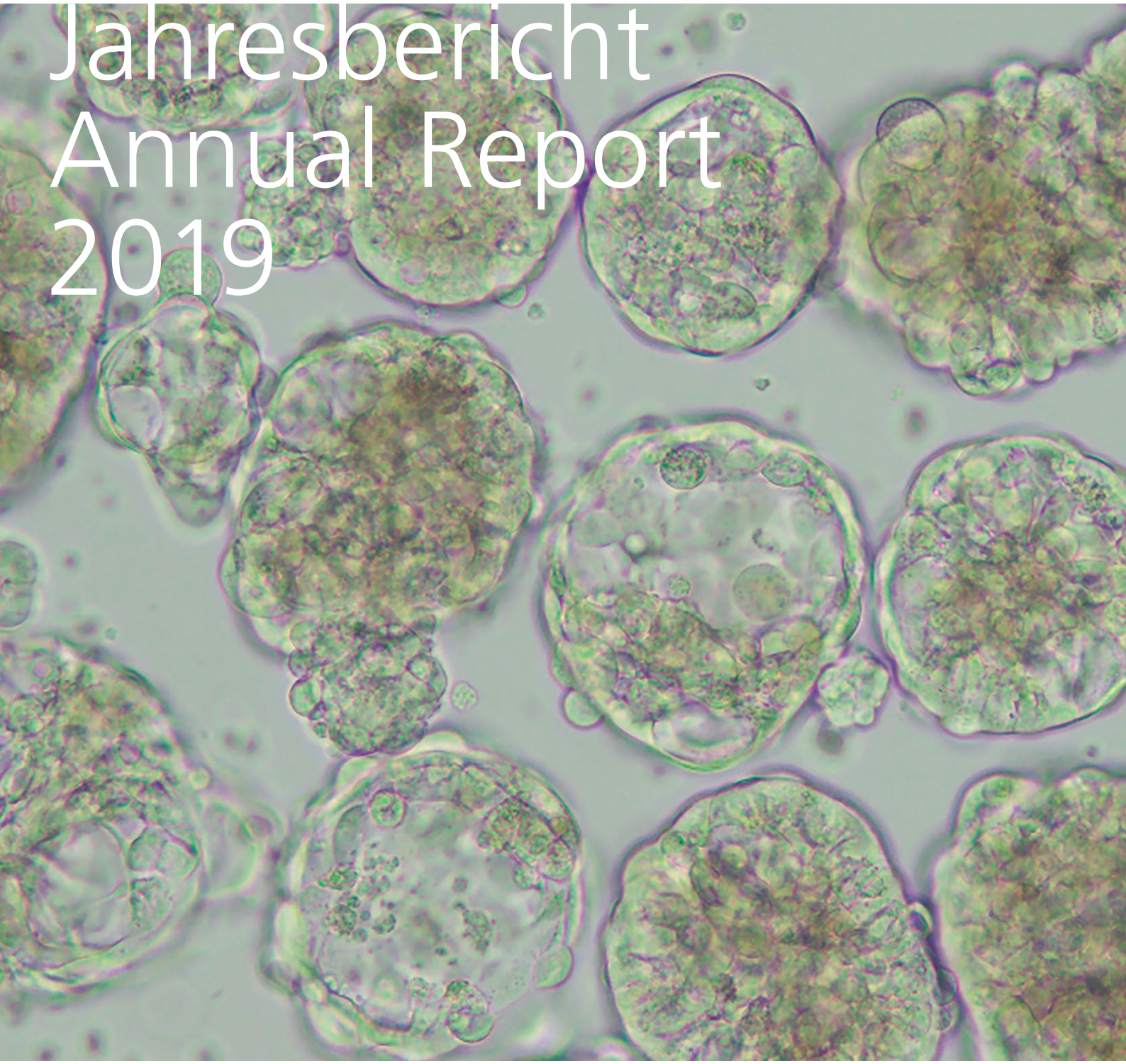
UNIVERSITÄT BERN

DEPARTMENT FOR BIOMEDICAL RESEARCH
www.dbmr.unibe.ch

Jahresbericht Annual Report 2019



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A copy of this report can be obtained online at:
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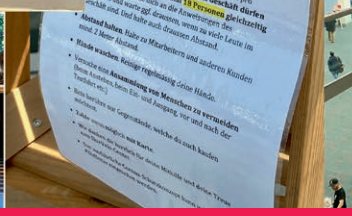
Cover:
Organoids
Image: PD Dr. Marianna Kruithof-de Julio

Contents


Neues Coronavirus
SO SCHÜTZEN WIR UNS.
Gründlich Hände waschen.
In Taschentuch oder Armbeuge husten und niesen.
Papiertaschentuch nach Gebrauch in geschlossenen Abfalleimer.
Hände schütteln vermeiden.
Bei Fieber und Husten zu Hause bleiben.
Nur nach telefonischer Anmeldung in Arztpraxis oder Notfallstation.
www.bag-coronavirus.ch Infoline Coronavirus: +41 58 463 00 00


Für IHRE und UNSERE
GESUNDHEIT
Bitte bezahlen Sie mit der Karte
Postcard
PAY
VISA


SAVAC
CORONA VIRUS
SCHÜTZEN WIR UNS


DON'T SHAKE ON IT!
It's cold and flu season.
It's okay not to shake hands.
How about a friendly smile instead?
USCAP

Foreword – Director's Report

Standing in front of the Los Angeles Convention Center in late February 2020, I ran into a Pathologist from Zurich, who informed me that he was heading back home, "immediately". There were new guidelines from his University Hospital regarding COVID-19 and travel. Reading his eyes, I also knew, guideline or not, it was time to return. There was little in the way of social distancing occurring at this international pathology meeting we were attending. All our colleagues from China had cancelled but otherwise attendance was almost normal. Except for signs suggesting not to shake hands, things were as usual. Arriving in record time from downtown LA to the airport, the taxi driver noted that he had never seen the parking lot as empty as on that day. I called home to let my wife know I was heading home early. She asked, "were there long lines at security?". Eerily, I was the line. No one was traveling.

What in February seemed unimaginable, soon became a reality to all of us in ways that we could not have anticipated. In Europe, Switzerland, at the University of Bern, the Insel Group, and the DBMR, we have gone from our normal activities to partial and then full shutdown due to the COVID-19 pandemic. This has been a difficult time for us all that impact our social and work life. In the biomedical research community, some laboratories have joined the efforts to address the immediate and pressing need to study COVID-19. But the reality for most was a complete shutdown of research. Now in June 2020 as I write this foreword to our annual report, I wanted to reflect on our measures to lift the lockdown and re-start biomedical research.

Coming out of lockdown has been a carefully orchestrated process, in which we have been working closely – but from a distance – with the leadership from the University and Insel Group to translate the guidelines from BAG into action. Many in the DBMR have helped to plan and implement our phased return. I am extremely grateful for your efforts. I do want to single out Prof. Willy Hofstetter, who has become our COVID-19 czar. We know that getting back to work was a high priority for all of our researchers but doing this safely was – and still is – our responsibility and Willy's dedication to this effort has been impressive to watch. A virtual – and eventually a real – round of applause is called for to honor his dedication to the DBMR community.

There is no question that the logistics of our buildings and the size of our groups has even made this opening-up phase difficult. It was of paramount importance to find effective ways to maintain social distancing. For this, we have implemented shifts, and also a system to allow contact tracing in the event cases emerge. Hopefully we will soon be in a new and less restricted phase. The important lessons and perspective we all have gained through this period will undoubtedly help us to adjust this new, but different normal.

A silver lining of this crisis has been the recognition of the importance of basic and biomedical research in the eyes of the general public. For researchers, this has also been an eye-opening experience. One that has shown that regardless what their specific field of research is, their expertise can suddenly become urgently needed in times of crisis. I am happy to say that many in the DBMR have responded with the biomedical research skills and innovative ideas to new research calls by the DoD, the SNF, and locally at the University level. We commend Profs. Andrew Macpherson, Stephanie Ganal-Vonarburg, and Deborah Keogh-Stroka for establishing in record time a COVID-19 diagnostic facility in our MEM building. I was impressed by their swift call to action, their attention to safety precautions, and how they rallied young investigators from the DBMR community to help with this important activity.

For many of us, this time of COVID-19 isolation has allowed to reflect on our work. I hope that as we return to active research, the focus on long term and important questions in biomedical research will remain our community's priority. This time away has allowed us to rethink and prioritize what is really essential. Maybe we will travel less, attend fewer meetings and continue to find alternative ways to communicate. As we move forward, I wish that we will continue to focus on the important work at hand and our local community.

Be well and stay safe in the coming year! I really look forward to seeing you!

Prof. Mark A. Rubin, MD

The DBMR at a Glance

The Department for BioMedical Research (DBMR) is a research department of the Faculty of Medicine at the University of Bern.

It was founded in 1994 with the mission to provide the best possible environment and infrastructures to researchers at the Inselspital, Bern University Hospital and at the Faculty of Medicine. In 2019, the DBMR celebrated its 25th anniversary. Forty-seven independent research groups, covering almost all fields of biomedical research, were affiliated with the DBMR.

The DBMR aims to bridge laboratory-based biomedical and patient-oriented clinical research through scientific support and by operating state-of-the-art technology core facilities and specialized animal core facilities. In addition, strong emphasis is placed on the development of translational approaches and the use of "omics" technologies.

Das DBMR auf einen Blick

Das Department for BioMedical Research (DBMR) ist ein Forschungsdepartement der Medizinischen Fakultät der Universität Bern.

Es wurde 1994 mit dem Auftrag gegründet, Forschenden des Inselspitals, Universitätsspital Bern und der Medizinischen Fakultät eine optimale Infrastruktur zur Verfügung zu stellen. Im Jahr 2019 feierte das DBMR das 25. Jahr seines Bestehens. 47 unabhängige Forschungsgruppen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken, waren dem DBMR angeschlossen.

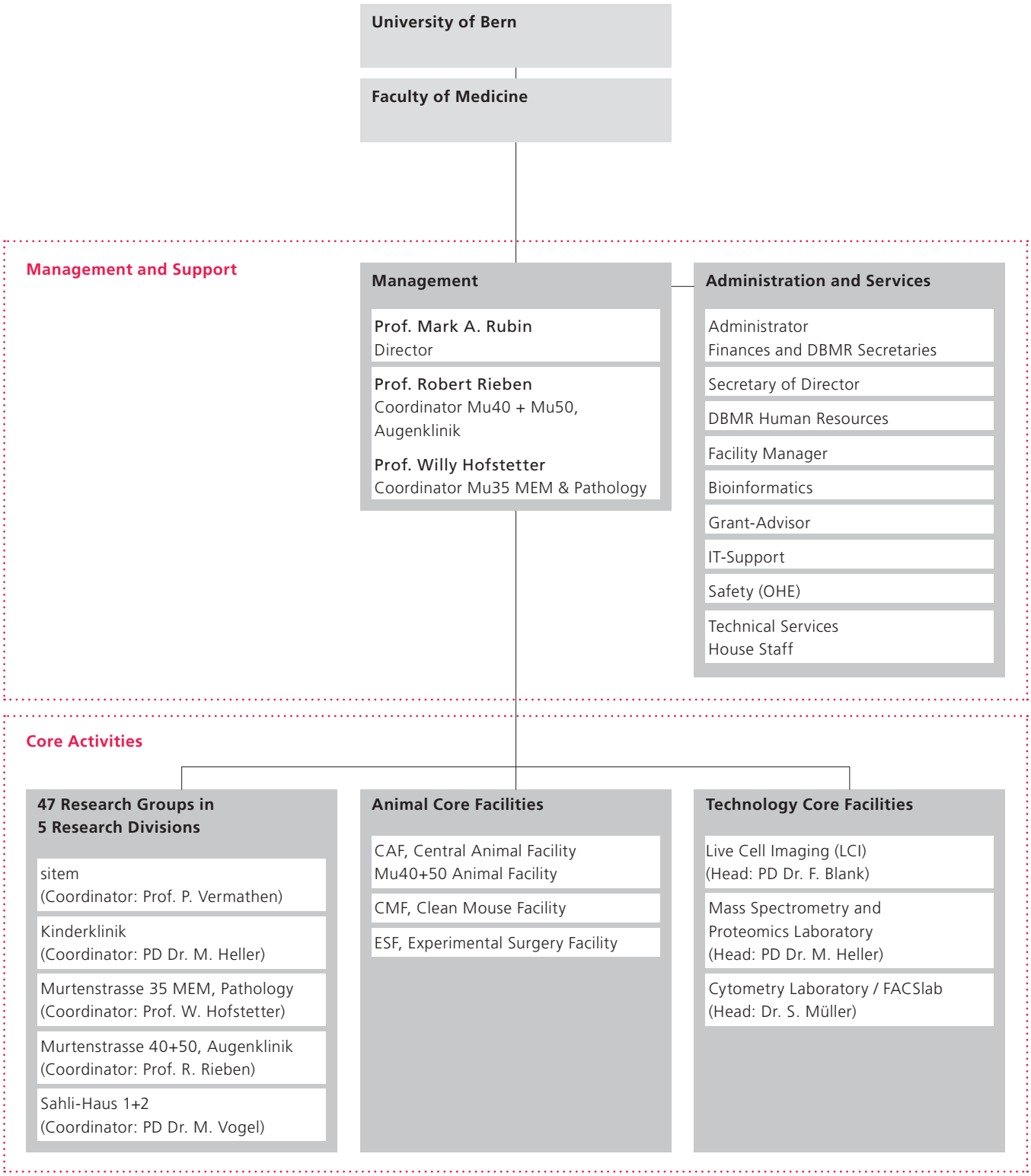
Ziel des DBMR ist es, Brücken zu schlagen zwischen laborbasierter biomedizinischer und patientenorientierter klinischer Forschung. Erreicht wird dies durch die wissenschaftliche Unterstützung der Forschungsgruppen, sowie dem Betrieb von, dem neusten Stand der Technik entsprechenden, technologischen Platformen und spezialisierten Tier Core Facilities. Ausserdem wird grosses Gewicht auf die Entwicklung translationaler Ansätze und der Anwendung von "omics" Technologien gelegt.

Organization

The role of the DBMR is to provide optimal infrastructures and scientific support to its research groups, of which there were 47 by the end of 2019. The vast majority (42) of these groups were from clinics of the Inselspital, Bern University Hospital. The remainder (5) are internal DBMR groups involved in the daily scientific support and coordination of equipment and infrastructures. The DBMR is divided into 5 research divisions. Equally important, the DBMR is responsible for operating the Technology and Animal Core Facilities. Furthermore, the department's groups are supported by central services responsible for administration, facility management, technical support, informatics, and bioinformatics.

Organigram

Department for BioMedical Research



1

M.E. Müller-Haus
Murtenstrasse 35

2

Murtenstrasse 50

3

Pathologie
Murtenstrasse 31

4

Kinderklinik
Freiburgstrasse 15

5

Sahli-Haus 1
Freiburgstrasse 14a

6

Sahli-Haus 2
Freiburgstrasse 14

7

Augenklinik
Freiburgstrasse 8

8

Murtenstrasse 40

9

sitem

10

Murtenstrasse 24
(under construction)

Key People

Management

Prof. Dr. Mark A. Rubin
Director

Prof. Dr. Robert Rieben
Coordinator Murtenstrasse 40+50, Augenklinik

Prof. Dr. Willy Hofstetter
Coordinator Murtenstr. 35 (MEM), Pathology

Administration and Central Services

Administration, Finances, and DBMR Secretariats

Basak Ginsbourger, Administrator
Ana Radovanovic, Secretary (since Sep.)
Deborah Re, Secretary (until July)
Marla Rittiner, Secretary
Beatrice Stalder, Secretary
Uyen Vo, Secretary

Secretariat of Director

Claudia Requeta (until May)
Cornita Rohda (since June)
Jasmine Stiefel

DBMR Human Resources

Silvia Rösselet
Marla Rittiner

Facility Manager

Bernhard Grossniklaus
Raschid Setoud
Alexia Roschi (Mar. – Dec.)

Occupational Safety, Health Protection, and Environmental Safety

François Achermann

IT-Support

Michael Ackermann
Max Pelletier (until July)
Thomas Späti
Luca Sulmoni
Ilker Yegit

Bioinformatics

Dr. Irene Keller

Technical Services

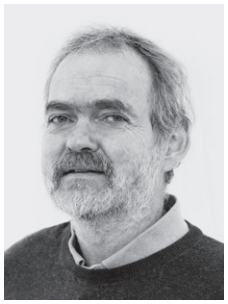
Patrick Furer, Head DBMR Workshop
Nivetha Ravindran, Intern

Coordinators of Research Divisions

PD Dr. Manfred Heller
Kinderklinik

Prof. Dr. Willy Hofstetter
Murtenstrasse 35 (MEM),
Pathology

Prof. Dr. Robert Rieben
Murtenstrasse 40+50,
Augenklinik



Prof. Dr. Peter Vermathen
sitem?

PD Dr. Monique Vogel
Sahli-Haus 1+2

Heads of Core Facilities

PD Dr. Fabian Blank
Live Cell Imaging (LCI)

PD Dr. Manfred Heller
Mass Spectrometry and
Proteomics Laboratory

Dr. Stefan Müller
Cytometry Laboratory,
FACS Lab

Cytometry Laboratory, FACS Lab

Dr. Stefan Müller
stefan.mueller@dbmr.unibe.ch

Microbiology studies at the University of Bern, PhD (1996). Postdoc (2000–2001) in intestinal mucosal immunology and Head of the Flow Cytometry Laboratory (2001), School of Cellular and Molecular Medicine, University of Bristol (UK). Senior Scientist in Gastroenterology (2004–2011) at the DBMR. Since 2010, Head of the DMBR Cytometry Laboratory / FACS Lab Core Facility.

Achievements 2019

In April, Isabelle Gsponer started her appointment in the FACS Lab as a lab technician. Due to her education and work experience in industry (Lonza AG) as well as at the Zürcher Hochschule für Angewandte Wissenschaften (ZHAW), Isabelle Gsponer brought, amongst other things, profound knowledge and experience about QC-management and elaboration of instrument or method-specific SOPs (Standard Operating Procedure) into the FACS Lab.

We were eventually able to upgrade our imaging flow cytometer, the Amnis ImageStreamX MK II, with the multi-magnification option (MultiMag) and the extended depth of field (EDF) module. The ×60 magnification now allows for the detection of more details in smaller primary cells. In addition, bacteria per se and host cell-bacteria interactions can be more reliably addressed. The higher magnification, together with the EDF, also allows the performance of flow-cytometry fluorescence *in situ* hybridization (Flow-FISH).

By the end of 2019, we launched our FACS course with a new modular concept. To obtain the two ECTS points, PhD students need to take a certain number of offered modules. Some of the modules are mandatory, while others can be selected according to the needs and interests of the course participants.

Performance Report 2019

After many years of a remarkably increasing demand of the use of our instruments, in 2019 there has been a slight decrease in the usage of our analyzers (-6.2%), and markedly fewer sorting requests (-20.5%). The latter was due, on one hand, to a heavily decreased demand by one former frequent user, and on the other hand, most likely because of the introduction of the markedly increased sorting-fees as of January 2019.

As an exception, and since its upgrade, the ImageStreamX has been used more frequently compared to 2018 (+ 13 %), and new research groups were using the equipment (18 groups compared to only 6 in 2018). This increased demand is a result of the long-awaited upgrade of the instrument, and it is even more remarkable because the instrument was not available during its upgrade process from March until the end of June.

FACS measurements were mostly performed by researchers from Inselspital clinics (51 %) and from the University of Bern institutes (48.6 %). Measurements by or for external parties made up 0.4 % of the total number. Regarding cell sorting, 68.7 % of the measurements were performed for Inselspital clinics and 30.4 % for University institutes, while 0.9 % were performed for external parties. A total of 51.4 % of measurements and 68.5 % of cell sorting runs were performed by or for DBMR groups.

Finances 2019

Due to the rather high age of many of our instruments, in 2019 we were again faced with the need to perform several rather expensive repairs. In addition, the service contract for our BD instruments did not pay off as expected, due to its restrictive regulations and exorbitant pricing regarding replacement parts. Nevertheless, thanks to the new user fee pricing scheme and the partial reimbursements for the costs of FlowJo licences, we expect a balanced budget for 2019, albeit with a delay of 3 to 6 months.

Outlook 2020

With the help of two BMA-diploma students, the FACS Lab will establish two methods of potential great interest and benefit to our users: Flow Cytometry-Fluorescent *In Situ* Hybridization (Flow FISH), and the simultaneous measurement of gene products at the mRNA and protein levels on a single cell level.

Regarding IT, our users will no longer be allowed to directly copy their data from our instrument workstations to any USB stick or external drive. Instead, we are currently installing disk stations in full RAID configuration, where data is transferred onto, and these can be retrieved by the users over the web. Furthermore, work-over of the new FACS Lab website will hopefully relaunch in 2020.

Staff Members

Dr. Stefan Müller, Head
Dr. Thomas Schaffer, Scientific, and Educational Support, Technical Assistance
Dr. Claudio Vallan, Scientific, and Educational Support
Bernadette Nyfeler, Lab Technician, and operational lead
MSc Isabelle Gsponer, Lab Technician, QC, and SOP (since Apr.)

www.dbmr.unibe.ch/services/core_facilities/cytometry_laboratory___facslab/index_eng.html

Live Cell Imaging (LCI)

PD Dr. Fabian Blank
fabian.blank@dbmr.unibe.ch

MSc in Cell Biology (2003) and PhD in Structural Biology (2006) at the University of Bern. Postdocs at the Institute of Anatomy, University of Bern (2007–2008) and Telethon Institute for Child Health Research, Perth (AU) (2008–2009). Since 2009, Senior Scientist, Pulmonary Medicine (Adults). DBMR since 2010, Commission Member, Microscopy Imaging Centre. Since 2012, Head of the Live Cell Imaging (LCI) Core Facility, DBMR. *Venia Docendi* (2016).

Achievements 2019

In the course of 2019, we have worked on refining our protocols for histological processing and analysis and provided a list of available services, which is now published on our webpage. In collaboration with the Microscopy Imaging Centre (MIC), the focus of our regular practical courses in histology and light microscopy has been further extended to digital image processing and analysis with a number of new lectures and practical exercises.

Since its launch in 2012, the LCI Core Facility is supported by the MIC, an interfaculty platform that coordinates, prioritizes, and supports funding applications in high-end microscopy as well as organizes the access to microscopy equipment for all members of the University of Bern.

Performance Report 2019

The total number of booked hours for using LCI equipment was 5,445 in 2019 (4,620 in 2018). These do not include systems that have to be booked daily, such as the IncuCyte S3 System. In 2019, LCI staff spent a total of 236 hours for introductory training on LCI microscopes (159 in 2018). The working hours spent for collaborations with other research groups from the DBMR decreased to 577 (672 in 2018). The number of hours spent on technical assistance increased to 265 (181 in 2018). As in previous years, the facility contributed to the advanced microscopy lectures and practical modules organized by the MIC. A total of 18 students received training in the practical modules of the LCI in 2019.

Finances 2019

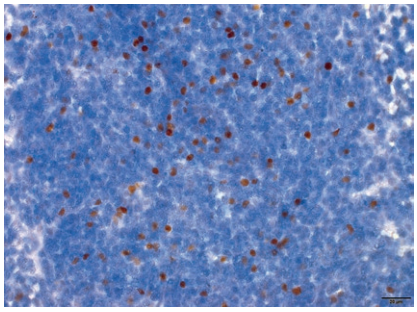
Revenues have increased slightly in 2019 in comparison to 2018. Several costly repairs on the Zeiss LSM710 confocal microscope (e.g., new argon laser) put considerable strain on the LCI budget in 2019. As in previous years, the facility has received a working credit of CHF 6'000 from the DBMR for general maintenance and repairs. The LCI Core Facility has again covered the yearly IMARIS software license fee for three floating licenses. The software is available for free for users of the facility and installed on the workstations available for booking.

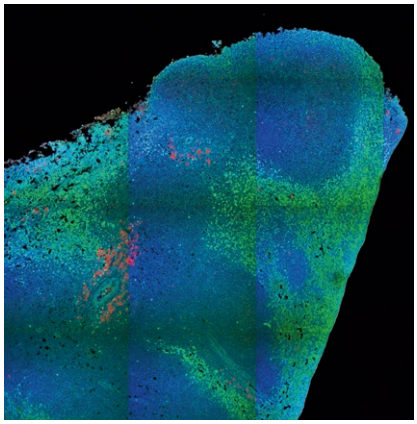
Outlook 2020

As in the previous year, the LCI Core Facility aims to acquire more expertise in the field of digital image processing, visualization, and analysis. LCI staff will receive training on the used software. Planning and coordination regarding the movement of the LCI Core Facility to Murtenstrasse 24 in 2021 will be continued and intensified. The new facility will include a larger histology lab and microscopy facility. In addition, new devices such as single-point confocal systems have been budgeted for, in the new location.

Staff Members

PD Dr. Fabian Blank, Head
Selina Steiner, Lab Technician
Carlos Wotzkow, Lab Technician





www.dbmr.unibe.ch/services/core_facilities/live_cell_imaging/index_eng.html

Mass Spectrometry & Proteomics Laboratory (Core Facility)

Protein & cell biology (research group)

PD Dr. Manfred Heller
manfred.heller@dbmr.unibe.ch

PhD in Biochemistry (1994) at the University of Bern. Postdoc at the University of Auckland (NZ) and in the University of Washington, Seattle (US). He returned to Switzerland in 1999 to the University of Geneva for one year as the Senior Assistant, followed by three years as a Senior Scientist at GeneProt Inc., Geneva, and at DiagnoSwiss, Monthey. Since 2003, he is the Head of Proteomics and Mass Spectrometry Laboratory, a DBMR Core Facility since 2008. He has twenty-two years of experience in mass spectrometry, proteomics, and bioinformatics.

Achievements 2019

Mass Spectrometry and Proteomics
As in recent years, the demand for our service has been constantly high, and we could assist in a variety of proteomics projects encompassing many different sample types collected from a variety of species. As a complement to our standard 15-cm column runs, we have started to offer shotgun proteome analysis based on 50-cm long columns and 2-3 hours of peptide separation gradients, in order to deepen the proteome coverage with only one single analysis run. We would like to thank all customers for their trust in our service.

The numbers presented in the performance report below illustrate the fact that we have reached a plateau for sample throughput. It was therefore a relief that our R'Equip proposal to the SNF for the acquisition of a fourth instrument based on ion-mobility technology was successful. Furthermore, we could extend the computing and storage power of our own server infrastructure.

Protein and Cell Biology
After composing a manuscript on the influence of the transport of blood on the protein composition of extracellular vesicles, we realized that more data was needed. With the great help of the Clinic of Haematology of the University Hospital of Bern in collecting new blood samples, we could extend our study and are about to redraft the manuscript. We also invested more time in order to stratify our phosphoproteome processing pipeline.

Plans for 2020

We aim to 1) publish our work on extracellular vesicles and the analysis pipeline for phosphoproteomics; 2) test at least two different nano LC-MS/MS instruments with ion mobility; and 3) publish a public tender for the purchase of a new instrument before the end of 2020.

Performance Report 2019

Mass Spectrometry and Proteomics
We processed around 1,370 samples during the year, submitted by laboratories from the Faculty of Medicine (49 %), Faculty of Science (32 %), Vetsuisse Faculty (12 %), and external institutions (8 %), which means that we processed more samples for the Medical Faculty than for any other organization for the first time. This is related to about 2,807 LC-MS/MS runs for publishable data production. This number is completed by 143 runs for developmental purposes, 1,379 QC standards, and 4,009 blanks for quality assurance. The number of QC standards increased by 63 % compared to the previous year, indicating that we processed more projects and upheld our urge for a high-quality standard.

Finances 2019

Mass Spectrometry and Proteomics
Our financial situation profited from the fact that we often do maintenance work ourselves. However, we had to spend more than CHF 20,000 on maintenance and repair costs. The facility received a working credit of CHF 10,000 from the DBMR to partially cover these costs.

www.pmscf.dbmr.unibe.ch

Staff Members

PD Dr. Manfred Heller, Group Leader (Research Group), and Head (Core Facility)
François Achermann, Lab Technician (40 % Core Facility and Research Group), DBMR Head of Occupational Safety, Health Protection, and Environmental Safety (OHE)
Sophie Braga, Lab Head and Assistant (Core Facility & Research Group)
Natasha Buchs, Lab Technician (Core Facility & Research Group)
Maïwenn Jornod, Master student, Scientific Assistant in Bioinformatics (Core Facility & Research Group)
Ilker Yegit, IT Specialist (20 % Core Facility)
Dr. Anne-Christine Uldry, Computational Scientist (80 % Core Facility & Research Group)

Collaborators

Bonadies N, University Hospital of Bern (CH)
Tiem A, Grether Y, INOFEA AG, Basel (CH)

Teaching activities

- MSc Biomedical Sciences: Tumour Biology – Proteomics Discussion
- MSc Biology: From Genomes to Metabolomes – Proteomics Lecture
- MSc in Bioinformatics: Mass Spectrometry to Systems Biology, Course, and Practical

Publications

Nasher, F., M. J. Kwun, N. J. Croucher, M. Heller, and L. J. Hathaway. "Peptide Occurring in Enterobacteriaceae Triggers Streptococcus Pneumoniae Cell Death." Front Cell Infect Microbiol 9 (2019): 320. http://dx.doi.org/10.3389/fcimb.2019.00320.

Muller, J., S. Braga, M. Heller, and N. Muller. "Resistance Formation to Nitro Drugs in Giardia Lamblia: No Common Markers Identified by Comparative Proteomics." Int J Parasitol Drugs Drug Resist 9 (Apr 2019): 112-19. http://dx.doi.org/10.1016/j.ijpddr.2019.03.002.

Kuhn-Nentwig, L., N. Langenegger, M. Heller, D. Koua, and W. Nentwig. "The Dual Prey-Inactivation Strategy of Spiders-in-Depth Venomic Analysis of Cupiennius Salei." Toxins (Basel) 11, no. 3 (Mar 19 2019). http://dx.doi.org/10.3390/toxins11030167.

Kehl, D., M. Generali, A. Mallone, M. Heller, A. C. Uldry, P. Cheng, B. Gantenbein, S. P. Hoerstrup, and B. Weber. "Proteomic Analysis of Human Mesenchymal Stromal Cell Secretomes: A Systematic Comparison of the Angiogenic Potential." NPJ Regen Med 4 (2019): 8. http://dx.doi.org/10.1038/s41536-019-0070-y.

Zahnd, S., S. Braga-Lagache, N. Buchs, A. Lugli, H. Dawson, M. Heller, and I. Zlobec. "A Digital Pathology-Based Shotgun-Proteomics Approach to Biomarker Discovery in Colorectal Cancer." J Pathol Inform 10 (2019): 40. http://dx.doi.org/10.4103/jpi.jpi_65_18.

Link to publication list:
www.pmscf.dbmr.unibe.ch/research/publications

Oncogenomics

Dr. Charlotte KY Ng
charlotte.ng@dbmr.unibe.ch

PhD (2012) at the University of Cambridge, UK
Postdoc (2012–2018) at the Institute of Cancer Research (London, UK), Memorial Sloan Kettering Cancer Center (New York, USA), and University Hospital Basel (Basel, CH). Head of the Oncogenomics Lab at the DBMR since 2019.

Research highlights of 2019 / outlook for 2020

The Oncogenomics Lab focuses on developing and applying computational approaches to address challenges in precision oncology. In particular, we are interested in leveraging the abundance of "omics" data derived from clinically annotated samples in computational frameworks to discover novel biomarkers and therapeutic targets.

Genomic characterization of metastatic breast cancer

In collaboration with Prof. Fabrice André (Institut Gustave Roussy, France), we profiled the exomes of 600+ cases of metastatic breast cancer. We found that NF1/RB1 mutations were associated with poor outcomes, suggesting that these patients may be prioritized for the use of investigational treatments. The genetic complexity of metastatic breast cancer and the frequent presence of mutations that lead to defective DNA repair mechanisms suggest that treatment should be offered as early as possible in the disease course.

Systematic identification of novel cancer genes from the perturbation screens

Systematic perturbation screens provide comprehensive resources for elucidation on cancer driver genes. We developed analysis of perturbation screens for identifying novel cancer genes (APSiC) and demonstrated its robustness in identifying drivers in perturbation screens, even with few samples. By applying APSiC to a deep shRNA screen, we identified and functionally demonstrated that LRRC4B, a putative novel tumor suppressor gene, inhibits the proliferation by delaying the cell cycle and modulating apoptosis in breast cancer.

A more accurate mutation calling on the Ion Torrent sequencing platform

Ion Torrent is the most used sequencing platform for diagnosis in Switzerland, but the proprietary software for data analysis requires an extensive manual review of the results and lacks an optimized workflow for custom panels. We developed 'Pipe-IT' and demonstrated its superior positive predictive value compared to the proprietary software (~100 % vs. ~74 %) in identifying somatic mutations from matched tumor-normal sequencing data, substantially reducing the need for manual curation of the results. PipeIT is being integrated into the SPHN/PHRT-funded SOCIBP infrastructure.

Dissecting the liver cancer ecosystem

In the Swiss Cancer League funded project, we will profile the transcriptome of hepatocellular carcinomas at the single-cell level to provide insights into the heterogeneity of cancer cells and the tumor microenvironment in liver cancer.

www.dbmr.unibe.ch/research/research_groups/oncogenomics/index_eng.html

Group Members

Dr. Charlotte K Y Ng, Group Leader (since Jan.)
Dr. Andrej Benjak, Senior Bioinformatician (since Mar.)

Collaborators

André F, Institut Gustav Roussy, Paris (FR)
Beerenwinkel N, ETH Zürich, Basel (CH)
Christofori G, University of Basel, Basel (CH)
Heim MH, University of Basel, Basel (CH)
Piscuoglio S, University of Basel (CH)
Roma G, Novartis (CH)

Teaching Activities

– Certificate of Advanced Studies in Personalized Molecular Oncology, University of Basel

Publications

Tang, F., R. Gao, B. Jeevan-Raj, C. B. Wyss, R. K. R. Kalathur, S. Piscuoglio, C. K. Y. Ng, S. K. Hindupur, S. Nuciforo, E. Dazert, T. Bock, S. Song, D. Buechel, M. F. Morini, A. Hergovich, P. Matthias, D. S. Lim, L. M. Terracciano, M. H. Heim, M. N. Hall, and G. Christofori. "Lats1 but Not Lats2 Represses Autophagy by a Kinase-Independent Scaffold Function." Nat Commun 10, no. 1 (Dec 17 2019): 5755. http://dx.doi.org/10.1038/s41467-019-13591-7.

Soysal, S. D., C. K. Y. Ng, L. Costa, W. P. Weber, V. Paradiso, S. Piscuoglio, and S. Muenst. "Genetic Alterations in Benign Breast Biopsies of Subsequent Breast Cancer Patients." Front Med (Lausanne) 6 (2019): 166. http://dx.doi.org/10.3389/fmed.2019.00166.

Garofoli, A., V. Paradiso, H. Montazeri, P. M. Jermann, G. Roma, L. Tornillo, L. M. Terracciano, S. Piscuoglio, and C. K. Y. Ng. "Pipeit: A Singularity Container for Molecular Diagnostic Somatic Variant Calling on the Ion Torrent Next-Generation Sequencing Platform." J Mol Diagn 21, no. 5 (Sep 2019): 884-94. http://dx.doi.org/10.1016/j.jmoldx.2019.05.001.

Bertucci, F. C. K. Y. Ng, A. Ptsouris, N. Droin, S. Piscuoglio, N. Carbuccia, J. C. Soria, A. T. Dien, Y. Adnani, M. Kamal, S. Garnier, G. Meurice, M. Jimenez, S. Dogan, B. Verret, M. Chaffanet, T. Bachelot, M. Campone, C. Lefeuvre, H. Bonnefoi, F. Dalenc, A. Jacquet, M. R. De Filippo, N. Babbar, D. Birnbaum, T. Filleron, C. Le Tourneau, and F. Andre. "Genomic Characterization of Metastatic Breast Cancers" Nature 569, no. 7757 (May 2019): 560-64. http://dx.doi.org/10.1038/s41586-019-1056-z.

Blumer, T., I. Fofana, M. S. Matter, X. Wang, H. Montazeri, D. Calabrese, M. Coto-Llerena, T. Boldanova, S. Nuciforo, V. Kancherla, L. Tornillo, S. Piscuoglio, S. Wieland, L. M. Terracciano, C. K. Y. Ng, and M. H. Heim. "Hepatocellular Carcinoma Xenografts Established from Needle Biopsies Preserve the Characteristics of the Originating Tumors" Hepatol Commun 3, no. 7 (Jul 2019): 971-86. http://dx.doi.org/10.1002/hep4.1365.

Bone Biology & Orthopaedic Research

Prof. Dr. Willy Hofstetter
hofstetter@dbmr.unibe.ch

MSc in Biochemistry at ETH Zurich; PhD in Biochemistry (supervisor Prof. N. Herschkowitz) at the Children's Hospital, Inselspital. Postdoc at the University of Georgia, US, with Prof. D. Dervartanian. Then, he joined the Institute of Pathophysiology, University of Bern (Prof. H. Fleisch). Since 1997, he is the head of the DBMR Research Group for Bone Biology & Orthopaedic Research.

Research Highlights of 2019 / Outlook on 2020

Highlights of our research on bone cell biology and fracture repair are described below

Highlights of our research on bone cell biology are described below:

– Iron is a major trace element with diverse functions and plays a part in oxidative phosphorylation and cellular energy metabolism, among other processes. In the recent past, we focused on the intracellular transport of iron in osteoclast lineage cells. After 2 h of iron uptake, iron in osteoclasts was found either in a soluble, cytoplasmic pool (corresponding to a labile iron pool) and in a vesicular pool. After incubation for another 4 h, the labile iron pool was greatly reduced and the intracellular iron was primarily associated with membrane vesicles and ferritin. Subcellular iron storage and trafficking will be the subject of further studies. This work was performed within the PhD Thesis of Romina Cabra, who defended her work successfully in December 2019 (supported by NCCR TransCure).
– Studies on the healing of bone defects in osteoporotic animals treated with bisphosphonates were continued. With a new PhD student (Franziska Strunz) and the support from the Alfred & Anneliese Sutter-Stöttner Stiftung, we started a project on the healing of critical size defects in mouse femora. For this purpose, a critical size defect model was established using the MouseFix System (RISystem, Landquart, CH). A pilot study was performed using Peek and Titanium osteosynthesis plates mounted on the femora of NMRI mice. The critical size defect of 3 mm was filled with a cylinder of beta-tricalcium phosphate (ßTCP) (M. Bohner, RMS Foundation, Bettlach, CH) that was coated with growth factors. The results from the pilot study allowed us to conclude that titanium plates are preferable over Peek plates and that a healing period of 12 weeks allowed for extensive bone formation when the ßTCP implants were coated with BMP2.
– In the recent past, we investigated novel potential roles of the BMP antagonist Noggin. Our data suggest that besides the canonical pathway of antagonizing the activities of bone morphogenetic proteins (BMP), BMP antagonists might exert autonomous cellular effects. Previously, we found that Noggin exerts direct and indirect effects on the development of osteoclast lineage cells. While we found a direct stimulatory effect of Noggin on the differentiation of osteoclast progenitor cells to be dependent on TGFß signaling, the indirect inhibitory effect on osteoclastogenesis was, at least in part, mediated through osteoblast-derived Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF). The underlying concept, however, regarding how a BMP antagonist provokes a cellular response, remains in the dark. For this purpose, a transcriptome study will be initiated to assess the whole repertoire of cellular responses induced by Noggin. The aim of this project was to identify receptors or receptor-like molecules that interact with Noggin and thus initiate a specific cellular response (PhD Project of Fatemeh Safari, in collaboration with PD Frank Klenke, University Clinics for Orthopaedic Surgery, Inselspital, Bern).
– Gadolinium (Gd) compounds are widely used as contrast agents in radiologic diagnostics. Recently it has become evident that Gd is stored in a multitude of tissues, i.e. CNS and bone. However, nothing

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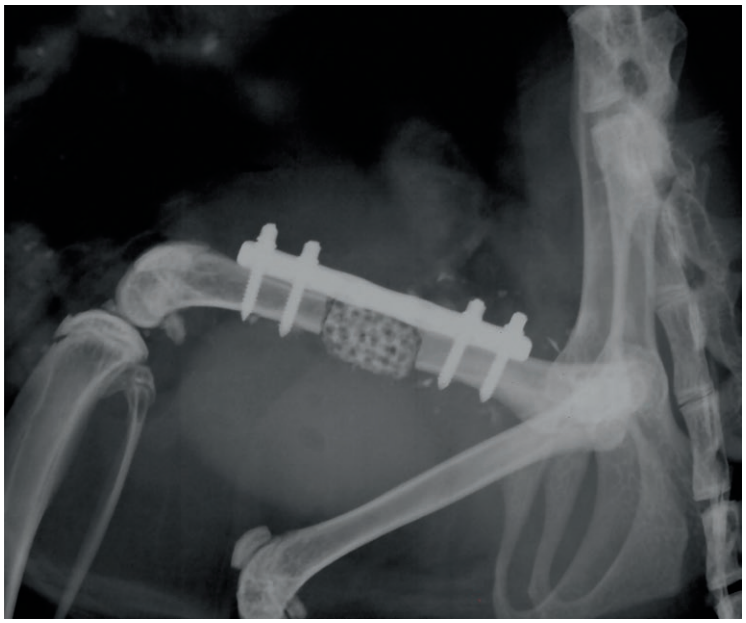

is known about the potential cellular effects of long-term exposure to Gd. In this project, we will first investigate the effects of free Gd and complexed Gd, as used in radiological contrast agents, on the development and activity of osteoblast and osteoclast lineage cells *in vitro*. In further studies, *in vivo* models will be used to assess the long-term effects of Gd on turnover and skeletal integrity (this work was initiated by Jana Stauffer, MEDI Intern, followed by Franziska Strunz, PhD student, in collaboration with Dr. Rainer Egli, Department for Radiology, Inselspital, Bern, and the Robert Mathys Foundation, and supported through a CTU Grant of the Inselspital).

Group Members

Prof. Dr. Willy Hofstetter, Group Leader
Silvia Dolder, Lab Technician
Mark Siegrist, Lab Technician
Romina Cabra, PhD Student
Fatemeh Safari, PhD Student
Franziska Strunz, PhD Student (since Nov.)
Roman Weber, Intern (since Nov.)

Clinicians with projects in the group
Dr. Rainer Egli, Project Leader
PD Dr. Frank Klenke, Project Leader

Collaborators

Bohner M, RMS Foundation, and Bettlach (CH)
Bonny O, University of Lausanne, Lausanne (CH)
Fuster D, Albano G, Inselspital, Bern (CH)
Krebs P, Pathology, Bern (CH)
Saulacic N, Inselspital, Bern (CH)
Siebenrock KA, Inselspital, Bern (CH)

Teaching Activities

- MSc Biomedical Engineering: Osteology course (Hofstetter)
- MSc Biomedical Engineering: Master student (6 months internship)
- 3rd-year dentistry students: Pathophysiology – Skeleton (Hofstetter)
- 2nd-year medical students: Kidney block – Calcium and phosphate metabolism (Hofstetter)
- MEDI Bern: Internship

Publications

Gallo, M., B. Le Gars Santoni, T. Douillard, F. Zhang, L. Gremillard, S. Dolder, W. Hofstetter, S. Meille, M. Bohner, J. Chevalier, and S. Tadier. "Effect of Grain Orientation and Magnesium Doping on Beta-Tricalcium Phosphate Resorption Behavior." Acta Biomater 89 (Apr 15 2019): 391-402. http://dx.doi.org/10.1016/j.actbio.2019.02.045.

Zhao, W., D. Michalik, S. Ferguson, W. Hofstetter, J. Lemaitre, B. von Rechenberg, and P. Bowen. "Rapid Evaluation of Bioactive Ti-Based Surfaces Using an in Vitro Titration Method." Nat Commun 10, no. 1 (May 2 2019): 2062. http://dx.doi.org/10.1038/s41467-019-09673-1.

Saulacic N., Munoz F., Kobayashi E., Chappuis V., Gonzales-Cantalapiedra A, Hofstetter W. (2019) "Alveolar ridge preservation using bisphosphonates: an experimental study in the Beagle dog". Clinical Oral Investigations (epub ahead of print)

May, R. D., D. A. Frauchiger, C. E. Albers, A. Tekari, L. M. Benneker, F. M. Klenke, W. Hofstetter, and B. Gantenbein. "Application of Cytokines of the Bone Morphogenetic Protein (Bmp) Family in Spinal Fusion – Effects on the Bone, Intervertebral Disc and Mesenchymal Stromal Cells." Curr Stem Cell Res Ther 14, no. 8 (2019): 618-43. http://dx.doi.org/10.2174/1574888X14666190628103528.

Link to publication list:
www.bonebiology.dbmr.unibe.ch/research/publications/

Link to DBMR Network for Bone and Joint Research:
https://www.dbmr.unibe.ch/unibe/portal/fak_medizin/ber_insklin/dept_bmr/content/e39405/e40552/e691896/files691909/180611ClusterDBMR_BoneJoint_eng.pdf

Cardiovascular Research

Prof. Dr. Robert Rieben
robert.rieben@dbmr.unibe.ch

Studies in Biology at the University of Bern; PhD in Immunology (1992). SNF postdoc on xenotransplantation (1995-1997) in Leiden (NL). Return to Bern in 1997 to establish a research group. Habilitation (2002); Associate Professor (2007). Sabbatical in Melbourne (AU) in autumn/winter 2015/2016. Since 2005, Group Leader of Cardiovascular Research, DBMR.

Research Highlights of 2019 / Outlook on 2020

Two new collaborators, Nicoletta Sorvillo (senior postdoc) and Anastasia Milusev (PhD student) joined our team in 2019 to work on our basic science SNF grant "Endothelial cell protection in ischemia / reperfusion injury: Investigation into the roles of the glycocalyx and the plasma cascade systems". They further developed the 3D microfluidic system for endothelial cell culture to investigate the role of the endothelial cell glycocalyx as a scavenger of plasma proteins. This state-of-the-art *in vitro* model, which could also be termed 'microvessels on a chip', should allow to study molecules like antithrombin III, superoxide dismutase, C1-inhibitor, and others, which are important for the anticoagulant, anti-inflammatory, and pro-fibrinolytic function of a healthy endothelium. In 2019 we isolated endothelial cells from different types of blood vessels of baboons, pigs, and rabbits. Characterization of these cells is still ongoing and goes in parallel with further technical optimizations of the *in vitro* model. With Nicoletta Sorvillo being an expert on neutrophil activation as well as neutrophil extracellular traps (NETs) we will also include these aspects in the future.

Supported by a grant of the US Department of Defense, an extracorporeal perfusion study was started with amputated porcine extremities. In October 2019, Josip Mikulic joined our group to work on this project as a postdoc. He successfully started the experimental study, for which we closely collaborate with the staff of the Experimental Surgery Facility, headed by Daniela Casoni, the Clinic of Plastic and Hand Surgery (Esther Vögelin, director, and Stefanie Hirsiger, staff surgeon), and the perfusionist's team of the Clinic of Cardiovascular Surgery, led by Hansjörg Jenni. The aim of this project is to prolong the time window of replantation of a traumatically amputated limb. For this, the amputated porcine limbs are exposed to different ischemia times and then reperfused on an extracorporeal perfusion circuit using anticoagulated, autologous pig blood.

The third project that started in 2019 is a large animal study on local immunosuppression in vascularized composite allotransplantation (VCA). In the summer of 2019, Isabel Arenas joined our group as a MD-PhD student focusing on this project. This study is led by our partner from the Clinic of Plastic Surgery, Radu Olariu, and supported by the SNF. Its final aim is to replace systemic immunosuppression in human VCA recipients and replace it by local, 'on demand' immunosuppression with significantly reduced side effects. In a first series of experiments, heterotopic, fully vascularized, osteomyocutaneous flaps from allogeneic donor pigs were grafted into the flank of recipient pigs. Immunosuppression was then either systemic or local, as previously successfully performed in a rat model. While immunological data are still pending, the feasibility of the study could already be proven.

www.cvrc.unibe.ch/research/ischemia___reperfusion/
www.dbmr.unibe.ch/research/research_groups/cardiovascular_research/index_eng.html

Group Members

Prof. Dr. Robert Rieben, Group Leader
Alain Despont, Lab Technician
Jane Shaw–Boden, Lab Technician
Josip Mikulic, Postdoc
Riccardo Sfriso, Postdoc (until Apr.)
Isabel Arenas, PhD Student
Anastasia Milusev, PhD Student
Nicoletta Sorvillo, Postdoc
Uyen Vo, Secretary and Web Administrator

Collaborators

Garweg J, Zandi S, Berner Augenklinik at Lindenhofspital, Bern (CH)
Guenat O, University of Bern (CH)
Heinis Ch, EPFL, Lausanne (CH)
Jenni HJ, Invital (CH)
Langelé B, Duisit J, Université Catholique de Louvain, Brussels (BE)
Luciani P, University of Bern (CH)
Yonglun L, Aarhus University (DK)
Olariu R, Constantinescu MA, Inselspital (CH)
Reichart B, Abicht J, Ludwig Maximilian University of Munich (DE)
Schnieke A, Fischer K, Technical University of Munich (DE)
Waskow C, Technical University of Dresden (DE)
Seebach J, Geneva University Hospital (CH)
Spirig R, CSL Behring AG (CH)
Vögelin E, Inselspital (CH)
von Gunten S, Frias Boligan K, University of Bern (CH)
Wolf E, Klymiuk N, Bähr A, Ludwig Maximilian University of Munich (DE)

Teaching Activities

- MSc in Biomedical Sciences: Elective modules, 2 Master students (6 month internship, each)
- Bachelor in Medicine: Elective course 33004 – Ihr Partner im Labor: Forschung auf den Gebieten Organtransplantation, Chirurgie und Herzinfarkt
- BSc in Life Sciences: Practical Course in Immunology, Research Internships
- MSc in Life Sciences: Lecture "Interactions of the Plasma Cascade Systems in Inflammation" (MOBIFLAM), 1 Master student (18 months internship)
- PhD students at the Graduate School for Cellular and Biomedical Sciences: Immunology Tutorial
- High school students: Patenschaften für Maturaarbeiten (6 students with a 2-week lab stay each)

Publications

Fischer, K., B. Rieblinger, R. Hein, R. Sfriso, J. Zuber, A. Fischer, B. Klinger, W. Liang, K. Flisikowski, M. Kurome, V. Zakhartchenko, B. Kessler, E. Wolf, R. Rieben, R. Schwinzer, A. Kind, and A. Schnieke. "Viable Pigs after Simultaneous Inactivation of Porcine Mhc Class I and Three Xenoreactive Antigen Genes Ggta1, Cmah and B4galnt2." Xenotransplantation 27, no. 1 (Jan 2020): e12560. http://dx.doi.org/10.1111/xen.12560.

Jandus, P., K. F. Boligan, D. F. Smith, E. de Graauw, B. Grimbacher, C. Jandus, M. M. Abdelhafez, A. Despont, N. Bovin, D. Simon, R. Rieben, H. U. Simon, R. D. Cummings, and S. von Gunten. "The Architecture of the Igg Anti-Carbohydrate Repertoire in Primary Antibody Deficiencies." Blood 134, no. 22 (Nov 28 2019): 1941-50. http://dx.doi.org/10.1182/blood.2019001705.

Sutter, D., D. V. Dzhonova, J. C. Prost, C. Bovet, Y. Banz, L. Rahnfeld, J. C. Leroux, R. Rieben, E. Vogelin, J. A. Plock, P. Luciani, A. Taddeo, and J. T. Schnider. "Delivery of Rapamycin Using in Situ Forming Implants Promotes Immunoregulation and Vascularized Composite Allograft Survival." Sci Rep 9, no. 1 (Jun 25 2019): 9269. http://dx.doi.org/10.1038/s41598-019-45759-y.

Zandi, S., I. B. Pfister, P. G. Traine, C. Tappeiner, A. Despont, R. Rieben, M. Skowronska, and J. G. Garweg. "Biomarkers for Pvr in Rhegmatogenous Retinal Detachment." PLoS One 14, no. 4 (2019): e0214674. http://dx.doi.org/10.1371/journal.pone.0214674.

Link to publication list:
www.cvrc.unibe.ch/research/ischemia___reperfusion/publications/

Precision Oncology

Prof. Dr. Mark A. Rubin
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Prof. Rubin is the Director of the Department for Biomedical Research and Head of the Bern Center for Precision Medicine. He is a leader in prostate cancer (PCa) biology and cancer precision medicine. His landmark studies have defined many molecular features of PCa and their involvement in disease progression. Many of his discoveries have been translated into clinical tests.

Research Highlights of 2019 / Outlook on 2020

Precision Oncology applies Precision Medicine approaches to understand the mechanisms of prostate cancer progression and therapy resistance. In 2019, the group has successfully secured additional funds, including SNF Sinergia project "Hijacking Transcription-Coupled DNA Repair for Cancer Therapy" in collaboration with Shana Sturla (ETHZ) and Orlando Schärer (IBS, Korea). In 2020, the group will continue to investigate the impact of epigenetic and epitranscriptomic events on gene regulation, particularly in the context of advanced PCa.

1) Defining the heterogeneity of brain metastatic PCa: a pan-Swiss project. In this pilot study within the larger SPHN-funded SOCIBP platform and sponsored by NCI, matched samples of primary and brain metastatic PCa were collected across seven Swiss cantons. Tumor heterogeneity and its molecular/genomic landscape were defined for a better understanding of this unexplored metastatic location.

2) Understanding non-canonical phosphatidylinositol kinases in the maintenance of prostate metabolism. In this SNSF and MSCA-funded project, we posit that the PI5P4K lipid kinases influence PCa metabolism. In 2019 we have produced "multi-omics" datasets to characterize the changes in cell metabolism using PI5P4K-depleted systems and generated the first prostate cell-type specific mouse to target expression *in vivo*.

3) Towards a precision therapy for speckle-type POZ protein (SPOP) mutant PCa. This project is funded by the Swiss Krebsliga in collaboration with Ruedi Aebersold (ETHZ) and focuses on the downstream effectors of SPOP by targeted proteomics. Further areas of SPOP biology were supported by an NCI grant.

4) Towards understanding and modulating neuroendocrine transdifferentiation in PCa. This project seeks to understand the lineage plasticity of neuroendocrine PCa (NEPC), which will help create therapeutic approaches that can delay or inhibit this terminal form of PCa and lead to earlier co-targeted therapies prior to disease progression.

5) Towards understanding the role of aberrant splicing in PCa progression. In PCa, a major clinical challenge is posed by the occurrence of constitutively active androgen receptor splice variants (e.g. AR-V7) that are C-terminal truncated and therefore resistant to AR signaling inhibitors (e.g. abiraterone or enzalutamide). This project seeks to understand how aberrant splicing participates in therapy resistance in PCa.

6) Understand the role of m6A methylation in gene regulation and PCa disease progression. This PCF- and NIH-funded project aims to explore the role of m6A modification of mRNAs in PCa. In 2019 we have combined transcriptomic and proteomic data to identify genes regulated by m6A at the mRNA and/or protein level.

7) Immune-radiation therapy for metastatic castration-resistant PCa. The aim of this PCF-funded project co-lead by George Coukos (Centre Hospitalier Universitaire Vaudois) is to expand on current approaches to immuno-oncology and elucidate on potential immunotherapeutic targets for metastatic PCa.

www.rubinlab.unibe.ch

Group Members

Prof. Dr. Mark A. Rubin, Group Leader
Dr. Anke Augspach, Postdoc
Dr. Laura Brandt, Postdoc
Dr. Kellie Anne Cotter, Postdoc
Dr. Joanna Triscott, Postdoc
Dr. Alison Ferguson, Postdoc (since Jan.)
Dr. med. Antonio Rodriguez, Resident Pathologist (since Jan.)
Dr. Stephan Christen, Lab Manager
Matthias Reist, Lab Technician
Muriel Jaquet, Lab Technician
Sina Maletti, Lab Technician (since Jan.)
Philip Rubin, Lab Technician (since Jan.)
Izzem Gemici, Lab Technician (since Nov.)
Phillip Thienger, PhD Student (since Nov.)

Collaborators

Emerling B, Stanford Burnham Prebys Medical Discovery Institute (USA)
Aebersold R, ETH Zurich (CH)
Moch H, University of Zurich (CH)
Coukos G, University of Lausanne (CH)
Rätsch G, ETH Zurich (CH)

Selected Publications

Abida, W., J. Cyrta, G. Heller, D. Prandi, J. Armenia, I. Coleman, M. Cieslik, M. Benelli, D. Robinson, E. M. Van Allen, A. Sboner, T. Fedrizzi, J. M. Mosquera, B. D. Robinson, N. De Sarkar, L. P. Kunju, S. Tomlins, Y. M. Wu, D. Nava Rodrigues, M. Loda, A. Gopalan, V. E. Reuter, C. C. Pritchard, J. Mateo, D. Bianchini, S. Miranda, S. Carreira, P. Rescigno, J. Filipenko, J. Vinson, R. B. Montgomery, H. Beltran, E. I. Heath, H. I. Scher, P. W. Kantoff, M. E. Taplin, N. Schultz, J. S. deBono, F. Demichelis, P. S. Nelson, M. A. Rubin, A. M. Chinnaiyan, and C. L. Sawyers. "Genomic Correlates of Clinical Outcome in Advanced Prostate Cancer." Proc Natl Acad Sci U S A 116, no. 23 (Jun 4 2019): 11428-36. http://dx.doi.org/10.1073/pnas.1902651116.

Augello, M. A., D. Liu, L. D. Deonarine, B. D. Robinson, D. Huang, S. Stelloo, M. Blattner, A. S. Doane, E. W. P. Wong, Y. Chen, M. A. Rubin, H. Beltran, O. Elemento, A. M. Bergman, W. Zwart, A. Sboner, N. Dephoure, and C. E. Barbieri. "Chd1 Loss Alters Ar Binding at Lineage-Specific Enhancers and Modulates Distinct Transcriptional Programs to Drive Prostate Tumorigenesis." Cancer Cell 35, no. 4 (Apr 15 2019): 603-17 e8. http://dx.doi.org/10.1016/j.ccell.2019.03.001.

Beltran, H., C. Oromendia, D. C. Danila, B. Montgomery, C. Hoimes, R. Z. Szmulewitz, U. Vaishampayan, A. J. Armstrong, M. Stein, J. Pinski, J. M. Mosquera, V. Sailer, R. Bareja, A. Romanel, N. Gumpeni, A. Sboner, E. Dardenne, L. Puca, D. Prandi, M. A. Rubin, H. I. Scher, D. S. Rickman, F. Demichelis, D. M. Nanus, K. V. Ballman, and S. T. Tagawa. "A Phase Ii Trial of the Aurora Kinase a Inhibitor Alisertib for Patients with Castration-Resistant and Neuroendocrine Prostate Cancer: Efficacy and Biomarkers." Clin Cancer Res 25, no. 1 (Jan 1 2019): 43-51. http://dx.doi.org/10.1158/1078-0432.CCR-18-1912.

Shen, M. M. and M. A. Rubin. "Prostate Cancer Research at the Crossroads." Cold Spring Harb Perspect Med 9, no. 7 (Jul 1 2019). http://dx.doi.org/10.1101/cshperspect.a036277.

Rubin, M. A. and F. Demichelis. "The Genomics of Prostate Cancer: A Historic Perspective." Cold Spring Harb Perspect Med 9, no. 3 (Mar 1 2019). http://dx.doi.org/10.1101/cshperspect.a034942.

DBMR Research Groups

Forty-two research groups from the departments of the Inselspital and other clinics were affiliated with the DBMR by the end of 2019. Below is a list of the groups. A few selected groups are featured on the following pages.

Anaesthesiology: Prof. Dr. Frank Stüber, PD Dr. Martin Luginbühl, and PD Dr. Andreas Vogt

Angiology: Prof. Dr. Iris Baumgartner

Audiology: Prof. Dr. Marco Caversaccio, Prof. Dr. Martin Kompis

Cardiology: Prof. Dr. Stephan Windecker, Prof. Dr. Christian Seiler, PD Dr. Stefan Stortecky, Prof. Dr. Thomas Suter, Prof. Dr. Hildegard Tanner, and PD Dr. Emrush Rexhaj

Cardiovascular Surgery: Prof. Dr. Thierry Carrel, Prof. Dr. Alex Kadner, Prof. Dr. Dominik Obrist, PD Dr. Sarah Longnus, PD Dr. Florian Schönhoff, PD Dr. Thomas Wyss, and Dorothée Keller

Clinical Radiopharmacy: Prof. Dr. Axel Rominger

Cranio-Maxillofacial Surgery: Prof. Dr. Tateyuki Iizuka, Dr. Matthias Mottini, and Dr. Benoît Schaller

Dermatology: Prof. Dr. Luca Borradori, Prof. Dr. Robert Hunger, Prof. Dr. Eliane J. Müller, Prof. Dr. Christoph Schlapbach, Prof. Dr. Dagmar Simon, and Prof. Dr. Nikhil Yawalkar

Endocrinology / Diabetology (Adults): Prof. Dr. Christoph Stettler, Prof. Dr. Markus Laimer, Prof. Dr. Lia Bally, Prof. Dr. Zeno Stanga, Dr. Roman Trepp, Prof. Dr. Regula Everts Brekenfeld, PD Dr. Michel Hochuli, and PD Dr. Maria Luisa Balmer

Endocrinology / Diabetology / Metabolism (Pediatrics): Prof. Dr. Christa F. Flück, PD Dr. Jean-Marc Nuoffer, and PD Dr. Amit V. Pandey

Endocrinology of the Breast: Prof. Dr. Petra Stute

Endometriosis and Gynaecological Oncology: Prof. Dr. Michel D. Müller, Dr. Thomas Andrieu

Endometrium & Ovary: Prof. Dr. Michael von Wolff

Experimental Haemostasis: PD Dr. Verena Schröder

Experimental Radiology: Prof. Dr. Johannes Heverhagen, Prof. Dr. Hendrik von Tengg-Kobligk

Gastroenterology / Mucosal Immunology: Prof. Dr. Andrew Macpherson, Prof. Dr. Stephanie Ganal-Vonarburg, and Dr. Mercedes Gomez de Agüero

Hand Surgery: Prof. Dr. Esther Vögelin

Hematology (Adults): Prof. Dr. Anne Angelillo-Scherrer, Prof. Dr. Gabriela Baerlocher, PD Dr. Elisabeth Oppliger Leibundgut, PD Dr. Nicolas Bonadies, Prof. Dr. Johanna Kremer Hovinga, and Prof. Dr. Ramanjaneyulu Allam

Hematology Oncology (Pediatrics): Prof. Dr. Jochen Rössler

Hepatology: Prof. Dr. Jean-François Dufour, Prof. Dr. Annalisa Berzigotti, Prof. Dr. Andrea De Gottardi, Prof. Dr. Nasser Semmo, and Dr. Guido Stirnimann

Human Genetics: PD Dr. André Schaller

Intensive Care Medicine: Prof. Dr. Stephan Jakob, Prof. Dr. Joerg C. Schefold, PD Dr. Carmen A. Pfortmüller, Prof. Yok-Ai Que, PD Dr. Matthias Hänggi, PD Dr. David Berger, and Marie-Madlen Jeitziner

Magnetic Resonance Spectroscopy and Methodology, AMSM: Prof. Dr. Roland Kreis, Prof. Dr. Peter Vermathen

Nephrology and Hypertension: Prof. Dr. Bruno Vogt, PD Dr. Geneviève Escher, Prof. Dr. Daniel Fuster, Dr. Michael Grössl, Dr. Matthias Hediger, Prof. Dr. Uyen Huynh-Do , Prof. Dr. Markus Mohaupt, PD Dr. Daniel Sidler, and Prof. Dr. Dominik Uehlinger

Neurology: Prof. Dr. Claudio Bassetti, Prof. Dr. Andrew Chan, Prof. Dr. Antoine Adamantidis, Prof. Dr. Urs Fischer, Prof. Dr. Arnold Marcel, Prof. Dr. Selma Aybek, Prof. Dr. Klemens Gutbrod, Prof. Dr. Simon Jung, Prof. Dr. Paul Krack, Prof. Dr. René Müri, Prof. Dr. Smita Saxena, Prof. Dr. Kaspar Schindler, and Prof. Dr. Werner Z'Graggen

Neurosurgery: Prof. Dr. Hans-Rudolf Widmer, PD Dr. Serge Marbacher

Oncology / Haematology (Adults): Prof. Dr. Thomas Pabst, PD Dr. Katja Seipel, PD Dr. Urban Novak, PD Dr. Julian Schardt, and Dr. Simon Häfliger

Ophthalmology: Prof. Dr. Sebastian Wolf, Prof. Dr. Martin Zinkernagel, Prof. Dr. Volker Enzmann, and Prof. Dr. Pascal Escher

Orthopedics: Prof. Dr. Klaus-Arno Siebenrock, Prof. Dr. Marius Keel, Prof. Dr. Ernst B. Hunziker, and Prof. Dr. Benjamin Gantenbein

Osteoporosis: Prof. Dr. Kurt Lippuner

Pediatric Surgery: Prof. Dr. Steffen Berger, PD Dr. Elizaveta Fasler-Kan

Plastic Surgery: Prof. Dr. Mihai Constantinescu

Prenatal Medicine: Prof. Dr. Daniel Surbek, PD Dr. Andreina Schoeberlein, PD Dr. Marc Baumann, and PD Dr. Martin Müller

Pulmonary Medicine (Adults): Prof. Dr. Thomas Geiser, PD Dr. Manuela Funke-Chambour, PD Dr. Amiq Gazdhar, and PD Dr. Fabian Blank

Pulmonary Medicine (Pediatrics): Prof. Dr. Thomas Geiser, Prof. Dr. Philipp Latzin, and Dr. Loretta Müller-Urech

Radiation Oncology: Prof. Dr. Daniel Aebersold, Prof. Dr. Yitzhak Zimmer, and Dr. Michaela Medova

Rheumatology: Prof. Dr. Peter M. Villiger, Prof. Dr. Martin Bachmann, Dr. Alexander Eggel, PD Dr. Frauke Förger, Dr. Stefan Kuchen, Prof. Dr. Burkhard Möller, Prof. Dr. Michael Seitz, Prof. Dr. Beat Trueb, PD Dr. Monique Vogel, and Dr. Daniel Yerly

RNA & Cancer (NCCR RNA & Disease): Prof. Dr. Rory Johnson

Thoracic Surgery: Prof. Dr. Ralph A. Schmid, Dr. Sean R.R. Hall, Dr. Thomas M. Marti, and PD Dr. Ren-Wang Peng

Tumor-Immunology: Prof. Dr. Adrian Ochsenbein, PD Dr. Carsten Riether

Urology: Prof. Dr. George Thalmann, PD Dr. Marianna Kruithof-de Julio, Prof. Dr. Katia Monastyrskaya, Prof. Dr. Fiona C. Burkhard, and PD Dr. Roland Seiler-Blarer

Visceral and Transplantation Surgery: Prof. Dr. Daniel Candinas, Prof. Dr. Deborah Keogh-Stroka, PD Dr. Vanessa Banz Wüthrich, Prof. Dr. Guido Beldi, and PD Dr. Lukas Brügger

Endocrinology / Diabetology / Metabolism (Pediatrics)

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MD (1992) at the University of Bern. Residency & Fellowships in Stans (1993), Lucerne (1994), Bern (1995–2000). FMH (1998); Deputy consultant (1999–2000), Bern. Postdoctoral Fellow (2001–2004) at the University of California, San Francisco (US). Venia Docendi (2006); Assistant Professor (2004–2010), Associate Professor (2010–2016) and since 2017, Professor of Pediatric Endocrinology and Diabetology at the University of Bern and Chief of the Division of Pediatric Endocrinology, Diabetology, and Metabolism in the Department of Pediatrics at the University Children's Hospital Inselspital Bern.

Research Highlights of 2019 / Outlook on 2020

Flück: Ongoing studies are on the topic of basic and translational research of disorders of human steroid biosynthesis and sex development (DSD). We studied the pathology of rare human genetic variants in *SRD5A2* and *CYP19A1* using cell models and steroid profiling. In the topic of DSD, we continued working on the hypothesis that such disorders may have an oligogenic mode of inheritance and were able to confirm that for individuals with variants in *MAMLD1*. Further studies with the same hypothesis are ongoing for genetic variations in *NR5A1* and a broader, unexplained phenotype in an extensive international collaboration with the I-DSD consortium. In addition, we started an innovative long-term project looking at the possible role of microRNAs for human adrenal cortex zonation and development, as well as for specific steroid hormone biosynthesis. We were granted associated membership to the NCCR RNA & Disease. A collaboration with Prof. Mihaela Zavolan, University of Basel, ha started.

Nuoffer: Clinical metabolism and orphan diseases. Mitochondrial diseases are continuously being discovered, and secondary dysfunctions play a role in almost every medical field. In our studies, we showed that using selective galactose culture conditions reveals distinct metabolic signatures in pyruvate dehydrogenase and complex I deficient cells. In collaboration with Prof. Peter Vermathen, we developed an in-cell NMR system, allowing the simultaneous online monitoring of bioenergetic and metabolomic variables. Further studies are ongoing to characterize the impact of bioenergetic dysfunction on the metabolome or vice versa. Other collaborative studies described novel molecular pathogenic mechanisms such as MRPS14 mutations that impair mitochondrial ribosomes during translation elongation or mitochondrial mRNA recruitment rather than in assembly.

Pandey: Human growth and development. Human growth hormone (GH) has a vital role in the physiology and metabolism, and its defects cause isolated GH deficiency (IGHD). We characterized GH variants in patients using a series of modern analytical tools, including Next-Generation-Sequencing, computational modeling, receptor-ligand interactions using surface plasmon resonance (SPR), and growth hormone bioactivation assays. We showed that both intronic, as well as exonic variations of the human GH gene, might cause IGHD. In 2020, we will continue to develop methods for the characterization and treatment of IGHD and study of GH production and secretion in humans.

Pandey: Molecular and computational biology of endocrine disorders. We use protein biochemistry to study variations in steroid metabolizing enzymes. In 2019, we focused on aromatase, an enzyme responsible for the production of estrogens. Using data from Next-Generation-Sequencing and population genetics, in collaboration with Val'd Hebron Hospital in Barcelona, Spain, we showed that mutations in P450 reductase protein could cause an aromatase deficiency in children, as well as maternal virilization during pregnancy. We explored an essential question about the role of multiple gene variants in humans. With the University of Torino, Italy, we showed that common polymorphisms in aromatase and P450 reductase genes could produce a different effect if present in the same individual.

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PD Dr. Amit V. Pandey, Group Leader
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Dr. Matthias Gautschi, Attending Physician, and Associated Clinical Researcher
Dr. Stefanie Graf, Attending Physician, and Associated Clinical Researcher
Dr. Marco Janner, Attending physician, and Associated Clinical Researcher
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Dr. Grit Sommer Senior, Research Fellow
Dr. Andrea Felser, Research Assistant
Sandra Kurth, Research Assistant
Patricia Rodriguez Castano, Research Assistant
Alexandra Nuoffer, Study Nurse
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Regula Küffer, Biomedical Analyst
Stefan Studer, Biomedical Analyst
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Selected Publications

Parween, S., M. Fernandez-Cancio, S. Benito-Sanz, N. Camats, M. N. Rojas Velazquez, J. P. Lopez-Siguero, S. S. Udhane, N. Kagawa, C. E. Fluck, L. Audi, and A. V. Pandey. "Molecular Basis of Cyp19a1 Deficiency in a 46,Xx Patient with R550w Mutation in Por: Expanding the Pord Phenotype." J Clin Endocrinol Metab 105, no. 4 (Apr 1 2020). http://dx.doi.org/10.1210/clinem/dgaa076.

Rodriguez Castano, P., S. Parween, and A. V. Pandey. "Bioactivity of Curcumin on the Cytochrome P450 Enzymes of the Steroidogenic Pathway." Int J Mol Sci 20, no. 18 (Sep 17 2019). http://dx.doi.org/10.3390/ijms20184606.

Malikova, J., T. Zingg, R. Fingerhut, S. Sluka, M. Grossl, S. Brixius-Anderko, R. Bernhardt, J. McDougall, A. V. Pandey, and C. E. Fluck. "Hiv Drug Efavirenz Inhibits Cyp21a2 Activity with Possible Clinical Implications." Horm Res Paediatr 91, no. 4 (2019): 262-70. http://dx.doi.org/10.1159/000500522.

Fluck, C. E., L. Audi, M. Fernandez-Cancio, K. S. Sauter, I. Martinez de LaPiscina, L. Castano, I. Esteva, and N. Camats. "Broad Phenotypes of Disorders/Differences of Sex Development in Mamld1 Patients through Oligogenic Disease." Front Genet 10 (2019): 746. http://dx.doi.org/10.3389/fgene.2019.00746.

Hertig, D., A. Felser, G. Diserens, S. Kurth, P. Vermathen, and J. M. Nuoffer. "Selective Galactose Culture Condition Reveals Distinct Metabolic Signatures in Pyruvate Dehydrogenase and Complex I Deficient Human Skin Fibroblasts." Metabolomics 15, no. 3 (Feb 28 2019): 32. http://dx.doi.org/10.1007/s11306-019-1497-2.

Link to the updated list of publications:
Christa E Flück:
https://scholar.google.com/citations?user=QMW4YW0AAAAJ&hl=en
Jean-Marc Nuoffer:
https://scholar.google.com/citations?user=3O7wmKgAAAAJ&hl=en
Amit V Pandey:
https://scholar.google.com/citations?user=dImQtXkAAAAJ&hl=en

Hematology (Adults)
Johanna Kremer Hovinga

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Our research focuses on the Von Willebrand factor (VWF)-cleaving protease, ADAMTS13, and disease states where VWF size regulation is absent. This is most prominent in thrombotic thrombocytopenic purpura (TTP), a rare and life-threatening disease. Two forms of TTP are recognized: hereditary TTP (hTTP) due to autosomal-recessively inherited ADAMTS13 mutations, and immune-mediated TTP (iTTP), where autoantibodies lead to a severe ADAMTS13 deficiency.

Research Highlights of 2019

The highlight of our hTTP research was our first large publication on 123 hTTP cases, enrolled between 2006 and 2017, in the Hereditary TTP Registry (www.ttpregistry.net), an international cohort study with participants from 44 sites in 18 countries worldwide. The systematic collection of clinical data of individual hTTP patients revealed substantial comorbidities, the most notable being a high prevalence of premature arterial thromboembolic events, mainly transient ischemic attacks, ischemic strokes and myocardial infarctions. At the relatively young age of ≥40 years, more than 50 % of hTTP patients had already suffered from at least one of these events. This publication and the ongoing project was awarded with the Günter Landbeck Excellence Award 2019. It is also worth to mention that we had an invitation to write a review on hTTP for the New England Journal of Medicine, together with my long-time collaborator, James George, at the University of Oklahoma.

The highlight in the field of acquired TTP was the authorization of Caplacizumab in Switzerland on October 1, 2019. We have been involved for nearly a decade in the development of this drug that effectively prevents platelet clumping on ultra-large Von Willebrand factor molecules and reduces ischemic organ damage and mortality in acute episodes of iTTP.

Outlook on 2020

We will continue our work on the Hereditary TTP Registry cohort, which has now 231 participants (patients and family members) and a prospective follow-up of a median of 5 years in patients. Important aspects to note are the annual TTP event rates under or without regular prophylactic plasma infusions, the identification of situations of increased risk of events to optimize therapy, and long-term outcomes in affected patients and their first-degree family members.

Although Caplacizumab will change iTTP treatment, it leaves the autoimmune response to ADAMTS13 unaddressed. During the past years, we have characterized this response of eight iTTP patients and generated small molecules (DARPins) that are able to bind and neutralize ADAMTS13 autoantibodies in plasma. These DARPins will be used to detect ADAMTS13 specific-memory B-cells in the circulation of iTTP patients by flow cytometry and ELISPOT, and in tissue sections. The promising candidates will be coupled to toxic substances to test their ability to destroy different EBV-immortalized ADAMTS13 specific-memory B-cell lines in culture. The ultimate goal over the next few years is to develop a treatment strategy to specifically target the ADAMTS13 autoimmune response in iTTP .

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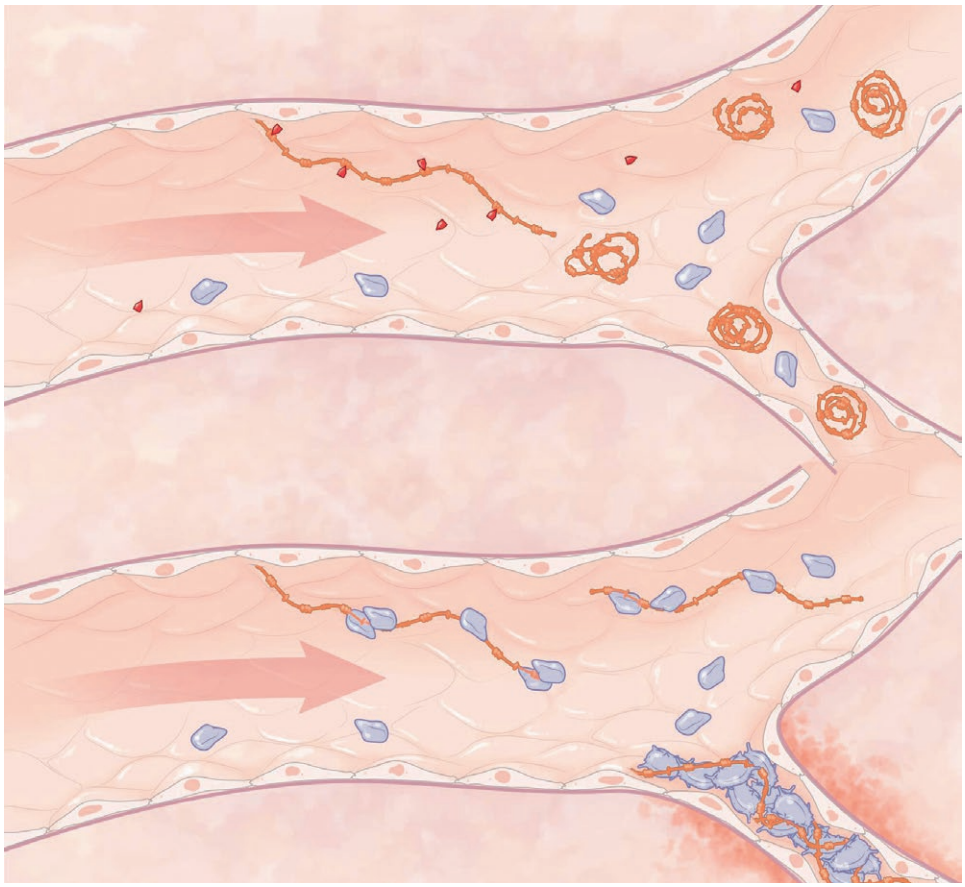

JA Kremer Hovinga, JN George. N Engl J Med 2019; 381:1653-1662.

Group Members

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PD Dr. phil. nat. Monica Schaller Tschan, Senior Scientist
Dr. phil. nat. Erika Tarasco, Research Associate (since July)
PD Dr. sc nat. H. Anette van Dorland, Research Associate (until May)
Silvan R. Heeb, MSc., PhD Student
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Selected Publications

van Dorland, H. A., M. M. Taleghani, K. Sakai, K. D. Friedman, J. N. George, I. Hrachovinova, P. N. Knobl, A. S. von Krogh, R. Schneppenheim, I. Aebi-Huber, L. Butikofer, C. R. Largiader, Z. Cermakova, K. Kokame, T. Miyata, H. Yagi, D. R. Terrell, S. K. Vesely, M. Matsumoto, B. Lammle, Y. Fujimura, J. A. Kremer Hovinga, and T. T. P. Registry Hereditary. "The International Hereditary Thrombotic Thrombocytopenic Purpura Registry: Key Findings at Enrollment until 2017." Haematologica 104, no. 10 (Oct 2019): 2107-15. http://dx.doi.org/10.3324/haematol.2019.216796.

Kremer Hovinga, J. A. and J. N. George. "Hereditary Thrombotic Thrombocytopenic Purpura." N Engl J Med 381, no. 17 (Oct 24 2019): 1653-62. http://dx.doi.org/10.1056/NEJMra1813013.

Robertz, J., M. Andres, B. Mansouri Taleghani, I. Koneth, I. Binet, and J. A. Kremer Hovinga. "Obinutuzumab in Two Patients Suffering from Immune-Mediated Thrombotic Thrombocytopenic Purpura Intolerant to Rituximab." Am J Hematol 94, no. 10 (Oct 2019): E259-E61. http://dx.doi.org/10.1002/ajh.25583.

Scully, M., S. R. Cataland, F. Peyvandi, P. Coppo, P. Knobl, J. A. Kremer Hovinga, A. Metjian, J. de la Rubia, K. Pavenski, F. Callewaert, D. Biswas, H. De Winter, R. K. Zeldin, and Hercules Investigators. "Caplacizumab Treatment for Acquired Thrombotic Thrombocytopenic Purpura." N Engl J Med 380, no. 4 (Jan 24 2019): 335-46. http://dx.doi.org/10.1056/NEJMoa1806311.

Link to the updated list of publications:
PubMed: https://www.ncbi.nlm.nih.gov/sites/myncbi/1HQIabMVC5Tkn/bibliography/46628237/public/?sort=-date&direction=descending

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https://ttpregistry.net/ttp-research-in-bern/about-us/

Cardiovascular Surgery
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Obtained a PhD with European Doctorate Mention in 2010 at the University of Salamanca (ES). Postdoctoral fellowships completed at Institute Cochin (2011-2013) and the University of Paris-Saclay (2013-2015) in Paris (FR). Since 2015, she has been a postdoctoral fellow at the Department of Cardiovascular Surgery, where she received research grants from the European Society of Cardiology and the International Society for Heart and Lung Transplantation and the Johanna Dürmüller-Bol DBMR Research Award.

Research Highlights of 2019

Heart failure is one of the leading causes of morbidity and mortality worldwide. In severe cases, heart transplantation is the sole option for improving the quality of life and survival of the patient. However, the number of patients requiring heart transplantation has consistently increased over the last 20 years, while the number of transplantations remains stable, limited by graft availability. Donation after circulatory death (DCD) has been revived as a solution for improving donor organ availability, providing an increase of up to 33% in heart transplant activity. More than 100 DCD heart transplantations have been reported worldwide in the last 5 years, and outcomes to date are comparable to those obtained with contemporary conventional donors.

Although its feasibility has been demonstrated, DCD heart transplantation raises concerns as it is accompanied by a potentially damaging period of warm ischemia prior to organ procurement. Ischemia and reperfusion are particularly detrimental to the heart, with mitochondria being among the most sensitive cellular organelles. Damage by warm ischemia and reperfusion results in several mitochondrial alterations: the inability to produce sufficient energy to maintain heart contraction and ion homeostasis, the production of damaging free radicals, and the release of mitochondrial components, called mitochondrial damage-associated molecular patterns (mtDAMPs). Recognized mtDAMPs include mitochondrial DNA (mtDNA), cytochrome c (cyt c), ATP, mitochondrial transcription factor A (Tfam), N-formyl peptides, succinate, and cardiolipin. mtDAMPs are known to activate the innate immune response, which in the case of graft transplantation, may ultimately contribute to the development of graft rejection.

We have previously demonstrated that mtDAMPs are released during the early reperfusion following warm, global ischemia in a rat model of DCD. Furthermore, mtDAMP release is inversely correlated with subsequent contractile recovery. Based on these results, Dr. Sanz hypothesized that minimizing mitochondrial damage in DCD hearts may prevent or reduce the release of mtDAMPs, which could limit sterile inflammation and promote recovery of the graft. In her future research, Dr Sanz will characterize the pattern of release of mtDAMPs and investigate their role in inflammatory responses and the recovery of contractile function in cardiac grafts from pre-clinical models of DCD. In these studies, Dr Sanz will focus on mitochondrial DNA, the most pro-inflammatory mtDAMP, which has been detected in the circulation of human DCD donors.

Support for this work has been awarded to Dr Sanz by the International Society of Heart and Lung Transplantation and the Johanna Dürmüller-Bol Foundation. A better understanding of the role of mtDAMPs in cardiac ischemia and reperfusion should aid in the optimization of clinical protocols for DCD heart transplantation, ultimately improving the outcome for patients with severe heart failure.

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Selected Publications

Sanz, M. N., E. Farine, P. Niederberger, N. Mendez-Carmona, R. K. Wyss, M. Arnold, P. Gulac, G. M. Fiedler, M. Gressette, A. Garnier, T. P. Carrel, H. T. Tevaearai Stahel, and S. L. Longnus. "Cardioprotective Reperfusion Strategies Differentially Affect Mitochondria: Studies in an Isolated Rat Heart Model of Donation after Circulatory Death (Dcd)." Am J Transplant 19, no. 2 (Feb 2019): 331-44. http://dx.doi.org/10.1111/ajt.15024.

Wyss, R. K., N. Mendez-Carmona, M. N. Sanz, M. Arnold, A. Segiser, G. M. Fiedler, T. P. Carrel, S. Djafarzadeh, H. T. Tevaearai Stahel, and S. L. Longnus. "Mitochondrial Integrity During Early Reperfusion in an Isolated Rat Heart Model of Donation after Circulatory Death-Consequences of Ischemic Duration." J Heart Lung Transplant 38, no. 6 (Jun 2019): 647-57. http://dx.doi.org/10.1016/j.healun.2018.12.013.

Sanz, M. N., L. Grimbert, M. Moulin, M. Gressette, C. Rucker-Martin, C. Lemaire, M. Mericskay, V. Veksler, R. Ventura-Clapier, A. Garnier, and J. Piquereau. "Inducible Cardiac-Specific Deletion of Sirt1 in Male Mice Reveals Progressive Cardiac Dysfunction and Sensitization of the Heart to Pressure Overload." Int J Mol Sci 20, no. 20 (Oct 10 2019). http://dx.doi.org/10.3390/ijms20205005.

Kjobsted, R., J. R. Hingst, J. Fentz, M. Foretz, M. N. Sanz, C. Pehmoller, M. Shum, A. Marette, R. Mounier, J. T. Treebak, J. F. P. Wojtaszewski, B. Viollet, and L. Lantier. "Ampk in Skeletal Muscle Function and Metabolism." FASEB J 32, no. 4 (Apr 2018): 1741-77. http://dx.doi.org/10.1096/fj.201700442R.

Niederberger, P., E. Farine, M. Arnold, R. K. Wyss, M. N. Sanz, N. Mendez-Carmona, B. Gahl, G. M. Fiedler, T. P. Carrel, H. T. Tevaearai Stahel, and S. L. Longnus. "High Pre-Ischemic Fatty Acid Levels Decrease Cardiac Recovery in an Isolated Rat Heart Model of Donation after Circulatory Death." Metabolism 71 (Jun 2017): 107-17. http://dx.doi.org/10.1016/j.metabol.2017.03.007.

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Research Highlights of 2019

Prelicinial Models for the Translational Study of Urological Cancers: We have generated patient derived organoids (PDOs) and patient derived xenografts (PDXs) of primary and metastatic PCa and other malignancies or tumor types. We have also developed and implemented a clinically relevant culture system for studying tumor tissue *ex vivo*. This technique allows the cultivation of tumor slices and needle biopsies in a tissue culture setting without the loss of the 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*). 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 provided us novel tools that overcome some of the limitations of traditional 2D and 3D *in vitro* models. It reduces the phylogenetic problem due to differences between human and animals and, if considered as a pre-screening tool, it significantly reduces the number of animals necessary for further *in vivo* validation. The 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 the generation and analysis of big gene expression data to reveal the triggers of LUTD. To achieve our goal of an unbiased classification of LUTD and the identification of molecular drivers of pathologic bladder remodeling, we apply machine learning algorithms to the transcriptome data. 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 LUTDs on bladder remodeling and functionally validate the findings in human patients. Our previous studies in bladder outlet obstruction have detected signs of macrophage infiltration by analyzing 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.

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Group Members

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PD Dr. Marianna Kruithof-de Julio, Group Leader
PD Dr. med. Roland Seiler-Blarer, Group Leader
Prof. Dr. Katia Monastyrskaya, Group Leader
Prof. Dr. Fiona Burkhard, Group Leader
Dr. Maria de Filippo, Postdoc
Dr. Marta de Menna, Postdoc
Dr. Sofia Karkampouna, Postdoc
Dr. Eugenio Zoni, Postdoc
Mirjam Kiener, PhD Student
Michelle Küffer, PhD Student
Federico La Manna, PhD Student
Martina Minoli, PhD Student
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Irena Klima, Lab Manager
Mustafa Besic, Lab Technician

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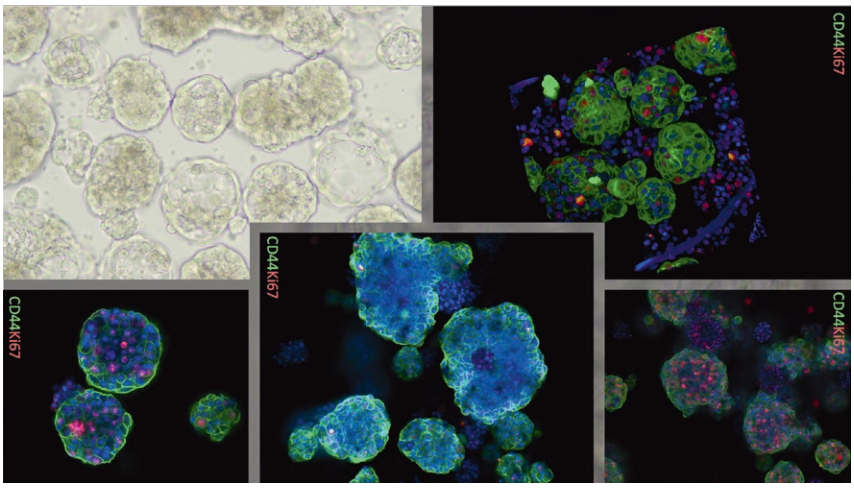
Selected Publications

Zoni, E., L. Astrologo, C. K. Y. Ng, S. Piscuoglio, J. Melsen, J. Grosjean, I. Klima, L. Chen, E. B. Snaar-Jagalska, K. Flanagan, G. van der Pluijm, P. Kloen, M. G. Cecchini, M. Kruithof-de Julio, and G. N. Thalmann. "Therapeutic Targeting of Cd146/Mcam Reduces Bone Metastasis in Prostate Cancer." Mol Cancer Res 17, no. 5 (May 2019): 1049-62. http://dx.doi.org/10.1158/1541-7786.MCR-18-1220.

Zoni, E., L. Chen, S. Karkampouna, Z. Granchi, E. I. Verhoef, F. La Manna, J. Kelber, R. C. M. Pelger, M. D. Henry, E. Snaar-Jagalska, Gjlh van Leenders, L. Beimers, P. Kloen, P. C. Gray, G. van der Pluijm, and M. Kruithof-de Julio. "Cripto and Its Signaling Partner Grp78 Drive the Metastatic Phenotype in Human Osteotropic Prostate Cancer." Oncogene 36, no. 33 (Aug 17 2017): 4739-49. http://dx.doi.org/10.1038/onc.2017.87.

Gheinani, A. H., M. Vogeli, U. Baumgartner, E. Vassella, A. Draeger, F. C. Burkhard, and K. Monastyrskaya. "Improved Isolation Strategies to Increase the Yield and Purity of Human Urinary Exosomes for Biomarker Discovery." Sci Rep 8, no. 1 (Mar 2 2018): 3945. http://dx.doi.org/10.1038/s41598-018-22142-x.

Gheinani, A. H., I. Kock, E. Vasquez, U. Baumgartner, A. Bigger-Allen, B. S. Sack, F. C. Burkhard, R. M. Adam, and K. Monastyrskaya. "Concordant Mirna and Mrna Expression Profiles in Humans and Mice with Bladder Outlet Obstruction." Am J Clin Exp Urol 6, no. 6 (2018): 219-33. https://www.ncbi.nlm.nih.gov/pubmed/30697578.



Nephrology
Membrane Transport
Discovery Lab

Dr. Matthias A. Hediger
matthias.hediger@ibmm.unibe.ch

Dr. sc. nat. (Biochemistry), ETH Zurich (1982). Postdoc at the University of Connecticut, CT, USA. (1982–1984). Postdoc at UCLA School of Medicine, Los Angeles, CA, USA (1984–1989). Assistant Professor, Harvard Medical School, Boston, MA, USA (1989–1995). Associate Professor, Harvard Medical School, Boston, MA, USA (1995–2005). Professor Ordinarius, Institute of Biochemistry and Molecular Medicine, University of Bern (2005–2019). Director of the Institute of Biochemistry and Molecular Medicine, University of Bern (2005–2017). Director of the NCCR TransCure, University of Bern (2010–2014). Since 2019, Group Leader and Head of the Membrane Transport Discovery Lab, Department of Nephrology and Hypertension, Inselspital Bern & Department for BioMedical Research, University of Bern.

Research Highlights of 2019

Research arising from the Hediger group has focused on the biology of medically important SLC solute carriers and calcium channels. Up to 10 % of the human genome is devoted to membrane transport processes and SLCs make up the largest class of transport proteins. SLCs play central roles as gatekeepers, controlling transport of nutrients, trace minerals, metabolites and drugs into and out of cells and cellular organelles. Originally, there were around 400 SLCs grouped into 52 SLC families. While specific SLCs serve as important drug targets such as the Na^+/glucose transporter SLC5A2/SGLT2 for glucose lowering drugs in diabetes, many SLCs are insufficiently characterized and around 30 % are orphan transporters, meaning that substrates and physiological roles are unknown. Recently, the Hediger group looked into potentially missing SLCs in different proteomes and identified 47 new putative human SLC families containing ~150 SLCs, of which 25 have known transport function. This gives rise to 99 human SLC families with ~ 556 SLCs (see circular dendrogram on the next page).

To accelerate scientific progress in the transporter field, Matthias Hediger initiated in year 2010 the NCCR TransCure network at the University of Bern. As part of these efforts, new inhibitors were developed for therapeutically important targets, including the divalent metal ion transporter SLC11A2/DMT1 and the epithelial calcium channel TRPV6.

SLC39A8/ZIP8 is another important metal ion transporter that is being studied. It has a unique SNP, rs13107325 (A393T), linked to different phenotypic traits such as obesity, reduced blood pressure and Crohn's disease. In collaboration with Bruno Vogt, Head of the Department of Nephrology and Hypertension, Inselspital Bern, and his research team, transgenic mice bearing this SNP are currently being characterized.

The lysosomal orphan transporter SLC15A4 is being studied in the context of autoimmune diseases, as it was reported to sustain the TLR signaling pathway. To generate SLC15A4 inhibitors, the Hediger group employs microscale thermophoresis to screen small-molecule compound libraries.

Another current project addresses the role of amino acids in colorectal cancer progression, since amino acid transporters play vital roles in mTOR activation and energy metabolism.

The recently completed SNSF Sinergia project on Orai store-operated calcium channels has generated new insight into STIM and Orai Proteins in calcium signalling in health and disease (see Figure Orai/STIM).

In collaboration with NCCR TransCure, Matthias Hediger organized the 11th international conference, entitled "Membrane transporters and channels: From basic research to drug development and clinical application" at the Swiss Museum of Transport, Lucerne, Switzerland from August 4 to 8, 2019, with over 200 participants (see https://www.bioparadigms.org).

www.bioparadigms.org

Outlook on 2020 – Membrane Transport Discovery Lab

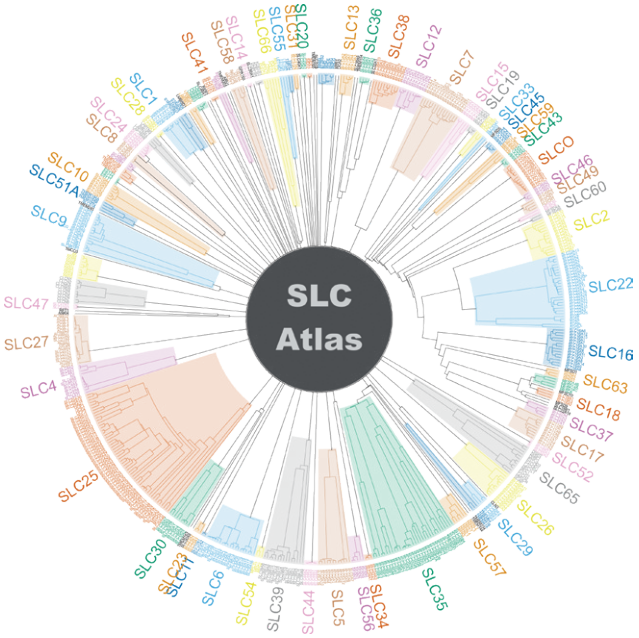
The SLC superfamily continues to harbor a wealth of unexplored therapeutic opportunities and extensive work is needed to leverage this potential.

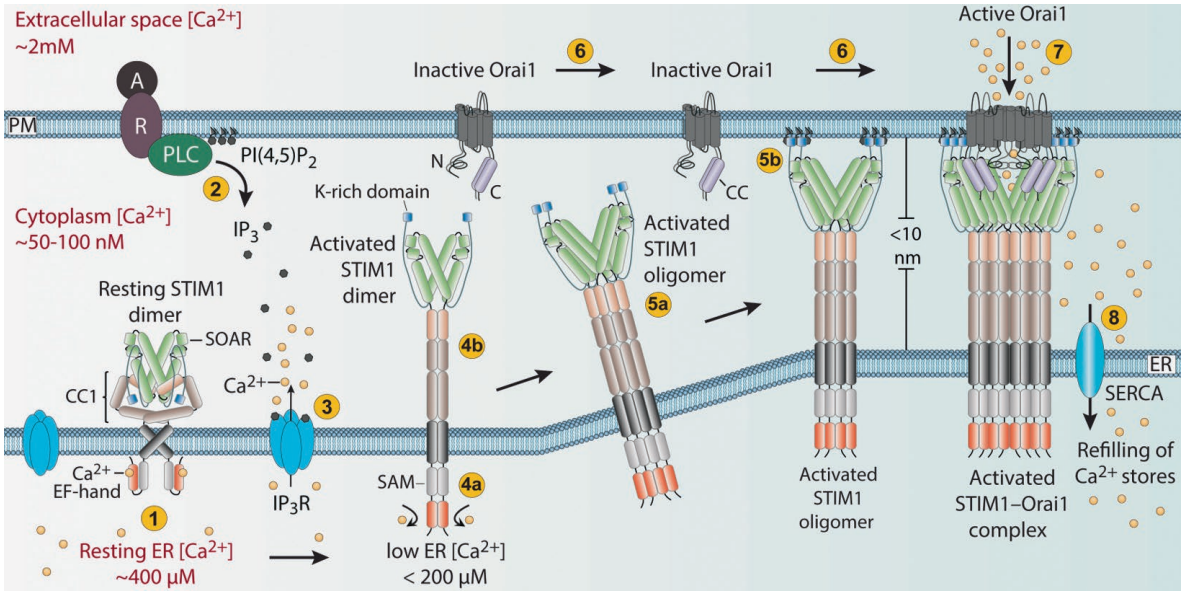
Group Members

Dr. Matthias A. Hediger, Group Leader
Dr. Rajesh Bhardwaj, Research Associate
Dr. Benjamin Clémençon, Research Associate
Dr. Bartłomiej Augustynek, Postdoc
Dr. Gergely Gyimesi, Postdoc
Dr. Palanivel Kandasamy, Postdoc
Dr. Jonai Pujol Giménez, Postdoc
Damian Nydegger, PhD Student
Verena Frazao, Secretary

Seleced Collaborators

Escher G, University of Bern, Bern (CH)
Demaurex N, University of Geneva, Geneva (CH)
Dutzler R, University of Zurich, Zurich (CH)
Lochner M, University of Bern, Bern (CH)
Peinelt C, University of Bern, Bern (CH)
Reymond J-L, University of Bern, Bern (CH)
Romanin C, Johannes Kepler University Linz, Linz (AT)
Vogt B, University of Bern, Bern (CH)





Rheumatology

Prof. Dr. Martin F. Bachmann
martin.bachmann@dbmr.unibe.ch

PhD at the Institute for Experimental Immunology at ETH in Zürich (1995). Postdoc at the Department of Immunology, Toronto, Canada (1995–1997). Member at the Basel Institute for Immunology, Basel (1997–2000). Chief Scientific Officer at Cytos Biotechnology AG, Schlieren-Zürich (2000–2012). Visiting Professor Immunology at the University of Zürich (2012–present). Associate Professor of Immunology at the University of Oxford (2013–present). Since 2015, he is the Head of Immunology at the Clinic of Rheumatology, Immunology, and Allergology and Professor of Immunology at the University of Bern. Visiting Professor at Anhui Agricultural University, Hefei, China.

PD Dr. Monique Vogel
monique.vogel@dbmr.unibe.ch

PhD at the Institute of General Microbiology, University of Bern (1989). Research Assistant and Senior scientist at the Institute of Immunology, University of Bern (1989–2015). Consulting Immunologist for the transplantation Diagnostic Laboratory at the Institute of Immunology (2004–2015). Head of Allergy Laboratory, INO, Inselspital, Bern (2011–2015). Since 2015, Deputy Head of Immunology at the Clinic of Rheumatology, Immunology, and Allergology.

Research Highlights of 2019

The University Clinic of Rheumatology, Immunology, and Allergology consists of two independent basic research groups and one clinically oriented research group that investigates immunological mechanisms with the aim of furthering our understanding of immune regulation and the development of potential new therapies in a single health framework. The highlights of the three research groups are as follows:

1) Development of vaccines using virus-like-particles and IgE regulation

Prof. Dr. Bachman and Dr. Vogel group focus on the development of therapeutic vaccines in the form of virus-like particles (VLPs)1,2 and on the mechanisms controlling IgE-mediated allergy class 3.

– *A vaccine against melanoma:* Melanoma is the most aggressive type of skin cancer, mostly due to its high metastatic potential. Active vaccination of cancer aims to treat the disease by inducing an effective cellular response. VLPs displaying melanoma-specific antigens are capable of eliciting efficient cytotoxic T (CTL) cell responses. Thus, the group utilized VLPs to build a novel platform for generating a personalized multi-target vaccine by combining both immunopeptidomics and whole exome sequencing techniques. The generated vaccine induced effective cytotoxic T-cell responses and conferred protection against tumor growth 1.
– *A vaccine against peanut allergy:* Peanut allergy is a severe and increasingly frequent disease. A causal, safe, and effective therapy is not yet available. Thus, the group generated vaccine candidates against peanut allergy based on a plant-virus-derived VLP coupled to the whole extract of roasted peanut or to the single major allergens Ara h 1 and Ara h 2 and tested them in a mouse model of peanut allergy. The vaccines demonstrated a strong immunogenicity and were able to strongly reduce systemic and local allergic reactions upon challenge with the whole allergen extract 2. This work suggests that vaccination using single peanut allergens displayed on VLP may represent a novel therapy against peanut allergy.
– *A non-inflammatory pathway for IgE–allergen complexes:* One key player of allergic reactions is Immunoglobulin E (IgE), which sensitizes the high affinity receptor for IgE, FcεRI on mast cells and basophils and drives an allergic inflammation upon a second contact with the allergen. CD23, the low affinity receptor, is known to play an important role in the regulation of IgE synthesis. The group found that in an complex with allergen, IgE loses its ability to sensitize FcεRI on effector cells while simultaneously increasing CD23 binding, resulting in IgE clearance and resistance to anaphylaxis.

PD Dr. Alexander Eggel
alexander.eggel@dbmr.unibe.ch

PhD at the Institute of Immunology, University of Bern; Postdoc at the Department of Neurology, Stanford University, Stanford, USA. Visiting Junior Specialist Microbiology and Immunology, Department of Microbiology and Immunology, University of San Francisco. Since 2013, Research Group Leader at the Clinic of Rheumatology, Immunology, and Allergology, at the University Hospital Bern.

Prof. Dr. Peter Villiger
peter.villiger@insel.ch

MD at the Department of RIA, University of Bern. Postdoc at Scripps and UCSD, California. Clinical positions at the University Hospital of Zürich, Kantonsspital St. Gallen. Sabatical at the Hopital Cochin in Paris (2009) and at the Ospedale Pini, in Milan (2017). Since 1999, Chairman and Head of the Clinic of Rheumatology, Immunology, and Allergology, University Hospital, Bern and Professor of Rheumatology and Clinical Immunology at the Faculty of Medicine, University of Bern.

2) Characterization of beneficial and detrimental type-2 immune responses

The group of PD Dr. Eggel aims to develop translational intervention strategies for the treatment of allergies and age-related disorders by modulating type-2 immune responses at the molecular, cellular, and systemic levels.

– *Disruptive IgE inhibitors – a novel class of anti-IgE molecules:*
About 20 years after the identification of immunoglobulin E (IgE) and its key role in allergic hypersensitivity reactions, scientists have started to generate monoclonal anti-IgE antibodies with the primary goal of neutralizing its pathogenicity. Subsequent humanization of these antibodies has paved the way for the development of therapeutic anti-IgE biologicals, as we know them today. Our research focuses on the development of alternative binding molecules (e.g., designed ankyrin repeat proteins) for the inhibition of IgE-mediated disorders. Recently, we have described a novel class of anti-IgE binders that not only neutralizes free IgE, but also actively removes IgE from its primary receptor on allergic effector cells. We expect that such novel modes-of-action will translate into an increased treatment efficacy.
– *Development of immune intervention strategies to promote healthy aging:*
Aging is a multifactorial process leading to the progressive loss of physiological integrity that affects almost every living organism. This unidirectional process is considered a time-dependent one-way road starting at birth and ending with death. However, recent studies have provided compelling evidence that aging is more plastic than previously assumed. We are currently investigating novel immunological concepts to systemically rejuvenate aged organisms. One key aspect of this work is the reversal of age-related systemic low-grade inflammation and the prevention of inflammation.

3) A novel treatment protocol for giant cell arteritis

Large vessel vasculitis, such as giant cell arteritis and Takayasuarteritis, are treated with long-term, high-dose glucocorticoids, leading to a broad range of severe side effects. IL-6 has been shown to play a central role in the pathogenesis of these diseases. Accordingly, inhibition of the IL-6 pathway using a monoclonal antibody against the IL-6R (tocilizumab) was successful in controlling disease remission and sparing steroids. Our current clinical study addresses the question of whether tocilizumab might replace steroids. We just finished recruitment of patients and will report about the 24-week outcome of 18 patients at the European annual meeting. Preliminary data support our hypothesis. As add-on studies, we developed a high-precision ultrasound protocol to monitor vessel wall inflammation of extracranial arteries and followed the disease course quantifying and qualifying T lymphocytes. We plan to submit our data to the annual congress of the American College of Rheumatology (ACR) in November in Washington.

Group Members

Prof. Dr. Martin F. Bachmann, Group Leader
PD Dr. Monique Vogel, Group Leader
Dr. Lisha Zha, Research Associate
Dr. Tasneem Arsiwala, Postdoc
Dr. Gustavo Cabral de Miranda, Postdoc
Dr. Mona Mohsen, Postdoc
Dr. Elisa Rösti, Postdoc
Gilles Augusto, Guest PhD Student
Xinyue Chang, PhD Student
Dr. Paul Engeroff, PhD Student
Zahra Gharailoo, PhD Student
Joana Jorge da Costa, PhD Student
Dr. Caroline Krüger, PhD Student
Xuelan Liu, PhD Student
Kevin Plattner, PhD Student
Salony Roongta, PhD Student
Jan Sobczak, PhD Student
Dr. med. Federico Storni, PhD Student
Varusha Veerapen, PhD Student
Simon Zinkhan, PhD Student
Marianne Zwicker, Lab Technician

PD Dr. Alexander Eggel, Group Leader
Dr. Daniel Brigger, Research Associate
Noemi Zbären, Research Associate
Pascal Gasser, PhD Student
Pascal Guntern, PhD Student

Prof. Dr. Peter Villiger, Group Leader
Prof. Dr. Stephan Reichenbach, Leading Physician
PD Dr. med. Florian Kollert, Leading Physician
Dr. Lisa Christ, Senior Physician
Dr. Godehard Scholz, Assistant Physician
Dr. med. Jennifer Amsler, Assistant Physician

Selected Collaborators

Allergy Therapeutics Ltd., Worthing (UK)
Department of Dermatology, University of Zurich, Zurich (CH)
Latvian Biomedical Research, University of Latvia, Riga (LV)
Jardetzky T, Standford University, Standford (US)
Wyss-Coray T, Standford University, Standford (US)

Selected Publications

Mohsen, M. O., M. D. Heath, G. Cabral-Miranda, C. Lipp, A. Zeltins, M. Sande, J. V. Stein, C. Riether, E. Roesti, L. Zha, P. Engeroff, A. El-Turabi, T. M. Kundig, M. Vogel, M. A. Skinner, D. E. Speiser, A. Knuth, M. F. Kramer, and M. F. Bachmann. "Vaccination with Nanoparticles Combined with Micro-Adjuvants Protects against Cancer." J Immunother Cancer 7, no. 1 (Apr 26 2019): 114. http://dx.doi.org/10.1186/s40425-019-0587-z.

Storni, F., A. Zeltins, I. Balke, M. D. Heath, M. F. Kramer, M. A. Skinner, L. Zha, E. Roesti, P. Engeroff, L. Muri, D. von Werdt, T. Gruber, M. Cragg, M. Mlynarczyk, T. M. Kundig, M. Vogel, and M. F. Bachmann. "Vaccine against Peanut Allergy Based on Engineered Virus-Like Particles Displaying Single Major Peanut Allergens." J Allergy Clin Immunol 145, no. 4 (Apr 2020): 1240-53 e3. http://dx.doi.org/10.1016/j.jaci.2019.12.007.

Engeroff, P., F. Caviezel, D. Mueller, F. Thoms, M. F. Bachmann, and M. Vogel. "Cd23 Provides a Nonin-flammatory Pathway for Ige-Allergen Complexes." J Allergy Clin Immunol 145, no. 1 (Jan 2020): 301-11 e4. http://dx.doi.org/10.1016/j.jaci.2019.07.045.

Delgado, S. J., S. Dehmel, E. Twisterling, J. Wichmann, D. Jonigk, G. Warnecke, P. Braubach, H. G. Fieguth, L. Wilkens, F. Dahlmann, F. J. Kaup, A. Eggel, S. Knauf, K. Sewald, and A. Braun. "Disruptive Anti-Ige Inhibitors Prevent Mast Cell-Dependent Early Airway Response in Viable Atopic Lung Tissue." J Allergy Clin Immunol 145, no. 2 (Feb 2020): 719-22 e1. http://dx.doi.org/10.1016/j.jaci.2019.11.002.

Gasser, P., S. S. Tarchevskaya, P. Guntern, D. Brigger, R. Ruppli, N. Zbaren, S. Kleinboelting, C. Heusser, T. S. Jardetzky, and A. Eggel. "The Mechanistic and Functional Profile of the Therapeutic Anti-Ige Antibody Ligelizumab Differs from Omalizumab." Nat Commun 11, no. 1 (Jan 8 2020): 165. http://dx.doi.org/10.1038/s41467-019-13815-w.

Key Events

Swiss Youth in Science: "Biology and Medicine" Study Week
17–22 March

Info Events DBMR 2019
10 April
16 October
Around 25 interested DBMR newcomers attended each of these events. The next Info Event will take place in October 2020.

Day of BioMedical Research 2019
12–13 November
As usual, a large and interested audience followed the presentations of Prof. Dr. Jacob Corn (ETH Zürich, Switzerland) entitled "CRISPR-Cas at work in human cells", and Prof. Dr. Eckhard Wolf (Ludwig-Maximilians-Universität, München, Germany) entitled "Genetically tailored pigs as disease models and organ donors for xenotransplantation".

Five candidates applied for the Johanna Dürmüller-Bol DBMR Research Prize 2019 (funded by the Johanna Dürmüller-Bol Foundation) and 148 abstracts were submitted for the Poster Prizes of the DBMR and the Research Prize Alumni MedBern. This prize for the Best Publication was introduced in 2019. The winners were. The winners were (left to right in photo below): Johanna Manuela Kurz, Philipp Zens, Dr. Maria Nieves Sanz Garcia, Prof. Dr. Mark A. Rubin (Director DBMR), Dr. Raja Prince, Narayan Schütz, Kristina Krempaska, and Federica Maria Conedera.

Johanna Dürmüller-Bol DBMR Research Award 2019
Dr. Maria Nieves Sanz Garcia
Department of Cardiovascular Surgery, Inselspital, University Hospital Bern
Research Group Cardiovascular Surgery, Department for BioMedical Research, University of Bern

Poster Prizes of the DBMR for:
- *best preclinical project*
  Kristina Krempaska
  Department for BioMedical Research, University of Bern, Research Group Pulmonary Medicine (Adults) and Department of Pulmonary Medicine, Inselspital, Bern University Hospital, University of Bern
- *best clinical project*
  Johanna Manuela Kurz
  Department for BioMedical Research, University of Bern, Research Group Pulmonary Medicine (Paediatrics) and Department of Pediatrics, Inselspital, Bern University Hospital, University of Bern
- *best project by a medical student*
  Philipp Zens
  Department of Neurology, Inselspital, Bern University Hospital, University of Bern
- *best publication 2018*
  Dr. Raja Prince
  Department for BioMedical Research, University of Bern, Research Group Hematology (Adults) and Department of Hematology and Central Hematology Laboratory, Inselspital, Bern University Hospital, University of Bern

Research Prize for Alumni MedBern
Narayan Schütz
Gerontechnology and Rehabilitation, ARTORG Center for Biomedical Engineering Research, University of Bern

Stem Cell Prize
Federica Maria Conedera
Research Group Ophthalmology, Department for BioMedical Research, University of Bern, Bern, Switzerland, and Department of Ophthalmology, Inselspital, Bern University Hospital, University of Bern

"Clinical Research" symposium for Biomedical Sciences students of the University of Fribourg

15 November

DBMR Research Conferences 2019

In 2019, we were pleased to present the following speakers:

4 Feb – Prof. Dr. Bruno Reichart
Walter Brendel Centre of Experimental Medicine, Ludwig Maximilian University, Munich (DE)
"Heart transplantation – from the first human allografts to life-supporting pig-to-baboon xenotransplantation"

4 Mar – Prof. Dr. Hendrik Jan Ankersmit
Department of Thoracic Surgery, Medical University of Vienna (AT)
"MNC secretome: from discovery to product science and patient: from ignorance to clinical trial"

1 Apr – Prof. Dr. Vera Regitz-Zagrosek
Institute of Gender in Medicine, Center for Cardiovascular Research (CCR), Charité -Universitätsmedizin, Berlin (DE)
"Sex and gender in basic and translational cardiovascular research"

6 May – Prof. Konstantin G. Birukov, MD
Department of Anesthesiology, University of Maryland School of Medicine, Baltimore, MD (US)
"Mechanical forces in endothelial function: Exercise with moderation!"

3 June – Prof. Dr. Tom van der Poll
Amsterdam University Medical Centers, Academic Medical Center, University of Amsterdam (NL)
"New insights in the pathogenesis of sepsis and a sneak preview to future therapy"

1 July – Prof. Dr. Ivan Martin
Department of Biomedicine, University Hospital, Basel (CH)
"Re-engineering developmental processes for cartilage and bone regeneration"

2 Sep – Prof. Dr. Livia S. Eberlin
Department of Chemistry, University of Texas at Austin (US)
"Ambient ionization mass spectrometry for cancer diagnosis and clinical use"

7 Oct – Prof. Dr. Boris W. Kramer
Head of Pediatric Research, Maastricht University (NL)
"Stem cell therapy for peripartum neuroregeneration and pulmonary regeneration"

2 Dec – Prof. Dr. Marius Ader
Technische Universität, Dresden
Center for Molecular and Cellular Bioengineering, Center for Regenerative Therapies, Dresden (DE)
"Photoreceptor transplantation into the mammalian retina"

Personnel Update

Academic Degrees

The following academic degrees were awarded to members of DBMR Research Groups:

Assistant Professor

Dr. Stephanie Ganal-Vonarburg
Gastroenterology / Mucosal Immunology

Associate Professor

Prof. Dr. Verena Schröder
Experimental Hemostasis

Lecturer (Privatdozent)

PD Dr. Laurence Feldmeyer
Dermatology

PD Dr. Thomas M. Marti
Thoracic Surgery

PD Dr. Loretta Müller
Pulmonary Medicine (Pediatrics)

PhD

(Supervisors in brackets)

Dr. Felix Baier
(Prof. Dr. Deborah Stroka)
Tight junctions of the liver: Expression, regulation and function in native, regenerating, and cholestatic livers

Dr. Pierre Balmer
(Prof. Dr. Eliane J. Müller and Prof. Dr. Petra Roosje)
Unraveling molecular and cellular functions of SUV39H2 and FAM83G in skin homeostasis

Dr. Romina Cabra
(Prof. Dr. Willy Hofstetter)
The roles of iron in osteoclast and osteoblast lineage cells

Dr. Simone Cazzaniga
(Prof. Dr. Dagmar Simon)
Semantic connectivity maps: A novel approach for the exploration of healthcare databases

Dr. Federica Conedera
(Prof. Dr. Volker Enzmann and Dr. Marcus Tschopp)
Glial involvement in retinal degeneration and regeneration in zebrafish and mouse

Dr. André Döring
(Prof. Dr. Roland Kreis)
Methods of diffusion-weighted MR spectroscopy as a probe for brain tissue-microstructure

Dr. Michel Dosch
(Prof. Dr. Guido Beldi)
ATP release mechanisms modulating inflammatory responses

Dr. Dorota Magdalena Dudka
(PD Dr. Kathrin Zaugg and PD Dr. Michaela Medová)
Unravelling the molecular response to dose-rate and delivery time of ionising radiation in 2D vs 3D cell culture

Dr. Jacopo Gavini
(PD Dr. Vanessa Banz)
Lysosomal compartment dysregulation as a treatment strategy for hepatocellular carcinoma

Dr. Mohsin Hassan
(Prof. Dr. Andrea De Gottardi)
Role of Intestinal microbiota and paneth cells in the development of liver fibrosis and Portal Hypertension

Dr. Jonas Koch
(PD Dr. Michaela Medová)
Characterization of a novel putative ATM/ATR/DNA-PK phosphorylation site on the MET receptor tyrosine kinase

Dr. Caroline Krüger
(Prof. Dr. Martin Bachmann)
Memory B and secondary plasma cell generation against virus-like particles

Dr. Andrés Lanzós
(Prof. Dr. Rory Johnson)
Bioinformatic analysis of cancer driver long non-coding RNAs

Dr. Sylvia Nyilas
(Prof. Dr. Philipp Latzin)
Comparison of different approaches to analyse lung diseases with imaging and functional methods

Dr. Elisa Rösti
(Prof. Dr. Martin Bachmann)
New therapeutic approaches against Type 2 Diabetes mellitus using virus-like particles

Dr. Selina Roth
(PD Dr. Michaela Medová and Prof. Dr. Yitzhak Zimmer)
Radiosensitization strategies in head and neck squamous cell carcinomas: Emphasis on DNA-PK inhibition and TPX2 targeting

Dr. Gierin Thomi
(Prof. Dr. Daniel Surbek and PD Dr. Andreina Schoeberlein)
Exosomes from Wharton's jelly mesenchymal stromal cells as a treatment for preterm brain injury

Dr. Karl-Leonhard von Meyenn
(Prof. Dr. Christoph Schlapbach)
PPARgamma modulates IL-9 expression in Th2 cells by regulating glycolysis

Dr. Rahel Wyss
(PD Dr. Sarah Longnus)
Mitochondria-based approaches to facilitate donation after circulatory death heart transplantation

Awards

The following DBMR group members received awards in 2019:

Federica Maria Conedera
Ophthalmology
Posterpreis SC&RM awarded by the Platform for Stem Cells in Regenerative Medicine at the Day of BioMedical Research 2019 for "Antagonistic effects of TGFβ isoforms on tissue repair in zebrafish and mouse"

Noëlle Dommann
Visceral and Transplantation Surgery
Best oral presentation in Association of Research in Surgery (ARS) session, 2019 SGC annual meeting
"LIM protein Ajuba promotes cancer cell proliferation and survival in hepatocellular carcinoma"

Prof. Dr. Stephanie Ganal-Vonarburg
Gastroenterology / Mucosal Immunology
Peter Hans Hofschneider Endowed Professorship from the Foundation for Experimental Biomedicine for the project "The role of maternal microbiota in durably shaping immunity and microbiota composition in the offspring through epigenetic mechanisms"

Dr. Michel Hauser
Bone Biology & Orthopaedic Research
Swiss Bone & Mineral Society President's Award 2019, Bern, Switzerland

Cristina Kalbermatter
Gastroenterology / Mucosal Immunology
Poster Price, 2nd Young Scientist Symposium, Bern, Switzerland

PD Dr. Marianna Kruithof-de Julio
Urology
DoD Impact Award by the Congressionally Directed Medical Research Programs, US Department of Defense (DoD), Arlington County, VA, USA

PD Dr. Gregor J. Kocher
Thoracic Surgery
Best Video Presentation by the Swiss Society for Thoracic Surgeryfor "3D video-assisted uniportal anatomical en bloc resection of lung segments 6 and 10 on the left"

PD Dr. Gregor J. Kocher
Thoracic Surgery
Best Experimented Publication by the Swiss Society for Thoracic Surgery for "Surgical smoke: still an underestimated health hazard in the operating theatre"

Dr. Andreas Kohler
Visceral and Transplantation Surgery
SGC Research Prize at the 2019 SGC Annual Meeting for "Effectiveness of prophylactic intraperitoneal mesh implantation for prevention of incisional hernia in patients undergoing open abdominal surgery"

Ana Maria Quintela Pousa
Ophthalmology
Pro-Retina Poster award by PRO RETINA Deutschland e. V. at the Potsdam-Meeting 2019 for "Retinal microglia signaling affects Müller cell behavior in the zebrafish following laser injury induction"

Prof. Dr. Robert Rieben
Cardiovascular Research
DoD Impact Award by the Congressionally Directed Medical Research Programs, US Department of Defense (DoD), Arlington County, VA, USA

Dr. Tim Rollenske
Gastroenterology / Mucosal Immunology
EMBO Long-term postdoctoral fellowship

Dr. Francesca Ronchi
Gastroenterology / Mucosal Immunology
PI of tomorrow price, LS2 Switzerland

Prof. Dr. Mark A. Rubin
Precision Oncology
ICPerMed Best Practice in Personalised Medicine 2019 for "Development and integration of organoid models in personalised medicine platforms"

Dr. Anna Wenning
Gastroenterology / Mucosal Immunology
Poster Price, 2nd Young Scientist Symposium, Bern, Switzerland

Dr. Bahtiyar Yilmaz
Gastroenterology / Mucosal Immunology
SGG 2019 Gastroenterology Prize – Best Gastroenterology Paper

Dr. Bahtiyar Yilmaz
Gastroenterology / Mucosal Immunology
SNF Ambizione Grant, "Evolutionary dynamics of bacteria in the intestines of IBD patients"

Staff Changes

New Staff

Andrej Benjak
Biostatisticians (100 %)
Oncogenomics (since Mar.)

Alison Ferguson
Postdoctoral Associate (100 %)
Precision Oncology (since Jan.)

Izzem Gemici
Lab Technician (100 %)
Precision Oncology (since Oct.)

Murielle Golomingi
PhD Student (75 %)
Experimental Haemostasis (since June)

Isabelle Gsponer
Lab Technician (80 %)
Cytometry Laboratory / FACS Lab (since Apr.)

Sina Maletti
Lab Technician (100 %)
Precision Oncology (since Jan.)

Josip Mikulic
Advanced Postdoc (100 %)
Cardiovascular Research (since Oct.)

Anastasia Milusev
PhD Student (75 %)
Cardiovascular Research (since May)

Charlotte Ng
Dozent (100 %)
Oncogenomics (since Jan.)

Philip Rubin
Lab Technician (100 %)
Precision Oncology (since Jan.)

Raschid Setoud
Facility Manager (80 %)
DBMR Services (since Jan.)

Ana Radovanovic
Secretary (70 %)
Administration (since Sep.)

Antonio Rodriguez
Assistant Physician (50 %)
Precision Oncology (since Jan.)

Cornita Rohda
Secretary of Director (100 %)
Administration (since June)

Karin Schmitter
Lab Technician (40 %)
Supply Center/Medical Oncology
(since May)

Senija Selimovic-Hamza
Postdoc (100 %)
Precision Oncology (since Oct.)

Nicoletta Sorvillo
Postdoc (100 %)
Cardiovascular Research (since July)

Franziska Strunz
PhD Student (75 %)
Bone Biology & Orthopaedic Research
(since Nov.)

Phillip Thienger
PhD Student (100 %)
Precision Oncology (since Nov.)

Song Xue
PhD Student (75 %)
Clinical Radiopharmacy (since Apr.)

Short employment

Maïwenn Jornod
Scientific Assistant (40%)
Proteomics (June to Dec.)

Alexia Roschi
Assistant Facility Manager (20%)
DBMR Services (Mar. to Dec.)

Resignations

Max Pelletier
Practical Student (100 %)
IT Support (until July)

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Coordination: Basak Ginsbourger & Marla Rittiner
Editing: Editage (www.editage.com)
Photos: DBMR Philipp Kellmann (Hepatology), Bern; Portrait MR John Abbott
Print: Länggass Druck AG Bern