

UNIVERSITÄT

Medical Faculty www.medizin.unibe.ch



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### **Foreword**

The University of Bern was founded in 1834 and has from the beginning included a Faculty of Medicine. In the last 185 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 Faculty of Medicine offers a full program of study in Medicine and Dental Medicine. In addition, Master studies in Biomedicine, Biomedical Engineering and newly also in Pharmacy 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. Beginning in September 2018, we accommodated an additional 100 students in the first year of study; the total first year medical class now numbers approximately 340. In the last years, 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 continue to offer a **problem-oriented** study program, which demands a high proportion of well-trained teaching staff. Currently, we are newly planning the master study which requires additional efforts to accommodate all medical students in our clinical departments.

The Faculty of Medicine 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, and 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 participation in large international trials, is performed with the support of the Clinical Trial Unit (CTU). Currently, we are in the process of developing a **new Department** of Clinical Research (DCR), which will accommodate the CTU as a service unit. The DCR will also develop its own research and teaching programs. It will be located in the Swiss Institute for Translational and Entrepreneurial Medicine (SITEM), in close

proximity to the clinical departments of the Inselspital. 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. For instance, we offer intramural grant opportunities (e.g. CTU grants, PhD student fellow ships, protected research time).

**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. Some ARTORG research groups were re-located in the SITEM. Other groups of the University and several units of the Inselspital also found space in SITEM in 2019 to promote collaborative interactions with partners of the industry. A good example here is the Diabetes Center Bern (DCB), in which new technologies are being developed to combat diabetes. Another strategic step to strengthen Translational Medicine was the decision to build up the Bern Center for Precision Medicine (BCPM) which has begun its work on 1 January 2019. Together with other local platforms (e.g. the unique Bern Liquid Biobank, several omics platforms, the Clinical Genomics Lab) and the University Hospital, this Center carries out research projects to develop the field of Precision Medicine and gives Bern a strong position within the Swiss Personalized Health Network (SPHN) initiative. These efforts require the development of additional expertise in the field of Computational Medicine. For this purpose, we are currently planning to create a new Center for Artificial Intelligence in Medicine (CAIM).

We hope that you will enjoy reading this report, which was prepared to promote familiarity with the breadth of knowledge and collaborations represented within and outside our University. We take this opportunity to thank all our employees and partners for their outstanding commitment which has made 2019 a very successful year for the Faculty of Medicine of Bern.

An . Um Dimo

Hans-Uwe Simon Dean

(on behalf of the Board of the Faculty of Medicine)

### Highlights

### January 2019

### 1.1.2019

In 2019, two internationally renowned research institutes in Bern merged: the Institute for Surgical Technology and Biomechanics and the ARTORG Center for Biomedical Engineering Research. Under the ARTORG brand, they form a national and international beacon for teaching, research and innovation in medical technology, in close connection with the Inselspital, Bern University Hospital, and the translational center sitem-insel AG.



### March 2019

### 1.3.2019 - Diploma Celebration in the Münster of Bern, Prizes & Honours 2018

### Faculty awards for the three best dissertations of the year 2018

1st price – Mr Dr. Georgios VASILAKOS for the Dissertation

"Superimposition of 3D-digital maxillary dental casts on palatal structures: Method validation and clinical application" under the direction of PD Dr. N. Gkantidis, Institute of Dental Medicine, Department of Orthodontics and Dentofacial Orthopedics, Bern

2<sup>nd</sup> price – Mrs Dr. Andrea Sara DULCEY-HUSI for the Dissertation

"Feasibility, Safety and Outcome of Recanalisation Treatment in Childhood Stroke" under the direction of Prof. Dr. M. Steinlin and Dr. S. Bigi, Department of Pediatrics, Inselspital Bern

2<sup>nd</sup> price – Mr Dr. Jonathan RÖCKEN for the Dissertation

"The role of TNIK in non-small cell lung cancer (NSCLC) development and Wnt pathway activation" under the direction of PD Dr. C. Riether and Dr. E.D. Bührer, Department for BioMedical Research, Research Group for Tumor-Immunology, University of Bern and Dr. M.A. Amrein, Department of Medical Oncology, Inselspital Bern

### Eduard-Adolf-Stein-Preis of the University of Bern for an outstanding dissertation

Mrs Prof. Dr. med. Lia BALLY

### **Recognition Prize of the Dental Society SSO**

For outstanding achievements in the study of dentistry (awarded at the Master's Ceremony on 13 September 2018) Mr Dr. med. dent. Fabrice DULLA

### Prize of the Medical Society of the Canton of Bern

For the best Federal examinations in human medicine 2018
Best Candidate for CS Examination – Mr Nicola Andrea BLASER
Best candidate for the MC-Examination – Mrs Laura Barbara ANDEREGG

### **CSL Behring Award**

For Excellence in the Master program Biomedical Sciences Mrs Vera IMBODEN & Mrs Anastasia MILUSEV & Mr Emilio FLINT

### **Alumni Biomedical Sciences Award**

For the best Master's thesis in the Master program Biomedical Sciences – Mr Akira NOMURA

### The RMS Foundation Award

For the best graduate in the Biomedical Engineering Master program – Mr Michael Andreas REBSAMEN

### Teacher of the Year

Dr. med. Stefan KUCHEN, Department of Rheumatology, Immunology and Allergology, Inselspital Bern



# College of Andreigher, National Cheng Kung University and Faculty of Busching Busching (Busching of Busching of Bu

# 6.3.2019 – Visit of the Dean to Taiwan

Dean Simon stayed in March 2019 for a few days at the College of Medicine of the National Cheng Kung University in Taiwan. On the occasion of his stay, a Memorandum of Understanding was signed by the representatives of the two universities.

# 26.3.2019 – World's first institute accredited for the detection of bacteria

The Institute for Infectious Diseases (IFIK) at the University of Bern is the world's first accredited laboratory that can identify bacteria using nanopore sequencing.



### **April 2019**



### 12.4.2019 - André Schroeder Research Award 2019

The André Schroeder Research Prize 2019 goes to Prof. Dr. Vivianne Chappuis from the Department of Oral Surgery and Stomatology and her co-authors for their study "Osseointegration of ultra-fine titanium with a hydrophilic nano-structured surface: an in vivo examination on mini pigs".

# 20.5.2019 – Bern Center for Precision Medicine inaugurated

The Bern Center for Precision Medicine (BCPM) of the University of Bern and Inselspital, University hospital of Bern, was officially opened today in the presence of Director of Education Christine Häsler. Häsler described the BCPM as a prime example of the development of new research centers, and strengthening Bern as a medical location.



### August 2019

# 9.8.2019 – A Bernese is "World Top Expert" for special immune cells

Eosinophils belong to the white blood cells and can render pathogens harmless. Hans-Uwe Simon, Director of the Institute of Pharmacology and Dean of the Medical Faculty, was recently appointed "World Top Expert" for these special immune cells.



# 15.8.2019 – Major award for two Bernese medical projects

Prestigious grants from the USA go to two Bernese researchers: the biomedical scientists Marianna Kruithof-de Julio and Robert Rieben were the only researchers in Switzerland to receive a grant under two "Congressionally Directed Medical Research Programs", which primarily support research in the USA. This underlines the unique quality of medical research at the University of Bern.





# 29./30.8.2019 – sitem-insel sets strong signal for Bern's role as a medical location

On Thursday and Friday, 29 and 30 August 2019, the opening of sitem-insel was celebrated. The first national competence center for translational medicine and entrepreneurship is supported by the public sector, science and industry and strengthens and expands Bern as a medical location. The University of Bern is a founding member and academic partner of sitem-insel.



### 16.9.2019 – Start of studies 2019

On 16 September, 357 students (human and dental medicine) began their medical studies in the newly created Alhambra auditorium (formerly the Alhambra Cinema). This is already the second study start with 100 additional study places in human medicine since this was decided by the government council to counteract the shortage of doctors in Switzerland. This increase of +100 places makes the Medical Faculty of the University of Bern the largest in Switzerland and strengthens Bern's position as a medical location.



# 17.9.2019 – Prestigious grant to use Artificial Intelligence for improved glucose control

The ARTORG Center for Biomedical Engineering Research of the University of Bern is the recipient of a grant from JDRF, the leading global funder for type 1 diabetes research. Thanks to the grant, a team led by Stavroula Mougiakakou will investigate a large, real-world dataset to develop advanced algorithms for automated insulin delivery that are capable of predicting dangerously low or high blood sugar levels. The goal is to optimize and personalize insulin treatment.

# 18.9.2019 – Al-based prognosis in intensive care: decision-relevant patterns identified in EEG of coma patients

A reliable prognosis for coma patients in the intensive care unit is crucial. Improved transparency will boost the use of Artificial Intelligence (AI) to support end-of-life decisions. For the first time, a research team has succeeded in identifying specific patterns in Electro-Encephalogram (EEG) analyses that the deep-learning network uses for making prognosis decisions. This is an important step towards decoding the "black box" of deep-learning processes and thus towards AI transparency.





# 25.9.2019 – Prestigious award for Bernese neurosurgeon

Prof. Andreas Raabe, Head of the Department of Neurosurgery at the Inselspital, Bern University Hospital, will be honored with an exceptional award at this year's congress of the European Association of Neurosurgical Societies EANS in Dublin: He will give the European Lecture as part of the Award Session. Prof. Raabe has merited the European Lecture Award with two inventions that have transformed neurosurgery worldwide and significantly improved patient safety.

# 23.10.2019 – Special cells contribute to regenerate the heart in Zebrafish

It is already known that zebrafish can flexibly regenerate their hearts after injury. An international research group led by Prof. Nadia Mercader of the University of Bern now shows that certain heart muscle cells play a central role in this process. The insights gained could be used to initiate a similar repair process in the human heart.





# 31.10.2019 – Removing liver tumors safely, noninvasively and efficiently

Many liver tumors have long been difficult or impossible to remove. Since 2015, however, it has been possible to treat these tumors by combining noninvasive surgical techniques, radiological imaging and a navigation system. For the first time, a new study by the University of Bern and Inselspital, Bern University Hospital has impressively demonstrated the success of this technique.

### **November 2019**

### 13.11.2019 – Day of BioMedical Research

This year's Johanna Dürmüller-Bol DBMR Research Award of the Department for BioMedical Research (DBMR) of the University of Bern has been awarded to Maria-Nieves Sanz. She receives the award, endowed with CHF 30'000, for her research on inflammatory processes during heart transplantations.



### The Medical Faculty in Numbers

1'983 students in Bac

**2**Bachelor programs

**4** Master programs

254 students in 30 CAS/DAS/MAS programs

313 Final Master Degrees

226 Medicine

**36** Dental Medicine

**28**MSc in Biomedical Sciences

20 MSc in Biomedical Engineering

Masters of Medical Education

107 Full Professors

17 Assistant Professors
134 Associate Professors

451 Lecturers

Faculty

**3**Organisations

16 Institutes

331
Doctorate Degrees

**231** Dr. med. **33** Dr. med. dent.

**60** from the Graduate School for Cellular and Biomedical Sciences

**7** from the Graduate School of Health Sciences

184'436'845

29'039'492

from the Swiss National Science Fondation

**44'834'102** third party funds for research

2168 Original Articles published

**136'878** hours of teaching

12 1:



# Historical

Glimpses of the History of the Faculty Deans of the Medical Faculty



Sahli presenting a clinical case at the Inselspital, circa 1905

# Glimpses of the History of the Faculty: Diagnostic Tools for the GP, Hermann Sahli and the Unity of Medicine

At the turn of the 20<sup>th</sup> century, Bern was famous for its quadrumvirate of highly acclaimed medical professors: the surgeon Theodor Kocher (1841-1817), the internist Hermann Sahli (1856-1933), the dermatologist Josef Jadasshon (1863-1936), and the pathologist Theodor Langhans (1839-1915).

Whereas it is rather easy to determine some of the major scientific achievements of Langhans, Jadassohn and Kocher, it is much more difficult to establish the scientific contribution of Sahli. This is not due to a lack of Sahli's originality but due to his ideal of medicine in an era of increasing specialization.

### The emergence of specialization

When Sahli, at the early age of 32, was elected as professor and head of the medical clinic in 1888, the buildings on the new hospital ground were just four years old. The whole hospital had a rather simple layout and was constructed around the two main clinics of surgery and medicine. Within a couple of years, this changed radically. Until 1910, new separate institutes and clinics of pharmacology, otorhinolaryngology, microbiology, dermatology, ophthalmology, radiology and pediatrics had been established. And a whole group of other specialities like neurology, cardiology and pneumology were calling for separate university teaching, professors and clinics.

This was not to Sahli's taste. In a 1914 paper on the relation between science and medicine, he stated that "in today's distractions and peculiarities of specialization, it is the duty of internal medicine to maintain the unity and simplicity of medicine. ...
They have recently started to open their offices: heart physicians, lung physicians, nerve physicians, kidney physicians, stomach physicians, bowel physicians.
What a brilliant idea! There is no objective justification for such separations. ... The human organism is a unity and it will not go unpunished if diagnosis and therapy are separated in such a manner according to organs."

Sahli bemoaned the tendency that patients would no longer go to their family doctor but directly to the specialist. This would be the reason why patients on the countryside were usually better off than those living in the cities. Such a development would neither be good nor necessary. Sahli stressed that the demands for a doctor's office could still be met with good education and experience. "And this will continue to be the case in hundred years when detailed knowledge will have increased tenfold." Sahli himself devoted the majority of his time to make this happening, to furnish physicians with the knowledge and the tools to become good GPs. He did so on three levels: by teaching, publishing and the invention of new diagnostic tools.

### **Holistic teaching**

In Sahli's teaching, the presentation of the single case took center stage. He prepared each case meticulously and it was usually discussed for several hours. "Each clinical case is considered as a problem and scrutinized as far as possible with all the means of examination and reasoning." This would lead to an discussion of all the areas of knowledge involved, especially physiology

In Sahli's teaching, the presentation of the single case took center stage

and pathology – but also psychological aspects had to be taken into consideration. Even younger students with little clinical knowledge would participate. Sahli was, in fact, a champion of problem-based learning. In his view, there was no simple case, and routine was not something physicians should strive for. Due to the complexity and interconnection of the body there was no need for specialized clinical teaching in e.g. neurology. As many internal diseases were related to or based on neurological pathologies, this could be done within internal medicine. In addition to clinical cases, the theoretical lectures would be restricted to some selected difficult areas like metabolism or pathology of infectious diseases. He stressed that there is no simple medicine, there is only scientific medicine which students have to be immersed in.

### A textbook: everything you need to know

True to his words, Sahli covered the whole range of internal medicine and – although an expert on blood pressure and circulation – published on such dissimilar topics as the development of antibodies, neurosis and hysteria, or insulin therapy. He criticized the increasing number of superficial, short-lived and irrelevant journal articles, arguing that World War One had at least one positive effect that not all the doctoral dissertations were printed anymore. As for himself, he announced many of his new findings only in his major work, the textbook on diagnostic methods. Published in seven increasingly voluminous editions from 1894 to 1928 and translated into English, Russian, Spanish and Italian, this is the work Sahli was mainly known for. He expected his students not only to use this massive textbook of almost 3,000 pages but to read it through carefully. In his view, diagnostic methods in his form of presentation, i.e. including physiological and pathological explanations, were "the basis of all our medical knowledge, thinking and skill."

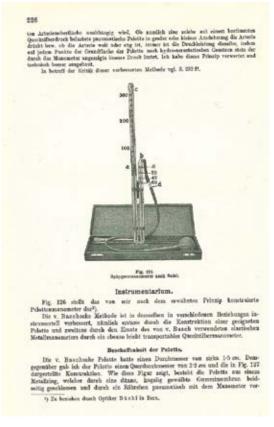
Such a synopsis of modern medical and technical knowledge was necessary more than ever and would help to strengthen the diagnostic skill of the general physician.

### Modernizing doctor's office: Sahli's hemometer

Situating diagnostic methods at the center of medicine and of his own scientific and clinical work, Sahli also developed a series of new methods and instruments himself, among other a manometer to measure blood pressure and – most famously – a hemometer to

measure hemoglobin. This latter instrument was based on a colorimetric comparison of diluted and dissolved blood with a standardized liquid. Being a simple yet reliable tool it was the worldwide (and often imitated) standard model in the early decades of the 20<sup>th</sup> century and present in many offices until the late 1950s. Today, it is still widely used in primary health care settings in developing countries. Sahli's aim in producing such an instrument was to allow the physician to keep up with the advancement of medicine but still maintain his independence.

Although Sahli helped to strengthen the coherence of internal medicine, the process of specialization continued relentlessly. His ideal, however, of the unity of medicine and of the importance of GPs is still of great importance.



From Sahli's textbook, 7th edition, 1928

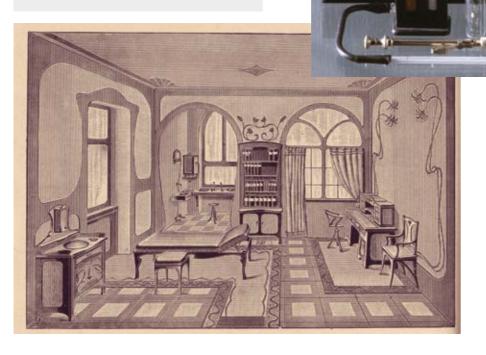
# **Deans of the Medical Faculty**

The Inselspital in 1908 showing Sahli's clinic (14), built in 1884, and newly established clinics and institutes of ophthalmology (8), otorhinolaryngology (12), bacteriology (22) and dermatology (34)



Sahli's hemometer (Institute for the History of Medicine)

Illustration of a doctor's office from a sales catalogue (Schaerer, Bern 1905), showing in the background a microscope and presumably a hemometer



1834–1835	Hugo Mohl
1835–1838	Hermann Askan Demme
1838–1843	Wilhelm Philipp Friedrich Vogt
1843–1847	Gabriel Gustav Valentin
1847–1849	Friedrich Miescher
1849–1852	Friedrich Wilhelm Theile
1852–1857	Wilhelm Rau
1857–1860	Wilhelm Philipp Friedrich Vogt
1860–1861	Wilhelm Rau
1861–1865	Gabriel Gustav Valentin
1865–1867	Daniel Jonquière
1867–1869	Christoph Theodor Aeby
1869–1871	Karl Emmert
1871–1874	Georg Albert Lücke / Henri Dor
1874–1876	August Breisky / Th. Kocher
1876–1878	Heinrich Irenäus. Quincke
1878–1880	Theodor Langhans
1880–1882	Ernst Pflüger
1882–1884	Ludwig Lichtheim
1884–1886	Marcellus Wilhelm von Nencki
1886–1888	Hugo Kronecker
1888–1890	Rudolf Demme
1890–1892	Ernst Pflüger
1892–1894	Hans Strasser
1894–1896	Hermann Sahli
1896–1898	Alexander Tschirch
1898–1900	Theodor Kocher
1900–1902	Arthur Carl Wilhelm Heffter
1902–1904	Theodor Langhans
1904–1906	Josef Jadassohn
1906–1908	August Siegrist
1908–1910	Wilhelm Kolle
1910–1911	Emil Bürgi
1911–1912	Leon Asher
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
.520 1550	Tians daygissery

1930–1932 Carl Wegelin

1963–1965 Adolf Zuppinger 1965–1967 Franz Escher 1967–1969 Johann Kuske 1969–1971 Eugen Läuppi 1971–1973 André Schroeder 1973–1978 Jürg Hodler 1978–1981 Beat Roos 1981–1983 Herbert A. Fleisch 1983–1985 Harald Reuter 1985–1987 Rudolf Berchtold 1987–1989 Max Hess 1989–1991 Georg Eisner 1991–1993 Alfred H. Geering 1993–1995 Hans-Rudolf Lüscher 1995–1997 Bernhard H. Lauterburg 1997–1999 Kurt Schopfer / HR. Lüscher 1999–2004 Emilio Bossi 2004–2008 Martin Täuber 2008–2016 Peter Eggli 2016– Hans-Uwe Simon
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# **Key people and Institutions**

Organigram
Board of Faculty
Institutional Overview
Structural Development of the Inselspital Area
Dean's Office
Dean's Office of Student's Affairs
Interview with Bernhard Pulver, Chairman of the Board
of Directors of the Insel Gruppe AG
New Professors at the Medical Faculty

# Organigram

### University Prof. Ch. Leumann **Faculty Council Faculty Executive Board** Dean Prof. H.-U. Simon **Deputy of the Dean** Prof. M. Egger Dean's office Dr. L. Stalder\* Vice-Dean Continuing Education & Clinics Prof. I. Baumgartner Vice-Dean Vice-Dean Vice-Dean **Head of Finance** Bachelor Research Master Prof. A. Perren Prof. C. Bassetti Prof. M. Egger Prof. Ch. Seiler Directorate Teaching Directorate Teaching **Medical Directorate Medical Directorate** Representative VDM & Research & Research UPD Insel Gruppe AG Insel Gruppe AG Prof. M. Arnold Prof. U. Mosimann Prof. T. Dierks Prof. S. Klöppel \*without suffrage



University Prof. Ch. Leumann



Prof. H.-U. Simon



Deputy of the Dean Prof. M. Egger



Dean's office Dr. L. Stalder



Vice-Dean **Bachelor Study** Prof. M. Egger



Vice-Dean Master Study Prof. Ch. Seiler



Head of Finance Prof. A. Perren



Vice-Dean

& Clinics

Continuing Education

Prof. I. Baumgartner

Directorate Teaching & Medical Directorate Research UPD Prof. T. Dierks



Vice-Dean

Prof. C. Bassetti

Research

Prof. S. Klöppel



Directorate Teaching & Research Insel Gruppe AG Prof. M. Gugger



Medical Directorate Insel Gruppe AG Prof. U. Mosimann



Representative VDM Prof. M. Arnold

## **Board of Faculty**

Prof. Claudio Bassetti Vice-Dean Research

Prof. Hans-Uwe Simon Dean

Prof. Christian Seiler Vice-Dean Master Study Prof. Iris Baumgartner Vice-Dean Continuing Education & Clinics

Prof. Marcel Egger Stellvertreter des Dekans Vice-Dean Bachelor Study



### **Institutional Overview**

## **Uni Mittelstrasse**

Institute for Medical Education (IML), Mittelstrasse 43 Institute of Primary Health Care (BIHAM), Mittelstrasse 43 Institute of Social and Preventive Medicine (ISPM), Mittelstrasse 43

## **Uni Muesmatt**

Institute of Anatomy, Baltzerstrasse 2
Institute of Biochemistry and Molecular Medicine, Bühlstrasse 28
Institute of Forensic Medicine, Bühlstrasse 20
Institute for the History of Medicine, Bühlstrasse 26
Institute of Physiology, Bühlplatz 5
Library Medicine, Baltzerstrasse 4
Microscopy Imaging Center (MIC), Freiestrasse 1
Theodor Kocher Institute (TKI), Freiestrasse 1

## von Roll Area

Institute of Complementary and Integrative Medicine (IKIM), Freiburgstrasse 46 & Fabrikstrasse 8

# **Insel Area**

Clinics and Institutes at the University Hospital, Inselspital

ARTORG Center for Biomedical Engineering Research, Murtenstrasse 50

Dean's Office, Office of student's affairs, Murtenstrasse 11

Department for BioMedical Research (DBMR), Murtenstrasse 35

Institute of Complementary and Integrative Medicine (IKIM), Freiburgstrasse 46 & Fabrikstrasse 8

Institute for Infectious Diseases (ifik), Friedbühlstrasse 51

Institute of Pathology, Murtenstrasse 31

Institute of Pharmacology, Inselspital, INO-F

Learning Center, Murtenstrasse 17

School of Dental Medicine, Freiburgstrasse 7

Swiss Institute for Translational and Entrepreneurial Medicine (sitem), Freiburgstrasse 18

University Cancer Center, Freiburgstrasse 10

University Neurocenter, Freiburgstrasse 16

# **Teaching facilities**

UniAlhambra UniZiegler

## **UPD**

University Psychiatric Services, Bolligenstrasse 111





Masterplan of the Inselspital area showing the expected allocation of the two planned projects on panel 03 and 07

### Structural Development of the Inselspital Area

With the construction of a new training building on panel 03 of the Inselspital and a research and training building on panel 07, the first significant expansion and modernization of the spatial infrastructure is taking place and the foundation stone for the concentration of University medical training on the area of the Inselspital is being laid.

The central location of the organizational units of the Faculty of Medicine of the University of Bern on the Insel site contributes on the one hand to strengthening the medical location of Bern, and on the other hand it promotes exchange in research and teaching and contributes to a practice-oriented learning and teaching environment.

# Panel 07: Construction of a research and training center on the Insel site

The new research and training building in construction area 07 will house a modern laboratory infrastructure for research, seminar rooms and parts of the practical training laboratories. The new building will bring together a large part of the medical institutes (including all preclinicians from the Muesmatt) at one location, lead to better utilization of the infrastructure and create synergies with the Inselspital. The competition projects have been submitted and are in the preliminary examination stage.

### Panel 03: the new base camp for medical students

In panel 03, the teaching and learning infrastructure for basic medical training for years 1-6 (Bachelor and Master) will be accommodated in the future. The main use of this training infrastructure will be teaching and seminar infrastructures (lecture halls, seminar and small group rooms), which will also be used for examinations, learning workstations for individual learning and learning in groups, a larger range of catering facilities, the Medical Faculty library and various organizational units responsible for the operation and management of the new training building.

The feasibility study for panel 03 was completed at the end of 2019, the next step is now the architectural competition. The commissioning of the new medical training building is planned for 2029.

# Murtenstrasse 24-28: A medical research and service building

North of the Insel site, between Murtenstrasse and the railway line, and adjacent to the Inselparking, a modern laboratory building for the Medical Faculty is being constructed. From autumn 2021 onwards, it will serve as the site concentration for the Institute of Forensic Medicine IRM, which is currently spread over seven locations. As one of four main sites, it will complement the research areas of the Department of Biomedical Research DBMR. In addition to accommodating research groups in large laboratories, the new



Murtenstrasse 24-28

The new modern laboratory building for the Faculty of Medicine is being constructed

Panel 12

Laying of the foundation stone for the main building of the Inselspital

building will allow the central services of the DBMR, the CoreFacilities, to be concentrated in one location.

The construction work is currently concentrating mainly on the interior fittings, while planning for the ELO project (Facility and Relocation Logistics) has started in parallel.

### Replacement building for the Dental clinics (ZMK)

As already reported last year, a new replacement building for the dental clinics (zmk) is planned. The current location, the building at Freiburgstrasse 7, is already significantly overcrowded and will continue to reach its capacity limits as the number of students, patients and staff increases as well as the upcoming digitalisation. With the move of the research department (Dental Research Center, DRC) into the sitem-insel building, space has been created to optimize the zmk. An improvement in the space situation will provide shortterm relief for users of the property at Freiburgstrasse 7. The selective conversion is expected to begin in summer 2020 and will take about one year. The zmk Bern's vision for the replacement building zmk Bern is strongly focused on the Insel site for a number of reasons, as the significant synergies in treatment, research and training are to be maintained. In the medium term, a modern infrastructure for the zmk Bern is to be created on the area of the Inselspital.

### sitem-insel: A unique cooperation starts

On Friday, 30 August 2019, sitem-insel, the Swiss Center for Translational Medicine, opened its doors to the general public (see also page 80). Several units of the University of Bern are rented in the sitem-insel building and work together with the other members of the community to "translate" innovations from medical research into a clinical product as quickly as possible - hence the English term "translation".

# Laying of the foundation stone for the main building of the Inselspital on panel 12

The foundation stone was laid with a dignified ceremony on 2 July 2019. This represents a further milestone in the "Inselcampus Masterplan" and the "Insel Areal III development plan", which was adopted by a large majority of Bernese voters in 2015. The aim is to modernise and harmonise the Insel area by 2030. From 2023, the new building will replace, among other things, the high-rise bed block and thus form the new heart of the Inselcampus.

With its digital planning and hospital building certified as Minergie-P-Eco, the complex new building is a true pioneering project. In addition to shorter distances, which should enable even more efficient processes, the well-being of the patients was the focus of the planning. In addition to central contact points and larger treatment rooms, they will also benefit from a pleasant atmosphere. A lot of daylight, views and bright and friendly materials were taken into account.

### Dean's Office

Dr. Lukas Stalder Head of the Dean's office

Dierk Matthäus IT Project Manager Lan Pham Finance/Human Resources Coordinator

Dr. Claudio Vallan PyRat Database

Pia Jäggi Finances Rita Meyer Appointments, Habilitations Dr. Max Müller Planning construction projects, Animal Welfare Officer



Nicole Peter Quality Manager Isabelle Salzmann Dissertations, Graduation ceremony

Sanche Schwab Successions, IT support

Svea Lehmann Gender Equality Coordinator José Schranz Teaching performance, Annual Report

Daniela Hügli – Faculty Secretary, Assistant to the Dean

Doris Haefelin Dean's Office Secretary, Assistant to the Head of the Dean's Office

Not on the picture: Brigitte Luginbühl – Exam fees, administration and projects

### Dean's Office of Student's Affairs

Sarah Habegger Student's Office Franziska Schmidhauser PBL Tutors

Dr. Sandra Trachsel Study Coordinator 2<sup>nd</sup> year Sara Vaz Clerkship Master Karin Erb Master Thesis, EKP Courses 4<sup>th</sup> year



Dr. Banu Yürüker Study Coordinator 1<sup>st</sup> year and Master Thesis Beatrice Ducret
Administration 1st year,
Leaves of Absence

Regula Walther Clinical Skills Training, courses 3<sup>rd</sup> year Dr. Peter Frey Head of Unit of student's affairs, Study Coordinator 3<sup>rd</sup> year

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Not on the picture: Christine Bögli – Lectures of the years 4, 5 and 6; Isabel Fahrni – Lectures 3<sup>rd</sup> year; Franziska Kolb – Administration 2<sup>nd</sup> year, courses SK1 (5<sup>th</sup> year) and SK2 (6<sup>th</sup> year)



### Interview with Bernhard Pulver Chairman of the Board of Directors of the Insel Gruppe AG

Dr. iur. Bernhard Pulver is Chairman of the Board of Directors of the Insel Gruppe AG since 2019. From 1999 to 2006 he was a member of the Grand Council of the Canton of Bern and from 2006 to 2018 he was a member of the government of the Canton of Bern. From 2010 - 2011 he was President of the Swiss University Conference (SUK) and from 2015 - 2018 Vice-President of the Swiss University Conference (SHK). Since 2019 he is also the lecturer for Political Governance in the Master in Public Management and Policy (Master PMP) at the University of Bern.

Mr. Pulver, you are the Chairman of the Board of Directors of the Insel Gruppe AG since 1 February 2019. You know the Inselspital well from your previous work as a member of the government council. How did you notice this change? What experiences have you had in this first year?

I had a great start! I was very positively received and the positive expectations on my part were exceeded. As Director of Education and from the Medical Task Force, I already knew a lot about the medical location. Now that I see more inside, I understand many things even better. But there are also major challenges - greater than I expected, for example in construction.

# One of the challenges is the tension between health and education or between services and academia. How do you see this tension?

I actually perceive it more as an interdependence than a tension. We are a hospital group with the University Hospital at its center, with an interweaving of education (teaching and research) and service. This is an identity-forming feature of the Insel Gruppe, which would otherwise not be one of the best hospitals in Switzerland. This is also the reason why so many excellent specialists work with us and I see the enthusiasm in the clinics.

When you look at the spatial visions, you can also see that teaching, research and services belong together. On the Insel campus, a University training building with the Medical Faculty is planned in panel 3 and a University research building in panel 7. The great advantage of Bern as a center of medicine is that we can combine many things in one campus: here we have two University Hospitals (Insel and UPD), University Institutes and the clinical departments of the Medical Faculty, the dental clinics of the University, the sitem-insel. This all belongs together, and we want to pursue the campus idea in this way.

The enthusiasm in the clinics is certainly one of the main reasons that this contributes to a higher quality of care. The active involvement in the front line of research is a major difference compared to standard treatment.

Exactly, and this combination enables patients to receive treatment at the highest level. It is also our task to find interfaces where this interlocking can lead to a crunch in the gears. We find this, for example, in the dual employment of a medical doctor who is simultaneously employed by the University as a lecturer and researcher and by the Insel Gruppe as a service provider. This can lead to high stresses. However, I see this combination primarily as an opportunity from which we can benefit.

«The keyword sustainability is on everyone's lips.»

# Now you have mainly talked about the opportunities and the friction surface. When the hospital is viewed as a business enterprise, the opportunities are emphasized, but do you also see dangers?

Swiss politics dictates that a hospital has to function like a business today. Hospital financing with DRGs (Diagnosis Related Groups) provides us with case-oriented income and we have to finance our costs and all investments - IT, construction and equipment ourselves. In my opinion, the prevailing basic statement in Swiss politics today that the healthcare system is too expensive and that hospitals must therefore function like a business is in principle too general, but this basic assumption has had a huge impact on Swiss healthcare policy over the last 20 years. The balancing act is to achieve the necessary profit margin in an institution that must by no means function according to purely economic logic. After all, we are not a manufacturing company. It is about people and health, it is about people's resources with relationships, prevention, aftercare. This is much more complex than simply a case that can be evaluated industrially. This is where I see the greater tension than in the combination of teaching, research and services. If we want to work in an entrepreneurial way and at the same time try to retain the human element, we could succeed in the "balancing act".

If we now once again build a bridge to teaching and research in this environment. One statement I often hear is: "Research is something I do in my leisure time". With this balancing act, how would you see future cooperation in terms of teaching and research? How do you think that should work?

When I visit clinics, they always present their research to me. I have not perceived this research activity as an activity in their free time. If you want to interpret this statement provocatively and take into account the long working hours of doctors, then it would indeed already be leisure time. For my feeling, the Insel Gruppe with its performance is not conceivable without this interlocking with teaching and research. We would not be where we are.

The key word is sustainability, which is on everyone's lips. How do you interpret sustainability and ecology in hospital and research operations? We make great efforts in the area of sustainability. This ranges from the kitchen, which uses regional products wherever possible, to the gardening, which tries to support biodiversity on the site. We are also making very good progress in the construction of the new main building, for example, which meets the Minergie® ecological standard, and I am proud that our management is strongly supporting this cause.

We as a society in general - and therefore we as a hospital group - will be challenged in the coming years to achieve net zero emissions by a year determined by politics.

### So the future plan is to achieve zero emissions?

Not only for our company - for the whole country! We do not yet have any concrete plans for the hospital, but we have received a number of measures from the sustainability office that will help us to move forward.

# Young talents and equality are two keywords that are omnipresent and one of the core issues in the area of future working models. Where do you see the development, where is the hospital heading?

The Insel Gruppe has set itself the goal of improving the promotion of young talent and equality. We have already received various awards in the promotion of diversity and equality, and we have also had ourselves certified. As an employer, the Insel Gruppe does a lot to be good at equality issues. But we have not yet reached our goal.

In view of the excessively low proportion of women in management positions, we see that further efforts are needed here. This begins with the top-down approach in our Board of Directors, where two out of eight members are women. We still have to increase this proportion. The same applies to the management. We are also working on the working time models - here too, great efforts are being made.

### Is there no chance at all that a part-time working time model will be implemented at any time, for example in the case of a cardiac or vascular surgeon?

Medical staff is indeed an area where it is difficult, but this too will have to be possible. The proportion of women in medical training is high. If we want to fill vacancies in the future, we need more women. We need appropriate working time models, we need to expand childcare facilities... a whole range of measures will be needed.

«Digitalisation will be a core issue. As one of the leading hospitals in the world, the Inselspital has now defined this as a vision.»

And now there is still a new generation at the very beginning, among the students. The education of the students is actually our core task. From your position as board member, what is your message to the students?

My message is that we are an exciting place to work. Working in our hospital is a highly meaningful task. And: We are a future-oriented industry - it is worthwhile to enter medical studies! With the "+100" project, we have increased the number of places in medical education by 100 students per academic year and have once again expanded pharmacy studies to full-time studies. This was an important concern for me at the time as Director of Education.

# If we go one step further now, is that the same message for assistant physicians and senior physicians?

For me it is the same message. It is not an ordinary job. It is a challenging job. Certainly, nobody becomes a doctor because they think they can have an easy job. I myself have great respect for this job because it involves dealing with people in difficult situations every day and demands an incredible amount of responsibility and flexibility.

# This is probably why the willingness to perform is so high.

Yes, that is enormous and at the same time certainly also a problem. When I ask the doctors how they can be on duty for so long on weekends, I hear that it is simply a calling for them as well. And when the work is finished, it often becomes even more interesting for them: now the patient is in the room, now they want to see how he is doing - and they don't want to go home yet. I still don't have an answer today as to how doctors can better manage their working hours.

### That is a very difficult question.

Maybe in a few years I'll have an answer... (laughs)

We have already addressed the topic of the medical location two or three times. The Center for Precision Medicine started at the beginning of 2019, and the next major topic will be digitalisation. How do you see the cooperation between the University and the Inselspital in this area? Politics, business, the population, the Inselspital, the University and Bern want to strengthen this medical

location. The Canton has stated in its 2030 commitment that it wants to be the number one medical location. The Insel Gruppe's vision states: "We want to be one of the world's leading hospital groups". [...]

At the moment we are in the process of building a leading medical location. With the +100 students we have expanded the Medical Faculty. With the sitem-insel, a translational research center has been created at the same time as the new Center for Precision Medicine. The ARTORG already exists and we have the Insel Data Science Center. A Center for Design and Health is coming, which will explore the potential of design in the broadest sense for medicine. Or the topic of artificial intelligence - our position in research into artificial intelligence in medicine in Switzerland is good, probably even leading the way in Switzerland.

My vision for 2050 is that the campus will continue to expand beyond today's perimeter, occupy more space, we will have even more start-up companies, and that even more research will take place. Digitalisation will be a core issue. As one of the leading hospitals worldwide, the Insel Gruppe has now defined this as a vision. Threads are being woven and ideas developed. We have a base where we are already excellent, and this is where we are building and want to improve.

# This is also noticeable outside of medicine. It is incredibly great what was unanimously approved at the session in the Grand Council regarding the medical site<sup>1</sup>.

As a former member of the government, I can say here that there have been few things that were approved so unanimously. Now I hope that we can still do a lot with it.

The area of digitalisation will be our next big topic. Within the next years, we plan to implement it in a structural form. From the University's point of view, of course, the question remains open as to how firmly this should be integrated into the services of the Insel or how tightly it could be cross-linked.

We are in the fortunate situation that we, as a University Hospital, have excellent cooperation with the Medical Faculty and the University. In artificial intelligence, knowledge is gained from an enormous amount of data. Here we can make progress by promoting research in the whole field of medicine,

digitalisation and artificial intelligence. Here we as a medical campus - together with the canton - should also give financial support to start-ups. These will bring in innovation from the background of the companies. We are currently at the very beginning of discussions, in the preliminary phase with the question of financing. The University has the know-how about the interesting projects and should be involved in the selection of the start-ups.

# You have said several times that the Inselspital is one of the leading hospitals and the largest medical location in Switzerland. We have achieved something in terms of power - is it also the best? Where are we already world class?

I think we are way ahead in terms of knowledge and innovation, especially in terms of recently acquired developments. Take the Theodor Kocher Prize 2018, which Mrs. Kathleen Seidel received with her "radar system" for brain tumor surgery. This technique is now used in 40 countries! This is a great example, and I could go on and on.

### If I may quote your statement on Dies Academicus: "The potential for shaping policy is often underestimated." In your new role as Chairman of the Board of Directors, what do you want from politics?

Politics can initiate economic and social developments. The Internet, for example, didn't just come into being, but massive government research and funding was used, for example by the military in America. My expectations of politicians are to trigger further developments with the aim of becoming the number one medical location.

Let me give you an example from another area: if Switzerland were to decide that no new cars with combustion engines would be registered after 2030, this would trigger something: Research, development and it will be good for the economy. The same applies to the medical location. This unanimous vote from the Grand Council sends signals to the economy.

# May I finally ask you 1-2 personal questions? Do you possibly have an anecdote from your activity as Chairman of the Board of Directors?

I have experienced many exciting moments. In Pneumology, for example, I was able to insert an endoscope into a doll and was shown how to get a candy out of the lungs in this way. Fortunately, it was a doll and not a human being!

An impressive moment for me was when a professor showed me his clinic - it was Prof. Gralla from Neuroradiology - and it started to flash on the screen during the visit as an indication that an emergency is coming in. He explained to me that a person with a stroke would arrive in 12 to 15 minutes and he would treat it. When I asked him if he had to

leave immediately, he replied that we could finish the conversation. He then continued talking to me for the next 7 or 8 minutes in peace. Afterwards he went quietly to his mission. At such moments - there were several such moments during my visits - I am always speechless.

But also the visit to the finishing of the patient menus in the central kitchen was very impressive for me

### Your job is challenging and probably also very time consuming. There is certainly also a balance that you sometimes seek.

The nice thing is that I don't have to make so many operational decisions and therefore have a balance in time that is right for me. In my life, I have seldom had such a good time, purely from a professional point of view, as I have now here with such an exciting task and at the same time the time autonomy that I have. Professionally, I am very happy at the moment. Nevertheless, I need a balance, and for me this is in the form of going fo a walk in the fresh air, at the Aare river, simply out and about, and in contrast to that at home, reading a book.

# Thank you very much for the great interview, I am looking forward to the exciting future developments!

The interview was conducted by Dr. Lukas Stalder, head of the Dean's Office



<sup>&</sup>lt;sup>1</sup> Editor's note: This statement refers to the project planning credit for the new research building, which was approved by the Grand Council.

### New Professors at the Medical Faculty

Raphael Sznitman joined the ARTORG Center in 2014 as head of the Ophthalmic Technology Laboratory research group. Previously, he was a postdoctoral fellow at the Computer Vision Laboratory of the École Polytechnique Fédérale in Lausanne. He holds a Bachelor's degree in Cognitive Science from the University of British Columbia (Canada) and a PhD in Computer Science from Johns Hopkins University (USA). As part of his research, Sznitman will establish the Artificial Intelligence in Medical Imaging group at ARTORG to develop applications in biomedical imaging, diagnostics, intervention, surgery and therapeutic decision making. Sznitman has successfully developed clinical applications in ophthalmology through artificial intelligence and machine learning, some of which are already in use at the Inselspital Eye Clinic.



Sznitman Raphael

Since 1 July 2019: Full Professor for Biomedical Engineering and new Director of the ARTORG Center for Biomedical Engineering Research

Vivianne Chappuis grew up in Winterberg in the canton of Zurich. She completed her studies in dentistry at the University of Zurich in 1997 and subsequently worked in private practice for 4 years. In 2004, she completed her specialization as a dental specialist for oral surgery. During her two-year research stay from 2009-2011 at the Harvard School of Dental Medicine in Boston (USA) she investigated the molecular basis of bone regeneration. The project was supported by the renowned Musculoskeletal Transplant Foundation (USA). She received a Certificate of Advanced Studies in Entrepreneurship in 2014 and a degree in Business Administration in 2017. In 2018 and 2019 she was awarded the André Schroeder Research Prize in Clinical and Preclinical Research. As an oral surgeon, she is involved in teaching and research, education and training at national and international courses and congresses with live operations, workshops and lectures.

Her research focuses on translational research in the field of soft tissue and bone regeneration. It combines clinical and experimental research methods with modern digital 3D imaging with the aim of optimizing treatment concepts for patients. As a service institute and competence center, its clinic is the point of contact for dentists, physicians and patients with oral surgical, stomatological and radiological problems in the oral cavity.

**Vivianne Chappuis** 

Since 1 August 2019: Full Professor at the Clinic for Oral Surgery and Stomatology

Andrew Chan grew up in Hamburg and completed his studies in human medicine at the University of Hamburg in 1995. After his doctorate at the Institute of Clinical Chemistry of the University of Hamburg and his training as a specialist in neurology at the University of Würzburg, he habilitated in 2006 at the University of Göttingen on microglial immunobiology. Until 2016 he worked as senior physician and associate professor at the Ruhr-University Bochum, until 2016 he started his work in Bern.

Andrew Chan's research focuses on neuroimmunological diseases, including multiple sclerosis. The research group focuses on mechanisms and markers for the optimization of immune therapies using different translational approaches.



**Andrew Chan** 

Since 1 February 2019: Professor for Outpatient Neurology

The Executive Board of the University has elected Lukas Hunziker as Associate Professor of Heart Failure with effect from 1 November 2019. He succeeded Paul Mohacsi. At the same time, he is the Chief Physician and Head of the Centre for Heart Failure at the University Cardiology Clinic of the Inselspital.

Lukas Hunziker (49) grew up in the Netherlands, Germany and Switzerland and graduated in human medicine from the University of Basel in 1995. After completing his doctorate, Lukas Hunziker completed the postgraduate course for basic immunological research at the Institute for Experimental Immunology at the University of Zurich. After a stay abroad at University College London, he habilitated at the University of Basel in 2006 in the field of internal medicine/immunology. In addition to his training as an FMH specialist in internal medicine, pneumology and intensive care medicine, he began training in invasive cardiology in Essen and at the University Clinic for Cardiology in Bern in 2013 and received a cardiology specialist in 2015. In 2016, he received his postdoctoral lecturing qualification in cardiology at the University of Bern. Since 2016 he has been a senior physician and since 2017 head of the Center for Heart Failure at the University Clinic for Cardiology of

Lukas Hunziker's research focuses on mechanical circulatory support and device based therapy/intervention of heart failure.



Lukas Hunziker

Since 1 November 2019: Professor for Heart Failure and Head of the Department for Heart Failure at the University Hospital of Cardiology

Prof. Campus graduated from dentistry a long time ago in Italy and spent some time in Jonkoping (Sweden). Under the supervision of Prof. Goran Koch he began to work in the field of preventive medicine and oral epidemiology which was also the focused topic of his doctorate. Since 1996 he worked at the University of Sassari as Assistant Professor and then as Associate Professor of Public Health Medicine, Preventive Cariology and Paediatric Dentistry.

Prof. Campus is coordinator of the Italian WHO Collaborating Centre for Epidemiology and Community Medicine. For the WHO Collaborating Centre, his role is to develop and coordinate actions to assess the oral health of the public in Italy and other countries such as Mexico and Burkina Faso. He is also working to develop strategies and recommend measures to promote healthy behaviour from childhood onwards, including reduced sugar consumption, stricter tobacco controls and affordable fluoride toothpaste.

The plans of Prof. Campus are to evaluate and develop new strategies to collect epidemiological data and then generate reliable data for prevention measures. His opinion is that prevention will be the key to future dentistry.



**Guglielmo Campus** 

Since 1 February 2019: Professor in Preventive Dentistry and Oral Epidemiology (Endowed Chair of Preventive Dentistry and Oral Epidemiology of the Lutz Zürrer Foundation)



Lorenz Räber grew up in Gelfingen, Canton Lucerne, and graduated from the University of Bern in 2004 with a doctorate in human medicine. After completing his training in internal medicine and cardiology, Lorenz Räber received a three-year scholarship from the Swiss National Science Foundation as part of the special program in University Medicine. From 2011 to 2012 he stayed at the Erasmus University Rotterdam and obtained a PhD in the field of intracoronary imaging. His habilitation followed in 2014 and his associate professorship in 2016. Clinically, he completed his training in interventional cardiology in 2013. In the same year, he took over the position of senior physician and from August 2015 the position of senior physician with head of the Department of Coronary Heart Disease at the Inselspital. Lorenz Räber's research focuses on the development, diagnosis and treatment of coronary heart disease, in particular with the aid of new methods such as optical coherence tomography or infrared spectroscopy. He is the author of over 180 publications and numerous book chapters as well as editor of the European Heart Journal.

Since 1 February 2019: Professor of Coronary Heart Diseases



# Teaching

School of Human Medicine
School of Dental Medicine
Local Student Committee of Bernese Medical Students
Start of studies 2019: "Firsties" are coming!
Teacher of the Year 2018: Stefan Kuchen
New Auditorium Alhambra
New Medicine Library
Bachelor and Master Program in Pharmacy
Master Program in Biomedical Sciences
Master of Science in Biomedical Engineering



Clinical skills training in the Renferhaus of the former Zieglerspital

### School of Human Medicine

Physicians and medical doctors have been trained at the Medical Faculty in Bern for more than 200 years. The Bern Faculty is currently the second largest institution for the education of medical professionals in Switzerland.

### **Profile**

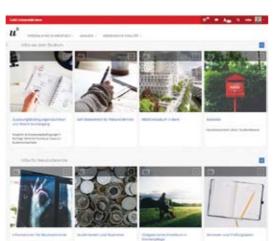
- Training of physicians and medical doctors for more than 200 years
- 2<sup>nd</sup> largest institution of Switzerland for the education of medical professionals
- Comprehensive and balanced training concept
- High practical relevance and patient-orientated training
- Increasing the number of study places by 100 for the second time
- Bachelor program based on the educational approach of problem-based learning
- Master program offers subject-specific and practice-oriented study model with a high emphasis on bedside teaching in hospitals and in general practices
- Comprehensive training at the Inselspital in more than 50 disciplines
- Learning objectives according to PROFILES, which forms the basis of the Federal examinations

### Start of studies in the new UniAlhambra

On 16 September 397 medical students, whereof 320 new and 28 repeaters in human medicine and 35 new and 14 repeaters in dental medicine started the first year of studies in the former cinema Alhambra, which has been transformed into UniAlhambra.

### New information system platforms for teaching

In summer 2019, the "Studmed" site of the Medical Faculty retired after 20 years of use. The student office had to learn how to program a new IT system called Kernsystem Lehre (KSL). Students and teachers had to switch to the ILIAS application. The data migration and the use of the two platforms meant a lot of work, but the start was almost trouble-free.



ILIAS - the new teaching website

### Clinical Skills Training (CST) in UniZiegler

The concept of Clinical Skills Training was completely revised. Many course modules now take place in the Renferhaus of the former Zieglerspital. The building has been renovated and there are now 4 seminar rooms, a simulator room, 41 examination rooms and a learning centre available. The OSCE examinations are also held in UniZiegler.

### **Bachelors of Medicine**

Study places 2019 320
Starters bachelor program 2016 217
Ending with bachelor degree 2019 213
including 20 repeaters from 2015 or earlier
Drop out 2016-2019 1,8%

### **Master of Medicine**

Study places 2019 260
Starters master program 2016 229
Ending with master degree 2019 229
Drop out in the master program 0%

### Federal exam Human Medicine 2019

Multiple choice exam:

230 candiates

230 passed

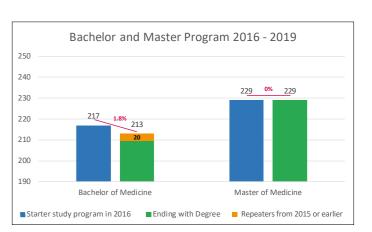
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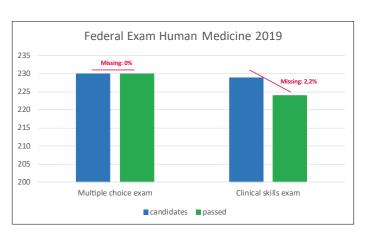
Clinical skills exam:

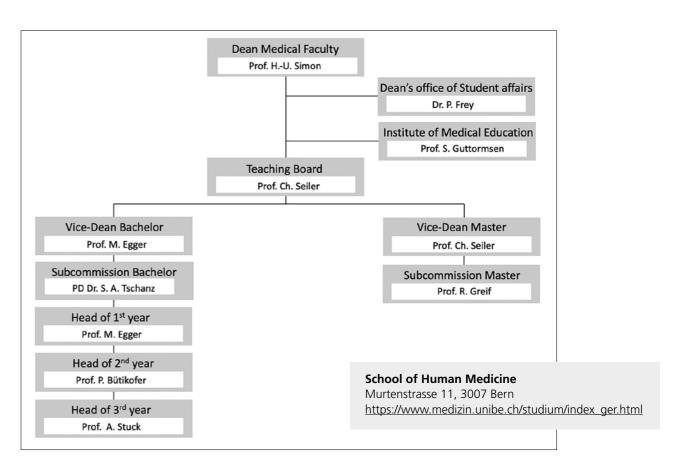
229 candidates

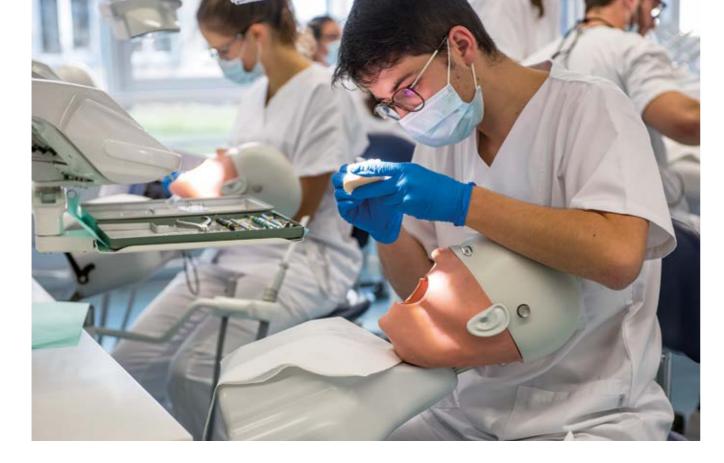
224 passed

2.2% missing









### School of Dental Medicine

The 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. The Bachelor and the Master programs in Dental Medicine at the University of Bern were accredited in December 2018 by the Rectors' Conference of the Swiss Universities based on the recommendation of the Swiss Center of Accreditation and Quality Assurance in Higher Education.

After completing the master program, candidates are tested on their ability to correctly and independently perform interdisciplinary treatment on patients as well as on their theoretical and analytical competence. Furthermore, they have to present a Master thesis that can consist of either

- 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 that is conducted simultaneously nationwide. The qualifications required by the national syllabus ensure a national standard of high quality.

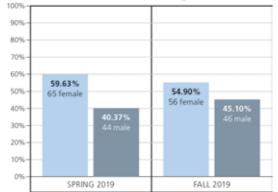
After the Master degree is awarded and the Swiss National Examination in dental medicine has been passed, the young dentists are qualified to treat patients independently in private practice.

### Master exams passed

In 2019 all 36 candidates successfully passed the Master exam as well as the Swiss National Examination in dental medicine.

The numbers of students and the male/female ratios are listed in the table below.

### Number of students 2019 (year 3-5)



### Optimizations according to accreditation requirements

In 2018, the Accreditation Council issued the accreditation of the University of Bern's Dentistry program with two conditions. In the accreditation report it was stated: "The zmk Bern must convert elective internships of the course into compulsory courses in such a way that all students are taught knowledge in complementary medicine, so that they are able to provide

appropriate information about the risks and limits of complementary medicine methods in the expected patient discussions". Fortunately, it was possible to implement this first edition from the autumn semester 2019 onwards. In the timetable of the 4<sup>th</sup> academic year a double lesson "complementary medicine" was introduced for the first time. This double lesson was successfully conducted by Prof. Dr. Ursula Wolf, Director of the IKIM (Institute for Complementary and Integrative Medicine).

The digitalisation of planning and treatment, which has been discussed for some time, was actively tackled. In the 3<sup>rd</sup> and 4<sup>th</sup> year of study, a joint module "digital impression" with theoretical and practical instruction was introduced by the clinics for tooth preservation and reconstructive dentistry and gerodontology. In the 5<sup>th</sup> academic year, the cross-clinic lecture series "Digital Reconstructive Technologies + Implant Dentistry" was established. In order to apply the newly acquired theoretical knowledge in the practical courses, an intraoral scanner, the corresponding

grinding unit and the sintering furnace was purchased for the synopsis course. The second edition consisted of introducing a digital medical history in the student clinic. The deadline for fulfilling this requirement is the end of 2020. The tender documents for the new hospital information system (HIS) were prepared in 2019. The requirements for the new HIS were recorded in all clinics and student courses and were prepared in the specifications and requirements catalogue.

# **Bachelor Information Days at the University**

Every year at the beginning of December, high school students in search of the ideal course of study have the opportunity to get to know various courses of study at the University of Bern within the framework of the "Bachelor Information Days". On the occasion of these "taster days" the zmk bern also puts together a comprehensive program. In addition to general explanations about the study of dentistry and presentations from the various clinics, interested parties can get involved themselves by means of a learning circuit.

A student is practicing the filling



### **School of Dental Medicine**

Freiburgstrasse 7, 3010 Bern www.zmk.unibe.ch, www.facebook.com/zmkbern



Board of the Local Student Committee in Autumn 2019

### Local Student Committee of Bernese Medical Students

# The fsmb (Fachschaft Medizin der Universität Bern)

- is created by students for students
- provides a link between the students and the faculty
- contributes to the optimization of studies
- has annual spokespersons in all study years, who are contact persons for the students and represent the academic year in the board of the student committee - mail: sj1@fsmb.ch, sj2@fsmb.ch
- acts as a mouthpiece for the interests of medical students in Bern: After a common reflection of a concern in the focus group with the annual spokesperson, an official feedback with proposals for solutions is submitted to the corresponding committee with the concern for open dialogue and cooperation
- represents the interests of medical students in Bern in educational matters in various commissions (representation and right of codetermination)
- offers several assistance services for the study and events besides the study: Clinical language courses for French and Spanish, ski and sports weekends, stethoscope sales, the "Medifest", book exchange, a welcome aperitif for master students from Fribourg, fondue dinner, etc. (see homepage)
- 's board is elected at the annual general meeting, interested students are welcome!



www.fsmb.ch

### Focus on psychiatry: Swiss Medical Students' Convention (SMSC) March 2019 in Bern

When suddenly 400 students with sleeping bags and sleeping mats under their arms, talking wildly in French, German, Italian and Rhaeto-Romanic, streamed from Bern's main railway station towards the VonRoll area, very few would have suspected this to be the future generation of Swiss doctors. Medical students from all over Switzerland came to Bern from 29 – 31 March 2019 to participate in the Swiss Medical Students' Convention. This national congress takes place once a semester in rotation at the various medical faculties in Switzerland. This year's organizing committee, consisting of around 20 committed medical students from Berne, had chosen psychiatry as its topic. Mr Graf's lecture entitled "the therapy of the pedophile x" was particularly memorable. In one hour the speaker succeeded in describing the "personal microcosm" as a flock of birds and questioned the "free will". In case studies, he showed us how this microcosm can lead to behaviour that is generally described as repulsive. As a psychiatrist, however, it is important not to look at patients' behaviour through the distorting mirror of one's own perception and history and thus directly categorize patients' behaviour. Rather, the goal should be for the patients themselves to realize where and how their thoughts and behavior patterns have led to criminal acts. At two further lectures and numerous workshops, for example on the topic "Children from families with a mentally ill parent", the participants of the SMSC received a lot of input on the topic of psychiatry during three days. On behalf of the entire organizing committee, we would

like to thank the speakers, the home service of the VonRoll and Muesmatt area, the Dean's Office and the numerous sponsors for their support. All this would not have been possible without the commitment of many people, whose mention would unfortunately go beyond this framework.

### National mental health campaign

In connection with the topic of the SMSC in Bern, swimsa together with the VSS (Verband Studierendenschaften Schweiz) has launched a national campaign on the mental health of students in Switzerland. In the spring of 2020, swimsa will conduct a national survey of all Swiss students, which will serve as an assessment of the current situation in order to introduce and promote evidence-based preventive measures to promote mental health at Swiss universities

In connection with this campaign, fsmb is organizing the mental health december in December 2019. Before the intensive learning and examination phase, we want to give students the opportunity to deal with the topic of mental health. On the one hand with lectures on efficient learning techniques and mental health, but also with social events such as joint yoga exercises, games evenings in the Wokermensa and movie nights in the former cinema Alhambra, which is now the Auditorium for Medical students of the first two years.



### Medical Students international

As a founding member of IFMSA (International Federation of Medical Students' Associations) in 1951, swimsa (Swiss Medical Students' Association) regularly takes part in the international meetings of medical students. These include the General Assemblies (GAs), which take place twice a year in March and August, and the European Regional Meeting (EuRegMe), which is held once a year in April. The Executive Board of swimsa assembles a committee of motivated students for each conference, with representatives from all Swiss faculties.

### EuRegMe April 2019 in St. Petersburg

Three Bernese medical students were selected for the EuRegMe in St. Petersburg from 20-24 April 2019: Gwen, Esma and Sebastian. During the congress, there were a variety of training opportunities, project presentations and workshops, where we were able to further educate ourselves together with the other international participants from all kinds of European countries. Through networking and the exchange of ideas, the new generation of doctors was inspired and our leadership and advocacy skills were developed. Gwen took part in a leadership training session that provided her with tools to explore her leadership style in a whole new way. On the Standing Committee for Human Rights and Peace, Sebastian learned about a Danish project to promote the health of refugees. We do not yet have any comparable projects in Switzerland. Esma visited the Standing Committee on Research Exchange and emphasized the opportunity of IFMSA meetings to inspire students: "IFMSA is an incredibly large community and every active person in it is committed to improving the lives of medical students. It's important to be aware of the purpose and importance of the work you do". The complete swimsa report on IFMSA EuRegMe 2019 Russia as well as an article on an alternative approach to travel (instead of using an airplane) "Hitchhiking to Russia" can be found at www.fsmb.ch.

### March Meeting 2019 in Portorož

One month before the EuRegMe the March Meeting of IFMSA took place in Slovenia. Four medical students from Bern were allowed to attend: Felice, Noemi, Alexander and Daniel. About 1'000 medical students from all over the world came together in Slovenia. The delegation from Berne reported on the special feeling when borders are overcome and thus a cooperation at eye level and international cooperation becomes possible. In the Standing Committee for Public Health, they learned about antibiotic resistance, diabetes and malaria and the associated problems in different countries and continents.

Sebastian Albermann

President of the Local Student Committee of Bernese medical students









### Start of studies 2019: "Firsties" are coming!

Since 16 September there have been new faces among the medical students in Bern - 355 firsties, or first year's students, to be exact. Here are a few insights into the life of the freshly baked students.

### Why exactly did you come to Bern?

Yuk Yi: Actually Bern was not my first choice. In the beginning I was a bit negative, but now I think it's pretty cool. The location is great because the Alhambra University is right next to the train station, and the city is very beautiful. I think it's great that we have a lot of lecture-free time, so you can organize everything yourself, but you also need a lot of self-discipline. That's what I'm still learning (laughs).

# What was the first thing that crossed your mind when you first stepped into the dissecting room?

Maria: I was really happy! Everything was still covered and they made a huge secret of it until the preparations were uncovered. Then for the first time we really had something medical, before we only had chemistry, physics and biology. In the anatomy internship we really noticed: Okay, we're studying medicine. Elia: Shit, it's cold in here!

Seraina: I was really surprised that we now have effective human preparations there. I hadn't thought about that at all.

Yuk Yi: I was very much looking forward to it and had already talked to others about it. That's why it wasn't bad for me at all.

# Is there something that's bothering you about med school?

Aurèle: So far it's a lot of repetition and very dry, I'm not used to that from studying biology before. But as soon as it goes into medicine, I find it very interesting. Yuk Yi: The few WCs in the Alhambra! One spends the whole break waiting in front of the toilet and misses the beginning of the lecture because of that. Maria: For commuters it is not easy that there are a lot of train delays and cancellations. And if you are late, you have to sit on the floor. And sometimes it's quite cold in the lecture hall.

# Which course has been the most exciting so far and why?

Elia: The anatomy course because it was the most exciting from a medical point of view. In addition, it best combined the theory learned so far with practice.

### Do you find the concept with a lot of self-study and few lectures combined with learning groups and internships useful?

Benjamin: I think that solving tasks in learning groups is a good approach. So far, however, I have always had the impression that the lectures and learning groups are not coordinated with each other. One solved tasks in the learning groups and only weeks later a lecture was added, or vice versa. In biology and veterinary medicine last year, the tasks were effectively coordinated with the lectures, which is not the case here. The interviews have been conducted by Florin Kalberer (1st year's student).







Dr. Stefan Kuchen: "I will probably learn more than you."

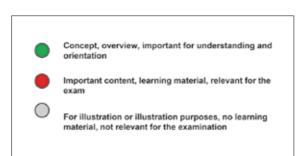
### Teacher of the Year 2018: Stefan Kuchen

Dr. Stefan Kuchen was selected as Teacher of the Year 2018 and honored at the graduation ceremony in March 2019.

With the words of the German psychologist Wolfgang Prinz: "We know a lot but understand little" the first immunology lecture began in the 3<sup>rd</sup> year of human medicine. The first part is probably especially true in the time before the exams, the second part is also true, but it also claims its validity in the time before and after the exams - so actually during the whole semester. In order to counteract this, we were introduced to the traffic light system. Slides marked green contain the concept and are important for understanding and orientation. Red dots mark slides with important and exam-relevant content. And grey slides are for illustration purposes and do not contain any learning material.

When I asked him what the teaching meant to him, Mr. Kuchen replied that there was the psychological aspect for him that it was nice to teach interested students. He was also aware that not everyone would have the same enthusiasm for his subject, but that it would be all the nicer if he felt the students' interest. On the other hand, it has a content aspect that can be particularly well understood when one has attended the Immunology in-depth seminar with Mr. Kuchen. There, one is encouraged to do something that one would otherwise rather avoid, namely to express answers or ideas that are certainly wrong. However, the Teacher of the Year 2018 does not only wish to expose himself to his ignorance from us students, but also likes to go into this position himself through these interactive courses - completely according to the motto "one only notices whether one has understood something completely when one explains it". And adds with a smile "I will probably learn more than you".

Mr. Kuchen sees the speed of medical development as a great challenge for the future. Both therapy and diagnostics are subject to rapid progress. Medical findings and knowledge are constantly increasing in quantity and complexity. But what always remains in this change is the patient with his needs, today as well as in the past. These have not changed and in order to do justice to them as new doctors, it is important never to lose sight of this. And in the flood of facts, mechanisms and principles to go back to the banal, to structure oneself as well as possible and not to lose orientation. Namely to want to understand and not only to know. This corrected version of the initial quotation is also based on the lectures of the Teacher of the Year. Because, among other things, the traffic light system gave Mr. Kuchen's lecture the structure that is so important to convey the content in such a way that it creates a solid basis that enables us to openly confront the dynamics of medical development. The interview was conducted by Recha Suter (4th year student), former secretary of the Local Student Committee of Bernese medical students.





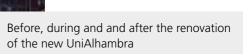
### New Auditorium Alhambra

The medical lectures promise a new big cinema in the UniAlhambra. Blockbusters and popcorn are history, new highlights are lectures on molecular genetics, history of brain research and many more.

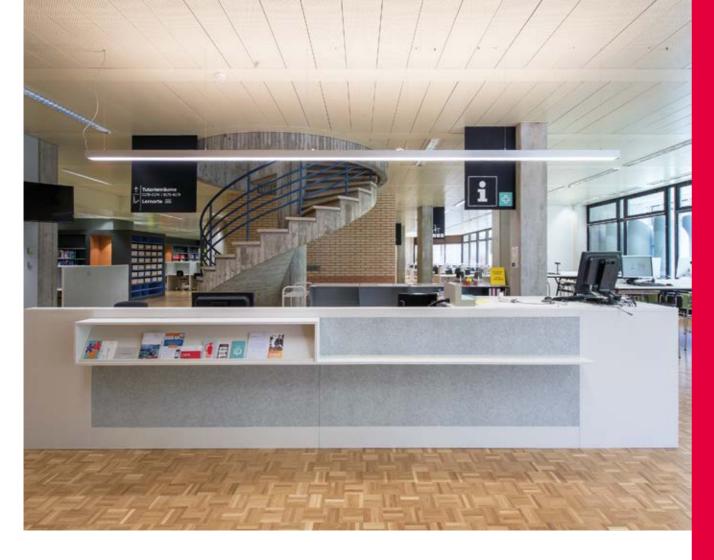
The spatial infrastructure of the University of Berne is facing major challenges as a result of the strengthening of Bern as a medical location and the associated increase in the number of students in human medicine as part of the +100 project. The former Alhambra cinema in Bern was rented and converted into the UniAlhambra in order to accommodate all medical students of the same year in the lectures. The schedule for the implementation of the measures was "sporty" the conversion time was just under 3 months.

In the short time it was possible to preserve the character of the former cinema through targeted structural interventions and still create the transformation to a modern classroom. The "UniAlhambra", the new auditorium of the Medical Faculty, has 364 seats and has been in full operation since autumn semester 2019.









## **New Medicine Library**

The department library Bühlplatz (FBB) has become a pure medicine library.

By early concentration of the natural science subjects in the library Muesmatt as well as the development of the roll rack arrangement, place for the Medical Faculty and their student increase (project +100) was created in the library at the Baltzerstrasse.

Thanks to the few but targeted measures, the medicine library is now shining in a new light and has been available to students, staff and visitors since the beginning of the 2019 autumn semester as a meeting place and place of learning.

Even among medical students, there is no "THE perfect learning workplace", which is why the creation of a diversified range of learning locations was the focus. Thus, in the course of the project, the various learning landscapes were developed together with the students, which can finally be found in the new library of medicine. In addition, the redesign of the back wall and the clear zoning provided an appropriate and dignified setting for the open-book collection, in which it is a pleasure to browse through the bookshelves.

By cleverly zoning the quiet learning workplaces on the ground floor and the group niches and tutorial rooms on the 1st floor, quiet and somewhat noisier uses could be separated from each other and the flows of people could be unbundled by separate entrances.



The Bachelor and Master Program in Pharmacy combines natural and biomedical sciences with clinical and patient-oriented training

### Bachelor and Master Program in Pharmacy

### **Profile**

- Upon completion of the Master of Science in Pharmacy, the Federal Exam in Pharmacy has to be passed to have the right to work as a pharmacist
- In close collaboration with institutes of the Medical Faculty (most prominently the BIHAM), clinics of the Inselspital, and practising pharmacists we aim at developing a high-quality, patient-oriented education of our future generations of pharmacists.

# Start of the new 3<sup>rd</sup> year Bachelor in September 2019

In the first half of 2019, all vacant positions could be filled and lecturers recruited, and the detailed curriculum of the new 3<sup>rd</sup> year was finalized to complete the Bachelor program in Pharmaceutical Sciences at the Department of Chemistry and Biochemistry (DCB) at the Natural Sciences Faculty. The new full professors are Prof. Paola Luciani (DCB) for Pharmaceutical Technology, Prof. Francesca Paradisi (DCB) for Pharmaceutical Chemistry, and Prof. Jürg Gertsch (IBMM, Medical Faculty) for Pharmaceutical Biology. In September 2019, 31 students were enrolled in the new 3<sup>rd</sup> year.

# Detailed planning for the start of the new Master in 2020 is ongoing

We are on track to launch the Master course in Pharmacy in September 2020. The contents of the curriculum have been finalized, vacant positions for professors, lecturers and administrative support are advertised, the regulatory documents are under revision, and the budget 2020 has been approved.

### Two new professorships for the Master course

The University has created and will finance a unique and innovative Professorship in Primary Healthcare in Pharmacy and Medicine at the BIHAM. This professorship will be shared by a pharmacist and a physician who together will develop a teaching and research program in interprofessional collaboration in primary healthcare. The election process in ongoing. pharmaSuisse has agreed to provide initial funding for an Assistant Professorship in Clinical Pharmacy. The structure and election committee will commence the process in early 2020.



### **Bachelor and Master Program in Pharmacy**

### Bachelor Program of the Natural Sciences Faculty

### Bachelor year 1&2

Natural sciences (e.g. chemistry, physics, cell biology) and biomedical sciences (e.g. biochemistry, anatomy, physiology, microbiology, plant biology)

### Bachelor year 3

Pharmaceutical sciences (pharmaceutical technology, pharmaceutical chemistry, pharmaceutical biology, pharmacology, epidemiology, clinical chemistry, nutrition, biotechnology, quality management)

### of the Medical Faculty

Master Program

### Master year 1

Diseases and pharmacotherapy, health promotion and disease prevention, the Swiss health system, pharmacoeconomics, scientific methodology; Master thesis (6 months)

### Master year 2

Clinical pharmacy and pharmaceutical care, clinical skills, vaccination, business management, law, manufacturing of medicines in the public pharmacy; Practical training in a public pharmacy (30 weeks)

The new Brochure is now available at <a href="https://www.philnat.unibe.ch">www.philnat.unibe.ch</a>.



UNIVERSE

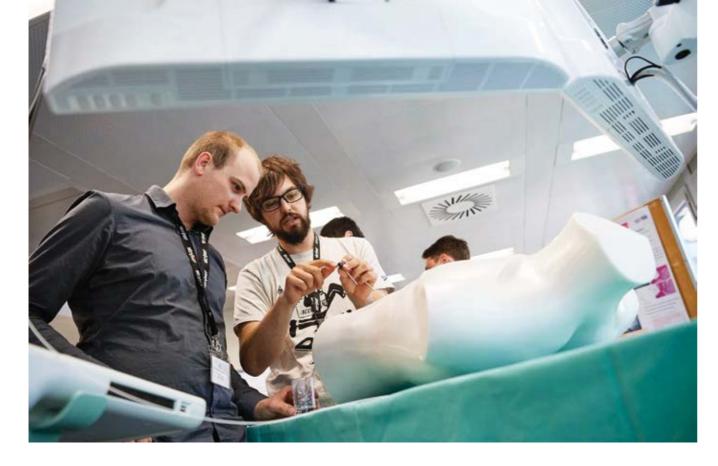
### Am richtigen Ort Pharmazie studieren in Bern





Prof. Verena Schröder, Director of Studies Master Program Pharmacy





### Master Program in Biomedical Sciences

Swiss Academic Institutions and Research Companies have been faced with considerable problems when recruiting young biomedical scientists for many years. Having the goal to ease this situation, educational opportunities in life sciences and biomedicine have multiplied in recent years.

Among these efforts, the Biomedical Science Studies of the Universities of Fribourg (Bachelor) and Bern (Consecutive Master) have played a pioneering role. Established in 2006, the harmonized curriculum of the two universities remains unique in Switzerland as it is focused on exposing the students to a translational teaching environment involving both basic and medical sciences. To achieve this goal, the first study year is dedicated to form a firm foundation in natural science while, in the second year, students share the curriculum of medical students thereby acquiring a comprehensive knowledge in human anatomy, physiology and biochemistry. During the third and the fourth year, students participate in a systematic introduction to the pathophysiology of all organ systems with lecturers being associated with basic research institutions, the university hospital and pharmaceutical companies. The Master Thesis is conducted in a laboratory of choice and includes collaborative projects with the industry. Based on the specific design of the curriculum, graduates in biomedical sciences have an exquisite and broad portfolio of both knowledge and skills at the interface between basic sciences and clinical research that endorses them to engage successfully in basic, translational and clinical research including emerging new research fields in human medicine like artificial intelligence and precision medicine.

### Profile

- Direct admission with a BSc in Biomedical Sciences of the University of Fribourg or a Bachelor in Human Medicine
- 1 1/2 year full time study program
- Human pathophysiology is lectured by basic researchers and clinicians
- Courses include practical work in research laboratories and training in modern experimental techniques
- 2 three-week laboratory internships in research fields chosen by the students
- Opportunities for conducting the master thesis in the industry
- Broad portfolio of systematic knowledge and skills at the interface between basic sciences and clinical research
- Graduates are in in high demand for doctoral positions in academia and for research positions in the industry

### **Figures**

- Diplomas since 2011: 178
- Presently enrolled students: 34
- Gender (f/m): 3/1
- 22 graduates in biomedical sciences in 2019



### **CSL Behring Prize 2019**

The CSL Behring Prize 2019 for the best Master degrees

went to:

1<sup>st</sup> rank: Imboden Vera \*5.82\* 2<sup>nd</sup> rank: Milusev Anastasia \*5.70\* 3<sup>rd</sup> rank: Flint Emilio \*5.62\*



### **ABS Animal Science and Ethics Day**

One-day event with talks, keynote lecture and workshops on animal science and ethics that drew 70 participants from the Universities of Bern, Zurich, Lausanne, Geneva and Neuchatel.



### Alumni Prize 2019

The prize for the best Master Thesis 2019 sponsored by the Alumni Organization went to Akira Nomura for his study on "Deciphering the importance of caveolin-1 for cardiac electrophysiology".

### **Master Program in Biomedical Sciences**

Bühlplatz 5, 3012 Bern www.medizin.unibe.ch/studium/studienprogramme/master in biomedical sciences/index ger.html



The Master's program in Biomedical Engineering is being presented at the opening of the new sitem-insel building in August of last year.

### Master of Science in Biomedical Engineering

The master's program in biomedical engineering is a full-time study program offered in cooperation with the Bern University of Applied Sciences. It aims at training multidisciplinary engineers to deliver scientifically-founded, sustainable and cost-effective solutions for biomedical problems in academia, medical care and industry.

### **Profile**

- Admission with BSc (FH/HES/SUP/Uni/ETH)
- Internation program in English
- Affiliated to a leading medical faculty hospital (Inselspital)
- Two-year full-time program but compatible with 40% working time
- Oriented towards clinical applications
- Attractive, central location

### **Figures**

- 148 students enrolled in academic year 2019/20
- 59 regular and 10 exchange or guest students new in 2019
- 25% of 2019 new students female
- 28 biomedical engineers graduated in 2019
- with excellent career perspectives

### **Swiss Engineering Master Thesis Awards 2019**

Jan Stapelfeldt received the award for innovation for his thesis "Smartphone-Based Perimetry for Fast and Low-Cost Visual Field Acquisition". Michael Rebsamen, was winner of the award for basic science for his work "Fast and Accurate Human Brain Morphometry Estimation with Deep Learning". The awards were presented by Valentin Herbez from Swiss Engineering.

### The Biomedical Engineering Day

The Biomedical Engineering Day is our annual BME career day and networking event. About 350 participants followed a broad and balanced speakers' program, which included highlights such as a live surgery by Prof. Siebenrock and a science slam. In addition, all research groups from the ARTORG Center and the HuCE, Bern University of Applied Sciences, as well as Swiss MedTech companies and research institutes presented themselves at a large exhibition with 29 booths.

### RMS Award 2019

Michael Rebsamen received the RMS Award 2019 from Philippe Zysset, Program Director Master Biomedical Engineering. Each year, the Robert Mathys Stiftung (RMS), an independent service laboratory and research institute, offers it to the BME student with the highest average grade.

### sitem-insel Open Doors

This summer, the Master's program in Biomedical Engineering moved to sitem-insel, the Swiss institute for translational and entrepreneurial medicine, located next to the university hospital. Sitem Open Doors at the end of August gave us the opportunity to increase public awareness for our unique program.

### Retirement Professor Lutz Nolte

In January, Professor Lutze Nolte, the founding father of our master's program in biomedical engineering, retired after 25 years of distinguished service as a faculty member at the University of Bern. Many colleagues and friends from Switzerland and all over the world joined us for a symposium in honour of his extraordinary work.

### **Master Thesis Award 2019**

Jan Stapelfeldt, Michael Rebsaman and Valentin Herbez (from left to right)



**BME Day 2019**Live surgery by Prof. Siebenrock

### RMS Award 2019

Michael Rebsamen receives the award from Philippe Zysset



**Retirement Professor Lutz Nolte** Lutz Nolte, Christian Leumann,

Stefan Weber (from left to right)

Master of Science in Biomedical Engineering

Freiburgstrasse 3, 3010 Bern www.bme.master.unibe.ch



# **Promotion of young academics**

sitem-insel School for Translation and Entrepreneurship in Medicine CAS, DAS and MAS Degree Programs PhD Education Grants Commission for Equality



On the occasion of the sitem-insel open doors, guests were introduced to the concept of the translational process in a playful way with a ladder game

# sitem-insel School for Translation and Entrepreneurship in Medicine

sitem-insel School aims to promote researchers and train specialists in the fields of translational medicine and biomedical entrepreneurship. 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.

### **Profile**

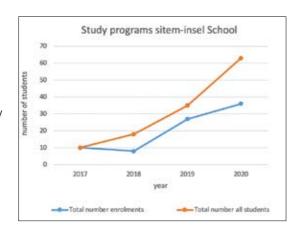
The sitem-insel school

- aims to teach students practice-oriented high-quality knowledge
- aims to facilitate a strong network between people involved in the translational process
- offers personalized continuing education using blended learning (presence lectures & e-learning).

### **Figures**

- Three continuing education programs:
- Translational Medicine and Biomedical Entrepreneurship (MAS/DAS/CAS)
- Artificial Intelligence in Medical Imaging (CAS, since Sept. 2019)
- Medical Device Regulatory Affairs and Quality Assurance (MAS/DAS in planning, starting September 2020)
- 35 students enrolled in the academic year 2019/20
- national and international students (Italy, Germany, Saudi- Arabia und USA) in 2019

- 7 start-ups and 6 companies in the incubator phase participate in the sitem-insel School continuing education
- The sitem-insel continuing educations offer excellent career perspectives



# Symposium "Artificial Intelligence in Medical Imaging"

The CAS "Artificial Intelligence in Medical Imaging" started with an international symposium at sitem-insel on 9 September 2019.

In this CAS, physicians are brought together with data scientists and specialists in AI to help shape digital technologies at the forefront. For more information see <a href="https://sitem-insel.ch/ai.">https://sitem-insel.ch/ai.</a>

### Symposium «Bringing Innovation to the Patient»

The new lecture hall at sitem-insel was crowded when people from industry, public offices and academia got together at the sitem-insel School Symposium «Bringing Innovation to the Patient». Keynote speaker Dr. Hans-Juergen Wildau, Biotronik, Berlin gave a fascinating talk on "Intelligent Digital Health".

### sitem-insel Open Doors

On the occasion of the sitem-insel open doors, guests were introduced to the concept of the translational process in a playful way. In a ladder game, the players virtually brought a product from the idea to the patient. At the various posts of the game, the players became familiar with the individual stages of the translational process and were able to learn more about its challenges and opportunities by drawing cards.

# Medical Device Regulatory Affairs and Quality Assurance (MAS / DAS)

The introduction of the new Medical Device (MDR) and In-vitro Diagnostic Medical Device (IVDR) regulations has created an enormous demand for further training in the Swiss medical technology industry. From September 2020, the sitem-insel School plans

to offer advanced studies to train specialists in "Regulatory Affairs". Graduates of the program will be able to carry out the approval of medical devices in cooperation with certification authorities ("Notified Bodies"). The course is currently in planning.

# Translational Medicine and Biomedical Entrepreneurship (MAS / DAS / CAS)

7 start-ups and 6 companies in the incubator phase are trained in the sitem-insel School personalized "Translational Medicine and Biomedical Entrepreneurship" continuing education, which includes topics such as R&D, quality management, regulatory affairs, clinical trials, biomedical entrepreneurship and others.

For more information see <a href="https://sitem-insel.ch/tmbe">https://sitem-insel.ch/tmbe</a>

### First national phageSuisse Symposium

phageSuisse has organized on 28.11.2019 its first symposium in collaboration with sitem-insel School and could welcome over 50 participants at the sitem-insel building. The need for novel and innovative phage treatments for resistant bacterial infections and the challenges in bringing them to the patients were discussed.





**sitem-insel School**Freiburgstrasse 3
www.sitem-insel.ch/school



### CAS, DAS and MAS Degree Programs

The Medical Faculty offers over 30 programs of advanced studies. All programs are held by teachers of the faculty who transmit practice-oriented and state of the art knowledge. They are addressed to professionals with a tertiary education.

### Existing advanced study programs

- Experimental and Translational Nephrology (CAS/DAS ETN Unibe)
- Hepatology (CAS/DAS HEP Unibe)
- Sleep, Consciousness and Related Disorders (CAS, DAS, MAS SCD Unibe USI)
- Clinical Nutrition (CAS)
- Spiritual Care (CAS SpC Unibe)
- Interprofessional Specialist Palliative Care (CAS PallCare Unibe)
- Swiss Exercise Therapy in Sports and Medicine (CAS/DAS SwissETSM Unibe)
- Swiss Cardiovascular and Diabetes Therapy (CAS SwissCDT Unibe)
- Exercise and sports therapy for mental illness (CAS PSY Unibe)
- Exercise and sports therapy in orthopedics, rheumatology and traumatology (CAS ORT Unibe)
- Public Health (CAS/DAS/MAS)
- Leadership in Health Care Organisations (CAS LHCO Unibe)
- Clinical Research in Health Care Organisations (CAS CRHCO Unibe)
- Managing Medicine in Health Care Organisations (CAS MMHCO Unibe)
- Translational Medicine and Biomedical Entrepreneurship (CAS/DAS/MAS Unibe)
- Master of Medical Education (MME Unibe)
- MAS in Leading Learning Health Care Organisations (MAS LLHCO Unibe)
- Master of Advanced Studies in Implant Dentistry (MAS IMPUnibe)
- Master of Advanced Studies in Orthodontics and Dentofacial Orthopedics (MAS ORTHO Unibe)
- Master of Advanced Studies in Cariology, Endodontology and Pediatric Dentistry (MAS REST Unibe)
- Master of Advanced Studies in Oral and Implant Surgery (MAS ORALSURG and IMPSURG Unibe)
- Master of Advanced Studies in Periodontology and Implant Dentistry (MAS PER and IMP Unibe)
- Master of Advanced Studies in Reconstructive and Implant Dentistry (MAS REC and IMP Unibe)

All study programs can be found on the wesbite:

www.medizin.unibe.ch/weiterbildung/cas das mas/index\_ger.html

### New advanced study programs

The main objectives of the Certificate of Advanced Studies (CAS) in Artificial Intelligence in Medical Imaging are to equip medical doctors (MDs) with the necessary skills to take a leading role in the Al-driven transformation of medicine. The course program was developed for medical professionals and provides them with the necessary knowledge and skills to translate medical problems into data science problems. By working on an Al project of their own, the participants will know and apply the fundamental concepts of Artificial Intelligence and can thus judge the feasibility and adequacy of proposed Al solutions.



CAS in Artificial Intelligence in Medical Imaging (CAS AIMI Unibe) for Outpatient Neurology



The CAS program in gender-specific medicine starts in May 2020 and is a part-time university continuing education program, jointly offered by the Universities of Bern and Zürich. It is aimed at people with a Master's degree in medicine or a related field who wish to deepen their knowledge of gender differences in medicine in order to shape their work according to the latest evidence. It teaches the concepts of so-called gender medicine and the effects of biologically and socio-culturally shaped gender on health and health care.

In the individual modules, the significance of gender in the various medical disciplines is shown. Tools, concepts and ideas are presented on how both health care and medical research can do justice to the sexes.

CAS in Sex and Gender Specific Medicine



### PhD Education

The Medical Faculty is associated with two graduate schools offering structured doctoral programs: the Graduate School for Cellular and Biomedical Sciences (GCB) and the Graduate School for Health Sciences (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 thesis projects for which the students get the best possible support from an expert supervisory committee in their specific research area. The emphasis is on high-quality training in research methods and study design. The PhD programs direct the candidates towards independent scientific work and enable them to assume scientific responsibility.

# Profile of the Graduate School of Cellular and Biomedical sciences GCB

The GCB offers 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.

There are two areas of specialization:

- Cutting-Edge Microscopy
- Stem Cell Research in Regenerative Medicine The requirement for the program is a master's degree in Molecular Life Sciences, Biomedicine, Medicine, Biomedical Engineering or a related field depending on the project.

There are five expert committees for the PhD program structure:

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

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

The curricula of the MD-PhD program for medical doctors focuses 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)

The MD-PhD-studies are supported by competing scholarships of the SNSF and SAMW.

# Profile of the Graduate School of Health Sciences GHS

The GHS offers a research-oriented curricula on psychological and physiological factors that determine the health of individuals and groups in their social contexts and physical environments.

The requirement for the program is a master's degree in Psychology, Medicine, Biomedicine, Epidemiology, Geography, Sport Science or other fields depending on the respective research project.

There are three expert committees for the PhD program structure:

- FKI: Preventive and Social Medicine, Public Health, Medical Education, Psychology, Rehabilitation and Patient-Related Studies
- FKII: Neurosciences
- FKIII: Clinical Sciences

Each candidate is supported by a thesis committee consisting of thesis advisor, co-referee and a member of an expert committee as mentor (only in FKIII). Awarded PhD title is:

- PhD in Health Sciences (specialist area) Curricula for medical doctors
- PhD in Clinical Sciences; 50:50 model: Patientoriented research and clinical career.
- Graduates receive the title: PhD in Health Sciences (Clinical Specialty)

### Highlights, important events at GCB

There is a new promotion regulation effective from 1 February 2020 for ALL students.

The following are the new mentors at GCB:

- Prof. Selma Aybek
- PD Michaela Medova PhD
- PD Dr. Andreina Schoeberlein Stehli
- Prof. Hildegard Tanner

Best PhD degree: Annina Bauer, Vetsuisse Bern

### Highlights, important events at GHS

- New GHS brochure
- 50% students increase from 2018 to 2019
- The new FKIII, Clinical sciences raises significant interest thanks to the 50:50 model
- GHS Symposium in Gunten

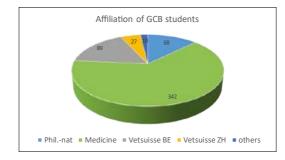
The following are the new expert committee members at GHS:

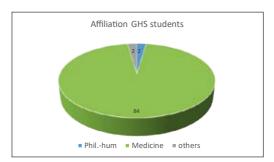
- Prof. Jennifer Inauen
- Prof. Stephanie Schmidt
- Dr. Cinzia del Giovane

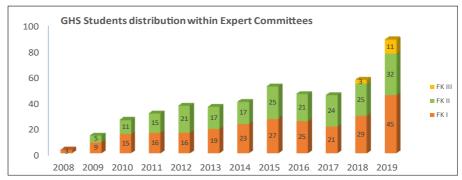
Starting 2019, the GCB & GHS have moved to the Mittelstrasse 43 and have new coordinators: Monica Schaller and Tullia Padovani have taken over the coordination from Marlene Wolf, who retired at the end of January 2019.



GCB: has a total of 511 students (excluding the 79 applications received on 15 December)







GHS has a total of 88 students (excluding the applications of 10 January 2020)

### **Graduate Schools GCB & GHS**

Mittelstrasse 43, 3012 Bern www.gcb.unibe.ch & www.ghs.unibe.ch

### **Grants**

### **Graduate School in Health Science (GHS)**

3 options: Health Sciences; Cognitive Neurosciences and Clinical Sciences

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

Duration: 3 – 5 years

Number of calls per 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 per year: continuously Funding source: Medical Faculty

### **CTU Grants**

Career stage: MD's before Habilitation

Duration: 1.5 year

Number of calls per year: 2x Funding source: University Hospital

### **Uni Bern Initiator Grant**

Career stage: postdocs and young PI

Number of calls per year: 2x 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 per year: 1x Funding source: Foundations

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

### **Travel Grants**

Career stage: during BSc or MSc

Duration: 1 – 6 years

Number of calls per year: continuously Funding source: Dean's office

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

### **Protected Research Time**

Career stage: Doctoral Students at the Graduate School for Health Sciences, Senior Physicians

Duration: 2 – 4 years

Number of calls per year: continuously Funding source: Dean's office

Additional information: open for doctoral students at the GHS or Senior Physicians with an academic degree, working at least 6 months at the Insel hospital, UPD or Service Institute of the University, >40 years old and not

habilitated

Women are explicitly encouraged to apply





Overcoming unconscious gender bias

### **Commission for Equality**

The Medical Faculty Commission for Equality (Innerfakultäre Kommission für die Gleichstellung, IFKG) supports the Medical Faculty in realizing measures ensuring effective equality of women and men. Together with the decision-makers of the institutes and clinics, the IFKG aims to improve conditions that facilitate the decision for women to pursue an academic career.

The immediate aim of the Commission for Equality is an increase of the number of women in leadership positions in the Medical Faculty. Among other measures, the IFKG aims to illustrate career options that improve working conditions such that they allow both women and men to combine their family live with their academic career pathway.

### **Profile**

- Mentoring 4 Women
- Ensuring implementation of equal opportunities in search committees and in the work environment of the Medical Faculty
- Contact point for all equal opportunity and diversity topics
- Contact point in case of discrimination
- External partners: Coordinator of the Office for Equality of the University of Zürich; Coordinator of the Office for Equality of the University Hospital of Basel

# Successful implementation of the Equal Opportunities Action Plan 2016-2019

All measures outlined in the Gender Equality Action Plan 2016 – 2019 for the Medical Faculty were successfully implemented. We would like to mention the following points in particular:

• Implementation of gender balance in cases discussed in problem based learning with medical

- students during their first years of education
- Initialization of quarterly strategic meetings between the University Bern, the Board of the Medical Faculty, the Board of the Inselspital Bern and the Medical Faculty Commission for Equality
- Equality checklist for search committees
- Implementation of consideration of unconscious biases as well as the DORA regulation in recruitment procedures
- Implementation of novel measures for the promotion of young talents
- further measures are taken to enhance the number of women pursuing an academic career

### Workshop in the «Haus der Universität»

The Medical Faculty Commission for Equality organized a workshop in June with female physicians pursuing an academic career at the Inselspital. The specific aim was to identify with this target group the obstacles prohibiting their academic career advancement. The following 3 focal points to improve attractiveness of an academic career for women in medicine were identified: Protected research time, networking and structural needs such as a flexible childcare, more jobsharing options for all employees.

### M4W – Mentoring for Women

We continuously work on improving our Mentoring for Women (M4W) program. We have introduced an initial interview with the applying mentee to optimize finding a suitable mentor. We have continuously increased the list of available mentors.

All mentees are regularly informed about interesting further trainings, speeches and equality related topics and events.

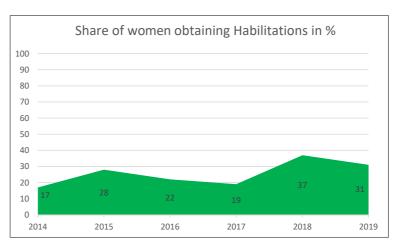
The mentees can furthermore benefit from a vast interfaculty cooperation and can attend interesting courses from mentee programs of the other faculties of the University of Bern. The M4W program is highly appreciated as underscored by select statements from our mentees:

- For me this is a very helpful program and provides a great opportunity to have an independent advisor.
   For the moment, I cannot provide any further ideas for improvement, as I am very happy with the program.
- This is exactly why programs like the M4W are important. This is about moral support and the role model function of the mentor.
- My experience continues to be extremely positive, I feel extremely supported and always very well advised. The conversations with my mentor are helpful, trendsetting and enriching for me on a human level.

### **Quarterly Conversations**

Every three months, the Vicerector Quality from the University of Bern, Members of the Board of the Faculty of Medicine and the Inselspital meet together with the President of the Medical Faculty Equality Committee to improve equal opportunities in the Medical Faculty and at the Inselspital.

Several important activities have already resulted from these meetings. Last June the workshop with female physicians pursuing an academic career at the Inselspital took place. The possibility of setting up a day nursery at the Inselspital has been identified and is now being examined. The idea of creating a networking platform for female physicians pursuing an academic career at the Inselspital is also followed up.



We are pleased about the positive development in the proportion of women in academic careers

### Gleichstellungsplan Medizinische Fakultät 2016-2018 /19

Nº	Handlungs- feld	end / neo	Massrahme	zustledig	Ownstand	indikator(en) qualitativ	indikator(en) quantitativ	Finan -cen
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2	Verankerung	nev	Die Vergabe von Masterarbeiten zum Thema Gleichstellung im Arbeite und Ausbildungsumfeld der Med Fakultät wird in der Medicinischen Ausbildung anerkanot	Vicedekan sehre	Ab Herbst- semester 2014	Verankerung im Ausbildungs- reglement	Einmaige Ansessing	V
3	Varankerung	Pex	Userprüfen von Möglichkeiten bur Schaffung von Annesen für den Aufbau gemischter Teams. Ziel: 10% des unterneitnetenen Geschichtes auf jeder Stide Assistentionen, Dereit Stimen-Werrassisterkinnen, Dazentöhnen, Professorienen	ING, MG	As 2017	ifeč kihre gemensom mit der AFG diese Machbarteits- studie durch	Esmoephpapier Antong 2018	0.00
4	Anstellungs- serfalsen	neu	Bei jedem Berufungsverfahren meissen mindestens S Personen des untervertretnen Geschlechts sicht und Bewerfung engelsden werden. Desser Teil des Geschäftes wird interguler Bestandssi des Kommissionsberichten zu Händen der Falsutzt. Sollte dies nicht mitglich sein, muss dies im Bericht schriftlich begründer werden.	Detan Kummia- sionsprisi- dentinnen	Ab Juli 2006	Der Dekan ergänet diese Klausel in den Anschroßen an die Kommissiona- präsiden-Cinnes	Betalten Berufungspr schäften	V
5	Anstellungs- serfahren	neu	Assochrößungen für zu besttende Professuren sollen grundsatzen Jestnamig all Option verteilen. Falls ein Joboharing für die zu werzebende Professur nicht möglich ist, misse dies im Berscht der Zeruktunformission begründet und der Palautist vergringt werden.	Dekan Kommis- sionspräsi- dentävnen	Ab.lull 2005	Der Dokan ergänet diese Klausel in den Anschnoben an die Komenbolons präsidentinnen	Bei allen Berufungge- schiften	0.00

Successful implementation of the Equal Opportunities Action Plan 2016-2019



MENTORING FOR WOMEN

### **Commission for Equality**

Murtenstrasse 11, 3008 Bern www.medizin.unibe.ch/ueber\_uns/gleichstellung/index\_ger.html

# **Centers and Platforms**



ARTORG Center for Biomedical Engineering Research
Bern Center for Precision Medicine (BCPM)
Department for BioMedical Research (DBMR)
Microscopy Imaging Center (MIC)
Swiss Institute für Translational and Entrepreneurial Medicine (sitem-insel)
University Cancer Center (UCI)
University Neurocenter
Clinical Trial Unit Bern (CTU)

# ARTORG Center for Biomedical Engineering Research

Murtenstrasse 50, 3008 Bern www.artorg.unibe.ch



Prof Raphael Sznitman ΔΙΙΛΙ



Prof Stefan Weber IGT



Prof. Philippe Zvsset MSB



Prof Olivier Guenat 000



Prof Dominik Obrist CVE



Mougiakakou ΔΙΗΝ



Marchal-Crespo Büchler MIN



Dr Francesco Clavica LIGE



Wimmer HRI



Prof Tobias

Nef

GER

# **Profile**

- Interdisciplinary medical technology research hub between the University of Bern, Inselspital, Bern University Hospital,
- 11 independent research groups, 5 of them at sitem-insel
- Teaching profile: The center mainly contributes to the Masters program in Biomedical Engineering. The postgraduate program currently has 55 full-time PhD students at the interface between technical and medical disciplines.
- Key collaboration partners: Inselspital; UPD; BFH; Imperial College London, UK; University of Nottingham, UK; University of Oxford, UK; Rutgers University, USA; University of British Columbia, Canada; Helmholtz Center, Germany; Universitätsklinikum Freiburg, Germany; University of Stuttgart, Germany; Vienna University of Technology, Austria; EMPA, EPFL, ETHZ, HUG, UZH

# **Grants**

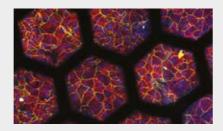
- Swiss National Science Foundation, SNSF (grant No. 163800; 165510; 173130; 176007; 176498; 182966; 182975; 183584; 185365; 188140; 180822; 190521)
- SNSF Sinergia: 183584; CRSII5\_189972 / 1; SNSF BRIDGE: 176498; 184179
- Innosuisse (grant No. 27813.1 PFL-LS; 29936.1 IP-ENG; 31010.1 IP-LS; 32213.1 IP-ICT; 33668.1 IP-SBM; 33780.1 IP-LS; 37855.1 IP-LS; 39409.1 SUIN-LS; 41236.1 IP-LS)
- Horizon 2020 (Marie Skłodowska-Curie): 722068 HiPerNav; 753878 GlimS; 786692 MIMetiCO; 812954 EUROOC
- Horizon 2020 (Eurostars): E!12712 IMAGE-R; E!12977 AIM4DoC
- NCCR Robotics / JDRF / Novostia: SOW#1 / Stiftelesen Promobilia / UniBE ID Grants

# Highlights

# Second-generation Lung-on-Chip

The Organs-on-Chip Technologies group developed the second-generation lung-on-chip that mimics the lung alveolar environment in an unprecedented way. An ultra-thin biological and stretchable membrane, made of collagen and elastin, two proteins found in the lung ECM, was created by surface tension using a gold mesh, and used to culture patients'cells (picture).

Zamprogno et al., bioRxiv 608919, 2019.



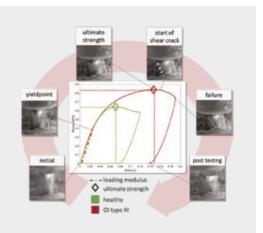
Immunostaining of patient cell cultures on a second-generation lung-on-chip (Picture: Pauline Zamprogno)

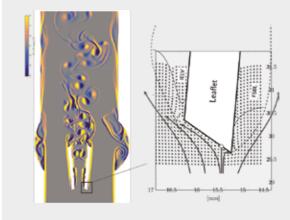
# Micro-Meso Scale Transition of Bone Strength

Osteogenesis imperfecta (OI) is a genetic disorder causing bone fragility, whose biomechanical origin remains unclear. Micro-pillar compression is an innovative technique characterizing the mechanical properties of bone at the ECM level. The Musculoskeletal Biomechanics group demonstrated that the micro-compressive property of adult OI bone is not inferior to those of healthy controls.

Indermaur et al., ASBMR 2019, Orlando, FL, USA.

Quasi static compression test of two representative micro-pillars (Picture: Michael Indermaur)





# Mechanical Heart Valves and Turbulent Blood

Mechanical heart valves have been linked to the production of unphysiological turbulent blood flow. As a first step toward a model for laminar-turbulent transition in this flow, the Cardiovascular Engineering group identified an absolute instability in the impinging leading-edge vortices which develop between the valve leaflets.

Zolfaghari et al., PhysRevFluids.00.003900, 2019.

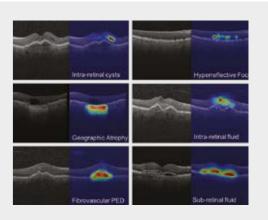
A pocket of absolute instability between the leaflets of a mechanical heart valve causes turbulent flow in ascending aorta.

# **Expert-level Automated Biomarker Identification**

Ophthalmologists today largely use Optical Coherence Tomography (OCT) to monitor chronic eye conditions, leading to an enormous amount of image data created. The Artificial Intelligence in Medical Imaging laboratory has developed a machine learning method that identifies a wide range of common retinal biomarkers from OCT scans fast, reliably and consistently for the use of physicians.

Kurmann et al., Nature Scientific Reports 9, 13605 (2019).

Automated detection and localisation of key biomarkers in OCT scans with human-level performance through an AI system.



# Prediction of Restenosis based on **Hemodynamical Markers**

Endovascular therapy in patients suffering from peripheral arterial disease shows high rates of restenosis. The Computational Bioengineering group developed personalized computational fluid simulations to understand the mechanisms responsible for this poor clinical outcome. Our models showed that flow parameters can be better predictors of restenosis than conventional clinical measures.

Gökgöl et al., Biomech Model Mechanobiol (2019) 18: 1883.

Distribution of wall shear stress (TAWSS) in a stented artery with arterial kinking during leg flexion, the atheroprone areas concentrated around the kinks or highly curved segments.

# Bern Center for Precision Medicine (BCPM)

Murtenstrasse 40, 3008 Bern www.bcpm.unibe.ch



Prof Mark Rubin Director



Prof Claudia Kühni



Prof Carlo Largiadèr



Leeb

Prof Tosso Dr Rémy Bruggmann



Prof Nadia Mercader Huber Chair of the Scientific Review

Board

# **Structure**

The Bern Center for Precision Medicine (BCPM) was established as an interfaculty center in 2019, based on the initiative and support of the canton, the university, and the university hospital (Inselspital). The BCPM is composed of the management board, headed by Prof. Mark Rubin; committees, such as the scientific review committee headed by Prof. Nadia Mercader Huber; the administration (currently two people, which makes the BCPM the smallest center of the Bern University); the academic members (the number is steadily growing, currently we count 65 members); most of its members come from the Medical Faculty.

# **Profile**

- Reporting back to the University board and the rector as well as to the University Hospital board
- Offers a platform for the researchers of both the University and Inselspital who are active in the field of precision medicine, with the goal to promote and further the establishment of precision medicine in Bern
- Aims to develop new medications and methods, increases the quality of treatment for patients, and relieves the healthcare system with more efficient therapies; in addition, it strengthens the national and international position of the University of Bern and the Inselspital in the area of precision medicine
- · Active in research, education, training and networking. In its first year of existence, it funded a total of 15 research projects selected from two separate project calls. The first call aimed at supporting the use of modern genomics in precision medicine. The second call aimed at improving the reproducibility and sustainability in PM research, and at improving the collaboration and connection among the various research groups and platforms of the Inselspital and the University of Bern. Further plans include the establishment of educational programs in the domain of precision medicine, in cooperation with the existing graduate schools. Promotion and outreach goals have also been tackled via the establishment of the Website (www.bcpm.unibe.ch), a Twitter channel (@PMBern), and the organization of various workshops and conferences, some of which gained international participation

# **Grants**

- Funds from the University
- Support of the canton and the Inselspital (invested in financing the Next Generation Sequencing infrastructure) These funds will support the first four years of BCPM activity (2019-2022)

# Highlights

In the first year of its existence, the center was able to align the technical and knowledge platforms active in precision medicine in a network (a comprehensive list can be found on the Website), and it reached out to the important external partners such as the Swiss Personalized Health Network (SPHN) in Bern, the Data Coordination Center (DCC) in Basel, other universities such as the ETH Zurich, and other hospitals such as the cantonal hospitals of Geneva, Lausanne or Basel-Landschaft.

# **BCPM Inauguration**

On 20 May 2019, the official inauguration of the BCPM took place in Bern, in the presence of Mrs Christine Häsler, Director of Education of the Canton of Bern, Prof. Christian Leumann, rector of the University of Bern, Dr. Uwe E. Jocham, President and CEO of the Insel Gruppe, Dr. Bernhard Pulver, President of the Board of the Insel Gruppe and Prof. Matthias Egger, President of the SNF. One of the highlights was the announcement of the first seven BCPM research projects.



From left to right: Christian Leumann, Mark Rubin, Christine Häsler, Uwe E. Jocham, Bernhard Pulver, Matthias Egger.

# 2 pilot project calls (February and July)

First project call: The primary goal of this call was to support innovative translational research projects that address key challenge areas in Precision Medicine, with a special focus on the usage of Next Generation Sequencing (NGS). 7 projects were

Second project call: Two topics were defined by the BCPM members for this call. Topic 1: Reproducibility and sustainability in Biomedical Research. Topic 2: Integrating Data from Multiple Platforms for Precision Medicine. 8 projects were selected.

The winners of both BCPM pilot project rounds

### **Precision Medicine seminars**

The first precision medicine seminar was organized in 2018 with the participation of Prof. Dr. William Sellers from the Broad Institute of MIT and Harvard, USA.

In 2019, two seminars were organized, the first one with Prof. Mark Bender Gerstein (co-director of the Yale Computational Biology and Bioinformatics program), the second one with Prof. Jean-Pierre Hubaux (ETH Lausanne, head of the laboratory in data security, invested in data security for personalized health issues).



Precision Medicine Seminar guest speakers



# General assembly and member workshops

In 2019, the BCPM gathered its members and stakeholders on three occasions: A first general assembly was held on 6 March, resulting in a first get-together. The inauguration took place on 20 May it showed the political buy-in. A strategy workshop was held on 3 June it formed an important basis for the subsequent project calls, and the research profile as a whole.

First General Assembly of the BCPM

# Department for BioMedical Research (DBMR)

University of Bern, Murtenstrasse 35, 3008 Bern www.dbmr.unibe.ch



Rubin Director DBMR



Rieben

40/50

Prof. Willy Prof Robert Hofstetter Directorate Directorate Coordinator Coordinator M.E.M.-Haus Murtenstrasse Pathologie Augenklinik





PD Dr. Manfred Prof Peter Heller Vermathen Coordinator Coordinator Kinderklinik



PD Dr. Monique Coordinator Sahli-Haus 1+2



Structure

The role of the Department for BioMedical Research (DBMR) is to provide its 47 research groups with optimal infrastructure and scientific support. The vast majority (43) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainders (4) are internal DBMR groups 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. Furthermore, the groups of the department are supported by central services responsible for administration, informatics, technical support and bioinformatics.



DEPARTMENT FOR BIOMEDICAL RESEARCH

# **Profile**

- Research department of the Faculty of Medicine of the University of Bern
- Mission: to provide the researchers of the Inselspital with the best possible environment and infrastructures
- Aim: to bridge laboratory-based and biomedical patient-oriented clinical research
- Most of the research groups host masters, PhD, MD-PhD-students, and post-doctoral fellows who are integrated in the research projects of the individual groups
- Organizing progress reports, seminars and conferences that can be credited by the PhD-students
- All group leaders of the department participate in teaching activities

# **Grants**

- Department of Defense (DoD), Prostate Cancer Research Program, Impact Award, The role of CRIPTO signaling in lethal prostate cancer, Pl- Marianna Kruithof-de Julio
- · Department of Defense (DoD), Peer Reviewed Orthopaedic Research Program, Applied Research Award, In Vivo and Ex Vivo Models to Study Ischemia / Reperfusion Injury, Endothelial Cell Protection and Limb Preservation in a Prolonged Field Care Scenario, PI- Robert Rieben
- SNF Sinergia, Hijacking Transcription-Coupled DNA Repair for Cancer Therapy, Pls Shana Sturla (ETH), Mark A. Rubin (Univ. Bern), Orlando Schärer (UNIST)
- Project PHRT, Pioneer Projects (3rd call), Characterization of Oncogenic Protein Isoforms as Targets for Myelodysplastic Syndromes, PI- Nicolas Bonadies
- Project SNF, Project (Div III), Tracing prostate cancer heterogeneity, PI Marianna Kruithof-de Julio
- Project SNF, R'Equip, Ion mobility enabled ion fractionation in the gas phase for deeper prote-ome characterization, PI - Manfred Heller

# **Highlights**

# Day of BioMedical Research 2019

Research Prize funded by Johanna Dürmüller-Bol Fondation, Poster Prizes of the DBMR, Best Publication 2018.



The Prize winners

# Johanna Dürmüller-Bol DBMR Research Award 2019

The Research Prize was awarded to Dr. Maria Nieves Sanz Garcia, Department of Cardiovascular Surgery, Inselspital, Bern University Hospital and Research Group Cardiovascular Surgery, Department for BioMedical Research, for the project "Mitochondrial preservation and mitochondrial damage-associated molecular patterns (mtDAMPs) in DCD heart transplantation".



Dr. Maria Nieves Sanz Garcia

# Microscopy Imaging Center (MIC)

c/o Theodor Kocher Institute, Freiestrasse 1, 3012 Bern www.mic.unibe.ch



Prof Britta Engelhardt President and Representative of the Medical Faculty



Prof Michael Stoffel Representative Faculty



Prof. Olivier Pertz Representative of the Vetsuisse of the Faculty of (30 %) Science



PD Dr. Ruth Lvck



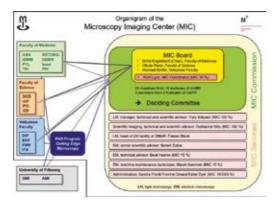
Dr Guillaume Witz BigData



MIC coordinator Biolmaging and Light Microscopy

# **Structure**

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 the Medical, Science and Vetsuisse Faculties of the University of Bern and from the University of Fribourg have joined forces to support high-end microscopy and image analysis. In 2019 the MIC Commission, which is the directive panel, involved 32 representatives. Currently, the MIC oversees 60 instruments including 48 light microscopes, 9 electron microscopes, two atomic force microscopy systems and one micro computed tomography (micro-CT) instrument. In 2019, this equipment was used by 341 researchers.



# **Profile**

- Mission. Expert knowledge and technical support. Implementation of new technologies. Central access to microscopy. Teaching, events and services.
- Teaching and events. Lecture series on Advanced Microscopy. MIC workshops and MIC trainings. PhD program Cutting Edge Microscopy (CEM). In 2019, the MIC organized a 3-day summer school, a 2-day visit of the European Molecular Biology Laboratory (EMBL), Heidelberg, Germany, a Mini-Symposium on Multi-Dimensional Image Processing, the MIC Research Day and the MIC Symposium on Machine Learning in Imaging.
- Portfolio. From live imaging of whole organisms to organs, cells and subcellular dynamics. High throughput setups. From 2D to 5D and from the mesoscopic scale to the ultrastructural level. Light microscopy, electron microscopy, micro computed tomography and atomic force microscopy.
- Service. Software for image analysis. Image data handling and processing. Sample preparation. Introduction into microscope operation. Bimonthly newsletter for visibility and information about microscopy related activities in Bern, Switzerland and abroad.
- Internal activities. The MIC Commission convened at four regular meetings and one retreat.
- External partners. Swiss Society for Optics and Microscopy (SSOM). Life Sciences Switzerland (LS2), Intersection Microscopy. Scientific Volume Imaging b.v. (SVI). Swiss Microscopy and Imaging Core Facility Network. Science IT Support Unit of the University of Bern

# Highlights



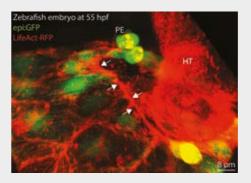
# MIC Research Day on 3 July 2019

This yearly event promotes networking of researchers of the University of Bern using microscopy. The keynote speaker Prof. Nicolas Thomas explained advanced imaging for material sampling on Mars. PD Dr. Fabian Blank and Dr. Guillaume Witz informed about MIC-services. Various researchers of University of Bern presented their microscopy applications.

# MIC Symposium on 29 November 2019

In 2019, MIC has selected the hot topic "Machine Learning in Imaging" as the theme of the MIC symposium. The scientific committee formed by Prof. Inti Zlobek, Prof. Raphael Sznitman, Prof. Mauricio Reyes and Dr. Guillaume Witz prepared a well-balanced and highly informative program which attracted more than 230 participants from Switzerland and abroad. Topics covered included most recent advances in the application of machine learning to various imaging modalities such as ultrasound, electron microscopy and light microscopy.





# **Research highlight Medical Faculty**

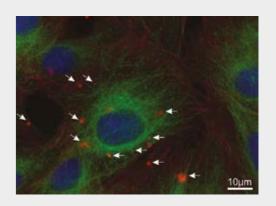
In vivo imaging of the developing zebrafish heart. Confocal microscope Zeiss LSM880 airy scan. Red color, LifeAct-RFP, labels F-actin. Green, epi:GFP, expressed in dorsal pericardium (DP) and proepicardium (PE). The PE protrudes close to the inflow tract (IFT) of the heart tube (HT). Actin filaments (white arrows) are involved in the cellular dynamics of PE formation. Research group of Prof. Nadia Mercader.

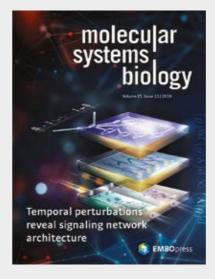
Published in Development 2019, doi: 10.1242/dev.174961.

# Research highlight Vetsuisse Faculty

Metabolic response of rat brain capillary endothelial cells to nanoparticles used in laser-assisted tissue soldering. Microscope Zeiss Axio Imager Z1. Red, internalized polymer-coated fluorescent nanoparticles (white arrows). Green, mitochondrial fusion protein optic atrophy 1 (OPA1). Blue, cell nuclei (DAPI). Purple, cytoskeleton (phalloidin). Research group of Prof. Meike Mevissen.

Published in Toxicology and Applied Pharmacology 2019, doi: 10.1016/j.taap.2019.114800.





# Research highlight Science Faculty

Programmable microfluidic circuits to stimulate living cells with pulses of growth factors applied at different frequencies and concentrations. Live cell imaging using genetically encoded biosensors to measure the activation dynamics of the MAP kinase ERK at the single cell level. Measuring ERK activity dynamics in response to dynamic perturbations and growth factors is combined with mathematical modelling. Such a quantitative and predictive model of MAPK signaling provides a novel understanding on how to target this important pathway in health and disease. Research group of Prof. Olivier Pertz.

Published in Embopress 2019, doi.org/10.15252/msb.20198947.

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

Freiburgstrasse 3, 3010 Bern www.sitem-insel.ch



Dr. Simon Rothen CEO



Prof. Juergen Burger Director sitem-insel School



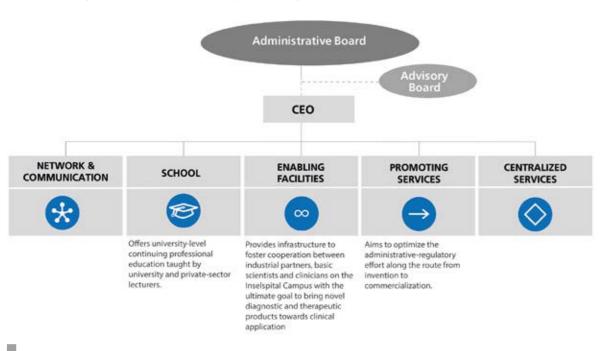
Prof. Rudolf Blankart Director sitem-insel Promoting Services



Dr. Christian Rosser Director sitem-insel Centralised Services

# Structure

sitem-insel brings innovation to the patient by connecting people



# **Profile**

- National center of excellence for translational medicine and entrepreneurship
- Non-profit oriented public private partnership
- Mission: to create and foster an enhanced environment for translational medicine in Switzerland
- Fosters the process of translational medicine by reducing silo building between the public and the private sector, between industries, between scientific disciplines, and within individual people
- Translational research platforms for Clinical Anatomy Training & Research and Biosafety Center
- Further tenants in the new building: parts of the Insel Group and the University, private companies and public organizations
- Network consisting of more than 100 partners such as Berner Fachhochschule BFH, Hamburg Center for Health

Economics, Fraunhofer Gesellschaft, Harvard T.H. Chan School of Public Health, Institut Straumann AG, Johns Hopkins University, KARL STORZ SE & Co, Siemens Healthcare AG, VCCI Foundation, and ZurRose Group (in alphabetical order)

• Shareholders: Berner Fachhochschule BFH; Catfil Schweiz AG, CSL Behring AG, Diabetes Center Berne Foundation, Energie Wasser Bern (ewb), Inselspital-Stiftung, Laboratorium und Grosse Apotheke Dr. G. Bichsel Holding AG, Universität Bern, VCCI Stiftung zur Förderung der medizinischen und translationalen Forschung, Zur Rose Group AG (in alphabetical order)

# Grants, received as center/platform

- HORIZON 2020 (H2020-SC1-2017): Pushing the boundaries of Cost and Outcome analysis of Medical Technologies (COMED)
- NRP74 SMARTER HEALTHCARE: Projecting the impact of health policy changes for Swiss patients with chronic conditions using simulation modeling
- DENTAL MINISCALER, Innosuisse project
- ONE-STEP BALLOON CATHETER, Innosuisse project
- COMPUTER ASSISTED PLANNING FOR ROTATOR CUFF REPAIR, Innosuisse project
- Analysis and simulation of the distal forearm stab. during pro-supination for improved surgical Planning, SNF project
- Innovative encapsulation thin films for neural implants, Innocheque
- European Medical Device (MDR) Regulations Experts for Industry, ZUW University of Bern

# Highlights



# **Promoting Services**

sitem-insel Promoting Services provides a network of regulatory agencies that are located within the building and beyond. This network allows translation specialists to access information and know-how such as IP, finance, regulatory, and more in a timely and tailored manner. In addition, regular events such as the MDR Support Panel is dedicated to preparing SMEs in the medical device industry for the upcoming changes in medical device regulation.

# **Research Platforms are Open and Running**

Starting in May 2019, several research platforms have started operating within sitem-insel AG's new building. At a capacity utilization of almost 95%, approximately 60% of the space is dedicated to medical device technologies, approximately 30% to medicinal and biotech products, and 10% to diagnostics. The blurring of the boundaries between medicinal products, medical devices, and other services makes sense particularly against the background of the ever-closer integration of technologies and people developing and ultimately using them.



The new building at the door of the Insel Campus

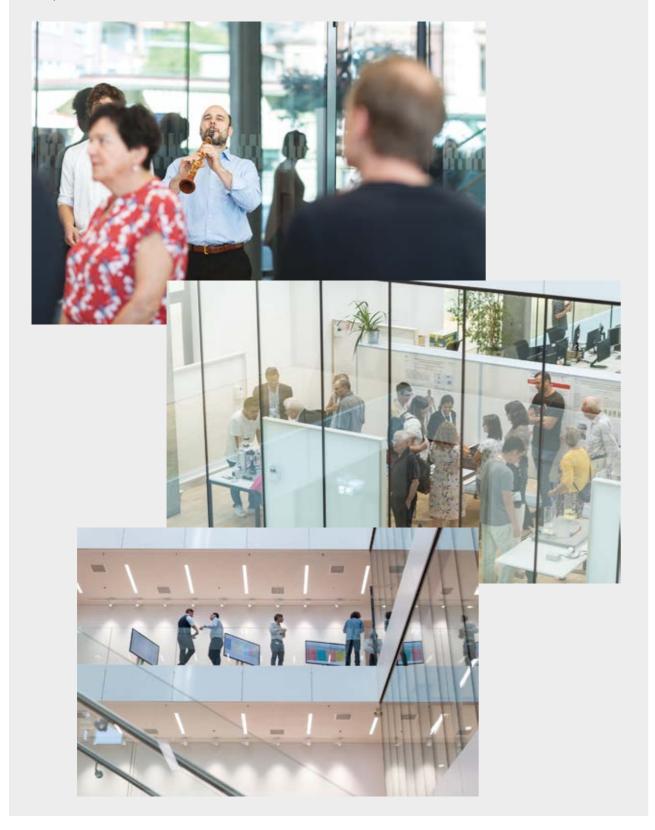
### sitem-insel school

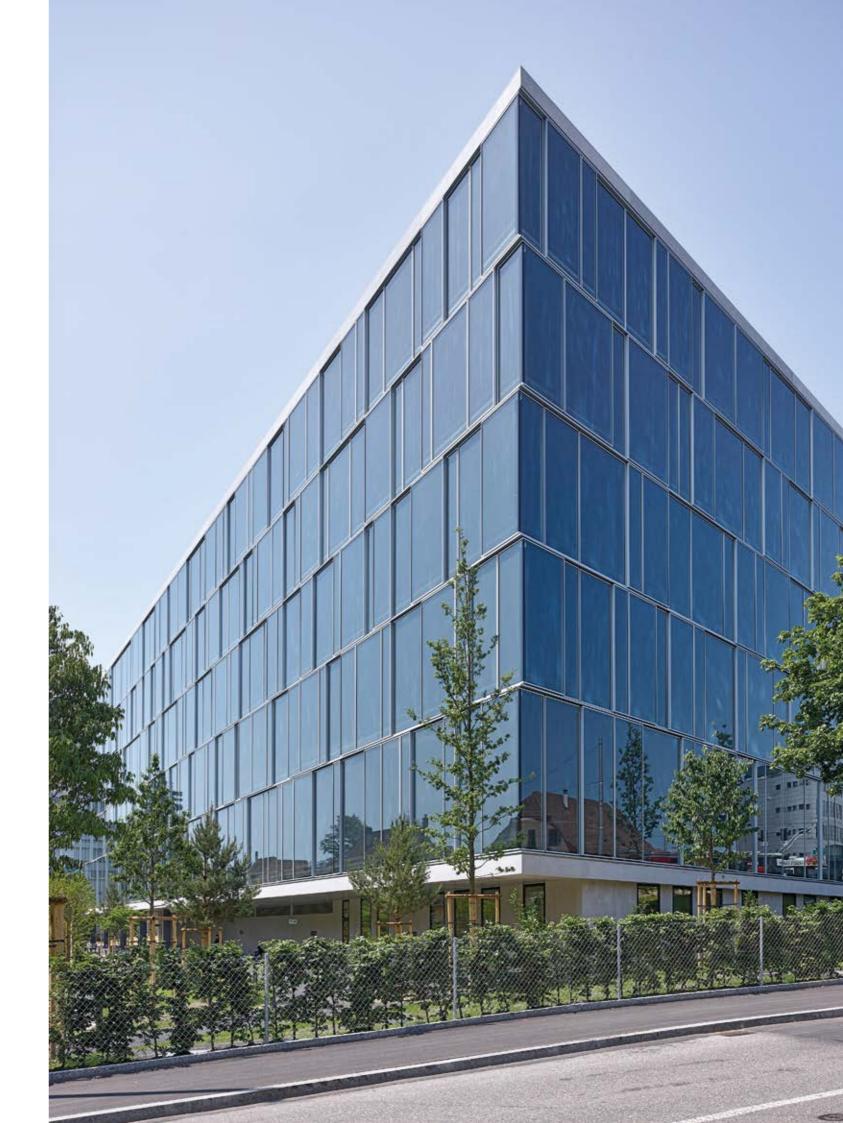
The sitem-insel school offers university education to professionals in medical devices and life science industry. The school's Continuing Professional Development (CPD) courses are taught by university faculty and private-sector lecturers. In September 2019, the new study program "Artificial Intelligence in Medical Imaging" started with an international symposium at sitem-insel.



# Official opening of the new sitem-insel AG building

From 28 August to 30 August 2019, sitem-insel AG has held opening festivities for its new building on the Insel Campus. The program featured several highlights such as:
Press conference with representatives from the Ministry of Economic Affairs of the Canton of Bern, the architectural team, and sitem-insel AG's management
Ceremonial occasion with invited guests from politics, the business and industry community, as well as public authorities
Open house with more than 2500 visitors





# **University Cancer Center (UCI)**

Inselspital, Bern University Hospital, Freiburgstrasse 10, 3010 Bern www.tumorzentrum.insel.ch



Prof Daniel M Aebersold Chairman and Board of Directors



Prof Michael Vice-Chairman and Board of Directors



Prof Daniel Candinas Board of Directors



Board of



Prof Adrian Ochsenbein Directors

Prof Aurel

Perren

Board of

Directors



Prof Andreas Raabe Board of Directors



Prof George Thalmann Board of Directors



Prof. Jörg Beyer Managing Director



Meyer-Soltys Head Coordination and Quality Management

# **Structure**

# University Cancer Center Inselspital (UCI)



The structure of the UCI is outlined in figure 1. Twelve organ-specific cancer centers constitute the core of the UCI – supported by interdisciplinary services and expert groups focusing on special aspects of cancer care.

# **Profile**

- Prevention, diagnosis, treatment and follow-up of cancer
- Aim: being the reference cancer center within the Canton of Bern and being among the top cancer centers of excellence
- Coordinates activities and services relating to cancer within the Inselspital and offers outside services to institutions, physicians, patients and their relatives
- Strong commitment to basic and translational cancer research with active clinical trials across all cancer diagnoses

# Highlights

# Launch of a cancer survivor clinic

Highlights of 2019 were the launch of a cancer survivor clinic to offer advice to patients and their family physicians as a cooperation of the Departments of Internal Medicine and Pediatrics together with the University Cancer Center Inselspital. As cancers are being increasingly cured, many pediatric and young adult patients survive into their late adulthood. Cancer survivors are often faced with multiple health problems resulting from late effects of their cancer treatment, which are often unrecognized and/or undertreated. Parallel to the Cancer Survivor Clinic, we offer reqular expert meetings to facilitate networking and develop guidelines for the care of such patients. Another vulnerable population with cancer are the old and very old. As many patients live well into their late eighties and early nineties, such patients often have similar expectations in respect to their cancer treatment as younger persons. Meeting

these expectations poses a particular challenge. In 2019, we launched an expert group to facilitate interdisciplinary and interprofessional exchange and develop guidelines for the care of such patients.

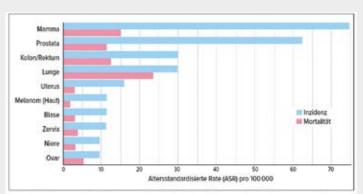


Abb. 1: Relation zwischen Inzidenz und Mortalität für die häufigsten Krebserkrankungen in der Schweiz (geschätzte altersstandardisierte Inzidenz/Mortalität 2018, Schweiz, beide Geschlechter, alle Altersgruppen; Quelle: IARC, GLOBOCAN 2018)

# Outreach

The UCI has close ties with the University of Bern, the cancer registry of the Canton of Bern as well as with national and international research organizations. Referring institutions and practicing physicians can participate in one of 16 organ-specific interdisciplinary tumor boards that offer expert advice on newly diagnosed cancer patients as well as on individual difficult-to-treat cases. In addition, outpatient clinics offer expert cancer care at each of the organ-specific centers for second-opinion.



# **University Neurocenter**

Inselspital, 3010 Bern www.insel.ch/de/das-inselspital/universitaeres-neurozentrum-bern

# **Structure**

The Neurocenter Bern, representing the clinical and scientific cooperation of the University clinic for Neurology, Neurosurgery and Neuroradiology as well as Neuropediatrics and Psychiatry has been founded in 2012. With 400 beds, >1400 collaborators, >60'000 ambulatory patients, >8000 stationary patients, and >3500 operations/interventions/angiographies each year and a budget of > 350 Mio CHF it is the largest of its kind in Switzerland, and leading in Europe.



# **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)
- Advanced neuroimaging, intraoperative imaging, post-processing and clinical implementation of machine learning (5/5)
- 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)
- 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

#### **Grants**

- Swiss National Science Foundation
- Neurology: 3 grants awarded in 2019: 185362, 188761, 189077. 18 running grants: 166827; 169975; 175615; 172952; 179929; 179436; 176985; 179595; 169789; 169379; 173081; 170060; 179667; 172676; 179277; 177520; 179565; 175984)
- Neuroradiology: SINERGIA Project "Predict and Monitor Epilepsy After a First Seizure: The Swiss-First Study
- SPHN Grant"Imagine" (USZ, UZH, Inselspital, USB, EOC, CHUV, HES-SO.)
- SNF SPARK "Using Deep Neural Networks to Bridge Clinical and Quantitative Analysis of Intracranial EEG in Epilepsy" Horizon 2020 (4 running grants): ERC Consolidator Grants (725850 and 725825)
- Neuropedriatrics: The Brainfit-Study, Krebsstiftung (4708-02-2019)
- Eurostars-2 (E! 12034/18/Q); Research and Innovation Programme (721098)
- Innosuisse (3 grants awarded in 2019: project no. 30664.1 IP-LS; 35656.1 IP-LS; 32213.1 IP\_ICT)
- "Suprafascial vancomycin powder for prevention of surgical site infections after instrumented posterior spinal fusion:
   A randomized controlled phase-II trial" TU-Research Grant and research grant form the Gottfried & Julia Bangerter-Rhyner Foundation
- "MAGNEURYSM: Real-time Augmented Visualisation of Vessel Perfusion with Automated Video Analysis" Inselspital CTU-Forschungsgrant
- "A proteomics discovery approach to identify candidate biomarkers of atherosclerotic plaque instability in endarterectomy specimens of patients with carotid disease." Schweizer Herzstiftung

# **Highlights**

### The Neuro Clinical Trial Unit

The Neuro Clinical Trial Unit (NCTU) is a platform of the Neurocenter Bern to support planning and realisation of clinical research in neurosciences. The NCTU works in close collaboration with the CTU Bern and the "Departement für Lehre und Forschung" and has substantiated expertise in the coordination of multicenter national and international clinical trials. Currently, the Neurocenter Bern is conducting over 80 clinical studies; including three large-scale multicenter investigator initiated clinical trials managed by the NCTU Bern:

- ELAN: Early versus Late initiation of direct oral Anticoagulants in post-ischaemic stroke patients with atrial fibrillation (ELAN) www.elan-trial.ch
- SWITCH: Swiss trial of decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral hemorrhage (SWITCH)
- www.switch-trial.ch
- SWIFT DIRECT: Solitaire™ With the Intention For Thrombectomy Plus Intravenous t-PA Versus DIRECT Solitaire™ Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke (SWIFT DIRECT) https://www.swift-direct.ch/



# Opening of the Magnetic Resonance Research Center at the sitem-insel AG – The Translational Imaging Center

The Translational Imaging Center is one of the core facilities of sitem-insel AG. This imaging platform enables translational research ranging from the chemical analysis of samples to model systems and organs to whole body clinical and ultra-high field (UHF) magnetic resonance imaging (MRI), which are integrally linked to the clinical environment and the clinical research of the University of Bern and the Inselspital. Magnetic resonance technology, in particular UHF, opens up a non-invasive examination option for investigating the structure and function of biological tissue. With the paradigm shift from cohort to personalised medicine, it marks a cornerstone for diagnostics and therapy monitoring and the research of new biomarkers.

The established research parameter including a 3 Tesla and a novel UHF 7 Tesla MRI in direct proximity to the Inselspital will foster clinical science in Bern. The MR-research has been an common interest of the Neurocenter in the past and will allow us to integrate and extend our research even further in the future.



# NeuroTec

NeuroTec is an innovative platform - located in the new sitem building - that enables efficient interactions between health and technology specialists from science and industry. The goal of NeuroTec is to promote new, flexible and

cost-efficient technologies improving outpatient diagnostics and therapy in neurology. A core infrastructure of NeuroTec is the "Neuro-Loft" - an instrumented apartment, in which new methods and devices can be tested under real-world conditions.



# Clinical Trial Unit Bern (CTU)

Mittelstrasse 43, 3012 Bern & sitem-insel, Freiburgstrasse 3, 3010 Bern www.ctu.unibe.ch



PD Dr. Sven Trelle Director



Prof. Urs Christina
Fischer Huf
Deputy Director Head Quality
Management



Muriel Helmers Head Data Management



Dr. Andreas Limacher Head Statistics and Methodology



Dr. Felix Rintelen Head Monitoring and Regulatory Affairs

# **Structure**

The CTU Bern is an institute of the Faculty of Medicine, works mainly in five areas and is structured accordingly:

- project coordination and management
- statistical analysis and study design
- data management
- monitoring and regulatory affairs
- clinical investigation

The CTU staff is supported by the institutional quality management of CTU to improve processes.

Consulting and project support are one of the main objectives of CTU Bern.

In 2019, CTU Bern conducted more than 330 consultings, mainly for researchers from Inselspital Bern, and supported more than 100 projects.

# Organigram CTU Bern Research Committee of the Faculty of Medicine (Forschungs suschuses) Executive Board DirectorDeputy Director DirectorDeputy Director Institutional Quality Management Institutional Qual

# **Profile**

- To provide the scientific, technical, and computing expertise needed to conduct patient-oriented clinical research at all stages, from conception to completion and dissemination
- Support is provided in a modular fashion and ranges from advice and general support to full development of the design and conduct of clinical studies
- Staff contributes to undergraduate teaching for 3<sup>rd</sup> and 6<sup>th</sup> year medical and biomedical sciences students
- Postgraduate teaching activities involve contribution to the Certificate of Advanced Studies course in Clinical Research (University of Bern) and the Certificate of Advanced Studies for Clinical Research Coordinators offered by the University of Applied Sciences Bern
- Research ethics and Good Clinical Practice (GCP) training form an important part of our teaching activities and are supplemented by special courses such as software trainings or a course on writing a study protocol and the monthly CTU lecture
- Research partners encompass all clinical departments and institutes of the Faculty of Medicine, members of the Swiss Clinical Trial Organization CTU network, and several Swiss cantonal and private hospitals

# Grants, received as center/platform

• CTU Bern supports the conduct of numerous projects financed by grants as partner

# **Highlights**

# Clinical Investigation moved to sitem-insel building

On 27 August it finally happened – The Clinical Investigation (CI) division of CTU Bern moved into its new facilities of sitem-insel. The new environment offers fully equipped state-of-the-art examination and treatment rooms. Smaller offices have been set up as a "touchbase" to allow presence of CTU staff located at Mittelstrasse 43. They offer the possibility to promote exchange between the CTU Bern and Inselspital investigators. Altogether, this move offers the possibility to occupy an important place on the sitem-insel agora of scientific exchange.





ISO 9001:2015 certification as a way of external review

# ISO 9001:2015 certification and audits

In the first quarter of 2019, CTU Bern had its quality management system (QMS) externally evaluated and assessed. Since April 2019, CTU Bern has successfully been ISO 9001: 2015 certified. Although an ISO certification is not a regulatory requirement, external review and feedback offer the opportunity to improve processes and to achieve higher quality. In summer 2019, CTU Bern was successfully audited as part of a clinical trial in which CTU Bern takes on major responsibilities. This external audit further assured CTU Bern, that internal processes are well established, generally aligned with study sponsor requirements and up to date in regard to regulatory expectations.

# SCTO/SERI platform statistics and methodology

In 2017, the Swiss network of clinical trial units received a four year grant from the State Secretariat for Education, Research, and Innovation to foster collaboration and improve the clinical research environment for multicentre clinical trials. Within this grant, CTU Bern is responsible for the statistics and methodology platform.

This year, CTU Bern hosted two events where statisticians of most CTUs as well as SAKK participated. In spring, a workshop on competing risk and multistate models was held with an internationally renowned faculty. In autumn, a workshop was held in Biel where quality aspects within the statistical workflow of a clinical study were discussed with a focus on improving the automatic and reproducible reporting of statistical information in publication-ready summary tables.



Networking among Swiss CTUs to facilitate and improve collaboration

# Department of Clinical Research: An outlook to 2020

So far, CTU Bern has been the only unit at the Faculty of Medicine dedicated to support academic clinical research activities. Complexity of clinical research has been growing steadily and faculty has acknowledged the importance of such research projects. Therefore, CTU Bern will move under a larger umbrella in 2020: the Department of Clinical Research. This new department will strengthen the clinical research activities at the Faculty of Medicine especially at Inselspital. It will be led by a full professor of clinical research. The department will be responsible for clinical research but also for education and especially promotion of young clinical researchers. CTU Bern will remain with its offices at Mittelstrasse 43. The other parts of the department will be located at the sitem-insel building on the Inselspital campus. A major focus there will be clinical investigation which will run an outpatient clinic for clinical research.



# **Institute at the University of Bern**

Institute of Anatomy

Institute of Biochemistry and Molecular Medicine (IBMM)

Institute for the History of Medicine (IMG)

Institute of Pharmacology (PKI)

Institute of Physiology

Institute of Social and Preventive Medicine (ISPM)

Theodor Kocher Institute (TKI)

Institute for Infectious Diseases (IFIK)

Institute of Pathology

Institute of Forensic Medicine (IRM)

Institute of Dental Medicine (ZMK)

Institute of Primary Health Care (BIHAM)

Institute of Complementary and Integrative Medicine (IKIM)

Institute for Medical Education (IML)

# Institute of Anatomy

Baltzerstrasse 2, 3012 Bern www.ana.unibe.ch



Djonov Director







Prof Nadia Mercader Huber Zuber Co-Director



Prof. Benoît Co-Director



PD Dr. Edik PD Dr Stefan Babiychuk Central Services Group Leader

Tschanz



PD Dr Gudrun Herrmann Group Leader



Hlushchuk Group Leader



PD Dr. Asparouh Schittny Group Leader



Prof. Johannes Group Leader

# **Profile**

- Teaching: The Institute of Anatomy is responsible for the comprehensive teaching of medical students (Human and Veterinary Medicine, Dentistry) and students of related paramedical fields (Biomedical Sciences, Pharmacy, Biomedical Engineering, Physiotherapy, Osteopathy). In addition, postgraduate education and advanced surgical training is provided. We also educate postgraduate medical students (Master/MD) as well as PhD students at the GCB, including the Interfaculty Cutting Edge Microscopy PhD Specialisation Course (responsible: Prof. N. Mercader Huber)
- 9 research groups with various research topics: microbeam radiation therapy; cellular damage control and liposomal nanotraps against bacterial toxins; cardiac development and regeneration; ultrastructure and function of synapses, protein structure; pulmonary development and function of cilia; neuroinflammation; microCT-based imaging
- External research partners: Australia: Australian Synchrotrone, University of Melbourne, University of Sydney, Monash University. Finland: Biomedicum Center Helsinki. France: IGMCB, CNRS, ESRF, University Hospital Henri Mondor, Institut du Fer à Moulin. Germany: MPI-HLR, University of Giessen, DZNE, MPIB, University of Münster. Israel: Hebrew University. Latvia: University of Latvia. Spain: CNIC. Sweden: Lund University. Switzerland: Idiap Research Institute, Anapath Services AG, University of Basel, Institut Straumann AG, University of Zurich, PSI, Lascco SA, ETH Zürich, CHUV. UK: University of Birmingham

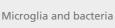
# **Grants**

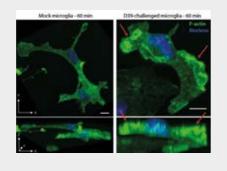
- ERC Consolidator Grant 819717- Transreg
- European Research Area Network (ERA-NET) Neuron grant (32NE30\_185536)
- European Industrial Doctorate Program (H2020-MSCA-ITN-2016) 4DHeart 722427 (2017-2021)
- HSFP RGP0016/2018 Handling OXPHOS structural heterogeneity and metabolic plasticity
- Swiss Cancer Research (KFS-4281-08-2017), 8 SNSF Grants and over 30 grants from other foundations and third parties

# Highlights

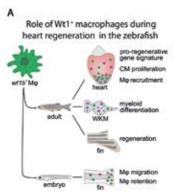
# Pneumolysin and pneumococcal capsule influence taxis and motility of microglia

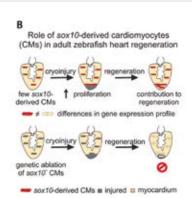
We show that microglia possess the capacity for a very agile response towards bacterial pathogens, but key pathogenic factors, such as pneumococcal capsule and pneumolysin, are able to abolish this response by interference with microglial taxis and motility. Hupp S. et al., J of Neuroinflammation (2019) 16:105.





# crophages (green) in a zebrafish caudal fi



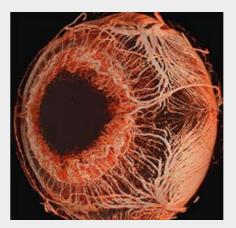


# **Cellular Mechanisms of Cardiac Regeneration**

(A) This year, the group of N. Mercader explored the role of macrophages during regeneration. They found a subset of macrophages with a pro-regenerative gene signature that has an important role during heart regeneration (Sanz-Morejón, García-Redondo et al., 2019 Cell Reports).

(B) Furthermore, the group identified a small subset of cardiomyocytes that expands in response to injury at a higher degree than the rest of cardiomyocytes and plays a fundamental role during myocardium regrowth (Sande et al., 2019 Cell Reports).





# First International Workshop on MicroangioCT

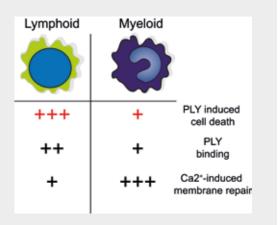
Institute of Anatomy (Prof. V. Djonov) and MicroCT Group (PD Dr. R. Hlushchuk) with the support of MIC (Prof. B: Engelhardt) have successfully conducted the first international workshop on "MicroangioCT: Vascular imaging using a contrast-enhanced microCT approach".

It will become a yearly event held in September. In 2021 it will be supported by COMULIS COST Action (CA17121).

MicroangioCT of a minipig eye

# Cell membrane structure and microvesicle shedding capacity determines differential survival of immune cells

We show here that myeloid cells are more resistant to cell death by pneumolysin (PLY), a pore-forming toxin from S.pneumoniae, as compared to lymphoid cells. Our results suggest that, immune cells important early in infections, i.e. myeloid cells, strongly benefit from an efficient cellular repair mechanism to ensure survival after PLY attack (Yu L et al., FASEB J 2019, in press).



# Institute of Biochemistry and Molecular Medicine (IBMM)

Bühlstrasse 28, 3012 Bern www.ibmm.unibe.ch



Prof Christiane Albrecht



Dr. Jin Li Ambizione Group Leader



Prof Christine Peinelt Co-Director



Abriel

Prof. Hugues Prof Peter Bütikofer Co-Director Head NCCR TransCure



Dr. Charles Roch-Philippe Dozent



Prof Dimitrios **Fotiadis** Managing Director



Gertsch



Lochner



Deputy Director Dozent

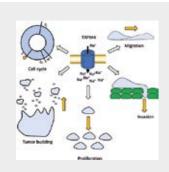
# **Profile**

- · Basic and specialized teaching in biochemistry, molecular and pharmaceutical biology, and molecular medicine, teaching activities in the faculties of Medicine, Natural Science and Vetsuisse to pre- and postgraduate students (GCB)
- Nine research groups
- Interdisciplinary research on structure, function, and pharmacology of membrane proteins (transporters, ion channels, and receptors), with a strong emphasis on the roles of these membrane proteins in human diseases such as cancer, neuropsychiatric and cardiac disorders, pre-eclampsia and pathogen infection
- · Aim: Unravel molecular working mechanisms of selected membrane proteins, discover new therapeutic targets
- Leading House of NCCR TransCure Excellence in Membrane Transport Research
- D-BSSE & D-CHAB, ETH Zürich, Switzerland, Swiss Institute of Bioinformatics, University of Geneva, School of Medicine, University of Nottingham, UK, Department of Pharmacology, University of Cambridge, UK, Novartis Institutes of Biomedical Research, Basel, Switzerland, Max-Planck- Institute, Munich, Germany, Laboratory of Molecular Electron Microscopy, The Rockefeller University, New York, USA, PeterMac Institute, Melbourne, Australia, NIH, NIAAA, Rockville, USA, Institute for Research in Biomedicine (IRB Barcelona), University of Barcelona, Spain

# **Grants**

- Swiss National Science Foundation (NCCR TransCure (Leading House), NCCR Molecular Systems Engineering
- SNSF project grants No. 31003A\_173155, 310030\_184783, 31003A\_162581, 31003A\_176175, 31003A\_163359, 310030\_184980, 31003A\_169355, 310030\_189220
- SNSF Sinergia grants No. CRSII5\_183481, CSRII5\_180326/1, CRSII5\_170923
- CTI Grant Feasibility Study, MS Foundation, Lindenhof Foundation Bern, Swiss Cancer League, BaseLaunch
- Ambizione Fellowship PZ00P3\_173961, SNSF Spark CRSK-3\_190182

# Highlights

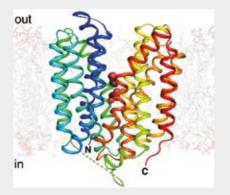


# TRPM4 in colorectal cancer (CRC)

In cooperation with the Translational Research Unit of the Institute of Pathology (UniBe) we showed that TRPM4 is highly expressed in human CRC tumor buds and associated with an infiltrative growth pattern. TRPM4 contributes to cell viability, proliferation, migration, invasion and cell cycle. TRPM4 plays a versatile role in cancer cell pathophysiology.

Kappel et al., Mol Oncology 2019: 13, 2393 - 2405.

TRPM4 in colorectal cancer



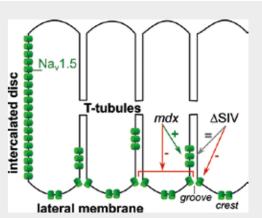
# First structure of a monocarboxylate transporter from the Solute Carrier 16 family

Monocarboxylate transporters play important roles in certain cancers. We have reported structures of an L-lactate-transporting solute carrier family 16 homolog with bound substrate and inhibitor. The structures show the transporter in the pharmacologically relevant outward-open conformation. Structure– function analysis provides insights into the molecular working mechanisms of ligand binding and L-lactate transport. Bosshart PD et al., Nature Commun 2019: 10, 2649.

Structure of the L-lactate transporter SfMCT: sideview, transmembrane helices and two L-lactate molecules are in rainbow colours, and black and red.

# Different modes of Nav1.5 reorganization at the cardiomyocyte lateral membrane and T-tubules

Mutations in the gene encoding the voltage-gated sodium channel Nav1.5 cause many different cardiac arrhythmias, but the causes of this variety remain unknown. We show in mice that different mutations (Nav1.5 truncation and dystrophin deficiency (mdx)) cause different modes of Nav1.5 reorganization in specific cardiomyocyte domains (T-tubules and lateral membrane). Nav1.5 mutations therefore seem to site-specifically affect Nav1.5 localization, distribution, and possibly function. Vermij et al., bioRxiv 674275.



Cardiomyocyte model showing the effects of dystrophin deficiency (mdx) and Nav1.5 truncation (DSIV) on Nav1.5 distribution (green).

# Interaction of antiemetics with serotonin-gated ion channels

We have synthesised several analogues of the clinically used antiemetic drug granisetron. These granisetron probes feature photo-crosslinking groups and our modifications did not affect their high affinity for the target, the serotonin-gated type-3 ion channel (5-HT3R). Furthermore, these granisetron derivates showed specific photo-crosslinking with the human receptor. Detailed analysis after photo-crosslinking by protein-MS/MS identified the exact residue in the receptor binding site that was covalently modified. Jack et al., ACS Chem Neurosci 2019: 10, 438-450.

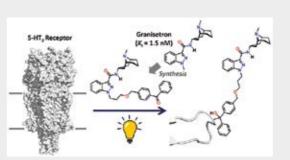
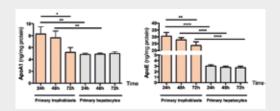


Photo-crosslinking of 5-HT3 receptor

# Placental versus hepatic secretion of apolipoprotein A1 and E

High levels of atherogenic lipids in pregnancy are associated with health complications for the mother, the fetus and the newborn. By ex vivo human placenta perfusion and primary cell culture experiments we demonstrated that the human placenta releases high amounts of anti-atherogenic apolipoproteins, particularly apoA1 and apoE. These data indicate that the placenta plays an important role in maternal and fetal cholesterol homeostasis during human

Melhem et al., Sci Rep. 2019, Sci Rep : 9, 6225.



Placental secretion of apolipoprotein A1 and E

# Institute for the History of Medicine (IMG)

Bühlstrasse 26, 3012 Bern www.img.unibe.ch



Prof Hubert Steinke Director



Dr Pascal

Germann

Stefan Hächler



Manuel Kaiser Head of Head of Archive Collection



Müller Head of Library



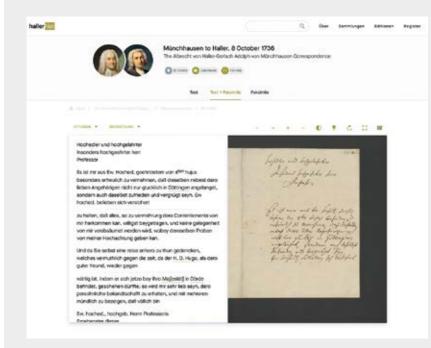
**Profile** 

- Teaching students of medicine at the Universities of Bern, Basel and Fribourg as well as history students and master students at the biomedical engineering program
- 1 professor, 1 assistant and further scientists in SNSF-funded projects
- Rich library (100,000 vols.), archive documenting local and Swiss medicine (paper and digital), large collection of medical objects from University and University Hospital
- Research on medical theory and practice 18th to 20th century, Albrecht von Haller and the 18th century Republic of Letters, history of medical ethics, history of the quality of life concept
- External partners: Institute of Biomedical Ethics and History of Medicine, University of Zurich; Institute for the History o Medicine and Health, University of Lausanne; School of Liberal Arts, Indiana University; Center for African Studies, University of Florida; Department of History, University of Montreal; Institute for History and Ethics of Medicine, University of Cologne

# **Grants**

- Swiss National Science Foundation (grants No. 100011\_159614; 100011\_184880; 10FE15-157963; 174862; 186439)
- Canton of Aargau, Departement of Health
- Swiss Academy of Medical Sciences

# Highlights



# Haller online

In this SNSF-funded longterm project we are editing thousands of bookreviews and letters from Albrecht von Haller's correspondence. These sources will allow us to get a better understanding of 18th century scientific networks.

The website has been launched in May 2019 and presents an ever increasing number of transcriptions. www.hallernet.org

Facsimile and text of a letter



# **Medical ethics in Switzerland**

In 2019 we finalized the process of digitizing and storing the whole archive of the Swiss Academy of Medical Sciences at our Institute (2,000 folders). Based on these sources, Dr. Magaly Tornay developed the SNSF-funded research project "Governing by Values: On the History of Medical Ethics and Bioethics in Switzerland", which started in October 2019.

Parts of the paper archive

# A new European Journal

The Institute hosted a conference with colleagues from 19 European countries in order to discuss the state of medico-historical research and the establishment of a new "European Journal for the History of Medicine and Health" in 2021. There is a need for a high quality journal serving as a platform for various European perspectives on medical history. Hubert Steinke will be Co-Editor-in-Chief of the journal.



Workshop with European colleagues



# **Psychiatric hospitalisation**

After five years of research, the Independent Expert Commission (IEC) on Administrative Detention published its Final Report, written by IMG staff member Urs Germann and Lorraine Odier. Among others, it shows the growing significance of psychiatric hospitalisation and calls for further research beyond the "watershed" of 1981.

# Institute of Pharmacology (PKI)

Inselspital, INO-F, 3010 Bern www.pki.unibe.ch



Prof. Hans-Uwe Simon Director



Prof. Andrea Huwiler Deputy Director



Prof. Thomas Kaufmann



SNF Prof. Georgia Prof. Stephan Konstantinidou von Gunten



Prof. Shida Yousefi



Prof. Uwe Zangemeister-Wittke

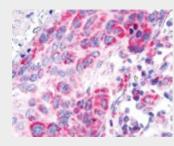
# **Profile**

- Teaching students of medicine, dental medicine, pharmacy, biomedicine and biology as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB)
- 7 research groups
- · Investigation of pathophysiological processes that contribute to inflammation and tumor diseases
- Aim: Discovering new drug targets
- External Partners: Institutes of Biochemistry, Experimental Immunology and Molecular Cancer Research, University of Zürich, Zürich, Switzerland; Department of Pharmacology, Toxicology and Clinical Pharmacy, Institute of Pharmacy, University of Tübingen, Tübingen, Germany; Pharmazentrum Frankfurt/ZAFES, University Hospital and Goethe University, Frankfurt/Main, Germany; Department of Medicine, University of Toronto, Toronto, Canada; Department of Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; Department of Clinical Immunology and Allergology, Sechenov University Moscow, Russia; Swiss EoE Research Group, Olten, Switzerland

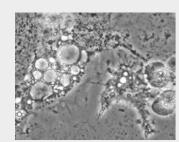
### **Grants**

- Swiss National Science Foundation (grant No. 310030-166473; 310030\_184816; 310030-175561; 31003A\_173215; 31003A\_149387; 310030-146215; 310030E-132762; 310030A-138201; 31003A\_170134; 310030\_184757)
- Swiss Cancer League (KFS-3703-08-2015; KFS-3941-08-2016)
- HORIZON 2020 (Marie Sklodowska-Curie Action): MEL-PLEX
- Novartis Foundation for Biological-Medical Research
- SNSF Professorship (PP00P3\_163929)

# Highlights



Lung cance



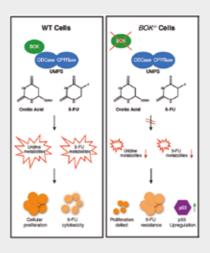
Cells undergoing oncosis

# Characterizing ATG12 as a novel drug target in cancer

ATG12 is known as an essential autophagy-regulating protein. We observed that cancer cells with reduced ATG12 expression undergo an oncotic cell death, owing to reduced mitochondrial biogenesis and function. Inducing oncosis by imposing an ATG12 deficiency in solid tumors might represent a novel anti-cancer therapy.

Top panel: Immunohistochemistry. High ATG12 expression in lung cancer. Bottom panel: Downregulation of ATG12 in lung cancer cells results in oncosis characterized by vacuolization and blister formation.

Liu H et al., Cell Death Differ. 2019 Dec 16. doi: 10.1038/s41418-019-0476-5.



# BCL-2 family protein BOK is a positive regulator of uridine metabolism

We report that the Bcl-2 family protein Bok activates a key enzyme involved in uridine metabolism (UMPS), and thereby nucleotide biosynthesis and activity of the chemotherapeutic drug 5-fluorouracil (5-FU). We propose Bok as potential biomarker for 5-FU resistance and to develop Bok mimetic compounds to re-sensitize 5-FU-resistant cancers. Srivastava R et al., PNAS 2019: 116, 15469 - 15474.

# Tumor glycosylation as an immune checkpoint

We demonstrated that one of the most common tumor glycosylation patterns (hypersialylation) provides tumor cells the capacity to escape the immune attack by cytotoxic CD8+ T cells. The attenuation of T cell anti-tumor responses involves the interaction of tumor glycans with the inhibitory Siglec-9 receptor. The recognition of sugar-structures as immune checkpoints may support immunotherapeutic approaches against cancer.

Right panel: Journal cover page with artistic representation of our results (May 2019).

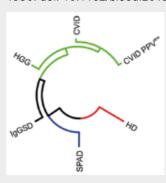
Haas Q et al., Cancer Immunol Res 2019: 7, 707 - 718.



# Glycan-specific antibodies in immunodeficiency

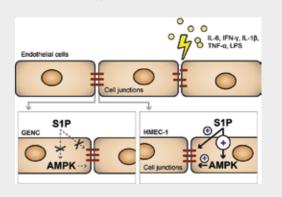
The surface of microbial pathogens and tumor cells is coated with glycans, which can be recognized by glycan-specific antibodies. An atlas of the glycan-specific IgG repertoire in primary antibody deficiency was established. We observed that individuals with immunodeficiency lack a significant proportion of antibodies not only to bacterial, but also to specific tumor antigens. Furthermore, our data suggest that broad antibody repertoire analysis may have advantages over current diagnostic approaches.

Jandus P et al., Blood. 2019 Nov 28;134(22):1941-1950. doi: 10.1182/blood.2019001705.



# The AMP kinase is a key mediator of the endothelial barrier-protective effect of S1P

Breakdown of the endothelial barrier is a critical step in the development of organ failure in severe inflammatory conditions such as sepsis. By measuring transendothelial resistance, we show a key role of the S1P-AMPK signalling axis in endothelial barrier stabilization in human microvascular endothelial cells (HMEC-1). This is not seen in glomerular endothelial cells (GENCs), thus proving a tissue-specific regulation of endothelial barrier integrity by S1P. Dennhardt S et al., Biochim. Biophys. Acta Mol. Basis Dis. 2019: 1865, 774 - 781.



# Institute of Physiology

Bühlplatz 5, 3012 Bern www.physio.unibe.ch



Prof. Thomas Nevian Managing Director



Prof Walter Codirector



Prof. Stephan Rohr Codirector



Prof Frnst Niggli Codirector



Prof Marcel

Egger

Prof Stéphane Ciocchi (SNF)



Kucera



Prof. Jüra

Streit





PD Dr. Sonia Kleinlogel



Prof. Jean-Pascal Dr. Shankar Pfister (SNF)



Sachidhanandam

# **Profile**

- Performs basic and translational research in cardiac- and neurophysiology.
- Five groups in cardiac physiology investigate the conditions that lead to heart failure and arrhythmias. They use electrophysiological and imaging techniques as well as computer simulations to elucidate the mechanisms of action potential propagation and excitation-contraction coupling on the subcellular, cellular and organ levels.
- 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, depression and perceptual vision are studied from molecules, over single cells to neuronal networks with electrophysiological, two-photon imaging, optogenetics and behavioural approaches.
- Two computational neuroscience groups develop probabilistic models of brain function at different levels, from single synapses to cognition.
- Predominantly engaged in the education of students of human and dental medicine, responsible for the entire field of physiology, covering all lectures and practical courses. Lecturers of our institute also participate in the training of students in veterinary medicine, pharmacy and the "Master in Biomedical Engineering". Our institute coordinates the master program in Biomedical Sciences (BMSc), contributes to the BeNeFri program in Neuroscience, as well as other interfaculty lecture courses.
- External research partners: Humbold University, Neurocure Cluster of Excellence, Berlin, Germany; Department of Pharmacy and Drug Science, University of Bari Aldo Moro, Bari, Italy; Department of Medicine, Wisconsin Institutes for Medical Research, University of Wisconsin, USA; Kirchhoff Institute of Physics, University of Heidelberg, Heidelberg, Germany; Medizinische Hochschule Hannover, Germany

# **Grants**

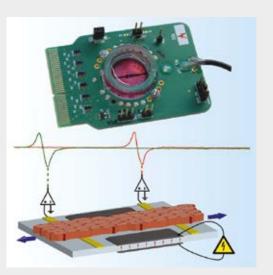
- ERC Consolidator Grant (Nevian)
- ERC Starting Grant (Ciocchi)
- SNF Professorship Grant (Pfister)
- Bertarelli Foundation Catalyst (Kleinlogel)
- Human Brain Project (Senn)
- IFK Decoding Sleep (Nevian, Senn)

# Highlights

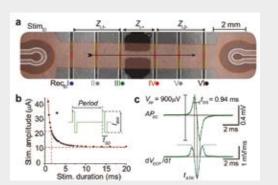
# Ultrafast stretch events and cardiac electrophysiology

A hefty blow to the chest can have entirely opposite outcomes. While, for instance, baseball players have died after being hit in the chest by a baseball, patients undergoing fatal cardiac tachyarrhythmias have been saved by an appropriately timed thump to the chest. In the past, investigations of electrophysiological mechanisms underlying these phenomena have been hampered by the lack of experimental systems that allow very fast stretching of cardiac tissues while simultaneously recording its electrophysiological properties. In collaboration with the EPFL Neuchatel, we developed such a device that is based on a stretchable, extremely thin silicone membrane containing integrated gold and carbon electrodes. Applying high voltage pulses to the carbon electrodes results in quasi-linear stretching of the membrane by up to 12% and at rates up to 100x those encountered by cardiomyocytes during normal heart function. Impulse propagation during strain application is recorded by extracellular gold electrodes positioned along the linear cardiomyocyte preparations. Much to our surprise, impulse conduction remained virtually unchanged even at the highest strain amplitudes and rates which suggests that the strain sensitive element of the heart may actually not be the contracting cardiomyocyte itself but adjacent electrotonically coupled connective tissue cells. The developed device is ideally suited to investigate this hypothesis and lends itself to systematic studies of the effect of specific drugs or gene therapies having beneficial effects on mechano-electrical coupling in the heart.

High-speed mechano-active multielectrode array for investigating rapid stretch effects on cardiac tissue. Nature Communications (2019), 10:834. Matthias Imboden, Etienne de Coulon, Alexandre Poulin, Christian Dellenbach, Samuel Rosset, Herbert Shea and Stephan Rohr. DOI: https://doi. org/10.1038/s41467-019-08757-2.



Mechano-active multielectrode array (MaMEA).

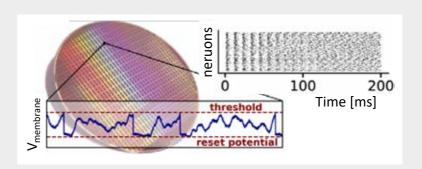


Preparate (a) with strength-duration curve (b) and example of an electrogram (c).

# Stochastic computation by spikes

When thinking of a visual scene, we imagine the different objects of the scene while the focus of attention jumps stochastically from object to another. We modeled this imagination process with a generative network of spiking neurons that serially "dream" visual objects seen before. A reduced version of the network is implemented in the Heidelberg neuromorphic hardware.

Stochasticity from function – why the Bayesian brain does not need noise. Dold, Bytschok, Kungl, Baumbach, Breitwieser, Senn, Schemmel, Meier, Petrovici; Neural Networks (2019), https://doi.org/10.1016/j.neunet.2019.08.002.



Wafer from the BrainScaleS neuromorphic hardware (left) with example of single neuron voltage time course (blue) and multi-neuron spike raster plot (top right)

# Institute of Social and Preventive Medicine (ISPM)

Mittelstrasse 43, 3012 Bern www.ispm.unibe.ch



Prof Oscar Franco Director



Prof Marcel Zwahlen Deputy Director



Prof Thomas Abel



Prof Matthias Egger



PD Dr Christian

Althaus

PD Dr. Julia **Bohlius** 



Prof Claudia Kuehni



Prof Nicola Low



Dr Taulant



Prof. Stephan Luciano Reichenbach Ruggia



Salanti



Prof Georgia Dr. Adrian Spoerri



PD Dr. Ben Spycher



Dr. Ana Maria Vicedo-Cabrera



Wanner

**Profile** 

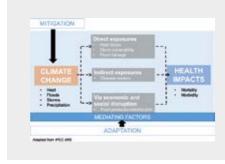
Muka

- Mainly academic and scientific activities with a primary interest in health across the lifecourse
- Research profile covers health areas from cardiometabolic to HIV, cancer, childhood and adolescents, NCDs to environmental influence, with the tiers of development of new methods and lifestyle and behavior reaching across all fields
- Participating in University teaching programs for students of medicine, biomedical engineering and biomedicine (including students from the University of Fribourg). Engaged in PhD and postgraduate programs of the University of Bern and SSPH+
- Offers three CAS
- 14 research groups
- External partners: Oeschger Center for Climate Change Research; Paraplegic Research Switzerland; University of Harvard, Schulich School of Medicine&Dentistry, University of Western Ontario, Canada; Fundacion Universitaria de Ciencias de la Salud, Colombia; Universidad de la Magdalena, Colombia; Federal State Budgetary Organization National Cardiology Research Center of the Ministry of Health of the Russian Federation; Department of Nuclear Medicine, University Hospital Zurich, Zurich, Switzerland; University of Lausanne; HELIUS, University of Amsterdam; School of Public Health, Imperial College London; Department of Epidemiology, Erasmus Medical Center, Rotterdam, the Netherlans; Institute of Community Medicine, University of Greifswald, Greifswald, Germany; Helmholtz Zentrum München, Munich, Germany; Epigenomics Research Group, King's College London; Institute of Applied Health Research, UKRI Innovation Clinical Fellow, Honorary Consultant in Public Health Medicine; Department of Epidemiology and Prevention, IRCCS Neuromed, Pozzilli (IS), Italy.

# **Grants**

- SNSF Ambizione (PZ00P3\_185923/1)
- Swiss National Science Foundation (31BL30\_185396)
- Horizon 2020 (EU 825162)
- Swiss Cancer Research (KLS/KFS-4825-01-2019, KFS-4722-02-2019, KLS 4592-08-2018)

# **Highlights**



# New research group on Climate Change and Health

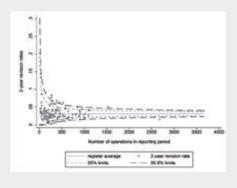
The group, led by Ana M. Vicedo-Cabrera, will investigate the impact of climate change on health, with particular focus on the evaluation of adaptation strategies, mitigation policies and their health co-benefits.

# **Cardiometabolic Health Group**

This newly established research group focuses on the aetiology of cardiometabolic disease including type 2 diabetes and cardiovascular disease and their associated factors such as dyslipidaemia, hypertension and obesity. The aim is to understand the role of lifestyle factors (e.g., diet, physical activity and sleep) on maintaining optimal cardiometabolic health and preventing cardiometabolic disease, as well as in identifying new biomarkers and pathways for prediction, diagnosis, prognosis and treatment of cardiometabolic disease.

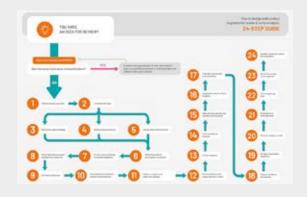
# **SwissRDL Medical Registries and Data Linkage**

SwissRDL maintains and analyses the national hip and knee implant registry on behalf of the SIRIS foundation. The annual report 2019 shows 2-years revision rates for primary hip and knee implant operations per hospital (panel shows hips only). With this report Switzerland presents a high-quality report comparable with others from long-standing registry world wide. Additionally, SwissRDL has negotiated and implemented new registries in 2019 and will be running the Swiss Heart Surgery Registry, the percutaneous coronary intervention registry and the idiopathic lung disease registry starting in 2020.



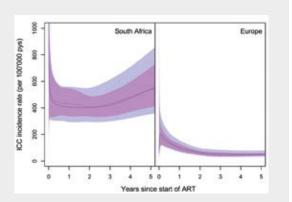
# 24-Step guide on how to design, conduct and succesfully publish a systematic review and meta-analysis in medical research

Together with researchers from the Netherlands and UK we have developed a clear step-by-step guide on how to perform a systematic review and metaanalysis of observational studies and clinical trials. This 24-step guide simplifies the process of conducting a systematic review, provides healthcare professionals and researchers with the tools to conduct methodologically sound systematic reviews and meta-analyses, and enhances the quality of synthesis efforts already underway. Read the abstract on PubMed.



# Global disparities in cervical cancer rates among women with HIV

A study by an international group of researchers led by a team at the Institute of Social and Preventive Medicine, University of Bern, found that the incidence rates of cervical cancer are particularly high among women living with HIV in South Africa or Latin America. For this study recently published in the International Journal of Cancer, researchers used data from a collaboration between global HIV cohort research networks to compare cervical cancer rates in 45 countries across Europe, South Africa, Latin, and North America among women living with HIV who initiated antiretroviral therapy between 1996 and 2014. Read the abstract on PubMed.



# Theodor Kocher Institute (TKI)

Freiestrasse 1, 3012 Bern www.tki.unibe.ch



Prof Dr Britta Engelhardt Director and Research Group Leader Leade



PD Dr Ruth Lvck Research Group Research



Dr. Urban Deutsch Group Leader



Dr. Giuseppe Locatelli Research Group Leader



Dr Steven Proulx Research Group Leader

Inflamed condition of the in vitro BBB (pMBMECs, II1b) led to significant stronger melanoma cell (B78chOVA) intercalation compared to control (Ctl).

# **Brain metastasis formation: Melanoma cells** breach the blood-brain barrier

Prior to colonization of the brain, metastatic melanoma cells breach the BBB. We have developed a high-throughput live cell imaging setup combined with an automated evaluation pipeline to identify inhibitors of this process. Proof-of-concept experiments confirmed applicability: Inflammatory conditions of the BBB accompanied by impaired barrier properties significantly increased melanoma cell intercalation with the BBB when compared to control conditions of the BBB.

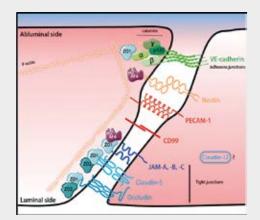
# **Profile**

- Teaching bachelor and master students of the Medical, Science and Vetsuisse faculties in lectures and practical classes in immunology, vascular and cell biology. Educating graduate students of the Graduate School for Cellular and biomedical Sciences (GCB). Coordinating national PhD programs "Cell Migration" and "Cutting Edge Microscopy".
- The TKI hosts 5 research groups studying central nervous system immunity in health and disease with a focus on multiple sclerosis, stroke, Alzheimer's disease and brain metastasis of tumors by employing advanced in vitro and in vivo imaging
- External partners: Prof. Thorsten Buch, University Zurich, Switzerland; Prof. Christer Betsholtz, Uppsala, Sweden, Dr. Yann Decker, University of the Saarland, Germany; Prof. Michael Detmar, ETH Zurich, Prof. Tobias Dick, University Heidelberg, Germany; Prof. Fabien Gosselet, University of Lens, France; Prof. Mikio Furuse, Kyoto University Faculty of Medicine, Japan; Prof. Jean-Charles Guery, INSERM, Toulouse, France; Prof. Jan Klohs, Neuroscience Center Zurich, Switzerland; Prof. Takashi Kanda, Yamaguchi University, Japan; Prof. Martin Kerschensteiner, LMU Munich, Germany; Prof. Harm-Anton Klok, EPFL, Lausanne, Switzerland; Prof. Hans Lassmann, Vienna, Austria; Prof. Roland Liblau, INSERM Toulouse, France; Prof. Gianluca Matteoli, KU Leuven, Belgium; Prof. James McGrath, University of Rochester, NY, USA; Prof. Renaud du Pasquier, CHUV, Lausanne, Switzerland; Prof. Marco Prinz, University Hospital Freiburg, Germany, Prof. Federica Sallusto, ETH Zurich, Switzerland; Prof. Eric Shusta, Univesity of Madison-Wisconsin, USA

# **Grants**

• Swiss National Science Foundation (grants 310030\_189080, 31003A\_170131, 310030\_189226), EU Horizon 2020 MSCA-ITN 2015-675619 BtRAIN and MSCS-ITN-2018-813294 ENTRAIN; Fidelity Bermuda Foundation; ARSEP, Swiss MS Society; Bangerter-Rhyner Foundation; Scherbarth Foundation, Theodor Ott Fund, David and Betty Koetser Foundation; Swiss Heart Foundation, UniBE ID grant, Synapsis Foundation, Heidi Seiler Stiftung, UniBern Forschungsstiftung

# **Highlights**



Schematic representation of the molecular composition of BBB tight junctions

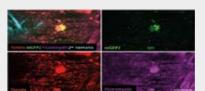
# Molecular composition and function of blood-brain barrier tight junctions

Complex tight junctions (TJs) between brain microvascular endothelial cells forming the blood-brain barrier (BBB) block uncontrolled paracellular diffusion of molecules across the BBB. Our studies advanced understanding of the molecular composition of BBB tight junctions and identified a novel role for BBB cell-to-cell contacts in regulating T-cell trafficking across these cellular junctions of the BBB ensuring central nervous system immune surveillance.

Castro Dias et al., 2019, Sci Rep. 9(1):203); Castro Dias et al., 2019, FBCNS, 16(1):30; Castro Dias et al., Int J Mol Sci. 20(21), pii: E5372; Wimmer et al., 2019 Front Immunol, 5;10:711.

# Oxidative pathology in mitochondria of oligodendrocytes

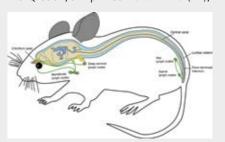
We have established a novel transgenic mouse model which allows imaging of oxidative pathology in oligodendrocyte mitochondria by 2-photon microscopy. By expressing a reporter protein sensitive to variations in oxidative agents (Orp1-roGFP2), specifically in mitochondria of myelin-producing oligodendrocytes, we can visualize - at a single organelle level - dynamic redox changes in the spinal cord of anesthetized animals. After establishing the surgical approach and data analysis, we now move toward dissecting the mechanisms of mitochondrial pathology during the development of anti-CNS inflammation.



Mitochondrial fluorescence from the cervical spinal cord of a MOG-mitoORP1-roGFP2 x Ai14 mouse image with 940 nm excitation by 2-photon microscopy. In cyan, collagen signal; in green, mitochondrial signal; in red, cytosolic ODC signal, in magenta, myelin sheaths. Scale bar, 20 um

# Clearance of cerebrospinal fluid from the sacral spine through lymphatic vessels

We have recently shown with dynamic in vivo imaging that routes of outflow of CSF in mice occur along cranial nerves to extracranial lymphatic vessels rather than directly to venous blood as commonly assumed. In this project, we used near-infrared and magnetic resonance imaging to demonstrate a cranial-to-caudal flow of CSF tracers within the spinal column and revealed that the major spinal pathways for outflow occurred to lymphatic vessels at the sacral region. Outflow of CSF from the spine to lymphatic vessels may have significance for many conditions, including multiple sclerosis and spinal cord injury. Ma Q et al., J Exp Med 2019: 216 (11), 2492-2502.



Overview of CSF efflux sites in mice

# Successful finalization of the international PhD program BtRAIN

The EU Horizon 2020 funded ITN BtRAIN coordinated by Britta Engelhardt was successfully finished. BtRAIN has created novel knowledge on the vertebrate brain barrier signature genes and their specific role in regulating brain barriers function in development, health, ageing and disease. BtRAIN has educated 12 young brain barrier researchers in an interdisciplinary manner allowing them to obtain unique skills and thus making them highly desired researchers in the academic and non-academic sector in the brain barriers field.



The 12 BtRAIN students at the final BtRAIN meeting

# Institute for Infectious Diseases (IFIK)

Friedbühlstrasse 51, 3012 Bern www.ifik.unibe.ch



Prof Stephen Leib Director



Dr Franziska Suter-Riniker Deputy Director



Keller

Dr Katharina Summermatter Head Innovation Head & Development



Prof Sieafried Hapfelmeier-Balmer, Deputy Biosafety Center Head Research



Prof Andrea Endimiani



Prof Bruno Gottstein





PD Dr. Markus PD Dr. Andreas Kronenberg



Niederhauser Head anresis ch



PD Dr. Christoph Dr. Alban

Ramette



Sendi

Prof Ronald

Dijkman

Prof. Parham

Head of Biorisk Management Network @ sitem-insel

# **Profile**

Hathaway

- · Covers the entire spectrum of microbiology integrated in research, education and diagnostic services under one roof, including virology, bacteriology, mycology, parasitology, molecular diagnostic and infection serology.
- Certified by Swissmedic and accredited for patient care in public hospitals by ISO/IEC 17025 (STS 0363).
- Home to the Swiss National Centre for Antibiotic Resistance (anresis.ch) and the Swiss National Reference Centre for Pneumococci, both mandated by the Federal Office of Public Health.
- 14 research groups in the fields of antimicrobial resistance, biosafety, central nervous system infection, diagnostic innova tion, experimental virology, microbial genomics and host-microbiota interaction, mucosal infections and parasitology.
- Teaching programs for students of medicine, dental medicine, pharmacology, biomedical sciences, and biology and for candidates of the FAMH postgraduate training in Clinical Microbiology.
- External Partners: Spiez Laboratory, Swiss Federal Office for Civil Protection; Department of Neurology and Neonatal Brain Disorder Center, University of California, San Francisco, USA; Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, South Africa; Department of Genetics, University of Leicester, UK; School of Life Sciences, University of Nottingham, UK; EPFL; Swiss Tropical and Public Health Institute, Basel; Medical Microbiology, University Hospital Basel; Department of Microbiology and Molecular Medicine, University of Geneva

# **Grants**

- Swiss National Science Foundation: project grants 162583; 162808; 169791; 170063; 179260; 189136; NRP 72 grants 177452; 177378; 177386; Sinergia grant 180317; Bilateral programme South Africa grant 170844
- European Union: EUREKA Eurostars grant "Hearlt"; Marie Skłodowska-Curie Action training network HONOURs
- University of Bern: Interfaculty Research Cooperations "One-Health" and "Decoding Sleep"
- The Gut Microbiology lab of Prof. Hapfelmeier was awarded participation in the new SNF NCCR "Microbiomes" (nccr.ch).

# Highlights



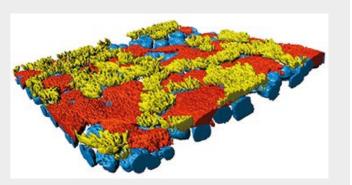
# First accredited nanopore sequencing laboratory worldwide

As of 21 January 2019, the IFIK) is the first laboratory worldwide to have received the ISO/ IEC 17025:2018 accreditation for sequence-based identification of bacterial pathogens using Oxford Nanopore Technologies devices in a medical diagnostic setting. The new sequencing technology enables to taxonomically identify pathogens more rapidly and cost-effectively. The IFIK sequencing laboratory is also the first certified Nanopore Service Provider in Switzerland.

Oxford nanopore sequening service at IFIK

# New research group: Experimental Virology

As of July, the Institute for Infectious Diseases (IFIK) has established the "Experimental Virology" research group headed by Prof. Ronald Diikman who currently holds a dual appointment as Assistant Professor at the Vetsuisse Faculty in Bern and IFIK. His research has an emphasis on characterizing critical determinants of species barriers for emerging respiratory pathogens, such as influenza viruses, for both epizootic and zoonotic risk assessment and the development of effective countermeasures against these diseases.



3D image representation of human airway epithelial cells



The INFECT by anresis App in action

# **INFECT** by anresis App

ANRESIS collects antibiotic resistance data from 30 representative laboratories all over Switzerland. But collecting is not enough, data should be used and help in decision making. Therefore, ANRESIS developed an interactive, user-friendly app showing real time local resistance rates and treatment guidelines from the Swiss Society of Infectious Diseases in a single interface.

# New zebrafish breeding and research laboratory to develop experimental models of infectious diseases

The IFIK inaugurated a zebrafish laboratory including a small breeding facility with a microinjection system and fluorescent imaging capability. This biosafety level 2 laboratory will allow the development of new experimental models of infectious diseases, including (but not restricted to) central nervous system and systemic infections.



Hindbrain infection of a zebrafish embryo by GFP-expressing Streptococcus pneumoniae

# **Biosafety Center Bern**

The biosafety center started its activities in August 2019. It is responsible for biosafety at sitem-insel and the ifik and advises both university institutes as well as partner institutions on questions related to biosafety. It offices are situated in the sitem-insel building. It will also conduct active biosafety research.

Kümin D., Gsell Albert M., K. Summermatter: Applied Biosafety 2019: Volume: 24 issue: 4, page(s): 200-206.



Biosafety Center, "Open House" day sitem-insel, 30 August 2019

# Institute of Pathology

Murtenstrasse 31, 3008 Bern www.pathology.unibe.ch



Aurel Perren Director



Alessandro Lugli Christoph Müller Inti Zlobec Clinical Pathology



Experimental Pathology



TRU

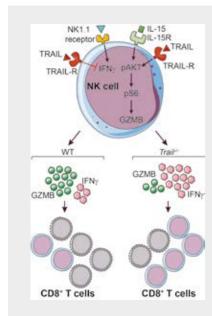
# **Profile**

- Teaching students of medicine, dental medicine, pharmacy, biomedicine and biology as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB)
- 10 research groups in experimental and clinical pathology
- External Partners: Institute of Pathologie University Hospital Basel; Helmholz-Zentrum München, Germany; University Children's Hospital Zürich; Division of Hematology, University Hospital Zürich; University of Calgary, Canada; Southwestern Medical Center, Dallas, USA; Universitätsklinikum Essen, Germany; Brigham Young University, Provo UT, USA; Institute of Pathology, Technisches Universität München, Germany; Université Libre de Bruxelles; University of Ghent; Institute of Molecular Systems Biology, ETH Zürich; Department of Biomedicine, University of Basel; Roche Pharma Research & Early Development F. Hoffmann-La Roche Ltd, Basel; Stanford University Medical Center, USA; Surgery Department, San Raffaele, Milan, Italy; Department of Pathology, Hostpital Beaujon, Clichy, France; University College London, UK; University of Pittsburgh Medical Center, Pennsylvania, USA; Department of Dermatology, CHUV, Lausanne; Department of Medicine Harbor-UCLA Medical Center, Los Angeles Biomedical Research Institute; Dpt. of Biology, University of Fribourg; Centre de Recherches en Cancérologie de Toulouse-CRCT, Toulouse, France; Ospedale Regionale di Lugano, Lugano

# **Grants**

- Swiss National Science Foundation (9x)
- Uniscientia Stiftung
- Peter Hans Hofschneider Stiftung für Experimentelle Biomedizin
- Wilhelm Sander Stiftung
- Swiss Cancer Research/Swiss Cancer League (5x)
- SAKK

# Highlights



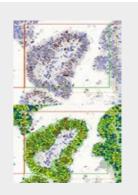
# A new pathway to "reprogram" killer cells

The so-called natural killer (NK) cells are cells of the innate immune system that recognize and eliminate infected cells or cancer cells. During a virus infection, NK cells also keep the body's own immune cells such as the T cells at bay to avoid excessive killing of intact body cells. Cardoso Alves et al. found a novel function of the death molecule TRAIL. NK cells without TRAIL sense various signals from their environment differently: they react more strongly to a signal that causes them to release more of the messenger molecule interferon (IFN)y. Yet NK cells lacking TRAIL are less susceptible to another trigger that leads them to release the cell toxin granzyme B (GZMB). Consequently, mice without TRAIL have more protective CD8+ T cells and are therefore better able to remove virus-infected cells (<a href="www.embopress.org/doi/10.15252/">www.embopress.org/doi/10.15252/</a> embr.201948789).

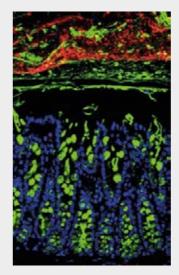
TRAIL programs NK cells by blocking the production of inflammatory messengers (IFN<sub>V</sub>) but promoting the formation of cell toxins (GZMB). NK cells lacking TRAIL produce more IFNy but less GZMB, which results in greater antivirus CD8+ T cell response in infected mice.

# Development of ngTMA pipelines

We investigate the role of machine and deep learning in addressing clinically relevant research questions, predominantly in gynecological and colorectal cancers. Pipelines for handling data from next-generation Tissue Microarray (ngTMA®) construction to assessment of immunostaining and integration of scores with clinical, histopathological and other research data for statistical analysis are performed by the group. We create and implement tools for quality control and optimization of digital workflows and apply these tools as a basis for our clinically oriented biomarker studies.



Example of digital p53 analysis in an endometrial cancer within an ngTMA experiment



# Changes in local immune cells during onset vs. remission of colitis

Understanding the mechanisms that drive remission induction and maintenance in the intestine is critical for a rational treatment of patients with inflammatory bowel diseases. We have recently established a reversible, relapsing-remitting mouse model of colitis with reproducible onset of colitis and induced remission (Brasseit et al., Mucosal Immunol 2016). In this model we monitor the composition of the intestinal microbiota during relapsing – remitting colitis and define its consequences on the metabolic profile in the feces and the host. Furthermore, we investigate how these changes influence the host immune response and vice versa at a single cell level. An ultimate goal is to identify strategies to specifically extend the remission period, or even prevent further relapses of the disease.

In the healthy intestine, luminal bacteria are separated by a mucus layer (green) from the intestinal epithelium (blue), containing mucus-secreting goblet cells (green) and the lamina propria, containing numerous immune cells

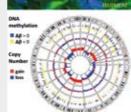
# Understanding the role of autophagy in retinoic acid therapy of breast cancer

associated fibroblasts influence cancer autophagy and therapy efficiency.

Epithelial-to-mesenchymal transition (EMT) plays a key role in therapy-resistance and metastasis formation. In the present study, we therefore aim at reversing the EMT phenotype of breast cancer cells using differentiation-based therapy based on all-trans retinoic acid (ATRA). Cellular differentiation is often associated with upregulation of autophagy. Autophagy is a lysosomal degradation and recycling system and may supports cellular differentiation by removing superfluous organelles, keeping energy levels or by regulating signalling by selective removal of proteins. Therefore, we study autophagy functions during therapy-induced MET and how modulation of autophagy can support differentiation-based therapy. Furthermore, we investigate how cancer



Cancer-associated fibroblasts co-cultured with SKBR3 breast cancer cells (green). Staining: autophagy marker LC3B (red).



# Role of DAXX and ATRX in PanNET

Almost, half of Pancreatic Neuro-endocrine Tumors (Pan NETs) showloss of expression of DAXXor ATRX. We could show that DAXX/ATRX loss correlates with an increased risk of metastasis.DAXX and ATRX negative tumors show chromosomal instability and ALT (Alternative Lengthening Telomeres) activation, a mechanism for telomeres length maintenance. We focus on unraveling the mechanism underlying this new cancer-associated pathway using in vivo mouse model, in vitro cell culture and ex-vivo human patient tissues. We specifically focus on the role of epigenetic changes occurring in DAXX/ATRX negative PanNETs.

Heterogeneous telomeric size as hallmark of ALT positive cells. Circos plot depicting different DNA methylation and chromosomal instability in DAXX/ATRX negative and positive PanNETs.

# Institute of Forensic Medicine (IRM)

Bühlstrasse 20, 3012 Bern www.irm.unibe.ch



Prof Christian Jackowski Director



Prof. Wolfgang Weinmann Deputy Director Forensic Forensic Toxicology Psychiatric and Chemistry



Prof Michael Liebrenz Services



PD Dr. Sandra Lösch Physical Anthropology

Pfäffli



Dr Matthias PD Dr Antoine Roggo Traffic Medicine Medical Law



Schvma Forensic Medicine and Imaging (F&E)





Forensic Molecular Forensic Medicine Biology and Imaging (DL)

# **Profile**

- Seven departments conducting research projects within the context of forensic sciences
- External fundings for the department of Forensic Medicine and Imaging, the department of Forensic Toxicology and Chemistry, the department for Physical Anthropology and the Forensic Psychiatry Service
- World leading in forensic physics and ballistics, forensic imaging and alcohol consumption markers
- · Successful performance of forensic genetic projects, traffic medicine projects and forensic psychiatry projects
- · Training and continuing education of students of medicine and jurisprudence, medical personnel and the institutions of the administration of justice and the police
- External Partners: Institute of Legal Medicine, University of Bonn; Center for Medical Image Science and Visualization, CMIV, Linköping University, Sweden; Institute of Forensic Medicine, University Medical Center Freiburg; Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital, University of Zürich; Netherlands Forensic Institute, Den Haag; Department of Forensic Anthropology, Center of Forensic Medicine, Medical University of Vienna, Austria; Max Planck Institute for the Science of Human History, Jena

# **Grants**

- Swiss National Science Foundation (grant No. CR31I3L\_157024; 320030\_179466/1)
- "Opioid maintenance therapy (OMT) in Belarus and Switzerland a multistep project to enhance methodological knowl edge and strengthen competencies in the further education of young scientists and physicians in the area of OMT", Swiss State Secretariat for Education, Research and Innovation (SERI) and Swiss Science and Technology Cooperation (SSCT)
- "Attitudes and beliefs of Swiss stakeholders towards patients with alcohol use disorder in Switzerland: comparison be tween primary care, specialists, insurance, and legal experts", Swiss Foundation for Alcohol Research Grant Program (SSA)

# **Highlights**

#### Forensic Science International: Mind and Law

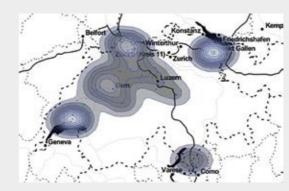
A new journal within the Forensic Science International family was launched with the aim of promoting the interdisciplinary exchange of ideas between psychiatric, psychological, legal, and other related fields within the forensic spectrum and beyond. «Forensic Science International: Mind and Law» will be edited by Michael Liebrenz, department of forensic psychiatry, and focus on mental disorders and how the sufferings of those affected are dealt with in the legal context in different regions of the world.



# A new comprehensive Swiss dataset for forensic genetics

In the past, forensic genetics in Switzerland suffered from a lack of comprehensive data. To fill this gap, we established a biobank, systematically collected throughout the whole country including a population sample from Ticino. We then established autosomal allele frequencies for the 23 most commonly used STR loci. Statistical evaluation of the data revealed only small genetic differences among regional subpopulations and among language subgroups. The autosomal allele frequencies can therefore be used for forensics and paternity / kinship testing as a valid nationwide dataset.

Zieger M, Utz S. A "forensic biobank" to establish comprehensive genetic frequency data for Switzerland, Forensic Sci Int Genet 40 (2019):46-51



"Forensic biobank": sample distribution

# Foundamental research in wound **ballistsics**

The formation of the temporary cavity (TC) in 12 cm long 10% gelatine cubes was recorded using high-speed-video. This was compared to cross sectional analysis of the cracks left by the TC in gelatine. However, the profiles of the TC in highspeed video did not correspond to the destruction found in gelatine. Moreover, neither the damage in gelatine nor the profile of the TC did reflect the deceleration of the bullet. But TC and damage in gelatine correlated with the energy deposited. The elastic behaviour of the target model might be the cause of this observation.

Schyma C (2020). Ballistic gelatine-what we see and what we get. International journal of legal medicine. Int J Legal Med. 2020 Jan; 134(1):309-315.



Deforming bullet (.32 auto) causing a pear-like shaped temporary cavity

# Multidisciplinary research on human remains from international excavations

Egypt, Turkey, Russia, and Madagascar - the team of the Department of Physical Anthropology joins international excavations every year providing their expertise on human remains to different research projects. The remains come from single or multiple graves, as skeletons or mummies, from burial mounds or rock-cut chambers and cover a time span from pre-roman to early

modern period. Apart from a thorough morphological investigation, samples for radiocarbon dating, stable isotope and ancient DNA analysis are taken in the field enabling interdisciplinary studies on diet, provenance, population genetics and kinship of the deceased.

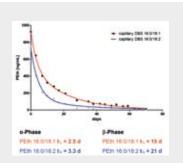
Haddow SD, Tsoraki C, Vasic M, Dori I, Knüsel CJ, Milella M. (2019). An analysis of modified human teeth at Neolithic Çatalhöyük, Turkey. Journal of Archaeological Science: Reports 28:102058.



Early medieval skulls from the excavation at the burial mound of Tunnug, Tuva Republic, Russia

# Monitoring of direct alcohol markers

Direct and indirect biomarkers are widely applied for the determination of alcohol consumption. They help to assess past or present alcohol consumption. In this study, different sampling strategies for the intermediary long-term marker phosphatidylethanol (PEth) were evaluated. Volumetric capillary DBS sampling for PEth is a simple and useful tool for compliance monitoring. Luginbühl M, Weinmann W, Butzke I, Pfeifer P. Monitoring of direct alcohol markers in alcohol use disorder patients during withdrawal treatment and successive rehabilitation. Drug Test Anal. 2019 Jun; 11(6):859-869.



Biphasic elimination

# Institute of Dental Medicine (ZMK)

Freiburgstrasse 7, 3010 Bern www.zmk.unibe.ch, www.facebook.com/zmkbern



Prof Anton Sculean Executive Director and Director of the Clinic of Periodontology



Chappuis

Surgery and

Stomatology

Prof Vivianne Buser Director of the Clinic of Oral



Prof em Daniel Director of the Clinic of Oral Surgery and Stomatology



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



Prof Urs Brägger Director of the Clinic of Reconstructive Dentistry and

Gerodontology



Schimmel Head of the Division of Gerodontology

# **Profile**

• Undergraduate dental curriculum (for 3rd, 4th and 5th year students) with theoretical and practical courses

Prof Hendrik

Director of

the Clinic of

Restorative.

Preventive

Dentistry

and Pediatric

Meyer-Lückel

- Postgraduate curricula (3–4 years) leading to specialty and / or MAS degrees
- Continuing Dental Education Master Courses
- Fundamental, translational and clinical resarch covering most aspects in dentistry
- WHO Collaborating Centre for Epidemiology and Community Dentistry, Milan, Italy; Department of Cariology, Institute of Odontology, Salhgrenska Academy, University of Gothenburg, Sweden; Department of Operative Dentistry, Periodontology and Preventive Dentistry RWTH Aachen, Germany; Department of Odontology, School of Dentistry, University of Copenhagen, Denmark; University of Texas Health, USA; University of Oslo, Norway; University of São Paulo - FOUSP / FOB, Brazil; Indiana University, USA; Federal University of Minas Gerais, Brazil
- The Department of Reconstructive Dentistry provides the following range of treatment: Treatment planning and prosthetic restoration; Interdisciplinary collaboration with other departments for complex cases; Computer-assisted all-ceramic crowns, bridges or long-term temporary restorations (CAD/CAM); Advice and prosthetic treatment for implant patients; Optimization of dental esthetics
- The Division of Gerodontology offers synoptic dental treatment for the elderly and frail taking into account their individual wishes and needs. It provides also service to the community in three outreach clinics

# **Grants**

- Endowed professorship for preventive dentistry and oral epidemiology of the Lutz Zürrer Foundation
- Swiss Government Excellence Scholarships for Foreign Scholars and Artists (ESKAS Scholarship; 2018.0515)
- Research Internships Abroad São Paulo Research Foundation (BEPE–FAPESP; 2019/08437-5)

# **Highlights**



# Resin infiltration to mask caries lesion

In this clinical study we found resin infiltration technique a very useful method to mask caries lesions having developed during treatment with fixed orthodontic appliances. Colour changes while re-wetting the lesions with ethanol seem to be a valuable indicator for the number of required

Kobbe C, Fritz U, Wierichs RJ, Meyer-Lueckel H.: J Dent 2019; 91: 103243.

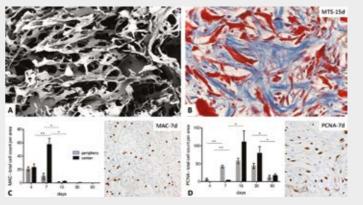
Caries lesion before and after caries infiltration

# Laboratory for Oral Molecular Biology

Van der Woude syndrome (VWS; OMIM # 119300) is an autosomal dominant condition and represents the most common syndromic form of orofacial clefts with a prevalence of 1/35'000 to 1/100'000 newborns. We are interested in a VWS patient, who harbors a novel undescribed disease-causing IRF6 mutation. Currently, we are establishing genotype-phenotype correlations using VWS patient-derived keratinocytes and over-expression systems of the pathogenic VWS-associated variant. Ultimately, our research will result in a better understanding of the pathogenesis of VWS and of IRF6 gene function.

(A) VWS patient with typical characteristics: cleft lip/palate and lip pits in the lower lip. (B) Genetic analysis revealed a novel undescribed pathogenic IRF6 (IRF6 VWS) mutation in the conserved protein binding domain (SMIR/IAD) resulting in a truncated IRF6 protein. (C) Forced expression of IRF6\_VWS shows weaker expression of the mutated protein compared to the IRF6 wild type (wt).





# **Research on Tissue Integration** of Biomaterials

A preclinical study of a novel collagen-based biomaterial used for soft tissue augmentation has shown a short inflammatory phase and rapid ingrowth of blood vessels and proliferating mesenchymal cells leading to fast tissue integration. These data form the biologic rational for the clinical application of this biomaterial for soft tissue augmentation around teeth and dental implants.

- (A) SEM image illustrating the porous structure of the biomaterial; (B) Filling of the pores after 15 days;
- (C) Quantitative and qualitative results of macrophage (MAC) labeling;
  (D) Quantitative and qualitative results of cell proliferation (PCNA labeling). MTS = Masson's trichrome staining.

# Laboratory of Oral Microbiology

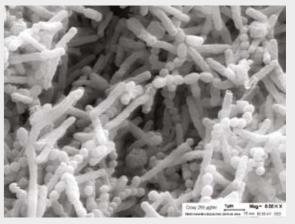
Grants: Innosuisse 26940.1 PFLS-LS

The laboratory evaluates in vitro new treatment options for periodontal and peri-implant therapy. Both standard microbiological methods as well as different biofilm models are used. A collaborative study of the three Swiss university laboratories of oral microbiology (Basel, Bern, Zurich) was finalized which determined antibiotic resistance incl. the mechanisms behind in two periodontopathogens.

Kulik et al., Antibiotics (Basel) 2019;8(4). pii: E253. doi: 10.3390.

Further, in vitro the effect of Porphyromonas gingivalis and its cysteine proteases (gingipains) on epithelial cell adhesion to titanium-zirconium alloy surfaces (a dental-implant surface) was investigated in collaboration with universities in Krakow (Poland) and Malmö

Eick et al. J Biomed Mater Res B Appl Biomater. 2019 Nov;107(8):2549-2556.



Bacteria in biofilm after exposure to 256 ug/ml doxycy-

# Institute of Primary Health Care (BIHAM)

Mittelstrasse, 43, 3012, Bern www.biham.unibe.ch



Prof Nicolas Rodondi Director



Prof Arnaud Chiolero Deputy Director



Prof. Reto Research



Dr. Cinzia Del Giovane Methodology and Biostatistics Coordination



Dr Martin

Research

Feller

Dr. Roman Teaching



Prof Sven Streit Career Development and Networking



Dr Flisavet Moutzouri Research Coordination

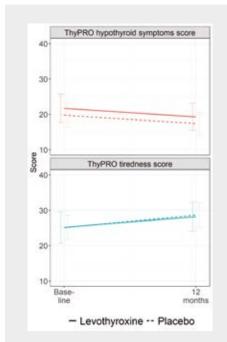
# **Profile**

- Training next generation of primary care physicians, medical students, researchers and teachers in primary care
- Research in primary health care and in primary health care, epidemiology and public health
- Promote evidence based, high value, safe and patient centered health care
- Strengthen the development of primary care at cantonal and national level
- External Partners: Department of Primary Care and Public Health, Leiden University Medical Center, The Netherlands; Department of Medicine & Epidemiology and Biostatistics, UCSF, CA, USA; Department of Epidemiology, McGill University, Montreal, Canada; Institute of Health Policy, Management and Evaluation University of Toronto, Canada; The Thyroid Studies Collaboration on 5 continents, University General Medicine and Public Health Centre (Unisanté), Lausanne University, Switzerland; Institute of Primary Care Zurich, University of Zurich, Switzerland; Italian Cochrane Centre, University of Modena and Reggio Emilia, Modena, Italy

# **Grants**

- OPERAM European Union's HORIZON 2020 (grant agreement 634238)
- Swiss National Science Foundation (grant No. 320030\_172676; NFP74 407440-167465; NFP74 407440\_167519; )
- SGAIM Foundation (LESS; SIGNATURE)
- ESTXENDS SNSF (IICT 33IC30\_173552), Swiss Cancer Research (KFS4744-02-2019), Tobacco Prevention Found (TPF 19.017477)
- Claims data colorectal cancer Swiss Cancer Research (HSR-4366-11-2017)

# Highlights



# No benefit of levothyroxine treatment in subclinical hypothyroidism among older adults aged 80 years and over

Subclinical hypothyroidism (SHypo), a mild dysfunction of the thyroid, is a common condition particularly among older adults. It is often treated with levothyroxine, but evidence for older adults is lacking. Among 251 adults aged 80 years and older with Shypo randomized to treatment with levothyroxine or placebo, we found that compared to placebo, treatment with levothyroxine was not associated with improvement in hypothyroid symptoms or fatigue. As mentioned in the Editorial linked to our trial, these results do not support treatment with levothyroxine in older adults with

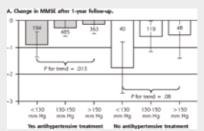
Mooijaart SP et a., JAMA 2019 Oct 30:1-11. doi: 10.1001/ jama.2019.17274.

Hypothyroid symptoms and tiredness scores at baseline and after 12 months of treatment with levothyroxine (solid line) or placebo (dashed line). Higher scores indicate more symptoms (range 0 – 100).

# The lower the better? Data on cognitive decline in multimorbid elderly patients and systolic blood pressure

Hypertension trials often exclude patients with multimorbidity and lack generalizability. We aimed in a Dutch cohort of >1'200 eldlerly patients to determine if systolic blood pressure (SBP) in patients undergoing antihypertensive treatment is associated with 1-year changes in cognitive/daily functioning or quality of life (QoL) in persons aged ≥75 years with or without complex health problems. We found an association between low SBP (<130mmHg) and more cognitive decline in those who were treatet with antihypertensive medication, and stronger among those with complex health problems. Our results suggest that SBP thresholds for treatment should be redefined, especially for frail older persons.

Streit S et al., Annals of Family Medicine 2019.

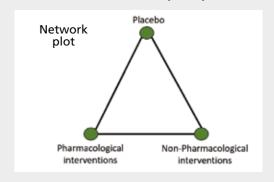


Associations between systolic blood pressure, antihypertensive treatment, and change in function after a 1-year follow-up

# The feasibility of Network Metaanalyses of Pharmacological and **Non-Pharmacological Interventions** in Psychiatry is challenging

The way how network meta-analyses (NMA) of pharmacological and non-pharmacological interventions in psychiatry are methodologically conducted is challenging. This could compromise their validity. In our meta review of 12 published NMAs, we found that the major issues are a) the definition and classification of the control node in the geometry of the network, b) differences in baseline participants' characteristics (i.e. previous medication exposure), study risk of bias and the level of masking between studies with pharmacological and non-pharmacological interventions.

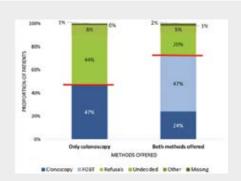
Del Giovane C et al., JAMA Psychiatry 2019.



# More refusals of colorectal cancer screening when only colonoscopy offered among patients in primary health care

Guidelines recommend primary care physicians (PCPs) offer patients a choice of colorectal cancer (CRC) screening methods. However, PCP screen mostly patients with colonoscopy and few screen with fecal occult blood testing (FOBT). We conducted a cross-sectional data collection among PCPs. 91 PCPs collected data on 3,637 50-75-yearold patients. PCPs who only offered colonoscopy had lower screening rates (47% vs. 71%) and higher refusal rates (44% vs. 20%) than PCPs who offered both methods. Encouraging PCPs to offer both methods could reduce the number of refusals and raise CRC screen-

Martin Y et al., J Gen Intern Med. 2019: 34(8), 1409-1411.



Decision patterns among patients who had a discussion on CRC screening (N patients = 770) and included by PCPs who only prescribed colonoscopy (N = 33) vs. PCPs who prescribed both colonoscopy and FOBT (N = 58), in the Sentinella Network in 2017



Thyroid gland

# New guidelines published with the BIHAM in the British Medical Journal (BMJ) recommend against the use of thyroid hormones in adults with subclinical hypothyroidism

SHypo is often treated with thyroid hormone therapy, despite weak evidence of benefits. In 2018 we published in JAMA a meta-analysis including more than 2'000 participants, showing no clinical benefit of thyroid hormone therapy in patients with SHypo. Based on that, we published new guidelines with the international MAGIC network in the BMJ, advising against the use of thyroid hormones in most adults with SHypo. Bekkering GE et al. BMJ 2019, 14;365:l2006.

# Institute of Complementary and Integrative Medicine (IKIM)

Inselspital, Freiburgstrasse 46, 3010 Bern; von Roll Campus, Fabrikstrasse 8, 3012 Bern www.ikim.unibe.ch



Director





Baumgartner Deputy Director



PD Dr Stephan PD Dr Johannes Fleckenstein

# **Profile**

- 3 research groups
- Teaching students of medicine and dental medicine
- Patient centered translational and clinical research in complementary and integrative medicine; investigating pharmacological and and non-pharmacological therapies, developing of new methodology
- Investigation of efficacy, effectiveness and mode of action of pharmaceutical preparations as used in Complementary and Integrative Medicine
- Investigation of underlying physiological mechanism; implementation of Chinese Medicine / Acupuncture technique into clinical routine
- External partners: Paracelsus Spital Richterswil, Switzerland; Hospital of Fribourg (HFR), Switzerland; Swiss Group for Clinical Cancer Research SAAK, Breast Cancer Group, Switzerland; EMPA, St. Gallen, Switzerland; NTB Buchs, Switzerland; Neuchâtel Platform of Analytical Chemistry, University of Neuchâtel, Switzerland; Society for Cancer Research, Arlesheim, Switzerland; Children's Hospital of Eastern Switzerland, St. Gallen, Switzerland; Institute of Integrative Medicine, University of Witten/Herdecke, Germany; Department of Sports Medicine, Goethe-University Frankfurt, Germany; Department of Clinical Pharmacology, University of Regensburg, Germany; Department of Anaesthesiology, University of Greifswald, Germany; ISS Inc.y Champaign, IL, USA; Multidisciplinary Laboratory of Pharmaceutical Sciences, Faculty of Pharmacy, Federal University of Rio de Janeiro, Brazil

#### **Grants**

- Swiss National Science Foundation: SNF Bridge Discovery 20B2-1\_180983 / 1 and 32473B\_162717
- Swiss Cancer League, Cancer Research Switzerland: 4259-08-2017
- Software AG Foundation (BA-P11425, SE-P12117, BA-P12916)
- University of Bern, UniBE Initiator Grant

# **Highlights**

# The Pulse-Respiration Quotient: A Powerful but Untapped Parameter for Modern Studies About Human Physiology and Pathophysiology

We describe why the PRQ is a powerful parameter that captures complex regulatory states of the cardiorespiratory system. We show that the PRQ (i) changes during human development, (ii) is time-dependent (ultradian, circadian, and infradian rhythms), (iii) shows specific patterns during sleep, (iv) changes with physical activity and body

posture, (v) is linked with psychophysical and cognitive activity, (vi) is sex-dependent, and (vii) is determined by the individual physiological constitution. We explain why and how the PRQ could be used for basic research on human physiology and for applications in medicine.

Scholkmann F, Wolf U. Front Physiol, 2019.

The Pulse-Respiration Quotient

# Swiss paediatrician survey on complementary medicine

Paediatricians attitude towards complementary medicine (CM) is positive, emphasised by great interest in CM training, a willingness to contribute to CM research and a high rate of paediatricians who use CM for themselves

and their families. The percentage of paediatricians offering CM is currently rather low despite strong demand for CM for children. This study provides key pointers for the future development of complementary and integrative medicine for children in Switzerland.

Huber BM, von Schoen-Angerer T, Hasselmann O, Wildhaber J, Wolf U. Swiss Med Wkly, 2019.

Swiss paediatrician survey on complementary medicine



Swiss paediatrician survey on complementary

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medicine

Original activity | Published No. June 2015 | 2010 octobury 2011 One time as: Towns Med 2001, 2019 545 w/2015

# Effects of integrative medicine pharmaceuticals in a fingerprint metabolomic analysis

We observed compelling evidence for specific effects of pharmaceuticals produced according to European Pharmacopoeia monograph 1038 (Praeparationes homoeopathicae) by a fingerprint metabolomic analysis in a highly controlled bioassay. We see this as a challenge to develop theoretical models to explain effects of such pharmaceuticals. Doesburg P, Andersen JO, Scherr C, Baumgartner S. Eur J Pharm Sci 2019: 137, 104987.

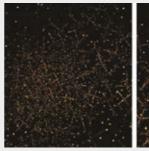
Circular radial region of interest (CRROI) of fingerprint metabolomic



# Impact of succussion on pharmaceutical preparations

We applied the Droplet Evaporation Method to investigate the effects of mechanical energy on phytopharmaceutical preparations. For all investigated preparations, significant differences were found between succussed samples and controls, calling for mechanistic studies to further characterize the effects induced.

Kokornaczyk MO, Würtenberger S, Baumgartner S. Sci Rep. 2020 Jan 17;10(1):570.





DEM image of succussed (right) and of unsuccussed (left) Echinacea extract

# Complementary medicine and its role in sports medicine

This review highlights the use and evidence for hands-on conservative pain treatments in athletes. Among complementary approaches it is neural therapy (injection techniques) providing best evidence. Acupuncture can be considered a Grade B recommendation.

Panel below: Journal article cover page. The abstract is bilingual adressing English and French

Fleckenstein and Banzer. Sci Spo 2019:34,e77-e100.



A review of hands-on based conservative treatments on pain in recreational and elite

Une revue des traitements conservateurs à visée antalgique chez les sportifs amateurs et professionnels

J. Fleckenstein a.b.c.\*, W. Banzer

Clinical Review

# Institute for Medical Education (IML)

Mittelstrasse 43, 3012 Bern www.iml.unibe.ch/en/iml



Dr. Sandra Trachsel Department Head MME

Dr. Kai Schnabel Department Head AUM

Prof. Sissel Guttormsen Director IML

Dr. Philippe Zimmermann Department Head

Prof. Sören Huwendiek Department Head AAE

# **Profile**

- Competence centre for medical education, serving the medical faculty in Bern and other medical schools and institutions nationally and internationally
- Contributing to innovative and sustainable development in medical education, supporting development of competency in health professionals aiming at optimal patient care
- Four departments: assessment and evaluation, teaching and media, IT-development and MAS Medical Education
- Investigating effectiveness of assessment and learning aids, innovative methods and fields of applications
- Developing tools for assessment and learning, complying with needs from digital transformation
- Partners: https://tinyurl.com/examic-partners, https://tinyurl.com/research-cooperations

### **Grants**

- EU-Project: «Developing, implementing, and disseminating an adaptive clinical reasoning curriculum for healthcare students and educators», Project coordinator: University of Augsburg, Project head: PD Dr. Inga Hege. Project partner IML: Prof. Sören Huwendiek, MME, Dr. Felicitas Wagner
- Swiss Cancer League: «Communication with cancer patients and their families about approaching death: Scaffolding conceptual and practical learning for health professionals.» Project head: Prof. Sissel Guttormsen. Project partner: Prof. Steffen Eychmüller, University Centre for Palliative Care (UCPC), Inselspital, University Hospital Bern
- Health 2030: «Precision Medicine frONtLINE a multi-support learning platform on Precision Medicine for the daily practice of frontline care professionals». Project head: Idris Guessous HUG/UNIGE. Co-Applicants: Prof. Sissel Guttormsen, Prof. Jacques Cornuz, Unisanté/UNIL, Prof. Gérard Waeber, CHUV/UNIL
- ERS (European Respiratory Society)/PhD-Grant: «How to improve continuing professional development to foster physician's competencies and patient treatment». PhD Advisor: Prof. S. Huwendiek, MME
- SGAIM: «Definition of Competencies for Attending Physicians in General Internal Medicine Departments in Swiss
  Hospitals: a multicenter qualitative study» SGAIM Foundation Award. Project partner: Dr. Christine Roten, MD, MME,
  Dr. Martin Perrig, MD, MME, Department of General Internal Medicine, Inselspital, University Hospital Bern, University
  of Bern, Dr. Christoph Berendonk, MD, MME, IML

# Highlights

# Professionalization of the work with simulated participants

Dr. med. B. Brem has been elected as Member of the Board of Directors of the Association of Standardized Patient Educators (ASPE). She will hold the position of Member Liaison for two years. ASPE engages in providing an international network for the new field of human simulation, develops "Standards of Best Practice" and basics for certification in working with simulated participants (SP).

# Research on effective health provider communication

Despite scientific breakthroughs, cancer remains the top two causes of death in Switzerland. So, "communication about approaching death" remains an important task for oncology professionals. We aim at supporting those professionals in performing such communication with confidence and positive impact for all involved. A new interactive eLearning module supports a blended learning approach and practical, safe training. Learning effects are investigated with RCT design. Partners: Palliative Care Unit, Inselspital; Swiss Cancer League.

https://tinyurl.com/project-swiss-cancer-league.



Communication is a key competence

# The IML is committed to interprofessionalism

Healthcare professionals face increasingly complex situations. One way to overcome this challenge is to improve interprofessional collaboration.

Together with the Bern Nursing Education Center and the Bern University of Applied Health Sciences, IML developed several interprofessional educational activities. Three of these were awarded by the Swiss Academy of Medical Sciences: https://tinyurl.com/Story-Interprofessionalism.



Practice cooperation in interprofessional teams (© Picture BZ Pflege and IML 2019)

# The IML participates in EU-project on clinical reasoning

Insufficient clinical reasoning (CR) skills are a major cause of cognitive errors in patient care. Yet, there is a lack of explicit teaching of CR in the training of healthcare professionals. To close this gap, an EU-wide project has been launched in which the University of Bern will work together with European partner universities and institutions to develop a CR-curriculum and a train-the-trainer course for lecturers.

https://tinyurl.com/Clinical-decision-making



Strengthen teaching of CR

# Supporting Clinical Skills Training with new videos

To manage the increasing number of students, Clincal Skills Training (CST) in the 3<sup>rd</sup> year was substantially redesigned. Students now exercise Clinical Skills CST in examing their peers before they practice on real patients. To support that the students are performing the tasks correctly, videos demonstrating the CST-Tasks were produced by the AUM. The video-production was supported by students and experts of the different clinical disciplines. IML's new video studio and team supports the high quality of the videos.



Examination of lymph nodes (© Picture IML 2019)



# Clinics at the University Hospital, Inselspital

Department of Anaesthesiology and Pain Medicine

Department of Angiology

Department of Cardiology

Department of Cardiovascular Surgery

Department of Clinical Chemistry

Department of Cranio-Maxillofacial Surgery

Department of Dermatology (DERK)

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

Department of Diagnostic and Interventional Neuroradiology

Department of Diagnostic, Interventional and Pediatric Radiology (DIPR)

Division of Magnetic Resonance Spectroscopy and Methodology (AMSM)

Department of Emergency Medicine

Department of ENT, Head and Neck Surgery

Department of General Internal Medicine

Department of Geriatrics

Department of Hematology and Central Hematology Laboratory

Department of Infectious Diseases

Department of Intensive Care Medicine

Department of Medical Oncology

Department of Nephrology and Hypertension

Department of Neurology

Department of Neurosurgery

Department of Nuclear Medicine

Department of Obstetrics and Gynecology

Department of Ophthalmology

Department of Orthopedic Surgery and Traumatology

Department of Osteoporosis

Department of Pediatrics

Department of Pediatric Surgery

Department for Plastic and Hand Surgery

Department for Pulmonary Medicine

Department of Radiation Oncology

Department of Rheumatology, Immunology and Allergology (RIA)

Department of Thoracic Surgery

Department of Urology

Department for Visceral Surgery and Medicine

# Department of Anaesthesiology and Pain Medicine

Inselspital, INO D, 3010 Bern www.anaesthesiologie.insel.ch



Prof Frank Stüber Director and



PD Dr. Lutz Lehmann Vice Chair



Prof Robert Greif Head of Education



PD Dr. Martin Luginbühl Chair Spital Tiefenau



Reto Thomann Head of Nursing



PD Dr. Markus Head of Research

# **Profile**

- Not only did we contribute to our 60 resident physicians' clinical skills and their knowledge of good clinical practice, but we were proud to have succeeded in lighting the fire of research in a number of them
- We continued our tradition of organising courses and symposia for certified anaesthesiologists, as well as overseeing the many successfully completed medical master and doctoral theses
- Reflecting the role of modern anaesthesiology as a provider of services for patients and surgeons alike, we conducted research in a broad range of topics
- Our close clinical ties to our surgical and interventional partners allowed us to address this interdependence in our research projects.
- Our goal was to contribute significantly to precision medicine in the fields of anaesthesiology and perioperative care, both nationally and internationally.
- We collaborated with partners in the US, Germany, France and Canada, as well as with 6 other Inselspital departments

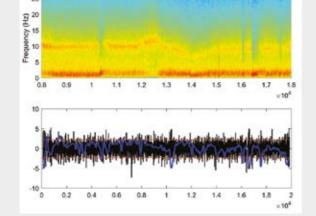
#### Grants

- European Society of Anaesthesiology (two grants, to PD Dr. Dominik Guensch & Dr. Kady Fischer)
- Gottfried and Julia Bangerter-Rhyner Stiftung, Basel, Switzerland (PD Dr. Heiko Kaiser)
- Velux Stiftung, Zurich, Switzerland (Prof. Dr. Patrick Wüthrich)

# Highlights

# Alpha power loss during general anaesthesia

EEG activity in the extended alpha frequency range (7-17 Hz) during maintenance of general anaesthesia is primarily determined by effect-site concentrations of the hypnotic and analgesic drugs used. Intermittent alpha loss during surgery could represent arousal of the cortex because of increased surgical stimulation. With a generalised linear model fitted to alpha power recorded from patients undergoing general anaesthesia from induction until waking using three variables, we showed that alpha power dropouts occurred in 73 of the 237 patients. Multivariate analysis showed that alpha dropouts were significantly associated with body cavity surgery and longer operations. This loss of alpha power, unexplained by changes in anaesthetic or opioid concentrations, is suggestive of thalamocortical depolarisation induced by body cavity noxious stimuli, and could provide a measure of nociception during surgery. Hight DF et al. Br J Anaesth 2019: 122, 635-642.



EEG during general anaesthesia showing alpha

# Achieving gender parity in acute care medicine

In this review article we bring together articles from business and human resource sciences, recommendations for involving women in leadership and gender diversity programs, and the experience and knowledge of women in leadership positions, in an attempt to move toward Sheryl Sandberg's vision of a world in which "there will be no female leaders – there will just be leaders". This approach will enable lasting and meaningful progress toward a universal standard that will work to the benefit of everyone. Fisler N. Anesth Analg 2019: 129, 1778-1783.



# A nationwide survery

Ultrasound has significantly increased safety and effectiveness in regional anaesthesia. Our nationwide survey including all active members of the Swiss Society for Anaesthesiology and Resuscitation (SSAR/SGAR) revealed that dual guidance appears to be the preferred approach for safely localizing nerves for PNB in Switzerland.

Luedi MM et al. Sci Rep. 2019: 9, 9178.

# Implementing Mini-CEX and DOPS for postgraduate medical trainees

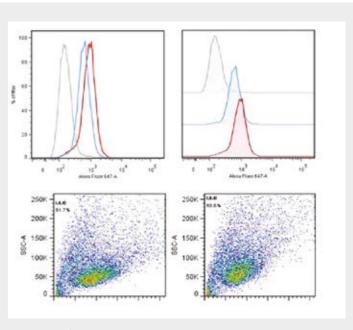
The way in which educational tools such as the Mini-Clinical Evaluation Exercise (Mini-CEX) and Direct Observation of Procedural Skills (DOPS) are implemented is of key importance, but many factors influence their implementation. We aimed to develop a comprehensive analysis of such factors and found 13 relating to four categories: organizational culture (e.g. value of teaching and feedback), work structure (e.g. time for Mini-CEX and DOPS, faculty development), instruments (e.g. content of assessment), and users (e.g. relationship between trainees and supervisors), and their interaction.

Lörwald et al. Med Teach 2019: 41, 448-456.

# ERK and p38 contribute to the regulation of nociceptin and the nociceptin receptor in human peripheral blood leukocytes

Mechanisms involved in the regulation of nociceptin and its receptor (nociceptin opioid peptide receptor, NOP) in response to inflammation and pain in humans are insufficiently studied. We investigated specific signaling pathways contributing to the regulation of nociceptin and NOP in human peripheral blood leukocytes and found that ERK and p38 are two major signaling pathways regulating nociceptin and its receptor in human peripheral blood leukocytes under inflammatory conditions.

Zhang L et al., Mol Pain 2019: 15.



FACS data of human leukocytes

# Department of Angiology

Inselspital, Freiburgstrasse, 3010 Bern www.angiologie.insel.ch/



Baumgartner Director



Prof Heinz Drexel Senior Consultant



PD Dr Alioscha Rastan Consultant Physician



PD Dr Marc Schindewolf Consultant Physician



until July 2019

Prof Christoph Dr lörn Thalhammer Dopheide Consultant Senior Physician Physician



Haine

Senior

Physician

Dr Axel

Dr Ulrike Hügel Senior

Physician

# **Profile**

- Teaching programs for students of medicine and sports-/ physiotherapists
- Regular student lectures and courses (clinical skills), weekly lectures (DHGE)
- Weekly internal education in the field of vascular medicine
- Multitude of divisional and interdisciplinary research projects
- Aim: To advance the field of vascular medicine
- Fundamental research as well as clinical trials
- Projects comprise analysis, classification and computational hemodynamic modeling of congenital vascular malformations, risk factor analysis and risk factor modulating therapies in peripheral artery disease, integration of omics technologies in research of vascular malformations and artherosclerosis expression, drug therapy and endovascular management of venous thromboembolism
- External Partners: Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria, University Hospital Basel, Department of Angiology, Basel, Switzerland, University Hospital Zürich, Department of Angiology, Zürich, Switzerland, University Hospital Munich, Institute of Epidemiology and Prophylaxis of Cardiovascular Diseases, Munich, Germany, University of Colorado Hospital, Heart and Vascular Center, Denver, Colorado, USA, University of Milan, Department of Pharmacological and Biomolecular Sciences, Milan, Italy, University of Cambridge, Cardiovascular Strategic Research Initiative Institution, Cambridge, United Kingdom, McGill University, Department of Human Genetics, Montreal, Canada

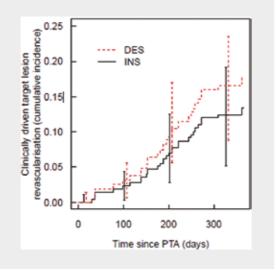
# **Grants**

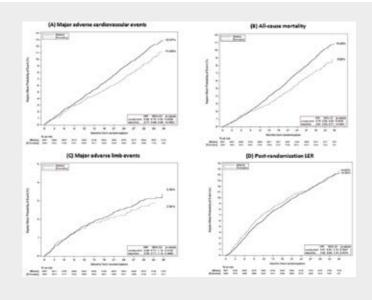
- Bangerter Rhyner Grant (Dr. Luise Adam)
- Förderungspreis Forschung 2019 der Union Schweizerischer Gesellschaften für Gefässerkrankungen (USGG): PD Dr. med. Marc Schindewolf

# **Highlights**

# Comparison of interwoven nitinol with drug-eluting stents for endovascular treatment of femoropopliteal artery disease

We analyzed efficiency of interwoven nitinol stents with drug-eluting stents for the femoropopliteal artery with regard to clinically-driven target lesion reintervention at 12 months in patients with symptomatic PAD. Data was prospectively collected. The results do not provide conclusive evidence to favor one stent over the other. Haine A et al., Eur J Vasc Endovasc Surg. 2019 Oct 25. pii: S1078-5884(19)31465-0. doi: 10.1016/j.ejvs.2019.09.002.





# **Sex-specific Differences in Risks** of Major Cardiovascular and Limb **Events in Symptomatic Peripheral Artery Disease**

The EUCLID trial showed no difference for either ticagrelor or clopidogrel, for reduction of major adverse cardiovascular events (MACE) and limb events in patients with symptomatic peripheral artery disease (PAD). We post-hoc analyzed sex-specific differences in these events. While women with PAD were at lower risk for MACE and all-cause mortality, risk for limb events was similar between sexes. Haine A et al., accepted for JACC publication 11/2019.

# Adherence to Statin Therapy Favours Survival of Patients with Symptomatic Peripheral Artery Disease (PAD)

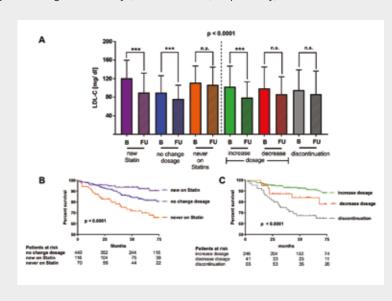
Patients with PAD are at a very high cardiovascular risk. Guidelines recommend a strict lipid lowering therapy with statins. However, adherence to statins is generally low. In our single center study we observed 691 symptomatic PAD patients. Those never receiving statins had a significant higher mortality rate (31%) compared to patients continuously on statins (13%) or new on statins (8%).

Moreover, patients on intensified statin medication had a low mortality of 9%, whereas those who terminated statin medication or reduced statin dosage had a higher mortality (34% and 20%, respectively).

Our data suggest that adherence to statin therapy is associated with reduced mortality in symptomatic PAD patients. A strategy of intensive and sustained statin therapy is therefore recommended.

Dopheide JF et al., accepted for publication in European Heart Journal - Cardiovascular Pharmacotherapy in Dec. 2019.

(A) Achieved mean LDL-C reductions depending on treatment incentives. (B) Kaplan-Meier survival curves of patients on and off statins. (C) Kaplan-Meier survival curves of patients with a switch in statin dosage.



# Broadening the categories of patients eligible for extended venous thromboembolism treatment.

VTE causes >500.000 deaths/year in Europe and the risk of recurrence after cessation of anticoagulation is up to 10%/year. Traditional treatment algorithms seem to be overly simplistic. More granular definitions of risk factor groupings, e.g. minor transient/persistent, environmental/non-environmental risk, in combination with new extended anticoagulation therapy options may provide refined management strategies for patients who commonly receive shorter-duration therapy.

Schindewolf M, Weitz Jl. Thromb Haemost. 2019 doi:10.1055/s-0039-3400302.

# Department of Cardiology

Inselspital, 3010 Bern www.kardiologie.insel.ch



Prof Stephan Windecker



Prof Lukas Hunziker



Prof Thomas

Räber



Prof Lorenz Prof Tobias Reichlin



Prof Markus

Schwerzmann

Prof Christian Seiler



Stortecky



Prof. Marco Valgimigli



Prof. Matthias



Pilarim

Wilhelm

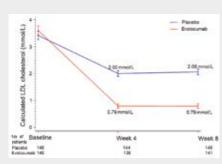
# **Profile**

- Teaching at multiple levels: clinical training, lectures for undergraduate and graduate students, supervision of MD, Master and PhD students
- Continuous medical education program
- Pre-clinical research (electrophysiology, arterial hypertension)
- Broad range of clinical research activities, ecompassing investigations of devices for the minimal-invasive treamtent of coronary artery disease and valvular heart disease; pharmacological therapies in patients with acute coronary syndromes; studies for the treatment of electrophysiological disorders as well as clinical trials of medicinal products.
- External partners: University and large hospitals in Switzerland and abroad, ETH, CSEM, industry

# **Grants**

- SNF Project "Efficacy of Permanent Internal Mammary Artery Occlusion in Stable Coronary Artery Disease: a Double-Blind, Randomized, Sham-Controlled Trial", Prof. C. Seiler
- SNF Project "Assisted reproductive technologies-induced alterations of the cardiac phenotype in mice and humans, underlying mechanisms and long-term consequences", PD Dr E. Rexhaj
- SWISSHEART Failure Network (SHFN) a Swiss Personalized Health Network (SPHN) Project (2018DRI14 PHRT122), Prof. S. Windecker
- SNF Project 32003B\_189077 Incidence of silent atrial fibrillation in patients with silent brain infarction Silent2 Study, PD Dr I Roten
- SNF-Spark "Value of transesophageal Phrenic Nerve Pacing" Dr. A. Häberlin

# **Highlights**



Change in LDL-C at week 4 and week 8 following the ACS (J Am Coll Cardiol.

# **EVOPACS Trial: PCSK-9 inhibitors to reduce LDL-C in** patients with Acute Coronary Syndrome (ACS)

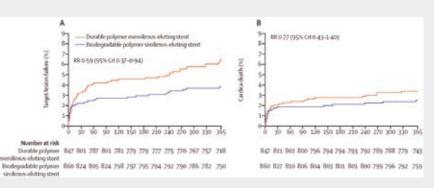
Decline of low-density lipoprotein cholesterol (LDL-C) levels effectively reduces the risk of adverse events in patients with established atherosclerotic cardiovascular disease. The clinical benefit of statins in improving clinical outcomes is proportional to the magnitude of LDL-C reduction and is more pronounced in patients with acute coronary syndromes (ACS) compared with stable coronary artery disease. A new randomized, multi-centric double-blind placebo controlled trial demonstrated the safety and the efficacy of a new PCSK-9 inhibitor on top of a therapy with statin to reduce the LDL level in patients with an ACS. Koskinas KC et al., J Am Coll Cardiol. 2019 Nov 19;74(20):2452-2462.

# **BIOSTEMI trial: Comparing two drug eluting stents**

Newer-generation drug-eluting stents that combine ultrathin strut metallic platforms with biodegradable polymers might facilitate vascular healing and improve clinical outcomes in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (PCI). The randomized, multi-centric investigator initiated trial in patients with acute myocardial infarction (STEMI) undergoing primary PCI indicated superiority of biodegradable

polymer sirolimus-eluting stents compared to durable polymer everolimus-eluting stents with respect to target lesion failure at 1 year. Iglesias JF et al., Lancet 2019 Oct 5: 394(10205) :1243-1253.

Time-to-event curves for target lesion failure (A), cardiac death (B) (The Lancet

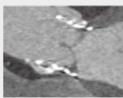


# SCOPE trial: Comparing two transcatheter aortic valve replacement systems

Transcatheter Aortic Valve Replacement (TAVR) represents an alternative treatment to surgery for patients with severe aortic valve stenosis. In this randomized, non-inferiority multi-centric international clinical trial, two commercially available TAVR devices were compared with regard to early safety and efficacy. The self-expanding device did not meet non-inferiority compared to the balloon expandable device. An early composite safety and efficacy endpoint was useful in discriminating the performance of the two devices. Lanz J et al., Lancet 2019 Nov 2; 394 (10209) :1619-1628.



A) Aortic valve leaflets thickening as a result of thrombi formation



B) Normal leaflets thickness following treatment with anticoagulants

Pictures: courtesy

# GALILEO / GALILEO 4D: Antithrombotic treatment after transcatheter aortic valve replacement

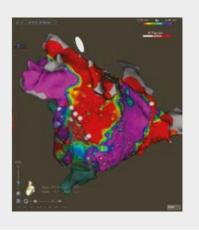
Following TAVR, medication to prevent thromboembolic events has to be balanced with the increased bleeding risk. A randomized, controlled trial has compared two strategies: an anticoagulation strategy based on factor Xa inhibition (Rivaroxaban) versus conventional therapy using platelet inhibition. The anticoagulation therapy was shown to be effective in reducing / dissolving the thrombus formation on the valve leaflets but the resulting increase in clinical risks (death, thromboemboli) led to the premature interruption of the trial.

De Backer et al., NEJM 2019, DOI: 10.1056/NEJMoa1911426. Dangas GD et al., NEJM 2019, DOI: 10.1056/NEJMoa1911425.

# Electrophysiology

The DEEP SEDATION study was started, an investigator initiated randomized controlled trial comparing Dexmedetomidine versus Propofol in the catheter ablation of atrial fibrillation. For ventricular tachycardia ablation, the novel approach of using stereotactic beam radiation therapy was newly implemented as an interdisciplinary project between the Divisions of Radio-Oncology, Radiology and Cardiology. In cardiac pacing, novel pacing modalities such as His-Bundle Pacing as well as leadless pacing are studied in clinical projects at the Inselspital as well as in translational projects in the SITEM.

Transvenous ablation on the mitral isthmus region of the left atrium



# Department of Cardiovascular Surgery

Inselspital, Freiburgstr. 18, 3010 Bern www.herzundgefaesse.ch



Prof. Thierry Carrel Director



Schmidli Deputy Director Head Physician



Englberger



Prof Dominik Obrist ARTORG Center for Biomedical Engineering, Head of

Cardiovascular

Engineering



Prof Alexander Kadner Consultant Physician, Surgery of Congenital

Heart Disease



PD Dr. Sarah

Longnus

Leader

PD Dr Florian Schönhoff Research Group Consultant Physician



Consultant Physician

# **Profile**

- Teaching at multiple levels: clinical training, lectures for undergraduate and graduate students, supervision of clinical and pre-clinical research work for MD, Master and PhD students
- Clinical and pre-clinical research: State-of-the-art research on multiple themes (eg. aortic pathologies, heart transplantation with donation after circulatory death, and cardiovascular fluid mechanics) is promoted through cooperation amongst clinicians, research scientists and biomedical engineers
- External partners: Integrated Actuators Laboratory Zentrum für künstliche Muskeln, EPFL Lausanne, Microcity Neuchâtel; Cardiac Surgery, University of Alberta, Edmonton, Canada; Department of Transplantation, Royal Papworth Hospital, Papworth Everard, Cambridge, UK; Laboratoire de Signalisation et Physiopathologie Cardiovasculaire, INSERM, Université Paris Sud, Université Paris Saclay, Châtenay-Malabry, France: St. Vincent's Hospital, University of New South Wales, Victor Chang Cardiac Research Institute, Sydney, Australia

#### **Grants**

- A collaborative platform for artificial muscles (collaboration with EPFL Lausanne & Nanocity Neuchâtel), Siemens Stiftung
- Prevention of paraplegia in thoraco-abdominal aneurysms PAPA-ARTiS, EU Horizon 2
- A publicly available collection of virtual and physical 3D models of congenital heart defects for surgical planning and training, Swiss Heart Foundation
- · Optimizing quality of cardiac grafts obtained with donation after circulatory death (DCD) using endothelial-targeted reperfusion strategies (Principal Applicant), Swiss Heart Foundation
- EXaCT: EXosomes based Combination Therapy to target multiple signaling within cardioprotective pathways (Co-Applicant) Swiss National Science Foundation (Project No. IZCOZ0\_182948)
- Role of mitochondrial damage-associated molecular patterns (mtDAMPs) in heart transplantation with donation after circulatory death (Principal Applicant), International Society for Heart and Lung Transplantation
- Cardioprotection with HOPE (Hypothermic Oxygenated PErfusion) in heart transplantation with Donation after Circulatory Death (Principal Applicant), Novartis Foundation for Biological-Medical Research

# Highlights



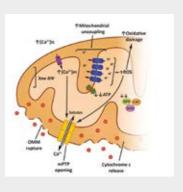
# Management of the aortic arch in patients with Loeys-Dietz syndrome

We present management strategies through a review of our clinical experience with the largest Loeys-Dietz patient population worldwide and a comparison with our experience in patients with Marfan

Schoenhoff FS, Alejo DE, Black JH, Crawford TC, Dietz HC, Grimm JC, Magruder JT, Patel ND, Vricella LA, Young A, Carrel TP, Cameron DE. Management of the aortic arch in patients with Loeys-Dietz syndrome. J Thorac Cardiovasc Surg. 2019; Sep 9. pii: S0022-5223(19)31737-4.

# Mitochondrial integrity during early reperfusion in an isolated heart model of donation after circulatory death

We report that mitochondrial dysfunction occurs with shorter periods of ischemia than those required to provoke contractile dysfunction and that mitochondrial function and circulating mitochondrial-related parameters can be used as specific indicators of cardiac ischemia-reperfusion injury. Wyss R et al., J Heart Lung Transplant 2019,38:647-57.



# Johanna Dürmüller-Bol DBMR Research Award and Jörg Vollmar-Prize from the German Society of **Vascular Surgery and Vascular Medicine**

Dr. Maria-Nieves Sanz was honoured for her research on mitochondrial-related inflammatory processes in heart transplantation. This is the second time that the Department of Cardiovascular Surgery was bestowed with this prestigious award in the last seven years.

The 2019 Jörg Vollmar-Prize from the German Society of Vascular Surgery and Vascular Medicine was awarded to Dr. Silvan Jungi. We report an estimated 4-year limb salvage of 84%, and excellent bypass patency rates despite poor runoff vessels. The considerable value and positive outcomes of open bypass surgery is emphasized. Jungi S et al., Eur J Vasc Endovasc Surg 2019,57:393-398.

# Symptomatic or aneurysmal aberrant subclavian arteries: results of surgical and hybrid repair

Surgical and hybrid repair provides satisfying results; however, the optimal procedure must be defined on an individual patient

Weiss S et al., Interact Cardiovasc Thorac Surg 2019:1-8.



# **Vertical Right Axillary Mini-Thoracotomy** for Correction of Ventricular Septal Defects (VSD) and Complete Atrioventricular Septal Defects (CAVSD)

Vertical right axillary mini-thoracotomy is a safe and effective approach for the repair of VSD and CAVSD in selected patient groups, and the outcome data appear comparable to those with median sternotomy. Heinisch PP et al., Ann Thorac Surg 2018;106:1220-8.



# Department of Clinical Chemistry

Inselspital, INO-F, 3010 Bern www.ukc.insel.ch



Prof Martin Fiedler Director



Prof Carlo Largiadèr Leichtle Deputy Director



Prof Alexander PD Dr Jean-Marc Nuoffer



PD Dr Ursula

Amstutz

PD Dr. Michaela

Fux

Nagler

PD Dr Michael

Masoodi

**Profile** 

- · Teaching students of medicine, biomedicine, bioinformatics, biochemistry, pharmacy, biology, epidemiology, as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB).
- 7 research groups
- Research focus: translational research, clinical research, and precision medicine
- Aim: to translate scientific knowledge into clinically useful bio markers and digital algorithms for more individualized
- Specific research topics: pharmacogenomics and drug metabolism, liquid biopsy, inherited metabolic diseases, clinical cytomics, thrombosis and haemostasis, and computational medicine
- External Partners: Canadian Pharmacogenomics Network for Drug Safety, University of British Columbia, Vancouver, Canada; Laboratory of Biometry, University of Thessaly, Greece; Department of Statistics and OR, Complutense University of Madrid, Madrid, Spain; Mayo Clinic Cancer Center, Mayo Clinic, Rochester, Minnesota, USA; Department of Medical Oncology & Hematology, Cantonal Hospital, St. Gallen, Switzerland; mitoNet (DACH-research Network for mitochondrial medicine); European Drug-Induced Agranulocytosis Consortium (EuDAC), Uppsala University, Uppsala, Sweden

# **Grants**

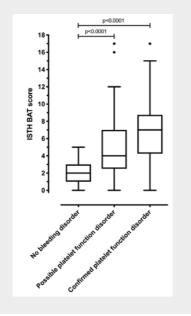
- Swiss National Science Foundation (grant No.310030- 163205; 31003A-160206; 310030-188762; 179334; BioLink 31BL30-185419; Spark CRSK-3\_190977 (co-applicant); Spark grant No:190686)
- Swiss Personalized Health Network: Project «L4CHLAB» (co-applicant)
- Fondation Johanna Dürmüller-Bol
- Hemmi-Stiftung (Forschungspreis 2019)

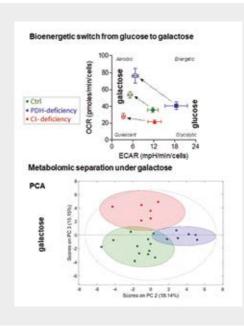
# Highlights

# The bleeding assessment tool of the ISTH is a useful diagnostic tool in patients with suspected platelet function disorders

Aiming to determine the diagnostic accuracy of the bleeding assessment tool (BAT) of the ISTH in clinical practice, we conducted a large prospective cohort study in 555 consecutive patients referred between 2012 and 2017 with a suspected bleeding disorder. Presence of a platelet function disorder was associated with substantially higher BAT scorings compared to patients without. Our data suggest that the ISTH-BAT provides a useful screening tool for patients with suspected platelet function disorders.

Adler, M. et al. Journal of Thrombosis and Haemostasis (2019) 17(7):1104-1112.





# Galactose based culture reveals distinct metabolic signatures in pyruvate dehydrogenase and complex I deficient human skin fibroblasts

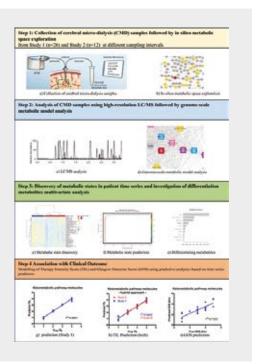
The bioenergetic profile of a cell influences the metabolism. Our results show that the switch from glucose to galactose based culture, leads to clearly distinctive bioenergetic profile of fibroblasts characterized by an increase in oxygen consumption (OCR) and decrease in extracellular acidification rate (ECAR). Further we could show that NMR metabolomic profiling revealed clear separation of mitochondrial defects from controls under galactose but not glucose using partial least squares discriminant analysis (PCA). Our results show the importance of selective culture methods and the influence of bioenergetics in discriminating normal from metabolic deficient cells using untargeted fingerprinting NMR profiles. Hertig et al., Metabolomics. 2019 Feb 28;15(3):32.

# Discovery and validation of temporal patterns involved in TBI brain metabolism in human

Traumatic brain injury (TBI) is recognized as a metabolic disease with acute impaired glucose metabolism, thus the utilization of alternative energy substrates could be beneficial for the patients. We assessed and identified different states of brain metabolism during the acute post-TBI critical care phase using cerebral microdialysis. Using combination of metabolomics and metabolic modeling, ketometabolism was identified as one of the key components associated to the patients' outcome, and the potential target for TBI neuro-repair. The identified metabolic signature could predict short- and long-term

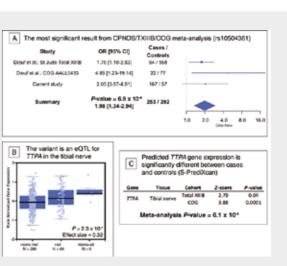
Eiden, M., N. Christinat, A. Chakrabarti, S. Sonnay, J. P. Miroz, B. Cuenoud, M. Oddo and M. Masoodi (2019). "Discovery and validation of temporal patterns involved in human brain ketometabolism in cerebral microdialysis fluids of traumatic brain injury patients." EBioMedicine 44: 607-617.

Schematic diagram outlining the workflow of the study



# Pharmacogenomics of Vincristine-**Induced Peripheral Neuropathy Implicates Pharmacokinetic and Inherited Neuropathy** Genes

Vincristine is an effective chemotherapeutic drug for various cancers but its use is restricted by dose-limiting vincristine-induced peripheral neuropathies (VIPN). This meta-analysis of three genetic association studies uncovered the first evidence that variants in genes causing inherited neuropathies (TTPA, SLC5A7), may contribute to VIPN susceptibility. The same study also replicated the association of a variant in the CEP72 gene with VIPN, strengthening the evidence for the potential clinical utility of this biomarker to identify patients at increased risk of VIPN. Wright et al. Clin Pharmacol Ther; 105(2): 402-10 (2019).



TTPA gene variant associated with vincristine-induced peripheral neuropathye

# Department of Cranio-Maxillofacial Surgery

Inselspital, 3010 Bern www.skg.insel.ch



Prof. Tateyuki lizuka Director Chief Physician



Prof Benoît Schalle Deputy Director



PD Dr Nikola Saulacic Chief Division Clinical Research



Dr Masako Fuiioka-Kobayashi Scientific Associate



Grigaitiene Laboratory Bone Biology



Senior Scientific Consultant

# **Profile**

- Teaching students of medicine and dentistry at the University of Bern, postgraduate education and training for specialization in Oral and Maxillofacial Surgery on the European level
- · Education and training of young academics by providing various clinical and scientific fellowship programs
- 3 research groups consisting of international team members
- Investigation of the biological process of bone and soft tissue regeneration in connection with the use of various bone substitutes and bone grafts
- Design and development of titanium and biodegradable osteosynthesis devices
- External Partners: Metal Physics and Technology, Department of Materials, ETH Zurich, Zurich, Switzerland; 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; International Bone Research Association (IBRA), Basel, Switzerland; Geistlich Pharma, Wolhusen, Switzerland

#### **Grants**

- Swiss National Science Foundation Synergia Grant (No. 180367/1)
- Swiss National Science Foundation (No. 31003A\_182350/1)
- ITI Research Grant (No. 1287\_2018)
- AO Foundation Research Fund (No. AOCMFS-19-15K)
- Osteology Young Researcher Grant, Osteology Fundation (No. 18-077)
- Clinical Research Grant Maxillofacial Surgery, International Bone Research Association/IBRA

# Highlights

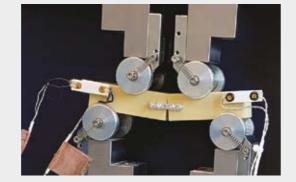
# Translational research on biodegradable magnesium plate/screw system for osteosynthesis

Our degradable magnesium osteosynthesis system consisting of plates and screws was successful for the midface fixation in a minipig fracture model. The degradation of a relatively large amount of magnesium did not lead to an accumulation of alloying elements in the organs. Hence, a significant step has been made for clinical application of magnesium-based osteosynthesis devises.

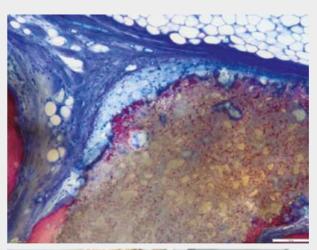
Application of magnesium plates in the mandible is still

challenge because of strong mechanical loading. The magnesium plate/screw system has continuously been improved by the newly initiated mechanical test.

Imwinkelried T et al., Mater Sci Eng C Mater Biol Appl. 2020 Mar;108:110389. doi: 10.1016/j.msec.2019.110389.



Mechanical test of osteosynthesis plates and screws





# **Bone Biology Lab**

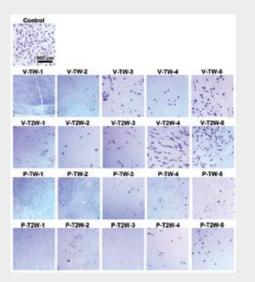
Focus of our research is the assessment of biphasic synthetic calcium phosphates and collagen-based scaffold for bone regeneration. The degradation kinetics and the formation of new bone can be affected by the level of biomimetic HA coating of  $\alpha$ -TCP. Mineralized collagen. but not the collagen alone, enhanced healing of the critical-size bone defects. Preliminary data indicated that the mode of periosteal manipulation influence the nature and kinetics of ectopic bone formation.

# Effect of the degree of conversion of resin-based composites on cytotoxicity, cell attachment, and gene expression

Resin-based composite (RBC) restorations are routinely used in dental practice. We comprehensively investigated the influence of the degree of conversion (DC), resin-based composites RBC composition, and the effect of additional violet light from one light curing unit (LCU) on cell attachment/growth, eluate cytotoxicity, and gene expression on human gingival fibroblasts (HGF).

The Panel shows Giemsa staining of HGF cells attached on a total of 20 combinations

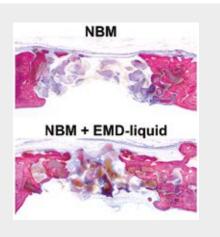
Fujioka-Kobayashi M et al., Dent Mater 2019: 35(8), 1173-1193.



# Use of enamel matrix derivative liquid in combination with a natural bone mineral on new bone formation

We have developed a new liquid carrier system for enamel matrix derivate (EMD-liquid) for improved adsorption of EMD to biomaterial surfaces. Using the derivate of EMD-liquid, bone regenerative potentials have been investigated in combination with a natural bone mineral (NBM) in vivo. The Panel shows the images of toluidine blue and fuchsin staining on the middle sections in the bone defects at 8 weeks in NBM alone and NBM + EMD-liquid groups.

Kobayashi E et al., Clin Oral Implants Res 2019: 30(6), 542-549.



# Department of Dermatology (DERK)

Inselspital, Switzerland www.dermatologie.insel.ch



Prof Luca Borradori Chairman



Prof Nikhil Yawalkar Deputy Chairman



PD Dr. Helmut Beltraminelli



Prof Dagmar

Prof. Robert

Hunge



Prof. Eliane

Müller



Favre



Dr. Bertrand Prof. Christoph Schlapbach

# **Profile**

- Investigation how T cell metabolism and T cell function are linked in inflammatory skin disease
- Study of the autoimmune response and the molecular events leading to skin blistering in pemphigus
- Assessing the mechanisms of the interaction of plakin family members with various intermediate filaments in epithelia and striated muscle cells
- Understanding how stem cells contribute to homeostasis of the skin
- Investigation of epithelial barrier dysfunction and type 2 inflammation
- Carrying out clinical trials with different targeted therapies for atopic dermatitis, psoriasis, hidradenitis suppurativa and melanoma
- External Partners: Genetic Skin Disease Group, King's College London, London, UK; Institute for Research in Biomedicine, Bellinzona; Department of Dermatology, Huashan Hospital, Fudan University, Shanghai China; Department of Immunology, University Hospital Zurich, Zurich; Dept. of Dermatology, University of Freiburg, Germany; The Regional Dermatology Training Centre, Tanzania; Department of Pathology, C.H. U. Henri Mondor, Paris, France; Department of Dermatology, University Hospital Düsseldorf, Düsseldorf, Germany; Hautklinik, Universitätsklinikum Marburg, Germany; Institute of Molecular Systems Biology, ETH, Zurich; Centro Studi GISED, Bergamo, Italy; Lübeck Institute for Experimental Dermatology, University of Lübeck; Institute for Biomedical Techniques, Department of Information Technology and Electrical Engineering, ETH Zürich

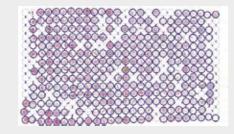
# **Grants**

- SNF Pemphigus-from pathogenesis to therapeutics (Pegasus): Epitope spreading in pemphigus
- SNF Sinergia: A One health approach to unravel novel genes and molecular pathways in dermatology
- 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
- Peter Hans Hofschneider Stiftungsprofessur für molekulare Medizin (Prof. Ch. Schlapbach)
- International Society for Dermatology -6<sup>th</sup> African Dermatopathology Conference, Tanzania
- Egyptian Cultural Office of the Republic of Egypt, Dermatopathology Training Scholarship

# **Highlights**

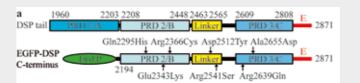
# A next-generation Tissue Microarray (ngTMA) automated analysis to find new markers to assess prognosis of melanoma

Finding new markers to assess prognosis of melanoma without the necessity to perform a surgical interventions is an important goal in melanoma research. We have developed in a completely automatic and random procedure a ngTMA block containing tissues from melanocytic nevi, primary and metastatic melanoma to evaluate the potential mark-

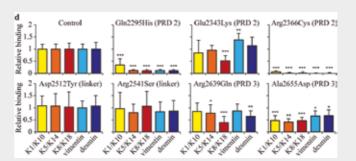


ers. Then sections cut from ngTMA-block undergo immunohistochemically stainings and expression of the proteins is investigated using full- automated image analysis and compared among the study groups. Seyed Jafari SM et al. PLoS One. 2018 Nov 8;13(11):e0207019.

# Identification and characterization of pathogenic variants of desmoplakin



Schematic structure of the DSP tail and EGFP-DSP C-terminus.



Fluorescence overlay assay. Result obtained with a DSP carrying a pathogenic mutation affecting binding of the DSP tail to all tested IF proteins. and EGFP-DSP C-terminus.

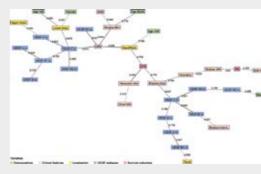
Desmoplakin (DSP) is a component of the desmosomes, cell-cell adhesion complexes. Genetic alterations of the DSP gene are associated with skin, hair and or heart pathologies. The genotype-phenotype relationship of DSP variants is still unclear. We have developed a biochemical method, which enables to identify deleterious versus silent variants in the tail domain of DSP. The tail of DSP tail anchors the intermediate filaments. Our results indicate that binding of DSP to epidermal keratins and the heart muscle-specific desmin relies on the same recognition sites. Deleterious DSP C-terminal variants, in a homozygous or compound heterozygous state, that are associated with a skin phenotype are most likely also pathogenic in the heart and lead to cardiomyopathy.

Favre B, et al Circ Genom Precis Med. 2018;11: e002241.

# Association of vascular endothelial growth factor subtypes with melanoma patients' prognosis

The expression of angiogenic factors, such as the Vascular Endothelial Growth Factor (VEGF) subtypes and their receptors is upregulated on vascular endothelial cells during tumor angiogenesis. By using semantic map analysis, we investigated the associations between VEGF subtypes and receptors by using next-generation Tissue Microarray, patients' characteristics and prognosis in a cohort of 137 melanoma patients. Low and high values of VEGF subtypes were distinguished in two clusters in the map. In particular, high values of VEGF, especially VEGF-C, were associated with thick MM, which was linked to disease-free survival and ulceration.

Cazzaniga S et al. Acta Derm Venereol. 2020 Jan 7;100(1).

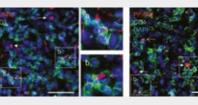


Semantic map showing the best linking among selected variables in the study population.

# Human "T" 9" cells are a subpopulation of PPARy<sup>+</sup> T<sub>u</sub>2 cells

While T<sub>1</sub>1, T<sub>2</sub>2, and T<sub>1</sub>17 cells are well-defined T<sub>1</sub> cell lineages in humans, it remains debated whether IL-9-producing T<sub>u</sub> cells represent a bona fide "T<sub>u</sub>9" lineage. Our understanding of the characteristics and role of IL-9-producing T<sub>u</sub> cells is still poor. Our work has provided evidence that human IL-9producing T<sub>ii</sub> cells are better described as a subpopulation of skin-homing and skin-resident T<sub>1</sub>2 cells. These IL-9+ T., 2 cells differ from "conventional" T., 2 cells in that they express the ligand-activated transcription factor PPARy. PPARy is required for full IL-9 production in human T<sub>u</sub> cells. IL-9+ T<sub>u</sub>2 cells infiltrate acute allergic skin inflammation in humans in high numbers. IL-9-producing T<sub>u</sub> cells are thus a phenotypically and functionally distinct subpopulation of T<sub>..</sub>2 cells.

Micossé C et al. Sci Immunol. 2019;4 (31). pii: eaat5943.



Detection of PPARy+ T helper cells in human allergic contact dermatitis: (A+B) Representative pictures of immunofluo-rescence for PPAR-v and CD3 (A) or CD4 (B) in lesional skin of acute allergic contact dermatitis. Scale bars: 50μm. Open arrows: PPAR-γ+/CD3+ cells (A) or PPAR-y+/CD4+ cells (B). Closed arrows: PPAR-y+/CD3cells (A) or PPAR-γ<sup>+</sup>/CD4<sup>-</sup> cells (B).

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

Inselspital, Freiburgstrasse 15, 3010 Bern www.udem.insel.ch



Prof. Christoph



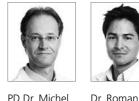






Prof Zeno

Stanga



Hochul



Bally





Prof Lia Prof. Regula **Everts** 

PD Dr Maria Balmer

**Profile** 

 Seven research groups covering the areas of: Diabetes Technology (artificial pancreas, closed-loop/hybrid-loop systems, smart sensing and devices, algorithms/artificial intelligence); Metabolic Science (exercise-related fuel metabolism, cardiometabolic studies, immuno-metabolism, deep phenotyping, metabolic imaging, physiological/mechanistic drug research); Metabolic Modelling (in-vivo, in-silico); Computer Vision and Food Science (automated food recognition, biometrics, body shape/composition analysis); Peptide Analytics, Biomarkers and Metabolomics (LC/GC MS, dry blood spot analytics); Inborn Errors of Metabolism; Neuroendocrinology (central regulation, functional imaging), Neuroendocrine Tumors; Thyroid Disease (MALDI-TOF mass spectrometry imaging)

Trepp

- Teaching students of medicine, dental medicine, pharmacy, biomedical sciences, graduate students of the Graduate School for Cellular, and Biomedical Sciences
- Postgraduate education (CAS in sex and gender-specific medicine, Certificate Course Clinical Nutrition)
- External partners: ETHZurich, ETHLausanne, HStGallen, CSEM Neuchatel, UniFR, University of Cambridge, Manchester, Swansea (UK), Rotterdam, Padova, Cologne, Graz, Toronto, Duke, Yale

# **Grants**

- SNF Sinergia Programm (Project CRSII5\_183569) Design and Evaluation of a Vehicle Hypoglycemia Warning System in Diabetes (HEADWIND Project) - PI Prof. C. Stettler
- SNF (32003B\_185019 / 1) Effects of SGLT-2 inhibitor dapagliflozin on hormonal glucose regulation and ketogenesis in patients with type 1 diabetes - PI Prof. M. Laimer
- Scherbath Foundation PI Prof. M. Laimer
- SNF Marie Heim-Vögtlin PI PD Dr. M. Balmer
- Dexcom ISS PI Prof. L. Bally
- Swiss National Kidney Foundation PI Prof. L. Bally
- Helmut Horten Foundation PI Prof. L. Bally
- Bangerter Foundation and Vontobel Foundation PI Prof. R. Everts and Dr. R. Trepp
- SNF Eccellenza (PCEGP3\_186978) Deciphering the Enigma of Postprandial Hyperinsulinaemic Hypoglycaemia after Bariatric Surgery (DEEP Project) – PI Prof. L. Bally

# Highlights

# **HEADWIND: Design and Evaluation of a** Vehicle Hypoglycemia Warning System in Diabetes

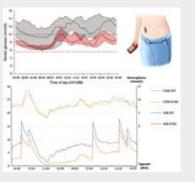
In collaboration with the ETHZ and the HSG (SNF sinergia program), we lead a program applying artificial intelligence to analyze driving behavior during hypoglycemia based on car-derived parameters as well as physiological parameters. The overall target is to detect and predict hypoglycemia while driving in real-time. To this aim, we induce hypoglycemia while human participants are driving first in a simulator and then in real cars. (SNF sinergia CRSII5\_183569; SGED 2019; ATTD 2020).



Hypoglycemia whilst driving in a simulator. Al analyses patterns of car-derived parameters.

# **Closed-Loop and Artificial Pancreas**

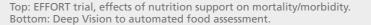
We are developing and evaluating a broad set of insulin-delivery algorithms in different target groups. Current studies address the safety, efficacy and utility of commercially available hybrid closed-loop systems (LINEAR: NCT NCT03932630) for type 1 diabetes, the Cambridge algorithm for fully-automated closed-loop in type 2 diabetes (APrenal: NCT04025775; Diabetes Obes Metab 2019; Lancet Diabetes Endocrinol 2019) and type 1 diabetes (AP04home: NCTNCT04055480, Diabetes Care 2019). In parallel we are evaluating "Do-it-yourself" (DIY) systems using elaborate in-silico environments (Diabetes Obes Metab 2019).

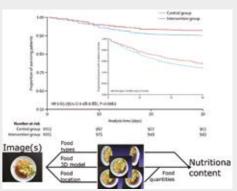


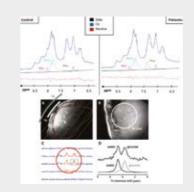
Top left: Glucose control during closed-loop versus conventional insulin therapy in dialysis patients. Top right: Concept of closed-loop/artificial pancreas. Bottom: Glucose control during DIY vs. commercial closed-loop system.

# **Innovation in Nutritional Medicine and Research**

Optimising nutrition support is a core interest of our clinical research. The EFFORT-trial has shown that an adequate nutritional therapy in patients significantly improves clinical outcomes (NNT 25) and reduces mortality (NNT 37) (Lancet. 2019, JAMA Network Open 2019). Leveraging novel technology (computer vision, artificial technology) to further enhance efficacy, effectiveness and personalisation of nutrition care is amongst our top priorities (DEEP VISION).







Top: Model with individual fitting of Phenylalanine in controls and PKU patients; Bottom: Deuterium Metabolic Imaging of human liver.

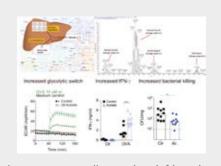
# **Metabolic Imaging**

The application of non-invasive non-radioactive magnetic resonance spectroscopy (MRS) offers the unique opportunity to map the concentration and utilisation endogenous and exogenous metabolites in target tissues. We take advantage of the technology to explore various metabolic diseases and responses to physiological challenges: ie, the quantification of phenylalanine in phenylketonuria (PICO: NCT03788343) and assessment of ectopic fat in the liver in prediabetic morbidly obese patients undergoing ketogenic diets (CaPrO: NCT03880162). The use of the ultra-high field 7T MR scanner within the novel translating imaging center (TIC) will further offer new avenues for metabolic imaging such as dynamic deuterium metabolic imaging (DMI). The technique is being developed in collaboration with Yale University to dynamically map body biochemistry in humans in 3D imaging mode.

# **Deep Metabolic Phenotyping**

We develop different mass-spectrometry (high resolution LC-MS/GC-MS/ IRMS) workflows with high throughput and quantitative capabilities to deepen our understanding of metabolic diseases and metabolic pathways and discover novel biomarkers (Metabolomics. 2019). We further apply MS for advanced peptide (e.g. insulin/proinsulin/gut peptides) and steroid analytics and stable isotope flux analyses. Non-targeted and targeted metabolomics approaches and flux analyses are critical to detect fuel switches,

not only in key metabolic organs such as liver, muscle and adipose tissue but also the immune system (SNF Marie-Heim Vögtli).



Metabolomics to profile glycogen storage diseases (top left); multi-plex LC-MS insulin profile (top right); Glycolytic switch leading to increased bacterial killing (bottom).

# Department of Diagnostic and Interventional Neuroradiology

Inselspital, Freiburgstrasse 4, 3010 Bern www.neurorad.insel.ch



Prof Jan Gralla Chairman and Physician in Chief



Wiest Deputy Chairman



PD Dr. Christoph Ozdoba Physician in Chief (SLS)



Michela Mordasini Head of Medical Technical Neuroradiology



Prof Marwan El-Koussy Consultant



PD Dr. Pasquale Mordasini Consultant

# **Profile**

- Neurovascular research: The research group focuses on treatment strategies for neurovascular diseases (aneurysms, Arterio-venous Malformations (AVMs) etc.) and especially the evaluation and treatment of acute ischemic stroke. The researchers combine preclinical development of techniques in bench-top and animal models and evaluate their application in large-scale international clinical studies (Swift direct). Furthermore, the group evaluated robotic approaches in neurovascular treatment.
- Advanced Neuroimaging and Artificial Intelligence Technology in Neuroradiology: The research of the Support Center of Advanced Neuroimaging (SCAN) focuses on the translation of quantitative imaging methods, artificial intelligence technology 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. ENINGMA Epilepsy and Parkinson's disease), neuroimaging challenges and data analysis networks in cerebrovascular research, neuro-oncology, neuro-immunology, sleep-related disorders, epilepsy and neurodegenerative disorders.
- CSF Disorders: 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
- Ultra High Field MRI: MR-pyhisicists and clinical neuroradiologists support the Translational Imaging Center (TIC) at the sitem-insel in MR methodology and explore new indications for UHF MRI in CNS disorders (as e.g. structural epilepsies, neuroimmunological and vascular disorders)
- Teaching activities: Medical Faculty, Faculty of Human Sciences, Biomedical Engineering, University of Applied Science Bern, European Academy of Neurology (EAN), European Stroke Organisation (ESO), Medical Image Computing and Computed Assisted Intervention Society (MICCAI)
- External Partners: Department of Neurology, UCLA, USA, Excellence Center for Ultra-High Field MRI, Austria, Department of Neuroradiology and Informatics, Technical University Munich, Germany, Division of Neuroradiology, Western Ontario Hospital Toronto, Canada

# **Grants**

- SINERGIA Project "Predict and Monitor Epilepsy After a First Seizure: The Swiss-First Study (PI Prof. Wiest)
- SINERGIA Project "Hydrogel" (PI Dr. Mosimann)
- SNF Project" Introduction of High Field Optimized Fast 3D MR Spectroscopic Imaging for IDH Typing of Gliomas and Assisted Surgical Neuro Navigation" (Pl Dr. Slotboom)
- HORIZON 2020 INSPIRE MED (CI Dr. Slotboom)
- Novartis Innovation Grant (PI Dr. McKinley)
- SPHN Grant"Imagine" (USZ, UZH, Inselspital, USB, EOC, CHUV, HES-SO.Local PI Bern: R. Wiest)
- SNF SPARK "Using Deep Neural Networks to Bridge Clinical and Quantitative Analysis of Intracranial EEG in Epilepsy"
- SISF Grant UniBe Translational developments of sequence and post-processing techniques for clinical applications of chemical exchange saturation transfer imaging (CEST) for ultra-high field MRI - a use case for a private-public partnership between TIC and Olea Medical®
- Heart Foundation (PI PD Dr. P. Mosimann)

# **Highlights**

The Translational Imaging Center at the siteminsel has become operational by the 1st of July 2019. The Bernese system is one of the first clinically approved UHF systems in the world and enables researchers to investigate specific pathologies obscured by conventional MRI (as e.g. subtle cortical dysplasias in epilepsy or cortical MS plagues). The TIC is granted support and expertise in MR physics by Siemens Healthineers, funding of the SNF and SISF, whereby the first scientific projects could be been started in 2019.



# **Biomedical Engineering Prize 2019**

M. Rebsamen received the Biomedical Engineering Prize 2019 for best MSc Thesis in Basic Science: "Fast and accurate human brain morphometry estimation with deep learning".



The Peter-Huber Preis of the Swiss society for neuroradiology has been granted to Dr. Thomas Dobrocky: "Assessing Spinal Cerebrospinal Fluid Leaks in Spontaneous Intracranial Hypotension With a Scoring System Based on Brain Magnetic Resonance Imaging Findings".



© swissneuroradiology.ch

# **Certificate of Advanced Studies in Neuroimaging (CAS)**

The SCAN and the sitem school at the Swiss Institute for Translational and Entrepreneurial Medicine have concepted a joint program to educate physicians in the emerging field of AI technology in imaging. The main objective of the CAS is to equip Medical Doctors with the necessary skills to take a leading role in the Al-driven transformation of medicine. The course program was developed for medical professionals and provides them with the necessary knowledge and skills to translate medical problems to data science problems. By working on an AI project of their own, the participants will know the fundamental concepts of Artificial Intelligence and can thus judge the feasibility and adequacy of proposed Al solutions.



# Department of Diagnostic, Interventional and Pediatric Radiology (DIPR)

Inselspital, Tiefenau Hospital, Hospitals in Aarberg, Münsingen, Belp, Riggisberg www.radiologie.insel.ch







Prof Hendrik v. Tengg-Kobligk Böhm Deputy Director Project Leader



PD Dr Ingrid



PD Dr Adrian Dr Verena Obmann Huber Senior Physician Senior Physician



Dr Nico

PostDoc

Ruprecht

Dr Danielle Bower Resident



Härmä, eMBA Senior Physician

# **Profile**

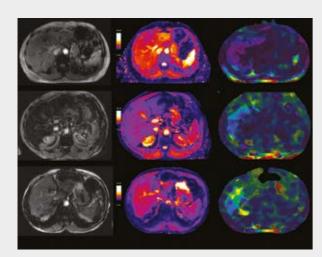
- Teaching medical students, students of biomedical engineering, FaGes (health specialists), and radiographers
- Performing currently 12 self-initiated studies, approx. 20 cooperation-studies, and additionally supporting approx. 80 ongoing clinical studies
- · Research topics include multiparametric imaging, advanced image analysis, structured reporting, and digitalisation of
- · Aiming at further improving diagnosis, navigation during intervention, and treatment and workflow planning
- External partners: Radiological Physics, Radiology and Nuclear Medicine, University of Basel; German Cancer Research Center (DKFZ), Heidelberg; ETH Zürich and EPFL/CHUV Lausanne; Ohio State University, Columbus, USA; Departments of Radiology and Biomedical Engineering at Case Western Reserve University, Cleveland, USA; University of Duke, NC, USA; Swiss Working Group for Clinical Cancer Research (SAKK), Bern; Switzerland Innovation Park, Biel

# **Grants**

- Innosuisse (34889.1 IP-ICT, 35656.1 IP-LS)
- 2 CTU Forschungs-Grants, UniBE ID Grant, Young Researcher Grant
- Stiftungen: Lindenhof, Gottfried & Julia Bangerter-Rhyner Stiftung, Lungen Liga Bern
- Swiss Personalized Health Network (2018DEV18 (PHRT531))
- SNF 320030\_188591 / 1

# Highlights

# Liver MRI susceptibility-weighted imaging (SWI) compared to T2\* mapping in the presence of steatosis and fibrosis



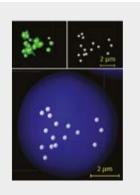
We demonstrated that both the SWI and T2\* relaxation times are strongly dependent on the liver steatosis grades, while SWI is more dependent than T2\*. Both parameters are useful predictors for liver fibrosis when using a multiparametric approach. However, the stage of fibrosis may be overestimated in the presence of steatosis, which should be taken into account when using SWI and T2\* in the assessment of fibrosis.

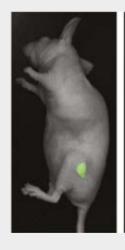
Obmann VC et al., Eur J Radiol. 2019 Sep;118:66-74.

# Improved identification of DNA double strand breaks: y-H2AXepitope visualization by confocal microscopy and 3D reconstructed images

Currently, in the context of radiology, irradiation-induced and other genotoxic effects are determined by visualizing DSB-induced DNA repair through y-H2AX immunofluorescence and direct counting of the foci by epifluorescence microscopy. This procedure, however, neglects the 3D nature of the nucleus.

Confocal microscopy and 3D reconstruction enables an improved identification of double strand break induced γ-H2AX foci, allowing for an unbiased, ameliorated quantification. Ruprecht N et al., Radiat Environ Biophys. 2019 May;58(2):295-302.







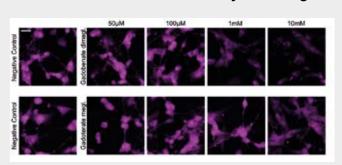


# Monitoring the tumor burden in vivo by optical imaging in a xenograft SCID mouse model

We transfected the human melanoma cell line MeWo with pEGFP-C1 or pDsRed1-N1, and investigated solid xenografts and metastases. EGFP-/DsRed-xenograft tumors had identical growth kinetics. In vivo the emitted light by DsRed tumors/metastases was much brighter than by EGFP. DsRed metastases were earlier (3 vs. 5 weeks) and much more sensitive detectable than EGFP metastases. Böhm I et al., Acta Radiologica 2019;60:315-26.

# Gadolinium-Based MRI Contrast Agents Induce Mitochondrial Toxicity and Cell Death in Human Neurons, and Toxicity Increases With Reduced Kinetic Stability of the Agent

This was the first study conducted in human neurons to assess for toxic effects on cellular function from MRI contrast agents routinely used in clinical practice. The results demonstrated that agents with lower kinetic stability broadly induce higher rates of cell death and greater impairment of mitochondrial function. Bower et al., Invest Radiol. 2019 Aug;54(8):453-463.







# A new predictive indicator in the diagnosis of endometriosis

The «Cloverleaf Sign» has been discovered on MRI and it has been shown that it accurately predicts significant longer OR times, increased intraoperative blood loss, as well as a higher rate of bowel resections. Therefore, it has a profound impact on OR planning and patient counselling.

Härmä K. et al., Invest Radiol. 2020 Jan;55(1):53-59.

# Division of Magnetic Resonance Spectroscopy and Methodology (AMSM)

sitem-insel, Freiburgstr. 3, 3010 Bern www.amsm.dkf.unibe.ch



Prof. Chris Boesch



Prof. Roland Kreis



Prof. Peter Vermathen



Karin Dr. Gabriele Zwygart-Brügger Bonanno



Joseph

Dr. André Döring



dy Maike



Hoefemann

Martyna

Dziadosz



Kadir Simsek

E

Damian

Hertig

Rizzo

# **Profile**

- Magnetic resonance imaging (MRI) and spectroscopy (MRS) methods in collaboration with clinical partners in prospective studies of different organs
- Development of novel methods to suit pertinent needs to study physiology and pathology
- MRI and MRS studies in brain, kidney, muscle, liver, and heart
- High resolution NMR studies on biopsies, cell cultures and body fluids
- Participating in University teaching programs for students of medicine, chemistry, biochemistry, and biomedical sciences
- External Partners: Max-Planck-Institute for Cognition- und Neurosciences, Leipzig, Germany; 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

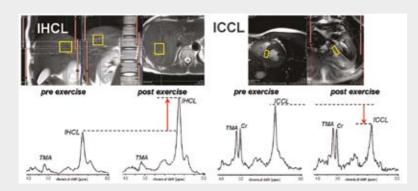
# **Grants**

- Swiss National Science Foundation (grant No. 320030\_175984; 320030\_170062)
- Marie-Curie Initial Training Network (H2020-MSCA-ITN-2018-813120)

# Highlights

# Overview

MRI and MR spectroscopy (MRS) are powerful and extremely versatile methods for non-invasive studies and diagnostic examinations in humans. We use MRI and MRS methods in collaboration with clinical partners primarily in prospective studies of different organs. We develop novel methods to suit pertinent needs to study physiology



and pathology, together with the underlying mechanisms, in situ. Most current studies are performed in brain, kidney, muscle, liver, and heart (see Figure). In addition, high resolution NMR studies are performed on biopsies, cell cultures, body fluids.

Effect of short term exercise on ectopic lipid reservoirs in liver and muscle

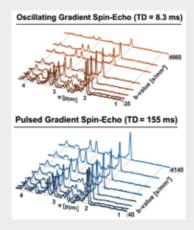
# **Group logistics**

After two years of "exile" at Erlachstrasse, we moved back to Freiburgstrasse, where our previous home, the old nephrology pavilions, have made room to the new sitem-insel building, where we moved into new offices and where we are part of the novel translational imaging center (TIC). This is equipped with a high-end 3T MR scanner, but also one of the worldwide few clinical 7T whole body MR scanners. With the move, the group now also hosts two Siemens MR Research Scientist (Dr. Bonanno and Dr. Joseph) in charge of support of clinical researchers from Inselspital performing research at 7 Tesla

Arrival of one of the new MR scanners for the Translational Imaging Center at sitem-insel

# **Brain Physiology**

An SNF grant aims at MR acquisition and postprocessing methods that are tailored to the observation of brain metabolism, yet are also transferable to other organs. Exchange processes between amide protons and water are studied. MRS is also optimized for reproducibility in longitudinal studies and for detection of low-concentrated metabolites like phenylalanine and NAD+. Diffusion properties of brain metabolites are investigated with dedicated methodology (see figure) in collaboration with the Clinic for Neurology to elucidate microstructural properties where we make use of the fact that metabolites, in contrast to water, are essentially confined to intracellular space. In collaboration with a Max Planck Institute in Leipzig, where we use a MR system with the strongest gradient system available for human research, we try to identify macromolecular signals to aid clinical MR spectroscopy.



Effect of diffusion time on brain spectra

# European Innovative Training network (ITN)

The newly funded Marie Curie ITN INSPIIRE-MED (inspire-med.eu) has started this year. It has a focus on multiparametric and multi-modal MRI/MRS and PET techniques in a European multicenter research and training network. The specific aim of our subproject includes novel synchronized acquisition and processing methods aiming at standard modeling evaluations in contrast to the use of dictionaries and machine learning methods.

# **Renal Function**

Renal Function in native and transplanted kidneys has been investigated by multi-modal MRI and MRS in preparation of a Sinergia Grant. In collaboration with the Nephrology Department 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. In clinical studies fMRI measurements were performed comparing living-donor versus deceased-donor kidney transplantation. Funded by sitem-insel Support Funds and in collaboration with the Nephrology we are currently preparing a study for localized non-invasive in vivo determination of potassium by 39K MR-Imaging and Spectroscopy on the 7T MR Scanner.

# **High-Resolution Magic Angle Spinning NMR**

High-resolution magic angle spinning (HR-MAS) NMR techniques were applied to correlate in vivo and in vitro NMR spectra of tissue and body fluids.

HR-MAS studies have been performed on biopsies and on cell cultures and analyzed by "metabonomical" methods. In collaboration with the vendor Bruker we established a perfused bioreactor system and performed measurements of living 3D cell cultures inside the NMR with changing conditions.



Bioreactor for online Metabolomics of living cells inside the NMR.

## Department of Emergency Medicine

Inselspital, INO-C, 3010 Bern www.notfallzentrum.insel.ch



Prof Aristomenis Dr Beat Exadaktylos FRCEM MSc Director and Chief Physician



Lehmann Deputy Chief Physician



Prof Wolf Hautz MME, Head of Research, Diagnostic Error Wilderness and Patient Safety



PD Dr. Monika Brodmann Maeder MME and Medicine



Dr Simone Ehrhard Infectious Diseases



PD Dr. Martin PD Dr. Thomas Müller Sauter Resource & Risk MME and Direct New Oral Management Anticoagulants

& Telemedicine



Srivastava Refugee Health

## **Profile**

- · Teaching medical students, residents and postgraduate nursing students in emergency medicine and point of care ultrasonography
- 7 research groups
- Investigation of research questions with direct relevance to emergency patients
- EURAC Bozen, CHUV Lausanne, HUG Genf, Max Planck Institute for Human Development Berlin, Institute of Educational Measurement Oslo, Sarah Lawrence College New York, Charité Berlin, Erasmus Medical Center Rotterdam

## **Grants**

- SNF and industry funding
- Foundational professorship for tele-emergency medicine and e-/m health
- BAG funded projects in migrant health
- Foundational career funding for young clinical scientists

## Highlights

## Foundational Professorship in tele-emergency medicine

Thanks to the support of the Touring Club Switzerland (TCS), the University of Bern is able to establish an assistant professorship for tele-emergency medicine. The professorship is concerned with "eHealth" in the field of emergency medicine. It is based at the University Emergency Centre (UNZ) at the Inselspital, University Hospital Bern. The professorship is unique in its academic orientation in German-speaking Europe and one of the very few in the world. With the support of a professorship for tele-emergency medicine, the increasing bottleneck in Swiss emergency care is to be counteracted, which is aggravated by the ageing population and the lack of doctors.

The endowed professorship will be advertised nationally and internationally; according to the UNZ and TCS, it is expected to be filled at the beginning of 2020.



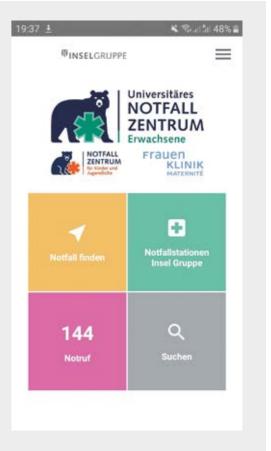


## 3<sup>rd</sup> Swiss symposium on refugee and migrant health

On 13 December 2019, we host the 3<sup>rd</sup> Swiss symposium on refugee and migrant health. The annual symposium is now a well established event in the communities of research and practice in the field. This year, the focus will be on the social aspects and the integration of refugees and migrants. The health of young adults and the work of "doctors without borders" are also key topics. In addition the importance of the social circumstances of asylum seekers and migrants will be adressed. We aim to achieve a more holistic view on the health of refugees and

## Swiss symposium on tele-emergency medicine and digital health

The rapid development of digitalisation in acute medicine encompasses all areas of medicine and all medical professionals in their everyday working environment from the use of apps and electronic decision aids with artificial intelligence to the support of rural areas through telemedically supported treatment systems. Whatever one may think of this development, it affects everyone who works in emergency medicine. Opportunities, such as the potential mitigation of a shortage of physicians in emergency care, and risks, such as the frequent lack of digital education, privacy concerns, and a lack of academic justification in the application of Digital Health products, must be addressed and discussed. The department thus hosts the first Swiss symposium on tele-emergency medicine and digital health on 13 February 2020. www.telenotfallmedizin.ch



## Department of ENT, Head and Neck Surgery

Inselspital, 3010 Bern www.hno.insel.ch



Prof Marco Caversaccio Chairman



Giger Deputy Director



Prof Martin Kompis Head of Audiology



Prof Fberhard Seifert Head of Phoniatry



Prof Georgios Mantokoudis Head of Cochlea-**Implants** 



Prof Dominique Vibert Head of Neurootology

## **Profile**

- Teaching students of medicine and dentists in ENT
- Teaching and supervising graduate students at the ARTORG Center
- Training of young ENT surgeons on a daily basis and in internal courses
- Courses in audiology, biomedical acoustics and phoniatrics for speech therapists
- Research collaboration with the Hearing Research Laboratory at the ARTORG Center to develop and integrate new technologies for the treatment of hearing loss
- Research projects in ENT oncology and the treatment of vestibular loss
- External Partners: Department of Otorhinolaryngology, University Hospital of Zurich, Switzerland; INRIA Research Center, Sophia Antipolis, France; ORL University Hospital Modena, Italy; Nottingham Hearing Biomedical Research Unit, University of Nottingham, UK; Johns Hopkins University, Department of Neurology, USA

#### **Grants**

- Eurostars-2, EU Horizon 2020 and Eureka (E! 11597 RCI)
- SNF PostDoc.Mobility Fellowship (Nr. 180822)
- SNF Grant, DETECT Study (320030\_173081)
- CTU-Forschungs-Grant 2019 (2018-08)
- Grant of Carigest SA
- Grant of the Gottfried and Julia Bangerter-Rhyner Stiftung

## Highlights



CORLAS 2019 meeting

## Collegium Oto-Rhino-Laryngologicum Amicitiae Sacrum (CORLAS)

CORLAS was founded in 1926 offering an international scientific setting where physicians could exchange their thoughts. Today, this meeting is still very popular to meet colleagues, to exchange new ideas and to present the latest findings to an interested and knowledgeable audience.

The annual CORLAS meeting 2019 took part in Bern and was hosted by the congress president Prof. Martin Kompis and the congress vice president Prof. Marco Caversaccio.

## **Politzer Society Award 2019**

The Politzer Society was founded in 1978 and has held an international conference every second year. The scientific focus is on research and the latest developments in otology and neurotology. This year, the 32<sup>nd</sup> meeting took place together with the World Congress in Otology in Warsaw, Poland. Dr. Stefan Weder was nominated for the Politzer Prize in the category "best paper in clinical science" with his research project "Towards a Better Understanding of Electrocochleography: Analysis of Real-time Recordings" and won the gold medal.



Award Winner

## **DGA: Young Scientist Award 2019**

At the annual conference of the German Society of Audiology (DGA) Tim Fischer received the Young Scientists Award 2019.

The prize was awarded for his research work on the influence of microphone directivity on the spatial hearing ability of bilateral cochlear implant wearers.



Award Winner

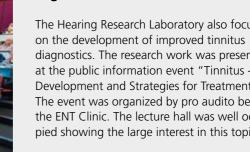
3D visualization of inner ear with detected modiolar axis

## **Cochlear Morphology Characterization**

In collaboration with the INRIA research group of the Université Côte d'Azur, France, we developed a novel method to characterize the shape of the cochlea. The method can be used to improve surgical planning approaches and to refine the postoperative fitting for cochlear implant patients.

Wimmer W et al., Med Image Comput Comput Assist Interv 2019:S3-10.





diagnostics. The research work was presented at the public information event "Tinnitus -Development and Strategies for Treatment". The event was organized by pro audito bern and the ENT Clinic. The lecture hall was well occupied showing the large interest in this topic.

Public audience about Tinnitus

## Department of General Internal Medicine

Inselspital, 3010 Bern www.inneremedizin.insel.ch



Prof Drahomir Aujesky Klinikdirektor und Chefarzt Allgemeine Innere Medizin



Prof Nicolas Rodondi Chefarzt und Leiter Poliklinik



Dr Martin Chefarzt und Leiter Bettenstationen



Prof Maria Wertli Leitende Ärztin und Stv. Leiterin Poliklinik



Prof Manuel Haschke Chefarzt und Leiter Klinische Pharmakologie

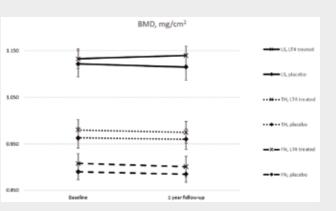


Dr Christine Baumgartner Leitende Ärztin

## Skeletal Effects of Levothyroxine for Subclinical Hypothyroidism in Older **Adults: A Randomized Trial**

Highlights

Both thyroid dysfunction and levothyroxine therapy (LT4) have been associated with bone loss, but studies on the effect of LT4 for subclinical hypothyroidism (SHypo) on bone yielded conflicting results. In a nested sub study of the double-blind placebo-controlled TRUST trial, 196 participants with SHypo were randomized to LT4 with dose titration vs. placebo. The unadjusted 1-year change in lumbar spine bone mineral density (BMD) was similar between LT4 (+0.8%) and placebo-treated groups (-0.6%; between-groups difference +1.4%: 95%CI -0.1 to 2.9, p=0.059). Likewise. there were no between-group differences in



1-year change in BMD (bone mineral density, left) at LS (lumbar spine, continuous line), TH (total hip, dotted line) and FN (femoral neck, broken line), in placebo (diamonds) and LT4 (cross) treated patients.

1-year change in Trabecular Bone Score (-1.3%: 95%CI -3.1 to 0.6, p=0.19) and total hip BMD (-0.2%: 95%CI -1.1 to 0.1, p=0.61). Over 1-year levothyroxine had no negative effect on bone health in older adults with SHypo. J Clin Endocrinol Metab. 2020 Jan 1;105(1). pii: dgz058. doi: 10.1210/clinem/dgz058.

## **Profile**

- Research focus: multimorbidity, venous thromboembolism, anticoagulation, variation in care, overtreatment, thyroid diseases, primary care, epidemiology, public health, chronic pain, opioid use, drug metabolism and safety, nicotine dependence, pharmacometrics, machine learning
- 8 research groups
- Overall aim: To improve quality of care and to promote evidence-based, high-value, safe, patient-centered, data-informed, and sustainable health care
- Teaching (lectures, clinical teaching, skills training, small group teaching) and assessment (practical and theoretical examinations) of students in medicine and dental medicine
- High-quality post-graduate training of general internal medicine and specialty residents
- International academic partners: Division of General Internal Medicine, University of Pittsburgh Medical Center, USA; Department of Medicine, Ottawa Hospital Research Institute, University of Ottawa, CA; Departments of Primary Care/Public Health and Internal Medicine, Leiden University Medical Center, NL; Division of Hospital Medicine and Clinical Pharmacology/Experimental Therapeutics, Department of Medicine, Department of Epidemiology and Biostatistics, and Center for Tabacco Control Research and Education, University of California, San Francisco, USA; The Thyroid Studies Collaboration on 5 continents; Department of Neurobiology, Care Sciences and Society, Institute of Environmental Medicine, Division of Physiotherapy, Karolinska Institutet, Stockholm, Sweden; Occupational and Industrial Orthopaedic Center, New York University Langone Orthopedic Hospital, New York, USA; Division of Research, Kaiser Permanente Northern California, Oakland, USA; The European Drug Emergencies Network Research Group; Global Health Institute Barcelona, Spain; Kenya Medical Research Institute, Nairobi, Kenya
- Swiss academic partners: Venous thromboembolism network including 22 Swiss university and non-university hospitals; Institute of Biostatistics, Epidemiology, Biostatistics and Prevention, University of Zürich; Department of Health Sciences, Helsana, Dübendorf; Horten Center for Patient Oriented Research and Knowledge Transfer, University of Zürich, Zürich; Department of Internal Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne; Swiss Tropical and Public Health Institute, Basel

### **Grants**

- Swiss National Science Foundation (grants no. 33IC30\_185616, NRP74 407440\_167339/1, 179346, 320030\_172676, 32003B\_189132, 31003A\_160206, 32003B\_179346)
- OPERAM- European Union's HORIZON 2020 (grant agreement 634238)
- Novartis Foundation for Medical-Biological Research, Bangerter-Rhyner Foundation, Swiss Society of General Internal Medicine Foundation, Eurospine Task Force Research Grant, UNITAID: BOHEMIA (Broad One Health Endectocide-based Malaria Intervention in Africa)
- Intramural grants: CTU grant (Inselspital), UniBE ID Grant

## Aspirin compared with anticoagulation to prevent venous thromboembolism after knee or hip arthroplasty: a large retrospective cohort study

Guidelines recently allowed the use of aspirin as an alternative to anticoagulants for venous thromboembolism (VTE) prophylaxis in patients undergoing knee or hip arthroplasty, but there is limited data on contemporary use and outcomes with aspirin in real-world practice. In a large retrospective cohort study using data from >100,000 patients undergoing knee or hip arthroplasty in the US MedAssets Health System, more than a fourth of all patients received

204 / 54,187 0.70 (0.56, 0.87) 0.93 (0.62, 1.38)

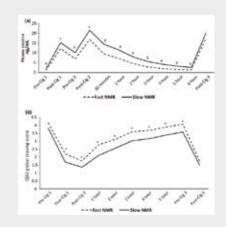
aspirin as the sole antithrombotic agent postoperatively. Thromboprophylaxis with aspirin-only was not associated with a higher risk of postoperative VTE compared with anticoagulants after knee or hip arthroplasty. J Gen Intern Med 2019;34:2038-2046.

Association between type of venous thromboembolism (VTE) prophylaxis and postoperative VTE in patients undergoing knee or hip arthroplasty.

## Effects of Nicotine Metabolic Rate (NMR) on withdrawal symptoms and response to cigarette smoking after abstinence

The NMR is a phenotypic biomarker that is highly correlated with the rate of nicotine clearance, an important determinant of smoking behavior and nicotine dependence. In our study fast metabolizers by NMR had lower blood nicotine concentrations and greater craving/withdrawal scores compared with slow metabolizers, but not greater reward after smoking, thus supporting the idea that fast metabolizers are likely smoking more to relieve craving/withdrawal symptoms. Selection of medications and/or doses of medications guided by NMR may be useful in optimizing smoking cessation therapies.

Clin Pharmacol Ther. 2019;105:641-51.



Nicotine plasma concentrations and craving scores in subjects with fast and slow NMR after smoking one cigarette after overnight and 6h daytime abstinence.

## **Department of Geriatrics**

Inselspital, Freiburgstrasse 46, 3010 Bern www.geriatrie.insel.ch



Prof. Andreas Stuck Department Director



Prof. Andreas Schönenberger Clinical Director



Dr. Dominic Bertschi Senior Research Assistant



Dr. Anna Stuck Senior Research Assistant

## **Profile**

- Inpatient geriatric rehabilitation unit (50 beds, Spital Belp), inpatient geriatric acute care unit (40 beds, Spital Tiefenau)
- Collaboration with department of orthopedics and ambulatory unit (Inselspital)
- Geriatric core curriculum in geriatrics for medical students at the University of Bern, courses for dental medicine students, residency training programs
- Methods and effects of geriatric assessment in clinical research, organized in collaboration with internal partners (audiology, cardiology, family medicine, osteoporosis, orthopedics, CTU, ARTORG and others)
- External partners: Department of Geriatrics, University of Basel, University Hospital Basel; Geriatrics, University of Geneva, University Hospital Geneva; Department of Geriatrics, University of Lausanne, University Hospital Lausanne; Department of Geriatrics, University of Zurich, University Hospital Zurich; Rehabilitation Center Kliniken Valens, Valens; Department of Internal Medicine, Hospital San Giovanni, Bellinzona; National Institute of Gerontology and Geriatrics, Ana Aslan, Bucharest, Romania; Department of Medicine and Surgery, University of Milano-Bicocca, Milan, Italy; Department of Geriatrics and Medicine, University of Florence, Florence, Italy

### **Grants**

• Swiss Personalized Health Network: Swiss Frailty Network and Repository 2018 to 2021 (Co-Investigator)

## **Highlights**

## **Towards a Swiss Electronic Frailty Index**

The Department of Geriatrics Bern, in collaboration with the four other University Geriatric Departments in Switzerland is participating in one of the seven initial driver projects of the Swiss Personalized Health Network. In this multisite project, frailty is measured clinically, as well as based on an algorithm based on electronic patient

record information. First results will be available in are expected in 2021, and the goal is to establish hospital-wide acute care treatment guidelines for senior patients at risk of or with established frailty and to prevent negative frailty-related outcomes.

Gagesch M, Edler K, Büla CJ, Stuck AE, Gold G, Kressig RW, Seematter-Bagnoud L, Zekry D, Meyer T, Bertschi D, Chocano P, Abderhalden L, Bischoff-Ferrari HA. Swiss Frailty Network & Repository: Rationale and design of a Swiss Personalized Health Network Driver Project (submitted).







## New standards for measuring muscle and bone function

For assessment of muscle function, standardized tests are needed to measure movement and strength of upper and lower extremities. However many tests have been insufficiently standardized or are not feasible for use in clinical settings. Based on systematic reviews, we propose a new standardization of gait speed assessment in older people. In addition, imaging techniques give additional information on muscle and bone quantity and quality. We are working on standards for measuring sarcopenia with body impedance analysis. In a joint collaboration with the CTU unit, the ARTORG center, and the osteoporosis unit we were able to develop a new standard for measuring bone strength (HR-pQCT-Based Distal Radius and Tibia Strenath).

Stuck AK, Bachmann M, Füllemann P, Josephson KR, Stuck AE. Effect of testing procedures (distance, starting, surface, timing) on gait speed measurement in older people: a systematic review (submitted).

Stuck AK, Schenk D, Zysset P. Bütikofer L, Mathis A, Lippuner K. Reference values and clinical predictors of bone strength for HRpQCT-based distal radius and tibia strength assessments in women and men (submitted).

# New technology for sensory assessment in hospital setting

Sensory function deficits are often not recognized at the time of hospital admission in older patients. However, reliable information on hearing and vision is key for optimal patient management, to ensure adequate patient-provider communication and to avoid in-hospital complications such as delirium and falls. In 2019, in a joint project with the audiology unit, we evaluated a prototype device using a calibrated voice recording as an alternative to the whispered voice test, and measured speech levels in patient-provider communication settings. The ultimate goal is to develop a feasible and clinically relevant brief hearing test for patients at hospital admission.

Comazzi GL, Stuck AE, Kompis M. Standardized testing of speech comprehension in hospitalized geriatric patients. Dissertation. Medical Faculty Bern, 2019.





## Department of Hematology and Central Hematology Laboratory

Inselspital, 3010 Bern www.hzl.insel.ch



Angelillo-Scherrer Rovó Director



PD Dr Alicia Deputy Director



Prof Sacha Zeerleder Head Transfusion Academic Head Medicine, Apheresis and Hematopoietic Stem Cell Transplantation



Prof Vera Ulrike Bacher of Morphology, Hematological Immunephenotypisation and Molecular Diagnosis



Prof. Johanna A. Kremer Hovinga Strebel Head Reference Laboratory Center/European Hemophilia Comprehensive Care Center and Academic

Head Hemostasis

Laboratory



Prof Gabriela

Head Stem Cell

Baerlocher

PD Dr. Elisabeth Leibundgut Group Leader



Ramanjaneyulu Group Leader



PD Dr. Nicolas Bonadies Head Clinical Study Management/ Biobanking



Dr Michael Daskalakis Head Laboratory Transfusion Medicine



Programm

## **Profile**

- · Teaching students of medicine, dental medicine, pharmacy, biomedical sciences as well as graduate students at the Graduate School of Graduate School for Cellular and Biomedical Sciences (GCB)
- 9 research groups
- Investigation of epidemiological and pathophysiological processes as well as diagnosis, prognosis and therapeutic approaches of blood-related disorders, pathophysiological processes that contribute to inflammation and tumor diseases
- External partners: INSERM & UMR-S 1176, Université Paris-Sud, University Paris-Saclay, Le Kremlin-Bicêtre, France; Department of Molecular Medicine, The Scripps Research Institute, La Jolla, CA, USA; Division of Developmental Therapeutics, Research Centre for Innovative Oncology, National Cancer Center Hospital Est, Chiba, Japan; Department of Biochemistry, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, The Netherlands; 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, MA, USA; Steering committee and Advisory Board of Hereditary TTP Registry (www.ttpregistry.net); Department of Internal Medicine- Infectious Diseases and Center of Molecular Medicine, University Medical Center Amsterdam Amsterdam, The Netherlands; Department of Experimental Immunohematology, Sanguin, Amsterdam, The Netherlands Departments of Biochemistry & Molecular Biology and Pathology, University of Oklahoma Health Sciences Center, Norman, OK, US; EBMT SAA Working Party, Late effects working party of the ASTCT; DCEG National Institutes of Health National Cancer Institute, Rockville, Bethesda, USA

## **Grants**

- Swiss National Science Foundation (grant No. 310030-185233; 314730\_173127; R'EQUIP 316030\_183501)
- SNF Professorship (PP00P3\_183721)
- Landsteiner Foundation for Blood Transfusion Research (LSBR1719), Amsterdam, The Netherlands
- Product and Process Development Cellular Products Sanquin (PPOC) program Sanquin (PPOC-14-010, PPOC-15-010, PPOC-16-34, PPOC-17-44), Amsterdam, The Netherlands
- Dutch Thrombosis Foundation (TSN 201604), Amsterdam, The Netherlands
- Health Services Research grant, Swiss Cancer Research (HSR-4085-11\_2016)
- 3rd Call for Proposals for Personalized Health and Related Technologies PHRT project #2019-717

## **Highlights**

## **The International Hereditary Thrombotic** Thrombocytopenic Purpura Registry

Congenital thrombotic thrombocytopenic purpura is an autosomal recessive inherited disease with a clinically heterogeneous course and an incompletely understood genotype-phenotype correlation. In 2006, the Hereditary TTP Registry started recruitment for a study which aimed to improve the understanding of this ultra-rare disease. We found a larger proportion of compound heterozygous than homozygous carriers of ADAMTS13 c.4143\_4144dupA with overt disease onset at < 3 months of age, despite the fact that ADAMTS13 activity was <1% in 18 of 20 homozygous, but in

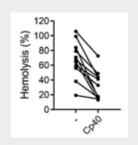


only 8 of 14 compound heterozygous carriers. An evaluation of overt disease onset in all patients with an available sensitive ADAMTS13 activity assay shows that residual ADAMTS13 activity is not the only determinant of age at first disease manifestation. Registered at clinicaltrials.gov identifier NCT01257269.

Van Dorland HA et al., Haematologica 2019: 104, 2101-2115.

## Complement C3 inhibition by compstatin Cp40 prevents hemolysis

Our results show that Cp40 can inhibit complement-mediated extravascular hemolysis of autoimmune hemolytic anemia (AIHA) sera opsonized RBCs. In addition our data show that complement regulation by Cp40 can be even more beneficial since both intra- and extravascular hemolysis are prevented. Together, we conclude that Cp40 is a promising new treatment for complement-mediated AIHA.



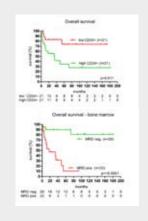
Baas I et al. Haematologica 2019, in press.

Hemolysis induced by opsonization of red blood cells with patient sera with or without Cp40

## Molecular minimal residual disease negativity and decreased stem cell mobilization potential predict

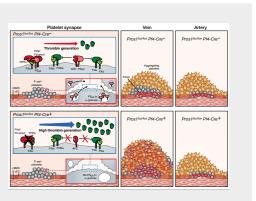
excellent outcome after autologous transplant in NPM1 mutant acute myeloid leukemia (AML) Outcomes varies if intensively treated NPM1mut AML receive consolidation treatment with autologous SCT in first complete remission depending on the NPM1mut minimal residual (MRD) status and on the stem cell mobilization potential. These results may contribute to improve the selection of appropriate candidates for autologous SCT within the subgroup of NPM1 mutated AML patients and to identify those that possibly should rather undergo allogeneic SCT if possible.

De Santiago de Benito A et al. Haematologica 2019, in press.



## Platelet protein S limits venous but not arterial thrombosis propensity by controlling coagulation in the thrombus

Platelet protein S (PSplt) controls platelet activation as well as coagulation in thrombi in large veins but not in large arteries. PSplt limits thrombin generation in the thrombus and insures that highly activated platelets and fibrin remain localized at the injury site. Calzavarini S et al., Blood 2019, in press.



## **Department of Infectious Diseases**

Inselspital, 3010 Bern www.infektiologie.insel.ch



Prof. Jonas Marschall Head of Infection Control

Prof. Hansjakob Furrer Chairman and Head of Department

Rauch
Deputy Head of
Department

## **Profile**

- Teaching students of medicine in Infectious Diseases; clinical skills training, problem based learning modules, practical months; teaching students of Dental Medicine and Biomedicine and Biology
- Accredited for postgraduate education in Infectious Diseases and Tropical Medicine
- Cohort Studies: 1. Swiss HIV Cohort Study (A. Rauch Chair of Scientific Board): Swiss and international collaborations.
   2. Swiss Transplant Cohort Study (C. Hirzel Chair of ID Board)
- Infection prevention: Healthcare-associated infections and research partnering with a number of clinical specialties of the Insel Group, IFIK, external surveillance systems Anresis and Swissnoso
- Clinical aspects and epidemiology of infectious diseases with clinical partners Insel Group and Institute for Infectious Diseases (IFIK); ID in people who inject drugs
- Research collaboration and implementation science within SubSaharan Africa: G. Wandeler via SNF, IEDA/NIH; C. Staehelin ESTHER project in Guinea-Conakry; Dr. S. Zimmerli, Harare Simbabwe
- Publications: https://boris.unibe.ch/view/divisions/DCD5A442BB13E17DE0405C82790C4DE2.html
- External Partners: Swiss Centre for Antibiotic resistance, Anresis; Swissnoso, Swiss HIV Cohort Study; leDEA, International Epidemiology Databases to Evaluate AIDS, NIH, Bethesda, USA; Swissnoso; Swiss Transplant Cohort Study; Fungal Infections Network of Switzerland; EUROSIDA; Swiss Tropical and Public Health Institute, Basel; Kirby Institute, Sydney, Australia; Centre Hospitalier Régional Spécialise Macenta Guinée-Conakry

## Grants

- SNF Project grants: 32003B\_179500 J. Marschall; 324730\_179567 A.Rauch; 33CS30\_177499 A. Rauch, H. Furrer; PMPDP3\_171259 B.Babouee
- SNF Professorship PP00P3\_176944 G.Wandeler
- SNF SPARK 19097, A. Atkinson
- SPHN Personalized Swiss Sepsis Study (PSSS), H.Furrer
- ESTHER Switzerland Partnership Project Grant 17G4, C.Staehelin

## Highlights

## **Congratulation to PD Christine Thurnheer for her Habilitation**

Mai 28, 2019 PD Dr.med. Christine Thurnheer Zürcher received the Venia docendi for Infectiology.

Her talk on "Reaching the Unreachable" mirrored the challenges in treatment of people who use intravenous drugs against HIV-Infection and Hepatitis.



## New Web-App for Antimicrobial Treatment Recommendations in the Insel Group

A great THANKYOU to Philipp Jent and Christoph Hauser who created the new web-App <a href="https://antibiotika.insel.ch/">https://antibiotika.insel.ch/</a> Try it!

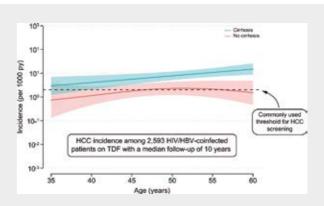
Web-App for Antimicrobial Recommendations Insel Group



#### **HCC Incidence in HIV/HBV coinfection**

Hepatocellular carcinoma (HCC) is a major cause of morbidity and mortality among HIV/HBV coinfected individuals. Among 3'625 study participants enrolled in a European multi-cohort study, 60 individuals (1.7%) developed an HCC. Age at initiation of HBV therapy and the presence of liver cirrhosis were predictors of HCC. The incidence of HCC remained below the commonly used screening threshold in patients without cirrhosis, who started on tenofovir disoproxil fumarate (TDF) when aged <46 years old.

Wandeler, G et al, J Hepatol. 2019 Aug;71(2):274-280.



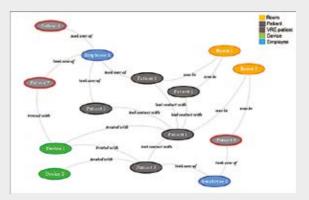
SSI-Safe-ID award for G. Wandeler's publication

## Successful ESTHER project: Introduction of point-ofcare HIV viral load measurement in Macenta, Forest Region, Guinea-Conakry, West Africa: «Go Viral»

Dr. Cornelia Staehelin and her coworkers in Guinea-Conakry have successfully implemented HIV viral load testing in Macenta within an ESTHER Project.



## Machine learning methods for understanding outbreak dynamics



Network of VRE transmission

During a large outbreak of vancomycin-resistant enterococci (VRE) we gathered all relevant data generated during medical routine on more than 60'000 admissions for data science purposes. This permitted an accurate analysis of risk factors for being affected by VRE. Machine learning methods were then employed to tie a network of VRE transmissions among patients. After securing funding from the SNF, we will continue delineating the dynamics of this outbreak with novel analytical methods in order to be prepared for future outbreaks.

For further information contact the PI of this SNF grant, Andrew Atkinson, PhD, <u>Andrew.atkinson@insel.ch</u>.

## **Department of Intensive Care Medicine**

Inselspital, 3010 Bern www.intensivmedizin.insel.ch



Matthias Theis Nursing Manager Prof. Stephan Jakob Director Chief Physician

Brigitte Hämmerli Head of IIMC Nursing Deputy Nursing

Felix Zürcher Head of Logistics

Prof. Jörg C. Schefold Chief Physician Head of Research

## **Profile**

- Key objective: to advance the pathophysiological understanding of critical illness and associated (multiple) organ failure and to develop innovative strategies to fight the increasing threat of antibiotic resistance. Special emphasis is placed on alternatives to antibiotics such as phage therapy and anti-virulence approaches.
- Clinical trials (including international multicenter trials) with internal and external partners focusing organ failure, metabolism/immune responses and severe infections.
- New translational research group "Immunosuppression in Critical Illness" founded in 2019. "European Group on Immunology in Sepsis, EGIS" co-founded by KIM
- Experimental research projects include animal models particularly on the pathophysiology of circulatory, cerebral and gastrointestinal function.
- Experimental research (including animal models particularly on the pathophysiology of circulatory, cerebral and gastrointestinal function) is performed in cooperation with other groups, including ARTORG and Institute for Infectious Diseases, University of Bern.
- Full spectrum of training in Intensive Care Medicine, including training to qualify as an ICU 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.
- Educational methods including simulator-based training, Echocardiography, Sonography and ECMO training
- External Partners: European Group on Immunology in Sepsis (EGIS): multiple research partners across Europe,
  Prof. M. Moller, Prof. A. Perner, Center for Research in Intensive Care (CRIC), Copenhagen, Denmark, Prof. K. Amrein,
  Medical University of Graz, Vienna, Austria, Prof. W. Doehner and Prof. von Haehling, Cachexia Research Groups,
  Charité University Medicine Berlin, and Goettingen University, Germany, Prof C. Storm, Charité Center of Excellence for
  Cardiac Arrest, Berlin, Germany, Marzia De Lucia, PhD PD, Head of EEG imaging, Centre for Research in
  Neuroscience Department of Clinical Neurosciences, CHUV UNIL, Laurence G. Rahme, Prof. of Surgery, Microbiology
  and Immunobiology, Harvard Medical School, Director of the MGH Molecular Surgical Laboratory, Center for Surgery,
  Innovation and Bioengineering, Massachusetts General Hospital, Boston, MA, USA

#### Grants

- Study grant: The international sham-controlled randomized clinical trial PhINEST to treat dysphagia in ICU patients post mechanical ventilation (Phagenesis Ltd.)
- ESICM Basic Science Award: Assessment of inhalative Phage Therapy in Methicillin Resistant Staphylococcus Aureus (MRSA) Ventilator Associated Pneumonia (VAP) in Rats AEROPHAGE
- Personalized Health and Related Technologies [PHRT-110] Grant: Personalized Swiss Sepsis Study (PSSS): Detection and modelling of sepsis using machine learning to analyse continuous ICU monitoring, laboratory, microbiology, and -omics data for personalized sepsis management



## Department of Medical Oncology

Freiburgstrasse 41, 3010 Bern www.onkologie.insel.ch







Prof Thomas Pabst



Prof Jöra Bever



PD Dr Urban Novak



PD Dr. Julian

Schardt

PD Dr Martin

Berger

Prof Rory Johnson

PD Dr. Carsten Riether



Häfliger

## **Profile**

- Teaching students of medicine, biomedicine and biology as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB)
- Research groups involved in basic, translational and clinical reserach
- GOLD lab with focus on long non-coding RAs (IncRNAs) links NCCR RNA and disease with clinical oncology
- Reserach focus in translational medicine in the field of Immuno-Oncology and Hematooncology
- up to 200 patients per year are treated in clinical interventional phase 1-3 trials
- fist clinic in Switzerland that treated patients with CAR-T cells 2019
- certified phase 1 trial unit

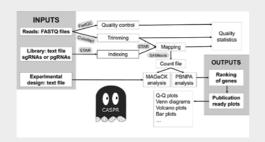
## **Grants**

- SNF Project 31003A\_182337
- SNF Sinergia CRSII5\_173738
- Krebsliga Schweiz 4534-08-2018
- Helmut Horten Stiftung
- Stiftung Für Klinisch-Experimentelle Tumorforschung (2019)
- SNFS Project 310030B\_13313
- SNFS Project 310030 179394
- Swiss Cancer League (= Krebsliga Schweiz): KFS-4389-02-2018, KFS-3815-02-2016
- Alfred and Anneliese Sutter-Stöttner Foundation (2019)

## Highlights

## Screening for novel targets in cancer using **CRISPR-Cas9**

New technological and scientific advances open new vistas for the discovery of drug targets. Long noncoding RNAs (IncRNAs) are an extremely numerous but poorly understood class of genes that have been linked to diverse cancers. The Johnson lab screens for new cancer lncRNAs using the latest CRISPR-Cas9 technology. As part of these projects, we have developed a new software pipe-

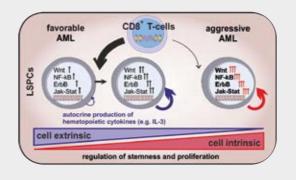


line that is capable of more accurately identifying IncRNA hits from CRISPR-screens, called CASPR (CRISPR Analysis for Single and Paired RNA-guides).

Bergadà-Pijuan J, Pulido-Quetglas C, Vancura A, Johnson R. Bioinformatics. 2020 Mar 1;36(6):1673-1680.

## CD8+ T cells expand stem and progenitor cells in favorable but not adverse risk acute myeloid leukemia

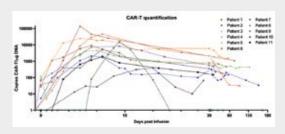
We characterized the molecular signature of leukemia stem/progenitor cells (LSPCs) and paired CD8+ T cells in patients with acute myeloid leukemia (AML). We found that CD8+ T cells support and expand LSPCs in favorable risk AML whereas intermediate and adverse risk AML possess the intrinsic molecular abnormalities to develop independently. Radpour et al., Leukemia. 2019; 33(10):2379-2392.



## Introduction of CAR-T treatment in lymphoma and ALL patients.

In January 2019, the first Swiss patient received CAR-T treatment at the University Hospital/ Inselspital. Up to 20 patients with relapsed/refractory ALL or lymphoma are treated 2019 at the Inselspital. We developed an assay to monitor persistence of CAR-T cells in the follow-up of such

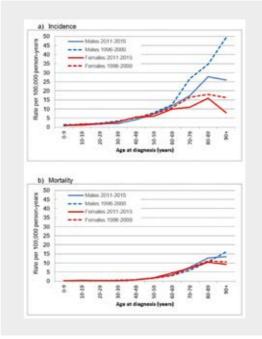
Pabst T et al; DGHO; oral presentation; Oct 13, 2019.



CAR-T persistence in lymphoma patients

### Identification of biomarkers in colon cancer

According to recent guidelines the state of the art first-line treatment of RAS wildtype (wt) metastatic colorectal cancer (mCRC) patients with a left-sided primary tumor is chemotherapy in combination with anti-EGFR antibodies, whereas right-sided tumor should be treated with chemotherapy in combination with an anti-VEGFR agent. However, to further optimize treatment we should identify a subgroup of RAS wt mCRC patients with a right-sided primary tumor, who will derive a benefit from cetuximab-based therapy in the first-line setting. Just recently, we could demonstrate that the assessment of genetic variations in both the CCR5 and CCL5 genes might help us to select those patients with right-sided RAS wt mCRC, who will benefit most from first-line cetuximab-based treatment. Suenaga M, Stintzing S, Cao S, Zhang W, Yang D, Ning Y, Okazaki S, Berger MD, Miyamoto Y, Schirripa M, Soni S, Barzi A, Heinemann V, Lenz HJ. Role of CCL5 and CCR5 gene polymorphisms in epidermal growth factor receptor signalling blockade in metastatic colorectal cancer: analysis of the FIRE-3 trial. Eur J Cancer. 2019 Jan; 107:100-114.



## first population-based data on incidence, mortality, and survival of soft tissue (STS) and bone sarcoma (BS) diagnosed in Switzerland

We performed a retrospective study with data from the National Institute for Cancer Epidemiology and Registration (NICER) database in Switzerland. The age-standardized incidence and mortality rates in 2011-2015 were 4.43 and 1.42 per 100,000 person-years for STS, and 0.91 and 0.42 for BS. Incidence rates of STS and BS have been stable since 2001. The longer RS in STS can be attributed to advances in sarcoma patient management.

Kollár et al. Cancer Epidemiol. 2019 Sep 11;63:101596.

Age-specific incidence and mortality of soft tissue sarcoma, 1996-2000 and 2011-2015

## Department of Nephrology and Hypertension

Inselspital, Kinderspital F, 3010 Bern www.nephrologie.insel.ch



Prof. Bruno Vogt Clinic Director



Prof. Dominik
Uehlinger
Deputy Clinic
Director
Prof. Uyen
Huynh-Do
Consultant
Physician



Prof. Daniel Fuster Consultant Physician



PD Dr. Geneviève Escher Lab Head

## Profile

- Teaching programs for students in medicine, biomedical sciences (BMS) and membrane biochemistry as well as supervision of bachelor and master students for their elective modules, master thesis and PhD students for Cellular and Biomedical Science (GCB)
- 8 research groups
- Investigation of the mechanims that contribute to renal function, loss upon hypoxyia and chronic allograft failure, formation of kidney stones, development of renal fibrosis and atherosclerosis, as well as factors influencing the steroid hormone metabolome and the role of the transportome in renal function
- Aim: improving diagnostic tools and implement of novel therapeutic approaches to enhance patient care
- External partners: Departement of Pharmacology and Toxicology, University of Lausanne, Switzerland; Institute of Social
  and Preventive Medicine, University of Lausanne, Switzerland; Institute of Pharmaceutical Sciences of Western
  Switzerland, Geneva, Switzerland; Institute des Cordeliers, Collège de France, Paris, France; Departement of Biochemistry
  and Biophysics, Stockholm, Sweden; University of Nottingham, Nottingham, UK; University of Cambridge, Cambridge,
  UK; Università Cattolica del sacro Cuore, Rome, Italy; University of Stellenbosch, South Africa; Baker Heart Research
  Institute, Melbourne, Australia: University of Texas Southwestern Medical Center, Division of Nephrology, Dallas, USA;
  Johns Hopkins University, Department of Physiology, Baltimore, USA

## Grants

- Swiss National Foundation (310030\_182482; 3100A\_172974; 310030\_188762/1; 331C30\_166785/1; 310030\_182272; CRSII5\_180326; CRSK-3\_190714)
- NCCR Kidney.ch
- NCCR-Kidney.CH Junior Grant Award
- NCCR TransCure
- Swiss Transplant Cohort study
- Swiss Cancer League (KFS 3966-08)
- Foundation Johanna Dürmüller-Boll

## Highlights

## Role of membrane transport proteins in health and disease

Solute Carrier (SLC) transporters play important roles in the maintenance of biological barriers in different organs, as well as intracellular organelles. Using information from various publicly available databases and scientific literature, we have recently identified ~150 putative new SLCs from human, of which ~25 have known transport function and 40% are orphans. SLCs are still relatively unexploited as therapeutic targets, and their characterization can potentially open the way for novel personalized therapeutic applications. Gyimesi & Hediger, manuscript in preparation.



SLC Atlas:
A circular
dendrogram
showing
hierarchical
clustering of
all known
human
transmembrane
transporters
of the SLC
solute carrier series.

The Human

Memo WT

Phenotype of distal femur of whole-body Memo cKO mice.

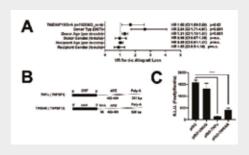
## Redox protein MEMO affects phosphotropic bone hormone FGF23 secretion and signaling

FGF receptor signaling in osteoblasts depends on the presence of the redox protein Mediator of Cell Motility 1 (MEMO). Ablation of MEMO in mice severely alters bone structure and energy metabolism. We investigate the interactions of MEMO with FGF23 biology using redox proteomics, experimental kidney disease models, bone tissue-specific mouse models and primary culture techniques of bone and kidney cells to define fundamental biological mechanisms. This may ultimately help to define diagnostic or therapeutic targets for CKD-MBD, a frequent complication of chronic renal failure that carries high morbidity and mortality. Moor et al., JBMR Plus 2018;195-200.

# Role of the TWEAK/Fn14 pathway in experimental Calcineurin Inhibitor Toxicity (CIT)

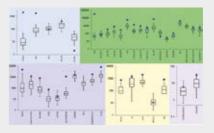
Memo cKO

Using clinical and gene-wide association data from the National Swiss Transplant Cohort Study, we demonstrated that a frequent single nucleotide polymorphism within TWEAK'S 3'UTR is predictive both for CIT lesions in the allograft and for premature allograft failure (A). We showed in vitro that the 3'UTR is critically involved in regulation of TWEAK expression potentially via post-transcriptional mRNA stabilization (B, C). We try currently to clarify the mechanisms of TWEAK's post-transcriptional regulation and its consequences on inflammation and renal fibrosis. Silder et al. Manuscript in preparation.



## Reference intervals for the urinary steroid metabolome

Circulating steroid hormones (glucocorticoids (incl. cortisol), corticosterones (incl. aldosterone) and sex steroids) mediate a wide variety of diseases, like obesity, arterial hypertension or adrenogenital syndrome. These steroids are converted into a large number of metabolites predominantly excreted via the urine. For the correct clinical interpretation of a urinary steroid profile (USP) a comparison with reference intervals is mandatory. We quantified 40 urinary steroid metabolites by gas chromatography-mass spectrometry in a large number of thoroughly characterized adults of European descent (SKIPOGH) and created sex- and age-specific reference intervals that can be used as diagnostic tools in routine clinical work. Ackermann et al., PLoS One. 2019;14(3):e0214549.

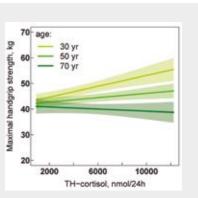


USP of a patient with a relapse of an adreno-cortical tumor producing corticosterones, glucocorticoids and sex steroids (blue dots) compared with age-matched

reference intervals (box plots). A surgical intervention can be planned after adrenal imaging.

# Association of urinary sex steroids and glucortoicoids with muscle mass and strength in healthy adults

We examined the association of urinary excreted sex steroids and gluco-corticoids with lean mass and grip strength in the SKIPOGH cohort. Our results strongly support a direct link between sex steroid and glucocorticoid hormones in a physiological range with muscle mass and function. Steroid hormones seem to exert age-specific anabolic effects on lean mass and handgrip strength: Deficits in physical performance in the aged muscle may be attenuated by androgens, whereas glucocorticoids in a physiological range seem to increase skeletal muscle mass at all ages, and muscle strength in particular in younger adults. Bochud et al., J Clin Endocrinol Metab. 2019;104(6):2195-2215.



Association of 24-hour urine TH-cortisol excretion with handgrip strength after multivariable adjustments

## Department of Neurology

Inselspital, 3010 Bern www.neurologie.insel.ch/



Prof Claudio Bassett Clinic Director



Prof Andrew Deputy Clinic Director



Prof Antoine Adamantidis Extraordinarius



Prof Urs Fischer Extraordinarius



Prof Marcel

Arnold

Saxena

Prof Selma Aybek



Prof Klemens Gutbrod



Prof Simon Prof. Paul Jung Krack



Prof Johannes Mathis



Prof. René

Müri





Schindler



Prof Werner Z'Graggen

**Profile** 

- Clinical, translational, basic and biotechnological research
- Topics and teams: sleep, stroke, epilepsy, neuroimmunology, neurorehabilitation, Parkinson/movement disorders, functional neurological disorders, Dementia/neurodegeneration
- Foundation of NeuroTec, located at sitem AG
- Teaching: Teaching students of medicine, biomedicine as well as graduate students of the Graduate School of Health Sciences (GHS) and Graduate School of Cellular and Biomedical Sciences (GCB); international postgraduate master in
- Promotion of Young Researchers: Internal funding schemes for young researchers (Research Grant in Neurology) as well as for excellent female researchers (Excellence in Diversity Fellowship)

## **Grants**

- Swiss National Science Foundation (3 grants awarded in 2019: 185362, 188761, 189077. 18 running grants: 166827; 169975; 175615; 172952; 179929; 179436; 176985; 179595; 169789; 169379; 173081; 170060; 179667; 172676; 179277; 177520; 179565; 175984)
- Horizon 2020 (4 running grants): ERC Consolidator Grants (725850 and 725825); Eurostars-2 (E! 12034/18/Q); Research and Innovation Programme (721098)
- Innosuisse (3 grants awarded in 2019: project no. 30664.1 IP-LS; 35656.1 IP-LS; 32213.1 IP\_ICT)
- Others: Swiss Heart Foundation, Swiss Academy of Medical Sciences, Gottfried & Julia Bangerter-Rhyner Foundation, Baasch Medicus Foundation, Parkinson Schweiz, Wyss Center

## **Highlights**

## Intra-arterial Urokinase as a promising treatment option after mechanical thrombectomy

Mechanical thrombectomy is the current standard of care in acute ischemic stroke patients presenting with a large vessel occlusion. In this work, it was shown that additional administration of intra-arterial Urokinase can be benefi-

cial in patients with failed procedures, without increasing the risk of systemic or intracranial bleeding. Multicenter validation of the findings and planning of a randomized-controlled trial is currently ongoing. Kaesmacher et al., JAMA Neurology 2019, in press.

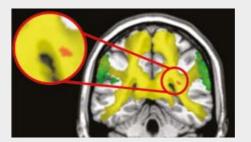


# Gain of Function Loss of Function (REM Sleep: Increase) Amblent ChR2 mics

## Dynamic REM sleep modulation by ambient temperature (T) and the Critical role of the melanin-concentrating hormone (MCH) system

Dr. Schmidt's research group show that mice dynamically increase REM sleep during thermoneutral Ta warming. Whereas optogenetic MCH activation overdrives REM sleep expression during Ta warming (gain of function), MCH silencing or lack of MCH receptor (MCHR1-KO) block the effect (loss of function). These data identify the MCH system as optimizing REM sleep timing to occur when the need for thermoregulatory defense is minimized.

Komagata et al., Current Biology, 2019, 29:1976-1987.



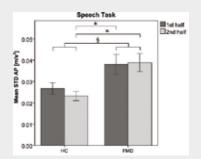
Voxels that were significantly more often lesioned in non-responders are depicted in red

## Theta burst stimulation in neglect after stroke: functional outcome and response variability origins

Using post-stroke spatial neglect as a model, we showed that the integrity of inter-hemispheric connections is a critical predictor of whether or not patients will respond to TMS. Patients with intact interhemispheric connections within the corpus callosum, in particular parieto-parietal connections, showed significantly improved and accelerated neglect recovery and general functional outcome after TMS. Nyffeler et al., Brain, 142(4): 992-1008.

## Abnormal postural behaviour in patients with functional movement disorders during exposure to stress

Patients affected by functional movement disorders (FMD) have abnormal processing of stress responses, and this could affect automatic motor defence behaviour, such as freeze response. We engaged nine FMD patients and thirteen healthy controls in the Trier Social Stress Test, while we measured their body movement. Compared to controls, FMD patients failed to show a reduction of body sway over time, i.e., freeze response, thus suggesting an impairment in the automatic defence behaviour. Zito et al., Psychoneuroendocrinology 101 (2019) 232-239.

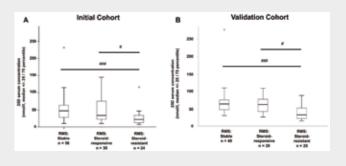


Amplitude of thorax sway, during the first and second half of the stress test. HC = healthy controls; FMD = functional movement disorders

## Vitamin D, mTOR inhibition and synergistic effects on anti-inflammatory alucocorticosteroids

We investigated whether vitamin D (VD) increases the efficacy of glucocorticosteroids (GC) for treatment of multiple sclerosis (MS) relapses. In T-cells VD upregulated the glucocorticoid receptor (GR) and methylprednisolone-induced apoptosis. In EAE, VD-GC therapy led to superior amelioration of disease compared to monotherapies; but only

if T-cell GR was present. In MS patients during GC-resistant relapse serum VD levels were decreased (figure). Using genetic/pharmacological approaches mTOR was identified to mediate the VD/GC combinatorial effect. Hoepner et al., Acta Neuropathol. September 2019.



25(OH)D serum concentrations of MS patients from 2 independent cophorts.

## Department of Neurosurgery

Inselspital, 3010 Bern www.neurochirurgie.insel.ch





Prof Claudio

Pollo







Prof Philippe

Schucht



Dr Christian

Ulrich



Prof Hans-Rudolf Prof Werne Widmer Z`Graggen

## Prof Andreas Raabe

**Profile** 

- 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
- Clinical studies or trials to investigate different managements or treatments: In our laboratory of regenerative experimental medicine we aim at the development and improvement of therapeutic strategies for neurodegenerative diseases
- Workshops for medical students, medical students in-house rotations, co-organizers of the lecture series "Disease and Repair at the CNS", supervision of master and doctoral students, mentor for PhD students
- External Partners: Laboratory of Hemodynamic and Cardiovascular Technology, EPFL Swiss Federal Institute of Technology Lausanne, Lausanne, Switzerland; Schweizer Zentrum für Elektronik und Mikrotechnologie, Neuchâtel, Switzerland; Department of Neurosurgery, Freiburg University Hospital, Freiburg, Germany

## **Grants**

- "Suprafascial vancomycin powder for prevention of surgical site infections after instrumented posterior spinal fusion: A randomized controlled phase-II trial" TU-Research Grant and research grant form the Gottfried & Julia Bangerter-Rhyner
- "MAGNEURYSM: Real-time Augmented Visualisation of Vessel Perfusion with Automated Video Analysis" Inselspital CTU-Forschungsgrant
- · "A proteomics discovery approach to identify candidate biomarkers of atherosclerotic plaque instability in endarterectomy specimens of patients with carotid disease." Schweizer Herzstiftung
- "Dynamic multimodal DBS programming tool for Parkinson Disease" Parkinson Schweiz Foundation
- "Hirnzelltransplantation bei Morbus Parkinson" HANELA Stiftung Aarau

## Highlights

## **Deep Brain Stimulation (DBS)**

Our research has pioneered the development of segmented leads and is focused on the development of a DBS algorithm to predict the most effective stimulation area in the Subthalamic Nucleus (STN) based on a comprehensive probabilistic stimulation map (PSM) of the STN integrating structural and connectivity imaging data, as well as electrophysiological biomarkers. Using computer-based biophysical electric field models, it is possible to estimate the stimulated nerve tissue around the electrode which is referred to as the volume of tissue activated (VTA). Reducing and confining the VTA to specific parts of the STN obtained from the PSM could improve outcome or even reverse stimulation induced cognitive impairments in STN DBS patients. Nguyen TAK et al., Brain Stimul. 2019.



Predicted optimized volume of tissue activated based on a probabilistic map of the best stimulation area and the patient specific location of the lead inside the Subthalamic Nucleus (orange)

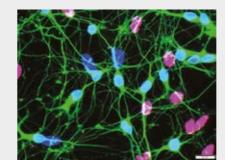
Example of computational fluid dynamic wall shear stress analysis of a brain arteriovenous malformation

#### Vascular

We have been building multidisciplinary databases for different cerebrovascular pathologies, allowing our team to participate and lead local, national and international collaborations and research projects. On the other hand, our key research activities have been focusing on different translational research projects in the fields of computer vision and machine learning applied to cerebrovascular microsurgery, intraoperative augmented reality, aneurysm microsurgery dry-lab simulation and education, computational fluid dynamic analysis of cerebrovascular diseases and proteomics approach applied to carotid atherosclerotic disease. Zuurbier SM et al., Lancet Neurol. 2019.

## Paracrine factors: A powerful tool for brain repair

In 2019 we investigated the potential of Endothelial progenitor cells-derived conditioned medium (EPC-CM) on the survival of cultured neuronal progenitor cells. Taken together, our findings identified EPC-CM as a powerful tool to promote survival of cultured neurons and further support the importance of paracrine factors in the actions of stem and progenitor cells for brain repair. Di Santo S et al., Cell Transplantation 2019.



Photomicrograph of cultured neuronal progenitor cells. Neurons with their processes are shown in green, nuclei in blue and new born cell in purple.

#### Trauma

The New England Journal of Medicine published the findings of the randomized controlled, blinded TOSCAN trial. The TOSCAN trial evaluated the role of routine CT scanning after evacuation of chronic subdural hematoma, and showed that doing CT scans only in cases of neurological evaluation decreased the number of second surgeries, had a positive impact on morbidity and mortality, and lowered costs.

Schucht et al., N Engl J Med, 2019.



CT-Images of a patient with chronic subdural hematoma

## Neurooncology

Research of the neuro-oncological team is focused on intra- and perioperative mapping and monitoring of neurological function as well as intra-operative differentiation of tumor tissue, infiltration and peri-lesional healthy brain. The team has published a key paper, which showed how post-operative transcranial magnetic stimulation can predict neurological outcome after surgery. The HORAO project reached its first milestone as the winners of the crowdsourcing competition were elected during the final conference. Preliminary studies are evaluation an array of technologies for improved tumor boarder identification, paving the way for larger trials starting 2020. Seidel et al., Clin Neurophysiol. 2019.



Winner of the HORAO crowdsourcing competition

## **Department of Nuclear Medicine**

## Inselspital www.nukmed.insel.ch



Prof Axel Rominger Director Head of Clinical Research



PD Dr Ali Afshar-Oromieh Cumming Deputy Director



Prof Paul

PD Dr. Kuangyu Scientific Head of Artificial Intelligence and Translational Theranostics



Dr Flen

## **Profile**

- Teaching students in the field of medicine, biomedical engineering, and chemistry; education of medical technical radiology assistants
- Research in radiopharmacy, oncology (theranostics), PET imaging in oncology and neurology, implementation of artificial intelligence and supprt of novel deep learning algorithms in Nuclear Medicine
- Aim: Improve PET and SPECT techniques in the field of oncology, neurology, and cardiology. Increase the therapeutic spectrum of Nuclear Medicine
- External partners: Dept. of Nuclear Medicine, University of Heidelberg; Dept. of Nuclear Medicine, Technical University Munich; Dept. of Nuclear Medicine, Ludwig-Maximilian-University Munich; Dept. of Nuclear Medicin, DKFZ Heidelberg; Fudan University Shanghai, China; Institute of Nuclear Chemistry, Johannes Gutenberg-University Mainz; Kindai University Osaka, Japan; MGH PET Core, Harvard Medical School, USA; Dept. of Molecular Pharmacology, UCLA, USA; School of Medical Technology, Peking University, Beijing, China; Dept. of Nuclear Medicine, Shanghai Jiaotong University, China

### **Grants**

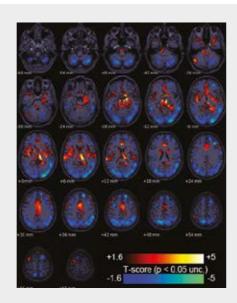
- Swiss National Science Foundation (grant no. 200021\_188914; IZKSW3\_188350)
- Swiss Cancer League (grant no. KFS-4723-02-2019)
- FreeNovation Fund, Novartis Foundation
- UniBern Forschungsstiftung (grant no. 43/2018)
- Deutsche Forschungsgemeinschaft (grnat no. RO5194/1-1)
- Berger-Janser Stiftung (grant no. 11/2019)

## Highlights

## Dopaminergic loss and its metabolic correlates in dementia with Lewy bodies

Relative glucose hypermetabolism and disturbed metabolic connectivity of limbic and basal ganglia curcuits correlated with the extent of nigrostriatal degeneration in DLB patients. The identification of specific metabolic network alterations in patients with early nigrostriatal degeneration may serve as an additional supporting biomarker for early diagnosis of DLB.

M. Huber et al. Mov Dis (2019) accepted.

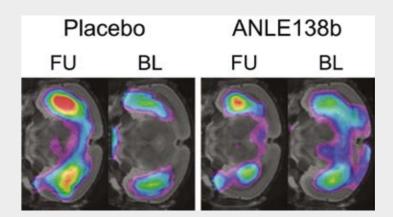


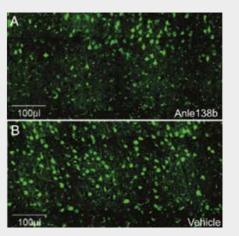
Correlation of DaT availability and FDG metabolism in DLB

## Anle138b treatment ameliorates tau pathology in a transgenic mouse model

Late-stage oligomer modulation effectively ameliorated tau pathology in hTau mice and consequently rescued metabolic function. Molecular imaging by FDG-PET could serve for monitoring effects of such treatment.

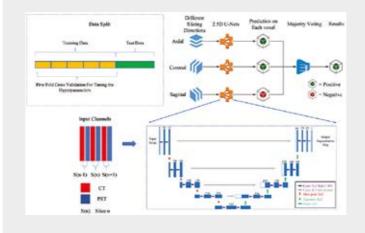
M. Brendel et al. Alzheimer's Res Ther (2019) 11(1):67.





Immunohistochemistry of frontal cortex, treatment (A) vs. vehicle (B)

Cerebral FDG-PET baseline and after 3 mo treatment vs. placebo



## Deep neural network automatically characterizes lesions on Ga-68-PMSA-PET/CT

We developed a deep neural network to characterize automatically the prostate cancer lesions on Ga-68-PSMA-PET/CT. The preliminary test within the pelvic area confirms the potential of deep learning methods.

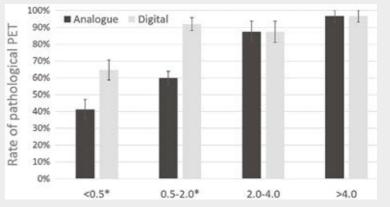
Y. Zhao, et al. EJNMMI (2019) Epub.

Architecture of the proposed framework

## **Digital PET/CT detects** more lesions compared to analogue PET/CT

Digital PET/CT detected more prostate cancer lesions compared to an analogue PET/CT. A significantly higher rate of pathological PET/CTs was found in the patient group with the lowest PSA levels. The differences could be plausibly explained by the measured imaging characteristics of the scanners.

I. Alberts, et al. EJNMMI (2019) Epub.



Frequency of pathological PSMA PET/CT findings

## Department of Obstetrics and Gynecology

Inselspital, Friedbühlstrasse 19, 3010 Bern

www.frauenheilkunde.insel.ch; www.dbmr.unibe.ch

#### **Division of Obstetrics and Feto-Maternal Medicine**



Prof. Daniel Surbek Director and Co- Deputy Director Group Leader

Laboratory

Prenatal

Medicine



Raio Head Research Group Leader



PD Dr. Beatrice Mosimann



PD Dr Marc Baumann Group Leader



PD Dr. Andreina Schoeberlein Co-Head Research

Prenatal Medicine

Laboratory

Group Leader

Group Leader

## **Profile**

Areas of Scientific Investigation:

- Stem cells, exosomes, non-coding RNA and sPIF in peripartum Neuroregeneration
- Basic function of Astroglia in peripartum hypoxia and inflammation
- Transmembrane transporter and biomarker in preeclampsia and preterm birth
- Clinical research in preterm birth, fetal neurosonography, labor induction, postpartum hemorrhage
- Teaching: preclinical and clinical at master, MD and PhD level; postgraduate preclinical / clinical training
- External Research partners: Dept. Pediatrics and Neonatology, Maastricht University; Dept. Neurosurgery, Cellular and Molecular Physiology, Yale University; Dept. Obstetrics, Peking Union Medical College Hospital (PUMCH); Dept. Obstetrics, Basel University; Dept. Obstetrics, Schiller University Jena; Dept. Obstetrics, University of Insubria, Varese; Risch Laboratory, Bern; BioIncept, LLC, Cherry Hill, New Jersey

## **Grants**

- SNF Grant: "Salt Supplementation in pregnancy at high risk to develop preeclampsia"
- EU Grant COST: "International network for translating research on perinatal derivatives"
- Bangerter Stiftung: "Mesenchymal stem cells-derived exosomes as a neuroregenerative therapy"
- CTU Grant: "Preimplantation factor: Biomarker for preterm birth?
- Grant Swiss Society of Obstetrics and Gynaecology / Bayer
- Investigator-initiated trial (Vifor): "Patient blood management in obstetrics"
- Investigator-initiated trial (Ferring): "Induction of labor: misoprostol vaginal insert vs tablets"
- Perinatal medicine intramural fund: Several grants for clinical studies

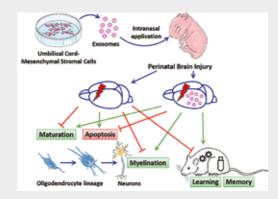
## Highlights

## Stem cells in peripartum brain damage: **Translation**

Thomi G et al. Intranasally Administered Exosomes from Umbilical Cord Stem Cells Have Preventive Neuroprotective Effects and Contribute to Functional Recovery after Perinatal Brain Injury. Cells 2019 Aug 8;8(8).

Thomi G et al. Exosomes derived from umbilical cord mesenchymal stem cells reduce microglia-mediated neuroinflammation in perinatal brain injury. Stem Cell Res Ther. 2019 Mar

Eggenberger S. et al. Stem cell treatment and cerebral palsy: Systemic review. World J Stem Cells. 2019;11:891-903.



Peripartum neuroregeneration mechanism

## **Division of Gynecology and Gynecological Oncology**



Mueller Director and Head Research



Prof. Annette



PD Dr. Sara Imboden



Konstantinos Nirgianakis



Andrieu

#### **Profile**

- Pathophysiology of endometriosis and associated pain
- Pathophysiology of gynaecologic cancers
- Quality of life before and after urogynaecologic interventions
- Physiologic and pathophysiologic changes of the pelvic floor during exercises
- Transgender studies
- External partners: Center for Gender Variance, Univ. of Basel; Berner Fachhochschule, Bern; Dell Medical School, Univ. of Texas, Austin; Croydon Univ. Hospital, London; Dept. of Obstetrics & Gynaecology, Inst. for Molecular Biosciences, Queensland; Clinical Pathology & Cytology, Karolinska Univ. Hospital, Stockholm; Dept. of Urogynaecology, Princess-N-Hospital, Southampton; Dept. of Obstetrics & Gynecology, Ospedale Santa Chiara di, Trento

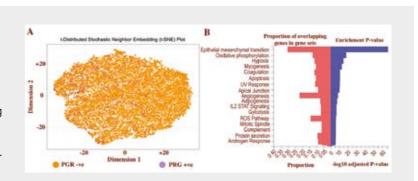
### Grants

- Swiss National Science Foundation
- Contura AG, Copenhagen, Denmark
- Bern Center for Precision Medicine (BCPM)
- Innosuisse Swiss Innovation Agency
- Stiftung für Klinisch-experimentelle Tumorforschung

## Highlights

## Progesterone resistance in endometriosis

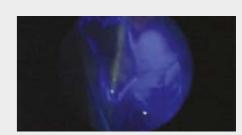
Dienogest is one of the promising options for the long-term hormonal management of endometriosis. By analyzing the prevalence of somatic mutations, cellular composition (progesterone receptor level in stromal cells, Fig. A), or transcriptomic profile between endometriotic lesions from non-responders



(GO, Fig B), we intend to unveil the mechanism of Dienogest resistance which occurs in several patients.

## Endometrial cancer (EmCa) with sentinel lymphnode (SLN) dissection

SLN removal offers a convincing balance between oncological safety and perioperative morbidity in early-stage EmCa. However, lymphovascular space invasion may represent a risk factors for recurrence and therefore lymph-node evaluation is crucial. Imboden S. et al. Eur J Surg Oncol. 2019



SLN marked with ICG (Indocyanine green)

## Department of Ophthalmology

Inselspital, 3010 Bern www.augenheilkunde.insel.ch



Prof. Sebastian Wolf Director



Früh

Anterior

Seament

Prof Martin Prof Beatrice Zinkernagel Outpatient Department



Prof Mathias Abegg Orthoptic Goldman Foundation



Prof Volker Enzmann Research Laboratories



Escher Ophthalmogenetics

## **Profile**

- Teaching students of medicine, biomedicine and biology as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB)
- 6 research groups
- 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
- External Partners: Dept. of Biology, University of Fribourg, 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

## **Grants**

- · A pragmatic, randomized, non-inferiority trial comparing the effectiveness of Botulinum toxin-based treatment with conventional strabismus surgery in acquired esotropia SNF 33IC30\_173533
- Molecular mechanisms of NR2E3-linked retinal degenerations SNF 33IC3031003A\_169237

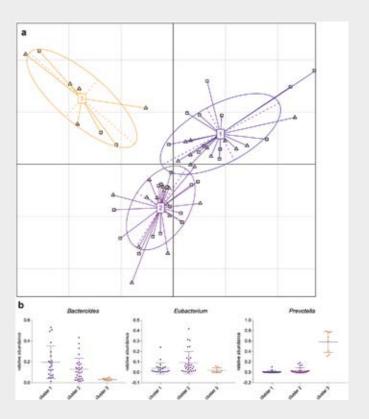


## Highlights

## Retinal artery occlusion is associated with compositional and functional shifts in the gut microbiome and altered trimethylamine-N-oxide levels

Retinal artery occlusion (RAO) is a sight threatening complication of cardiovascular disease and commonly occurs due to underlying atherosclerosis. As cardiovascular disease and atherosclerosis in particular has been associated with compositional alterations in the gut microbiome, we investigated this association in patients with clinically confirmed non-arteritic RAO compared to age- and sex-matched controls. On the phylum level, the relative abundance of Bacteroidetes was decreased in patients with RAO compared to controls, whereas the opposite applied for the phylum of Proteobacteria. Several genera and species such as Actinobacter, Bifidobacterium spp., Bacteroides stercoris, Faecalibacterium prausnitzii were relatively enriched in patients with RAO, whereas others such as Odoribacter, Parasutterella or Lachnospiraceae were significantly lower. Patient's gut microbiomes were enriched in

genes of the cholesterol metabolism pathway. The gut derived, pro-atherogenic metabolite trimethylamine-N-oxide (TMAO) was significantly higher in patients with RAO compared to controls (p = 0.023) and a negative correlation between relative abundances of genera Parasutterella and Lachnospiraceae and TMAO levels and a positive correlation between relative abundance of genus Akkermansia and TMAO levels was found in study subjects. Our findings proposes that RAO is associated with alterations in the gut microbiome and with elevated TMAO levels, suggesting that RAO could be targeted by microbiome-altering interventions. Gut enterotypes in the cohort. Three enterotypes exist in the cohort based on the abundance of microbial genera. Patients (n = 29) and controls (n = 30) are denoted by squares ( $\square$ ) and triangles ( $\Delta$ ), respectively (a). Boxplots represent the abundance of Bacteroides, Eubacterium and Prevotella, the proposed drivers of the three enterotypes (b). Blue is enterotype 1, purple is enterotype 2 and orange is enterotype 3. Scientific reports (2019) 9:15303.



## Evaluation of different Swept-Source optical coherence tomography angiography (SS-OCTA) slabs for the detection of features of diabetic retinopathy

The purpose of the study was to compare different 12 9 12 mm SSOCTA slabs centred on the fovea (retinal, superficial and in addition the deep slab) to see if there is a significant difference in the detection rate of features of diabetic retinopathy depending on the slab examined. Consecutive patients with DR were evaluated using SS-OCTA. The central 12 3 12 mm scan was used to generate the retinal, superficial and deep slab. The grading results of the slabs were then compared to determine if one specific slab is superior to detect respective features. A total of 348 eyes (190 patients; mean age 58.1 \_ 14.5 years) were graded for features of DR. The retinal slab detected most frequently MAs and IRMAs, however with no significant difference compared to the superficial slab (p = 0.93 and p = 0.93, respectively). Small capillary dropout was most frequently found on the superficial slab, but there was no significant difference compared with the retinal (p = 0.78) and deep slab (p = 0.45). The only statistically significant difference was found for large capillary dropout, where the retinal and superficial slab showed a higher detection rate compared with the deep slab ( $p \le 0.0001$  and p = 0.001, respectively). The superficial and retinal slabs are equally suitable for grading with no statistically significant difference in the detection rate of the diabetic features

Acta Ophthalmol. doi: 10.1111/aos.14299

## Department of Orthopedic Surgery and Traumatology

Inselspital, 3010 Bern www.orthopaedie.insel.ch



Prof Klaus A Siebenrock Chairman



Prof Lorin M Benneker Head Spine Surgery



Dr Michael Schär Head Shoulder, Elbow and Sports



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

PD Dr Fabian

Head Foot and

Ankle Surgery

Krause



PD Dr. Johannes D. Bastian Head Orthogeriatrics



PD Dr Sven Translational Medicine and Spine Research



Dr. Moritz Deml Pediatric Spine Surgery



Prof. Matthias 7umstein and Sports



Prof Marius Shoulder, Elbow Consultant Hip and Spine Surgery

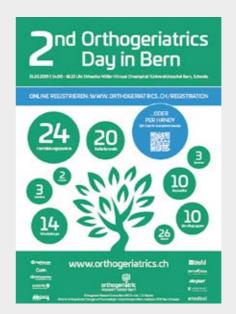
## **Profile**

- Hip research focus on the development of osteoarthritis and pre-arthritic deformities like femoroacetabular impingement
- Spine research is focused on disc degeneration models and tissue-engineered disc regeneration and the treatment of osteoporotic fractures
- The shoulder & 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
- 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
- Arthrosis of the ankle joint, innovative treatment of ankle fractures and AMIC plastic in osteochondral lesions is the main focus in foot & ankle research
- Orthogeriatrics investigates the impact of orthogeratric pathways and rehabilitations protocols on the clinical outcome in
- Translational medicine is the latest research field which will come to focus the during the next years
- External Partners: 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: RMS Foundation, Bettlach: SUVA

### **Grants**

- Zumstein M, Dommer L: Timepoint and direction of secondary dislocation in early conservative treatment in distal radius fractures using 3D imaging. Hans Neuenschwander Fonds, 2019
- Gantenbein B, Benneker L: «Working Package 1 of the H2020 Project "iPSpine- Project Agreement #825925 Induced pluripotent stem cell-based therapy for spinal regeneration»
- Siebenrock KA, Beckmann NA, Fellowship Hip Surgery, Hans Neuenschwander Fonds & Depuy Synthes, 2019

## **Highlights**



## Second Swiss Orthogeriatric Day, 31.10.2019

The number of elderly patients in orthopaedics and traumatology is steadily increasing and represents a new challenge in interdisciplinary and interprofessional treatment. Accordingly, in 2018 the «1st Swiss Orthogeriatrics Day Bern» was initiated by PD Dr. med. J. D. Bastian and hosted together with Prof. Dr. med. A. E. Stuck to provide a platform for all occupational groups involved in the treatment of the elderly for a rich and informative interdisciplinary exchange. On the 31 October in 2019, we were able to build on our previous success with the «2<sup>nd</sup> Swiss Orthogeriatrics Day» and hosted that symposium with PD Dr. med. J. D. Bastian together with Prof. Dr. med. A. Schönenberger. The program included the following sessions: Session 1:

«Key Note Session» Gerontotraumatology from an emergency medicine point of view

Session 2.

«Parallel Workshop-Sessions of different disciplines» with «Handson» about «The hands in old age - The key to independence» (Ergotherapy), «Malnutrition in orthogeriatrics» (Nutrition Counselling),

«Geriatric assessment» (Geriatrics), «Co-management in the Rhine Valley» (Geriatrics), «Guided Tour around the Emergency Department, Inselspital» (Emergency Medicine), «Sonography in Gerontotraumatology» (Emergency Medicine), «Challenges in an acute-care hospital» (Nursing Staff), «The orthogeriatric patient» (Physiotherapy), «Patient discharges in succession scenarios» (Social Services), «Osteoporotic vertebral fractures» (Orthopaedics), «ADAPT system for Gamma3 nail» (Orthopaedics), «Tricky Trauma Cases – think outside the box!» (Orthopaedics), «TFN-A on the sawbone» (Orthopaedics)

Session 3:

Unstable joint fractures - how does post-treatment work? As a debate session with specialist contributions with «Pros» and «Cons» for one or another treatment.

About 170 participants from 16 different cantons in Switzerland joined this event and made it a great success. For 2020, the 3<sup>rd</sup> Orthogeriatrics Day is already under preparation.

## Sarcoma Center Bern

Sarcomas are a group of rare cancers originating from bone and the soft tissues. The Sarcoma Center Bern is one out of five university centers specialized on the care of sarcoma patients in Switzerland. Currently, the Sarcoma Center Bern is the only Swiss center fully certified according to ISO 9001:2015 and the German Cancer Society (DKG). The center, led by the Department of Orthopaedic Surgery, belongs to the University Cancer Center Inselspital (UCI). At the Sarcoma Center Bern 17 medical disciplines make use of state of the art diagnostic and treatment modalities and provide personalized care in order to ensure the best treatment for sarcoma patients.

A recent multicenter population-based retrospective registry study performed together with the National Institute for Cancer Epidemiology and Registration (NICER) was the first study analyzing population-based data on the temporal trends of incidence, mortality and survival of soft tissue and bone sarcomas diagnosed in Switzerland. The study showed a stable, low incidence rate of approximately five soft tissue sarcomas (STS) and one bona sarcoma (BS) per 100'000 person years, respectively. This related to an overall annual incidence of 366-448 STS and 63-77 BS in Switzerland between 1996 and 2015.



## **Department of Osteoporosis**

Inselspital, Imhoof-Pavillon, 3010 Bern www.osteoporose.insel.ch





Prof Kurt Lippuner Director and Head Physician

Hunziker Head Translationa Research Group

## **Profile**

- Epidemiological Research: focused on the epidemiology of fractures and the socioeconomic burden of osteoporosis and fractures; continued development and update of the country-specific fracture risk prediction tool (FRAX)
- Translational research: development of bone strength prediction and clinical fracture risk assessment by finite element analysis using high resolution peripheral quantitative CT (HR-pQCT) at the forearm and the tibia
- Clinical research (Phase II-IV): development of new investigational drugs for the treatment of osteoporosis and the reduction of fracture risk
- Experimental first in man clinical research: investigation of local bone remodeling and mechanoregulation of bone fracture healing in healthy, aged, and osteoporotic humans; targeted stimulation of bone anabolism with in situ bone active agents; osseointegration of bone implants
- Osteoporosis lectures for medical students in the context of geriatrics (year 4), practical courses on pharmaceutical medicine for students of human medicine (year 2); module "bone measurement technologies" of the "Biomechanics Labs" for students of biomedical engineering
- External research partners: Centre for Metabolic Bone Diseases, University of Sheffield, UK; ETH Zurich, Institute for Biomechanics, Zurich; Free University of Amsterdam (ACTA), Amsterdam, the Netherlands; Swiss Paraplegic Center, Clinical Trial Unit, Nottwil, Switzerland; University Hospitals of Geneva, Service of Bone Diseases, Department of Rehabilitation and Geriatrics, Geneva; Zhejiang Chinese Medical University, Hangzhou, China

#### Grants

- MICROMESO SNF project grant no 165510 until 2020 (Co-Pl)
- PARATY Fondation pour l'Ostéoporose until 2020 (PI)
- AFFIRM-CT SNF sinergia grant no 183584 until 2023 (Partner)
- 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, Univ. Hospital Innsbruck, Univ. Ulm. —>2021

## Highlights

## **BMP-7 for Implant Osseointegration in Osteoporosis**

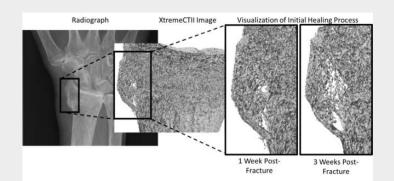
Osseointegration of dental and orthopaedic implants is seriously impaired in an osteoporotic environment. By using bone morphogenetic protein-7 (BMP-7) we are able to significantly improve implant healing when used at a low dose in a delayed drug-release system, and were also able to prevent drug-related side-effects (ectopic bone formation, inflammation, cyst formation etc.). Hunziker et al: The Slow Release of BMP-7 at a Low Dose Accelerates Implant Healing in an Osteoporotic Bony Environment. Ready for submission, 2019.



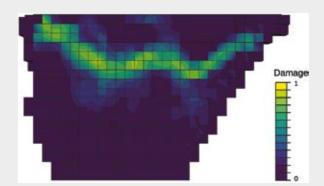
Osseointegrated experimental dental implant in the osteoporotic bone

## SNSF DACH Fracture study (DACH-Fx)

In collaboration with ETH Zurich, University Hospital Innsbruck, Ulm University, and Insel Orthopaedics, this study follows distal radius fracture patients over one year. Detailed clinical assessment and HR-pQCT imaging are performed at six time points. This study will characterize fracture healing at the level of single trabeculae as well as the outcome contribution of age, osteoporosis, and bone biomarkers. In addition, computational models are built to study local mechanical regulation and to simulate the healing process.



2D radiograph of a right wrist showing a fracture of the radius (left). Cut away of the radius with region of fracture healing after 1 and 3 weeks, respectively. Image courtesy of Penny Atkins.



Failure zone of the distal radius calculated by homogenised finite element analysis

## **HR-pQCT-Based Estimation of Bone** Strength

High-resolution peripheral computed tomography (HR-pQCT) allows to reconstruct the in vivo geometry of distal fracture sites, including at the radius and the tibia, with a resolution of 61 microns. A novel measurement protocol with multiple bone sections and a homogenised finite element methodology was developed for evaluation of bone strength at the distal radius and tibia. An extensive in vivo reproducibility study was conducted to determine the precision of this methodology. Finally, reference values and clinical predictors of bone strength for HR-pQCT-based distal radius and tibia strength were established in young Swiss women and men.

Schenk D, Mathis A, Lippuner K, Zysset P, Annual Meeting of the American Society of Bone and Mineral Research (ASBMR), Orlando, September 20-23, 2019.

### Periodontitis and Periimplantitis in Osteoporosis

Periodontitis (POIS) and periimplantitis (PIIS) are very frequent diseases in dentistry and patients with osteoporosis. We investigated the differences between the two diseases in generally used experimental in vivo-models. Bone resorption was found to be significantly higher in the PIIS model. Huang et al.: What are the differences in the inflammatory process between experimental periimplantitis and periodontitis? Submitted for publication, 2019.



Top panel: in situ photograph of a ligature-induced paradontitis (tooth) and an implant with periimplantitis. Bottom panel: same set-up as above, imaged by CBCT.

## **Department of Pediatrics**

Inselspital, 3010 Bern www.kinderkliniken.insel.ch/de/kinderkliniken/kinderheilkunde



Prof Steffen Berger Director a.i.



Prof Christoph Extraordinarius and Head Paediatric Infectiology



Prof Christa Flück Extraordinaria and Head Paediatric Endocrinology, Diabetology and and Allergology Metabolism



Prof. Philipp Latzin Extraordinarius and Head Paediatric Pneumology



Prof Jochen PD Dr André Rössler Schaller Head Paediatric Head a.i. Haematology Genetics and Oncology



Prof Maia Steinlin Extraordinaria and Head Paediatric Neurology and Neurodevelopmental

## **Profile**

- Teaching at every level of the School of Medicine and other courses at the University of Bern
- Providing training in Paediatrics and all its subspecialities as well as in Medical Genetics (FMH, FAMH)
- Offering PhD training in programs of the Graduate Schools of the University of Bern
- Very broad research spectrum ranging from basic to translational to clinical projects
- Genetics: Projects to identify novel disease-associcated genes in rare diseases. Partners: University Hospitals Switzerland
- Haematology/Oncology: Strategies to manage fever in neutropenia; Trying to understand the situation of childhood cancer survivors (in collaboration); Studies on mechanisms of genomic instability hematological malignancies (in cooperation with the DKFZ); Preclinical research focusing on new drugs and delivery for pediatric sarcoma
- Infectiology: Multidimensional research of pediatric sepsis as host organization of the Swiss Pediatric Sepsis Study; Partners: Children's Hospital, University of Queensland, Australia; University Children's Hospital, Zürich; Department of Pediatrics, University of Lausanne, CHUV, Lausanne
- Neuropaediatrics: SNPSR and CP registry studies in collaborations with other Swiss Children's Hospitals; Brainfit-Study in collaboration with the University Children's Hospital Zürich and Neuroimaging Center Salzburg, Austria; HERO-Study (reorganisation after paediatric stroke, collaboration); Onset-Study (influence of age at acute brain problem collaboration)
- Pneumology: Research topics: lung development in health and disease, novel lung function tests and state-of-the-art diagnostics in rare diseases; key projects: BILD (www.bild-cohort.ch), SCILD (www.scild.ch) lwith worldwide partners a
- The list of the above mentioned research topics and collaborators is noncomprehensive

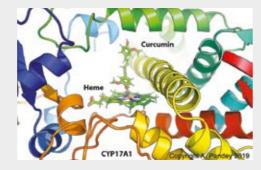
## **Grants**

- HORIZON 2020 PERFORM, Partner (2017-2020), DIAMONDS, Partner (2020-2024), Infectiology
- SNF Nr. 182719 (Latzin), 179905 (Yammine), 168173 (Ramsey), 182871 (Frey), Pneumology
- Uniscientia, Novartis and IFCAH-ESPE grants; Endocrinology
- Krebsforschung Schweiz-4709-02-2019 (Leibundgut), Oncology

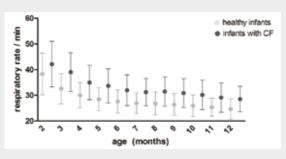
## **Highlights**

## Curcuminoids as potential drugs against breast and prostate cancer

Curcumin, the major component of commonly used spice turmeric, can inhibit activities of steroid metabolizing enzymes CYP17A1, a target of drugs for prostate cancer, and CYP19A1, a target for drugs against breast cancer. Our results propose that curcuminoids may be modified to generate better lead compounds for potential drugs against prostate and breast cancer. Rodríguez Castaño P et al., Int J Mol Sci. 2019 20(18).



Curcumin docked into active site of steroid metabolizing enzyme CYP17A1.



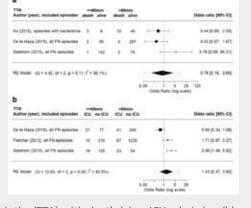
Respiratory rate is higher in infants with CF (black dots) compared to healthy infants (grey dots) throughout the first year of life.

## Respiratory rate is increased in infants with cystic fibrosis throughout the first vear of life

In more than 5000 measurements from 153 infants, we were able to show that infants with cystic fibrosis had a higher respiratory rate throughout the whole first year of life than healthy controls. This suggest that subtle pulmonary changes occur already that early in life. Korten et al., J. of Cystic Fibrosis, 18 (1), Jan. 2019, 118-126.

## Association of time to antibiotics and clinical outcomes in patients with fever and neutropenia during chemotherapy for cancer: a systematic review

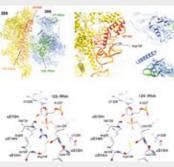
Time to antibiotics refers to the timespan until intravenous antibiotics are administered in a neutropenic patient developing fever. Meta-analysis suggest after quality assessment that there is an association between longer TTA and impaired safety. Triage bias, i.e. faster treatment of patients with worse clinical condition, was identified as a relevant confounding factor. Koenig C et al. Support Care Cancer. 2020 Mar;28(3):1369-1383.



Meta-analysis Time to antibiotics (TTA) with death (a) or ICU admission (b).

## A variant in MRPS14 (uS14m) causes perinatal hypertrophic cardiomyopathy with neonatal lactic acidosis, growth retardation, dysmorphic features and neurological involvement

We identified a homozygous variant in the mitochondrial small ribosomal protein 14 (MRPS14, uS14m) in a patient manifesting with perinatal hypertrophic cardiomyopathy, growth retardation, muscle hypotonia, elevated lactate, dysmorphy and mental retardation. Our data demonstrates a novel molecular pathogenic mechanism that impairs the function of mitochondrial ribosomes during translation elongation or mitochondrial mRNA recruitment Jackson et al., Hum Mol Genet 2019 Feb;28(4):639-649.



Modelling of uS14m mutation R108C within the 55S mitochondrial initiating Ribosome.

## Functional resting state MR in childhood

Functional resting state MR is increasingly important for research of brain development and effects of brain lesions as stroke, brain tumors trauma during childhood. We analyzed different networks in healthy children and also in children after stroke or brain tumors. We could show, that especially cognitive networks do develop after the early childhood with increasing connections not only in cortical networks but especially in thalamocortical networks. In children after stroke or brain tumors network alterations correlate with cognitive and motor outcome. Steiner et al., submitted.

## **Department of Pediatric Surgery**

Inselspital, 3010 Bern www.kinderkliniken.insel.ch/de/kinderkliniken/kikli-chirurgie





Fasler-Kann









PD Dr. Thoralf Liebs

PD Dr. Ulf Kessler

Profile

- Participates in University teaching programs for students of medicine (PBL-teaching, bedside teaching, practical year, clinical skills training, surgical rotation for students)
- Oncobiology research (laboratory research in childhood malignancies); study of the expression of Tim-3 and Gal-9
  molecules and their roles in leukemia and in pediatric and adult solid tumors: PD Dr. E. Fasler-Kan
- Research of Necrotizing enterocolitis of the newborn (Hosting of the Swiss national NEC registry): Prof. S. Berger, PD Dr. U. Kessler, Dr. M. Kordasc
- Research of Pathophysiology of necrotizing enterocolitis and appendicitis: PD Dr. U. Kessler
- Health related quality of life research after pediatric extremity fractures (clinical research and follow up studies): PD Dr. T. Liebs, Dr. N. Kaiser
- Development of new operative strategies in pediatric hip surgery and clinical outcome research after surgical treatment of
  paediatric hip and knee diseases, including slipped capital femoral epiphysis and ruptured anterior cruciate ligaments. PD
  Dr. K. Ziebarth

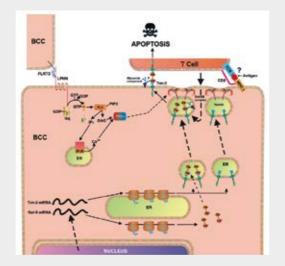
#### **Grants**

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

## Highlights

# The Tim-3-Galectin-9 Pathway and Its Regulatory Mechanisms in Human Breast Cancer

Human cancer cells operate a variety of effective molecular and signaling mechanisms which allow them to escape host immune surveillance and thus progress the disease. We have recently reported that the immune receptor Tim-3 and its natural ligand galectin-9 are involved in the immune escape of human acute myeloid leukemia (AML) cells. We now found that studied breast tumors expressed significantly higher levels of both galectin-9 and Tim-3 compared to healthy breast tissues of the same patients and that these proteins were co-localized. Surface-based galectin-9 was able to protect breast carcinoma cells against cytotoxic T cell-induced death. Furthermore, we found that cell lines from brain, colorectal, kidney, blood/mast cell, liver, prostate, lung, and skin cancers expressed detectable amounts of both Tim-3 and galectin-9 proteins. We conclude that the Tim-3-galectin-9 pathway is operated by a wide range of human cancer cells and is possibly involved in prevention of anti-tumor immunity. Yasinska et al., Front. Immunol. 2019; 10:1594.

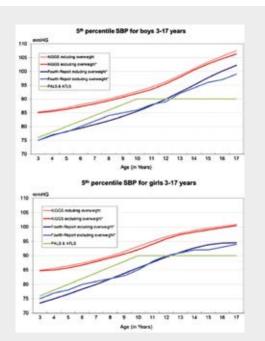


Breast cancer cell-based pathobiochemical pathways showing LPHN-induced activation of PKCa, which triggers the translocation of Tim-3 and galectin-9 onto the cell surface which is required for immune escape.

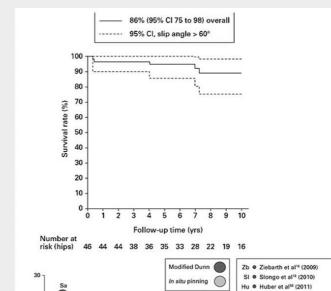
## Definition of pediatric hypotension: Gaps between two percentile-based definitions and Pediatric Advanced Life Support/Advanced Trauma Life Support guidelines

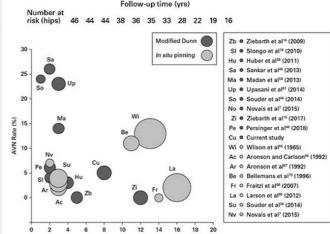
Data are lacking to provide cutoffs for hypotension defining shock in children based on outcome studies. Pediatric Advanced Life Support (PALS), and Advanced Trauma Life Support (ATLS) definitions are based on normal populations. We compared different normal population based cutoffs including fifth percentile of systolic blood pressure (P5-SBP) in children and adolescents from the German Health Examination Survey for Children and Adolescents (KiGGS, 12.199 children aged 3-17 years), US population data (Fourth Report), and cutoffs from PALS and ATLS guidelines. The KiGGS P5-SBP was on average 7 mm Hg higher than Fourth Report P5-SBP (5–10 mm Hg depending on age-sex group). For children aged 3 to 9 years, KIGGS P5-SBP at median height follows the formula 82 mm Hg + age; for age 10 to 17 years, the increase was not linear. Current PALS/ATLS guidelines largely underestimate the rate of hypotension in children with

Sarganas et al., J Trauma Acute Care Surg. 2019;86: 448-453.



Fifth SBP percentiles curves for boys (upper panel) and girls (lower panel) aged 3 to 17 years according to the KIGGS population (red), the Fourth Report references (blue); thresholds of the PALS and the ATLS (green).





## Long term results of modified Dunn procedure in SCFE

AIMS: The modified Dunn procedure has the potential to restore the anatomy in hips with severe slipped capital femoral epiphyses (SCFE). However, there is a risk of developing avascular necrosis of the femoral head (AVN). In a retrospective analysis involving 46 hips in 46 patients treated with a modified Dunn procedure for severe SCFE (slip angle > 60°) between 1999 and 2016. At nine-year-follow-up, 40 hips were available for clinical and radiological examination. Mean preoperative age was 13 years, and 14 hips (30%) presented with unstable slips. Mean preoperative slip angle was 64°.

The modified Dunn procedure for severe SCFE resulted in a low rate of AVN, low risk of progression to OA, and high functional scores at long-term follow-up. The slip deformities were mainly corrected but secondary impingement deformities can develop in some hips and may require further surgical treatment. Lerch et al., Bone Joint J 2019;101-B:403-414.

Upper panel: Kaplan–Meier analysis with the cumulative ten-year hip survival rates.

Lower panel: Avascular necrosis of the femoral head (AVN) rate and follow-up time for studies reporting outcome after in situ pinning and the modified Dunn procedure. Bubble size represents the number of patients per study.

## **Department for Plastic and Hand Surgery**

Inselspital, Freiburgstrasse 10, 3010 Bern www.plastichandchirurgie.insel.ch





Prof. Mihai Constantinescu

Prof. Est ı Vögelin

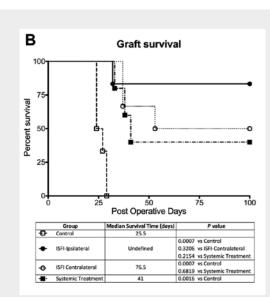
## **Profile**

- Conducting clinical and basic research in the fields of Plastic, Reconstructive and Aesthetic Surgery, under the lead of Prof. Mihai Constantinescu, and Hand Surgery and Surgery of the Peripheral Nerve, under the lead of Prof. Esther Vögelin
- Focus of the Plastic Surgery clinical research: implementation of 3D models of aesthetic tissue reconstruction and innovative strategies for the diagnosis and treatment of critical ischemic tissue and malignant skin tumors
- Focus of the Hand surgery research: developing new treatment modalities for hand injuries by application of new drugs and evaluation of innovative modalities for repair of peripheral-nerve injuries
- Conducting several basic research projects in the field of vascularized composite allotransplantation (VCA)
- Investigating the possibility to use vascularized composite tissue-engineering (VCE) and innovative nanoparticle-based modalities for the treatment of nerve injuries and surgical complications Teaching programs for students of Medicine, Biomedical Science and Molecular Life Science, 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
- External Partners: 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 Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences, ETH Zurich, Switzerland.; Swiss Federal Laboratories for Materials Science and Technology, St Gallen, Switzerland

## **Grants**

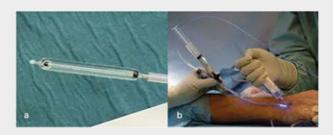
• SGH Forschungspreis Stefanie Hirsiger (Nov. 2019) "Diagnostic Case-Control Study: Ultrasound 'in Carpal Tunnel Syndrome: Outlet Ratio"

## Highlights



Delivery of Rapamycin Using In Situ Forming Implants Promotes Immunoregulation and Vascularized Composite Allograft Survival

Scientific Reports, 9(1), p. 9269. Nature Publishing Group 10.1038/s41598-019-45759-y.





# Osteosynthesis of fifth metacarpal neck fractures with a photodynamic polymer bone stabilization system

Figure 1: (a) Polyethylene terephthalate balloon filled with monomer ex situ. (b) After implantation the resin is cured in situ by application of visible light.

Figure 2: Fifth metacarpal neck fracture in posteroanterior and 45° oblique radiographs (a) preoperatively and (b) after fracture reduction and osteosynthesis with an intramedullary photodynamic polymer. (c) Radiological follow-up 3 months after operation.

Journal of hand surgery. European volume, p. 1753193419880775.

Sage 10.1177/1753193419880775.



## Non-vascularized partial joint transfer for Finger Proximal Interphalangeal joint reconstruction: a series of 9 patients

In this study, non-vascularized partial joint transfer provides a mobile and stable PIP joint up to 4 years after reconstruction. The surgical technique presented herein is complex depending on additional soft tissue, tendon and nerve injuries but results in great patient satisfaction.

Archives of orthopaedic and trauma surgery Springer 10.1007/s00402-019-03301-9.

### LIMIT Sudy

We investigated whether intradermally administered indocyanine green (ICG) and near infrared fluorescence imaging (NIRFI), sentinel lymph nodes (SLNs) in malignant melanoma and Merkel cell carcinoma can be identified transcutaneously as well as by traditional lymphoscintigraphy (LS).

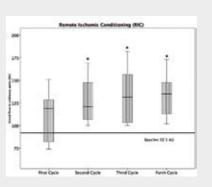
Lese I, Leckenby JI, Taddeo A, Constantinescu M, Olariu R. Medicine (Baltimore). 2019 Nov;98(44):



e17839. doi: 10.1097/MD.000000000017839

# Quantitative impact analysis of remote ischemic conditioning and capsaicin application on human skin microcirculation

Clinical hemorheology and microcirculation, 71(3), pp. 291-298. IOS Press 10.3233/CH-180373.



## Department for Pulmonary Medicine

Inselspital, 3010 Bern www.pneumologie.insel.ch







Prof. Christophe PD Dr. Manuela von Garnier



Funke-

Chambour

Dr Anne-Kathrin PD Dr Jacqueline Dr Nikolav Brill



Pichler Hefti

Pavlov

Dr Sabina Guler







PD Dr. Fabian Blank



Guenat

## **Profile**

- Focus: airway and lung parenchymal lung diseases, vascular lung diseases and sleep-related breathing disorders
- Performing experimental lung research at the DBMR Lung Research Laboratory but also translational studies in collaboration with the clinical research team at the Inselspital
- Interests: lung inflammation, lung immunology, lung regeneration and fibrosis
- Focusing on novel therapeutic treatment modalities including stem cells and their secretome, virosomes/liposomes, mRNA and targeting novel pathophysiological pathways in obstructive and fibrotic lung diseases
- · Providing training in respiratory medicine for students in medicine, biomedicine, dentistry, sport sciences and biomedical research
- Teaching physiotherapists at the Bern University of applied sciences and the Swiss neurophysiologists in respiratory medicine
- Training specialists in respiratory medicine and provide post-graduate training for other specialists and general
- External partners: SINERGIA Team (PD Hostettler, Basel, Prof. Lars Knudsen, Hannover, F. Baty, St. Gallen); Prof. Dr. Phil Stumbles, Murdoch University, Western Australia; Prof. Bruno Crestani, Université Paris Diderot, Paris; AlveoliX, sitemInsel AG, Bern

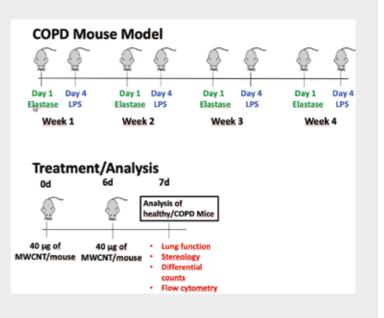
## **Grants**

- Swiss National Science Foundation SINERGIA SNF grant nr. CRSII3\_160704/1 (Prof. Thomas Geiser)
- Lungenliga Schweiz Patient specific pluripotent stem cell derived organoids a step to precision medicine\_2019 (Prof. Thomas Geiser)
- OPO-Stiftung Zürich and Lungenliga Bern: Efficient Pulmonary Mucosal Allergen Immunotherapy in allergic Airways Disease Employing Virosomes as Nanocarriers for Antigen and Adjuvant (PD F. Blank)
- Lungenliga Schweiz/Lindenhofstiftung: mRNA in pulmonary hypertension (PD J. Pichler Hefti)
- CTU-Forschungs-Grant: Clinical impact of dehydroepiandrosterone sulfate on disease severity & physical performance in fibrotic interstitial lung disease (Dr. Sabina Guler)
- Lungenliga Schweiz 2015 (PD Dr. Manuela Funke-Chambour)
- Lungenliga Bern 2019 (PD Dr. Manuela Funke-Chambour)

## Highlights

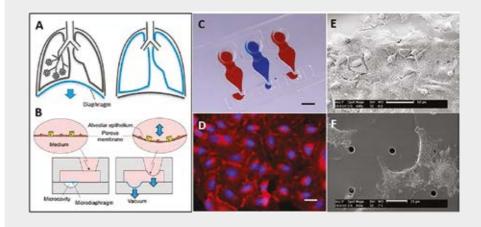
## Multi-walled carbon nanotubes (MWCNTs) as a hazard in chronic obstructive pulmonary disease (COPD)

We have shown in a mouse model of COPD that MWCNTs instilled intra-tracheal in a realistic occupational dosage induce mucus hypersecretion, and phenotypic shifts and activation in macrophage and dendritic cell populations in the lung. These findings demonstrate enhanced susceptibility for adverse health effects induced by MWCNT in individuals suffering from COPD (PD Dr. Fabian Blank).



## Impaired Wound Healing of Alveolar Lung Epithelial Cells in a **Breathing Lung-On-A-Chip**

In collaboration with ARTORG Lung, we developed a microfluidic in vitro system to study lung epithelial wound repair on a lung-on-chip system that includes breathing movements. The data support the development of novel therapeutic strategies in chronic lung diseases such as lung fibrosis or emphysema (Prof Th. Geiser/Prof. O. Guenat).



#### Awards

Kristina Krempaska (Supervison: PD Dr. Manuela Funke-Chambour) received a Poster Award by the Swiss Society of Pneumology for the project "Anti-fibrotic and apoptotic effects of Azithromycin in IPF and control fibroblasts". Moreover, she was awarded with the best preclinical project at the DBMR research day: "Azithromycin has enhanced anti-fibrotic properties on IPF fibroblasts" (Supervision: PD Dr. Manuela Funke-Chambour). Dr. Sabina Guler was awarded by the Swiss Society of Pneumology by the Poster Discussion award.

#### Honors

Prof. Thomas Geiser was appointed as individual member of the Swiss Academy of Medical Sciences (SAMW).

## Department of Radiation Oncology

Inselspital, Freiburgstrasse 10, 3010 Bern www.radioonkologie.insel.ch



Prof Daniel M Aebersold Director



Dr Kristina Lössl



Dr. Evelvn Herrmann



Eliçin

Dr. Olgun Dr Mohamed Shelan



Eychmüller

Prof Steffen



PD Dr Peter Manser



Prof Michael K



Prof. Yitzhak Medova



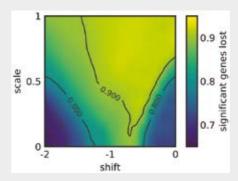
## **Profile**

- Teaching: Undergraduate lectures are provided for students in medicine, physics, 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
- · Clinical Research: (a) Prostate cancer: salvage radiotherapy in biochemical failure, metabolomic signatures; (b) head neck cancer: Role of upfront neck dissection in the context of primary radiotherapy; single vocal cord irradiation, outcome of immune checkpoint inhibitor and chemotherapy followed by dose and volume adapted chemo-radiotherapy; (c) brain tumor: Automatic segmentation of brain tumors, postoperative radiosurgery; (d) palliative care: Advanced care planning/anticipation; best care for the dying; community palliative care
- Medical physics research: (a) Dynamic Trajectory Radiotherapy (DTRT) and Modulated Electron Beam Radiotherapy (MERT); (b) Independent Dose Calculation and Radiation Protection in the Context of Robotic Stereotactic Radiotherapy; (c) Efficient Quality Assurance for External Beam Radiotherapy and Accurate Dose Calculation for Brachytherapy; (d) Medical Imaging Related Research Topics
- Radiation Biology: (a) 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); (b) Roles of novel posttranslational modifications (phosphorylations, ubiquitinations, acetylations) in cellular responses to DNA-damaging agents and targeted therapies; (c) Translational research to explore new prognostic and predictive biomarkers
- Collaborations: Multidisciplinary and multiinstitutional national and international collaboration within the SAKK & EORTC networks; Institute for Biomedical Engineering, Swiss Federal Institute of Technology (ETH), Zürich, Switzerland; Princess Margaret Cancer Center, Toronto, Canada; Laboratory of Artificial Intelligence in Medicine and Biomedical Physics, Stanford Medicine, USA; ACRF Image X Institute, University of Sidney, Australia

## **Grants**

- Swiss National Science Foundation
- Innosuisse
- Rising Tide Foundation
- Research Framework Agreement, Varian Medical Systems Inc.
- Swiss Bridge Foundation
- sitem-insel Support Funds
- Werner und Hedy Berger-Janser Stiftung
- Krebsforschung Schweiz

## Highlights



The impact of imputation on differential expression analysis

## Bypassing the imputation of missing values in differential expression analysis of proteomic data

Imputation of missing values in proteomic datasets significantly affects results of differential expression analyses. We developed ProtRank as a new method that identifies differentially expressed proteins by ranking their observed changes with respect to changes of other proteins and thus overcomes the need to impute missing

Medo M et al., BMC Bioinformatics. 2019 Nov 9;20(1):563. doi: 10.1186/s12859-019-3144-3.

## **Disease Control With Delayed Salvage** Radiotherapy for Macroscopic Local Recurrence Following Radical Prostatectomy

For patients with isolated local recurrence after radical prostatectomy, dose-escalted salvage radiotherapy to the prostate bed provides inferior tumor control compared to early intervention. Despite dose escalation, no increased incidence of high grade toxicities was observed.

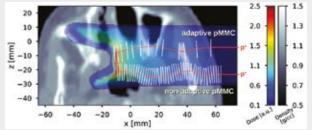
Shelan M et al, Front Oncol. 2019 Feb 28;9:12. doi: 10.3389/ fonc.2019.00012.



Dose-escalted salvage radiotherapy to macroscopic recurrence after radical prostatectomy.

## Adaptive step size algorithm to increase efficiency of proton macro Monte Carlo dose calculation

Accurate and efficient dose calculation is essential for treatment planning purposes in radiation therapy and Monte Carlo (MC) simulations are commonly known as the most accurate method to perform this task. Our group works on this topic and developed an adaptive macro Monte Carlo method for efficient dose calculations of proton beams. Kueng R et al., Radiation Oncology, 14:165, 2019.



Proton Macro Monte Carlo transport

## Metabolomics reveals tepotinib-related mitochondrial dysfunction in MET-activating mutations-driven models

Inhibition of the MET oncogene by small molecule inhibitor tepotinib alters metabolic signature of cancer cells and affects their mitochondrial function. Metabolic state of cancer cells upon MET inhibition can serve as an early indicator of efficacy of anti-MET

Poliaková M et al., FEBS J. 2019 Jul;286(14):2692-2710. doi: 10.1111/febs.14852. Epub 2019 May 11.

Changes of mitochondria-related metabolites upon MET inhibition.

## Department of Rheumatology, Immunology and Allergology (RIA)

Inselspital, Sahli Haus 1-2, 3010 Bern www.ria.insel.ch; www.bachmannlab.ch; www.eggellab.ch



Villigei





Prof. Martin PD Dr. Monique Bachmann Vogel



e PD Dr. Alexander Eggel

## **Profile**

- Participating in University Teaching programs for students of medicine, biomedicine and biology; master students of biology are also coming from foreign Universities
- 3 Basic research groups and one clinically oriented research group
- Aim: Understanding of immune regulation and the development of potential new therapies for inflammatory and other diseases
- Rheumatology, Clinical Immunology and Allergology offered optional teaching courses for last-year medical students, in addition to regular courses and lectures; these interactive workshops were again very popular
- Clinical research focuses large-vessel vasculitides, immune regulation in pregnancy, pathogenesis of arthritides and osteo-immunological interaction; in Allergology drug-hypersensitivity and immune-deficiencies are in the research focus
- Collaboration with a variety of partners within the medical faculty of Bern, with partners in Germany, France, the USA and Italy are ongoing
- External Partners Immunology: The Jenner Institute, University of Oxford, Oxford; Department of Dermatology, Zürich University Hospital, Zürich; Allergy Therapeutics (UK) Ltd. Domininion Way, UK; BRSC, Riga, Latvia; Vifor Fresenius Medical Care, Renal Pharma Ltd, St-Gallen, Zürich; Ludwig Institute, Lausanne, Switzerland; Nanyang University, Singapore; Kennedy Institute of Oxford, UK; Anhui Agricultural University, Hefei, China; 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; Instituto Nazionale di Genetica Molecolare, Milano, Italy; Novartis Pharma AG, Basel, Switzerland; Prof. Theodore Jardetzky, Stanford University, USA; Prof. Tony Wyss-Coray, Stanford University, USA; Immunologie de l'allergie cutanée et vaccination, CIRI, Université Claude Bernard, Lyon France

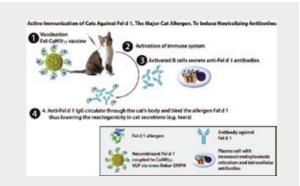
## **Grants**

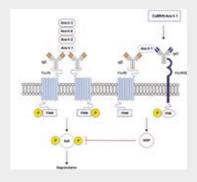
- Cancer Research Switzerland, Bern. Project: Development and exploration of a novel personalized cancer vaccine based on virus-like particles incorporating patient-specific melanoma T-cell epitopes. Project period: 1.1.2018-31.12.2020
- Swiss National Science Foundation (SNF), Bern. Project. "Unraveling the role of CD23 in the context of allergy". Project period: 1.04.2018-31.03.2022
- Swiss National Science Foundation (SNF), Bern. Project. "Understanding the role of antibody affinities in the regulation of allergic responses". Project period: 1.04.2019-31.03.2023
- SNF Bridge Discovery, Bern Zürich. Project: "Self-assembling glycoprotein nanoparticles vaccines" Project period: 01 01 2019 31 12 2022
- National Institute of Health R01 Subaward with Prof. Theodore Jardetzky from Stanford University, Project: "Suppression of basophil activation by IgE glycovariants". Project period: 15.04.2018-31.03.2022
- Research Fund of the Swiss Lung Association, Berne and the Uniscientia foundationa. Project: "Assessment of novel therapeutic strategies for the treatment of allergic asthma". Project period: 01.06.2017-31.05.2020

## Highlights

## A new vaccine for cat allergies

Cat allergy in human subjects is usually caused by the major cat allergen Fel d 1 and is found in approximately 10% of the Western population. Currently, there is no efficient and safe therapy for cat allergy available. We developed a new virus-like particle based vaccine to treat Fel d 1-induced allergy in human subjects by immunizing cats against their own major allergen, Fel d 1. The vaccine successfully induces Fel d 1 binding antibodies in cat and these antibodies neutralize the allergen thereby reducing symptoms of allergy in owners. Thoms F et al., JACI 2019: 144, 193-203.





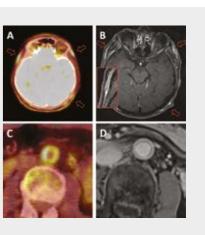
## A new vaccine for peanut allergy

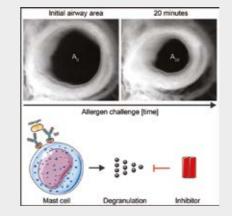
Peanut allergy is a severe and increasingly frequent disease. We generated vaccine candidates against peanut allergy based on the plant-virus derived VLP coupled to the whole extract of roasted peanut or to the single major allergerns Ara h 1 and Ara h 2 in a mouse model of peanut allergy. The vaccines demonstrated strong immunogenicity and were able to protect allergic reactions to allergen extracts.

Storni F et al., J Allergy Clin Immunol. 2019 Dec 19. pii: S0091-6749(19)31709-9.

## A novel treatment protocol for giant cell arteritis

Large vessel vasculitides such as giant cell arteritis and Takayasuarteritis are still treated with long-term, high-dose glucocorticoids, leading to a broad range of severe side effects. After our first RCT (published in Lancet 2016) which showed a glucocorticoid-sparing effect of >50%, we sought to prove that blockade of the IL-6 pathway can induce disease remission and replace glucocorticoids. The interim analysis shows a very successful outcome, and, in addition, it proves that high-resolution ultrasound qualifies to monitor inflammatory changes in the arterial vessel wall.





# Disruptive anti-IgE inhibitors prevent mast-cell dependent early airway response in viable atopic lung tissue

IgE plays a central role in the pathophysiology of allergic asthma. In patients suffering from allergic asthma, airway mast cells are loaded with allergen-specific IgE. Inhalation of allergens leads to rapid activation and degranulation of these cells and the induction of allergic symptoms. In this study we demonstrate that disruptive anti-IgE inhibitors prevent mast cell activation in atopic precision-cut lung slices.

Jiménez Delgado S et al., JACI 2019; 145, 719-722.e1

## Department of Thoracic Surgery

Inselspital, 3010 Bern www.thoraxchirurgie.insel.ch; www.thorax-schweiz.ch



Prof Ralph A Schmid Director



PD Dr. Gregor Kocher Deputy Director Consultant



Dr Roland Kuster



Dr. Ion Andri



Dr Patrick

Dorn

Dr Adrian Zehnder Senior Physician Senior Physician Senior Physician



PD Dr Ren-Wand Research Group



Hall



PD Dr. Thomas M. Marti Research Group Research Group

## **Profile**

- Teaching students of medicine as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB)
- Evaluation and therapeutic improvements by uniportal minimally-invasive thoracic surgery techniques
- Investigation of different clinical and functional parameters with the aim of achieving better outcome and improvement of
- Determine the immunosuppressive potential of the tumor-derived mesenchymal subset, which may serve as a novel therapeutic target in lung cancer; further, we are interested in identifying the molecular mechanisms underlying T cell dysfunction in the setting of lung cancer
- Dentify the molecular mechanisms conferring resistance to clinical standard therapies, with the goal to unravel druggable vulnerabilities - the 'Achilles' heel' - of therapy-resistant cancer cells for development of innovative strategies to treat lung
- Investigate how the mitochondria-related nucleotide metabolism and the DNA damage response machinery is associated with the tumor initiating capacity and chemotherapy response of NSCLC cancer stem cells
- External Partners: Institute General Physiology, University of Ulm, Germany

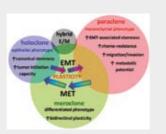
## **Grants**

- Swiss Cancer League (KFS-4265-08-2017; KFS-3772-08-2015)]
- China Scholarship Council (201606230238; 201708530258; 201606740067; 201808170004; 201906240084)
- Bernese Cancer League (160901; 170907; 180401)
- Lungenliga Bern (NCT03924206)
- Bern Center for Precision Medicine (190402)

## Highlights

#### Not all cancer cells are equal

Cell lines are essential tools to standardize and compare experimental findings in basic and translational cancer research. The current dogma states that cancer stem cells feature an increased tumor initiation capacity and are also chemoresistant. Here, we identified and comprehensively characterized three morphologically distinct cellular subtypes in the non-small cell lung cancer cell line A549, and challenge the current cancer stem cell dogma. Tièche et al., Neoplasia, 2019, 21 (2), 185-196.



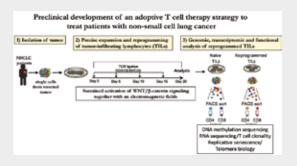
### Surgical smoke project

Surgical fumes that arise when electrocautery is used during surgery contain a variety of carcinogenic compounds. Our team has recently analyzed the exposure to these fumes in our operating rooms (OR's) during surgery, using real-time mass spectrometry analysis. The results of our study will be used to further improve already existing smoke evacuation systems as well as to develop additional preventive and protective measures against hazardous volatile substances in the OR. Kocher et al. Eur J Cardiothorac Surg, 2019, 55 (4), 626-631.



### Adoptive T cell therapy (ACT) project

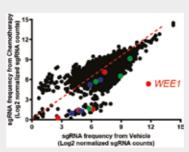
Antigen-specific tumor infiltrating lymphocytes (TILs), represents a transformative living immunotherapy for the treatment of cancer. In lung cancer patients, we previously demonstrated that TILs show hallmarks of exhaustion coupled with downregulation of Wnt/B-catenin signaling and reduced expression of TCF7, an end effector of Wnt signaling. Therefore, we are testing a novel intervention aimed at targeting Wnt/B-catenin to generate ex vivo expanded TILs with renewed and sustained functional ability to eliminate malignant lung cancer cells.



## WEE1 is a drug target that promotes standard chemotherapy in MPM

Malignant pleural mesothelioma (MPM) is a rare but very deadly cancer, notoriously known for dearth of therapeutic options. In a kinome CRISPR/Cas9 knockout screen, we identified the G2-M checkpoint kinase WEE1, whose inhibition synergistically enhances the efficacy of standard chemotherapy, leading to enhanced MPM cell death in vitro and in vivo.

Xu et al. Mol Cancer Ther, 2019 Nov 6 [Online].

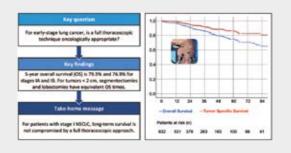


Scatterplot of sgRNAs in chemotherapyversus vehicle-treated MPM cells.

## Thoracoscopic approach does not compromise survival

The full thoracoscopic approach to major pulmonary resections is considered challenging and controversial as it might compromise oncological outcomes. The aim of this work was to analyse the results of a full thoracoscopic technique in terms of nodal upstaging and survival in patients with non-smallcell lung carcinoma (NSCLC).

We found that long-term survival is not compromised by a full thoracoscopic approach. Our results compared favorably with those of video-assisted techniques. Lutz JA et al. Eur J Cardiothorac Surg. 2019, 1;55(2):263-270.



## Influence of an early assessment and management of dysphagia after lung resection

Aspiration resulting from oropharyngeal dysphagia has been recognized as a serious complication after lung resection. In a single-center, randomized controlled trial, we investigated the influence of a clinical dysphagia assessment before the initiation of oral intake after surgery. The risk of pneumonia and the median length of hospital stay were compared between the intervention and the control group. We demonstrated that early detection of postoperative dysphagia can significantly decrease the risk of postoperative pneumonia. Schmidt Leuenberger et al., Ann Thorac Surg, 2019, 108 (4), 1059-1064.



## Department of Urology

Inselspital, Freiburgstrasse 4, 3010 Bern www.urologie.insel.ch













Prof Fiona Prof George N Thalmann Burkard

PD Dr Marianna Prof Katia Kruithof-de Julio Monastyrskaya

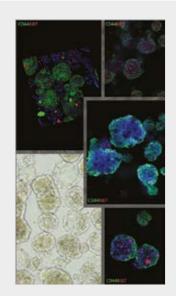
## **Profile**

- Teaching students of medicine, biomedicine and biology as well as graduate students at the Graduate School for Cellular and Biomedical Sciences (GCB) at the University of Bern, CH and Leiden, NL
- 4 Groups
- Investigation of pathophysiological processes that contribute tumor diseases and bladder disfunction
- Aim: Understand the molecular processes of urological cancer progression and bladder disfunction
- External Partners: Alvaro Aytes Institut d'Investigació Biomèdica de Bellvitge, Program Against Cancer Therapeutic Resistance / Prostate Cancer Lab, Barcelona, Spain; Theodore Alexandrov EMBL-Heidelberg, Structural and Computational Biology / Spatial Metabolomics Lab, Heidelberg, Germany; Cristina Müller, Center for Radiopharmaceutical Sciences ETH-PSI-USZ, Paul Scherrer Institut, Zürich, Switzerland; Sylvia LeDevedec, Leiden Academic Centre for Drug Research, Leiden University, Leiden, The Netherlands; Rosalyn Adam, Urological Diseases Research Center, Boston Children's Hospital, Boston, USA; Duke University, Durham USA; Swiss Institute for Bioinformatics, HEIG-VD, ETH Zürich

## **Grants**

- Swiss National Science Foundation (#179265, #189149, #184933, #189369, #175773/1, #182966/1)
- Department of Defense (W81XWH-19-1-0432)
- Swiss Cancer League (KFS 4718-02-2019)
- HORIZON 2020 (Marie Sklodowska-Curie Action) (STOPa 748836)
- Bern Center for Precision Medicine
- Wings for life Spinal Cord Research Foundation
- Novartis Foundation for medical-biological Research
- Innosuisse Grant Nr 41236.1 IP-LS

## Highlights



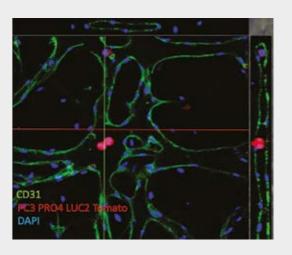
## **Preclinical Models for the Translational Study of Urological**

We have generated patient derived organoids (PDOs) and patient derived xenografts (PDXs) of primary and metastatic PCa and other malignancies or tumor types (Karkampouna et al. 2018). We have also developed and implemented a clinically relevant culture system for studying tumor tissue ex vivo. This technique allows cultivation of tumor slices and needle biopsies in a tissue culture setting without loss of normal architecture, viability, proliferative properties, or expression of specific markers. 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).

**Prostate Cancer Organoids** 

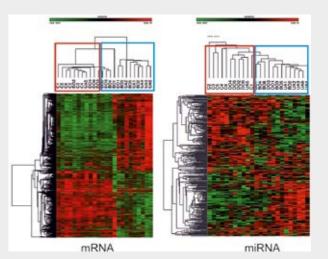
#### Microvasculature on CHIP

Metastasis spread is a multistep process that depends on the capacity of specific cancer cells to leave the primary tissue, intravasate in the lymphatic and/or vascular network, transit and survive in the flow, extravasate and colonize the distant tissue. Organ on chip technology has provide us novel tools that overcome some of the limitations of traditional 2D and 3D in vitro models, reduce the phylogenetic problem due to differences between human and animals and if considered as a pre-screening tool significantly reduces the number of animals for further in vivo validation.



## Discovery of diagnostic and prognostic biomarkers of the "point of no return" for bladder function

Lower urinary tract dysfunction (LUTD) has different underlying mechanisms and multiple confounding factors. LUT symptoms are often shared between the diseases of different origin, delaying and complicating therapy. We are in the possession of a unique collection of human biopsy samples from patients with well-characterized bladder functional phenotypes. Our approach relies on generation and analysis of big gene expression data to reveal the triggers of LUTD. To achieve our goal of unbiased classification of LUTD and identification of molecular drivers of pathologic bladder remodelling, we apply machine learning algorithms to the transcriptome



Hierarchical clustering of significantly regulated mRNAs and miRNAs in benign prostatic obstruction patients

Myeloid cells (green) and infiltrating macrophages (red) in control mouse bladder

## Urodynamic studies in awake mice with obstruction and SCI.

Along with recruiting the human spinal cord injury (SCI) patients for a longitudinal study of gene expression changes during neurogenic LUTD, we carry out a translational project to perform urodynamic studies in awake mice with obstruction and SCI. We investigate the impact of obstructive and neurogenic LUTD on bladder remodeling and functionally validate the findings in human patients. Our earlier studies in bladder outlet obstruction have detected signs of macrophage infiltration by analysing the total RNA in the BPO patients' biopsies for macrophage-specific gene expression markers. We are now using mouse models of SCI and pBOO to investigate the role of infiltrating macrophages in bladder dysfunction. Our aim is to develop tools to mitigate the impact of cellular inflammatory pathways, preserving bladder contractility.

## Department for Visceral Surgery and Medicine

Inselspital – Bauchzentrum Bern, Freiburgstrasse 18, 3010 Bern www.bauchzentrum-bern.ch





Managing

Director and





Prof Andrew Macpherson Director and

Dufour Chief Physician Chief Physician Chief of Surgery Gastroenterology Hepatology

Prof Jean-François Director and

#### Staff members

PD Dr. Vanessa Banz, Senior Surgeon Visceral Surgery Prof. Guido Beldi, Senior Surgeon Visceral Surgery PD Dr. Lukas Brügger, Senior Surgeon Visceral Surgery Prof. Beat Gloor, Senior Surgeon Visceral Surgery PD Dr. Reto Kaderli, Senior Surgeon Visceral Surgery Prof. Deborah Keogh-Stroka, Senior Scientist Visceral Surgery Prof. Markus Laimer, Chief Physician Diabetology and Metabolism UDEM PD Dr. Philipp C. Nett, Senior Surgeon Bariatric and Metabolic Surgery

PD Dr. Beat Schnüriger, Senior Surgeon Visceral Surgery Prof. Katharina Staufer, Senior Surgeon Transplantation Surgery Prof. Annalisa Berzigotti, Senior Physician Hepatology Prof. Andrea De Gottardi, Senior Physician Hepatology Prof. Nasser Semmo, Senior Physician Hepatology Prof. Stephanie Ganal-Vonarburg, Senior Scientist Gastroenterology PD Dr. Pascal Juillerat, Senior Physician Gastroenterology

Prof. Reiner Wiest, Chief Physician Gastroenterology

## **Profile**

- Visceral Surgery Gastroenterology Hepatology
- Endoscopy Unit; Transplantation
- External Partners: ETH Zurich, Systems Biology; Karolinska Institutet, Stockholm. Department of Surgery; University of Geneva, Molecular Biology; University of Neuchâtel, Department of Psychology
- University of Freiburg, Clinic for Hepatology, Germany; SCCS (Swiss Hepatitis C Cohort Study); STCS (Swiss Transplant Cohort Study); FLIP Kohorte (European Tatty Liver: Inhibition of Progression); CLIF Consortium (European Foundation for the study of Chronic Liver Failure); VALDIG Consortium (Worldwide Vascular Liver Disease Group)

## **Grants**

- Fondation Alcon: Adult stem cells for regenerative medicine. PCSK9 and cholesterol metabolism in HCC. (Prof. Daniel Candinas, Prof. Deborah Keogh-Stroka)
- Health 2030 EPFL ENT-R CPH: Personalizing surgical care. (Prof. Guido Beldi)
- EU Grant: HHMM-Neonates. (Prof. Andrew Macpherson)
- SNF: The sequence of functional public and private antibody repertoire development in response to transient exposures to non-pathogenic intestinal microbes. (Prof. Andrew Macpherson)
- EU-Grant: Liver Investigation: Testing Marker Utility in Steatohepatitis (LITMUS). (Prof. Jean-François Dufour)
- SNF: Hint1, Hin2 and MAMs. (Prof. Jean-François Dufour)

## Highlights



### **Computer Assisted Liver Surgery**

In October 2019 we hosted the 7<sup>th</sup> annual meeting of the European Computer-Assisted Liver Surgery Society where more than 100 experts from 19 different countries discussed the latest developments in computer-navigated liver surgeries and interventions. The meeting was extended to a pre-conference workshop where participants could watch a life case demonstration of a stereotactic liver ablation sharing our experience from more than 600 stereotactic liver tumor ablations since 2015.

## First Swiss national Kidney Paired Exchange Donation and **Transplantation**

On 20 November 2019 a kidney from a living donor from Bern was implanted in Zurich and vice versa a kidney from Zurich was transplanted in Bern. This was the result of a joint effort of all transplant centres in Switzerland and Swisstransplant to offer living donor transplantation for couples with immunological contraindication to transplant in their respective combinations, either due to HLA or bloodgroup incompatibility. Using a novel software, two compatible donor and recipient pairs were identified among 12 candidates and cross over transplantation performed. Both procedures in Zurich and Bern went well and were finished early afternoon on the same day. Both recipients were discharged without complications and with good kidney function.

## Terlipressin in surgical patients

A randomized placebo controlled trial was concluded and revealed that the splanchnic vasopressor terlipressin can reduce the incidence of renal but not hepatic complications after major liver surgery.



Prof. Semmo, supervisor of the curriculum, hands over the diploma to Dr. Yulv Mendoza

## New curriculum in Hepatology

The University of Bern has new a curriculum in Hepatology. In 2019 Dr. Abdoul Sow and Dr. Daye Ka, both from Senegal, were the first to receive a Certificate of Advanced Studies in Hepatology and Dr. Yuly Mendoza from Colombia a Diploma of Advanced Studies in Hepatology. This unique curriculum allows physicians interested in liver diseases to follow a structured teaching covering all aspects of hepatology in a leading university clinic in this field.

## Outreach into the undeveloped world

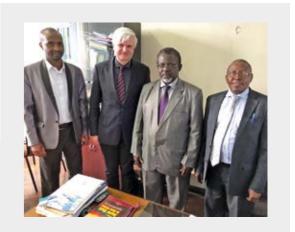
In 2019 we have started collaborative work with colleagues at the University Hospitals of Harare and Nairobi. Our objective is to address why there is intestinal failure in young children causing stunting with poor physical and cognititive development as

a result of abnormal colonization of the intestine by microbes that do not normally cause any problems. The work is funded by the generosity of the Botnar foundation in collaboration with colleagues at the ETH and University of Basel. As a result of this outreach, we have already hosted colleagues from Zimbabwe in Bern, and Benjamin Misselwitz and Andrew Macpherson have been working in Harare and Nairobi.



## **CAS in Sex- and Gender-Specific** Medicine established

In cooperation with the Medical Faculty of the University of Zurich, the University Clinic for Visceral Surgery and Medicine established the first continuing education course in gender medicine in Switzerland. National and international experts will reveal the importance of gender in the various medical disciplines.





## Clinics at the University Hospital, Universitäre Psychiatrische Dienste (UPD)

University Hospital of Old Age Psychiatry and Psychotherapy (APP)
University Hospital of Child and Adolescent Psychiatry and Psychotherapy (KJP)
University Hospital of Psychiatry and Psychotherapy (PP)

## University Hospital of Old Age Psychiatry and Psychotherapy (APP)

Murtenstrasse 21, 3008 Bern www.upd.ch





Klöppel

PD Dr. Jessica

## **Profile**

- Teaching students of medicine as well as graduate students at the Graduate School for Health Science (GHS)
- 2 research groups
- Investigation of retrospective as well as prospective memory with cognitive assessment, brain imaging, and non-invasive brain stimulation in healthy aging and cognitive impairment
- Aim: Development of non-pharmocological interventions to counteract cognitive decline
- External partners: Department of Neuroradiology, University of Zürich, Switzerland; Department of Basic Psychological Research and Research Methods, University of Vienna, Austria; Cobtek (Cognition, Behavior, Technology) Research Lab, University Cote d'Azur, France, Neuroscience Center, University of Geneva, Switzerland; German Research Center for Artificial Intelligence (DFKI), Saarbrücken, Germany

#### **Grants**

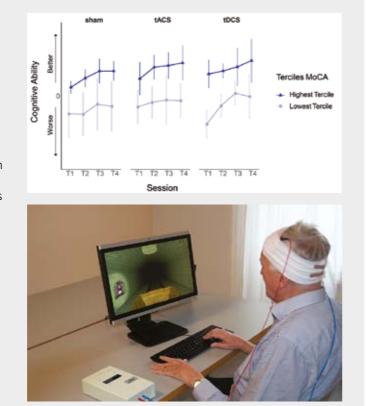
- Swiss National Science Foundation (320030 173880, 100014 185105)
- Velux Foundation
- Stiftung Synapsis, Heidi Seiler Stiftung und Peter Bockhoff Stiftung

## **Highlights**

## Transcranial electrical stimulation enhances cognitive training in initially poorly performing healthy elderly

We combined a cognitive training with transcranial electrical stimulation and were able to show that participants with low performance in a cognitive screening tool (i.e. MoCA) before the training benefitted from direct current stimulation (tDCS) in a cognitive composite score directly after the training (T2) when compared to the scores before the training (T1). This cognitive composite score quantifies the general cognitive ability of a person. There was no such effect for alternating current stimulation (tACS) when compared to a group with no stimulation (sham group). The effect vanished after 6 and 12 months (T3, T4) when corrected for repeated testing.

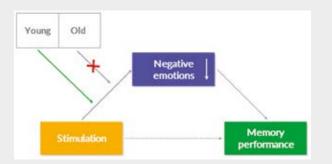
Improvement in cognitive ability through the combination of transcranial electrical stimulation and cognitive training



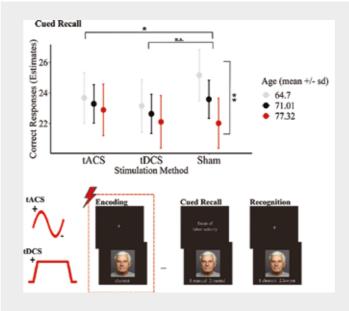
## **Electrical stimulation reduces negative** emotions and therby improves memory

We applied transcranial direct current stimulation (tDCS) to the prefrontal cortex in 94 healthy individuals (n = 43 young, n = 51 elderly) while they performed an episodic memory task. In young but not in older participants, moderation models indicated that the reduction of negative emotions via tDCS led to better memory performance.

Our study provides a further link between emotion and memory: as increased activity in the prefrontal cortex is crucial for successfully coping with affective interference, anodal tDCS seems to help preventing negative and probably distracting thoughts.



Electrical stimulation reduces negative emotions in healthy young adults and thereby improves memory performance. This was not the case in older adults.

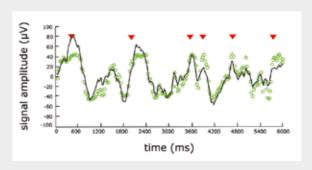


## Alternating direct current stimulation improves memory performance

Associative memory is among the first cognitive functions negatively affected by aging. In a randomized, sham-controlled, and double-blind study, healthy older adults (n=28; mean age 71) received anodal transcranial direct current stimulation(tDCS), alternating current in the theta range (tACS), and sham stimulation over the left ventrolateral prefrontal cortex each once during encoding of an associative memory task. Our results suggest that tACS might be more effective to improve associative memory performance than tDCS - at least in higher aged samples.

## Boosting slow wave sleep by closed loop acoustic stimulation to enhance memory performance in older adults

Reduced slow wave sleep is associated with cognitive decline and recent work suggests that it might even causally contribute to its development. As part of ongoing collaborations, we successfully adapted a closed loop acoustic stimulation approach that is able to detect slow waves in a sleeping person's electroencephalogram and presents short and soft tones temporally aligned with the peaks of the slow waves. This procedure has shown to improve slow wave sleep as well as specific forms of short-term memory functions. In our project we are particularly interested in a range of cognitive tasks as well as the long-term effects of our intervention in an at risk group.



The black line represents the ongoing EEG activity in a sleeping person during slow wave sleep. The red signs show successful detection and triggering of acoustic stimulation during the peaks of these waves.

## University Hospital of Child and Adolescent Psychiatry and Psychotherapy (KJP)

University Psychiatry Department (UPD), Haus A, Bolligenstrasse 111, 3000 Bern 60 www.upd.unibe.ch













PD Dr Julian Koenig

Kindler

## **Profile**

- 4 research groups, 22 staff members
- Investigating mental disorders with an onset during childhood and adolescence up to emerging adulthood
- Focus on: neurobiological mechanisms, early precursors, innovative treatment development, psychotherapy research, E-mental health
- Teaching students of Medicine and Psychology at all educational levels
- External Partners: Department of Child and Adolescent Psychiatry, Psychiatric Clinics of the University of Basel, Basel, Switzerland; Institute of Pharmacology and Toxicology, University of Zurich, Zurich, Switzerland; Department of Economics, 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; University Hospital of Child and Adolescent Psychiatry, Medical University Vienna, Vienna, Germany; Orygen, The National Centre of Excellence in Youth Mental Health, University of Melbourne, Australia; Division of Sleep Medicine, Harvard Univesity, USA; Department of Psychology, University of Zurich, Switzerland; Psychiatry and Human Behavior, University of California, Irvine, USA; Department of Psychiatry and Human Behavior, Brown University, USA; Child Psychiatry Branch, National Institute of Mental Health, USA; Upstate Medical University, Syracuse, New York, USA; School of Psychiatry, University of New South Wales, Sydney, Australia & Neuroscience Research, Sydney, Australia; Center for Psychiatric Neuroscience, Department of Psychiatry, Lausanne University Hospital, Lausanne, Switzerland

#### **Grants**

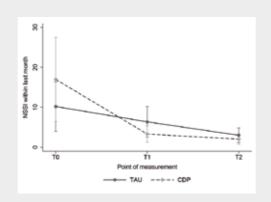
- Interfaculty Research Cooperation Grant Decoding Sleep: Sleep subtypes in adolescent depression: Sleep physiology and treatment (PI: Dr. Tarokh)
- SNF Scientific Exchange Grant (182891): The Neurobiological Mechanisms of Auditory Verbal Hallucinations in Youth with Borderline Personality Disorder (PI: Dr. Michel)
- SNF Project Grant (182639): Neurobiological Mechanisms of Pain Dependent Stress-Regulation in Adolescent Non-Suicidal Self-Injury (Pls: Prof. Dr. Kaess & PD Dr. Koenig)
- SNF Project Grant (184943): Sleep Neurophysiology: A Window onto Adolescent Mental Health (Pl: Dr. Tarokh)

## Highlights

## **Effective Brief Psychotherapeutic Intervention** for Adolescent Non-Suicidal Self-Injury

We developed a manualized brief cognitive behavioral intervention for the treatment of adolescent nonsuicidal self-injury (NSSI). Within a randomized controlled trial, the brief psychotherapeutic intervention conducted by trainees in psychotherapy led to an equal and guicker reduction of NSSI when comparing it to more intensive outpatient psychotherapy conducted by professional psychotherapists.

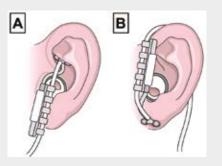
Kaess et al. European Child and Adolescent Psychiatry, in press.



Frequency of NSSI at baseline, after 4 months,

## **Promising Findings for Transcutaneous Vagus Nerve Stimulation in Adolescent Depression**

In a first experimental trial, we investigated the effects of transcutaneous vagus nerve stimulation (tVNS) on emotion recognition in adolescents with major depressive disorder (MDD). Compared to sham stimulation, tVNS decreased the recognition of briefly presented stimuli of negative valence in patients with MDD. These findings suggest a potential antidepressant effect of tVNS by reducing the negativity bias in adolescents with MDD. Further research is needed, addressing the potential of tVNS as treatment option for MDD in children and adolescents. Koenig et al. Psychological Medicine, in press



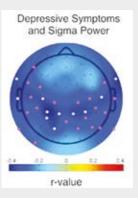
Electrode placement for tVNS (A) versus sham (B) stimulation

## Depressed Adolescents Show Altered Sleep Neurophysiology

Depression is often accompanied by subjective sleep complaints and alterations in sleep neurophysiology. In this study, we show that more depressive symptoms are associated with less sleep spindle activity. Sleep spindles, a unique feature of the sleep EEG, have been hypothesized to protect sleep against environmental disturbances. Thus, diminished spindle activity may be a subtle sign of disrupted sleep and its association with depressive symptoms in early adolescence may signal vulnerability for depression.

Hamann et al. Journal of Child Psychology and Psychiatry, 2019.

Depressive symptoms in early adolescence associated with sleep EEG spindles



First Brain Imaging of Abnormal Involuntary Movements in Early Psychosis

We measured motor symptoms, regional cerebral blood flow (rCBF) and cortical grey matter volume (GMV) in patients with first episode psychosis (FEP), clinical high risk (CHR) and controls. Our video-based analysis demon-

strated that abnormal involuntary movements were more frequent in CHR and FEP as compared to clinical controls and correlated with increased rCBF but decreased GMV in the premotor cortex. Thus, our study shows for the first time an association between motor symptoms and biological markers such as rCBF and GMV in early psychosis. Kindler et al. Schizophrenia Research, 2019.

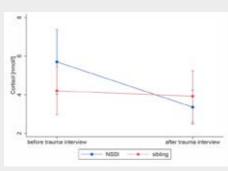


Functional correlates (rCBF) of abnormal involuntary movements in psychosis risk and first episode psychosis

## Sibling Study Shows Altered Cortisol Response to Memories of Early Adversity in Adolscent Non-Suicidal Self-Injury

We compared adolescents engaging in non-suicidal self-injury (NSSI) and their siblings with regard to hair cortisol concentrations as well as salivary cortisol concentrations before and after an interview assessing experiences of childhood adversity within the family environment. Our results showed that adolescents engaging in NSSI reported more severe experiences of childhood adversity, exhibited higher hair cortisol levels and had a significantly higher decrease in salivary cortisol levels during the trauma interview. The results point to increased basal hypothalamic-pituitary-adrenal axis functioning but decreased reagibility to stress such as traumatic memories in adolescents with NSSI.

Reichl et al. Psychoneuroendocrinology, 2019.



Salivary cortisol levels in adolescents engaging in NSSI and their siblings before and after a trauma interview

## University Hospital of Psychiatry and Psychotherapy (PP)

Bolligenstrasse 111, 3000 Bern 60 www.upd.unibe.ch















König



Prof Thomas Strik Dierks Walther

Prof Sebastian Prof Franz Moggi

Prof Daniela Hubl

Prof Andrea Federspiel

Prof Thomas

Prof Wolfgang Tschacher

## **Profile**

- Teaching students of medicine, biomedical science, and psychology within the curriculum, supervision of masters and doctoral theses projects, as well as teaching at various graduate schools at the University of Bern
- Clinical translational research topics include psychosis pathobiology and treatment, sleep, addiction, stress, and depression
- Aims: understand the etiology of psychiatric disorders and develop novel non-pharmacological treatment options
- External partners: Dept. of Psychiatry, Northwestern University, Chicago, USA; Dept. of Psychiatry, Vanderbilt University, Nashville, USA; Dept. of Psychiatry, Philipps-University Marburg, Germany; Dept. of Psychiatry, Karolinska Institute, Stockholm, Sweden; Dept. of Psychiatry, University of Freiburg, Germany; Dept. of Psychiatry, University of Würzburg, Germany; University of Amsterdam, The Netherlands; University of Milano, Italy; Depts. of Psychiatry, University of Basel and University of Zurich; Neurocenter of the University of Lugano

## **Grants**

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- Novartis-Foundation, Velux-Foundation, Frutiger-Foundation, Volkswagen-Foundation, Swiss Foundation for Alcohol Research
- IFK "decoding sleep" University of Bern

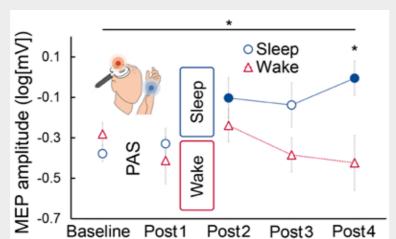
## Highlights

## Sleep orchestrates indices of neural plasticity

Animals and humans spend on average one third of their lives in sleep, but its functions remain to be specified. We used electrophysiological (TMS, EEG), behavioral (memory, vigilance) and molecular (BDNF, cortisol) indices and provide first integrative evidence in humans that sleep strengthens relevant connections between neurons while keeping overall neural network func-

tion stable.

Maier JG, Kuhn M, Mainberger F, Nachtsheim K, Guo S, Bucsenez U, Feige B, Mikutta C, Spiegelhalder K, Klöppel S, Normann C, Riemann D, Nissen C (2019). Sleep orchestrates indices of local plasticity and global network stability in the human cortex. Sleep, 42(4).



Effects of sleep on MEP amplitudes

## Review on Catatonia presentation and neurobiology

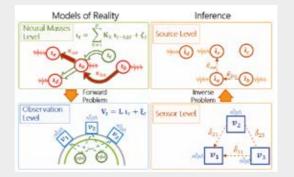
Catatonia is a complex psychomotor syndrome that can occur in several conditions and has increased mortality. The current knowledge on the clinical presentation, suspected neurobiology, and clinical management have been summarized in this review.

Walther S, Stegmayer K, Wilson JE, Heckers S (2019). Structure and neural mechanisms of catatonia. Lancet psychiatry 6(7):610-619.

## **Electrophysiological Brain Connectivity**

Leading EEG experts provided a consensus review on the current state of the theory and the available algorithms for the estimation of brain connectivity based on electrophysiological data. They developed a common theoretical framework, and explained the common pitfalls.

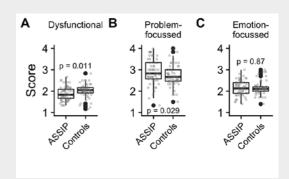
Bin He B, Astolfi L, Valdés-Sosa PA, Marinazzo D, Palva SO, Bénar CG, Michel CM, and Koenig T (2019). Electrophysiological Brain Connectivity: Theory and Implementation. IEEE Transactions of Biomedical Engineering, 66(7): 2115-2137.



Levels of neuronal connectivity estimation based on EEG and MEG

## Coping styles improved with specialized interventions after suicide attempts

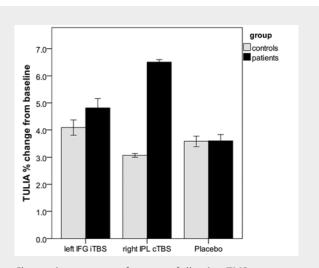
Coping strategies are critical for secondary suicide prevention. We demonstrated 11% less dysfunctional coping in the ASSIP group and 6% more problem-focussed coping compared to the control group after 24-months. Thus, specialized psychotherapy was superior over treatment as usual. Gysin-Maillart A, Soravia L, Schwab S (2020). Attempted Suicide Short Intervention Program Influences Coping Among Patients with a History of Attempted Suicide. Journal of Affective Disorders, 264:393-399.



Changes in coping strategies with ASSIP or control treatment

## Hand gestures improved with single session TMS

Schizophrenia patients have severe gesture deficits, that are linked to alterations in the cerebral praxis network. This double-blind, randomized controlled trial tested the effects of single sessions of transcranial magnetic stimulation and detected one superior protocol. This protocol is now being tested in a parallel-arm RCT. Walther S, Kunz M, Müller M, Zürcher C, Vladimirova I, Bachofner H, Scherer KA, Nadesalingam N, Stegmayer K, Bohlhalter S, Viher P. Single session transcranial magnetic stimulation ameliorates hand gesture deficits in schizophrenia. Schizophrenia Bulletin, in press.



Change in gesture performance following TMS



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Cover Picture: Graphic illustrating the influence of individual genes and proteins in a medical treatment. Khrystyna Okhrim and the Bern Center for Precision Medicine, Prof. Dr. Mark Rubin.

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