. The Department of Pulmonary Medicine trains specialists in respiratory medicine and also provides post-graduate training for other specialists and general practitioners.

Highlights 2017

Identification and Characterization of a Dendritic Cell Precursor in Parenchymal Lung Tissue

A network of pulmonary dendritic cells (DC) and macrophages ($m\phi$) provides continuous surveillance of inhaled antigens to maintain immunological homeostasis. How bone marrow-derived precursors replenish resident pulmonary DC and $m\phi$ remains unclear. We employed a mouse model for whole body irradiation and bone marrow reconstitution to identify a common DC progenitor (PC) population that rapidly depleted and reconstituted in parallel to DC by Days 7-9 and significantly faster than $m\phi$ that reached 50% repopulation only by Days 16-21. During in vitro maturation, purified PC gained antigen-presenting function, cell surface phenotype and morphology consistent with that of a pulmonary myeloid DC.

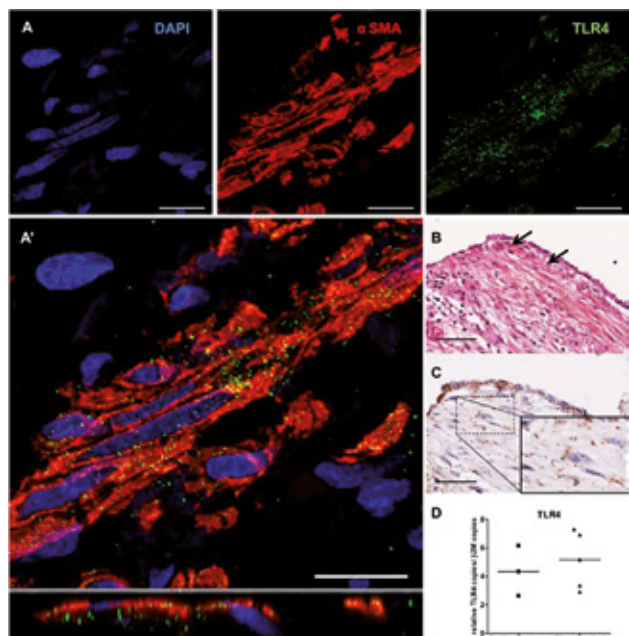
The SERVE-HF safety notice in clinical practice- experiences of a tertiary sleep center

The results of the SERVE-HF trial addressing adaptive servo-ventilation (ASV) in chronic heart failure (CHF) patients with central sleep apnea (CSA) prompted a field safety notice. It was recommended to identify potentially endangered patients and to advise the discontinuation of ASV. Our study reports on the first „real world“ experience of the patient identification process and effect of ASV discontinuation after the safety warning. Only 10% of our patients fulfilled the risk criteria but 38% required an additional echocardiogram implying a need for a more precise phenotyping of sleep apnea patients. ASV could be withdrawn without severe complications in most patients, but nearly all of them rapidly redeveloped CSA after ASV was withdrawn.

Toll-like receptor 4 (TLR4) activation attenuates pro-fibrotic response in control fibroblasts but not fibroblasts from IPF patients

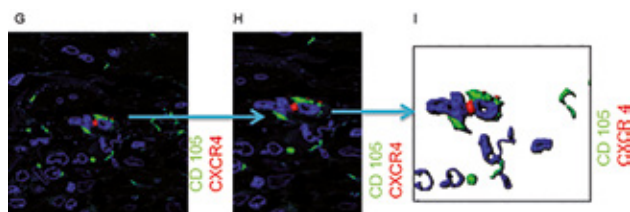
Idiopathic pulmonary fibrosis (IPF) deteriorates after infection although pneumonia in healthy lungs rarely induces fibrosis. Bacterial lipopolysaccharide (LPS) activates Toll-like receptor

4 (TLR4). We investigated the role of TLR4 in IPF. TLR4 is expressed in IPF lungs, primary normal human lung fibroblasts (NL-FB) and IPF-FB. Cells were co-exposed to LPS and TGF- β modeling pneumonia. NL-FB produced less pro-fibrotic factors upon co-stimulation compared with TGF- β stimulation alone, but IPF-FB showed increased pro-fibrotic markers after co-stimulation. Downregulation of TGF- β receptor type 1 in NL-FB contributes to the reduced pro-fibrotic response. Normal and IPF fibroblasts differ in their pro-fibrotic response upon TLR4 stimulation.



Multipotent mesenchymal stem cells in lung fibrosis

Stem cells have been identified in the human lung; however, their role in disease is unclear. We isolated mesenchymal stem cells (MSC) from human lungs. MSC were cultured from fibrotic, emphysematous and healthy lung tissue. Immunofluorescence expression of CD44, CD90 and CD105 characterized the MSC. Cells stained positive for the pluripotency markers and markers indicating bone marrow origin. Our study demonstrates enhanced numbers of MSC in fibrotic lung tissue as compared to emphysema and normal lung. The cells inhibit fibroblast proliferation and enhance epithelial repair. Further studies are needed to elucidate their role in the treatment of lung fibrosis.



Selected Competitive Grants

- Swiss National Science Foundation (Sinergia grant nr. CRSII3_160704/1)
- Swiss National Science Foundation (nrs. 320030-149752; 320030-166827)
- Lungenliga Schweiz (nr. 2015-06)
- Lungenliga Schweiz (nr. 2014-15)
- Johanna Dürmüller-Bol DBMR Research Grant Award 2017

Selected Publications

- von Garnier C, Blank F, Rothen-Rutishauser B, Goethert JR, Holt PG, Stumbles PA, Strickland DH. Identification and Characterization of a Dendritic Cell Precursor in Parenchymal Lung Tissue. *Am J Respir Cell Mol Biol.* 2017 Mar; 56(3):353-361
- Ebener S, Barnowski S, Wotzkow C, Marti TM, Elena Lodrigez, Crestani B, Blank F, Schmid RA, Geiser T, Funke M. Toll-like receptor 4 (TLR4) activation attenuates pro-fibrotic response in control fibroblasts but not fibroblasts from IPF patients. *Am J Physiol Lung Cell Mol Physiol.* 2017 Jan 1;312(1):L42-L55
- Brill A-K, Pichler Hefti J, Geiser T, Ott SR: The SERVE-HF safety notice in clinical practice-experiences of a tertiary sleep center. *Sleep Med.* 2017 Sep;37:201-207
- Hostettler KE, Gazdhar A, Khan P, Savic S, Tamo L, Lardinois D, Roth M, Tamm M, Geiser T. Multipotent mesenchymal stem cells in lung fibrosis. *PLoS One.* 2017 Aug 21;12(8):e0181946
- Funke M, Azzola A, Adler D, Barazzone-Argiroffo C, Benden C, Boehler A, Bridevaux P-O, Brutsche M, Clarenbach C, Hostettler K, Kleiner-Finger R, Nicod LP, Soccia PM, Tamm M, Geiser T, Lazor R. Idiopathic pulmonary fibrosis in Switzerland - Diagnosis and Treatment Position of the Working Group for Interstitial and rare lung diseases of the Swiss Respiratory Society, *Respiration.* 2017;93(5):363-378

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- Institute for Surgical Technology and Biomechanics, University of Bern, Bern, Switzerland
- Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland
- Swiss Group for Clinical Cancer Research, Bern, Switzerland
- GEC-ESTRO-Breast-Working-Group, Brussels, Belgium
- Paul Scherrer Institute, Villigen, Switzerland
- Institute for Biomedical Engineering, Swiss Federal Institute of Technology (ETH), Zurich, Switzerland
- Princess Margaret Cancer Center, Toronto, Canada
- Institute of Molecular Systems Biology, Swiss Federal Institute of Technology (ETH), Zurich, Switzerland
- The Netherlands Cancer Institute, Amsterdam, The Netherlands

Research Profile

The Department of Radiation Oncology along with its three alliance centers represents the largest provider of radiation therapy in Switzerland. Three main branches of research are established as follows: Clinical research with roughly 20 open clinical trials, among them six trials initiated and chaired by the department; Research in medical physics, headed by the division of medical physics; Research in radiation biology, conducted in three research groups.

Clinical Research

- Prostate cancer: salvage radiotherapy in biochemical failure, metabolomic signatures
- Head neck cancer: Role of upfront neck dissection in the context of primary radiotherapy; outcome of immune checkpoint inhibitor and chemotherapy followed by dose and volume adapted chemo-radiotherapy
- Breast cancer: Partial breast irradiation with multi-catheter brachytherapy
- Brain tumor: Automatic segmentation of brain tumors, postoperative radiosurgery
- Palliative care: Advanced care planning/anticipation; best care for the dying; community palliative care

Medical Physics

- Dynamic trajectory radiotherapy (DTRT) and modulated electron beam radiotherapy (MERT)
- Independent dose calculation and radiation protection in the context of robotic stereotactic radiotherapy
- Efficient quality assurance for external beam radiotherapy and accurate dose calculation for brachytherapy
- Medical imaging related research topics

Radiation Biology

- Omics-related (transcriptomics, (phospho-)proteomics and single-cell proteomics, metabolomics) studies on receptor tyrosine kinase (MET) signaling, radiation therapy response and resistance and head and neck squamous cell carcinoma (HNSCC)
- Roles of novel posttranslational modifications (phosphorylations, ubiquitinations, acetylations) in cellular responses to DNA-damaging agents and targeted therapies
- Translational research to explore new prognostic and predictive biomarkers
- Radiobiological impact of dose rate

Teaching Profile

Undergraduate lectures are provided for students in medicine, biomedical engineering, molecular and biomedical sciences as well as in dental medicine at the University of Bern. Undergraduate teaching does also include practical training for medical students. Postgraduate lectures in medical physics are given at the department of physics at the Swiss Federal Institute of Technology in Zurich. A CAS program for palliative care is run in cooperation with various faculties of the University of Bern and the Bern University of Applied Sciences. Various PhD and MD-PhD positions are provided in radiation biology and medical physics.

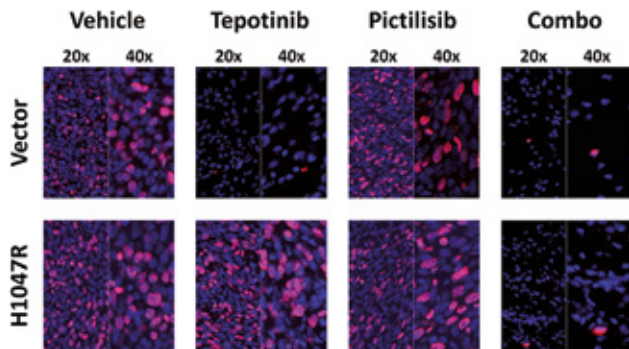
Highlights 2017

Two multicentric prospective trials, which are led by the department, were opened and funded: the PROMET trial (SAKK 0815, international phase III) and the upfront neck dissection trial (national phase II). S. Mueller's paper (Phys

Med Biol. 2017, see below) was chosen as „Editor’s choice“. We published more than 35 original articles, including the following three papers.

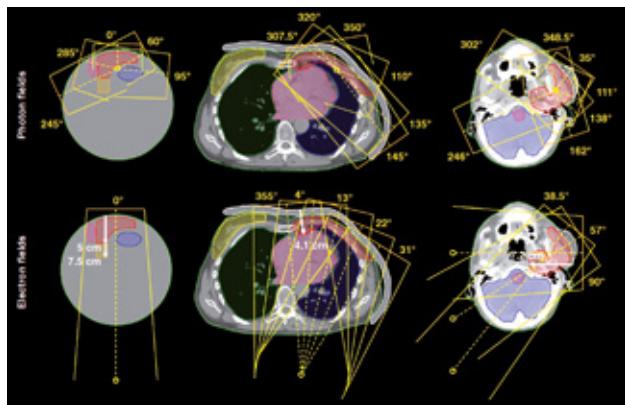
Nisa L, et al. PIK3CA hotspot mutations differentially impact responses to MET targeting in MET-driven and non-driven preclinical cancer models. Mol Cancer. 2017 May 22;16(1):93.

PIK3CA mutations can lead to resistance to MET inhibition, supporting future clinical evaluation of combinations of PI3K and MET inhibitors in common scenarios of malignant neoplasms featuring aberrant MET expression and PIK3CA mutations.



Mueller S, et al. Simultaneous optimization of photons and electrons for mixed beam radiotherapy. Phys Med Biol. 2017 Jun 26;62(14):5840-5860.

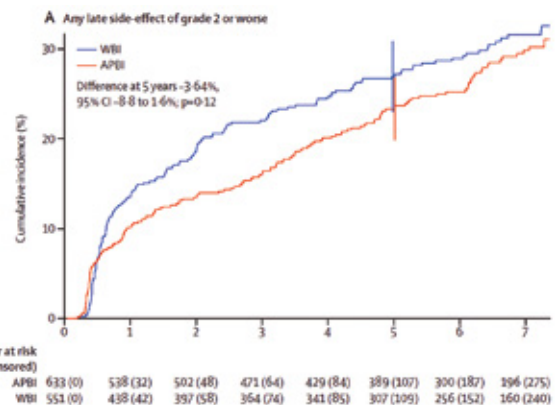
A treatment planning process for mixed beam radiotherapy (MBRT) including simultaneous optimization is successfully implemented and the dosimetric superiority of MBRT plans over modulated electron radiotherapy, photon IMRT and VMAT plans is demonstrated for academic and clinical situations including superficial targets with and without deep-seated part.



Polgár C, et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. Lancet Oncol. 2017 Feb;18(2):259-268.

5-year toxicity profiles and cosmetic results were similar in patients treated with breast-conserving surgery followed by either accelerated partial breast irradiation (APBI) with interstitial brachytherapy or conventional whole-breast irradiation, with significantly fewer grade 2-3 late skin side-effects after APBI with interstitial brachytherapy. These

findings provide further clinical evidence for the routine use of interstitial multicatheter brachytherapy-based APBI in the treatment of patients with low-risk breast cancer who opt for breast conservation.



Selected Competitive Grants

- Swiss Cancer Research and Rising Tide: PROMET - Multicenter, Randomized, Double Blind, Placebo Controlled Phase II Trial of Salvage Radiotherapy +/- Metformin for Patients with Prostate Cancer after Prostatectomy. (A. Dal Pra, D. Aebbersold)
- Swiss Cancer Research: Is early palliative care associated with a reduction in intensity and costs of care at the end of life in patients with advanced cancer? A randomized controlled trial. (S. Eychmüller)
- SNF project funding: Impact of MET receptor tyrosine kinase inhibition on the DNA damage response-related phosphoproteome. (Y. Zimmer)
- Werner und Hedy Berger-Janser Stiftung: Characterization of a novel putative ATM/ATR/DNA-PK phosphorylation site on the MET receptor tyrosin kinase. (M. Medova)
- Bernische Krebsliga: Cutting-edge radiation therapy: effect of delivery time and dose-rate on tumour cell survival and invasion and its clinical impact. (K. Zaugg)

Selected Publications

- Herrmann E, et al. External beam radiotherapy for unresectable hepatocellular carcinoma, an international multicenter phase I trial, SAKK 77/07 and SASL 26. *Radiat Oncol.* 2017 Jan 13;12(1):12
- Polgár C, et al. Late side-effects and cosmetic results of accelerated partial breast irradiation with interstitial brachytherapy versus whole-breast irradiation after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: 5-year results of a randomised, controlled, phase 3 trial. *Lancet Oncol.* 2017 Feb;18(2):259-268
- Nisa L, et al. PIK3CA hotspot mutations differentially impact responses to MET targeting in MET-driven and non-driven preclinical cancer models. *Mol Cancer.* 2017 May 22;16(1):93
- Mueller S, et al. Simultaneous optimization of photons and electrons for mixed beam radiotherapy. *Phys Med Biol.* 2017 Jun 26;62(14):5840-5860
- Henzen D, et al. Evaluation of clinically applied treatment beams with respect to bunker shielding parameters for a Cyberknife M6. *J Appl Clin Med Phys.* 2017 Nov 10. doi: 10.1002/acm2.12215

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- BRSC, Riga, Latvia
- Vetsuisse Faculty, University of Bern, Switzerland
- Vifor Fresenius Medical Care Renal Pharma Ltd., St. Gallen
- Ludwig Institute, Lausanne
- Nanyang University, Singapore
- Kennedy Institute, University of Oxford
- Tumor-Immunologie, Prof. Dr. med Ochsenbein, DBMR, University of Bern, Bern
- Laboratory of Clinical Immunology Allergy and Advanced Biotechnologies, Arcispedale Santa Maria Nuova-IRCCS, Reggio Emilia, Italy
- University of Piemonte Orientale, Dept. of Translational Medicine, Italy
- Istituto Nazionale di Genetica Molecolare Via Francesco Sforza, Milano, Italy
- Dr. Marc Vocanson, CIRI, Lyon, France
- Prof. David A. Ostrov, Department of Pathology, Immunology and Laboratory Medicine, University of Florida, College of Medicine, Gainesville, FL, USA

Research Profile

The division of Immunology is linked to the Department for BioMedical Research (DBMR) at the University of Bern and to the University Clinic of Rheumatology, Immunology and Allergology (RIA) at the Inselhospital, Bern. It consists of three independent basic research groups and a clinically oriented research group that investigate immunological mechanisms with the aim of furthering our understanding of immune regulation and the development of potential new therapies in the framework of one health. In the first group (Bachmann/Vogel) the research is dominated by the question how T and B cells responses are induced and influenced by innate immunity. Viruses, virus-like particles and bacteria are used to probe the protective capacity of the induced immune response. Understanding the cellular networks of the immune system is of significant medical interest since i) prophylactic vaccines, which are the most effective medical intervention known to date, are based on the induction of long-lived immune responses and ii) a deregulated immune system is the underlying cause of many chronic diseases and autoimmunity. Several diseases serve as models i.e. Typ II Diabetes, cancer, and in particular inflammatory diseases mostly on type 2 immunity such as allergic inflammation of the skin. Monoclonal antibodies

and virus-like particles based vaccines are the primary agents developed for therapy. In the field of allergy the focus is on the study of basic and applied aspects of IgE regulation and mast cell biology and the role of CD23 in driving IgE and IgG responses. Development of a vaccine against peanut- as well as cat allergy are also important goals in this field.

In the second group (Eggel) the focus lies on the investigation of biologic mechanisms underlying both beneficial as well as pathogenic type 2 immune responses. Key questions are: 1) how allergies evolve and how treatments directly interfering with the allergic cascade may be developed 2) how age-related disorders and how they are linked to alterations in type 2 immune responses.

The domain of interest of the third group (Yerly) lies in drug allergy. In order to treat and prevent such reactions, it is important to understand how small molecules like drugs can become immunogenic. As the symptoms of drug allergy are very heterogeneous, efforts are also being made to study the link between the phenotype of drug reacting immune cells and the clinical picture.

The clinical research group (Villiger) is active in the study of pathogenic mechanisms and the testing of novel treatment strategies of large vessel vasculitides such as Giant Cell Arteritis, Takayasuarteritis and Behçet's disease. In addition, there is a long-term interest in the field of pregnancy and rheumatic diseases (Foerger). There is a strong interaction with international groups, in particular with Italy, Germany and the USA.

Teaching Profile

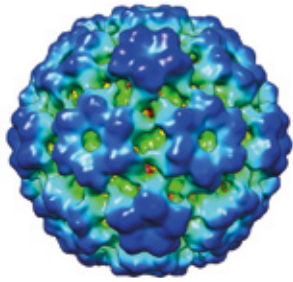
The Immunology groups participate in university teaching programs for students of medicine, biomedicine and biology. Master students of biology are also coming from foreign Universities.

Highlights 2017

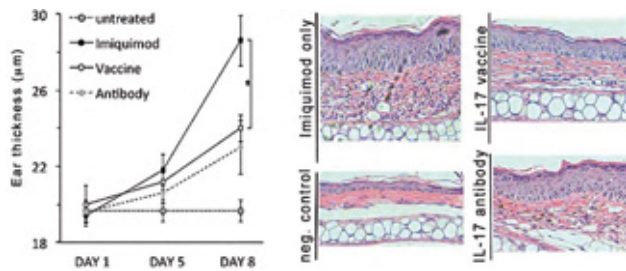
Incorporation of Tetanus-epitope into virus-like particles results in a vaccine platform optimized for the old age

The use of Virus-like particles (VLPs) as antigen-carrier confers robust B cell activation, by mimicking the repetitive three-dimensional scaffold common to viral intruders. Vaccine-induced IgG responses are usually limited by Th cells. To improve IgG responses overall, we incorporated a universal T-cell epitope derived from the tetanus vaccine, which is recognized by essentially all individuals and for which everyone has memory T help. VLPs derived from Cucumber Mosaic Virus were engineered to incorporate a T-cell-stimulatory epitope derived from Tetanus toxoid. By displaying cytokines and allergens on these VLPs, we were able to treat chronic inflammatory (Psoriasis, IL-17), neurodegenerative

(Alzheimer's, β -amyloid) and allergic diseases (cat allergy, Fel d 1). Vaccine responses were uniformly strong, selective, efficient *in vivo*, observed and improved in old mice.



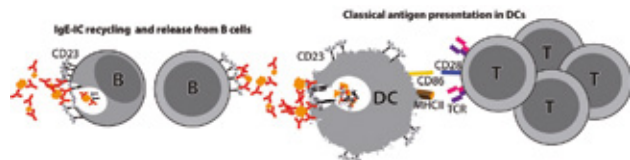
Cryo-electron microscopy image of engineered CMV VLPs.



Demonstration of improved symptoms psoriasis anti-IL-17 vaccinated mice.

A novel recycling mechanism of native IgE-antigen complexes in human B cells facilitates transfer of antigen to dendritic cells for antigen presentation

IgE-immune complexes have been shown to enhance antibody and T cell responses in mice by targeting CD23 (Fc ϵ RII), the low-affinity receptor for IgE on B cells. In humans, the mechanism by which CD23-expressing cells take up IgE-immune complexes (IgE-IC) and process them is not well understood. In this study, we investigated the fate of IgE-IC in human B cells and in CD23 expressing monocyte-derived dendritic cells (moDCs) that represent classical APCs and aimed at studying IgE-dependent antigen presentation in both cell types. The results showed efficient internalization of CD23 IgE-ICs in both cell types. While IgE-ICs were degraded in moDCs, B cells did not degrade the complexes but recycled them in native form to the cell surface enabling IgE-IC shuttling to moDCs in cocultures and antigen specific T cell proliferation. That led us to propose a new CD23-depending recycling mechanism allowing antigen delivery from B cells to dendritic cells for T cell proliferation.



An unexpected protective role of low affinity allergen-specific IgG via the inhibitory receptor Fc γ RIIb

Induction of allergen-specific IgG antibodies is a critical parameter for successful specific immunotherapy (SIT). In this study, we tested the affinity thresholds of allergen-specific IgG antibodies for inhibition of mast cell activation by using 2 different monoclonal antibodies against the major cat allergen, Fel d 1. We generated low affinity versions by mutating the variable regions back to their germ-line sequence resulting in low affinity (10^{-7}) antibodies of the exact same

specificity. Using *in vitro* and *in vivo* models we demonstrate that high affinity antibodies block cellular activation by allergen neutralization and engaging Fc γ RII β while low affinity antibodies fail to neutralize the allergen but are still effective via the inhibitory mechanism. These data indicate that despite inefficient allergen-binding, low IgG affinity antibodies may still efficiently block allergic responses *in vivo*.

Selected Competitive Grants

- Cancer Research Switzerland, Bern. Project: Bispecific anti-tumour antibodies: combining tumour-specificity with cytokine agonism. Project period: 1.7.13-31.3.17
- Allergy Therapeutics (UK) Limited, United Kingdom. Project: Investigating the efficacy of MCT and DOPS adjuvants in combination with VLPs-based vaccines in melanoma murine models via different administrative routes. Project period: 1.8.17-30.7.19
- Vifor Fresenius Medical Care Renal Pharma Ltd., St. Gallen. Project: Uptake of non-biological complex drugs by immune cells. Project period: 1.6.17-31.5.19
- EHVA, Horizon 2020, SBFI, Bern. Project: European HIV Vaccine Alliance (EHVA): a EU platform for the discovery and evaluation of novel prophylactic and therapeutic vaccine candidates. Project period: 1.1.16-31.12.2020
- Lungenliga Bern, Schweiz: Assessment of alternative strategies for the treatment of allergic asthma, Project period: 01.01.17 – 31.12.18
- Allergie-Stiftung Ulrich Müller-Gierok, Bern, Schweiz: Etablierung eines funktionellen, zellbasierten Assays zur Diagnose von Typ-1 Allergien. Project period: 01.10.17 – 30.09.18
- Lungenliga Schweiz, Schweiz: Assessment of novel therapeutic strategies for the treatment of allergic asthma, Project period: 01.06.17 – 30.05.20

Selected Publications

- Zeltins A, West J, Zabel F, El Turabi A, Balke I, Haas S, Maudrich M, Storni F, Engeroff P, Jennings GT, Kotecha A, Stuart DI, Foerster J, Bachmann MF. Incorporation of tetanus-epitope into virus-like particles achieves vaccine responses even in older recipients in models of psoriasis, Alzheimer's and cat allergy. *npj Vaccines*. 2017
- Engeroff P, Fellmann M, Yerly D, Bachmann MF, Vogel M. A novel recycling mechanism of native IgE-antigen complexes in human B cells facilitates transfer of antigen to dendritic cells for antigen presentation. *J Allergy Clin Immunol*. 2017 Oct 23. pii: S0091-6749(17)31591-9
- Zha L, Leoratti F, Storni F, Vogel M, Bachmann MF. An unexpected protective role of low-affinity allergen-specific IgG through the inhibitory receptor Fc γ RIIb. *J Allergy Clin Immunol*. 2017; in press
- Mohsen MO, Zha L, Cabral-Miranda G, Bachmann MF. Major findings and recent advances in virus-like particle (VLP)-based vaccines. *Semin Immunol* 2017 Dec;34:123-132. doi: 10.1016/j
- Engeroff P, Caviezel F, Storni F, Thoms F, Vogel M, Bachmann MF. Allergens displayed on virus-like particles are highly immunogenic but fail to activate human mast cells. *Allergy* 2017 Aug 8. Doi: 10.1111
- Yerly D, Pompeu YA, Schutte RJ, Eriksson KK, Strhyn A, Bracey AW, Buus S, Ostrov DA. Structural Elements Recognized by Abacavir-Induced T Cells. *Int J Mol Sci*. 2017 Jul 7;18(7). pii: E1464

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- Advanced Research Center, School of Life Dentistry at Niigata, Nippon Dental University, Japan
- National Dental Centre Singapore, SingHealth, Duke-National University of Singapore, Singapore
- Department of Periodontology, College of Dental Medicine, Nova Southeastern University, Florida, USA
- Department of Veterinary Clinical Sciences, Faculty of Veterinary, University of Santiago de Compostela, Lugo, Spain
- Bone Biology & Orthopaedic Research, Department for BioMedical Research (DBMR), University of Bern, Bern, Switzerland
- International Bone Research Association (IBRA), Basel, Switzerland
- Geistlich Pharma, Wolhusen, Switzerland

Research Profile

The Department of Cranio-Maxillofacial Surgery at the University of Bern is made up of an international team who perform a wide range of oral and maxillofacial surgeries. Facial fractures, bony deficits due to atrophy and growth disturbances, and facial bone defects are the main focus of our work.

The formation of new bone in the facial skeleton is influenced by several factors related to the type and location of a defect.

Our department is investigating the biological process of bone regeneration in connection with the use of various bone substitutes and bone grafts for different indications. In light of the steady development in surgical techniques, we have broadened our focus and are now exploring how implants – such as osteosynthesis devices made of titanium and biodegradable materials – influence bone regeneration. Another new field of interest is computer-assisted planning and production of materials for reconstruction, with special emphasis on 3-D printing technologies. Following the principle of translational research, the hypotheses of our studies are closely linked to clinical practice.

Teaching Profile

Our department is involved in a range of undergraduate teaching programs in both medicine and dentistry at the University of Bern. We also offer complete postgraduate clinical training and specialization curriculums for Oral and Maxillofacial Surgery. These meet official Swiss and

European standards and are based on so-called double full qualification for degrees in both medicine (MD) and dentistry (DDS/DMD). In addition, we provide clinical and scientific fellowship programs in Oral and Maxillofacial Surgery which are designed for international candidates who are pursuing professional careers, particularly in academics.

Highlights 2017

Osteosynthesis of partial rib osteotomy using standard-sized magnesium plate/screw systems

Magnesium is considered the biodegradable osteosynthesis material for the next generation. Our research group was the first in the world to conduct a series of in vivo studies applying a plate and screws system made of magnesium alloy. The implants were modified with a plasma-electrolytic surface to inhibit adverse gas formation during biodegradation. Our most recent study focused on the evaluation of the newly developed implants in a minipig rib fracture model. Amounts of gas formation were significantly lower and properties of the surrounding bone were better around the coated than around the uncoated implants. The results clearly suggest that the coating technique applied here is a promising solution to the problem of gas formation.

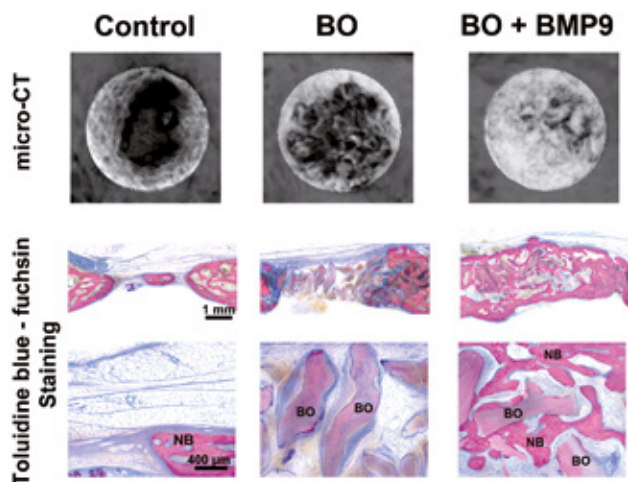


Computed tomography 6 months after rib osteosynthesis with the coated new magnesium plate/screw system.

Dramatic bone regenerative potential of recombinant human bone morphogenetic protein 9 (rhBMP9) therapy

Bone morphogenetic protein 9 (BMP9) has been recognized as one of the most osteogenic growth factors among BMP-family. In this project, we investigated the effects of rhBMP9 on bone regenerative potential using bone guided bone regeneration (GBR) model in a rabbit. New bone formation was quantified in a rabbit calvarial defect by means of micro-CT analysis and histomorphometry.

Apparently, rhBMP9 loaded on deprotonized bovine bone mineral (BioOss®, BO) promoted bone regeneration when compared with control (empty) and BO alone groups. rhBMP9 application may be an excellent option for bone regenerative therapy in future. A future in vivo preclinical study is necessary to optimize effective doses and carriers, to seek and fully characterize its realistic potential for future human use.



MicroCT and histological images (Toluidine blue – fuchsin staining) of Control, BO alone, and BO + rhBMP9 in bone defects 8 weeks post implantation. NB shows new bone.

Stereographic measurement of orbital volume, a digital reproducible evaluation method

To date, no reproducible orbital volume measurement method is available. Our team developed a new measurement method which delineates the boundaries of the orbital cavity in three dimensions. Results of repeated measurements made by two investigators were compared to assess the accuracy of the method. The difference in mean orbital volume measured by the investigators was minimal. The intra-class correlation coefficient showed excellent inter-rater agreement, suggesting that the method provides a standardized, reproducible and useful approach to the measurement of orbital volume in clinical practice.



Selected Publications

- Schaller B, Saulacic N, Beck S, Imwinkelried T, Liu EWY, Nakahara K, Hofstetter W, Iizuka T. Osteosynthesis of partial rib osteotomy in a miniature pig model using human standard-sized magnesium plate/screw systems: Effect of cyclic deformation on implant integrity and bone healing. *J Craniomaxillofac Surg.* 2017;45(6):862-871, doi: 10.1016/j.jcms.2017.03.018
- Fujioka-Kobayashi M, Schaller B, Shirakata Y, Nakamura T, Noguchi K, Zhang Y, Miron RJ. Comparison of two porcine collagen membranes combined with rhBMP-2 and rhBMP-9 on osteoblast behavior in vitro. *Int J Oral Maxillofac Implants.* 2017 Jul/Aug;32(4):e221-e230, doi: 10.11607/jomi.5652
- Fujioka-Kobayashi M, Kobayashi E, Schaller B, Mottini M, Miron RJ, Saulacic N. Effect of recombinant human bone morphogenetic protein 9 (rhBMP9) loaded onto bone grafts versus barrier membranes on new bone formation in a rabbit calvarial defect model. *J Biomed Mater Res A.* 2017;105(10):2655-2661, doi: 10.1002/jbm.a.36125
- Saulacic N, Fujioka-Kobayashi M, Kobayashi E, Schaller B, Miron RJ. Guided bone regeneration with recombinant human bone morphogenetic protein 9 loaded on either deproteinized bovine bone mineral or a collagen barrier membrane. *Clin Implant Dent Relat Res.* 2017;19(4):600-607, doi: 10.1111/cid.12491
- Mottini M, Wolf CA, Seyed Jafari SM, Katsoulis K, Schaller B. Stereographic measurement of orbital volume, a digital reproducible evaluation method. *Br J Ophthalmol.* 2017;101(10):1431-1435, doi: 10.1136/bjophthalmol-2016-309998

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Oberarzt



Dr. Adrian Zehnder
Oberarzt



The research team of the thoracic surgery laboratory.

Research Partners

- Department of Oncology, University Hospital, Bern
- Department of Pulmonology, University Hospital, Bern
- Department of ENT, Head and Neck Surgery, University Hospital Bern
- Visceral and Transplantation Surgery, University Hospital, Bern
- Department of Radiation Oncology, University Hospital, Bern
- Institute of Pathology, University of Bern
- Swiss Institute of Bioinformatics (Interfaculty Bioinformatics Unit), University of Bern
- Genome Plasticity - Department of Biomedicine, University of Basel
- Institute General Physiology, University of Ulm, Germany
- ARTORG Center for Biomedical Engineering Research, University of Bern

Research Profile

The Department of Thoracic Surgery in Bern is with 27 beds (together with the Department of Pulmonology) and over 170 anatomical resections per year one of the largest centers in Switzerland with a considerable experience in all fields of this specialized medicine area, e.g. oncological

surgery, chest wall resection and reconstruction, treatment for chest wall deformities, lung volume reduction surgery, thoracic trauma management, etc.

Main Research Goals

- Evaluation and therapeutic improvements by minimally-invasive thoracic surgery techniques
- Investigation of different clinical and functional parameters with the aim of achieving better outcome and improvement of patient's comfort
- Determine the potential of the tumor-derived mesenchymal subset to serve as a novel therapeutic target in lung cancer. Further, we are interested in identifying cell subsets that are critical for lung regeneration
- Identification and therapeutic targeting of molecular mechanisms conferring resistance to standard therapies, with the goal to unravel the vulnerabilities - the 'Achilles' heel' - of therapy-resistant cells for development of innovative strategies to treat lung cancer and MPM
- Identification and characterization of differentially regulated DNA damage repair factors in tumor initiating cells compared to tumor bulk cells, which will subsequently allow us to identify novel targets for pharmacological or genetic intervention to treat lung cancer

Teaching Profile

Teaching at our Department is characterized by a specialized knowledge of team members from different educational sections. Undergraduate teaching is therefore provided for students of medicine, biomedicine and biology. By giving lectures at the University of Medicine, by organizing students courses and bedside-teachings and by supporting students by writing of thesis or doing their PhD programs, we offer a wide range of teaching and knowledge support services.

Highlights 2017

Our translational research part focused on 1.) the biology of stem cells in lung development and disease and on 2.) drug resistance in lung cancer and malignant pleural mesothelioma (MPM). In the clinical context, we investigated functional parameters as prognostic factors for postoperative complication with the future aim for better prediction. We published a total of 29 original publications, including the following 3 papers.

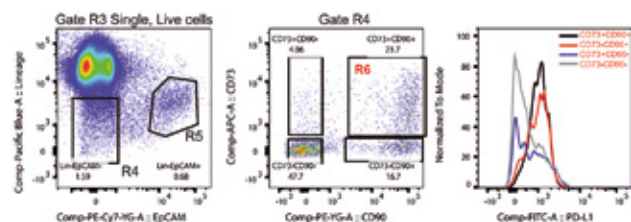
Perioperative Lung Function Monitoring for Anatomic Lung Resections

Kocher GJ, Gioutsos KP, Ahler M, Funke-Chambour M, Ott SR, Dorn P, Lutz J, Schmid RA. *Ann Thorac Surg.* 2017 Nov;104(5):1725-1732. Daily bedside spirometry might be a helpful diagnostic adjunct for early recognition, and hence, timely treatment, of pulmonary infection after open anatomic lung resections. In addition, minimally invasive techniques not only resulted in a lower rate of pulmonary infections but also resulted in faster postoperative recovery of pulmonary function and shorter hospital stay.

Increased PD-L1 expression and IL-6 secretion characterize human lung tumor-derived perivascular-like cells that promote vascular leakage in a perfusable microvasculature model

Bichsel CA, Wang L, Froment L, Berezowska S, Müller S, Dorn P, Marti TM, Peng RW, Geiser T, Schmid RA, Guenat OT, Hall SRR. *Sci Rep.* 2017 Sep 6;7(1):10636. doi: 10.1038/s41598-017-09928-1.

Our data show that perivascular-like cells present in NSCLC retain functional abnormalities in vitro. Perivascular-like cells as an eventual target in NSCLC warrants further investigation.

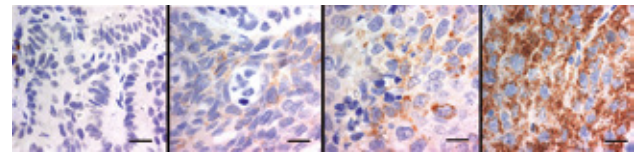


Characterization of mesenchymal cell subset in NSCLC by multicolor flow cytometry.

Glycine decarboxylase and HIF-1 α expression are negative prognostic factors in primary resected early-stage non-small cell lung cancer

Berezowska S, Galván JA, Langer R, Bubendorf L, Savic S, Gugger M, Schmid RA, Marti TM. *Virchows Arch.* 2017 Mar;470(3):323-330. We show that the combination of GLDC and HIF-1 α expression is an independent prognostic

factor in early-stage NSCC. Our results will assist future development of therapeutic approaches targeting GLDC or exploiting tumor hypoxia.



Immunohistochemical staining of GLDC in early-stage NSCC.

Selected Competitive Grants

- Bernese Cancer League: Characterization and therapeutic targeting of chemoresistance-driving pathways in lung cancer. PD Dr. Ren-Wang Peng
- Swiss Cancer League: Unravelling and reversing drug resistance of human lung cancer. PD Dr. Ren-Wang Peng
- Bernese Cancer League, Role of PD-1/PD-L1 in NSCLC. Dr. Sean R. Hall
- China Council Scholarship: Targeting the DNA damage response in lung cancer tumor initiating cells. Prof. Ralph A. Schmid
- Bernese Cancer League: Targeting mitochondrial activity to enhance lung cancer therapy. Dr. Patrick Dorn

Selected Publications

- Kocher GJ, Gioutsos KP, Ahler M, Funke-Chambour M, Ott SR, Dorn P, Lutz J, Schmid RA. Perioperative Lung Function Monitoring for Anatomic Lung Resections. *Ann Thorac Surg.* 2017 Nov;104(5):1725-1732
- Berezowska S, Galvan JA, Langer R, Bubendorf L, Savic S, Gugger M, Schmid RA, Marti TM: Glycine decarboxylase and HIF-1 α expression are negative prognostic factors in primary resected early-stage non-small cell lung cancer. *Virchows Arch* 2017, 470(3):323-330
- Bichsel CA, Hall SR, Schmid RA, Guenat OT, Geiser T: Primary Human Lung Pericytes Support and Stabilize In Vitro Perfusable Microvessels. *Tissue Eng Part A* 2015, 21(15-16):2166-2176
- Zehnder A, Kocher GJ, Seitz M, Schmid RA. IgG4-related disease of the lung: a rare differential diagnosis to lung cancer after positive positron emission tomography and biopsy. *Eur J Cardiothorac Surg.* 2017 Nov 1;52(5):1003-1004. doi: 10.1093/ejcts/ezx265
- Kocher GJ, Sharafi S, Azenha LF, Schmid RA. Chest wall stabilization in ventilator-dependent traumatic flail chest patients: who benefits? *Eur J Cardiothorac Surg.* 2017 Apr 1;51(4):696-701. doi: 10.1093/ejcts/ezw365

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- Theodore Alexandrov, EMBL-Heidelberg, Structural and Computational Biology / Spatial Metabolomics Lab, Heidelberg, Germany
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- David Gfeller, University of Lausanne, Ludwig Center for Cancer Research, Lausanne, Switzerland
- Sylvia LeDevedec, Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands
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- Thomas Grewal, Faculty of Pharmacy, University of Sydney, Sydney, Australia

Research Profile

Genital-Urothelial (GU) Cancer Research Group

Our research is focused on the role of cancer stem cells and the supportive stroma in the progressive and metastasising GU cancers. We are establishing a personalized GU platform that well integrates effective therapeutic treatments for individual patients, testing not only *in vitro* but also *ex vivo* and *in vivo*. This platform consists of 1. Patient Derived Organoids (PDOs), which facilitate the integration of genomic, transcriptomic, proteomic and metabolomics data with drug screening of patients' tumor samples, 2. Patient Derived Xenografts (PDXs), that allow the growth of tumor material 3. zebrafish model that allows the (fast) assessment of the metastatic potential of the individual PDO lines.

Bladder Dysfunction Research Group

Lower urinary tract dysfunction, characterized by urgency, frequency and incomplete emptying, has multiple causes including bladder outlet obstruction and neurological diseases including spinal cord injury. Our group has pioneered the study of the role of miRNAs in the pathogenesis of lower urinary tract diseases. Our experimental approach combines the analysis of human biopsy material with the *in vitro* cell-based models. Altered miRNAs serve as biomarkers and might be used to optimise the timing of treatment, and we determined combinations of 3 mRNAs and 3 miRNAs sufficient to discriminate between bladder functional states. We

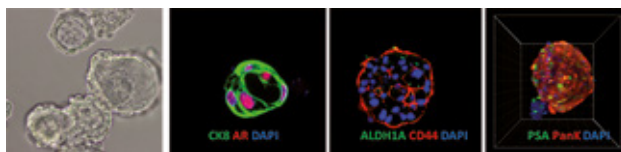
are currently quantifying these miRNAs in urinary exosomes with the aim of developing a non-invasive tool for reliable diagnosis of bladder dysfunction.

Teaching Profile

The Genital-Urothelial group participates in University teaching programs for students of medicine, biomedicine, veterinary medicine and biology.

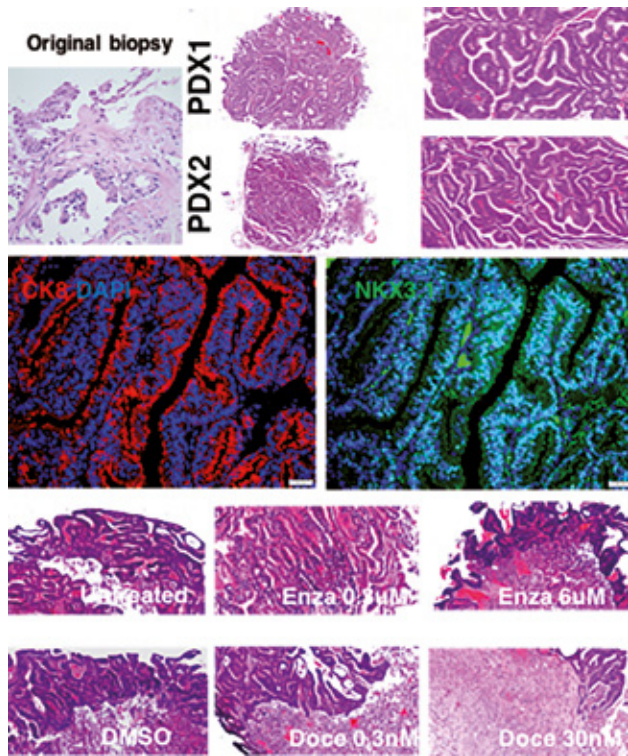
Highlights 2017

The use of preclinical models is a core component in every aspect of translational cancer research ranging from efforts to understand the biological basis of the disease to the development of new treatments. A major goal of our work has been to increase the tools at our disposal for the study of tumor heterogeneity, its role in cancer progression and the development of novel therapies. We have generated PDXs by subcutaneous implantation in immunocompromised NOD scid gamma (NSG) mice and established organoid lines, both from needle biopsies. In order to generate organoid lines that mimic "castrated" and "intact" conditions *in vivo*, we have established cultures in the presence and absence of androgen and tested for metastatic potential by zebrafish inoculation and implantation in mice. We additionally have determined cell type composition (immunofluorescence) using 3D imaging by confocal, light-sheet microscopy and FACS.



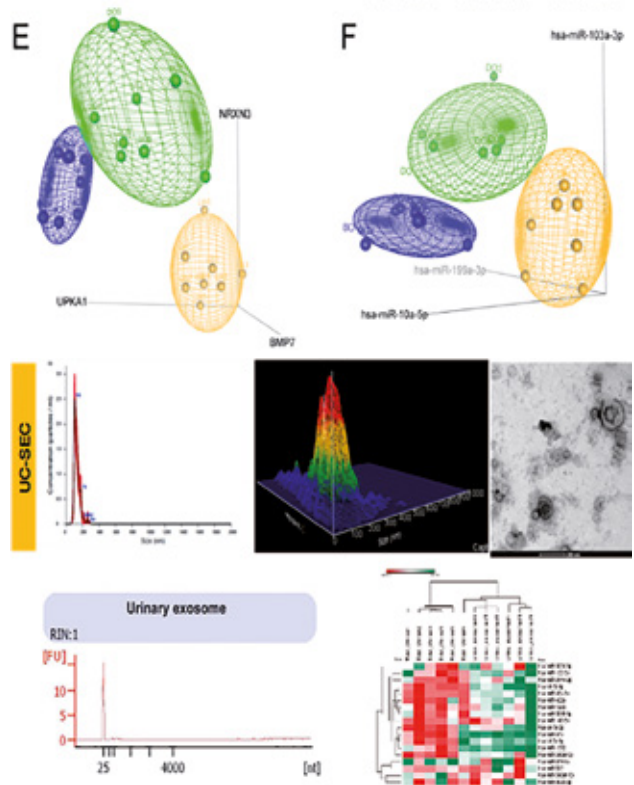
Metastasis-initiating cells (MICs) characterization. Patient Derived Organoids (PDOs) expressing prostate-specific and MICs markers: cytokeratin 8 (CK8, green), androgen receptor (AR, red); Aldehyde Dehydrogenase (ALDH1A1, green), CD44 (red); Prostate Specific Antigen (PSA, green), pancytokeratine (PanK, red). Images are acquired bright field, confocal and Light sheet.

In addition to our PDOs and PDXs, we have developed and implemented a clinically relevant culture system for studying tumor tissue *ex vivo*. This technique allows cultivation of tumor slices and needle biopsies without loss of normal architecture, viability, proliferative properties, or expression of specific markers. Moreover, we have shown that the effects of drug treatment in this system are consistent with those observed on organoids (*in vitro*) and PDXs (*in vivo*).



Patient derived xenograft and “Near-patient” ex-vivo tumor tissue slices. Biopsy of PCa penile metastasis and corresponding Patient Derived Xenograft passage 1 and 2 HE. Cytokeratine 8 and NKX3.1 expression in the PDX and ex vivo treatments.

Assessment of specific molecular alterations in the bladder wall could aid diagnosis and optimize timing of treatment. We validated the biomarkers for distinguishing urodynamic BOO phenotypes in an independent patient cohort before and after TURP and found mRNA and/or miRNA combinations, sufficient to accurately discriminate between urodynamic phenotypes before and after relief of obstruction. Specific miRNA and mRNA signatures allow discrimination between urodynamically-defined bladder states with high sensitivity and specificity and present a potential tool to evaluate disease progression during BOO and the symptom recovery after surgery. In order to facilitate the assessment of the bladder function, relevant for diagnostic of LUTS and obstruction, we developed an optimized ultracentrifugation and size exclusion chromatography approach for highly reproducible isolation for 50-150 nm uEVs, corresponding to the exosomes, from urine. We profiled the miRNA content of uEVs and total urine from the same samples with the NanoString platform and validated the data using qPCR.



Scatterplots show high discriminative potential of mRNA and miRNA signatures. Urinary exosome isolation and characterization. Exosome vesicles (50-150 nm) from 50 ml urine contain miRNAs detectable by RT-qPCR.

Selected Competitive Grants

- Swiss National Science Foundation (grant No. 31003A_169352; 310030_175773/1;)
- HORIZON 2020 (Marie Skłodowska-748836 - STOPCa):
- Novartis (grant No. 17B076)
- PHRT (301)
- KWF (grant No. UL2015-7599)

Selected Publications

- Zoni et al. CRIPTO and its signaling partner GRP78 drive the metastatic phenotype in human osteotropic prostate cancer. *Oncogene*. (2017) Aug 17;36(33):4739-4749.
- Gheinani AH et al. Characterization of miRNA-regulated networks, hubs of signaling, and biomarkers in obstruction-induced bladder dysfunction. (2017) *JCI Insight*, Jan 26;2(2):e89560. doi: 10.1172/jci.insight.89560
- La Manna et al. Cold Spring Harbor book on Prostate Cancer (book chapter). (2017). Accepted
- Astrologo et al. ALK1Fc Suppresses the Human Prostate Cancer Growth in in Vitro and in Vivo Preclinical Models. *Frontiers Cell and Developmental Biology*. (2017). Dec 5;5:104

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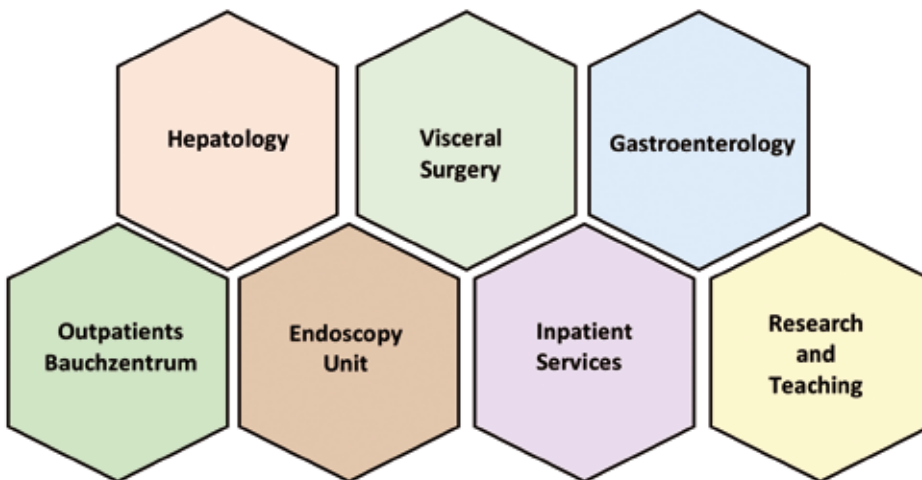
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Gastroenterologie



Clinic for Visceral Surgery and Medicine

Research Partners

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- Novartis
- University of Neuchâtel, Department of Psychology
- University of Freiburg, Clinic for Hepatology, Germany
- SCCS (Swiss Hepatitis C Cohort Study)
- FLIP Kohorte (European Fatty Liver: Inhibition of Progression)
- CLIF Consortium (European Foundation for the study of Chronic Liver Failure)
- VALDIG Consortium (Worldwide Vascular Liver Disease Group)

Research Profile

The research interests of Visceral Surgery include regenerative medicine and the image guidance of surgical procedures. Specific topics of interest within regenerative medicine include the molecular basis of liver regeneration and sphincter muscle augmentation and regeneration. For both aspects, elements of adult liver stem cell physiology are explored in detail in order to enhance the regrowth of hepatic parenchymal cells, and of the various compartments of sphincter muscle. In Gastroenterology the main research interests are interactions between bacteria and host in health and diseases. Therefore new genetically engineered bacterial strains have been developed. Such bacteria are used to measure antibody response against commensals, and whether the immune system in the gut 'remembers' previous encounters with commensal bacteria and generates a stronger response on the second occasion (as in medical vaccinations).

We play a leading role in liver disease research (liver cancer, hepatitis, liver cirrhosis, etc.) with the aim of providing our outpatient and inpatient patients with the best possible treatment, and our students and assistants the latest in liver research. Our liver research team covers all areas of hepatology and looks after patients before and after liver transplantation. We explore vascular diseases such as portal hypertension in a cirrhotic and non-cirrhotic liver. A main focus are novel treatments of hepatocellular carcinoma and non-alcoholic steatohepatitis for which we currently include patients in multiple trials.

Teaching Profile

Training in our clinic is offered with fellowships in visceral surgery, gastroenterology and hepatology. In visceral surgery the fellows receive a training in highly specialized procedures for all visceral and endocrine organs and profit from our team structures. For students we offer a broad spectrum ranging from basic teaching in the field to specialized tuition.

Highlights in 2017

In the past year our collaborators won several prestigious awards and prizes and were engaged in a multitude of panels and committees, both at national and international level. In particular, we are very proud that Prof. Macpherson was awarded a substantial ERC senior investigator grant and that the first interfaculty research cooperation (IRC) grant by the University of Bern was attributed to an interdisciplinary project between Gastroenterology, Veterinary Sciences and Plant physiology. This work will elucidate the cascading multitrophic effects in the chain between humans, animals, soil and plants.

Selected Competitive Grants

- SNF: Role of maternal microbiota and aryl hydrocarbon receptor signaling in establishing neo-natal skin. (CHF 598'901; M. Gomez)
- HHMM-Neonates-EU-Grant: (CHF 2'200'000; A. Macpherson)
- TSNF: The microbial-dependent hemodynamic response to partial portal vein ligation is regulated by the microbiota via mucosa-derived angiogenic factors (CHF 348'396; A. DeGottardi)
- SNF: Purinergic control of innate lymphoid cells in liver injury and repair (CHF 390'110, G. Beldi)
- SNF: fueling hepatic resistance against irradiation-induced damage and disease (CHF 255.892, D. Stroka)

Selected Publications

- Andrew J. Macpherson, Mercedes Gomez de Agüero and Stephanie C. Ganai-Vonarburg. How nutrition and the maternal microbiota shape the neonatal immune system. *Nat Rev Immunol.* 2017 Aug;17(8):508-517
- Hebbandi Nanjundappa R, Ronchi F, Wang J, Clemente-Casares X, Yamanouchi J, Sokke Umeshappa C, Yang Y, Blanco J, Bassolas-Molina H, Salas A, Khan H, Slattery RM, Wyss M, Mooser C, Macpherson AJ, Sycuro LK, Serra P, McKay DM, McCoy KD, Santamaria P. A Gut Microbial Mimic that Hijacks Diabetogenic Autoreactivity to Suppress Colitis. *Cell.* 2017 Oct 19;171(3):655-667.e17
- Lofrese G, Malinka T, Keogh A, Baier F, Simillion C, Montani M, Halazonetis TD, Candinas D, Stroka D. Impaired liver regeneration in aged mice can be rescued by silencing Hippo core kinases MST1 and MST2. *EMBO Mol Med.* 2017 Jan;9(1):46-60
- Tinguely P, Fusaglia M, Freedman J, Banz V, Weber S, Candinas D, Nilsson H. Laparoscopic image-based navigation for microwave ablation of liver tumors - A multi-center study. *Surg Endosc.* 2017 Oct; 31(10):4315-4324
- Kolly P, Knöpfli M, Dufour JF. Effect of smoking on survival of patients with hepatocellular carcinoma. *Liver Int.* 2017 Nov;37(11):1682-1687

Department of Emergency Medicine

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PD Dr. Wolf
Hautz
MME
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Error and Patient
Safety



Dr. Thomas
Sauter
AG Direct
New Oral
Anticoagulants



Dr. David
Srivastava
AG Refugee
Health

Research Partners

- Institut für Gebirgsnotfallmedizin EURAC, Bozen
- CHUV Lausanne
- HUG Genf
- Max Planck Institute for Human Development Berlin, Germany
- Institute of Educational Measurement, University of Oslo, Norway
- Sarah Lawrence College, New York University School of Medicine, USA
- Charité Berlin, Germany
- Erasmus Medical Center Rotterdam, The Netherlands

Research Profile

The Department of Emergency Medicine focuses its research on questions of clinical relevance and applicability - under the lead of Prof. Exadaktylos - in an attempt to improve emergency care. Five working groups currently investigate different aspects of emergency care, including diagnostic error and patient safety (PD Dr. Hautz), direct new oral anti-coagulants (Dr. Sauter), refugee health (Dr. Srivastava), geriatric emergency medicine (Dr. Jegerlehner) and wilderness medicine (Dr. Brodmann Maeder). We heavily invest in the scientific training of medical students and young graduates and supervise around 10 master thesis and 10 dissertation projects annually.

Teaching Profile

The Department of Emergency Medicine is actively involved in undergraduate and postgraduate medical education and hosts a continuous education curriculum for emergency physicians. In undergraduate education, we both lead and participate in numerous interdisciplinary teachings and offer a maximum of 12 concurrent two-month internship positions to final year students. We train medical graduates in emergency medicine and emergency ultrasound and host a variety of interprofessional education activities. The Department received two national awards for its interprofessional training programs and a national award from the swiss institute for research and education in medicine (SIWF) for exceptional postgraduate teaching (Dr. Sauter). We further received a competitive grant from Berne university to fund a teaching improvement project in undergraduate education.

Currently, the educational activities of the department are coordinated by three consultants with a formal qualification

in education (Master in medical education) and we bi-annually fund a junior colleague in the participation in that program as part of our capacity building efforts.

Highlights 2017

The Department of Emergency Medicine hosted the 1st Swiss Minisymposium on Refugee Health in 2017, which was attended by a number of distinguished speakers and 120 guests. We further had the chance to welcome Prof. A Brown from NY as a Fulbright specialist on Mental Health in Refugees and Minorities. This collaboration is an important step in becoming a Center of Excellence in Migration and Refugee Health.



The 1st Swiss Minisymposium on Refugee Health.

We also were appointed host of the 2nd European conference on Diagnostic Error, which will take place in August 2018 at Inselspital Bern and already confirmed a number of renown speakers, among them Sir Liam Donaldson, WHO

Envoy for Patient Safety, and Professor Gerd Gigerenzer, Director of the Max Planck Institute for Human Development Berlin.

We further established the first prospective European registry of emergency patients treated with direct new oral anticoagulants and concluded data acquisition on the world's first prospective study on diagnostic error in emergency care.

Selected Competitive Grants

- Project Partner on the SNF Project DETECT - Dizziness Evaluation Tool for Emergent Clinical Triage
- Bangarter-Rhyner Stiftung for the BerNOAC Registry
- Bundesamt für Gesundheit and 2 Fulbright Specialist Stipends for a cross-sectional study on migrants ED use
- CTU-Grant of the Department of Research at Inselspital for the investigation of diagnostic error in emergency care
- competitive grant from Berne university, Förderung Innovative Lehre, a teaching improvement project in undergraduate education

Selected Publications

- Hautz W, Sauter TC, Lehmann B, Exadaktylos AK (in press). Professionalization rather than monopolisation is the future of emergency medicine in Europe - a response to De Robertis and colleagues. *European Journal of Anaesthesiology*. 2018 Mar;35(3):234-235. doi: 10.1097/EJA.0000000000000744
- Kämmer JE, Hautz WE, Herzog SM, Kunina-Habenicht O, Kurvers RHJM (2017). The Potential of Collective Intelligence in Emergency Medicine: Pooling Medical Students' Independent Decisions Improves Diagnostic Performance. *Med Decis Making*. Aug;37(6):715-724
- Pfortmueller CA, Müller M, Guignard C, Schefod J, Leichtle B, Exadaktylos AK. Utility of quick sepsis-related organ failure assessment (qSOFA) to predict outcome in patients with pneumonia. *PLOS one*. 2017 Dec 21;12(12):e0188913. doi: 10.1371/journal.pone.0188913. eCollection 2017
- Sauter TC, Hegazy K, Hautz WE, Krummrey G, Ricklin ME, Nagler M, Borner U, Exadaktylos AK. (2017) Epistaxis in anticoagulated patients: Fewer hospital admissions and shorter hospital stays on rivaroxaban compared to phenprocoumon. *Clin Otolaryngol*. May 16. 2018 Feb;43(1):103-108. doi: 10.1111/coa.12904. Epub 2017 Jun 5.



The 1st Swiss Minisymposium on Refugee Health.

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Mordasini

Research Partners

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- Department of Neurosurgery, University Hospital Bern and University of Bern
- University Hospital of Psychiatry, Bern, Switzerland
- Division of Child Neurology, Department of Pediatrics, University Hospital Bern and University of Bern
- Institute for Surgical Technology and Biomechanics, University of Bern
- Department of Psychology, University of Bern
- Division of Neuroradiology, Toronto Western Hospital, Toronto, Canada
- Department of Clinical Neurology, University of California Los Angeles (UCLA), USA

Research Profile

Neurovascular research

The research group focuses on treatment strategies for neurovascular diseases (stroke, aneurysms, AVM etc.). The researchers combine preclinical developments of techniques in bench-top and animal models and evaluate their application in clinical studies.

Advanced Neuroimaging

The research of the Support Center for Advanced Neuroimaging (SCAN) focuses on the translation of quantitative imaging methods and automated image analysis into clinical practice, sequence development and methodological counselling for neuroimaging studies. In this domain, the researchers of the SCAN have participated in international neuroimaging trials (e.g. the ENIGMA epilepsy and parkinson projects), neuroimaging challenges and data analysis networks in cerebrovascular research, neuro-oncology, neuro-immunology and epilepsy/neurodegeneration.

CSF Hypo- und Hypertension Syndromes

The multidisciplinary group of the Neurocenter develops new imaging modalities and interventional/surgical treatment options for patients with CSF leakage syndromes and idiopathic intracranial hypertension.

Teaching Profile

The Department has been involved in educational activities and public events, e.g. the annual CNB scientific meeting and various activities during the annual brain week (e.g. the science slam).

In 2017 the Departments of Neuroradiology and Neurology organized the European Stroke Winter School for the fourth time. The meeting is dedicated to young stroke physicians in

and is endorsed by the relevant European Societies (ESMINT, ESO, ESNR). Participants from 18 countries join the course. The Institute has hosted the annual meeting of the Alpine Chapter of the Organization for Human Brain Mapping (OHBM) dedicated to advanced neuroimaging in life science, physics and clinical neuroimaging with more than 100 participants from the US and Europe, including an international EEG/fMRI workshop.

Highlights 2017

The Departments of Neuroradiology and Neurology in cooperation with the Neuro-Clinical Trial Unite have organized an international stroke trial (Global PIs: Prof. Jan Gralla, Prof. Urs Fischer). The Swift Direct Trial (www.swift-direct.com) is a RCT, focusing on the value of intravenous thrombolysis in combination with mechanical thrombectomy for large intracranial vessel occlusions (funded by Medtronic, USA). The trial will enroll and randomize 404 patients in 30 sites throughout Europe and Canada and has started in October 2017.

A joint workgroup of the ISTB and SCAN was awarded 2nd at the international Brain Tumor Segmentation Challenge (BRATS) at MICCAI 2017 in the category "prediction of outcome".

Selected Competitive Grants

SNF grants, accepted 2017:

- Effects of serotonergic neuromodulation on behavioral recovery and motor network plasticity (CISS). (PI Prof. Wiest CHF 429.000)
- Stroke treatment goes personalized (Stray Cats). (CHF 474.000; PI: J. Gralla)

Selected Publications

- Bellwald S, Weber R, Dobrocky T, Nordmeyer H, Jung S, Hadisurya J, Mordasini P, Mono ML, Stracke CP, Sarikaya H, Bernasconi C, Berger K, Arnold M, Chapot R, Gralla J, Fischer U. Direct Mechanical Intervention Versus Bridging Therapy in Stroke Patients Eligible for Intravenous Thrombolysis: A Pooled Analysis of 2 Registries. *Stroke* 2017; 48(12); 3282-3288
- McKinley R, Hani L, Gralla J, El-Koussy M, Bauer S, Arnold M, Fischer U, Jung S, Mattmann K, Reyes M, Wiest R. Fully automated stroke tissue estimation using random forest classifiers (FASTER). *J Cereb Blood Flow Metab* 2017; 37(8); 2728-2741
- Piechowiak E, Zibold F, Dobrocky T, Mosimann PJ, Bervini D, Raabe A, Gralla J, Mordasini P. Endovascular Treatment of Dural Arteriovenous Fistulas of the Transverse and Sigmoid

Sinuses Using Transarterial Balloon-Assisted Embolization Combined with Transvenous Balloon Protection of the Venous Sinus. *AJNR Am J Neuroradiol* 2017; 38(10); 1984-1989

- Rummel C, Slavova N, Seiler A, Abela E, Hauf M, Burren Y, Weisstanner C, Vulliemoz S, Seeck M, Schindler K, Wiest R. Personalized structural image analysis in patients with temporal lobe epilepsy. *Sci Rep.* 2017; 7:10883. doi: 10.1038/s41598-017-10707-1
- Whelan CD, Altmann A, Botía JA, Jahanshad N, Hibar DP, Absil J, Alhusaini S, Alvim MK, Auvinen P, Bartolini E, Berge F et al for the ENIGMA-Epilepsy Working Group. *Brain* 2017; in press

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- Switzerland Innovation Park Biel/Bienne
- ETH Zürich
- EPFL Lausanne / CHUV Lausanne
- Clinical Departments, Inselspital
- Swiss Working Group for Clinical Cancer Research (SAKK), Bern
- University of Duke, NC, USA
- Fraunhofer Institute MEVIS, Bremen, DE

Research Profile

DIPR maintains an innovative research culture in order to provide high standard performance and for the purpose of the well-being of all patients. Various measures have improved the cooperation with other research partners. At present we are involved in 20 cooperation-studies as well as 10 DIPR-IIT projects; on top of it we are delivering support to 50 ongoing clinical studies.

Three permanent staff positions in Medical Physics and Computer Vision Engineering support the development of new MR sequences and an imaging processing platform, this platform is being established in the imaging laboratory. In close collaboration with many clinical sites including pediatric partners, multiparametric imaging and advanced image analysis are in the process of being translated into clinical routine to further improve diagnosis, treatment planning and navigation during intervention. Our productive collaboration with e.g. the ARTORG center in Bern allows us to work with biomedical engineers of various clinical fields that help us to test and apply innovative imaging methods and image processing. Since 2014 DIPR is building up an

experimental radiology laboratory at the Department for BioMedical Research, University of Bern to perform tumor cell ex vivo experiments as well as studies with focus on contrast media.

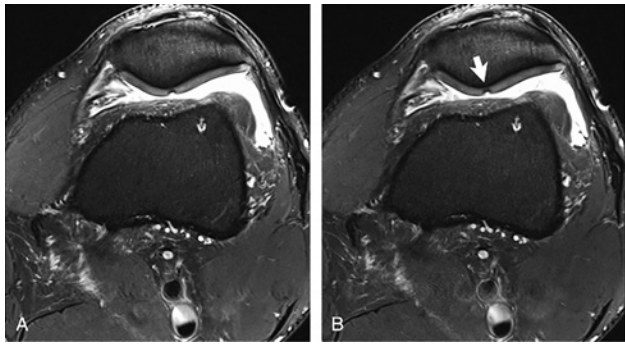
Teaching Profile

DIPR is an active member of the SIWF/ISFM (Schweizerische Institut für ärztliche Weiter- und Fortbildung) and takes responsibility for residents, who are members of the European School of Radiology (ESOR). Our teaching program is also engaged with Medical and Biomedical Engineering students. Our Department is the largest training site in the German speaking part of Switzerland for the Registered Radiographer Advanced Federal Diploma of Higher Education. DIPR is also a member of the training program for commercial employees and Healthcare Assistants.

Highlights 2017

Higher Acceleration ("Speed") in Clinical Magnetic Resonance

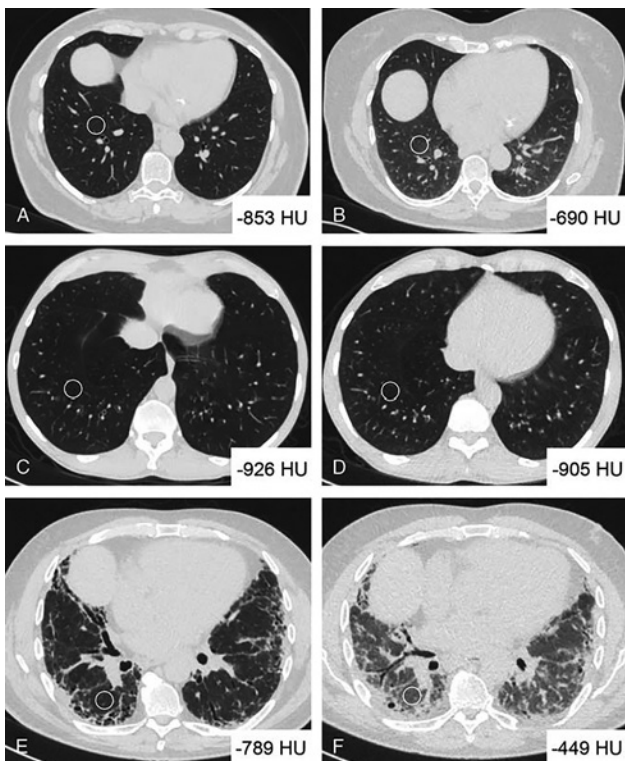
The most relevant clinical accelerated magnetic resonance techniques that are currently available for routine patient examinations are reviewed to present and discuss the benefits therein when compared with more conventional scans. The publication is divided into 3 sections focusing on these techniques' clinical use and practicality. Improvements in 3-dimensional acquisition are first discussed, specifically controlled aliasing in parallel imaging results in higher acceleration, related radial techniques, and CAIPI-Dixon-TWIST-VIBE. Simultaneous multislice imaging is then reviewed, focusing on current implementation for 2-dimensional imaging, including both echo-planar and fast spin echo techniques. The final topic is that of sparse reconstruction, discussing the principles therein, challenges, and current applications. Guidance in terms of clinical use for accelerated techniques is provided, focusing on enabling faster and improved clinical scan results.



Axial TSE T2-weighted scans of the knee at 3 T depicting patellar cartilage damage (arrow), in a patient with prior medial collateral ligament and anterior cruciate ligament surgery, on images (A) without and (B) with SMS (2 acceleration). As in the previous figure, image quality and SNR are essentially equivalent, with a reduction in scan time from 7:14 to 3:48 min:s. The scan time with SMS is sufficiently short to make such a high spatial resolution acquisition (with a 0.4 0.4 mm² pixel) clinically feasible.

Increased expiratory CT-Density reveals possible Abnormalities in radiologically preserved Lung Parenchyma in Idiopathic Pulmonary Fibrosis

Idiopathic pulmonary fibrosis (IPF) is a progressive lethal chronic lung disease with unclear pathogenesis. Radiological hallmark is the pattern of usual interstitial pneumonia accentuated in peripheral and basal areas with otherwise preserved lung structure. One hypothesis is that alveolar collapse and consequent induration lead to fibrotic transformation of lung tissue. The aim of the study was to investigate normal-appearing tissue during expiration for signs of collapsibility and differences from other diseases or controls.



Representative computed tomography density measurements of lower lung lobes in inspiration (left) and expiration (right) in (A and B) a control subject, (C and D) COPD patient, and (E and F) idiopathic pulmonary fibrosis patient. White circle depicts region of interest.

Therefore we retrospectively assessed a total of 43 patients with non-enhanced computed tomography (CT) in inspiration and expiration, performed for routine clinical workup. Densitometry of visually unaffected lung tissue was conducted in all lung lobes with a region of interest of 15-mm in diameter on soft tissue kernel reconstruction during inspiration and expiration.

We gained following findings: One-factor analysis of variance analysis yielded significant difference in attenuation changes between inspiration and expiration of unaffected lung parenchyma among all subject groups in all lung lobes. For IPF patients, the highest differences in densities were observed in the lower lobes, which is the predominantly affected site of usual interstitial pneumonia. In the chronic obstructive pulmonary disease group, the density remained rather equal in the entire lung.

Summary means that High CT attenuation changes between inspiration and expiration in IPF patients might suggest altered lung parenchyma in normal-appearing tissue on CT. Density changes during the respiratory cycle might be explained by alveolar collapse of radiologically unaffected lung tissue possibly preceding fibrosis. These results support the concept of alveolar collapse preceding lung fibrosis in IPF.

Selected Competitive Grants

- SAKK Life Grant, awarded to PD Dr. Martin Maurer for his research project, Impact of Diffusion-weighted Magnetic Resonance Imaging to Evaluate Treatment Response of Patients undergoing Neoadjuvant Therapy with Borderline Resectable or Locally Advanced Pancreatic Carcinoma
- Dr. Adrian Huber - Stiftung zur Krebsbekämpfung – for MR Elastography equipment, application 414
- Prof. Dr. Harriet Thöny - Personalized imaging for active surveillance of prostate cancer patients. Swiss National Science Foundation (SNF): 32003B_176229/1
- Prof. Dr. Andreas Christe – Stiftung Lindenhof support INTACT – lung project 17-08-F

Selected Publications

- Petroulia V, Funke M, Zumstein P, Berezowska S, Ebner L, Geiser T, Torbica N, Heverhagen J, Poellinger A. Increased Expiratory Computed Tomography Density Reveals Possible Abnormalities in Radiologically Preserved Lung Parenchyma in Idiopathic Pulmonary Fibrosis. *Invest Radiol.* in press
- Runge VM, Richter JK, Heverhagen JT. Speed in Clinical Magnetic Resonance. *Invest Radiol.* 2017 Jan;52(1):1-17
- Barbieri S, Broennimann M, Boxler S, Vermathen P, Thoeny HC. Differentiation of prostate cancer lesions with high and with low Gleason score by diffusion-weighted MRI. *Eur Radiol.* 2017 Apr;27(4):1547-1555
- Ebner L, Tall M, Choudhury KR, Ly DL, Roos JE, Napel S, Rubin GD. Variations in the functional visual field for detection of lung nodules on chest computed tomography: Impact of nodule size, distance, and local lung complexity. *Med Phys.* 2017 Jul;44(7):3483-3490
- Christodoulidis S, Anthimopoulos M, Ebner L, Christe A, Mouggiakakou S. Multisource Transfer Learning With Convolutional Neural Networks for Lung Pattern Analysis. *IEEE J Biomed Health Inform.* 2017 Jan;21(1):76-84

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Dr. Nicole Fichtner



André Döring



Maike Hoefemann

Research Partners

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- Hepatology, University Clinic for Visceral Surgery and Medicine, Inselspital, Bern University of Bern
- Department of Neurology, Inselspital, Bern University of Bern
- Department of Nephrology and Hypertension, Inselspital, Bern University of Bern
- Department of Orthopaedic Surgery and Traumatology, Inselspital, Bern University of Bern
- Institute for Biomedical Engineering, University and ETH Zurich
- Center of Laboratory Medicine, Inselspital, University of Bern
- Max Planck Institute for Biological Cybernetics, Tuebingen, Germany
- University Children's Hospital and Children's Research Center, Zurich, Switzerland
- Department of Physiology, University of Lausanne, Lausanne, Switzerland
- Department of Biochemistry and Molecular Biology Universitat Autònoma de Barcelona, Spain

Research Profile

Magnetic resonance imaging (MRI) and spectroscopy (MRS) are powerful and extremely versatile methods for non-invasive studies and diagnostic examinations in humans. Our group is using these MRI and MRS methods in close collaboration with clinical partners primarily in prospective studies of different organs. We also combine the methodological development with applications to study physiology and pathology, together with the underlying mechanisms, in situ. Currently most MRI and MRS studies are performed in muscle, liver, kidney, brain, and heart. In addition, high resolution NMR studies are performed on biopsies, cell cultures and body fluids.

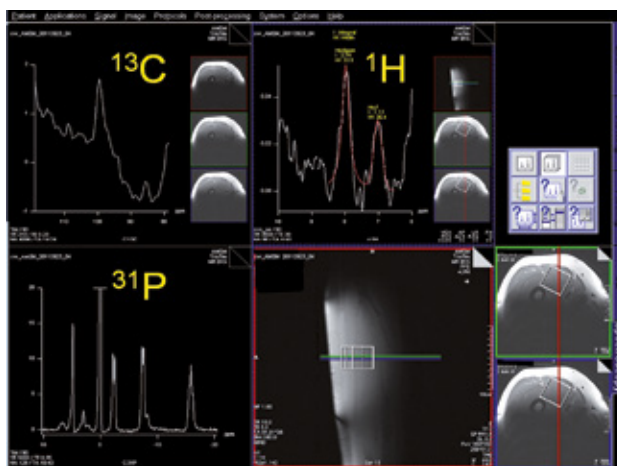
Teaching Profile

The AMSM group participates in University teaching programs for students of medicine, chemistry, biochemistry, and biomedical sciences.

Highlights 2017

Insulin Resistance

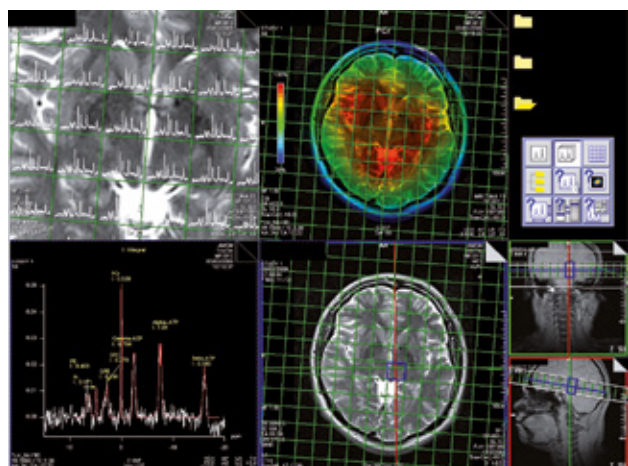
One SNF grant has been finished successfully in 2017 with the retirement of the PI. It targeted insulin resistance, which has been a major research topic of our group for more than a decade. Since insulin resistance is a major cause of cardiovascular diseases such as stroke and myocardial infarction, better understanding of this phenomenon will help us to prevent these acute diseases. We study effects of chronic or acute exercise and different kinds of carbohydrates, lipids, and amino acids on muscle and liver metabolism. Several strong collaborations are based on this research topic (several clinics of the Inselspital and externally with Lausanne (CH), Pittsburgh (US), Lyon (FR), and Tübingen (DE).



Brain Physiology

A second SNF grant aims at the development of MR methods and synergistic postprocessing methods that are tailored to the observation of brain metabolism, yet are also transferable to other organs. In collaboration with the ETH and University of Zurich, as well as the MPI in Tübingen, exchange processes between amide protons and water are studied in human brain at the highest field strengths available for investigation of human subjects. General acquisition parameters for MRS of neurotransmitters (glutamate and GABA) have been optimized using a general error estimation

technique, while diffusion properties of brain metabolites are investigated with optimized methodology in collaboration with the Clinic for Neurology.



TRANSACT

TRANSACT (TRANSforming Magnetic Resonance Spectroscopy into A Clinical Tool) is an EU-funded Marie Curie Initial Training Network (<http://www.transact-itn.eu/>), which aims at improving and automating MRS methods and postprocessing tools such that the clinical use of MRS becomes more robust and widespread. The specific aim of our subproject is the definition and automatic recognition of spectral quality and clinical usability such that radiologists without specific methodological knowledge should be better able to use MRS in their routine. Machine learning networks are shown to yield similar accuracy as human experts for quality assessment in spectra acquired for brain tumor assessments and deep learning is used for artifact detection.

Renal Function

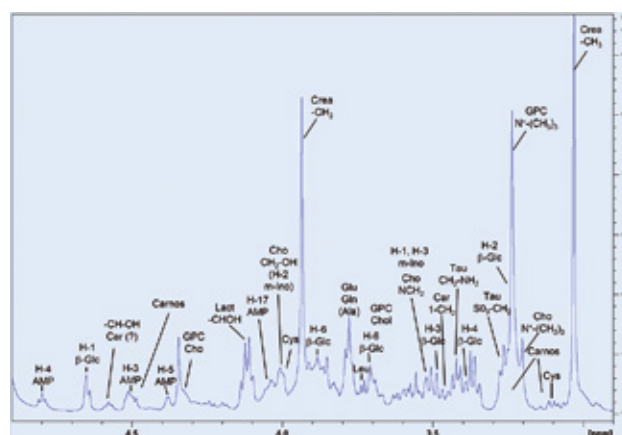
Renal Function in native and transplanted kidneys has been investigated by multi-modal MRI and MRS funded by an UniBe ID Grant in preparation of a Sinergia Grant. Renal function deteriorates after kidney transplantation for multiple reasons. The functional MR modalities differ in terms of sensitivity for cortical or medullary renal tissue and in their assessed determinants. We aim at a better perception of the physiologic basis behind functional MR-parameters and why they may be changed in renal disease. Reproducibility and comparability studies have been performed employing several functional MR methods, such as diffusion weighted imaging, arterial spin labelling, and oxygen dependent MRI. In collaborations with ISTB, image post processing was developed to minimize respiratory motion related problems of the MR acquisition. This may allow for omitting respiratory triggering and thus accelerate the acquisitions. For detection of renal ectopic lipids, MRS and MRI methods have been optimized. In a clinical study, living renal allograft donors and their corresponding recipients were longitudinally followed by diffusion-weighted MR Imaging.

High-Resolution Magic Angle Spinning NMR

Since MR spectra *in vivo* have a limited spectral resolution, high-resolution magic angle spinning (HR-MAS) NMR techniques are currently being developed in order to correlate spectra of tissue *in vivo* and *in vitro*. HR-MAS makes NMR spectroscopy applicable also to semi-solid materials including biological tissues or cell cultures, which under static

conditions yield only poorly resolved NMR spectra with very broad lines providing only little information. Fast spinning around an axis inclined at an angle of 54.7° ("magic angle") with respect to the axis of the external magnetic field (B_0) can average orientation dependent effects close to zero, thereby significantly reducing the linewidth and increasing both the spectral resolution and sensitivity.

HR-MAS allows to metabolically characterize tissue types like brain, muscle (see Fig), prostate, breast, liver, or kidney. Several HR-MAS studies have been performed on biopsies like muscle or sheep brain as well as on cell cultures and analyzed by statistical "metabonomical" methods.



Selected Competitive Grants

- Swiss National Science Foundation (grant No. 320030_156952; 320030_175984; 325230_147153, 320030_170062; 32003B_156167)
- EU 7th Framework Programme (Marie-Curie Initial Training Network, PITN-GA-2012-316679)

Selected Publications

- Diserens G, Hertig D, Vermathen M, Legeza B, Flück CE, Nuoffer JM, Vermathen P. Metabolic stability of cells for extended metabolical measurements using NMR. A comparison between lysed and additionally heat inactivated cells. *Analyst*. 2017;142:465-471
- Fichtner ND, Giapitzakis IA, Avdievitch N, Mecke R, Zaldivar D, Henning A, Kreis R. In vivo characterization of the downfield part of 1H MR spectra of human brain at 9.4T: Magnetization exchange with water and relation to conventionally determined metabolite content. *Magn Reson Med* (2017), epub; doi: 10.1002/mrm.26968
- Kyathanahally SP, Mocioiu V, Pedrosa de Barros NM, Slotboom J, Wright AJ, Julia-Sape M, Arus C, Kreis R. Quality of clinical brain tumor MR spectra judged by humans and machine learning tools. *Magn Reson Med* (2017) epub; doi: 10.1002/mrm.26948
- Lévy PL, Duponchel S, Eiseid H, Molle J, Michelet M, Diserens G, Vermathen M, Vermathen P, Dufour JF, Dienes HP, Steffen HM, Odenthal M, Zoulim F, Bartosch B. Hepatitis C virus infection triggers a tumor-like glutamine metabolism. *Hepatology*. 2017;65:789-803
- Vermathen P. Diffusion MRI and MRS outside the brain: from methodology to practice. *NMR Biomed* (2017) epub; doi: 10.1002/nbm.3703
- Pouymayou B, Buehler T, Kreis R, Boesch C. Test-retest analysis of multiple 31P magnetization exchange pathways using asymmetric adiabatic inversion. *Magn Reson Med* 2017;78: 33-39

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Prof. Martin Fiedler
Director



Prof. Carlo Largiadè
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PD Dr. Jean-Marc Nuoffer



PD Dr. Ursula Amstutz



PD Dr. Alexander Leichtle



Dr. Michaela Fux

Research Partners

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- Institute of Pharmacology, University of Bern, Bern, Switzerland
- Canadian Pharmacogenomics Network for Drug Safety, University of British Columbia, Vancouver, Canada
- Respiratory Medicine, Department of Clinical Research, University of Bern, Bern, Switzerland
- Department of Emergency Medicine, University of Bern, Bern, Switzerland
- Department of Neurology, University of Bern, Bern, Switzerland
- Mayo Clinic Cancer Center, Mayo Clinic, Rochester, Minnesota, USA
- Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands
- Institute of Pathology, University of Bern, Bern, Switzerland
- Department of Ophthalmology, University of Bern, Bern, Switzerland
- Laboratory of Biometry, University of Thessaly, Volos, Greece

Research Profile

The research focus of the Institute of Clinical Chemistry is on translational research and precision medicine. Specific research topics encompass pharmacogenomics and drug metabolism, inherited metabolic diseases, clinical cytomics, and computational medicine. Of the five research groups, two focus their research on the factors and mechanisms underlying inter-individual variability in drug response with an emphasis on genetic and metabolomic factors. Their ultimate aim is to translate scientific knowledge into clinically useful genetic and pharmacological markers for individualized drug prescription or dosing. The clinical cytomics group is mainly evaluating whether and how human basophils perpetuate chronic allergic asthma by studying different factors and circumstances that have the potential to mount or dampen the immune-regulatory and effector functions of human basophils. The fourth group focuses on the biochemical, enzymatic, and genetic characterization of selected rare inherited metabolic diseases. This involves the study of the genetic and pathophysiological mechanisms underlying mitochondriopathies and ammonia detoxification defects of the urea cycle. The computational medicine group focuses on predictive modeling of clinically relevant outcomes from laboratory data, on deep evaluation of "-omics" data, especially metabolomics, and on the development and application of bioinformatics tools for laboratory medicine.

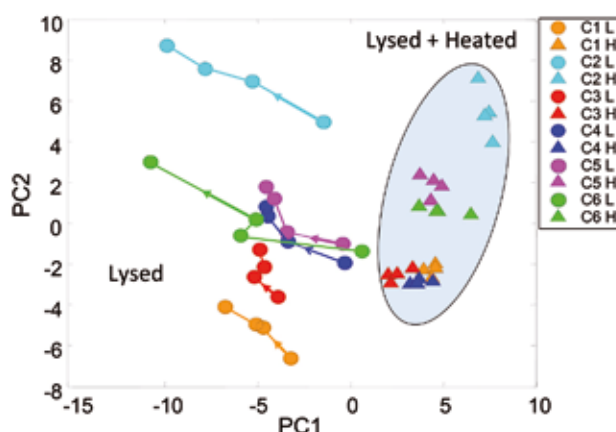
Teaching Profile

The institute participates in University teaching programs for students of medicine and biomedicine (including students of the University of Fribourg), biology and biochemistry.

Highlights 2017

Metabolic stability of cells for extended metabolomic measurements using NMR. A comparison between lysed and additionally heat inactivated cells

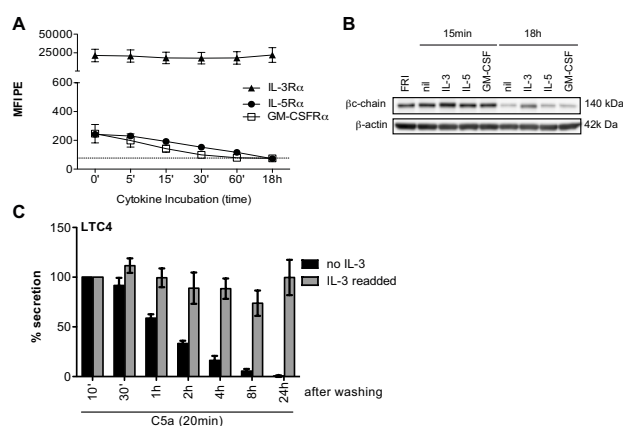
NMR measurements for metabolic characterization of biological samples, may take several hours. Preanalytical issues, such as sample preparation and stability, may have a high impact on metabolite content, and potentially lead to misinterpretation. In this study, we investigated by 1H HR-MAS NMR the impact of different content over the measurement time. Interestingly the results showed similar metabolite concentrations between lysed and lysed-heated cells at the beginning of the measurement, but increasing differences after some hours of measurement. In lysed cells, metabolism was ongoing, producing metabolite changes over time, contrary to a stable metabolite content of the lysed-heated cells. These results were confirmed in both fibroblasts and adrenal cells. Therefore, in order to minimize metabolite content modifications over the measurement time, it is suggested to use cell lysis in combination with heat inactivation for extended HR-MAS NMR measurements.



PCA score plot (PC1 vs. PC2) of lysed (circle – L) and lysed-heated (triangle – H) fibroblast spectra, obtained from the six different cell lines at four different time points (directly after preparation, after 160 min, 277 min, and 394 min). The six different cell lines are named C1 to C6 and are represented by different colours. Connecting lines between the 4 different measurements indicate the evolution of the metabolite content over time for each of the lysed cell samples.

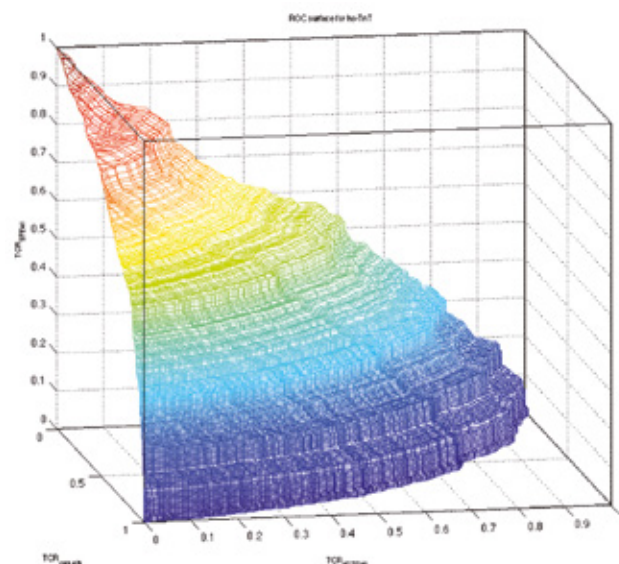
Sustained IL-3-mediated activation of human basophils is concomitant with a stable and high expression of IL-3R α and a replenishment of the common β -chain

Human basophils function as effector and immunoregulatory cells in allergic diseases. The GM-CSF cytokine family (IL-3, IL-5, GM-CSF), which is present at sites of allergic inflammation, regulates cellular function of human basophils. The receptors of the GM-CSF family share a common signaling chain (β c), which is co-expressed together with the cytokine-specific α -chain (IL-3R α , IL-5R α , GM-CSFR α). Among the members of the GM-CSF cytokine family, only IL-3 has the capacity to induce sustained functional changes in human basophils. The reason for these late effects of IL-3 has remained unclear. We report that the capacity of IL-3 in maintaining cellular responses is due to a constant high expression of IL-3R α accompanied with re-synthesis of β c. Continuous IL-3 receptor signaling was mandatory for the induction of late responses.



A) Flow cytometric analysis of surface expression of cytokine-specific α -chains demonstrate that upon addition of the respective cytokine, the expression of IL-3R α remains constantly high while IL-5R α and GM-CSFR α are rapidly down-regulated. B) IL-3 treatment provides replenishment of β c synthesis as shown here by western blot. C) Analysis of LTC₄ formation upon removal of IL-3 revealed that IL-3 has to be continuously present to induce late effects.

Modeling of the specificity of high-sensitive Troponin T
 With our publication "High sensitive cardiac troponin T: Testing the test" we could demonstrate that the specificity of hs-TnT for AMI is very low in a quaternary care hospital and trace a large proportion of the "false positives" back to myocardial stress of any origin (e.g. sepsis). Our modeling approach showed that the elevation of cardiac troponin alone therefore does not substantiate a diagnosis of acute myocardial infarction (AMI). Our manuscript sparked fruitful discussions (e.g. Badertscher et al.) and has been incorporated in a recent "state of the art review (Twerenbold et al.).



3-dimensional ROC surface analysis of hs-TnT including all 3 groups (controls n=964, NSTEMI n=323 and STEMI n=286). Volume under the surface=34% (95% CI: 30–38%).

Selected Competitive Grants

- Swiss National Science Foundation (grant No.310030-163205; 31003A-160206)
- Swiss Personalized Health Network: Project «L4CHLAB» (co-applicant)

Selected Publications

- Wortmann SB, Mayr JA, Nuoffer JM, Prokisch H, Sperl W. A Guideline for the Diagnosis of Pediatric Mitochondrial Disease: The Value of Muscle and Skin Biopsies in the Genetics Era. *Neuropediatrics*. 2017 Aug;48(4):309-314
- Amstutz U, Henricks LM, Offer SM, Barbarino J, Schellens JHM, Swen JJ, Klein TE, McLeod HL, Caudle KE, Diasio RB, Schwab M. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update. *Clin Pharmacol Ther*. 2018 Feb;103(2):210-216. doi: 10.1002/cpt.911. Epub 2017 Nov 20
- Hamzic S, Kummer D, Milesi S, Mueller D, Joerger M, Aebi S, Amstutz U, Largiadèr CR. Novel genetic variants in carboxylesterase 1 predict severe early-onset capecitabine-related toxicity. *Clin Pharmacol Ther*. 2017; 102 (5): 796-804
- Kämpfer S, Odermatt A, Dahinden CA and Fux M: Late IL-3 induced phenotypic and functional alterations in human basophils require continuous IL-3 receptor signaling. *Journal of Leukocyte Biology* 2017 101:227-238
- Haider DG, Klemenz T, Fiedler GM, Nakas CT, Exadaktylos AK, Leichtle AB. High sensitive cardiac troponin T: Testing the test. *International Journal of Cardiology* 228, 779–783 (2017)

University Hospital of Old Age Psychiatry and Psychotherapy (APP)

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Prof. Stefan
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MD

Research Partners

- ARTORG Center for Biomedical Engineering Research, University of Bern, Bern, Switzerland
- Division of Experimental Psychology and Neuropsychology, University of Bern, Bern, Switzerland
- University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland
- Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Department of Neuroradiology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
- Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland
- Image Analysis Lab Department of Computer Science University of Freiburg, Freiburg, Germany
- Freiburg Brain Imaging, University Medical Center Freiburg, Freiburg, Germany

Research Profile

Being a component unit of the University Psychiatric Services (UPD) Bern, the University Hospital of Old Age Psychiatry and Psychotherapy attends to psychiatric conditions in elderly patients. Likewise, the associated research group, that was established under the new directorship of Prof. Stefan Klöppel in January 2017, conducts clinically focused research on neurodegenerative pathologies, with special emphasis on dementia processes. To ultimately improve patient care, our efforts range from providing early and differential diagnoses



as well as prognoses with regard to the therapeutic effect by means of MRI-based machine learning algorithms (currently deployed in the interdisciplinary rapport at the local Memory Clinic) to exploring novel personalised treatment options. Concerning the latter, the primary focus is on non-invasive brain stimulation methods, such as transcranial electric stimulation (tES) and transcranial magnetic stimulation (TMS), applied independently or in combination with computerized cognitive training (Photo). Additionally, we are pursuing more fundamental research questions regarding the neuronal mechanisms underlying learning to later inform practical implementations.

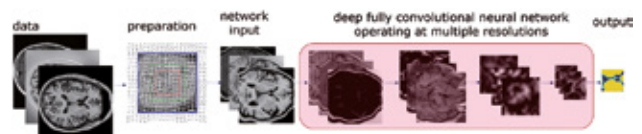
Teaching Profile

The University Hospital is involved in the University curriculum for students of medicine while also offering master thesis projects for students of medicine and psychology. Furthermore, Prof. Stefan Klöppel is participating in the newly formed Expert Committee III Clinical Sciences as part of the Graduate School for Health Sciences.

Highlights 2017

MRI-based pattern recognition techniques in dementia diagnostics

Patients suffering from dementia often receive unspecific diagnoses and consequentially no specialised treatments. While brain imaging can improve diagnostic accuracy, the interpretation of the results relies on the neuroradiologists' experience. Within this project, which attracted SNF funding, we plan to apply convolutional neuronal networks (CNNs) to integrate all analysis procedures from raw data to diagnostic decision. Moreover, an uncertainty rating will be assigned to each diagnostic decision to inform the clinicians about the reliability. Currently, the procedure is tested on existing data from the local memory clinic in weekly interdisciplinary case conferences.

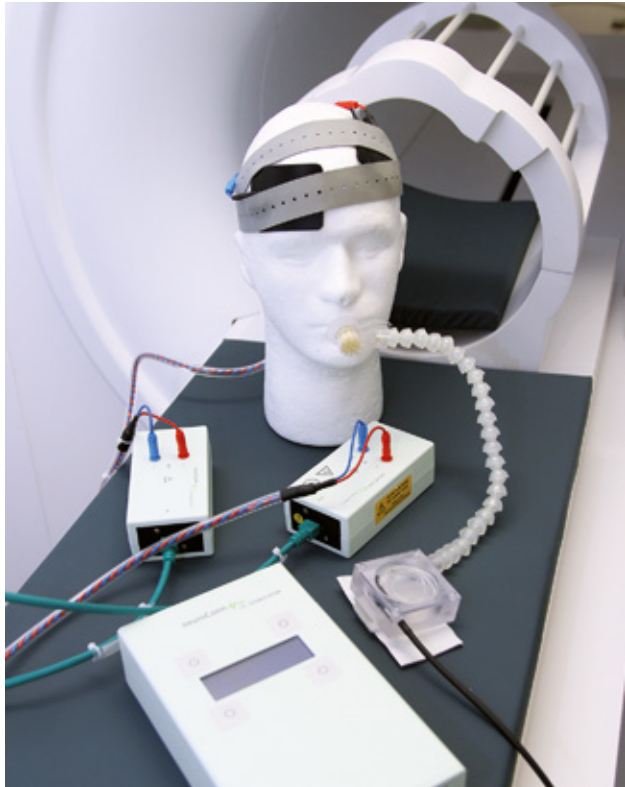


Deep learning segmentation of multimodal MRI data.

Anodal tDCS enhances verbal episodic memory in initially low performers

While transcranial direct current stimulation (tDCS) boosts neuronal excitability in the stimulated cortical areas and has

been proposed as a method to improve cognitive skills, previous studies have reported mixed behavioural effects. The present study aimed to investigate whether performance at baseline could predict stimulation-induced benefits. Despite the absence of a significant tDCS effect at group level, we found that the initial performance significantly moderated the stimulation effect insofar as initially low performers experienced the highest gain from real as compared to sham stimulation. A follow-up project will extend those findings by including MRI measurements, notably magnetic resonance spectra acquisitions of neurotransmitter levels in the stimulated cortical area, first, to monitor tDCS-induced neurophysiological changes and second, to identify biomarkers for the anticipated stimulation benefit.



Setup for tDCS in MRI scanner.

Selected Competitive Grants

- Swiss National Science Foundation (Grant #173880)
- German Alzheimer Forschung Initiative e.V. (AFI-Grant #16040)
- German Federal Ministry for Economic Affairs and Energy,
- Central Innovation Programme for SMEs (KF3223201)

Selected Publications

- Lora Minkova, Annegret Habich, Jessica Peter, Christoph P. Kaller, Simon B. Eickhoff, Stefan Klöppel: Gray matter asymmetries in aging and neurodegeneration: A review and meta-analysis. *Hum. Brain Mapp.* (2017), doi: 10.1002/hbm.23772
- Elisa Scheller, Jessica Peter, Lena V. Schumacher, Jacob Lahr, Irina Mader, Christoph P. Kaller, Stefan Klöppel: APOE moderate compensatory recruitment of neuronal resources during working memory processing in healthy older adults. *Neurobiol. Aging* (2017), 56, 127-137, doi: 10.1016/j.neurobiolaging.2017.04.015
- Annegret Habich, Stefan Klöppel, Ahmed Abdulkadir, Elisa Scheller, Christoph Nissen, Jessica Peter: Anodal tDCS enhances verbal episodic memory in initially low performers. *Front. Hum. Neurosci.* (2017), doi: 10.3389/fnhum.2017.00542
- Lora Minkova, Sarah Gregory, Rachael I. Scahill, Ahmed Abdulkadir, Christoph P. Kaller, Jessica Peter, Jeffrey D. Long, Julie C. Stout, Ralf Reilmann, Raymund A. Roos, Alexandra Durr, Blair R. Leavitt, Sarah J. Tabrizi, Stefan Klöppel, TRACK-HD Investigators: Cross-sectional and longitudinal voxel-based grey matter asymmetries in Huntington' disease. *NeuroImage Clin.* (2018), doi:10.1016/j.nicl.2017.10.023
- Jessica Peter, Lena V. Schumacher, Verena Landerer, Ahmed Abdulkadir, Christoph P. Kaller, Jacob Lahr, Stefan Klöppel: Biological Factors Contributing to the Response to Cognitive Training in Mild Cognitive Impairment. *J. Alzheimers Dis.* (2018), doi:10.3233/jad-170580

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Prof. Michael
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Prof. Frauke
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Deputy Head of
Research

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- Institute of Pharmacology and Toxicology, University of Zurich, Zurich, Switzerland
- Developmental Clinical Psychology Research Unit, Faculty of Psychology and Educational Sciences, University of Geneva, Geneva, Switzerland
- Department of Child and Adolescent Psychiatry, Heidelberg University, Heidelberg, Germany
- Department of Child and Adolescent Psychiatry and Psychotherapy, University of Ulm, Ulm, Germany
- Orygen, The National Centre of Excellence in Youth Mental Health, University of Melbourne, Australia
- Child Psychiatry Branch, National Institute of Mental Health, Washington, USA
- Harvard Medical School, Boston, USA
- Neuroscience Research Australia, Sydney, NSW, Australia

Research Profile

With the recent appointment of Prof. Dr. Michael Kaess as new director and head of research, the research department of the University Hospital of Child and Adolescent Psychiatry and Psychotherapy is realigning its research priorities. Previous research focussed on early detection and intervention in children and adolescents at risk for psychosis, studies on the impact of sleep on brain development and well-being as well as the evaluation of novel psychotherapy approaches based on transdiagnostic mechanisms of change. Spanning the spectrum from basic research to randomized controlled trials, the department will maintain its translational character, thereby directly informing clinical services, such as the Early Detection and Intervention Centre for mental crisis (FETZ Bern). Strategic developments in the near future include the establishment of a competence centre (research and clinical care) for adolescents with risk-taking and self-injurious behaviour in the context of personality disorders and methodological extensions in neuroendocrine and psychophysiological research.

Teaching Profile

This department participates in University teaching for students of Medicine and Psychology at all educational levels.

Highlights 2017

Prevalence and clinical relevance of psychosis-risk symptoms in the young adult community

The utility of ultra-high risk and basic symptoms in the psychosis assessment of community-based samples has been questioned, given a lack of knowledge about their prevalence and clinical relevance. The study sought to rectify this situation, using semi-structured telephone interviews with established psychosis-risk instruments in a representative sample from the young adult community (N = 2683; age 16–40 years; response rate: 63.4%). The point-prevalence of psychosis-risk symptoms was 13.8%. Psychosis-risk criteria were uncommon (2.4%), indicating little risk of falsely labelling individuals from the community at-risk for psychosis. However, both psychosis-risk symptoms and diagnostic criteria seem to possess sufficient clinical relevance to justify broader attention in clinical practice, especially if ultra-high risk and basic symptoms occur together.

Electrical sources underlying sleep oscillations are trait-like

Slow waves are low frequency, high amplitude waves characteristic of the sleep EEG and support sleep dependent plasticity and learning. Deficits in slow waves have been described for a number of psychiatric disorders including depression, schizophrenia and ADHD. Using source localization to examine the brain regions that generate this rhythm in a population of healthy adults, we found that slow waves have a frontal focus and show an increase following sleep deprivation. The spatial distribution of the source of these waves was unique to an individual and stable over time. Given that slow waves are altered in psychiatric disorders and play a key role in sleep dependent learning our findings inform the source of these waves and show that they are trait specific.

Cerebral blood flow as a biomarker for patients with psychosis-risk

There is an ongoing search for meaningful biomarkers for the early detection of patients with clinical high risk for psychosis (CHR). Cerebral blood flow (Figure 1A) can be measured with arterial spin labelling magnetic resonance imaging and correlates with neuronal activity in brain regions of interest. In the study cerebral blood flow was measured in a sample of CHR (n = 29) patients and clinical controls (CC, n = 18). In patients with CHR, cerebral blood flow was significantly increased in the striatum (Figure 1B; CHR > CC)

and significantly decreased in prefrontal areas (Figure 1C; CHR < CC) compared to CC. Increased neuronal activity in the striatum is suggested to reflect elevated dopaminergic turnover in these regions, whereas decreased cerebral blood flow in frontal areas could be an early marker for cognitive dysfunction in patients with CHR. Thus, the study emphasizes abnormal metabolic activity preceding the onset of full-blown psychosis.

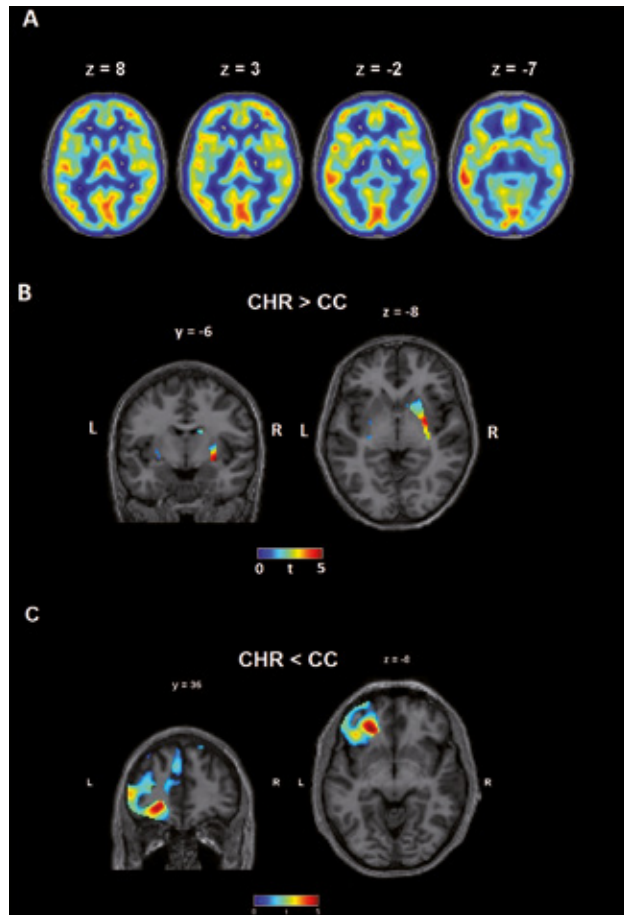


Figure 1.

Selected Competitive Grants

- Swiss National Science Foundation (Grant No. 155951; 144100)

Selected Publications

- Bersagliere A, Pascual-Marqui RD, Tarokh L, Achermann P. Mapping Slow Waves by EEG Topography and Source Localization: Effects of Sleep Deprivation. *Brain Topography* [E-Pub ahead of print] doi: 10.1007/s10548-017-0595-6
- Kindler J, Schultze-Lutter F, Hauf M, Dierks T, Federspiel A, Walther S, Schimmelmann BG, Hubl D. Increased Striatal and Reduced Prefrontal Cerebral Blood Flow in Clinical High Risk for Psychosis. *Schizophrenia Bulletin*. 2017; doi: 10.1093/schbul/sbx070
- Schmidt SJ, Schultze-Lutter F, Bendall S, Groth N, Inderbitzin N, Michel C, Schimmelmann BG, Hubl D, Nelson B. Psychological and symptomatic mediators linking childhood adversities and trauma to suicidal behavior in adolescents and adults at clinical high risk for psychosis. *Frontiers in Psychiatry*. 2017; 8(242):1-12
- Schultze-Lutter F, Michel C, Ruhrmann S, Schimmelmann BG. Prevalence and clinical relevance of interview-assessed psychosis-risk symptoms in the young adult community. *Psychological Medicine*. 2017; doi: 10.1017/S0033291717002586
- Koenig J, Weise S, Rinnewitz L, Parzer P, Resch F, Kaess M. Longitudinal covariance of resting-state cardiac function and borderline personality disorder symptoms in adolescent non-suicidal self-injury. *World Journal of Biological Psychiatry*. [E-Pub ahead of print] doi: 10.1080/15622975.2017.1342046

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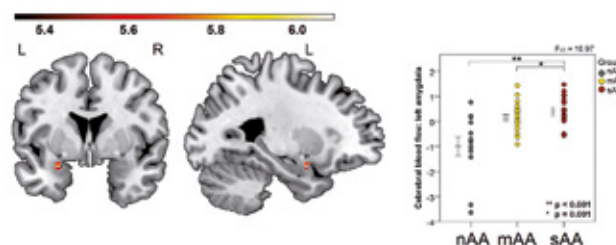
Research Partners outside of the University of Bern, among others

- Alzheimer Research Center, Karolinska Institute, Stockholm, Sweden
- Campus Biotech, University of Geneva
- Collaborative Psychiatric Research Institute, University of Antwerpen, Belgium
- Feinstein Institute for Medical Research, Northwell Hofstra University, New York, USA
- Department of Economics, University of Zurich
- Department of Neuroscience, University of Groningen, Netherlands
- Department of Psychiatry, Northwestern University, Chicago, USA
- Department of Psychiatry, University of Tokyo, Japan
- Department of Psychiatry and Psychotherapy, Ludwig-Maximilians-Universität, Munich, Germany
- Department of Psychology, University of Jyväskylä, Finland

Research Profile

The research of the University Hospital of Psychiatry und Psychotherapy is coordinated in the Translational Research Center. Thus, the translational aspect of the research is pivotal and reflected in four research sections, clinical research support, clinical research, systems neuroscience of psychopathology and molecular psychiatry, covering the spectrum from methodological research in neuroimaging, electrophysiology and non-invasive stimulation technologies to introducing novel diagnostic criteria improving therapy and prognosis in psychiatry. A large number of independent researchers are covering clinical topics like psychosis, hallucinations, aberrant motoric behaviour, formal thought disturbances, affective disturbances, psychotherapy, sleep and neuroplasticity, molecular psychiatry and addiction. Most of these groups are working transdisciplinary within UPD, Insel-Hospital as well as other faculties at the University of Bern and within international cooperations. Recently it has been recognized that the currently used diagnostic criteria in psychiatry has led to a deadlock in the clinical development.

In the project SyNoPsis we aim to identify neurobiological patterns characteristic for defined psychopathologies and not disease categories and thus to improve prediction outcome and therapy. Innovative therapy studies using novel approaches like transcranial magnetic stimulation as well as deep brain stimulation, partly in close cooperation with the Neurocenter at the Inselhospital, have led to alternative therapeutic strategies improving the outcome in patients and reducing the burden of stigma of patients and relatives.



Neuronal activity in the left amygdala associated with altered affectivity in schizophrenia, the more the affectivity is altered, the higher the neuronal activity in amygdala (Stegmayer K, Strik W, Federspiel A, Wiest R, Bohlhalter S, Walther S (2017) Specific cerebral perfusion patterns in three schizophrenia symptom dimensions. Schizophrenia Research 190: 96-101)



Interdisciplinary approach of deep brain stimulation for treatment-resistant severe major depressive disorder at the Neurocenter of the University Hospital Insel.

Teaching Profile

The University Hospital of Psychiatry and Psychotherapy is involved in the University curriculum for students of medicine and psychology including master and doctoral thesis projects. Furthermore, the Department is involved in various Graduate Schools of the University of Bern.

Highlights 2017

Considering that the unitary model of schizophrenia has failed as a medical diagnosis we published a disruptive perspective of psychosis introducing Synopsis, a concept where psychopathological symptoms are mapped upon functional neuronal circuits like language, emotion and motor behavior. Several papers have supported our concept. E.g. motor abnormalities in schizophrenia include several impairments and despite their frequent occurrence, the underlying causes of motor abnormalities remain unclear. We demonstrated that no single abnormality within the cerebral motor system is linked to all motor abnormalities. Instead, specific local dysfunctions within the motor system are associated with distinct behavioral abnormalities. These results stimulate treatment approaches, where we currently conduct a randomized clinical trial with transcranial magnetic stimulation targeting this system.

Early detection of emerging psychosis is one strategy to improve prognosis in schizophrenia. This has been a challenging task and unsatisfactorily resolved. We could now demonstrate that increased neuronal activity in the striatum combined with a reduction prefrontal are reflecting metabolic abnormalities preceding the onset of psychosis. These results may improve the therapeutic outcome and reduce the burden of schizophrenia.

One aspect of behavior regarding mental health and personal growth is that they depend on wise choices on how much effort to invest in seeking expected rewards. We could demonstrate that bulimia, a severe but common eating disorder, is associated with impaired effort-reward integration due to a dysfunction of brain's dopamine system. Our work provides crucial insights into the causes of food addiction. It encourages treatment studies combining dopamine-modifying drugs with psychotherapy in bulimia nervosa.

Sleep is frequently disturbed in psychiatric disorders and here traditional models of sleep-wake regulation in mammals emphasize the importance of the ascending reticular arousal system ('bottom-up' pathway). We further integrate evidence on a cortico-thalamic 'top-down' pathway and provide a systematic framework for non-invasive brain stimulation (NIBS) techniques in humans to modulate arousal and sleep. This line of research may contribute to the development of novel treatments for clinical conditions of disrupted arousal and sleep.

Regarding addiction research we could demonstrate, in an important clinical study, that the use of the Alcohol Withdrawal Scale can reduce risks and health care costs significantly in alcohol withdrawal treatment.

Selected Competitive Grants

- SNF (320030_146789, 32003B_152619, 105319_159286)
- Schweizerische Stiftung für Alkoholforschung SSA (283)
- Japan Science and Technology Agency (JST) Tokyo: Joint Research Grant

Selected Publications

- Krone L, Frase L, Piosczyk H, Selhausen P, Zittel S, Jahn F, Kuhn M, Feige B, Mainberger F, Klöppel S, Riemann D, Spiegelhalder K, Baglioni C, Sterr A, Nissen C. Top-down control of arousal and sleep: Fundamentals and clinical implications. *Sleep Med Rev.* 2017; 31:17-24. doi: 10.1016/j.smrv.2015.12.005
- Mueller SV, Morishima Y, Schwab S, Wiest R, Federspiel A, Hasler G (2017). Neural Correlates of Impaired Reward-Effort Integration in Remitted Bulimia Nervosa. *Neuropsychopharmacology* (in press)
- Soravia LM, Wopfner A, Pfiffner L., Bétrisey S., Moggi F (2017). Symptom-triggered detoxification using the Alcohol Withdrawal-Scale reduces risks and health care costs. *Alcohol and Alcoholism* (in press)
- Strik W, Stegmayer K, Walther S, Dierks T. (2017) Systems Neuroscience of Psychosis: Mapping Schizophrenia Symptoms to Brain Systems. *Neuropsychobiology* (in press)
- Walther S, Stegmayer K, Federspiel A, Bohlhalter S, Wiest R, Viher P (2017) Aberrant Hyperconnectivity in the motor system at rest is linked to motor abnormalities in schizophrenia spectrum disorders. *Schizophrenia Bulletin* 43 (5):982-992

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