UNIVERSITÄT BERN

DEPARTMENT OF CLINICAL RESEARCH
www.dkf.unibe.ch

Jahresbericht Annual Report 2015

Contents

The DCR at a Glance

The Department of Clinical Research (DCR) 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 infrastructure to researchers at the Inselspital, Bern University Hospital and at the Faculty of Medicine. In 2015, 47 independent research groups covering almost all fields of biomedical research were affiliated with the DCR.

The DCR aims to bridge laboratory-based biomedical and patient-oriented clinical research through the scientific support of its groups and by operating state-of-the-art Technology Core Facilities and specialised Animal Core Facilities. It also hosts the Clinical Trials Unit (CTU) Bern. In addition, a strong emphasis is put on the development of translational approaches and the use of omics technologies.

Das DKF auf einen Blick

Das Departement Klinische Forschung (DKF) ist ein Forschungsdepartement der Medizinischen Fakultät der Universität Bern.

Es wurde 1994 mit dem Auftrag gegründet, Forschenden vom Inselspital, Universitätsspital Bern und von der Medizinischen Fakultät eine optimale Infrastruktur zur Verfügung zu stellen. Im Jahr 2015 waren 47 unabhängige Forschungsgruppen dem DKF angeschlossen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken.

Ziel vom DKF ist es, Brücken zu schlagen zwischen laborbasierter biomedizinischer und patientenorientierter klinischer Forschung. Erreicht wird dies durch die wissenschaftliche Unterstützung seiner Forschungsgruppen, sowie den Betrieb von, dem neusten Stand der Technik entsprechenden, Technologie und spezialisierten Tier Core Facilities. Die Clinical Trials Unit (CTU) Bern ist auch dem DKF angegliedert. Ausserdem wird ein starkes Gewicht auf die Entwicklung von translationalen Ansätzen und der Anwendung von Omics-Technologien gelegt.

Foreword – Director's Report

It is my pleasure to write this foreword for the sixth time in the name of the DCR Directorate. The first word that comes to mind when I think about the DCR in 2015 is "dynamic"! Over the past years, the DCR has been in a constant remodelling process, with groups coming and leaving, with laboratory spaces being created and disappearing, and with Core Facilities adding new instruments and services. The general trend has been towards growth and, we hope, more qualitative output in scientific knowledge!

In 2015, two new research groups joined the DCR. The Pediatric Surgery group, headed by Prof. Steffen Berger, is located in the research division of the Kinderklinik. In addition, following the Inselspital's fusion of the former Institute of Immunology with the Department of Rheumatology, Clinical Immunology and Allergology, the new research group of Prof. Martin Bachmann was created in the Sahli-Haus. We wish these two groups a productive year and much success in their research. The DCR is glad to host such a diverse and broad range of research areas!

The DCR Research Clusters were initiated a few years ago in order to increase the scientific collaboration and education activities of research groups with common interests, from both inside and outside the DCR. Two new, important clusters started their activities in 2015. The DCR Cluster for Cardiovascular Research is coordinated by PD Dr. Sarah Longnus from the Department of Cardiovascular Surgery, Inselspital. The DCR Cluster for Lung Development, Regeneration and Respiratory Diseases is coordinated by Dr. Thomas Marti from the Department of Thoracic Surgery, Inselspital. Both clusters organised a series of seminars and symposia that were very well attended. One of the goals with the Research Clusters is to initiate a process whereby we hope in the future to regroup the various main research topics of the DCR under the same roof, i.e., cardiovascular research, neuroscience, immunology and oncology, lung research, and muscular-skeletal research.

A first step towards this goal will be achieved in early 2016 with the opening of the new laboratories at Murtenstrasse 40 (located below the blood transfusion service). This new facility will host all the different groups of the Department of Hematology, the stem cell research cluster and the Genomics Core Facility. This regrouping will reduce the number of locations of the DCR research groups, in particular by giving up the sixth floor in the Institute of Pathology building. However, it is a fact that the DCR laboratories are still quite scattered over the Inselspital campus, making it very difficult to create an "under the same roof" collaborative spirit for the researchers with similar interests. While we can dream about a single research building hosting all the 47 research groups of the DCR on the Inselspital campus, the only concrete solution for the future is the so-called "InselNord" project at Murtenstrasse 20. The construction of this new building was recently suported by the Bernese voters. We are pleased that it will be possible to regroup the DCR research groups and Core Facilities more efficiently after 2021 and that the planning work can recommence.

One of the important tasks of the DCR is to maintain the Technology Core Facilities, offering state-of-the-art services and instruments. In 2015, we were again very active in upgrading the instruments in the Mass Spectrometry and Proteomics Laboratory Core Facility, with a very sensitive new mass spectrometer, and in the Live Cell Imaging (LCI) Core Facility, with a new micro-fluidic set-up and the Airyscan instrument, allowing much higher resolution confocal microscopy images. If you are interested in using these new instruments, please check the details on the respective homepages and contact the heads of these Core Facilities.

In addition to all the above changes, 2015 was a year of transition for the DCR Directorate. Since March 2015, Prof. Willy Hofstetter has been acting as DCR Managing Director because of my extra duties as the new Director of the NCCR TransCure. This period of transition will continue in 2016. It is foreseen that an interim directorate will be in place by April 2016. The future structure and direction of the DCR will be decided upon by the Faculty of Medicine following a report that is currently being written by an ad hoc committee. I take this opportunity to warmly thank all the DCR Coordinators and my DCR colleagues, in particular Prof. Hofstetter, for their outstanding work to keep the department running and developing so dynamically.

It only remains for me to wish you success with your research activities within the DCR in 2016.

Prof. Hugues Abriel, MD PhD

Vorwort – Bericht des Direktors

Es ist mir eine Freude, dieses Vorwort zum sechsten Mal im Namen der Direktion an Sie zu richten. Wenn ich über das DKF im Jahr 2015 nachdenke, kommt mir als erstes Wort „dynamisch“ in den Sinn! In den letzten Jahren war das DKF in einem ständigen Umformungsprozess, mit Forschungsgruppen, die kamen und gingen, mit Laborflächen, die geschaffen wurden und wieder verschwanden und mit Core Facilities, die durch neue Geräte und Dienstleistungen ergänzt wurden. Der generelle Trend zeigt in Richtung Wachstum und, wir hoffen, auf einen höheren qualitativen Output von wissenschaftlichem Wissen!

Im Jahr 2015 wurden zwei neue Forschungsgruppen im DKF aufgenommen: Die Gruppe Kinderchirurgie unter der Leitung von Prof. Steffen Berger im Forschungsbereich Kinderklinik und, im Anschluss an die Zusammenlegung des ehemaligen Instituts für Immunologie mit der Universitätsklinik für Rheumatologie, Klinische Immunologie und Allergologie, die neue Forschungsgruppe von Prof. Martin Bachmann im Sahli-Haus. Wir wünschen diesen beiden Gruppen einen guten Start im DKF und viel Erfolg in ihrer Forschungstätigkeit. Das DKF schätzt sich glücklich, ein derart vielfältiges und breites Spektrum an Forschungsthemen unter einem Dach zu vereinen!

Die DKF Forschungsclusters wurden vor ein paar Jahren initiiert, um die wissenschaftlichen Zusammenarbeiten und Aktivitäten von Forschungsgruppen mit gemeinsamen Interessen, sowohl innerhalb als auch ausserhalb des DKF, zu verstärken. Zwei neue, wichtige Cluster begannen ihre Tätigkeit im Jahr 2015: Der „Cluster for Cardiovascular Research“ wird von PD Dr. Sarah Longnus, Herz- und Gefässchirurgie, Inselspital und der „Cluster for Lung Development, Regeneration and Respiratory Disease“ von Dr. Thomas Marti, Thoraxchirurgie, Inselspital, koordiniert. Beide Clusters organisierten Seminare und Symposien, die sehr gut besucht waren. Eines der Ziele der Forschungsclusters besteht darin, die Voraussetzungen zu schaffen, um in Zukunft die Forschungsschwerpunkte des DKF zusammenzufassen, z. B. Herz-Kreislaufforschung, Neurowissenschaften, Immunologie und Onkologie, Lungenforschung und Muskulo-Skeletale-Forschung.

Ein erster Schritt in diese Richtung wird Anfang 2016 mit der Eröffnung der neuen Labors in der Murtenstrasse 40 gemacht werden. An diesem neuen Standort sind die Gruppen der Universitätsklinik für Hämatologie, der Forschungscluster Stammzellen und die Genomics Core Facility untergebracht. Diese Umgruppierung wird die Anzahl Standorte von DKF Forschungsgruppen, insbesondere durch die Aufgabe des sechsten Geschosses im Institut für Pathologie, reduzieren. Aber noch immer sind die DKF Labors auf dem Inselspital Campus verstreut, und es ist schwierig, einen „unter einem Dach“-Geist der Zusammenarbeit für Forschende mit ähnlichen Interessen zu schaffen. Wir können zwar von einem Forschungsgebäude auf dem Insel Campus träumen, in dem alle 47 Forschungsgruppen des DKF untergebracht werden können, die einzige konkrete Annäherung an dieses Ziel ist jedoch das so genannte „InselNord“ Projekt an der Murtenstrasse 20. Die bernischen Stimmbürger haben kürzlich dem Bau des neuen Gebäudes zugestimmt, und wir freuen uns, dass, ab 2021, DKF Forschungsgruppen und Core Facilities effizienter zusammengeführt werden und die Planungsarbeiten wieder beginnen können.

Eine der wichtigsten Aufgaben des DKF ist der Betrieb von dem neusten Stand der Technik entsprechenden Dienstleistungen und Geräten in den Technologie Core Facilities. Im Jahr 2015 waren wir wieder sehr aktiv in der Beschaffung neuer und leistungsfähigerer Geräte. In der Massenspektrometrie- und Proteomics Core Facility wurde ein sehr empfindliches, neues Massenspektrometer angeschafft. Der Gerätepark in der Live Cell Imaging (LCI) Core Facility wurde um ein neues Mikrofluid-Set-Up und ein Airyscan, welcher eine viel höhere Auflösung der konfokalen Mikroskopie Bilder erlaubt, ergänzt. Wenn Sie interessiert sind, diese neuen Geräte zu benutzen, überprüfen Sie bitte die Hinweise auf der jeweiligen Homepage und kontaktieren Sie die Leiter dieser Core Facilities.

Zu all den obgenannten Veränderungen, war das Jahr 2015 ein Jahr des Übergangs für die DKF Direktion. Wegen meiner zusätzlichen Aufgaben als neuer Direktor des NCCR TransCure ist Prof. Willy Hofstetter seit März 2015 als Geschäftsführender Direktor DKF tätig. Diese Übergangszeit wird im Jahr 2016 weiter gehen. Es ist geplant, dass bis April 2016 eine interim Direktion eingesetzt sein wird. Die künftige Struktur und Ausrichtung des DKF wird von der Medizinischen Fakultät entschieden werden, einem Bericht folgend, der gerade von einer ad hoc Kommission verfasst wird. Bei dieser Gelegenheit möchte ich mich herzlich bei allen DKF Koordinierenden und meinen DKF Kollegen, insbesondere bei Prof. Hofstetter, für ihre herausragende Arbeit bedanken, die den dynamischen Betrieb und die Weiterentwicklung des Departements möglich gemacht hat.

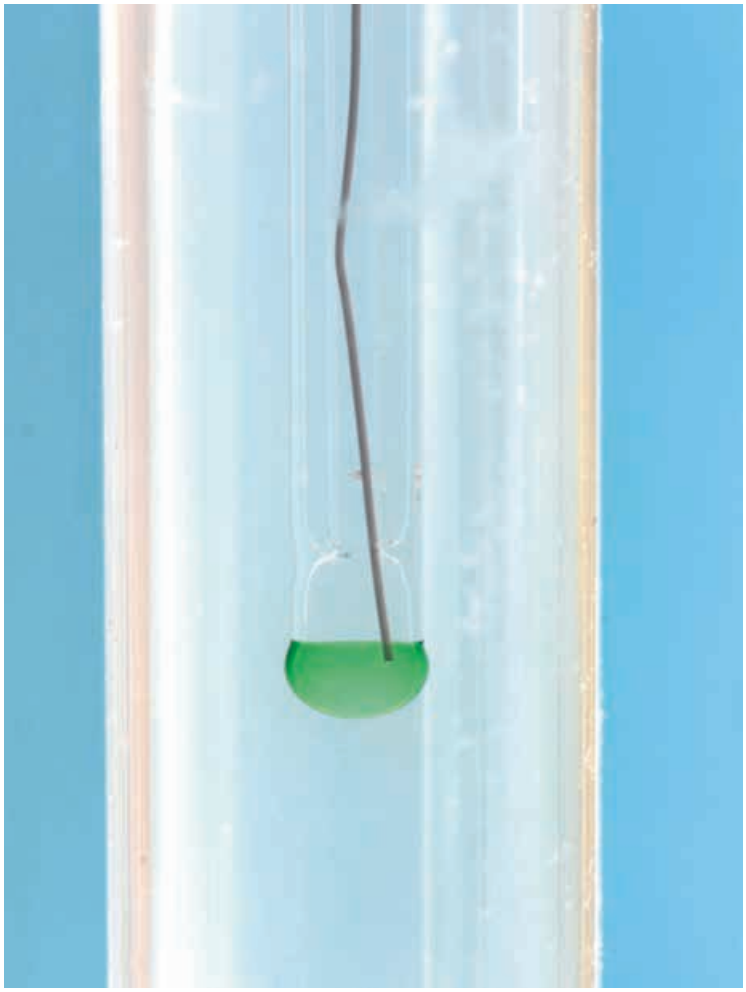
Ich wünsche Ihnen viel Erfolg mit Ihren Forschungsaktivitäten im 2016!

Prof. Hugues Abriel, MD PhD

Organisation

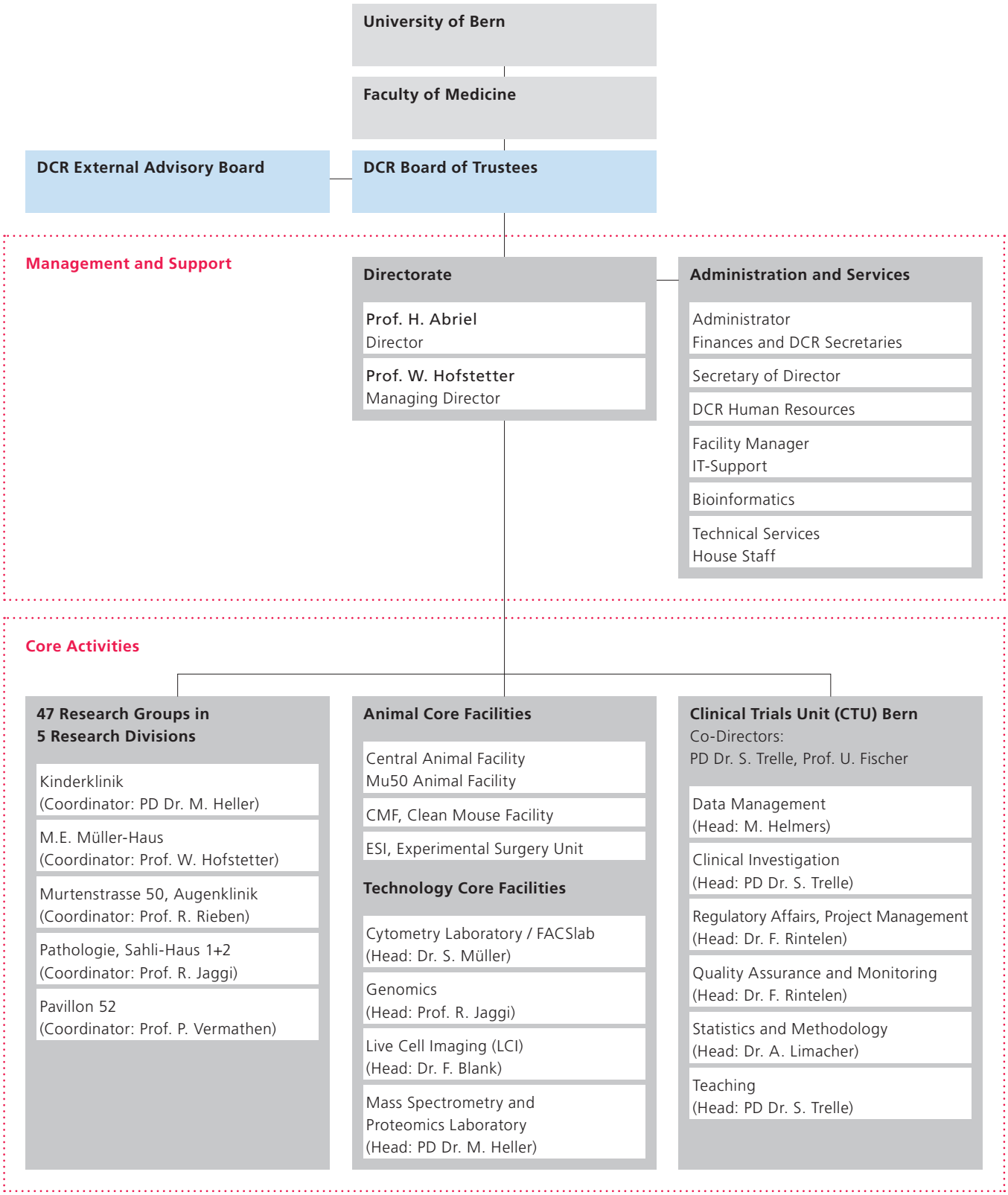
The role of the DCR is to provide optimal infrastructure and scientific support to its research groups, of which there were 47 at the end of 2015. The vast majority (42) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainder (5) are internal DCR groups, involved in the scientific support and coordination of equipment and infrastructure on a daily basis. The 47 groups are divided into 5 Research Divisions. Equally important, the DCR is responsible for operating Technology and Animal Core Facilities. It also hosts the Clinical Trials Unit (CTU) Bern. Furthermore, the groups of the department are supported by central services responsible for administration, informatics, technical support and bioinformatics.

The DCR Directorate, which comprises the Director and Managing Director, is supported by a Facility Manager. The Board of Trustees (Kuratorium) oversees DCR strategy and is involved in the decision-making process for resource distribution to the DCR groups. The External Advisory Board evaluates the overall strategies and operation of the DCR.



Organigram

December 2015



1

M.E. Müller-Haus
Murtenstrasse 35

2

Murtenstrasse 50

3

Pathologie
Murtenstrasse 31

4

Pavillon 52
Freiburgstrasse 3

5

Kinderklinik
Freiburgstrasse 15

6

Sahli-Haus 1
Freiburgstrasse 14a

7

Sahli-Haus 2
Freiburgstrasse 14

8

Augenklinik
Freiburgstrasse 8

Key People

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Prof. Dr. Lutz-Peter Nolte
Prof. Dr. Anton Sculean
Prof. Dr. Christian Seiler
Dr. Katharina Stegmayer

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Elisabeth Albertson (until June)
Dr. Lukas Stalder (since Oct.)

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Director

Prof. Dr. Willy Hofstetter
Managing Director

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EPF Lausanne (CH)

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University of Oxford (UK)

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University of Geneva (CH)

Prof. Dr. Radek Skoda
University of Basel (CH)

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Deborah Re, Secretary
Uyen Schmutz, Secretary
Beatrix Stalder, Secretary

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IT-Support
Michael Ackermann
David Schär
Thomas Späti

Bioinformatics
Dr. Irene Keller
Dr. Cedric Simillion
Ilker Romann

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Otto Aeby, Head DCR Maintenance

Coordinators of Research Divisions

PD Dr. Manfred Heller
Kinderklinik

Prof. Dr. Willy Hofstetter
M.E. Müller-Haus

Prof. Dr. Rolf Jaggi
Pathologie, Sahli-Haus 1+2

Prof. Dr. Robert Rieben
Murtenstrasse 50,
Augenklinik

Prof. Dr. Peter Vermathen
Pavillon 52

Heads of Core Facilities

Dr. Fabian Blank
Live Cell Imaging (LCI)

Prof. Dr. Urs Fischer
Clinical Trials Unit (CTU)
Bern

PD Dr. Manfred Heller
Mass Spectrometry and
Proteomics Laboratory

Prof. Dr. Rolf Jaggi
Genomics

Dr. Stefan Müller
Cytometry Laboratory /
FACSlab

PD Dr. Sven Trelle
Clinical Trials Unit (CTU)
Bern

Clinical Trials Unit (CTU) Bern

www.ctu-bern.ch
www.dkf.unibe.ch/core-facility/93/

Achievements 2015

Since the beginning of 2015, CTU Bern has found itself in a phase of change and development. Since January, two co-directors are responsible for the operational management: PD Dr. Sven Trelle, former associate director of CTU, is the methodological, managing co-director. He is responsible for the day-to-day business of the unit. Prof. Dr. Urs Fischer, Professor for Acute Neurology and Stroke, is the new medical co-director of CTU Bern. He acts as a liaison between CTU and the clinical departments of the Inselspital. A broadly based Board of Trustees was elected to supervise the co-directors, that is to support and approve their strategic and financial decisions and to represent the interests of clinical researchers. The members of the Board of Trustees, headed by Prof. Dr. Iris Baumgartner and Prof. Dr. Claudio Bassetti, are listed below.

This new organisational structure, as well as the newly appointed personnel, will not simply guarantee the established CTU services but will also enhance their quality and methodological expertise, and further expand the range of services for clinical researchers.

In collaboration with the Board of Trustees, the CTU co-directors have defined the main short- and long-term goals for the future development of CTU Bern:

- The new Human Research Act ("Humanforschungsgesetz") sets new and high requirements for patient-oriented clinical research and observational studies. Accordingly, CTU Bern is expanding its support for researchers with regard to regulatory affairs.
- The collaboration between the clinical departments of the Inselspital and CTU Bern should be closer and be continually improved. CTU is therefore offering a new, regular consulting service and lectures for researchers on the campus of the Inselspital.
- CTU Bern should be strengthened and enlarged so as to be able to enhance the field and the importance of clinical research in Bern.

PD Dr. Sven Trelle
sven.trelle@ctu.unibe.ch

Studies in medicine (2002). Research Fellow at Department I of Internal Medicine, Cologne (DE) (2003-2005) and Institute of Social and Preventive Medicine, University of Bern (2005-2008). Associate Director (2008-2015) and since 2015, Co-Director (methodological), CTU Bern.

Prof. Dr. Urs Fischer
urs.fischer@insel.ch

Studies in medicine (2000). Research Fellow (2008) at Stroke Prevention Research Unit, University of Oxford (UK). Head, Neurological Emergency Team and Associate Professor for Clinical Neurology (2014); Co-Chair, Stroke-Center (2015), Department of Neurology, Inselspital. Associate Professor for Acute Neurology and Stroke (2015), University of Bern. Since 2015, Co-Director (medical), CTU Bern.

Board of Trustees

Prof. Dr. H. Abriel
Department of Clinical Research, University of Bern
Prof. Dr. C. Aebi
Department of Paediatrics, Inselspital
Prof. Dr. D. Aujesky
Department of General Internal Medicine, Inselspital
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Department of Neurology, Inselspital
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Department of Angiology, Inselspital
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Department of Visceral Surgery and Medicine, Inselspital
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Directorate of Teaching and Research, Inselspital
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Department of General Internal Medicine, Inselspital
Prof. Dr. D. Surbek
Department of Gynaecology and Obstetrics, Inselspital
Prof. Dr. G. Thalmann
Department of Urology, Inselspital

Performance Report 2015

As in previous years, we were active in providing consultancy services for again more than 200 contacts within various clinical departments of the Inselspital as well as other institutes of the Faculty of Medicine. Due to the new Human Research Act, the number of consulting inquiries for the Data Management workflow remained high but we also saw an increase in requests for methodological consulting.

Finances 2015

As in previous years, the Inselspital provided core funding for senior staff and parts of our administration. Nevertheless, project funds and service charges needed to cover approximately two thirds of our budget. Thanks to the revenues in previous years and the acquisition of new projects, we were able to break even.

Outlook 2016

CTU Bern will be involved in large-scale international trials in the fields of general internal medicine and cardiology, all starting in spring/summer 2016. We have also been involved in several grant applications within the new Investigator Initiated Clinical Trials call of the SNF and will be involved in several applications within the new National Research Program 74 "Smarter Health Care".

Staff Members

PD Dr. Sven Trelle, Co-Director (methodological)
Prof. Dr. Urs Fischer, Co-Director (medical)
Hafeezul Adnan, Clinical Data Manager
Sarah Berner, Clinical Research Coordinator (since June)
Renata Bünter, Clinical Research Coordinator
Dr. Lukas Bütikofer, Senior Statistician
Madeleine Dähler, Study Coordinator
Dina Diatta Ibrahim, Statistical Data Manager (since Feb.)
Dr. Niklaus Fankhauser, Statistician (since Nov.)
Veronika Fiege, Statistician (since Mar.)
Dr. Alan Haynes, Statistical Data Manager
Dr. Dik Heg, Head, Cardiovascular Health
Sarah Heldner, Research Fellow (since Mar.)
Muriel Helmers, Head, Clinical Data Management
Stefanie Hossmann, Project Manager
Regula Jaeggi, Clinical Research Coordinator
Lucia Kacina, Clinical Trial Monitor
Dr. Andreas Limacher, Head, Statistics and Methodology
Lena Maurer, Junior Research Assistant
Julie Rat-Wirtzler, Clinical Data Manager
Dr. Stephan Reichenbach, Head, Clinical Investigation (until Apr.)
Dr. Felix Rintelen, Head, Monitoring and Regulatory Affairs
Martina Rothenbühler, Statistician
Dominique Rubi, Clinical Data Manager
Ursina Sager, Clinical Research Coordinator (until Mar.)
Dr. Georgia Salanti, Senior Statistical Consultant (since Aug.)
Dr. Roger Schürch, Senior Statistician
Nathalie Schwab, Clinical Trial Monitor (since June)
Malcolm Sturdy, Clinical Data Manager (until May)
Brigitte Wanner, Head, Quality Management
Simona Wanner, Assistant
Miriam Wegmann, Clinical Data Manager
Selina Wegmüller, Junior Research Assistant
Priska Wölfli, Clinical Data Manager (since July)
Janine Wyniger, Clinical Trial Monitor
Adrian Wyss, Clinical Data Manager
Serge Zaugg, Statistician
Katrin Ziegler, Clinical Data Manager

Acknowledgements in publications

A pilot test of the new Swiss regulatory procedure for categorizing clinical trials by risk: A randomized controlled trial. Cevallos, M et al. (2015) in: Clin Trials, 12(6), p. 677-687.

Efficacy and effectiveness of an rVSV-vectored vaccine expressing Ebola surface glycoprotein: interim results from the Guinea ring vaccination cluster-randomised trial. Henao-Restrepo, AM et al. (2015) in: Lancet, 386(9996), p. 857-866.

Predicting recurrence after unprovoked venous thromboembolism: prospective validation of the updated Vienna Prediction Model. Tritschler, T et al. (2015) in: Blood, 126(16), p. 1949-1951.

Improvement of antibiotic prescription in outpatient care: a cluster-randomized intervention study using a sentinel surveillance network of physicians. Hurlimann, D et al. (2015) in: J Antimicrob Chemother, 70(2), p. 602-608.

Bivalirudin or Unfractionated Heparin in Acute Coronary Syndromes. Valgimigli, M et al. (2015) in: N Engl J Med, 373(11), p. 997-1009.

Link to publication list:
www.ctu.unibe.ch/research/publications/index_eng.html

Cytometry Laboratory / FACSlab

www.facslab.unibe.ch
www.dkf.unibe.ch/core-facility/48/

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

Studies in microbiology at University of Bern; PhD (1996). Postdoc in intestinal mucosal immunology (2000-2001) and Head, Flow Cytometry Laboratory (2001), School of Cellular and Molecular Medicine, University of Bristol (UK). Senior Scientist in gastroenterology (2004-2011) at DCR. Since 2010, Head, DCR Cytometry Laboratory / FACSlab Core Facility.

Achievements 2015

New requirements for participants of our FACS course were implemented. First, participants who want to earn 2 ECTS points now need to fulfil more stringent criteria regarding investment of time and FACS-related impact. Second, participants need to catch up on missed parts of the course to obtain a course certificate.

All the bugs and problems with our imaging flow cytometry instrument (ImageStream^X) were finally sorted out during 2015. Thus, we are now able to offer a well-structured introduction according to the official recommendations of the manufacturer.

Thomas Schaffer, who has a PhD in Immunology and Cell Biology, was hired part time (50%) to deal with the increasing demand in cell sorting and scientific and educational support.

An agreement was setup between the Department of Clinical Chemistry (Inselspital) and the DCR FACSlab, with the aim of sharing their BD FACS ARIA III cell sorter.

Performance Report 2015

Compared to 2014, FACS measurements increased by 31% and sorting by 33%! 59% of the FACS measurements were performed by researchers from Inselspital clinics and 41% by researchers from University of Bern institutes. Cell sorting numbers were 64% and 35%, respectively. Use by external people made up only 1%. 59% of acquisitions and 63% of cell sorting were performed by DCR groups.

As expected, the introduction of charging for excessively booked time on our FACS analysers resulted in a more careful estimation and, thus, more accurate booking of our instruments. This freed up sufficient time to cope with the increased demand in 2015.

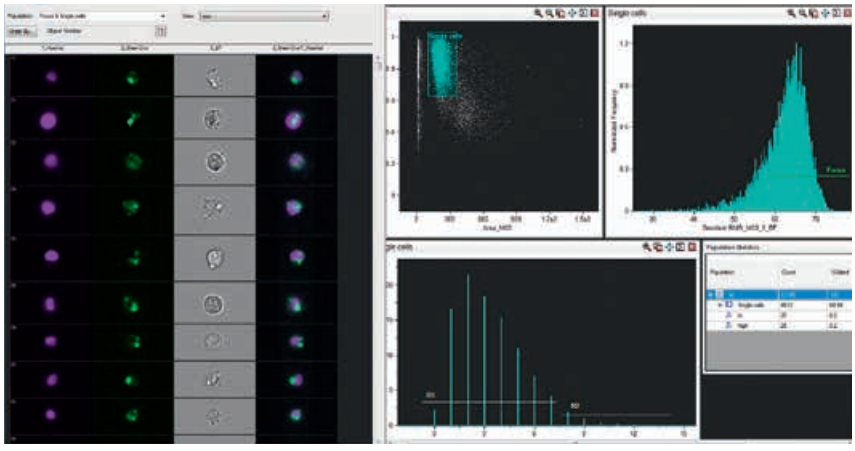
Finances 2015

The increased use of our instruments was also reflected by increased revenues in 2015 compared to 2014. The costly repair of the FACSArray analyser as well as the yearly license fee for the FlowJo analysis software was covered by the "Ressourcenausschuss" of the Faculty of Medicine. This allowed us to order comprehensive preventive maintenance services for all our high-end instruments.

The facility received a working credit of CHF 8,000 from the DCR for general maintenance and repairs.

Outlook 2016

In 2016, we plan to improve our website with: (i) new sections for general information about FACS and our Core Facility; (ii) a section with experimental protocols that are continuously being established in our Core Facility and which will cover, in particular, methods for the ImageStream^X and the HyperCyt; and (iii) a personalised online sort-form. A new instrument, the NanoSight NS300, which allows to assess and characterise nano particles between 10 and 2000 nm, will be installed in our facility.



Staff Members

Dr. Stefan Müller, Head
Dr. Thomas Schaffer, Scientific and Educational Support, Technical Assistance
Dr. Claudio Vallan, Scientific and Educational Support, Technical Assistance
Bernadette Nyfeler, Laboratory Technician

Live Cell Imaging (LCI)

www.lci.dkf.unibe.ch/
www.dkf.unibe.ch/core-facility/92/

Dr. Fabian Blank
fabian.blank@dkf.unibe.ch

MSc in Cell Biology (2003) and PhD in Structural Biology (2006) at University of Bern. Postdocs at 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), DCR. Since 2010, Commission Member, Microscopy Imaging Centre. Since 2012, Head, Live Cell Imaging (LCI) Core Facility, DCR.

Achievements 2015

A Nikon spinning disk confocal system with LED illumination was installed for automated high-speed imaging of microfluidic cell cultures. This system will soon be available to users in need of ultrafast 4D imaging of complex in vitro systems. The Zeiss LSM 710 confocal microscope was recently upgraded with an Airyscan module. This upgrade provides a significant improvement in lateral and axial resolution, and a substantial increase in signal-to-noise ratio. Users of the LSM 710 in need of high-resolution imaging or working with dyes of low signal will benefit from this upgrade soon.

Since its launch in 2012, the LCI Core Facility has been a unit of and is supported by the Microscopy Imaging Centre (MIC). The MIC is an interfaculty platform that coordinates, prioritises and supports funding applications in high-end microscopy, as well as organising access to microscopy equipment for all University members.

Performance Report 2015

A total of 72 users (2014: 53) from 30 different research groups (2014: 25) acquired microscopy data with the help of the Facility and spent a total of 5,144 booked hours (2014: 3,555) using its equipment during the last year. The Facility provided one two-day MIC Module on fluorescence microscopy, laser scanning microscopy, immunofluorescence labelling and image processing, and a five-day MIC Module on immunohistochemistry and immunofluorescence in paraffin-embedded sections, for a total of 20 students. In addition, the Facility contributed to the cutting-edge lectures and practical parcours in light microscopy organised by the MIC. Furthermore, the Facility is continuously advising, supporting and collaborating with a number of research groups from the DCR and other institutes.

Finances 2015

Revenues increased again due to the increased use of our equipment. The Facility received a working credit of CHF 6,000 from the DCR for general maintenance and repairs. In addition, the invoice for the yearly IMARIS software license fee (CHF 16,194) was covered by the "Ressourcenausschuss" of the Faculty of Medicine and the replacement of the Argon laser unit for the Zeiss LSM 710 (CHF 30,012) by the DCR. The new Nikon spinning disk microscope was financed from an SNF R'Equip grant by Olivier Guenat (ARTORG), with matching funds from the Inselspital "Fonds der Chefärztinnen und Chefärzte für Forschungsinfrastruktur". The Zeiss Airyscan upgrade (CHF 184,157) was covered by the University of Bern. Furthermore, the MIC provided financial support (CHF 1,000) for the practical courses organised in the Facility.

Outlook 2016

The LCI Core Facility will expand to Murtenstrasse 40, where new research labs, currently being built for the DCR, will be ready in February 2016. In the new labs, the Facility will provide a microscopy room for basic and advanced imaging with light microscopy as well as a powerful workstation for image processing and visualisation. In addition, provision will be made for safe central storage of imaging data acquired in the Facility.

Staff Members

Dr. Fabian Blank, Head
Carlos Wotzkow, Laboratory Technician

Genomics (Core Facility)

www.gcf.dkf.unibe.ch / www.dkf.unibe.ch/core-facility/83/

Molecular Biology (Research Group)

www.molbiol.dkf.unibe.ch
www.dkf.unibe.ch/research-group/11/

Prof. Dr. Rolf Jaggi
rolf.jaggi@dkf.unibe.ch

Studies and PhD (1982) at University of Bern. Postdoc (1984-1988) at Ludwig Institute for Cancer Research, Bern. Head of research group (1988-1996) at Institute of Clinical and Experimental Cancer Research, Bern. Several residences in the group of Prof. F. Martin, University College, Dublin (IE). Habilitation (1990); Professor (1996) at University of Bern. Group Leader, DCR and since 2011, Head of Genomics Core Facility.

Achievements 2015 / Outlook 2016

Molecular Biology

Our research is focused on the role of the oestrogen (ER) and progesterone (PR) receptors in human breast cancer. The ER is expressed in about 70% of all breast cancers, where it acts as a promoter of proliferation. These patients are usually treated with drugs that antagonise the endogenous oestrogen or that block the synthesis of new oestrogen. The drugs are applied alone or in concert with cytostatic drugs to reduce the risk of recurrence after surgery. The role of PR is less clear: multiple studies have documented that PR expression is controlled at least in part by ER but PR can also be expressed in the absence of ER. The PR may be expressed at different levels in individual cancer cells of the same tumour. Drugs that block the PR or some of its effects are not yet available.

We used the newly developed and highly specific "Crisper/Cas9" system to modulate PR expression in breast cancer cells. The system is based on short nucleic acids that bind specifically to the coding regions of genes in the nucleus of living cells. The Cas9 introduces a double-strand break. Mutations in the repaired DNA block the normal function of the encoded protein. The system is well tolerated by cells and it can be adapted to essentially any gene. We used this approach to inactivate the PR gene in well-characterised breast cancer cells. In 2016, we will use RNA-seq to measure the transcriptome of PR-positive and PR-negative cells and the consequences of PR extinction. We will then study expression of several de-regulated genes in human breast cancer. A more detailed understanding of PR and its role will hopefully help to develop strategies to control proliferation of some cancer cells that tend to escape therapy and lead to recurrence.

Our group was also involved in several clinical studies in 2015. In one of them, our collaborators Bernhard Pestalozzi and Stefan Aebi studied the acceptance of molecular parameters among Swiss oncologists. More than 200 patients with primary breast cancer participated. Normal diagnostic procedures were extended by measuring the recurrence score (RS), which is widely used and accepted in the USA. The primary goal was to compare treatment decisions with and without the RS results. We obtained histological sections from each tumour and determined our own molecular score, RISK, which was developed and validated in Bern.

It was surprising to find that the agreement between RISK and RS was only about 65%, although both scores measure the risk of recurrence in the tumour of each patient. The discrepancy between RISK and RS was much higher than the expected technical and biological variation. Interestingly, a similarly poor consensus was found when other prognostic scores based on molecular parameters were compared. The meaning of these findings was recently discussed at the 40th ESMO European Cancer Congress in Vienna (AT) but could not be explained.

Several other clinical studies were either continued or newly initiated in 2015. The Genomics Core Facility supported these studies by isolating RNA or DNA and performing molecular analyses.

Performance Report 2015 / Outlook 2016

Genomics

The Genomics Core Facility supported several users of the Faculty of Medicine with either next generation sequencing on the Ion Torrent PGM or on the Illumina Hi-Seq. One study used Sanger sequencing. Two groups

measured gene expression using Nanostring. We provided support at the level of planning, sample preparation, data acquisition and analysis of results.

Finances 2015

Genomics
The Genomics Core Facility received a working credit of CHF 6,000 from the DCR, which was used for repairs and maintenance.

Staff Members

Prof. Dr. Rolf Jaggi, Group Leader and Head of Genomics Core Facility
Dr. Irene Keller, Bioinformatician (Core Facility)
Ilker Romann, IT Specialist (Core Facility)
Mariana Bustamante, PhD Student (Research Group)
Michèle Ackermann, Laboratory Technician (Core Facility) (until Feb.)
Muriel Fragnière, Laboratory Technician (Research Group & Core Facility) (until Feb.)
Nathalie Schuster, Laboratory Technician (Research Group & Core Facility) (from June)

Collaborators

Aebi S, Gautschi O, Günthert A, Lucerne Cantonal Hospital (CH)
Krestel H, Inselspital (CH)
Ochsenbein A, Inselspital (CH)
Pestalozzi B, University Hospital Zurich (CH)
Popovici V, Masaryk University (CZ)
Rothschild S, University Hospital Basel (CH)
Zweifel M, Inselspital (CH)

Grants

Amounts allocated for 2015:
Molecular Biology
- W.+H. Berger-Janser Foundation: Characterization of ER-negative cancer cells in ER-positive breast cancer (R. Jaggi) CHF 59,100
- SAKK studies: Analysis of molecular score and adjuvant treatment recommendations (R. Jaggi) CHF 33,200
- Various donors: (R. Jaggi) CHF 14,100

Teaching Activities

- 1st year medical students: Problem Based Learning
- Selected topics in molecular pathology: Molecular Processes of Disease lecture

Publications

Molecular Biology
Bevacizumab, Pemetrexed, and Cisplatin, or Bevacizumab and Erlotinib for Patients With Advanced Non-Small-Cell Lung Cancer Stratified by Epidermal Growth Factor Receptor Mutation: Phase II Trial SAKK19/09. Gautschi, O; Mach, N; Rothschild, SI; Li, Q; Stahel, RA; Zippelius, A; Cathomas, R; Fruh, M; Betticher, DC; Peters, S; Rauch, D; Feilchenfeldt, J; Bubendorf, L; Savic, S; Jaggi, R; Leibundgut, EO; Largiader, C; Brutsche, M; Pilop, C; Stalder, L; Pless, M; Ochsenbein, AF (2015) in: Clin Lung Cancer, 16(5), p. 358-365.

Comprehensive validation of published immunohistochemical prognostic biomarkers of prostate cancer – what has gone wrong? A blueprint for the way forward in biomarker studies. Huber, F; Montani, M; Sulser, T; Jaggi, R; Wild, P; Moch, H; Gevensleben, H; Schmid, M; Wyder, S; Kristiansen, G (2015) in: Br J Cancer, 112(1), p. 140-148.

Mass Spectrometry and Proteomics Laboratory (Core Facility)

Protein and Cell Biology (Research Group)

www.pmscf.dkf.unibe.ch

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

PhD in Biochemistry (1994) at University of Bern. Postdocs at University of Auckland (NZ) and Washington, Seattle (US). Return to Switzerland in 1999 to University of Geneva, followed by three years as Senior Scientist at GeneProt Inc., Geneva and DiagnoSwiss, Monthey. Since 2003, Head of Proteomics and Mass Spectrometry Laboratory, a DCR Core Facility since 2008. Eighteen years of experience in mass spectrometry, proteomics and bioinformatics.

Achievements 2015 / Outlook 2016

Mass Spectrometry and Proteomics

We experienced some very varied work phases in 2015. While it was business as usual during the first half of the year, there was a significant decrease in sample analysis requests during the second half. At the same time, several researchers approached us for collaborations. Two projects involved tissue and leukaemia phosphoproteomics. We have some preliminary workflows but we need to invest more time for improvements in 2016. Two other projects are about biomarker discovery on colon cancer tissue, with the Zlobec lab (Department of Pathology), and on virus-affected grapevine leaves, with Bioreba AG (CH). For the former, we have already conducted some reproducibility studies on fresh and frozen tissue samples, whereas formaldehyde-fixed and paraffin-embedded samples need more work. For the later, we have secured CTI funding, with the project start scheduled for March 2016.

Since 2013, we have been advocating replacing the orbitrap XL with a new mass spectrometer. In spring, we were finally able to bring together the decision makers of the three life science faculties (Vetsuisse, Phil. nat. and Medicine) in order to discuss possibilities for co-financing. A financing scheme was agreed upon but we were granted the necessary money from the University of Bern in June, rendering it obsolete. After fulfilling the necessary procedures of a public tender and some intense negotiations with ThermoFisher Switzerland, we ordered the latest orbitrap technologies in the form of a Fusion Lumos ETD and a second-hand QExactive HF, replacing the orbitrap XL and the VELOS iontrap.

Unfortunately, the orbitrap XL broke down about a month before the installation of the Fusion Lumos. The QExactive HF was shipped and installed after the Lumos, reducing our productivity for quite some time. Additionally, we had to get accustomed to the new instruments, which was however accelerated by good training support from ThermoFisher and the hard work of Sophie Braga. The two new instruments now produce very rich data of excellent quality, which results in unprecedentedly large datasets. Processing of these puts demands on the hardware and software infrastructure, and raises the need for dedicated bioinformatics support to keep up with the instrument performance.

Protein and Cell Biology

We analysed the microparticle proteome of patient plasma samples from a former clinical study and finalised data production for two manuscripts. With the help of an intern, we made some progress on an old project idea about the impact of shear stress on the proteome of endothelial cells. We also made progress in the automated sample digestion workflow on an RTC PAL liquid handling system and hope to solve the last issues of hard- and software compatibilities early in 2016.

Plans for 2016

The central focus will be the translation of acquired data and developments into publications. Furthermore, we anticipate heavy workloads on samples provided by collaborators who made progress in getting their research projects financed, including our own CTI-funded project. One central task will be to secure the financial resources in order to hire a bioinformatician and last but not least, finding such an expert.

Performance Report 2015

Mass Spectrometry and Proteomics
A total of 1,339 samples were processed during the year, submitted by laboratories from the Vetsuisse Faculty (2%), external institutions (3%), Faculty of Medicine (25%), Faculty of Science (30%), and our own projects and collaborations with other groups (40%).

Finances 2015

Mass Spectrometry and Proteomics
Despite lower income for provided services compared to former years, we had a positive accounting balance of about CHF 8,000 thanks to relatively few instrument breakdowns and hence only modest repair bills. The Facility received a working credit of CHF 8,000 from the DCR for general maintenance and repairs.

Staff Members

PD Dr. Manfred Heller, Group Leader (Research Group) and Head (Core Facility)
François Achermann, Laboratory Technician (Core Facility & Research Group), Radio-safety and JHE Deputy and Biosafety Officer, DCR
Sophie Braga, Laboratory Assistant (Core Facility & Research Group)
Natasha Buchs, Laboratory Technician (Core Facility & Research Group)
Dr. Cedric Similion, Bioinformatician (Core Facility)
Ilker Romann, IT Specialist (Core Facility)

Collaborators

Böhm G, CTC Analytics AG (CH)
Debonneville C, Bioreba AG (CH)
Müller M, Swiss Institute of Bioinformatics (CH)
Saxena S, University of Bern (CH)
Zlobec I, University of Bern (CH)

Grants

None for 2015

Teaching activities

- MSc Biomedical Sciences: Tumour Biology – proteomics lectures
- MSc Biology: From Genomes to Metabolomes – proteomics lecture
- MSc in Bioinformatics: Mass Spectrometry to Systems Biology course

Publications

Trypanosoma brucei RRM1 is a nuclear RNA-binding protein and modulator of chromatin structure. Naguleswaran, A; Gunasekera, K; Schimanski, B; Heller, M; Hemphill, A; Ochsenreiter, T; Roditi, I (2015) in: MBio, 6(2), p. e00114.

Doxorubicin Affects Expression of Proteins of Neuronal Pathways in MCF-7 Breast Cancer Cells. Petrovic, M; Simillion, C; Kruzliak, P; Sabo, J; Heller, M (2015) in: Cancer Genomics Proteomics, 12(6), p. 347-358.

FUS/TLS contributes to replication-dependent histone gene expression by interaction with U7 snRNPs and histone-specific transcription factors. Raczynska, KD; Ruepp, MD; Brzek, A; Reber, S; Romeo, V; Rindlisbacher, B; Heller, M; Szweykowska-Kulinska, Z; Jarmolowski, A; Schumperli, D (2015) in: Nucleic Acids Res, 43(20), p. 9711-9728.

Aberrant association of misfolded SOD1 with Na/KATPase-alpha3 impairs its activity and contributes to motor neuron vulnerability in ALS. Ruegsegger, C; Maharjan, N; Goswami, A; Filezac de, L'E; Weis, J; Troost, D; Heller, M; Gut, H; Saxena, S (2015) in: Acta Neuropathol, e-pub ahead of print.

A Drosophila XPD model links cell cycle coordination with neuro-development and suggests links to cancer. Stettler, K; Li, X; Sandrock, B; Braga-Lagache, S; Heller, M; Dumbgen, L; Suter, B (2015) in: Dis Model Mech, 8(1), p. 81-91.

Link to publication list:
www.pmscf.dkf.unibe.ch

Bone Biology & Orthopaedic Research

www.bonebiology.dkf.unibe.ch
www.dkf.unibe.ch/research-group/1/

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

MSc in Biochemistry at ETH Zurich; PhD in Biochemistry (supervisor Prof. N. Herschkowitz) at Children's Hospital, Inselspital. Postdoc at University of Georgia (US). Then joined Institute of Pathophysiology, University of Bern. Since 1997, Head, Bone Biology & Orthopaedic Research Group, DCR and since 2015, DCR Managing Director.

Research Highlights 2015 / Outlook 2016

Bone Biology & Orthopaedic Research Group

Highlights of our research on bone cell biology, inflammatory diseases and molecular transport systems include the projects described below:

- In vivo experiments using a rat model investigated the osseointegration and turnover of composite materials of poly-lactate nano-fibres and CaP cement. These studies were extended to in vitro studies with osteoblast lineage cells to assess toxicity and biological activity. (NFP64 / Alfred and Anneliese Sutter-Stöttner Foundation, PhD project N. Ruef).
- Iron was found to regulate osteoclast development and to modulate the resorption activity of mature osteoclasts. Excess extracellular iron directed the development of haematopoietic progenitors towards the macrophage/monocyte lineage, while deprivation of iron did not impair in vitro osteoclast development. Next, osteoclast lineage-specific DMT1 and ferroportin knock-out mice will be generated to elucidate the role of cellular iron homeostasis in bone physiology (NCCR TransCure, PhD project R. Cabra).
- Bone healing in osteoporotic bones treated with the bisphosphonate alendronate (Ale) was observed under rigid and non-rigid fixation. Ale was found to exert strong effects on the formation of a fracture callus in non-rigidly fixed osteotomies. We expect to gain mechanistic insights into the repair processes upon completion of the RNA sequencing experiments that are currently running (Alfred and Anneliese Sutter-Stöttner Foundation, PhD project M. Hauser).
- We continued our studies into the loss of chondrogenic potential in primary bovine chondrocytes during in vitro expansion. TGF-β signalling has been identified as an essential component for cartilage formation. We aim to elucidate the molecular mechanisms governing chondrocyte differentiation and chondrogenesis by characterising the transcriptomes of cells grown in monolayers and high-density cultures. (Robert Mathys Foundation, R. Egli)
- We carried out detailed studies of the mechanisms of the effects of bone morphogenetic proteins and their agonists in integration and turnover of materials. Biofunctionalisation is a means to improve the osseointegration and turnover of CaP ceramic-based bone substitute materials. (ITI Foundation, E. Hartmann; PI: F. Klenke).

Osteo-Articular Research Group

Highlights of our research on cartilage biology and degeneration include studies of the small calcium-binding proteins S100A1 and S100B in human articular chondrocytes (HAC). We demonstrated their co-expression with cartilage matrix-specific components, namely proteoglycans and collagen type II, in healthy and diseased cartilage, in biopsies upon AMIC treatment, and in de-differentiated (in monolayer) and re-differentiated (in micromass pellet) HAC. Furthermore, induction of chondrogenic factors – including S100A1 and S100B – in monolayer by high osmolarity and BMP4 in HAC at different stages of de-differentiation increases their re-differentiation (neochondrogenic) potential in micromass pellet culture.

Group Members

Bone Biology & Orthopaedic Research Group
Prof. Dr. Willy Hofstetter, Group Leader
Dr. Rainer Egli, Senior Scientist (until Oct.)
Dr. Antoinette Wetterwald, Senior Scientist
Eliza Hartmann, Research Assistant (since Apr.)
Silvia Dolder, Laboratory Technician
Mark Siegrist, Laboratory Technician
Romina Cabra, PhD Student (since Apr.)
John Choy, PhD Student (until May)
Michel Hauser, PhD Student
Nina Ruef, PhD Student
Wenjie Xie, PhD Student (until June)

Osteo-Articular Research Group
PD Dr. Dobrila Nesic, Group Leader

Clinician with projects in the group
PD Dr. Frank Klenke, Project Leader

Collaborators

Aeberli D, Inselspital (CH)
Fuster D, Inselspital (CH)
Luginbuehl R, RMS Foundation (CH)
Seitz M, Inselspital (CH)
Siebenrock KA, Inselspital (CH)
Kohl, S, Inselspital (CH)

Grants

Amounts allocated for 2015:
Bone Biology & Orthopaedic Research
- SNF: NCCR TransCure sub-project: Role of ion transporter TRPV6 and other transporters in bone homeostasis (M. Hediger, W. Hofstetter) CHF 75,000
- SNF: NFP64 – Nanofibres reinforced bone substitute materials: Effect of delayed fibre degradation on cells and tissues (R. Luginbuehl, K. Maniura, W. Hofstetter) CHF 90,408
- ITI Foundation: Functionalization of CaP bone substitutes with growth factors (F. Klenke, W. Hofstetter)
- Alfred and Anneliese Sutter-Stöttner Foundation: Heilung von Frakturen in osteoporotischen Knochen (W. Hofstetter) CHF 87,000
- Alfred and Anneliese Sutter-Stöttner Foundation: Faser-verstärkte Knochenersatzmaterialien – Verbesserung der Biokompatibilität und des Umbaus (W. Hofstetter) CHF 85,000

Teaching Activities

- MSc Biomedical Engineering: Tissue Engineering course (Nesic)
- MSc Biomedical Engineering: Osteology course (Hofstetter)
- 3rd-year dentistry students: Pathophysiology – Skeleton (Hofstetter)
- 1st-year medical students: Molecular biology practical courses (Hofstetter)
- 2nd-year medical students: Kidney block – Calcium and phosphate metabolism (Hofstetter)

Publications

Sodium-dependent phosphate transporters in osteoclast differentiation and function. Albano, G; Moor, M; Dolder, S; Siegrist, M; Wagner, CA; Biber, J; Hernando, N; Hofstetter, W; Bonny, O; Fuster, DG (2015) in: PLoS One, 10(4), p. e0125104.

The Role of Cells in Meniscal Guided Tissue Regeneration: A Proof of Concept Study in a Goat Model. Julke, H; Mainil-Varlet, P; Jakob, RP; Brehm, W; Schafer, B; Nesic, D (2015) in: Cartilage, 6(1), p. 20-29.

Comparison of two protocols of periosteal distraction osteogenesis in a rabbit calvaria model. Saulacic, N; Nakahara, K; Iizuka, T; Haga-Tsujimura, M; Hofstetter, W; Scolozzi, P (2015) in: J Biomed Mater Res B Appl Biomater, e-pub ahead of print.

Platelet-rich concentrates differentially release growth factors and induce cell migration in vitro. Schar, MO; Diaz-Romero, J; Kohl, S; Zumstein, MA; Nesic, D (2015) in: Clin Orthop Relat Res, 473(5), p. 1635-1643.

Transforming growth factor beta signaling is essential for the autonomous formation of cartilage-like tissue by expanded chondrocytes. Tekari, A; Luginbuehl, R; Hofstetter, W; Egli, RJ (2015) in: PLoS One, 10(3), p. e0120857.

Extracellular Iron is a Modulator of the Differentiation of Osteoclast Lineage Cells. Xie, W; Lorenz, S; Dolder, S; Hofstetter, W (2015) in: Calcif Tissue Int, e-pub ahead of print.

Link to publication list:
www.bonebiology.dkf.unibe.ch/lit/literature_2000.html

Cardiovascular Research

www.cvrc.dkf.unibe.ch
www.dkf.unibe.ch/research-group/61/

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

Studies in biology at the University of Bern; PhD in Immunology (1992). SNF postdoc on xenotransplantation (1994-1997) 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, Cardiovascular Research, DCR.

Research Highlights 2015 / Outlook 2016

The work of our group focuses on transplantation and ischemia/reperfusion injury. Both subjects are close to clinical application and complex in the sense that many different pathophysiological mechanisms are involved. It is our ambition to understand and deal with these processes as a whole, which means that we often have to use animal models in our projects. However, we constantly strive to adhere to the '3R' principles of animal experiments (Refinement, Reduction, and Replacement). We will therefore dedicate this annual report to two of our recent 3R projects.

Refinement – Ischemia/reperfusion injury

Surgeries on extremities, like the hand, elbow, shoulder, foot, knee and hip, often need a bloodless environment. A tourniquet is therefore applied, which leads to a temporary ischemia in the affected limb, followed by reperfusion at the end of the operation. However, tissue subjected to ischemia and reperfusion may suffer from an inflammatory reaction that can lead to more tissue damage than ischemia alone, a phenomenon which is called ischemia/reperfusion injury. In clinical practice, this means swelling, pain, loss of muscle mass, and increased recovery time for the patient. We have been using a hind limb ischemia/reperfusion injury model in rats to simulate this clinical situation, understand the pathophysiology, and test potential treatment options. Recently, we refined the anaesthesia protocol used for these experiments in order to improve their clinical relevance. We compared anaesthesia with 100%, 60% and 40% oxygen in the inhalation gas mixture and found that use of 40% oxygen led to a significantly higher reperfusion injury. Because 40% oxygen is within the clinically used range, switching our animal experiments to this concentration will lead to a refined, more clinically relevant model.

Reduction – in vitro system of endothelial cells

A second 3R project aims at 3D culture and analysis of endothelial cells under physiological pulsatile flow conditions. Endothelial cells form the inner surface of blood vessels. They carry a layer of sulfated sugar molecules on the luminal side, which is important for the anti-coagulant and anti-inflammatory properties of healthy endothelium. In currently available in vitro systems, this so-called 'glycocalyx' is not fully functional and we need animal models to study the interactions between endothelial cells and the coagulation system. In collaboration with Olivier Guenat's group (ARTORG Center for Biomedical Engineering Research), we have developed a new in vitro system in which endothelial cells grow under pulsatile flow on the inner surface of tubular channels on a microfluidics device. Characterisation of the glycocalyx of the endothelial cells grown in the microfluidics system is currently ongoing, with the final aim to have an in vitro system that can be used with whole, non-anticoagulated blood and thereby considerably reduce the number of animal experiments.

Group Members

Prof. Dr. Robert Rieben, Group Leader
PD Dr. Yara Banz, Research Associate (Pathology, until July)
Julie Denoyelle, Laboratory Technician and MSc Student (until May)
Alain Despont, Laboratory Technician
Jane Shaw-Boden, Laboratory Technician
Oliver Steck, Laboratory Technician (since Mar.)
Uyen Schmutz, Secretary and Web Administrator
Mai Abdelhafez, PhD Student
Dzhuliya Dzhonova, PhD Student (since May)
Riccardo Sfriso, PhD Student (since Feb.)
Shengye Zhang, PhD Student
Pavan Garimella, Research Assistant (since Mar.)

Collaborators

Abicht J, Reichart B, Ludwig Maximilian University of Munich (DE)
Ahrens H, Niemann H, Friedrich Loeffler Institute (DE)
Ayares D, Revivicor Inc. (US)
Bovin N, Korchagina E, Titov A, Russian Academy of Sciences (RU)
Constantinescu MA, Olariu R, Inselspital (CH)
Cowan P, St Vincent's Hospital Melbourne (AU)
Guenat O, University of Bern (CH)
Jenni HJ, Inselspital (CH)
Karp JM, Harvard Medical School (US)
Klymiuk N, Wolf E, Wünsch A, Ludwig Maximilian University of Munich (DE)
Miescher S, Spirig R, Spycher M, CSL Behring AG (CH)
Mollnes T, Oslo University Hospital (NO)
Seebach J, Geneva University Hospital (CH)
Taddeo A, Schnider J, Sutter D, Vögelin E, Inselspital (CH)
Vemula P, inStem (IN)

Grants

Amounts allocated for 2015:

- SNF: Endothelial cell protection in xenotransplantation and ischemia/reperfusion injury: Assessing the effect of multiple transgenes and the pathophysiological role of the plasma cascade systems (R. Rieben) CHF 160,000
- SNF: Composite tissue preservation by extracorporeal blood perfusion and vascular cytoprotection to extend the time limit to replantation or transplantation (E. Vögelin, M.A. Constantinescu, R. Rieben) CHF 60,000
- SNF: Effect of locally delivered immunosuppressives encapsulated in self-assembled hydrogel systems on vascularized composite allotransplantation. Joint Research Project with India (R. Rieben, E. Vögelin, P. Vemula) CHF 60,000
- CSL Behring AG: Effect of C1INH on oxidative stress in rat hind limb ischemia/reperfusion injury (R. Rieben) CHF 50,000

Teaching Activities

- MSc Biomedical Sciences: Elective module – Composite tissue preservation by extracorporeal blood perfusion and vascular cytoprotection to extend the time limit to limb replantation
- Medical students: Elective course 5034 – Ihr Partner im Labor: Forschung auf den Gebieten Organtransplantation, Chirurgie und Herzinfarkt
- BSc in Life Sciences: Practical Course in Immunology
- PhD students in Graduate School for Cellular and Biomedical Sciences: Immunology tutorial
- High school students: Patenschaften für Maturaarbeiten (3 students with 2-week lab stay each)

Publications

Porcine extrahepatic vascular endothelial asialoglycoprotein receptor 1 mediates xenogeneic platelet phagocytosis in vitro and in human-to-pig ex vivo xenoperfusion. Bongoni, AK et al. (2015) in: Transplantation, 99(4), p. 693-701.

Transgenic Expression of Human CD46 on Porcine Endothelium: Effect on Coagulation and Fibrinolytic Cascades During Ex Vivo Human-to-Pig Limb Xenoperfusions. Bongoni, AK et al. (2015) in: Transplantation, 99(10), p. 2061-2069.

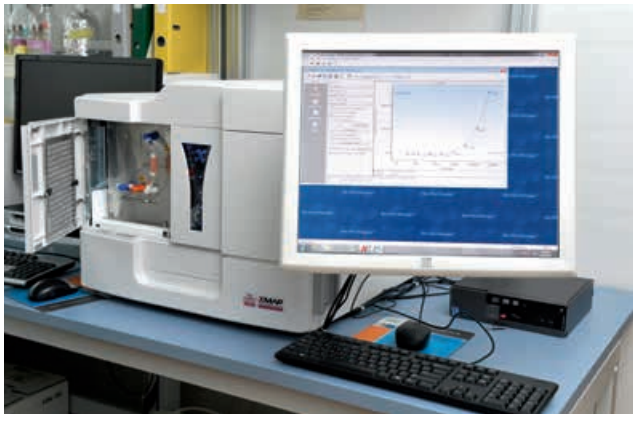
Organ inflammation in porcine Escherichia coli sepsis is markedly attenuated by combined inhibition of C5 and CD14. Egge, KH et al. (2015) in: Immunobiology, 220(8), p. 999-1005.

siRNA Mediated Knockdown of Tissue Factor Expression in Pigs for Xenotransplantation. Ahrens, HE et al. (2015) in: Am J Transplant, 15 (5), p. 1407-1414.

Endothelial- and Platelet-Derived Microparticles Are Generated During Liver Resection in Humans. Banz, Y et al. (2015) in: J Invest Surg, e-pub ahead of print.

Inhalation anesthesia of rats: influence of the fraction of inspired oxygen on limb ischemia/reperfusion injury. Zhang, S et al. (2015) in: Lab Anim, e-pub ahead of print.

Link to publication list:
www.boris.unibe.ch/view/divisions/DCD5A442C26FE17DE0405C-82790C4DE2.html



Ion Channels and Channelopathies

www.ionchannels.dkf.unibe.ch
www.dkf.unibe.ch/research-group/66/

Prof. Dr. Hugues Abriel
hugues.abriel@dkf.unibe.ch

Training both as a biologist at ETH Zurich and physician at University of Lausanne. After two years at Lausanne University Hospital, postdoc at Columbia University (US). In 2002, SNF Professorship and start of independent research studying the role of ion channels in human disorders. Since 2009, Professor of Pathophysiology, University of Bern and DCR Director. Since 2012, Member, SNF National Research Council. Since 2015 Director, NCCR TransCure.

Research Highlights 2015 / Outlook 2016

Similar to previous years, our research focused on the roles of ion channels in human diseases, so-called 'channelopathies'. On the one hand, we are characterising genetic variations in ion channel genes found in patients with pathological phenotypes, and on the other, we are studying new molecular mechanisms regulating the function of ion channels. Last year, with the help of SNF project funding, we continued to study the molecular determinants of the cellular localisation of the cardiac sodium channel Nav1.5 in cardiac cells. In particular, we investigated the roles of two Nav1.5 interacting proteins, alpha1-syntrophin and CASK. Diana Shy obtained her PhD title with this project. Valentin Sottas also finished his thesis work in the group. His main contribution was to decipher some of the molecular mechanisms involved in the phenomenon of negative dominance of mutant Nav1.5 proteins towards the normal (wild-type) proteins. This project will be continued by a PhD student, who will be hired in 2016. In 2016, PhD students Morgan Chevalier and Sarah Vermij, who started in summer 2015, will mainly work on the roles of CASK in murine heart.

In the frame of the NCCR TransCure project, Beatrice Bianchi continued the characterisation of several mutants of the genes coding for the TRPM4 cation channel that were found in patients with different types of cardiac arrhythmias. Some of the TRPM4 mutations were provided by Argelia Medeiros Domingo (Inselspital) with whom we have started to collaborate. Beatrice will also soon start to address the question of TRPM4 and TRPM4 inhibitors in a mouse model of multiple sclerosis. At the beginning of 2015, Lijo Ozhathil, an expert electrophysiologist, started as a postdoctoral fellow in the group. His main task has been to work in collaboration with the groups of Jean-Louis Reymond (Department of Chemistry and Biochemistry) and Jürg Gertsch (Institute of Biochemistry and Molecular Medicine) to set up a screening assay for small-molecule compounds that modulate the activity of TRPM4. These studies will be continued in 2016 and it is our goal to publish the first results of this collaboration soon.

Lastly, we also started a new transdisciplinary project with the CALIPHO group (Swiss Institute of Bioinformatics, University of Geneva) headed by Amos Bairoch. This project, funded by the SNF, aims to develop new tools to better predict the pathogenicity of variations found in the genes coding for the several voltage-gated sodium channels expressed in excitable cells. We will soon be hiring an electrophysiologist for this project, to validate the predictions made by the new tools developed by our colleagues in Geneva.

Group Members

Prof. Dr. Hugues Abriel, Group Leader
Dr. Jean-Sébastien Rougier, Research Assistant and Senior Teaching Assistant
Dr. Ludovic Gillet, Postdoctoral Fellow (until July)
Dr. Lijo Ozhathil, Postdoctoral Fellow
Maria Essers, Laboratory Technician
Sabrina Guichard, Laboratory Technician (since July)
Sabine Nafzger, Laboratory Technician (until July)
Verena Frazao, Secretary
Beatrice Bianchi, PhD Student
Morgan Chevalier, PhD Student
Diana A. Shy, PhD Student (until Sep.)
Valentin Sottas, PhD Student (until Nov.)
Sarah Vermij, PhD Student (since Aug.)

Collaborators

Bairoch A, SIB Swiss Institute of Bioinformatics (CH)
Decosterd I, University of Lausanne (CH)
Gaudet P, SIB Swiss Institute of Bioinformatics (CH)
Gertsch J, NCCR TransCure (CH)
Hatem SN, French National Research Agency, INSERM (FR)
Kucera JP, University of Bern (CH)
Lochner M, NCCR TransCure (CH)
Medeiros Domingo A, Inselspital (CH)
Remme CA, University of Amsterdam Academic Medical Center (NL)
Reymond JL, NCCR TransCure (CH)
Swan H, University of Helsinki (FIN)
Zaklyazminskaya EV, Moscow (RU)
Zambelli T, ETH Zurich (CH)

Grants

Amounts allocated for 2015:

- SNF: Molecular determinants of Nav 1.5 multiprotein complexes in cardiac cells (H. Abriel) CHF 214,000
- SNF: NCCR TransCure subproject: Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (M. Hediger, H. Abriel) CHF 260,000
- SNF: Interdisciplinary project: Force-controlled patch clamp (pc-FluidFM) (T. Zambelli, H. Abriel) CHF 59,000
- SNF: NavMutPredict, an interdisciplinary project to assess the severity of patients mutations with sodium channel channelopathies (A. Bairoch, H. Abriel) CHF 40,000
- DCR Grants-in-Aid: Regulation of L-type voltage-gated cardiac calcium channel Cav1.2 via a "new partner": CASK (J.-S. Rougier) CHF 5,000

Teaching Activities

- Dentistry students: Coordination of pathophysiology lectures
- Dentistry students: Kidney and electrolytes pathophysiology
- MSc Biomedical Sciences: Ion channels in cardiac diseases
- BSc Life Sciences: Cardiac ion channels in health and disease

Publications

Ion channel macromolecular complexes in cardiomyocytes: roles in sudden cardiac death. Abriel, H; Rougier, JS; Jalife, J (2015) in: Circ Res, 116(12), p. 1971-1988.

Cellular hyper-excitability caused by mutations that alter the activation process of voltage-gated sodium channels. Amarouch, MY and Abriel, H (2015) in: Front Physiol, 6, p. 45.

Inherited progressive cardiac conduction disorders. Baruteau, AE; Probst, V; Abriel, H (2015) in: Curr Opin Cardiol, 30(1), p. 33-39.

Na+ channel function, regulation, structure, trafficking and sequestration. Chen-Izu, Y; Shaw, RM; Pitt, GS; Yarov-Yarovoy, V; Sack, JT; Abriel, H; Aldrich, RW; Belardinelli, L; Cannell, MB; Catterall, WA; Chazin, WJ; Chiamvimonvat, N; Deschenes, I; Grandi, E; Hund, TJ; Izu, LT; Maier, LS; Maltsev, VA; Marionneau, C; Mohler, PJ; Rajamani, S; Rasmusson, RL; Sobie, EA; Clancy, CE; Bers, DM (2015) in: J Physiol, 593(6), p. 1347-1360.

Cardiac-specific ablation of synapse-associated protein SAP97 in mice decreases potassium currents but not sodium current. Gillet, L; Rougier, JS; Shy, D; Sonntag, S; Mougenot, N; Essers, M; Shmerling, D; Balse, E; Hatem, SN; Abriel, H (2015) in: Heart Rhythm, 12(1), p. 181-192.

Post-translational modifications of voltage-gated sodium channels in chronic pain syndromes. Laedermann, CJ; Abriel, H; Decosterd, I (2015) in: Front Pharmacol, 6, p. 263.

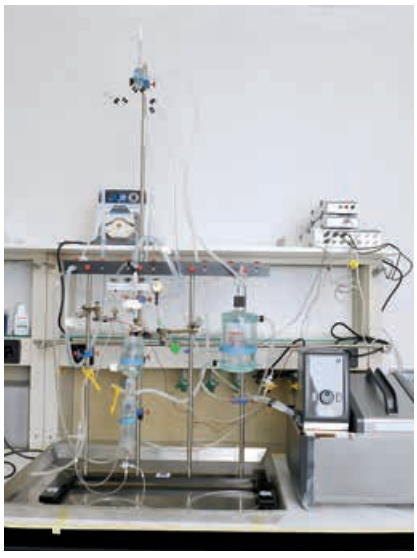
Regulation of the cardiac Na+ channel NaV1.5 by post-translational modifications. Marionneau, C and Abriel, H (2015) in: J Mol Cell Cardiol, 82, p. 36-47.

Force-controlled patch clamp of beating cardiac cells. Ossola, D; Amarouch, MY; Behr, P; Voros, J; Abriel, H; Zambelli, T (2015) in: Nano Lett, 15(3), p. 1743-1750.

Ubiquitin-specific protease USP2-45 acts as a molecular switch to promote alpha2delta-1-induced downregulation of Cav1.2 channels. Rougier, JS; Albesa, M; Syam, N; Halet, G; Abriel, H; Viard, P (2015) in: Pflugers Arch, 467(9), p. 1919-1929.

Complex genetic background in a large family with Brugada syndrome. Saber, S; Amarouch, MY; Fazelifar, AF; Haghjoo, M; Emkanjoo, Z; Alizadeh, A; Houshmand, M; Gavrilenko, AV; Abriel, H; Zaklyazminskaya, EV (2015) in: Physiol Rep, 3(1).

p.L1612P, a novel voltage-gated sodium channel Nav1.7 mutation inducing a cold sensitive paroxysmal extreme pain disorder. Suter, MR; Bhuiyan, ZA; Laedermann, CJ; Kuntzer, T; Schaller, M; Stauffacher, MW; Roulet, E; Abriel, H; Decosterd, I; Wider, C (2015) in: Anesthesiology, 122(2), p. 414-423.



Cluster for Regenerative Neuroscience

www.dkf.unibe.ch/downloads/forschungscluster/cluster-for-regenerative-neuroscience-engl.pdf

PD Dr. Volker Enzmann
volker.enzmann@insel.ch

PhD in Cell Biology (1995) and postdoc (1995-2000) at University of Leipzig (DE). Postdoc (2001-2005) and Assistant Professor (2005-2006) at University of Louisville (US). Since 2006, Head of Research, Ophthalmology, DCR. Venia Docendi (2010).

Prof. Dr. Stephen L. Leib
stephen.leib@ifik.unibe.ch

MD at University of Basel (1988). Certified in Internal Medicine (1995) and Infectious Diseases (1999). Research Fellow (1994-1996), University of California, San Francisco (US). Since 1997, Consultant Physician, Department of Infectious Diseases, Inselspital; SNF-Professorship (2002). Head, Division of Biology, Swiss Federal Office for Civil Protection, Spiez (2012-2015). Since 2015, Chair and Full Professor, Institute for Infectious Diseases, University of Bern.

PD Dr. Pascal Senn
pascal.senn@insel.ch

MD at University of Bern (1998). Certified in Ear, Nose & Throat Medicine (2005). Research Fellow Harvard Medical School, Boston (2005) and Stanford School of Medicine (2006) (US). Since 2007, Head of Inner Ear Research Laboratory, Department of Ear, Nose and Throat Diseases, Head and Neck Surgery, Inselspital. Venia docendi, University of Bern (2013) and University of Geneva (2014). Since 2014, Head of Ear Surgery, Audiology and Cochlear Implant Unit, Geneva University Hospitals.

Research Highlights 2015 / Outlook 2016

Institute for Infectious Diseases: We continued to characterise in detail the pathogenesis of inner ear damage in an infant rat model of pneumococcal meningitis (collaboration with P. Senn). We demonstrated for the first time that the bacterial dose / inoculum concentration used for infection directly correlates with the severity of sensorineural hearing loss. Thus, this disease model bridges the translational gap between basic and clinical science. Furthermore, we developed an in vitro assay capable of detecting the biological activity of *botulinum* neurotoxins on neurons derived from mouse embryonic stem cells, using electrophysiological recording on multi-electrode arrays. Given a further increase in sensitivity, this assay may replace the murine LD50-assay.

Neurosurgery: Our main research focus is to find innovative ways to improve cell transplantation approaches for Parkinson's disease (PD). In a rat model of PD, Stefanie Seiler found that a combination of cell grafts with concomitant infusion of neutralising Nogo-A antibodies results in significantly improved behaviour and a higher number of graft-derived dopaminergic fibres growing into the host brain (PhD project). This supports the view that inhibition of Nogo-A may offer a novel intervention for cell transplantation therapies in PD.

Obstetrics and Gynecology: Our research focused on the neuroregeneration following peripartum brain damage, using novel therapeutic approaches. The intranasal administration of mesenchymal stem cells led to neuroregeneration in a neonatal rat model. In the same model, subcutaneous injection of synthetic PreImplantation factor (sPIF) was able to reduce cell death, neuronal loss and restore cortical architecture. We attribute the effect to the inhibition of microRNA let-7 biosynthesis and the activation of cAMP-dependent protein kinase / calcium-dependent protein kinase signalling, leading to the expression of downstream factors that regulate neuronal growth, survival and remodelling.

Ophthalmology: In 2015, research continued on retinal degeneration and its stem cell-based endogenous and exogenous regeneration. Importantly, we found not only remnants of regenerative capacity in mammalian Müller cells in the degenerated retina but could also differentiate adult human stem cells in vitro into retinal pigment epithelium-like cells. Both results could take us further towards new treatment strategies for age-related macular degeneration, the leading cause of blindness in the elderly in the industrialised world.

Otorhinolaryngology, Head and Neck Surgery: In 2015, research continued on two EU FP7-funded, international research projects with the aim to improve cochlear implants, prostheses to restore hearing in the deaf, and to develop possible future therapies for hearing loss based on stem cells. In the NANOCI project, we were able to substantially improve the auditory nerve-electrode interface. In the OTOSTEM project, the above-mentioned model of meningitic hearing loss was developed (collaboration with S. Leib).

Prof. Dr. Daniel Surbek
daniel.surbek@insel.ch

MD at University of Basel (1988); FMH Obstetrics and Gynecology (1996). Research Fellow at Johns Hopkins University, Baltimore and Children's Hospital of Philadelphia (US) (1996) and Harris Birthright Centre, King's College Hospital, London (UK) (2000). Subspecialist in Maternal-Fetal Medicine (2000). Venia docendi (2002), University of Basel. Since 2005, Full Professor and Acting Chair, Department of Gynaecology and Obstetrics; Head, Division of Obstetrics and Feto-Maternal Medicine, Inselspital.

Prof. Dr. Hans Rudolf Widmer
hanswi@insel.ch

PhD at University of Zurich (1989). Postdoc (1991-1993) at University of Southern California, Los Angeles (US). Venia docendi (2003). Since 1996, Director, Research Laboratory, Department of Neurosurgery, Inselspital. Associate Professor for Neuroscience (2008), University of Bern.

Other Cluster Members

PD Dr. Marc Baumann, Research Associate
Dr. Stefano Di Santo, Research Associate
Dr. Denis Grandgirard, Research Associate
Dr. Marianne Jörger-Messerli, Research Associate
Dr. Martin Müller, Research Associate
Prof. Dr. Luigi Raio, Research Associate and Senior Consultant
Dr. Marta Roccio, Research Associate
PD Dr. Andreina Schoeberlein, Co-Head Research and Group Leader
Monika Kilchenmann, Laboratory Technician
Stephanie Lötscher, Laboratory Technician
Ursula Reinhart, Laboratory Technician
Philipp Schneider, Laboratory Technician
Anelia Schweri-Olac, Laboratory Technician
Susanne Wälchli, Laboratory Technician
Stefan Hahnewald, PhD Student
Stephen Jenkinson, PhD Student
Camilla Marini, PhD Student
Byron Oppliger, PhD Student
Michael Perny, PhD Student
Miriam Reisenhofer, PhD Student
Stefanie Seiler, PhD Student
Marialuigia Spinelli, MD-PhD Student
Carolyn Trepp, PhD Student

Selected Collaborators

Bordey A, Yale University School of Medicine (US)
Jazwinska A, University of Fribourg (CH)
Leppert D, Novartis Pharma AG, Basel (CH)
Meyer M, University of Southern Denmark (DK)
Rask-Andersen H, University of Uppsala (SE)

Selected Grants

Amounts allocated for 2015:

- SNF: Improving the outcome of bacterial meningitis: combination versus single drug adjuvant therapies (S. Leib) CHF 127,000
- SNF: NCCR TransCure – From transport physiology to identification of therapeutic targets (D. Surbek) CHF 100,000
- SNF: Regulation and Role of ABCA1-mediated Cholesterol Transfer in the Human Placenta in Health and Disease: Protecting the Fetal Environment and/or Maintaining Placental Endocrine Function? (C. Albrecht, D. Surbek) CHF 90,000
- SNF: Novel ways for improved cell replacement strategies in Parkinson's: The potential of Nogo-A neutralization (H.R. Widmer) CHF 80,000
- EU: NANOCI – Improving cochlear implants with nano- and stem cell technology (P. Senn) CHF 190,000
- EU: OTOSTEM – Stem cell based therapy of hearing loss (P. Senn, S. Leib) CHF 180,000
- Cryosafe: Neurogenic potential of umbilical cord-derived mesenchymal stem cells and extracellular vesicles (D. Surbek) CHF 60,000
- Novartis Foundation: 3D culture system for in vitro differentiation of sensory hair cells from somatic cochlear stem cells and pluripotent stem cells for ototoxic and regenerative compounds screening (M. Roccio, Senn Group) CHF 60,000
- Sutter-Stöttner Stiftung: Müller cells – possible candidates for endogenous repair of the degenerated mammalian retina? (V. Enzmann) CHF 50,000

Selected Publications

The antidepressant fluoxetine protects the hippocampus from brain damage in experimental pneumococcal meningitis. Liechti, FD; Grandgirard, D; Leib, SL (2015) in: Neuroscience, 297, p. 89-94.

Retinal differentiation of human bone marrow-derived stem cells by co-culture with retinal pigment epithelium in vitro. Mathivanan, I et al. (2015) in: Exp Cell Res, 333(1), p. 11-20.

PreImplantation Factor bolsters neuroprotection via modulating Protein Kinase A and Protein Kinase C signaling. Mueller, M et al. (2015) in: Cell Death Differ, 22(12), p. 2078-2086.

Cell cycle reactivation of cochlear progenitor cells in neonatal FUCCI mice by a GSK3 small molecule inhibitor. Roccio, M et al. (2015) in: Sci Rep, 5, p. 17886.

Loss of Nogo-A-expressing neurons in a rat model of Parkinson's disease. Schawkat, K et al. (2015) in: Neuroscience, 288, p. 59-72.

DCR Research Groups from the Inselspital

Forty-two research groups from departments of the Inselspital were affiliated with the DCR at the end of 2015. Below is a list of the groups and the names of the Chairs of Department, Heads of Research/ Laboratory and/or Group Leaders. Thirteen of the groups are featured on the following pages. Other groups will be featured in future annual reports.

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

Angiology: Prof. Dr. Iris Baumgartner

Audiology: Prof. Dr. Marco Caversaccio, Prof. Dr. Martin Kompis, PD Dr. Pascal Senn

Cardiology: Prof. Dr. Stephan Windecker, Prof. Dr. Paul Mohacsi, PD Dr. Stefano Rimoldi, Prof. Dr. Urs Scherrer, Prof. Dr. Christian Seiler, Prof. Dr. Thomas Suter, Prof. Dr. Hildegard Tanner

Cardiovascular Surgery: Prof. Dr. Thierry Carrel, Prof. Dr. Hendrik Tevaearai, PD Dr. Sarah Henning Longnus, PD Dr. Henriette Most

Clinical Radiopharmacy: Prof. Dr. Thomas M. Krause, PD Dr. Martin A. Walter

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

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

Endocrinology of the Breast: PD Dr. Petra Stute

Endocrinology / Diabetology (Adults): Prof. Dr. Peter Diem

Endocrinology / Diabetology / Metabolism (Paediatrics): Prof. Dr. Primus E. Mullis, Prof. Dr. Christa F. Flück, PD Dr. Jean-Marc Nuoffer, PD Dr. Amit V. Pandey

Endometriosis and Gynaecological Oncology: Prof. Dr. Michel D. Mueller, Prof. Dr. Nick A. Bersinger, Dr. Brett D. McKinnon

Endometrium & Ovary: Prof. Dr. Michael von Wolff

Experimental Haemostasis: Prof. Dr. Hans-Peter Kohler, PD Dr. Verena Schröder

Gastroenterology / Mucosal Immunology: Prof. Dr. Andrew Macpherson, Prof. Dr. Kathy McCoy, Dr. Markus Geuking, PD Dr. Jan Hendrik Niess

Geriatrics / Medicine of Ageing: Prof. Dr. Andreas Stuck, PD Dr. Andreas Schoenenberger

Haematology / Oncology (Paediatrics): Prof. Dr. Kurt Leibundgut, PD Dr. Alexandre Arcaro, Prof. Dr. Beatrice U. Müller

Hand Surgery: Prof. Dr. Esther Voegelin, Dr. Adriano Taddeo

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

Hepatology: Prof. Dr. Jean-François Dufour, PD Dr. Andrea de Gottardi, Prof. Dr. Jeff Idle, PD Dr. Nasser Semmo, Dr. Guido Stirnimann

Human Genetics: Prof. Dr. Sabina Gallati, PD Dr. André Schaller

Intensive Care Medicine: Prof. Dr. Jukka Takala, Prof. Dr. Stephan Jakob

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

Nephrology and Hypertension: Prof. Dr. Bruno Vogt, PD Dr. Geneviève Escher, Prof. Dr. Daniel Fuster, Prof. Dr. Uyen Huynh-Do, Prof. Dr. Stephan Krähenbühl, Prof. Dr. Markus Mohaupt, PD Dr. Andreas Pasch, Prof. Dr. Dominik Uehlinger

Neurology: Prof. Dr. Claudio L. Bassetti, Prof. Dr. Antoine Adamantidis, Prof. Dr. Marcel Arnold, Prof. Dr. Urs Fischer, Dr. Christian P. Kamm, Prof. Dr. René Müri, Prof. Dr. Kaspar Schindler, PD Dr. Michael Schüpbach, Prof. Dr. Roland von Känel

Neurosurgery: Prof. Dr. Andreas Raabe, Prof. Dr. Hans Rudolf Widmer

Oncology / Haematology (Adults): Prof. Dr. Martin Fey, Prof. Dr. Thomas Pabst

Ophthalmology: Prof. Dr. Sebastian Wolf, PD Dr. Volker Enzmann, PD Dr. Martin Zinkernagel

Orthopaedic Surgery: Prof. Dr. Klaus-Arno Siebenrock, Prof. Dr. Ernst B. Hunziker, Prof. Dr. Marius Keel, PD Dr. Dobrila Nesic

Osteoporosis: Prof. Dr. Kurt Lippuner, Dr. Shintani Nahoko

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

Plastic Surgery: Prof. Dr. Mihai Constantinescu

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

Pulmonary Medicine (Adults): Prof. Dr. Thomas Geiser, Dr. Manuela Funke, Prof. Dr. Christophe von Garnier

Pulmonary Medicine (Paediatrics): Prof. Dr. Thomas Geiser, PD Dr. Philipp Latzin

Radiation Oncology: Prof. Dr. Daniel Aebersold, PD Dr. Yitzhak Zimmer, Dr. Michaela Medová, PD Dr. Kathrin Zaugg

Radiology: Prof. Dr. Johannes T. Heverhagen, PD Dr. Hendrik von Tengg-Kobligk, PD Dr. Ingrid Böhm, Prof. Dr. Christof Granzow

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

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

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

Urology: Prof. Dr. George Thalmann, Dr. Marco Cecchini, Prof. Dr. Katia Monastyrskaya

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

Cardiology

www.cvrc.dkf.unibe.ch
www.dkf.unibe.ch/research-group/8/

Prof. Dr. Stephan Windecker
stephan.windecker@insel.ch

MD (1992) at University of Heidelberg (DE); FMH certification in Cardiology. Currently, Chair and Professor of Cardiology, University of Bern and Inselspital. President, European Association of Percutaneous Cardiovascular Interventions.

Prof. Dr. Paul Mohacsi
paul.mohacsi@insel.ch

MD at University of Zurich. Postdoc at Stanford University Medical Center (US). Since 1993, Medical Director, Heart Failure and Cardiac Transplantation and Head of Research (CHF/HTx), Department of Cardiology, Inselspital. Visiting Professor (2008, 2011) at University of British Columbia, Vancouver (CA). EMBA (2009) at University of Zurich. Since 2013, Full Professor and Chief Cardiologist, University of Bern.

PD Dr. Stefano Rimoldi
stefano.rimoldi@insel.ch

MD (2001) at University of Bern; FMH certification in Internal Medicine (2007) and Cardiology (2012). Postdoc (2010-2011) at University of Lausanne. Since 2013, Chief Resident, Inselspital. Venia legendi (2013).

Research Highlights 2015 / Outlook 2016

Mohacsi Group

We aim to minimise the side effects of immunosuppression often observed in heart transplant patients by studying mechanisms for optimisation of tailored immunosuppressive therapy. In collaboration with the Department of Clinical Chemistry, we investigated whether genetic polymorphisms in drug metabolism, transport and targets of immunosuppressants affect the drug dose required to achieve therapeutic blood trough drug levels in cardiac allograft recipients.

Rimoldi/Scherrer Group

Epidemiological studies demonstrate a relationship between pathological events in foetal life and increased cardiovascular risk in later life. We showed for the first time that assisted reproductive technologies (ART) cause premature atherosclerosis and hypertension in humans and mice. In mice, it is related to epigenetic changes of the eNOS gene, resulting in decreased vascular expression and function of this major regulator of cardiovascular homeostasis. Recently, we showed that modification of the culture media attenuates ART-induced phenotypic alteration in mice and that antioxidants attenuate ART-induced vascular dysfunction in humans, opening up avenues to prevent/restore ART-induced damage.

Suter Group

We seek to improve the prevention of and clinical management strategies for cancer drug-associated cardiovascular side effects. Ischemia and cardiotoxic compounds can lead to cellular damage and irreversible decline of cardiac function. Thus, it is critically important to understand the cardiovascular complications of cancer therapies in order to provide better diagnostics and therapy. In the lab, we investigated mechanisms of cardiotoxicity of old and new anti-cancer therapies in rodent and human iPSC-derived cardiomyocytes in 3D culture conditions.

Tanner Group

In 2015, we finished a prospective international multicentre trial studying the diagnostic yield of external prolonged electrocardiogram monitoring in unexplained syncope and palpitations. We also started the STAR-FIB Study Program, in which patients with high thromboembolic risk and prolonged atrial electromechanical interval are systematically screened for silent atrial fibrillation. Together with the Bern University of Applied Sciences, we continue to develop novel tools and software for long-term monitoring of cardiac arrhythmias. Leadless and batteryless pacing technologies are under development. The newly established cardiac-arrhythmia programme studies the molecular basis of arrhythmia syndromes and sudden cardiac death.

Windecker Group

We evaluated intracoronary device-related medication therapy (antithrombotic treatment) and imaging techniques for the treatment of coronary diseases. Our research is related to structural heart disease, including transcatheter aortic, mitral and tricuspid valve intervention, patent foramen ovale and left atrial appendage occlusion.

Prof. Dr. Urs Scherrer
urs.scherrer2@insel.ch

MD (1975) at University of Zürich. Professor emeritus (2011) at University of Lausanne. Since 2011, Visiting Professor, Department of Cardiology, Inselspital.

Prof. Dr. Christian Seiler
christian.seiler@insel.ch

Studied medicine (1979-1985) at University of Bern. Postdoc (1990-1992) at University of Texas Health Science Center, Houston (US). Since 1997, Director of Echocardiography; since 1998, Staff Physician Interventional Cardiology, Department of Cardiology, Inselspital. Venia docendi (1997); Associate Professor (2000); Full Professor (2010). Co-Head, Faculty of Medicine MSc curriculum. President, Bern Cantonal Ethics Committee.

Prof. Dr. Thomas M. Suter
thomas.suter@insel.ch

MD (1986) at University of Zurich. Cardiology and CCU/ICU Fellowship in internal medicine at University of Zurich. Fellowships (1992-1998) in cardiovascular physiology and cardiology at Boston University. Internship (1998) at Brigham and Women's Hospital, Boston (US). Since 2005, Associate Professor, University of Bern.

Prof. Dr. Hildegard Tanner
hildegard.tanner@insel.ch

MD (1994) at University of Bern; FMH certification in Internal Medicine (2001) and Cardiology (2003). Fellow in electrophysiology and cardiology in Bern. Research Fellow in electrophysiology (2003-2005) at Heart Center, University of Leipzig (DE). Since 2005, Attending Electrophysiologist, Department of Cardiology, Inselspital. Venia docendi (2009); Associate Professor of Cardiology (2014).

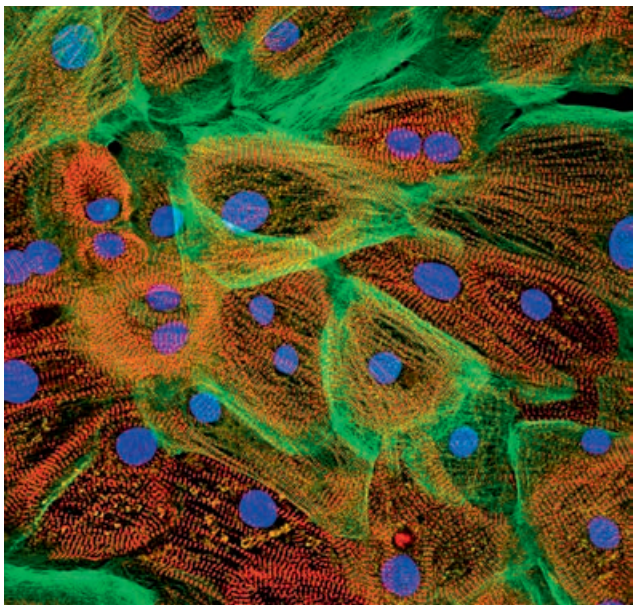
Group Members

Prof. Dr. Stephan Windecker, Chair
Dr. André Frenk, Head, Study Group
Prof. Dr. Thomas Pilgrim, Consultant
PD Dr. Lorenz Räber, Consultant
PD Dr. Stefan Stortecky, Consultant
Dr. Masahiko Asami, Research Associate
Dr. Anna Franzone, Research Associate
Dr. Raffaele Piccolo, Research Associate
Dr. Kyohei Yamaji, Research Associate

Prof. Dr. Paul Mohacsi, Group Leader
Dr. Raschid Setoud, Senior Scientist
Tina Borella, Laboratory Technician (since Jan.)

PD Dr. Stefano Rimoldi, Group Leader
PD Dr. Claudio Sartori, Group Leader (Lausanne)
Prof. Dr. Urs Scherrer, Group Leader
Dr. Emrush Rexhaj, Senior Scientist
Dr. David Cerny, Clinical Research Associate
Dr. Theo Meister, Clinical Research Associate
Dr. Rodrigo Soria Maldonado, Postdoctoral Fellow
Elisa Bouillet, Laboratory Technician

Prof. Dr. Christian Seiler, Group Leader
Dr. Nicolas Brugger, Research Assistant
Dr. Stefano de Marchi, Consultant
PD Dr. Steffen Gloekler, Consultant
PD Dr. Michael Stoller, Research Assistant
Prof. Dr. Thomas Suter, Group Leader
Dr. Christian Zuppinger, Senior Scientist
Prof. Dr. Hildegard Tanner, Group Leader
Dr. Jürg Fuhrer, Head of Rhythmology
Dr. Fabian Noti, Consultant
PD Dr. Laurent Roten, Consultant



Dr. Jens Seiler, Consultant
Dr. Helge Servatius, Consultant
Dr. Argelia Medeiros Domingo, Consultant and Research Associate
Dr. Andreas Häberlin, Research Associate
Dr. Anna Lam, Postdoctoral Fellow (since Feb.)
Helene Eigensatz, Study Nurse (since Jun.)
Nicole Klossner, Study Nurse (until May)
Babken Asatryan, PhD Student (since Sep.)

Selected Collaborators

Abriel H, University of Bern (CH)
Bailey D, University of South Wales (UK)
Jacomet M, Bern University of Applied Sciences (CH)
Largiadèr C, Inselspital (CH)
Locati TE, Ospedale Niguarda Ca' Granda, Milano (IT)

Selected Grants

Amounts allocated for 2015:

- SNF: Birth weight and hypertension (S. Rimoldi) CHF 168,000
- SNF: Insulin-resistance in offspring of assisted reproductive technologies (C. Sartori) CHF 150,000
- SNF: Predicting Silent Atrial Fibrillation in Patients at High Thrombo-embolic Risk (STAR-FIB Study Program) (L. Roten) CHF 179,392
- SNF: Natural IMA bypasses to the human collateral circulation: pathophysiologic and therapeutic aspects (C. Seiler) CHF 158,000
- SNF: Assessment of arrhythmias in patients undergoing TAVI using a small insertable cardiac monitoring device (F. Praz, G. Siontis, L. Rauten, S. Windecker) CHF 168,000
- SNF Nano-Tera.ch: Night Ambulatory Monitoring of Blood Pressure (S. Rimoldi, J. Sola) CHF 52,000
- Fondation Professeur Placide Nicod: Fetal programming (U. Scherrer, S. Rimoldi) CHF 100,000

Selected Publications

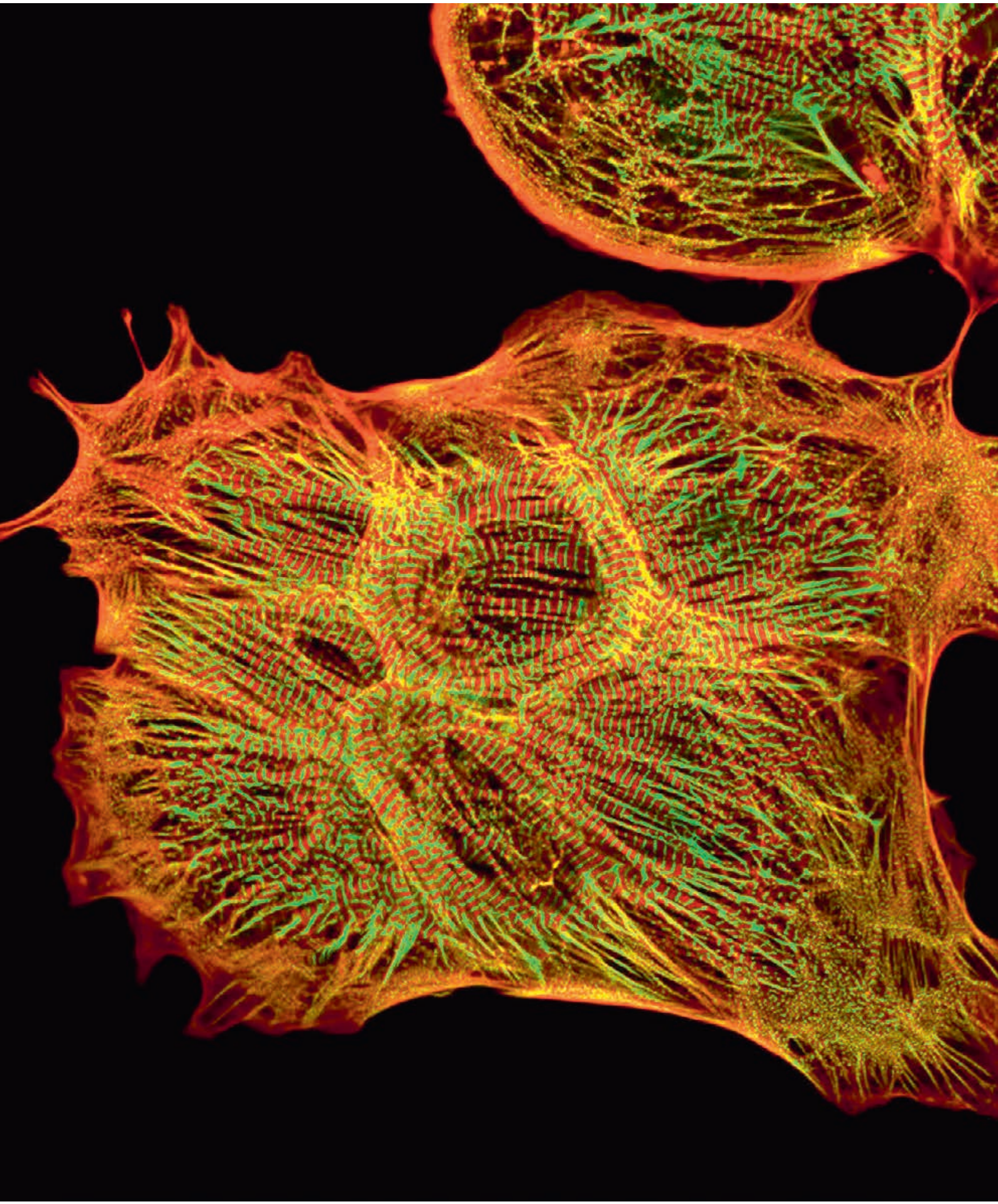
Prevention of vascular dysfunction and arterial hypertension in mice generated by assisted reproductive technologies by addition of melatonin to culture media. Rexhaj, E; Pireva, A; Paoloni-Giacobino, A; Allemann, Y; Cerny, D; Dessen, P; Sartori, C; Scherrer, U; Rimoldi, SF (2015) in: Am J Physiol Heart Circ Physiol, 309(7), p. H1151-H1156.

Development and Characterization of a Scaffold-Free 3D Spheroid Model of Induced Pluripotent Stem Cell-Derived Human Cardiomyocytes. Beauchamp, P; Moritz, W; Kelm, JM; Ullrich, ND; Agarkova, I; Anson, BD; Suter, TM; Zuppinger, C (2015) in: Tissue Eng Part C Methods, 21(8), p. 852-861.

The first batteryless, solar-powered cardiac pacemaker. Haeberlin, A; Zurbuchen, A; Walpen, S; Schaerer, J; Niederhauser, T; Huber, C; Tanner, H; Servatius, H; Seiler, J; Haeberlin, H; Fuhrer, J; Vogel, R (2015) in: Heart Rhythm, 12(6), p. 1317-1323.

Clinical impact of gastrointestinal bleeding in patients undergoing percutaneous coronary interventions. Koskinas, KC; Raber, L; Zanchin, T; Wenaweser, P; Stortecky, S; Moschovitis, A; Khattab, AA; Pilgrim, T; Blochlinger, S; Moro, C; Juni, P; Meier, B; Heg, D; Windecker, S (2015) in: Circ Cardiovasc Interv, 8(5).

Influence of CYP3A5 genetic variation on everolimus maintenance dosing after cardiac transplantation. Lesche, D; Sigurdardottir, V; Setoud, R; Englberger, L; Fiedler, GM; Largiader, CR; Mohacsi, P; Sistonen, J (2015) in: Clin Transplant, e-pub ahead of print.



Dermatology

www.dermatologie.insel.ch/de/lehreundforschung/
www.dkf.unibe.ch/research-group/72/

Prof. Dr. Luca Borradori
luca.borradori@insel.ch

MD (1986) at University of Bern; Resident in dermatology (1989-1993) at University Hospitals of Paris (FR), Lausanne and Geneva. Postdoc at National Cancer Institute, NIH, Bethesda (US) (1993-1995) and Division of Cell Biology, Netherlands Cancer Institute (NL) (1995-1997). Since 2005, Associate Professor, Geneva University Hospitals. Since 2008, Chair and Head, Department of Dermatology, Inselspital.

Dr. Arnaud Galichet
arnaud.galichet@dkf.unibe.ch

PhD (1999) at University of Reims (FR). Postdoc (1999-2004) at University of California at Berkeley (US) and ETH Zurich. Senior Postdoc (2005-2008) at Department of Pediatrics, University Children's Hospital Zurich and at Division of Psychiatry Research, University of Zurich (2005-2008). Since 2008, Group Leader at Institute of Animal Pathology and since 2015, also at Department of Dermatology, Inselspital.

Prof. Dr. Robert Hunger
robert.hunger@insel.ch

Studied medicine (1984-1990) at Universities of Freiburg (DE) and Bern; MD-PhD (1996) at University of Bern; board certification in Dermatology (2001). Postdoc (2001-2003) at Department of Dermatology, University of California, Los Angeles (US). Since 2011, Associate Professor, Department of Dermatology, Inselspital.

Research Highlights 2015 / Outlook 2016

Allergies

Acute generalised exanthematous pustulosis (AGEP) and generalised pustular psoriasis (GPP) are rare pustular skin disorders with systemic involvement. Interleukin-17 (IL17) is a key cytokine in the pathogenesis of neutrophilic inflammatory disorders. In collaboration with Mariagrazia Uguccioni (IRB, Bellinzona), we found that IL-17A/F-expressing cells were significantly increased in subcorneal pustules, epidermis and dermis of AGEP and GPP compared to normal skin. Innate immune cells such as neutrophils and mast cells are important cellular sources of IL-17A/F.

Eosinophils play a role in host defence as part of the innate immune system. They are able to kill bacteria by generating extracellular DNA traps (EETs). Eosinophilic oesophagitis (EoE) is characterised by oesophageal dysfunction owing to an eosinophil-predominant inflammation. We found that EETs in EoE tissue samples were proportional to the abnormally high number of eosinophils, which correlated with both a decreased expression of epithelial barrier proteins and an increased level of several cytokines. The formation of EETs could therefore serve as a firewall against the invasion of pathogens in oesophagi with impaired epithelial barrier function.

Autoimmune diseases

Pemphigus vulgaris (PV) autoantibodies mainly target an intercellular adhesion molecule of the desmosomal cadherin family in skin and mucous membranes. Our group and others discovered that these adhesion molecules act as receptors to transmit outside-in signals, which are required for normal skin homeostasis and are deregulated in PV. In 2015, we identified another pathogenic signalling pathway in PV implicating proliferation and the non-apoptotic level of caspase-3 activity. Furthermore, we found that deregulated Wnt and epidermal growth factor signalling in PV result in a transient loss of stem cell potential affecting normal skin renewal.

Chronic skin diseases

Hidradentitis suppurativa (HS) mainly affects the anogenital and axillary regions. Although the disease is relatively common (1% prevalence), our knowledge about the pathogenesis is very limited. In an ongoing project, we are analysing the molecular and cellular mechanisms leading to the chronic inflammation. We found that the antimicrobial peptide LL37 is up-regulated in the inflamed lesions and might maintain the chronic inflammation by directly stimulating resident T cells.

Cancer

Human T helper (TH) cells are crucial mediators of the immune system in health and disease. TH9 cells, a novel subset of TH cells that produce interleukin 9, mediate strong anti-tumour immunity in mouse models of melanoma. However, their identity and function in humans remain largely unknown. We therefore aim to define the surface phenotype of these cells in order to easily isolate them from human blood and tissues, and investigate their effector functions, phenotypic stability, and genetic regulation. A better understanding of TH9 cells will guide innovative T cell-based tumour immunotherapies.

Prof. Dr. Eliane J. Müller
eliane.mueller@dkf.unibe.ch

PhD (1991) at University of Fribourg. Postdocs at University of Sherbrooke (CA) (1991-1993) and Institutes of Microbiology (1993-1995) and Animal Pathology (1995-1997), University of Bern. Since 2008, Associate Professor, Institute of Animal Pathology and since 2014, also at Department of Dermatology, University of Bern. Head of DermFocus, Vetsuisse Faculty and Platform for Stem Cells and Regenerative Medicine, University of Bern.

Dr. Christoph Schlapbach
christoph.schlapbach@insel.ch

MD (2008) and MD-PhD (2012) at University of Bern. Postdoc (2011-2012) at Harvard Skin Disease Research Center, Boston (US). Since 2012, Resident and Group Leader, Department of Dermatology, Inselspital.

Prof. Dr. Dagmar Simon
dagmar.simon@insel.ch

MD (1989) at Friedrich Schiller University Jena (DE). Research fellowship (1991-1992) at Women's College Hospital, University of Toronto (CA). Board certifications in Dermatology (1993) and Allergy and Clinical Immunology (2003); PD (2006) at University of Bern. Since 2010, Associate Professor, Department of Dermatology, Inselspital.

Prof. Dr. Nikhil Yawalkar
nikhil.yawalkar@insel.ch

MD (1988) at University of Basel. Board certifications in Dermatology (1995) and Allergy and Clinical Immunology (1998) at University of Bern. Postdocs in USA at Department of Dermatology, UCSF School of Medicine (1995) and Harvard Skin Disease Research Center, Boston (US) (2000-2002). Since 2006, Associate Professor, Department of Dermatology, Inselspital.

Group Members

Prof. Dr. Luca Borradori, Chair and Head, Group Leader
Dr. Arnaud Galichet, Group Leader
Prof. Dr. Robert Hunger, Group Leader
Prof. Dr. Eliane Müller, Group Leader
Dr. Christoph Schlapbach, Group Leader
Prof. Dr. Dagmar Simon, Group Leader
Prof. Dr. Nikhil Yawalkar, Group Leader
Dr. Bertrand Favre, Laboratory Head
Dr. Dominik Waluk, Head of Research, DermFocus Lab
Dr. Beyza Sayar, Postdoctoral Fellow
Nadja Begré, Research Assistant
Fabiana Jakob, Laboratory Technician, DermFocus Lab
Ursula Läderach, Laboratory Technician
Evelyne Seger, Laboratory Technician
William Hariton, PhD Student
Claire Micossé, PhD Student
Dr. Jafari Morteza, PhD Student
Rahel Thomi, PhD Student

Selected Collaborators

Hertl M, Philipp University of Marburg (DE)
Knöpfel T, Imperial College London (UK)
Leeb T, University of Bern (CH)
Simon H-U, University of Bern (CH)
Uguccioni M, Institute for Research in Biomedicine (CH)

Selected Grants

Amounts allocated for 2015:

- SNF Sinergia: A One Health approach to Genodermatoses (subproject E. Müller) CHF 268,562
- Hans-Sigrist Foundation: Adhesion-dependent repair mechanisms in the hair follicle stem cell niche (E. Müller) CHF 58,493
- Martha Foundation: Unraveling EGFR-related signal pathways in pemphigus vulgaris (E. Müller) CHF 91,062
- Olga Mayenfisch Foundation: The role of human Th9 cells in cutaneous inflammation (C. Schlapbach) CHF 60,000
- Werner and Hedy Berger-Janser Foundation: Characterization of human interleukin 9 producing T helper cell (C. Schlapbach) CHF 60,000

Selected Publications

Immune response in pemphigus and beyond: progresses and emerging concepts. Di, ZG; Amber, KT; Sayar, BS; Muller, EJ; Borradori, L (2015) in: Semin Immunopathol, e-pub ahead of print.

Preclinical studies identify non-apoptotic low-level caspase-3 as therapeutic target in pemphigus vulgaris. Luyet, C; Schulze, K; Sayar, BS; Howald, D; Muller, EJ; Galichet, A (2015) in: PLoS One, 10(3), p. e0119809.

Homozygous missense mutation in IL36RN in generalized pustular dermatosis with intraoral involvement compatible with both AGEP and generalized pustular psoriasis. Navarini, AA; Simpson, MA; Borradori, L; Yawalkar, N; Schlapbach, C (2015) in: JAMA Dermatol, 151(4), p. 452-453.

The continuing evolution of targeted therapy for inflammatory skin disease. Schlapbach, C and Navarini, AA (2015) in: Semin Immunopathol, e-pub ahead of print.

Active eosinophilic esophagitis is characterized by epithelial barrier defects and eosinophil extracellular trap formation. Simon, D; Radonjic-Hosli, S; Straumann, A; Yousefi, S; Simon, HU (2015) in: Allergy, 70(4), p. 443-452.

Endocrinology / Diabetology / Metabolism (Paediatrics)

www.dkf.unibe.ch/research-group/15/

Prof. Dr. Primus E. Mullis

MD (1981) at University of Bern. Fellowships in Chur (1981-1982), Lucerne (1983-1985), Bern (1986) and University College London (UK) (1988-1990); FMH (1987); Deputy Consultant (1991-1992), Bern. FMH Pediatric Endocrinology (1991). Venia docendi (1992). Head (1993-1996), Professor (1997) and since 2000, Chair, Paediatric Endocrinology, Diabetology and Metabolism, Inselspital.

Prof. Dr. Christa E. Flück
christa.flueck@dkf.unibe.ch

MD (1992) at University of Bern. Residency and fellowships in Stans (1993), Lucerne (1994) and Bern (1995-2000); FMH (1998); Deputy Consultant (1999-2000), Bern. Postdoctoral Fellow (2001-2004) at University of California, San Francisco (US). Venia docendi (2006); Assistant Professor (2004-2010); since 2010, Associate Professor, Paediatric Endocrinology, Diabetology and Metabolism, Inselspital.

PD Dr. Jean-Marc Nuoffer
jean-marc.nuoffer@insel.ch

MD (1991) at University of Bern; FMH certification (1997). Postdoctoral Fellow (1997-1999) at Necker Hospital – Sick Children, Paris (FR). Venia docendi (2012). Since 2000, Head, Polyclinic of Metabolism, Paediatrics. Since 2003, Head, Clinical Metabolism and Orphan Diseases, Department of Clinical Chemistry.

Research Highlights 2015 / Outlook 2016

Our research groups study endocrine and metabolic disorders in children.

Mullis: Human growth and development

Human growth hormone (GH) has an important role in physiology and metabolism, and its defects cause isolated GH deficiency (IGHD). We characterised GH variants by GH secretion studies, in silico mutagenesis and molecular dynamics simulations. We performed detailed structural analyses of the GH-L76P mutant by generating recombinant wild type and mutant protein in *E. coli*. Using novel methods of fast proteolysis and thermal unfolding, we defined precise molecular mechanisms responsible for causing IGHD type 2 in patients. In 2016, we will continue to develop novel methods for characterisation of IGHD-causing mutations, and study GH production and secretion in humans.

Flück: Cellular and molecular biology of human steroid metabolism

We study androgen biosynthesis in sex development and reproduction. Using gene expression profiling, we searched for androgen regulators and identified retinoic acid receptor beta and angiopoietin-like protein 1. With Aurel Perren (Institute of Pathology), we described the alternative backdoor pathway for dihydrotestosterone synthesis in human ovary and confirmed its existence in the adrenal and testis. With the GC/MS team, (Bruno Vogt, Nephrology), we described the urine steroid metabolome (67 steroids) in babies, setting the standards needed to offer urine profiling as a diagnostic tool. In patients with disorders of sex development with NR5A1/SF-1 mutations, we investigated the role of LRH1 and described a larger cohort of 46,XY DSD patients with MAMLD1 mutations and their role in sex development.

Nuoffer: Clinical metabolism and orphan diseases

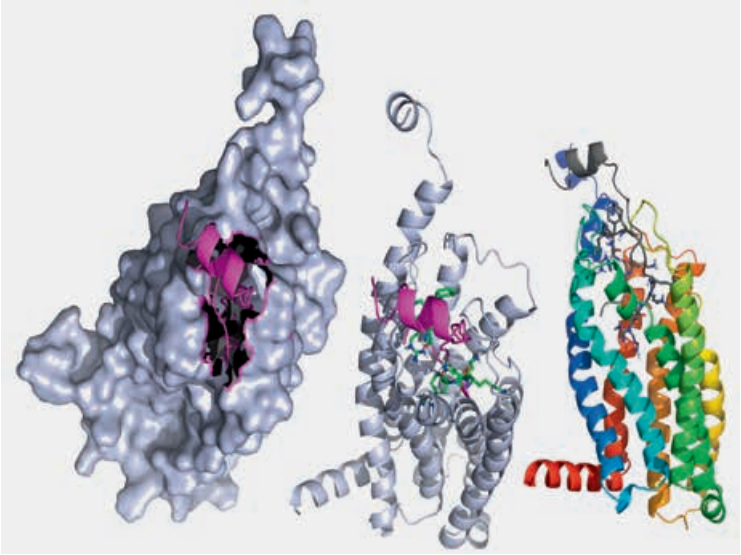
Argininosuccinate lyase (ASL) has a broad clinical spectrum ranging from life-threatening severe neonatal to asymptomatic forms. In 2015, we defined the molecular characteristics underlying the phenotypic variability in the variant forms of argininosuccinate lyase deficiency. These findings led to a new therapeutic approach (Chaperon therapy), tested in vitro. The second highlight was the description of a new disease: short-chain enoyl-CoA hydratase (ECHS1) deficiency (Ann Clin Transl Neurol, 2015 May; 2(5), p. 492-509). In 2016, we will focus on further investigation of ECHS1 and the use of HR-MAS NMR in the diagnosis of inborn errors of metabolism.

Pandey: Molecular and computational biology of metabolic disorders

We use spectroscopy and molecular dynamics to study variations in steroid metabolising enzymes. In an SNF-funded project, we characterised several mutations in P450 reductase protein and worked out the action and binding of anti-prostate cancer drugs with CYP17A1 enzyme. This allowed us to search for better candidate molecules to target prostate cancer. With the Flück Group, we created a 3D model of human MC2R receptor and designed inhibitors to treat congenital adrenal hyperplasia. This project will continue with funding from the IFCAH foundation (FR). In 2016, we will continue our collaboration with the University of Copenhagen (DK) on single-molecule microscopy studies of conformational changes in proteins.

PD Dr. Amit V. Pandey
amit.pandey@dkf.unibe.ch

PhD (2000) at Central Drug Research Institute (IN). Postdoctoral Fellow (2000-2003) and Research Scientist (2003-2005) at University of California, San Francisco (US). Research Scientist (2005-2007), Theodor Kocher Institute, Bern. Venia docendi (2010). Since 2007, Group Leader, Paediatric Endocrinology, Inselspital.



Group Members

Prof. Dr. Primus E. Mullis, Chair and Group Leader
Prof. Dr. Christa E. Flück, Group Leader
PD Dr. Jean-Marc Nuoffer, Group Leader
PD Dr. Amit V. Pandey, Group Leader

Dr. Marco Janner, Consultant
Dr. Matthias Gautschi, Deputy Consultant
Dr. Marie-Anne Burckhardt, Clinical Fellow (until Oct.)
Dr. Tanja Haamberg, Clinical Fellow
Dr. Dagmar Hahn, Research Associate
Dr. Nuria Camats, Postdoctoral Fellow (until July)
Dr. Balàzs Legeza, Postdoctoral Fellow
Dr. Jana Malikova, Postdoctoral Fellow (since Sep.)
Dr. Maria C. Miletta, Postdoctoral Fellow
Dr. Shaheena Parween, Postdoctoral Fellow
Dr. Sameer S. Udhane, Postdoctoral Fellow
Andrée Eblé, Laboratory Technician
Annemarie Haeberli, Laboratory Technician
Beatrice Lottaz, Laboratory Technician
Kay Sara Sauter Etter, Laboratory Technician
Thuvaraka Senthuran, Laboratory Technician (until Nov.)
Sandra Schlatter, Secretary
Nesa Marti, PhD Student

Selected Collaborators

Audi L, Vall d'Hebron University Hospital, Barcelona (SP)
Häberle J, University Children's Hospital Zurich (CH)
Hotzakis N, University of Copenhagen (DK)
Perren A, University of Bern (CH)
Vogt B, Inselspital (CH)

Selected Grants

Amounts allocated for 2015:

- SNF: Towards a better understanding of human androgen biology in health and disease (C.E. Flück) CHF 183,363
- SNF: Pathogenesis and therapy of mutations in human P450 oxidoreductase (A.V. Pandey) CHF 165,000
- Gottfried und Julia Bangerter-Rhyner Foundation: Human Sex Development – Gaining Further Insight by Studying Human Mutations (C.E. Flück, N. Camats) CHF 50,000
- Novo Nordisk Pharma: Understanding and rescuing growth hormone deficiency – molecular studies (P.E. Mullis) CHF 70,000

Selected Publications

Estimation of reference curves for the urinary steroid metabolome in the first year of life in healthy children: Tracing the complexity of human postnatal steroidogenesis. Dhayat, NA; Frey, AC; Frey, BM; d'Uscio, CH; Vogt, B; Rousson, V; Dick, B; Fluck, CE (2015) in: J Steroid Biochem Mol Biol, 154, p. 226-236.

Unstable argininosuccinate lyase in variant forms of the urea cycle disorder argininosuccinic aciduria. Hu, L; Pandey, AV; Balmer, C; Eggimann, S; Rufenacht, V; Nuoffer, JM; Haberle, J (2015) in: J Inherit Metab Dis, 38(5), p. 815-827.

A novel mutation in BCS1L associated with deafness, tubulopathy, growth retardation and microcephaly. Jackson, CB; Bauer, MF; Schaller, A; Kotzaeridou, U; Ferrarini, A; Hahn, D; Chehade, H; Barbey, F; Tran, C; Gallati, S; Haeberli, A; Eggimann, S; Bonafe, L; Nuoffer, JM (2015) in: Eur J Pediatr, e-pub ahead of print.

Retinoic acid receptor beta and angiopoietin-like protein 1 are involved in the regulation of human androgen biosynthesis. Udhane, SS; Pandey, AV; Hofer, G; Mullis, PE; Fluck, CE (2015) in: Sci Rep, 5, p. 10132.

IGHD II: A Novel GH-1 Gene Mutation (GH-L76P) Severely Affects GH Folding, Stability, and Secretion. Miletta, MC; Eble, A; Janner, M; Parween, S; Pandey, AV; Fluck, CE; Mullis, PE (2015) in: J Clin Endocrinol Metab, 100(12), p. E1575-E1583.

It is with great sadness that we inform you of the death of Prof. Dr. Primus E. Mullis. He passed away in January 2016.

Endometriosis and Gynaecological Oncology

www.dkf.unibe.ch/research-group/41/

Prof. Dr. Michel D. Mueller
michel.mueller@insel.ch

MD (1989) at University of Bern. Residencies in Aarberg, Biel, Münsterlingen, Bern. Postdoc (1998-2000) at University of California, San Francisco (US). Vice Chair (2005); currently Co-Chair, Department of Gynaecology and Obstetrics; Head, Gynaecology and Gynaecological Oncology, Inselspital.

Prof. Dr. Nick A. Bersinger
nick.bersinger@dkf.unibe.ch

PhD (1982) at University of Geneva. Postdocs at Department of Obstetrics and Gynaecology, University of Aberdeen, Aberdeen Royal Infirmary (UK) (1982-1984) and Reproductive Biochemistry and Immunology, Royal North Shore Hospital, University of Sydney (AU) (1990-1991). Venia docendi (2000). Associate Professor of Clinical Chemistry (2010). Currently Group Leader, Endometriosis and Gynaecological Oncology, DCR.

Dr. Brett McKinnon
brett.mckinnon@dkf.unibe.ch

PhD (2008) at University of Queensland (AU). Postdoc (2008-2014) at DCR. Since 2014, Group Leader, Endometriosis and Gynaecological Oncology, DCR. Associate Editor for Human Reproduction and Review Board Editor for Frontiers in Surgery (Obstetrics and Gynaecology section).

Research Highlights 2015 / Outlook 2016

Bersinger Group: Endometriosis and Inflammation

Endometriosis is a gynaecological condition with chronic pain and reduced fecundity, and is related to inflammation. It affects 15-20% of reproductive age women. Globally, 120 million women suffer from endometriosis and the European economy loses €30 billion each year due to pain-related absenteeism. The most widely accepted theory of endometriotic lesion development is retrograde menstruation – reflux into the peritoneal cavity of viable endometrial cells that attach to the underlying tissue and grow. However, as retrograde menstruation occurs in 80-90% of all women, additional factors must be involved.

Our research focus in 2015 and preceding years was on inflammation produced by the implantation and growth of endometriotic lesions. We study inflammatory cytokines, angio- and neurogenic factors in the peritoneum at both the gene expression and protein level. RT-qPCR is performed for these markers on RNA obtained from eutopic endometrium. At the protein level, ELISA and multiplexed double fluorescence-based immunoassays are run for these molecules present in the laparoscopically collected peritoneal fluid adjacent to the lesions. To date, we have collected samples from 887 patients. Results are set in relation to the levels of different types of pain reported by the patient and to the hormonal treatment received. Cultures of primary endometrial cells and cell lines are used as models for studying pathways of cytokine, angiogenic and neuro-stimulatory marker production.

McKinnon Group: Gynaecological Oncology

Epidemiological and genetic studies have confirmed a link between ovarian endometriosis and clear-cell and endometrioid ovarian cancer. Inflammation at the endometriotic lesions stimulates the development of the malignancy and we have postulated that this environment may contribute to its increased incidence. The inflammatory response is however considered a universal phenomenon; only a small percentage of women with endometriosis will have lesions that progress to a malignant phenotype. There must therefore be an innate or acquired attribute of the underlying epithelial or endometriotic cells that predispose them to malignant transformation. Kinase signalling pathways transmitting inflammatory signals may be dysregulated in ovarian cancer. We are therefore looking for aberrant kinase activity that can lead to neoplasia when coupled with an extracellular environment characteristic of endometriosis.

Endometrial carcinoma is the most common gynaecological malignancy and the prognosis is only good if detected early. Genetic mutations have been identified with links to endometrial cancer. Currently, these cancers are treated with extensive surgery but this increases the risk of overtreatment. As an addition to surgical improvement, we wish to develop a reliable method to identify women with specific genetic mutations that carry a recurrence risk in the early stages of the disease progression.

Group Members

Prof. Dr. Michel D. Mueller, Chair
Prof. Dr. Nick A. Bersinger, Group Leader
Dr. Brett McKinnon, Group Leader
Dr. Sara Imboden, Consultant
Dr. Laura Knabben, Consultant
Dr. Konstantinos Nirgianakis, Consultant
Anne Vaucher, Laboratory Technician
Juliette Wanner, Study Nurse

Selected Collaborators

Haouzi D, Saint Eloi Hospital (FR)
Greaves E, Queen's Medical Research Institute (UK)
Grandi G, University of Modena and Reggio Emilia (IT)

Selected Grants

Amounts allocated for 2015:

- SNF: Inflammation stimulated angiogenesis in endometriosis and ovarian cancer (M. Mueller) CHF 120,000
- SNF: Improving treatment of early stage endometrial cancer (M. Mueller) CHF 51,000

Selected Publications

H19 lncRNA alters stromal cell growth via IGF signaling in the endometrium of women with endometriosis. Ghazal, S; Mckinnon, B; Zhou, J; Mueller, M; Men, Y; Yang, L; Mueller, M; Flannery, C; Huang, Y; Taylor, HS (2015) in: EMBO Mol Med, 7(8), p. 996-1003.

A Comparison of Radiocolloid and Indocyanine Green Fluorescence Imaging, Sentinel Lymph Node Mapping in Patients with Cervical Cancer Undergoing Laparoscopic Surgery. Imboden, S; Papadia, A; Nauwerk, M; Mckinnon, B; Kollmann, Z; Mohr, S; Lanz, S; Mueller, MD (2015) in: Ann Surg Oncol, 22(13), p. 4198-4203.

Comparison of ovarian cancer markers in endometriosis favours HE4 over CA125. Mckinnon, B; Mueller, MD; Nirgianakis, K; Bersinger, NA (2015) in: Mol Med Rep, 12(4), p. 5179-5184.

Inflammation and nerve fiber interaction in endometriotic pain. McKinnon, BD; Bertschi, D; Bersinger, NA; Mueller, MD (2015) in: Trends Endocrinol Metab, 26(1), p. 1-10.

Induction of the neurokinin 1 receptor by TNFalpha in endometriotic tissue provides the potential for neurogenic control over endometriotic lesion growth. McKinnon, BD; Evers, J; Bersinger, NA; Mueller, MD (2013) in: J Clin Endocrinol Metab, 98(6), p. 2469-2477.

Experimental Haemostasis

www.dkf.unibe.ch/research-group/96/

Prof. Dr. Hans-Peter Kohler
hanspeter.kohler@spitaltiefenau.ch

MD (1991) at University of Bern; FMH certification in Internal Medicine (1998). Research fellowship (1996-1998) at University of Leeds (UK). Venia docendi (2001); Titular Professor (2006); Honorary Professor (2007) at University of Bern. Head of Internal Medicine (2000-2006) at Department of Emergency Medicine, Inselspital. Since 2000, Group Leader, FXIII Research Group, DCR and Inselspital. Since 2008, Head of Internal Medicine, Tiefenauspital, Insel Gruppe.

PD Dr. Verena Schröder
verena.schroeder@dkf.unibe.ch

MSc in Pharmacy (1999) at University of Basel; PhD (2003) at University of Basel with research conducted at Laboratory for Thrombosis Research, DCR. Postdocs at University of Bern (2003-2008) and University of Leeds (UK) (2008-2010). Since 2010, Senior Researcher and Group Leader, Experimental Haemostasis, DCR; venia docendi (2013).

Research Highlights 2015 / Outlook 2016

Our research deals with factors that influence thrombus formation and have implications for cardiovascular and thromboembolic diseases. One focus of our research is on coagulation factor XIII (FXIII), another is the complement system, and we also combine these two areas by studying interactions between FXIII, fibrin formation and components of the complement system.

Role of AP-FXIII

We continued to study the role of the FXIII activation peptide (AP-FXIII). By expressing novel missense mutants, we were able to identify amino acids that crucially contribute to the stabilisation of the FXIII-A2 dimer. We recently proposed for the first time a threefold role of AP-FXIII: 1) stabilising the FXIII-A2-dimer, which is not expressed at protein level when AP-FXIII is missing or shortened, 2) regulating FXIII activity by occluding the active site cavity, and 3) locally toning down further FXIII activation by free AP-FXIII released into plasma upon cleavage by thrombin.

Congenital FXIII deficiency

Together with our collaborators in Karachi (PK), we characterised further patients with congenital FXIII deficiency. We identified two novel mutations leading to this rare bleeding disorder that give further clues to the structure/function relationship of FXIII protein domains.

Mechanism of prothrombin activation by complement MASP-1

Mannan-binding lectin-associated serine protease 1 (MASP-1) of the complement lectin pathway interacts with several coagulation factors due to its similarity to thrombin. We and others have previously shown that MASP-1 cleaves the thrombin substrates fibrinogen, FXIII, TAFI and the PAR4 receptor on endothelial cells. We have demonstrated that MASP-1 induces clot formation via prothrombin activation. By expressing and studying several prothrombin mutants in which individual cleavage sites were abrogated, we showed for the first time the mechanism underlying prothrombin activation by MASP-1. Our finding may be of clinical relevance, as MASP-1 can directly promote clot formation and thus links inflammatory conditions with thrombotic complications.

A novel microvascular flow model

In spring 2015, Lorenz Jenny (PhD student with Verena Schröder) spent two months at the Georgia Institute of Technology (US) in the lab of Wilbur Lam, developer of a novel microvascular flow model [Tsai M, et al. J Clin Invest 2012; 122:408]. We have now set up this model in our lab. The model combines many features of blood vessels, including endothelial cells, whole blood, vessel structure with a diameter similar to human arterioles, and blood flow of physiological shear rates. It allows us to study clot formation and vessel occlusion in real time under the microscope. This model will enable us to investigate the complex interplay of endothelial and blood cells, the coagulation system, and the complement system in a more physiological environment and under certain pathological conditions.

Group Members

Prof. Dr. Hans-Peter Kohler, Group Leader
PD Dr. Verena Schröder, Group Leader
Lorenz Jenny, PhD Student

Selected Collaborators

Ajjan R, University of Leeds (UK)
Borhany M, National Institute of Blood Disease and Bone Marrow Transplantation (PK)
Dobó J, Gál P, Hungarian Academy of Sciences (HU)
Lam W, Emory University and Georgia Institute of Technology (US)
Thiel S, Aarhus University (DK)

Grants

Amounts allocated for 2015:

- SNF: Further characterisation of the activation steps of blood coagulation factor XIII, the role of its activation peptide and B-subunits, and their impact on clot formation, structure and lysis (H.-P. Kohler) CHF 77,400
- SNF: Interactions between complement and coagulation in cardio- and cerebrovascular diseases: Role of MASP-1 in clot formation (V. Schröder) CHF 86,406

Selected Publications

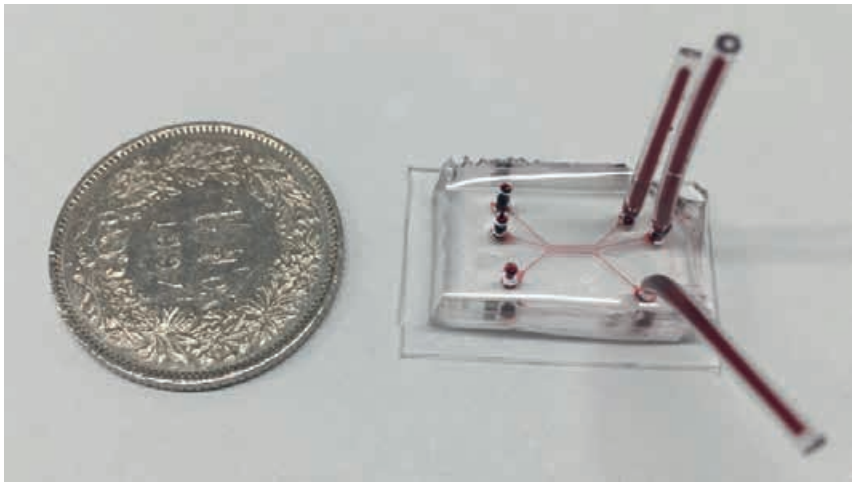
Identification of two novel missense mutations causing severe factor XIII deficiency. Handrkova, H; Borhany, M; Schroeder, V; Fatima, N; Hussain, A; Shamsi, T; Kohler, HP (2015) in: Haemophilia, 21(3), p. e253-e256.

The activation peptide of coagulation factor XIII is vital for its expression and stability. Handrkova, H; Schroeder, V; Kohler, HP (2015) in: J Thromb Haemost, 13(8), p. 1449-1458.

Plasma levels of mannan-binding lectin-associated serine proteases MASP-1 and MASP-2 are elevated in type 1 diabetes and correlate with glycaemic control. Jenny, L; Ajjan, R; King, R; Thiel, S; Schroeder, V (2015) in: Clin Exp Immunol, 180(2), p. 227-232.

MASP-1 of the complement system promotes clotting via prothrombin activation. Jenny, L; Dobo, J; Gal, P; Schroeder, V (2015) in: Mol Immunol, 65(2), p. 398-405.

Free factor XIII activation peptide affects factor XIII function. Schroeder, V; Handrkova, H; Dodt, J; Kohler, HP (2015) in: Br J Haematol, 168(5), p. 757-759.



Gastroenterology / Mucosal Immunology

www.dkf.unibe.ch/research-group/4/

Prof. Dr. Andrew Macpherson
Andrew.Macpherson@insel.ch

PhD in Biochemistry (1983); MB (1985) at University of Cambridge (UK). Research Group Leader and Senior Medical Staff (1998-2004) at University Hospital Zurich. Professor of Medicine (2004-2008) at McMaster University, Hamilton (CA). Since 2008, Chief of Gastroenterology and Co-Chair, Department of Visceral Surgery and Medicine, Inselspital.

Prof. Dr. Kathy McCoy
kathleen.mccoy@dkf.unibe.ch

PhD in Immunology (1997) at Otago University, Dunedin and Malaghan Institute of Medical Research, Wellington (NZ). Postdoc (1998-2000) and Senior Research Scientist /Group Leader (2000-2006) at Institute for Experimental Immunology, University Hospital Zurich. Assistant Professor (2006-2010) and Director of Axenic/Gnotobiotic Facility (2008-2010) at McMaster University, Hamilton (CA). Since 2010, Assistant Professor and Group Leader, Gastroenterology / Mucosal Immunology, DCR.

Dr. Markus Geuking
markus.geuking@dkf.unibe.ch

PhD in Molecular Biology and Immunology (2006) at University of Zurich and ETH Zurich. Postdoctoral Fellow (2006-2010) at McMaster University, Hamilton (CA). Since 2010, DCR Group Leader, Gastroenterology / Mucosal Immunology.

Research Highlights 2015 / Outlook 2016

Translational research into microbiome composition and function

We are studying the intestinal microbiome composition and function in ulcerative colitis and Crohn's disease patients. The collection of intestinal biopsies in the biobank of the Swiss Inflammatory Bowel Disease Cohort (http://ibdcohort.ch/) and biopsy samples from the Department of Gastroenterology, Inselspital allow us to study the mucosa-associated microbiome in a large number of patients. We aim to determine 'who is there' and 'what they are doing'. By combining metabolomic, metagenomic and metatranscriptomic approaches, we can study how metabolism of the intestinal microbes affects the mucous membranes and the immune system. The goal is to understand the biochemical processes that underlie intestinal inflammatory disease and the differences in the severity of the conditions, in order to improve therapies.

Host-microbial mutualism

Immunoglobulin A (IgA) is strongly induced in response to microbial colonisation. Many aspects of intestinal IgA function remain unclear, including its role in modulating microbiota composition or protecting the epithelial surface from microbes and their molecular products. We have been investigating the function of intestinal IgA using a system of reversible colonisation to pre-induce bacterial-specific IgA. This is followed by colonisation with metabolically labelled bacteria to determine the ability of specific IgA to protect from penetration of microbial products or modify the host metabolic response.

Maternal microbiota in postnatal development of innate immune system

Colonisation of the intestine of newborns occurs immediately after birth but exposure to microbial metabolites likely occurs in utero. We have found that the maternal microbiota extensively shapes the immune system of the offspring, with alterations in innate lymphoid and mononuclear cells and extensive reprogramming of intestinal transcriptional profiles. We aim to extend this study by characterising the mechanisms by which this occurs.

Mechanisms of hygiene-mediated immune dysregulation

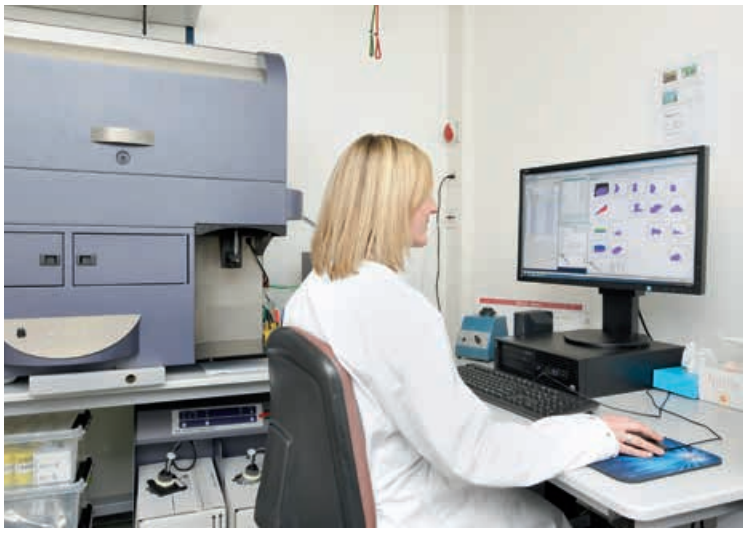
Microbial colonisation is critical for proper development and regulation of the immune system. We have been studying the pathways and cell types involved in sensing intestinal bacteria and regulating the immune system. In 2015, we focused on the microbial impact on gastrointestinal eosinophils, which are abundant in the small intestine. We also looked at how microbial colonisation regulates B cell development and the repertoire of naive B cells.

Impact of microbial composition early in life on immune regulation

We studied the minimal microbial diversity and the early life colonisation dynamics that limit induction of hygiene-mediated immunoglobulin E and protect from immune dysregulation. We are determining the metabolic capacity and activity of the microbiota required to induce immune regulation, with the aim to provide insight into the immune regulatory effects of microbial composition and diversity early in life.

PD Dr. Jan Hendrik Niess
jan.niess@insel.ch

MD (2002) at Friedrich Schiller University, Jena (DE). Postdoctoral Fellow (2001-2006) at Massachusetts General Hospital, Harvard Medical School, Boston (US). Group Leader and training in internal medicine and gastroenterology (2006-2012) at University of Ulm (DE). Since 2012, Attending Physician, Department of Visceral Surgery and Medicine, Inselspital.



Group Members

Prof. Dr. Andrew Macpherson, Chief of Gastroenterology and Co-Chair of Department
Prof. Dr. Kathy McCoy, Group Leader
Dr. Markus Geuking, Group Leader
Dr. Jan Niess, Group Leader
Prof. Dr. Reiner Wiest, Senior Consultant
PD Dr. Pascal Juillert, Consultant
Dr. Yilmaz Bahtiyar, Postdoctoral Fellow
Dr. Stephanie Ganal, Postdoctoral Fellow
Dr. Mercedes Gomez de Aguero, Postdoctoral Fellow
Dr. Li Hai, Postdoctoral Fellow
Dr. Julien Limenitakis, Postdoctoral Fellow
Dr. Francesca Ronchi, Postdoctoral Fellow
Dr. Yasuhiro Uchimura, Postdoctoral Fellow
Sarah Brand, Laboratory Technician
Beatrice Flogerzi, Laboratory Technician
Jessica Rieder Harrell, Laboratory Technician
Yasmin Köller, PhD Student
Cheong KC Kwong Chung, PhD Student (until July)
Catherine Mooser, MD-PhD Student
Sandra Rupp, PhD Student
Marcel Sorribas, PhD Student
Anna Steinert, PhD Student
Madeleine Wyss, PhD Student

Selected Collaborators

Hardt WD, ETH Zurich (CH)
Harris N, EPF Lausanne (CH)
Mueller C, University of Bern (CH)
Sauer U, ETH Zurich (CH)
Stecher B, Ludwig Maximilian University (DE)

Selected Grants

Amounts allocated for 2015:

- SNF: Secretory IgA in host-microbial reciprocity (A. Macpherson) CHF 254,097
- SNF: Swiss IBD Cohort Study – Microbiome-analysis in phenotypically and genotypically well characterized IBD patients (A. Macpherson) CHF 305,525
- SNF: Investigation into the effects of reduced or altered microbial composition early in life on immune regulation (K. McCoy) CHF 168,416
- SNF Sinergia: The host-microbial superorganism (A. Macpherson, C. Mueller, W.-D. Hardt, U. Sauer) CHF 736,675
- European Research Council: Mechanisms of hygiene-mediated immune dysregulation and impact on the susceptibility to allergic and autoimmune diseases (K. McCoy) CHF 300,000
- SystemsX.ch MRD: GutX-Systems biology of intestinal microbial metabolism in inflammatory bowel disease (A. Macpherson, U. Sauer, J. Stelling, C. von Mering) CHF 361,433

Selected Publications

The outer mucus layer hosts a distinct intestinal microbial niche. Li, H; Limenitakis, JP; Fuhrer, T; Geuking, MB; Lawson, MA; Wyss, M; Brugiroux, S; Keller, I; Macpherson, JA; Rupp, S; Stolp, B; Stein, JV; Stecher, B; Sauer, U; McCoy, KD; Macpherson, AJ (2015) in: Nat Commun, 6, p. 8292.

The bilateral responsiveness between intestinal microbes and IgA. Macpherson, AJ; Koller, Y; McCoy, KD (2015) in: Trends Immunol, 36(8), p. 460-470.

Standardised animal models of host microbial mutualism. Macpherson, AJ and McCoy, KD (2015) in: Mucosal Immunol, 8(3), p. 476-486.

New developments providing mechanistic insight into the impact of the microbiota on allergic disease. McCoy, KD and Koller, Y (2015) in: Clin Immunol, 159(2), p. 170-176.

CD4 T cells are required for both development and maintenance of disease in a new mouse model of reversible colitis. Brasseit, J; Althaus -Steiner, E; Faderl, M; Dickgreber, N; Saurer, L; Genitsch, V; Dolowschiak, T; Li, H; Finke, D; Hardt, WD; McCoy, KD; Macpherson, AJ; Corazza, N; Noti, M; Mueller, C (2015) in: Mucosal Immunol, e-pub ahead of print.

Link to publication list:
www.mucosalimmunology.ch/de/The-lab-University-of-Bern/Publications

Hand Surgery

www.handchirurgie.insel.ch
www.dkf.unibe.ch/research-group/64/

Prof. Dr. Esther Vögelin
esther.voegelin@insel.ch

Studied medicine at University of Basel. Clinical training in plastic/reconstructive surgery at Mount Vernon Hospital, Northwood (UK). Research Fellow in hand and microsurgery at University of California, Los Angeles (US). Since 2007, Head and Co-Chair, Hand Surgery and Surgery of the Peripheral Nerves, Department of Plastic and Hand Surgery, Inselspital.

Dr. Adriano Taddeo
adriano.taddeo@dkf.unibe.ch

Studied molecular medicine and immunology; PhD (2009) at University of Milan (IT). Postdoctoral Fellow (2010-2015) at German Rheumatism Research Center (DRFZ), Berlin (DE). Since 2015, Senior Researcher and Head of the Research Laboratory, Hand Surgery, DCR.

Research Highlights 2015 / Outlook 2016

Vascularised composite allotransplantations (VCA), particularly hand and face transplantations, have become valid reconstructive options for individuals suffering from injuries not amenable to traditional techniques. Currently, broader application of VCA is limited by the side effects of the lifelong immunosuppression required to avoid rejection. Our research focuses on the development of new therapies aimed at local drug delivery, in order to reduce toxicity and improve therapeutic outcomes. In collaboration with the DCR Cardiovascular Research Group, we designed and tested two different drug delivery systems: 1) Hydrogels loaded with the immunosuppressive drug tacrolimus (TAC), and 2) In situ forming implants (ISFI) loaded with the immunomodulatory drug rapamycin. The first system releases the drug 'on-demand' only under inflammatory conditions, the second modulates the graft milieu, promoting the development of regulatory T cells, a key cell type in transplantation tolerance. Using an in vivo model of VCA, we showed that local immunosuppression, both with TAC-hydrogel and rapamycin-ISFI, is able to prevent graft rejection for more than 100 days. These results could lead to a paradigm shift in clinical immunosuppression in VCA, tipping the risk-benefit ratio in favour of the recipients. In 2016, we will analyse the kinetics of drug release of the TAC hydrogel in physiological and inflammatory conditions as well as the immunological mechanisms by which prolonged survival of VCA is achieved during treatment.

In collaboration with the DCR groups of Cardiovascular Research, Plastic Surgery, and Cardiovascular Surgery, we established a system to perfuse amputated pig extremities with whole blood. We previously demonstrated that extracorporeal limb perfusion can be used to prolong time to replantation. Moreover, we performed experiments to investigate rejection mechanisms and the role of different genes in the context of xenotransplantation. In 2015, we used the extracorporeal perfusion system to investigate cytoprotective agents for prevention of ischemia/reperfusion injury. Our data showed that treating the amputated limb with the cytoprotective drug C1-inhibitor significantly reduced activation of the complement system, and deposition of immunoglobulin and fibrin observed during ischemia/reperfusion injury. In 2016, the analysis of the effects of the treatment will be continued and further markers of coagulation analysed to better understand whether this drug could be used to preserve traumatically amputated limbs.

In 2015, we organised the first "Advanced Course in Microsurgery" for surgeons of the Inselspital, in collaboration with the ESI, Experimental Surgery Unit and Matthias Hänggi (Intensive Care Medicine). Thanks to the positive feedback of participants, we would like to open up this course in 2016 to residents, surgeons, researchers or technicians interested in microsurgery.

Group Members

Prof. Dr. Esther Vögelin, Co-Chair and Head
Dr. Adriano Taddeo, Laboratory Head (since Mar.)
Dr. Bettina Juon, Consultant
Dr. Frank Leclère, Consultant
Dr. Jonas Schnider, Staff Surgeon
Dr. Damian Sutter, Research Assistant (until July)

Selected Collaborators

Costantinescu MA, Olariu R, Inselspital (CH)
Gorantola V, University of Pittsburgh (US)
Leroux JC, Luciani P, Plock JA, ETH and University Hospital Zurich (CH)
Rieben R, University of Bern (CH)
Vemula P, inStem (IN)

Selected Grants

Amounts allocated for 2015:

- SNF: Composite tissue preservation by extracorporeal blood perfusion and vascular cytoprotection to extend the time limit to replantation or transplantation (E. Vögelin, M.A. Constantinescu, R. Rieben) CHF 60,000
- SNF: Effect of a locally delivered immunosuppressives encapsulated in self-assembled hydrogel systems on vascularized composite allotransplantation (R. Rieben, E. Vögelin, P. Vemula) CHF 60,000
- Insel-Grant: Site specific immunosuppression with rapamycin encapsulated hydrogel in vascularized composite allotransplantation (J. Schnider, E. Vögelin, R. Rieben) CHF 70,000

Selected Publications

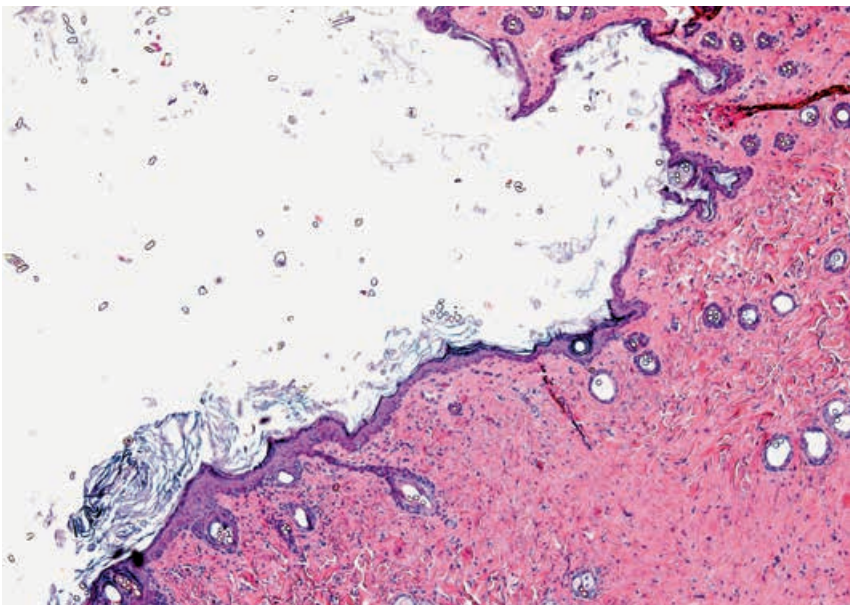
Porcine extrahepatic vascular endothelial asialoglycoprotein receptor 1 mediates xenogeneic platelet phagocytosis in vitro and in human-to-pig ex vivo xenoperfusion. Bongoni, AK; Kiermeir, D; Denoyelle, J; Jenni, H; Burlak, C; Seebach, JD; Vogelin, E; Constantinescu, MA; Rieben, R (2015) in: Transplantation, 99(4), p. 693-701.

Transgenic Expression of Human CD46 on Porcine Endothelium: Effect on Coagulation and Fibrinolytic Cascades During Ex Vivo Human-to-Pig Limb Xenoperfusions. Bongoni, AK; Kiermeir, D; Schnider, J; Jenni, H; Garimella, P; Bahr, A; Klymiuk, N; Wolf, E; Ayares, D; Voegelin, E; Constantinescu, MA; Seebach, JD; Rieben, R (2015) in: Transplantation, 99(10), p. 2061-2069.

Nerve Transfers for Persistent Traumatic Peroneal Nerve Palsy: The Inselspital Bern Experience. Leclere, FM; Badur, N; Mathys, L; Vogelin, E (2015) in: Neurosurgery, 77(4), p. 572-579.

A single localized dose of enzyme-responsive hydrogel improves long-term survival of a vascularized composite allograft. Gajanayake, T; Olariu, R; Leclere, FM; Dhayani, A; Yang, Z; Bongoni, AK; Banz, Y; Constantinescu, MA; Karp, JM; Vemula, PK; Rieben, R; Vogelin, E (2014) in: Sci Transl Med, 6(249), p. 249ra110.

Un modèle animal simple pour l'apprentissage des techniques de microanastomoses vasculaires de congruences différentes. Leclere, FM; Kolb, F; Lewbart, GA; Casoli, V; Vogelin, E (2014) in: Plast Surg (Oakv), 22(1), p. 30-33.



Hematology (Adults)

www.dkf.unibe.ch/research-group/68/

Prof. Dr. Anne Angelillo-Scherrer
anne.angelillo-scherrer@insel.ch

MD (1989) at University of Geneva; FMH certification (1999). Postdoc (1998-2000) at Catholic University of Leuven (BE). Attending Physician / Group Leader (2000-2005) at Division of Angiology and Hemostasis, University Hospitals Geneva. SNF Professor (2005-2011); Associate Professor (2011-2013); Director, Hemophilia Center and Hemostasis Laboratory, Lausanne University Hospital. Since 2013, Full Professor of Hematology and Chair, Department of Hematology, Inselspital.

Research Highlights 2015 / Outlook 2016

Mouse Models of Hematophysiology and Hematopathology and their Translation to Human Hematological Disorders Group

Both Gas6 and protein S (PS) belong to the vitamin K-dependent protein family and bind to the receptor tyrosine kinases Tyro3, Axl and Mer. We generated and studied Gas6- and PS-deficient mice to gain insights into the role of Gas6/PS in haemostasis and inflammation. In 2015, we focused on preclinical studies of PS-targeting for use in haemophilia treatment, and on investigating the mechanism of purpura fulminans and the role of Gas6/PS in inflammation and sepsis. Perspectives include clinical trials involving Gas6/PS agonists or antagonists to treat human diseases such as bleeding disorders, thrombosis and sepsis.

Prof. Dr. Gabriela M. Baerlocher
gabriela.baerlocher@insel.ch

MD (1990) at University of Bern; FMH and FAMH certification (1999, 2002). Postdoc at University of Southern California, Los Angeles (US) (1991-1992) and Terry Fox Institute, Vancouver (CA) (1999-2002). Venia docendi (2006). Associate Professor (2010). Since 2005, Head, Clinical Stem Cell Laboratory and since 2014, Vice-Chair, Department of Hematology, Inselspital.

Hematopoiesis and Molecular Genetics Group

We published a clinical study demonstrating the effect of a novel therapy for myeloproliferative neoplasms (MPNs). In MPNs, such as essential thrombocythemia, the telomerase inhibitor imetelstat selectively inhibits neoplastic cell growth. In a phase II clinical study, all patients reached rapid and sustained clinical and molecular responses. Next generation sequencing revealed additional mutations that were mostly suppressed by imetelstat treatment. Telomere length measurement and mutational screening of 12 telomere-associated genes was performed for patients with bone marrow failure syndromes. Characterisation of endothelial cells in MPN revealed a procoagulant and inflammatory signature by the JAK2 V617F mutation. In 2016, N. Bonadies will set up a biobank linked to the Swiss Registry for Myelodysplastic Syndromes (MDS) and start a study integrating the biological layers of genome, transcriptome and phospho-proteome, to characterise the patterns of individual clonal dynamics in MDS patients under therapy.

Prof. Dr. Johanna A. Kremer Hovinga
johanna.kremer@insel.ch

MD (1990) at University of Bern; FMH certification (1999 and 2004). Postdoc (1999-2001) at Academic Medical Center, Amsterdam (NL). Venia docendi (2009). Since 2007, Head, Hemostasis Research Laboratory and since 2013, Head, Hemophilia Consultation, Department of Hematology and Central Hematology Laboratory, Inselspital. Associate Professor of Hematology (2015).

Hemostasis Group

Severe ADAMTS13 deficiency, hereditary or acquired due to (inhibitory) autoantibodies leads to thrombotic thrombocytopenic purpura (TTP). Long-lasting remission can be achieved in frequently relapsing TTP by splenectomy. We are working on the characterisation of the ADAMTS13-specific autoimmune response using single cell sorting and deep sequencing of splenic B-cells and generation of monoclonal anti-ADAMTS13 antibodies. The latter are used to select small molecules (DARPINs) with broadly neutralising capacity in large numbers of acquired TTP patients. Another focus is on the natural course and long-term outcome in rare hereditary TTP.

Inflammation and Hematopoiesis Group

Haematopoiesis is a complex process by which mature blood cells of distinct lineages are produced from pluripotent haematopoietic stem cells. Defects in this process lead to several haematological malignancies. Recent studies suggest that inflammation influences haematopoiesis and that chronic inflammation might contribute to the development of haematopoietic malignancies. We are studying this relationship and the detailed molecular mechanism of the inflammation-associated malignancies. This group started in 2015, with the award of an SNF Professorship to R. Allam.

PD Dr. Elisabeth Oppliger Leibundgut
elisabeth.oppliger@insel.ch

MSc in Pharmacy (1986); PharmD (1996). Postdoc (1997-1999) at University of Bern. FAMH certification in Medical Genetics (2004). Venia docendi (2013). Since 1999, Head, Hematological Molecular Diagnostics, Department of Hematology, Inselspital.

Prof. Dr. Ramanjaneyulu Allam
allam.ramanjaneyulu@dkf.unibe.ch

PhD (2010) at University of Munich (DE). Postdoc at University of Lausanne (2010-2014) and University of Bern (2014-2015). Since 2015, SNF Professor, Department of Hematology, Inselspital and Group Leader, Inflammation and Hematopoiesis, DCR.

Group Members

Translational Hematology Research
Prof. Dr. Anne Angelillo-Scherrer, Group Leader
Dr. Peter Keller, Staff Physician
Dr. Michael Nagler, Staff Physician
Dr. Sara Calzavarini, Postdoctoral Fellow
Dr. Natacha Dewarrat, MD Student
Federica Bisignani, Laboratory Technician
Claudia Quarroz, Laboratory Technician
Luca Bologna, PhD Student
Raja Prince, PhD Student

Hematopoiesis and Molecular Genetics
Prof. Dr. Gabriela M. Baerlocher, Group Leader
PD Dr. Elisabeth Oppliger Leibundgut, Group Leader
Dr. Nicolas Bonadies, Staff Physician
Dr. Monica Haubitz, Postdoctoral Fellow
Dominik Gygax, Laboratory Technician
Ingrid Helsen, Laboratory Technician
Dania Hiltbrunner, Laboratory Technician
Anna Pham, PhD Student

Hemostasis
Prof. Dr. Johanna A. Kremer Hovinga, Group Leader
Prof. Dr. Kenneth J. Clemetson, Senior Scientist
PD Dr. Monica Schaller Tschan, Senior Postdoctoral Fellow
Isabella Aebi-Huber, Laboratory Technician
Irmela Sulzer, Laboratory Technician
Corinne Eschler, PhD Student
Magdalena Skowronska, PhD Student

Inflammation and Hematopoiesis
Prof. Dr. Ramanjaneyulu Allam, Group Leader
Dr. Nicola Andina, Postdoctoral Fellow and Staff Physician
Giuseppe Bombaci, PhD Student
Aubry Tardivel, Research Associate

Selected Collaborators

Crow Y, University of Manchester (UK)
George JN, University of Oklahoma (US)
Heinis C, EPFL (CH)
Hoang T, University of Montreal (CA)
Röth A, University of Essen (DE)

Selected Grants

Amounts allocated for 2015:

- SNF: Role of Ribonuclease inhibitor (RNH1) in Hematopoiesis and Inflammation (R. Allam) CHF 372,436
- SNF: Gas6 and protein S pathways in hemostasis, thrombosis and inflammation (A. Angelillo-Scherrer) CHF 252,000
- Bayer Hemophilia Award: Blocking protein S to treat haemophilia (A. Angelillo-Scherrer) CHF 95,000
- Baxalta Innovations GmbH: Hereditary TTP registry (J.A. Kremer Hovinga)
- Geron Corporation: Dynamics of mutations in patients with ET treated with Imetelstat (G.M. Baerlocher, E. Oppliger Leibundgut)
- Research Grant of the Inselspital for early stage researchers: Convergence of Recurrent Somatic Mutations and Epigenetic Alterations towards Targetable Oncogenic Signaling Pathways in High-risk Myelodysplastic Syndromes and Secondary Acute Myeloid Leukaemia (N. Bonadies) CHF 80,000

Selected Publications

Epithelial NAIPs protect against colonic tumorigenesis. Allam, R et al. (2015) in: J Exp Med, 212(3), p. 369-383.

A Synthetic Factor XIIa Inhibitor Blocks Selectively Intrinsic Coagulation Initiation. Baeriswyl, V et al. (2015) in: ACS Chem Biol, 10(8), p. 1861-1870.

Telomerase Inhibitor Imetelstat in Patients with Essential Thrombocythemia. Baerlocher, GM et al. (2015) in: N Engl J Med, 373(10), p. 920-928.

Establishment of the WHO 1st International Standard ADAMTS13, plasma (12/252): communication from the SSC of the ISTH. Hubbard, AR; Heath, AB; Kremer Hovinga, JA (2015) in: J Thromb Haemost, 13(6), p. 1151-1153.

IL-33 signaling contributes to the pathogenesis of myeloproliferative neoplasms. Mager, LF et al. (2015) in: J Clin Invest, 125(7), p. 2579-2591.

Link to publication list:
www.hzl.insel.ch/de/aerzte-klinik/lehre-forschung/publikationen/

Magnetic Resonance Spectroscopy and Methodology (AMSM)

www.amsm.dkf.unibe.ch
www.dkf.unibe.ch/research-group/40/

Prof. Dr. Chris Boesch
chris.boesch@insel.ch

PhD in Physics with Kurt Wüthrich at ETH Zurich. Swiss State License and MD at University of Zurich. Postdoc (1985-1990) at University Children's Hospital Zurich. Since 1991, Professor at University of Bern; DCR since 1995; Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital since 2011. Visiting Professor (2006) at Université Lyon 1 (FR). President of MR Societies (ESMRMB 1997, ISMRM 2001). Silver medallist (ISMRM) and Fellow (ISMRM and ESMRMB). President of SNF Research Commission, University of Bern (2008-2013). Since 2013, Member, SNF National Research Council.

Prof. Dr. Roland Kreis
roland.kreis@insel.ch

PhD in Chemistry with Richard Ernst at ETH Zurich. Postdoc and Boswell Fellow at Caltech and HMRI (US) (1989-1992). At University of Bern since 1992; Habilitation (2000), Titular Professor, later converted to Associate Professor (2006). Fellow of ISMRM (2011) and ESMRMB (2012).

Prof. Dr. Peter Vermathen
peter.vermathen@insel.ch

PhD in Physical Chemistry with Prof. Müller-Warmuth at University of Münster (DE). Postdoc (1995-1996), DFG Fellow (1996-1998), Assistant Specialist (1998-2000) at University of California, San Francisco (US). At University of Bern since 1999; Habilitation (2008); Associate Professor (2013).

Research Highlights 2015 / Outlook 2016

Magnetic resonance imaging (MRI) and spectroscopy (MRS) are powerful and extremely versatile methods for non-invasive studies and diagnostic examinations in humans. Our group uses these methods primarily in prospective studies and combines methodological development with applications to study physiology and pathology, together with the underlying mechanisms, in situ. Three SNF grants with PIs in our group, five SNF grants in collaboration with other groups, and one EU-funded training network define the direction of our research.

For more than a decade, insulin resistance has been a major research topic of our group and is supported by ongoing SNF grants. While insulin resistance is a major cause of cardiovascular diseases such as stroke and myocardial infarction, we study the effects of chronic or acute exercise and different kinds of carbohydrates, lipids and amino acids on muscle and liver metabolism. Several strong collaborations are based on this research topic (Internal – Inselspital: Endocrinology, Diabetology, Hepatology; University of Bern: pre-clinical institutes. External – Lausanne (CH), Pittsburgh (US), Lyon (FR), and Tübingen (DE)).

A second SNF grant aims to develop MR acquisition and synergistic post-processing methods that are tailored to the observation of brain metabolism yet are also transferable to other organs. In collaboration with the ETH and University of Zurich as well as the Max Planck Institute, Tübingen (DE), exchange processes between amide protons and water, diffusion-weighted MRS as well as general MRS at very high fields were studied in human brain and skeletal muscle. Three PhD students are currently working in this area.

We are investigating renal function in native and transplanted kidneys by multi-modal MRI and MRS in another SNF project in collaboration with the Department of Nephrology. Repeatability studies employing functional MRI have been performed. In collaboration with groups from the Institute for Surgical Technology and Biomechanics, image post processing was developed to minimise motion artefacts (PhD project M. Seif).

High-resolution magic angle spinning (HR-MAS) was applied to metabolically characterise tissue spectra and correlate in vivo and vitro spectra. Several HR-MAS studies have been performed on biopsies like brain, muscle, breast, liver, or kidney and on cell cultures and analysed by metabonomic methods (PhD project G. Diserens, MSc project D. Hertig). Numerous internal and external collaborations have been established for these studies.

TRANSACT (TRAnsforming Magnetic Resonance Spectroscopy into A Clinical Tool) is an EU-funded Marie Curie Initial Training Network (www.transact-itn.eu) that aims at improving and automating MRS methods and post-processing tools such that the clinical use of MRS becomes more robust and widespread. The specific aim of our subproject is the definition and automatic recognition of spectral quality and clinical usability such that radiologists without specific methodological knowledge are better able to routinely use MRS.

Group Members

Prof. Dr. Chris Boesch, Head of Research
Prof. Dr. Roland Kreis, Group Leader
Prof. Dr. Peter Vermathen, Group Leader
Dr. Tania Buehler, Postdoctoral Fellow
Karin Zwygart-Brügger, Technician
Anja Elstner, Research Assistant (until Sep.)
Victor Adalid, PhD Student
Gaëlle Diserens, PhD Student
Sila Dokumaci, PhD Student
André Döring, PhD Student
Nicole Fichtner, PhD Student
Bertrand Pouymayou, PhD Student
Sreenath Pruthviraj Kyathanahally, PhD Student
Maryam Seif, PhD Student (until Dec.)
Marc Stadelmann, PhD Student

Selected Collaborators

Carlier P, Wary C, Pitié-Salpêtrière Hospital (FR)
Möller H, MPI for Human Cognitive and Brain Sciences (DE)
Prüssmann K, Kozerke S, ETH Zurich (CH)
Tappy L, Amati F, Pralong F, Zurich MG, University of Lausanne (CH)
Thomas AM, University of California, Los Angeles (US)

Selected Grants

Amounts allocated for 2015:

- SNF: Multi-nuclear magnetic resonance spectroscopy (MRS) and imaging (MRI) on a clinical whole-body MR-system: Lipid organelles and mitochondria (C. Boesch) CHF 177,450
- SNF: Magnetic resonance techniques to determine metabolite levels: extending scope and clinical robustness (R. Kreis) CHF 169,382
- SNF: Advanced multi-modal MR Imaging and Spectroscopy for Comprehensive Characterization of Renal Function in Native and Transplanted Kidneys (P. Vermathen) CHF 86,922
- EU: Marie Curie ITN "TRANSACT" (R. Kreis) CHF 68,076

Selected Publications

Comparison of (31)P saturation and inversion magnetization transfer in human liver and skeletal muscle using a clinical MR system and surface coils. Buehler, T; Kreis, R; Boesch, C (2015) in: NMR Biomed, 28(2), p. 188-199.

Separation of small metabolites and lipids in spectra from biopsies by diffusion-weighted HR-MAS NMR: a feasibility study. Diserens, G; Vermathen, M; Precht, C; Broskey, NT; Boesch, C; Amati, F; Dufour, JF; Vermathen, P (2015) in: Analyst, 140(1), p. 272-279.

Motion-insensitive determination of B1+ amplitudes based on the bloch-siegert shift in single voxels of moving organs including the human heart. Dokumaci, AS; Pouymayou, B; Kreis, R; Boesch, C (2015) in: Magn Reson Med, e-pub ahead of print.

Does superficial fat affect metabolite concentrations determined by MR spectroscopy with water referencing? Kyathanahally, SP; Fichtner, ND; Adalid, V; Kreis, R (2015) in: NMR Biomed, 28(11), p. 1543-1549.

Image registration for triggered and non-triggered DTI of the human kidney: reduced variability of diffusion parameter estimation. Seif, M; Lu, H; Boesch, C; Reyes, M; Vermathen, P (2015) in: J Magn Reson Imaging, 41(5), p. 1228-1235.

Link to publication list:
www.amsm.dkf.unibe.ch/paper-0.htm

Neurology

www.neuro-bern.ch/
www.dkf.unibe.ch/research-group/14/

Research Highlights 2015 / Outlook 2016

In 2015, Urs Fischer was elected "Professor Extraordinarius" for acute neurology and stroke. A total of 14 SNF grants were running in our department. A Sinergia grant was received by a consortium including Prof. Bassetti (PI), Prof. Adamantidis, Prof. Müri, Prof. Huber (Zurich), and Prof. Massimini (Milano) on a project about sleep, neuroplasticity and stroke recovery. A total of 61 original publications were published, including the 'highlight' paper on the identification of a new wakefulness circuit that signals the termination of light sleep (Gutierrez et al., Nat Neurosci).

In 2016, Prof. Chan, who was elected the new Chair of the Ambulatory Neurocenter, will start his work in Bern. His research interests include the investigation of mechanisms of autoimmune inflammatory reactions in the nervous system in vitro, in animal models and in humans. He is also interested in the identification of molecular and clinical markers to predict the risk of disease progression and to assess benefit/risk profiles under different immunotherapies.

Sleep-Wake Mechanisms/Disorders and Epilepsy Group

In rodents, we developed and implemented high-density electrophysiology and cellular network imaging in freely moving mice to further dissect the brain mechanisms of sleep-wake states/functions and sleep-related neuroplasticity after stroke. In humans, a data-driven statistical model of intracranial EEG (iEEG) was developed to simulate the effect of localised therapeutic interventions and was shown to replicate key features of functional intracranial networks (Steimer et al., Neuroimage, 2015). We also succeeded in recording multi- and single-unit neuronal activity in human epilepsy patients undergoing pre-surgical evaluation.

Stroke Group

In 2015, five international trials (one with Bern: Saver et al., New Engl J Med) showed that mechanical thrombectomy in addition to intravenous recombinant tissue-type plasminogen activator improves outcome in patients with large artery anterior circulation stroke. These reports confirm our pioneering work on endovascular therapy in stroke. A second highlight was a joint publication with our neuropaediatric team on the long-term outcome of children/young adults after stroke (Goeggel et al., Neurology).

Neurorehabilitation/Cognitive Disorders Group

In 2015, two collaborative SNF research projects, granted in 2014, with Prof. Annoni (Fribourg) and Prof. Bohlhalter (Lucerne) were started. The focus is on executive functions and language, and on interference of gesture control and transcallosal white matter integrity.

Movement/Motor Disorders Group

Following a proof of concept study (Pollo et al., Brain, 2014), the team began new studies on directional deep-brain stimulation using segmented electrodes.

Neuropsychosomatic Group

Several prospective studies on an increased thrombotic risk in sleep apnoea and depression were published. In the first longitudinal study, a prominent increase in prothrombotic factors in patients with new-onset sleep apnoea was found.

Prof. Dr. Claudio L. Bassetti
claudio.bassetti@insel.ch

MD (1985) at University of Basel; Neurology residency in Bern/Lausanne; FMH certification (1992). Research fellowships in neurophysiology (1985-1986) at University of Basel and sleep medicine (1995-1996) at University of Michigan, Ann Arbor (US). Venia docendi (1997). Professor and Vice-Chair of Neurology (2001-2009) at University Hospital Zurich. Director (2009-2011) at Neurocenter of Southern Switzerland. Since 2012, Full Professor of Neurology; Chair, Department of Neurology, Inselspital.
Clinical and animal research, sleep, stroke.

Prof. Dr. Antoine Adamantidis
antoine.adamantidis@dkf.unibe.ch

PhD (2005) at University of Liege (BE). Postdoc (2006-2010) at Stanford University School of Medicine, Palo Alto (US). Since 2010, Assistant Professor, Department of Psychiatry, Douglas Mental Health University Institute, McGill University, Montreal (CA). Since 2013, Tenure Track Assistant Professor, Department of Neurology, Inselspital.
Animal research, sleep.

Prof. Dr. Urs Fischer
urs.fischer@insel.ch

MD (2000) at University of Bern; Neurology residency in Bern; FMH certification (2007). Research fellowship (2008) and MSc (2009) in Clinical Neurology, University of Oxford (UK). Venia docendi (2011). Since 2011, Head, Neurological Emergency; since 2013, Head, Neuro Clinical Trial Unit; Associate Professor (2014); since 2015, Co-Chair Stroke-Center, Department of Neurology, Inselspital. Since 2015, Co-Director, CTU Bern. Since 2015, Professor for Acute Neurology and Stroke, University of Bern.
Clinical research, stroke.

Prof. Dr. Marcel Arnold
marcel.arnold@insel.ch

MD (1994) at University of Bern; Neurology residency in Bern; FMH certification (2000). Research fellowships in clinical neurology (2005) at Lariboisière Hospital, University of Paris 7 (FR). Venia docendi (2007). Since 2010, Associate Professor of Neurology. Currently Chair, Stroke Center, Department of Neurology, Inselspital.
Clinical research, stroke.

Dr. Christian P. Kamm
christian.kamm@insel.ch

MD (2003) at Heidelberg University (DE); Venia docendi (2003); Neurology residency in Bern; FMH certification (2011). Research fellowship (2013) at Department of Neurology, VU University Medical Center Amsterdam (NL). Since 2009, Senior Physician, Department of Neurology, Inselspital.
Multiple sclerosis, neuroimmunology.

Prof. Dr. René Müri
rene.mueri@insel.ch

MD (1984) at University of Bern; Neurology residency in Bern and Basel; FMH certification (1991). Postdoc at INSERM U 289, Hôpital de la Salpêtrière, Paris (FR) (1993-1995). Venia docendi (1997). Since 2004, Senior Attending and Head, Unit of Cognitive and Restorative Neurology, Department of Neurology, Inselspital. Associate Professor of Neurology (2008).
Clinical research, visuo-perception/eye movement, neurorehabilitation.

Group Members

Sleep-Wake Mechanisms/Disorders and Epilepsy Group
Prof. Dr. Claudio L. Bassetti, Group Leader
Prof. Dr. Antoine Adamantidis, Group Leader
Prof. Dr. Kaspar Schindler, Consultant, Group Leader
Prof. Dr. Johannes Mathis, Senior Consultant
Dr. Heidemarie Gast, Consultant
Dr. Ulf Kallweit, Consultant
Dr. Markus Schmidt, Consultant
Dr. Thomas Horvath, Research Assistant
Dr. Michael Oberholzer, Research Assistant
Dr. David Schreier, Research Assistant
Dr. Andrea Seiler, Research Assistant
Dr. Mostaba Bandarabadi, Postdoctoral Fellow
Dr. Simone Duss, Postdoctoral Fellow
Dr. Thomas Gent, Postdoctoral Fellow
Dr. Andreas Steimer, Postdoctoral Fellow
Dr. Frédéric Zubler, Postdoctoral Fellow
Dr. Carolina Gutierrez Herrera, Research Associate
Laura Facchin, PhD Student
Lukas Oesch, PhD Student
Marta Pace, PhD Student

Stroke Group
Prof. Dr. Marcel Arnold, Group Leader
Prof. Dr. Urs Fischer, Group Leader
PD Dr. Simon Jung, Group Leader
Prof. Dr. Werner Z'Graggen, Group Leader
Prof. Dr. Claudio L. Bassetti, Head of Department
Prof. Dr. Heinrich Mattle, Senior Consultant
Dr. Anne Broeg, Consultant
Dr. Aikaterini Galimanis, Consultant
Dr. Barbara Goeggel-Simonetti, Consultant
Dr. Mirjam Heldner, Consultant
PD Dr. Marie-Luise Mono, Consultant
PD Dr. Hakan Sarikaya, Consultant
Dr. Rupa Balasubramaniam, Research Fellow
Dr. Monika Bühlmann, Research Fellow
Dr. Ariane Cavelti, Research Fellow
Dr. Rebekka Kurmann, Research Fellow
Dr. Kai Liesirova, Consultant
Marianne Kormann, Study Nurse
Andrea Surtmann, Study Nurse

Neurorehabilitation/Cognitive Disorders Group
Prof. Dr. René Müri, Group Leader
Prof. Dr. Thomas Nyffeler, Head Research
Prof. Dr. Stephan Bohlhalter, Project Leader
Prof. Dr. Klemens Gutbrod, Senior Research Associate
PD Dr. Roger Kalla, Senior Consultant
Dr. Jurka Meichtry, Senior Researcher
Dr. Tim Vanbellingen, Postdoctoral Fellow
Diego De Leon Rodriguez, PhD Student
Noëmi Eggenberger, PhD Student
Simone Hopfner, PhD Student
Basil Preisig, PhD Student
Rahel Schumacher, PhD Student
Denise de Jong, Research Assistant

Movement/Motor Disorders Group
PD Dr. Michael Schüpbach, Group Leader
Prof. Dr. Claudio L. Bassetti, Head of Department
Prof. Dr. Kai Rösler, Senior Consultant
Prof. Dr. Mathias Sturzenegger, Senior Consultant
Dr. Ines Debove, Consultant
Dr. Lenard Lachenmayer, Consultant
Dr. Niklaus Meier, Consultant
Dr. Julia Müllner, Consultant
Dr. Panagiotis Bargiotas, Research Fellow
Dr. Gerd Tinkhauser, PhD Student

Neuropsychosomatic Group
Prof. Dr. Roland von Känel, Group Leader
PD Dr. Stefan Begré, Consultant
Dr. Niklaus Egloff, Consultant
Dr. En-Young Wagner Cho, Postdoctoral Fellow
Rebecca E. Meister, PhD Student
Fiorenza A. Meyer, PhD Student
Mary Princip, PhD Student
Kathleen Schwarzkopf, PhD Student

Neuro CTU Group
Prof. Dr. Urs Fischer, Group Leader
Dr. Corrado Bernasconi, Co-Chair NCTU
Dr. Stefanie Lerch, Co-Chair NCTU
PD Dr. Michael Schüpbach, Vice-Chair
Prof. Dr. Jürgen Beck, Consultant

Prof. Dr. Kaspar Schindler
kaspar.schindler@insel.ch

MD (1995) at University of Bern; MD-PhD (1996-1999) at Institute of Neuroinformatics, ETH Zurich and University of Zurich; doctorates (1999) at Faculty of Mathematics/Natural Sciences (PhD) and Medical Faculty (MD) at University of Zurich; residency in Neurology in Zurich and Bern; FMH certification (2005). Research Fellow (2006-2007) at Epileptology Center, University of Bonn (DE). Venia docendi (2010). Since 2013, Associate Professor and Head of Epilepsy Center, Department of Neurology, Inselspital.
Clinical research, epilepsy.

PD Dr. Michael Schüpbach
michael.schuepbach@insel.ch

MD (1995) at University of Bern; Resident (1996-1999) at Institute of Physiology, Bern; residency in Neurology in Bern; FMH certification (2002). Research fellowship (2003-2008) at Salpêtrière Hospital, Paris (FR). Since 2008, Attending Physician; since 2010, Chair, DBS program; since 2014, Chair, Movement Disorders Center, Department of Neurology, Inselspital. Venia docendi (2014).
Clinical research, movement disorders.

Prof. Dr. Roland von Känel
roland.vonkaenel@insel.ch

MD (1993) at University of Bern; residency in Internal Medicine; FMH certification (1999); residency in Psychiatry and Psychotherapy; FMH certification (2008). Postdoc (1999-2001) at University of California, San Diego (US). Chair, Psychosomatic Medicine (2004-2014). Associate Professor of Somato-Psychosocial Medicine (2004-2012); Full Professor of Psychosomatic Medicine (2012-2014), Inselspital. Since 2014, Head, Clinic Barmelweid.
Clinical research, neuropsychosomatics.

Prof. Dr. Thomas Dierks, Consultant
Dr. Sebastian Grunt, Consultant
Dr. Christian Kamm, Consultant
Prof. Dr. Schindler, Consultant
Prof. Dr. Roland Wiest, Consultant
Prof. Dr. Werner Z'Graggen, Consultant
Jenny Bressan, Research Coordinator

Multiple Sclerosis/Neuroimmunology Group
Dr. Christian Kamm, Group Leader
Dr. Robert Hoepner, Consultant
Dr. Anke Salmen, Consultant
Saskia Steinheimer, Research Fellow
Kirsten Schanzmann, PhD Student
Lisa Schrewe, PhD Student
Dr. Monika Käser, Study Nurse
Karin Streit, Study Nurse

Selected Collaborators

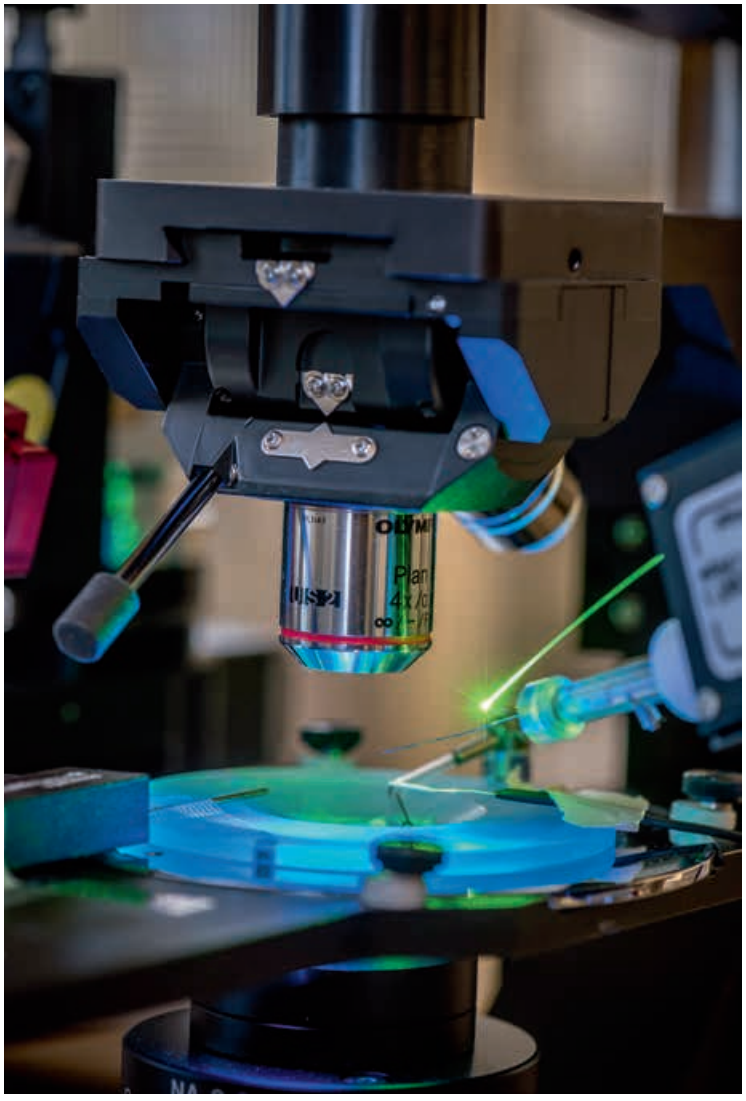
Andrzejak R, Pompeu Fabra University (ES)
Albrecht U, Annoni J-M, University of Fribourg (CH)
Bacon SL, Concordia University (CA)
Baumann C, University Hospital Zurich (CH)
Beck J, Gralla J, Meier B, Pollo C, Raabe A, Schroth G, Wiest R, Inselspital (CH)
Bloch J, Hirt L, University Hospital of Lausanne (CH)
Bohlhalter S, Nyffeler T, Lucerne Cantonal Hospital (CH)
Bousser MG, Debette S, Stapf C, University of Paris 7 (FR)
Brandt T, Grond-Ginsbach C, University of Heidelberg (DE)
Burdakov D, National Institute for Medical Research (UK)
Burgunder JM, Siloah Clinic (CH)
Cereda C, Fulda S, Galati S, Kaelin A, Manconi M, Neurocenter of Southern Switzerland (CH)
Coutinho J, Stam J, University of Amsterdam (NL)
Deuschl G, University of Kiel (DE)
Diniz Behn C, Colorado School of Mines (US)
Engelter S, Lyrer P, University of Basel (CH)
Gabriels L, Nuttin B, Catholic University of Leuven, (BE)
Hamel E, Jones B, Seguela P, Williams S, McGill University Montreal (CA)
Hartmann A, Pitié-Salpêtrière Hospital Paris (FR)
Henke K, Mast F, Mosimann UP, Nef T, University of Bern (CH)
Huber R, University Children's Hospital Zurich (CH)
Kent D, Thaler D, Tufts Medical Center (US)
Khatami R, Nedeltchev K, Remonda L, Cantonal Hospital Aarau / Barmelweid Clinic (CH)
Korotkova T, Ponomarenko P, NeuroCure, Berlin (DE)
Lammers GJ, Leiden University Medical Centre (NL)
Löffelholz G, Schmitt W, University of Bern (CH)
Luppi PH, University Lyon 1 (FR)
Malan L, North-West University, Potchefstroom (ZA)
Massimini M, University of Milan (IT)
Mausbach BT, University of California, San Diego (US)
Mormannn F, University Hospital of Bonn (DE)
Nobili L, Niguarda Hospital (IT)
Ptak R, University of Geneva (CH)
Schnitzler A, Vesper J, University Hospital Düsseldorf (DE)
Tatlitsumak T, University of Helsinki (FI)
Thurston RC, University of Pittsburgh (US)
Wirtz PH, University of Konstanz (DE)

Selected Grants

Amounts above CHF 50,000 allocated for 2015:

- SNF: Optogenetic dissection of hypothalamic regulation of sleepwake states (A. Adamantidis) CHF 120,000
- SNF: Etiopathogenesis, Diagnosis, Imaging and Treatment of Cervicocerebral Artery Dissections: A Multifactorial, Multidisciplinary and Translational Approach (EDIT-CAD-II-Study) (M. Arnold; U. Fischer, Co-Applicant) CHF 356,593
- SNF: Autonomic Function and Cardiovascular Risk in Restless Legs Syndrome – the AUTO-REST Study (C. Bassetti; M. Manconi, PI) CHF 184,333
- SNF: Sleep loss and sleep disorders and their impact on the short and long termin outcome of stroke (C. Bassetti) CHF 185,224
- SNF: Magnetic resonance techniques to determine metabolite levels: extending scope and clinical robustness (C. Bassetti; R. Kreis, PI) CHF 169,382

- SNF: Swiss study of initial decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral hemorrage (switch): a randomized controlled trial (U. Fischer) CHF 168,596
- SNF: Motion and spatial neglect (R. Müri; T. Nyffeler, PI) CHF 65,000
- SNF: Aphasia and co-speech gestures (R. Müri) CHF 72,000
- SNF: Role of executive functions on language: an experimental and clinical approach with application to mother language and second language (R. Müri; J.-M. Annoni, PI) CHF 208,000
- SNF: Interference with gesture control and transcallosal white matter integrity: A theta-burst stimulation and diffusion tensor imaging study in apraxia after stroke (R. Müri; S. Bohlhalter, PI) CHF 112,000
- SNF: A Bayesian Inference Approach to intracranical EEG Seizure dynamics (K. Schindler) CHF 90,000
- SNF: MI-SPRINT (Myocardial Infarction – Stress Prevention INTervention): A randomized-controlled minimal early behavioral intervention trial to reduce the development of posttraumatic stress caused by acute myocardial infarction (R. von Känel) CHF 104,000
- SNF: Contrast enhanced ultrasound imaging for cerebral perfusion measurement in cerebral vasospasm after subarachnoid haemorrhage (W. Z'Graggen; J. Beck, PI) CHF 107,188
- Human Frontiers Science Program: Neural basis of behavioral multitasking and coordination by hypothalamic circuit (A. Adamantidis; D. Burdakov, PI) CHF 125,000
- Swiss Heart Foundation: Predictive Swallowing Score (PRESS)-Validation of a prognostic score of impaired oral intake after ischemic stroke (M. Arnold; G. Kägi, PI) CHF 80,774
- Medtronic: DBS Nurse (M. Schüpbach) CHF 51,192
- Boston Scientific: Latestim. Prospective, randomized, controlled trial of bilateral pallidal stimulation in patients with advanced Parkinson's Disease with motor complications and relative or absolute contraindications for subthalamic stimulation (M. Schüpbach) CHF 77,724



Selected Publications

Long-term outcome after arterial ischemic stroke in children and young adults. Goeggel, SB; Cavelti, A; Arnold, M; Bigi, S; Regenyi, M; Mattle, HP; Gralla, J; Fluss, J; Weber, P; Hackenberg, A; Steinlin, M; Fischer, U (2015) in: Neurology, 84(19), p. 1941-1947.

An integrated microprobe for the brain. Herrera, CG and Adamantidis, AR (2015) in: Nat Biotechnol, 33(3), p. 259-260.

Identification of Sleep-Modulated Pathways Involved in Neuroprotection from Stroke. Pace, M; Baracchi, F; Gao, B; Bassetti, C (2015) in: Sleep, 38(11), p. 1707-1718.

Chow-Liu trees are sufficient predictive models for reproducing key features of functional networks of periictal EEG time-series. Steimer, A; Zubler, F; Schindler, K (2015) in: Neuroimage, 118, p. 520-537.

Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. Saver, JL; Goyal, M; Bonafe, A; Diener, HC; Levy, EI; Pereira, VM; Albers, GW; Cognard, C; Cohen, DJ; Hacke, W; Jansen, O; Jovin, TG; Mattle, HP; Nogueira, RG; Siddiqui, AH; Yavagal, DR; Baxter, BW; Devlin, TG; Lopes, DK; Reddy, VK; du Mesnil de, RR; Singer, OC; Jahan, R (2015) in: N Engl J Med, 372(24), p. 2285-2295.

Link to publication list:
www.neurologie.insel.ch/de/forschung/

Pulmonary Medicine (Adults)

www.pneumologie.dkf.unibe.ch/research/
www.dkf.unibe.ch/research-group/36/

Prof. Dr. Thomas Geiser
thomas.geiser@insel.ch

MD (1989) at University of Bern. Internal medicine, pulmonary medicine and research fellowships (1991-1998) at University of Bern. Postdoc (1998-2000) at University of California, San Francisco (US). Senior Attending Physician (2000-2008); since 2008, Professor and Chair, Department of Pulmonary Medicine, Inselspital. Head of Pulmonary Medicine (Adults), DCR.

Dr. Manuela Funke-Chambour
manuela.funke-chambour@insel.ch

MD (2001) at University of Bonn (DE). Internal medicine fellowship (2001-2005) at Lausanne University Hospital and in pulmonary medicine at Rolle Hospital (2005) and Inselspital (2005-2007). Postdoc (2007-2011) at Massachusetts General Hospital, Harvard Medical School, Boston (US). Since 2011, Attending Physician, Pulmonary Medicine, Inselspital. Currently, Attending Physician and Group Leader, Pulmonary Medicine (Adults), DCR.

Prof. Dr. Christophe von Garnier
christophe.vongarnier@insel.ch

MD (1993) at University of Lausanne. Internal medicine (2001) in Basel. Pulmonary medicine fellowship (2002, 2006) at University of Basel and postdoc (2002-2005) at Telethon Kids Institute and Sir Charles Gairdner Hospital in Peth (AU). Attending Physician (2008-2012), Pulmonary Medicine, Inselspital. Venia docendi (2011); Associate Professor (2015). Since 2013, Head of Pulmonary Medicine, Spital Tiefenau, Insel Group. Group Leader, Pulmonary Medicine (Adults), DCR.

Research Highlights 2015 / Outlook 2016

Geiser/Gazdhar Group

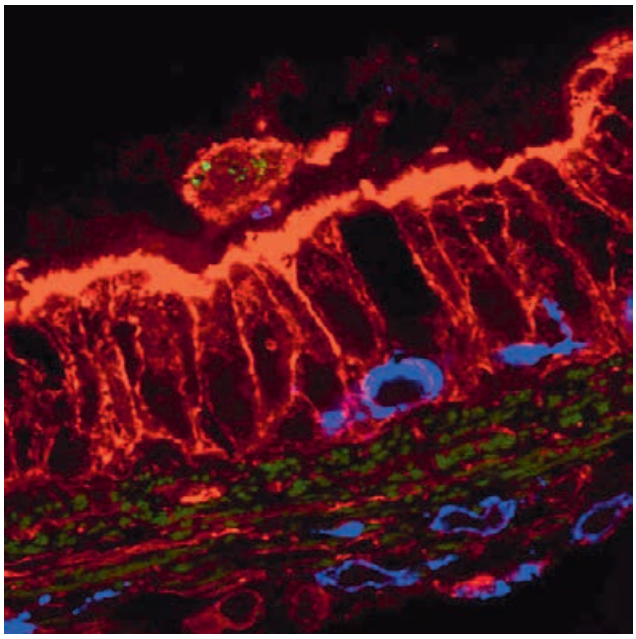
Our group focuses on stem cells in lung repair and regeneration in pulmonary fibrosis (PF). The exact pathophysiology of this devastating progressive disease is unknown, with limited therapeutic options. Alveolar epithelial cell (AEC) injury and impaired repair after repeated injuries initiate fibrosis. We demonstrated that lesions in mitochondria are possible disease perpetuators due to mitochondrial DNA (mtDNA) mutations. We are now investigating the mtDNA genome in PF. Moreover, we previously demonstrated that the cell-specific gene transfer of hepatocyte growth factor (HGF) to AECs increases lung repair and that HGF-expressing bone marrow-derived stem cells attenuate PF in an animal model. We are now focusing on the antifibrotic effects of induced pluripotent stem cells, their secretome and lung resident stem cells, using proteomics, RNA sequencing and bioinformatics to study the mechanisms that govern the antifibrotic effects.

Funke Group

We investigate inflammatory pathomechanisms of idiopathic pulmonary fibrosis (IPF), the most prevalent form of idiopathic interstitial pneumonia (IIP). Impaired lung repair is involved in lung fibrosis development, however increasing evidence suggests that inflammation or immune responses might also be contributory factors. We found divergent responses towards activation of toll-like receptor 4 (TLR4) in fibroblasts isolated from patients with IPF or without. We also investigated the role of lysophosphatidic acid receptor 1 during lung development in mice. This receptor is known to be a potent pro-fibrotic mediator and is involved in inflammation. In 2015, the Department of Pulmonary Medicine initiated a Cohort Study for IIP. The translational study will start in 2016. The aim of the study is to gather data about IIP in Switzerland, to monitor new treatments for PF and to facilitate translational research.

Von Garnier/Blank Group

We focus on interactions between engineered biomedical or environmental nanoparticles and antigen-presenting cells (APCs) of the respiratory tract. Particle-cell interactions and potential changes in APC phenotype and function are routinely monitored by flow cytometry and advanced light microscopy. Our three main projects are: (1) Assessment of immunomodulatory effects of multi-walled carbon nanotubes in chronic-obstructive pulmonary disease (COPD); (2) Pulmonary immune responses to bio-mimetic antigen carriers for novel therapeutic approaches for allergic asthma; and (3) Lung microbiome and macrophage polarisation in COPD. APCs, like pulmonary dendritic cells and alveolar macrophages, orchestrate innate and adaptive immunity in the respiratory tract and therefore represent potential targets for immunomodulatory approaches to treat chronic lung diseases like allergic asthma.



Group Members

Prof. Dr. Thomas Geiser, Chair, Group Leader and Head of Research
Dr. Manuela Funke-Chambour, Group Leader
Prof. Dr. Christophe von Garnier, Group Leader
Dr. Izabela Magdalena Nita, Research Scientist
Dr. Fabian Blank, Postdoctoral Fellow
Dr. Amiq Gazdhar, Postdoctoral Fellow
Sandra Barnowski, Laboratory Technician
Anna-Barbara Tschirren, Laboratory Technician
Rahel Holderegger, Secretary
Seraina Beyeler, PhD Student
Rebecca Blom, PhD Student
Simone Ebener, PhD Student
Paulius Ruzgys, PhD Student (until Oct.)
Emilie Seydoux, PhD Student (until June)
Luca Tamò, PhD Student

Selected Collaborators

Hostettler K, University of Basel (CH)
Knudsen L, University of Hannover (DE)
Marsland B, University of Lausanne (CH)
Stumbles P, University of Western Australia (AU)
Tager A, Massachusetts General Hospital, Harvard Medical School (US)

Selected Grants

Amounts allocated for 2015:

- SNF: Paracrine soluble factors released by induced pluripotent stem cells in lung regeneration and repair (T. Geiser) CHF 80,000
- SNF: Pulmonary immune responses to bio-mimetic antigen carriers for novel therapeutic approaches to treating allergic asthma (C. von Garnier) CHF 115,000
- SNF Sinergia: Lung resident stem cells for treatment of pulmonary fibrosis (T. Geiser) CHF 120,000
- SNF Sinergia: Dysregulation of the Lung Microbiota in Chronic Obstructive Pulmonary Disease (C. von Garnier) CHF 120,000
- SNF NRP 64: Biomedical nanoparticles as immune-modulators (C. von Garnier) CHF 50,000
- Swiss Lung League: Azithromycin Study in IPF (M. Funke) CHF 61,398
- OPO Foundation: Cell and gene therapy for AAT deficiency (I. Nita, A. Gazdhar, T. Geiser) CHF 70,000
- Unrestricted grants (Intermune, Boehringer Ingelheim and Roche): IIP Cohort Study (M. Funke) CHF 58,377

Selected Publications

Time-dependent and somatically acquired mitochondrial DNA mutagenesis and respiratory chain dysfunction in a scleroderma model of lung fibrosis. Gazdhar, A; Lebrecht, D; Roth, M; Tamm, M; Venhoff, N; Foocharoen, C; Geiser, T; Walker, UA (2014) in: Sci Rep, 4, p. 5336.

Size-dependent accumulation of particles in lysosomes modulates dendritic cell function through impaired antigen degradation. Seydoux, E; Rothen-Rutishauser, B; Nita, IM; Balog, S; Gazdhar, A; Stumbles, PA; Petri-Fink, A; Blank, F; von Garnier, C (2014) in: Int J Nanomedicine, 9, p. 3885-3902.

The secretome of induced pluripotent stem cells reduces lung fibrosis in part by hepatocyte growth factor. Gazdhar, A; Grad, I; Tamo, L; Gugger, M; Feki, A; Geiser, T (2014) in: Stem Cell Res Ther, 5(6), p. 123.

Alveolar derecruitment and collapse induration as crucial mechanisms in lung injury and fibrosis. Lutz, D; Gazdhar, A; Lopez-Rodriguez, E; Ruppert, C; Mahavadi, P; Gunther, A; Klepetko, W; Bates, JH; Smith, B; Geiser, T; Ochs, M; Knudsen, L (2015) in: Am J Respir Cell Mol Biol, 52(2), p. 232-243.

LPA Signaling through the LPA1 Receptor is Required for Alveolarization. Funke, M; Knudsen, L; Lagares, D; Ebener, S; Probst, C; Fontaine, B; Franklin, A; Kellner, M; Kuehnel, M; Matthieu, S; Grothausmann, R; Chun, J; Roberts, J; Ochs, M; Tager, A in Am J Respir Cell Mol Biol. Accepted for publication January 2016.

Radiology

www.dkf.unibe.ch/research-group/95/

Prof. Dr. Johannes T. Heverhagen
johannes.heverhagen@insel.ch

Studied physics (1997), University of Kaiserslautern (DE). Medical licence (2004), Junior Professor (2006); Dr. med. (2007), University of Marburg (DE). Research Scientist (2004-2006) at Department of Radiology, Ohio State University, Columbus (US). Assistant Professor (2006-2012); Director of Research (2009-2012); Vice Chair (2010-2012), Department of Radiology, Philipps University, Marburg (DE). Since 2012, Chair, Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital.

Prof. Dr. Hendrik von Tengg-Kobligk
hendrik.vontengg@insel.ch

MD (2001), Ruprecht Karls University, Heidelberg (DE). Postdoc (2003), German Cancer Research Center and University of Heidelberg (DE). Board Certification in Diagnostic Radiology (2010); Venia docendi (2012). Since 2007, Adjunct Instructor, Department of Radiology, Ohio State University, Columbus (US). Since 2010, Senior Radiologist, University of Heidelberg. Since 2013, Vice Chair, Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital. Since 2014, Group Leader, Radiology, DCR. From 2016, Associate Professor at University of Bern.

PD Dr. Ingrid Böhm
ingrid.boehm@insel.ch

Group Leader, Molecular Radiology and Contrast Agent Safety groups (2008-2013); Research Group Leader (2012-2013) at Faculty of Human Medicine, University of Marburg (DE). Venia docendi (2012). Since 2014, Scientific Project Leader, Department of Diagnostic, Interventional and Paediatric Radiology, Inselspital. Since 2015, Project Leader, Radiology, DCR.

Research Highlights 2015 / Outlook 2016

The Radiology Lab serves as a research platform for various scientific radiology projects:

Interventional radiology: diagnostic tissue sampling

The aim of this project is to improve the standardisation and quality of image-guided tissue sampling. Together with the Institute for Pathology, we are evaluating the quality and quantity of tissue samples. The results will enable us to predict the number of samples needed per patient for diagnostic purposes. Furthermore, it will be possible to determine which biopsy device is the most efficient.

Ex vivo-simulation of chemotherapy options for advanced lung tumours

For the majority of patients with advanced tumours, personalised oncological treatment strategies are still lacking. Our ex vivo approach to this problem relates to the phenotypical chemotherapy response of tumour cells. Several agents have been identified as effective sensitisers for platinum analogues in in vivo platinum-resistant lung tumours, e.g., pemetrexed (WO 2014/206387 A1 "Method for the creation of a database for initial assessment of the effectiveness of active agents in tumour therapy"; international publication date: 31.12.2014). To enable future individualised chemotherapy scheduling, the project aims at studying this sensitisation effect more closely under in vitro and ex vivo conditions. Conditions in vitro are a priority, since experiments need to be both reproducible and independent of the availability of clinical tumour specimens. A series of platinum-resistant cell strains, derived from wild type cells of the human lung adenocarcinoma strain A240286S, are now available and suited to performing sensitisation experiments in vitro.

Molecular biology

This research project aims at characterising the involvement of excision repair cross-complementation group 1 (ERCC1) isoforms and their interplay in cell responses to cisplatin. As a first step towards potential clinical applications, this project includes the study of the association between the protein level of the isoforms and cells resistance to cisplatin.

DNA strand breaks

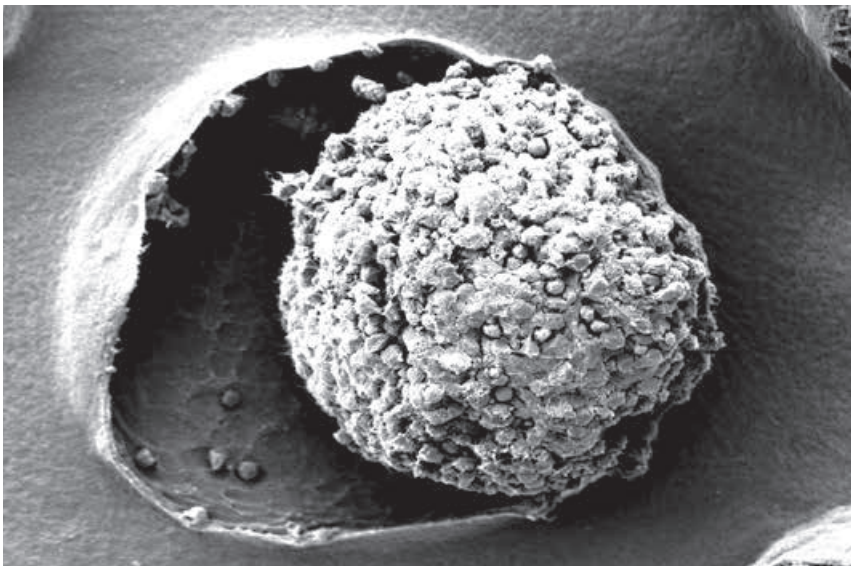
Contrast agents per se and in combination with either X-rays or MR-RF pulses may disturb cellular functions and can lead to DNA double-strand breaks (DSB). In 2016, we plan to study and compare various methods of analysing DSB in vitro, and to implement these methods in different radiological applications after ethical approval.

Imaging phantoms (design and production)

We are designing and producing phantom models for in vitro testing of new magnetic resonance and computed tomography imaging protocols and new contrast materials. The phantoms allow us to evaluate contrast media effects, e.g., signal intensity, blood and air flow, diffusion properties, and tissue sampling (see above).

Prof. Dr. Christof Granzow
christof.granzow@dkf.unibe.ch

Retired Professor of Biochemistry (2006) at German Cancer Research Center, Heidelberg (DE) and University of Heidelberg (DE). Inventor of methods for experimental oncology. CEO of FLACOD GmbH, Heidelberg (DE). Since 2014, Experimental Project Leader, Radiology, DCR.



Group Members

Prof. Dr. Johannes T. Heverhagen, Chair
Prof. Dr. Hendrik von Tengg-Kobligk, Vice Chair and Group Leader
PD Dr. Ingrid Böhm, Project Leader
Prof. Dr. Christof Granzow, Experimental Project Leader
Dr. Isabelle Schepens, Senior Research Scientist and Laboratory Head
Martin Hungerbühler, Laboratory Technician

Selected Collaborators

Berezowska SA, Hewer E, University of Bern (CH)
Haenni B, University of Bern (CH)
Marti T, Ott S, University of Bern (CH)
Ochsenbein A, University of Bern (CH)
Schmid RA, University of Bern (CH)

Selected Grants

Amounts allocated for 2015:

– Allergy Foundation Ulrich Müller-Gierok: Analysis of allergic phenomena in non-allergic contrast agents reactions (I. Böhm) CHF 75,000

Selected Publications

Intravenous Iodinated Contrast Agents Amplify DNA Radiation Damage at CT. Piechowiak, EI; Peter, JF; Kleb, B; Klose, KJ; Heverhagen, JT (2015) in: Radiology, 275(3), p. 692-697.

Brain-borne IL-1 adjusts glucoregulation and provides fuel support to astrocytes and neurons in an autocrine/paracrine manner. Del, RA; Verdenhalven, M; Lorwald, AC; Meyer, C; Hernangomez, M; Randolf, A; Roggero, E; Konig, AM; Heverhagen, JT; Guaza, C; Besedovsky, HO (2015) in: Mol Psychiatry, e-pub ahead of print.

Contrast agents and ionization with respect to safety for patients and doctors. von Tengg-Kobligk, H; Kara, L; Klink, T; Khanicheh, E; Heverhagen, JT; Bohm, IB (2015) in: Contrib Nephrol, 184, p. 59-74.

Thoracic Surgery

www.dkf.unibe.ch/research-group/50/

Prof. Dr. Ralph A. Schmid
ralph.schmid@insel.ch

MD at University of Zurich; Residency, Division of Surgery (1988-1994). Fellowship (1994-1995) at Department of Thoracic and Cardiovascular Surgery, Washington University Medical School, St. Louis (US). Staff Surgeon (1996-1999) at Division of Surgery, University Hospital Zurich. Since 1999, Professor of Surgery and Chair, Department of Thoracic Surgery, Inselspital

Dr. Sean R.R. Hall
sean.hall@insel.ch

PhD in Pharmacology and Toxicology at Queen's University (CA). Postdoc (2008-2010) at Brigham and Women's Hospital, Harvard Medical School (US). Senior Scientist (2011) at NeoStem Inc, Boston (US). Senior Scientist (2011-2012) at Erasmus Medical Center, Division of Transplantation and Intestinal Surgery, Rotterdam (NL). Since 2013, Group Leader, Department of Thoracic Surgery, Inselspital.

Dr. Thomas M. Marti
thomas.marti@insel.ch

PhD in Biology at University of Bern. Postdoc (2003-2006) at UCSF Comprehensive Cancer Center (US). Principal Investigator (2006-2012) at Laboratory of Molecular Oncology, University Hospital Zurich. Since 2012, Group Leader, Department of Thoracic Surgery, Inselspital.

Research Highlights 2015 / Outlook 2016

Hall Group

There is emerging evidence to suggest that the tumour (mesenchymal) microenvironment acts in concert with the cancer cell-centric changes driving tumour phenotype. We have recently identified rare mesenchymal stromal cells in primary human lung adenocarcinomas and are interested in how these cells promote tumour growth. Initially, mesenchymal stromal cells were shown to possess broad immunomodulatory properties. We postulate that these cells may act as key effectors in regulating the composition and function of infiltrating leukocytes within the tumour microenvironment, tipping the balance towards immunosuppression. Therefore, our aim is to use a combined pharmacological and genetic approach (patient-derived samples and inducible mouse models of human lung adenocarcinoma) to determine the potential of this tumour-derived mesenchymal subset to serve as a novel therapeutic target in lung cancer. In a second project, we are interested in identifying cell subsets that are critical for lung regeneration. To achieve this, we plan to utilise genetic fate mapping tools to identify cellular hierarchies in alveolar development and cell fate during injury and alveolar regeneration.

Marti Group

Lung cancer is the most common cause of cancer-related mortality worldwide. More than 80% of lung tumours are non-small-cell lung cancers (NSCLC). It has been postulated that tumour initiation and propagation are mediated by so-called 'tumour-initiating cells' (TICs) that can self-renew and spawn differentiated progeny. The DNA damage response (DDR) is a complex signalling network that maintains genome integrity, essential for the proper function and survival of all organisms. We were able to identify TICs in cell lines and primary NSCLC samples. Subsequent analysis indicated that factors of the DDR and nucleotide synthesis pathways are deregulated in TICs. Our aim is to identify differentially regulated DDR factors in TICs compared to tumour bulk cells, which will subsequently allow us to identify novel targets for pharmacological or genetic intervention to treat lung cancer.

Peng Group

Resistance to anticancer therapies causes tumour relapse, treatment failure and mortality. This forms the motivation for our research, which is mainly oriented towards identification of therapy-resistant tumour cells and of the underlying molecular mechanisms accounting for the phenomenon. We focus on cancer stem cells in the resistance of lung cancer to standard therapies currently used in the clinic, with the ultimate goal of unravelling the vulnerabilities – the 'Achilles' heel' – of therapy-resistant cells, and of developing new and more effective therapeutic strategies for the treatment of human lung cancer.

Dr. Ren-Wang Peng
renwang.peng@insel.ch

PhD in Biochemistry at Chinese Academy of Sciences, Beijing (CN). Research scientist (1998-2005) at Max Planck Institute for Biophysical Chemistry, Göttingen (DE) and Visiting Scholar (1999) at Dartmouth Medical School (US). Group Leader (2006-2010) at ETH Zurich. Since 2012, Group Leader, Department of Thoracic Surgery, Inselspital.

Group Members

Prof. Dr. Ralph A. Schmid, Chair
Dr. Sean R.R. Hall, Group Leader
Dr. Thomas M. Marti, Group Leader
Dr. Ren-Wang Peng, Group Leader
Laurène Froment, Laboratory Technician
Ming Qiao, Laboratory Technician
Dr. Patrick Dorn, Clinical Fellow
Dr. Gregor Kocher, Clinical Fellow
Andreas Keil, PhD Student
Liang Shunqing, PhD Student
Colin Tièche, PhD Student
Limei Wang, PhD Student

Selected Collaborators

Berezowska, S, University of Bern (CH)
Galetta, D, European Institute of Oncology (IT)
Ochsenbein A, University of Bern (CH)
Stroka, D, University of Bern (CH)
Vassella, E, University of Bern (CH)

Selected Grants

Amounts allocated for 2015:

- Cancer League Bern: Role of PD-1/PD-L1 in NSCLC (S.R.R. Hall) CHF 60,000
- Cancer League Switzerland: Characterization and Targeting of Cancer Initiating Cells in Lung Cancer (T. Marti) CHF 84,616
- Cancer League Bern: Functional identification and molecular targeting of human lung cancer stem cells (R.-W. Peng) CHF 72,000

Selected Publications

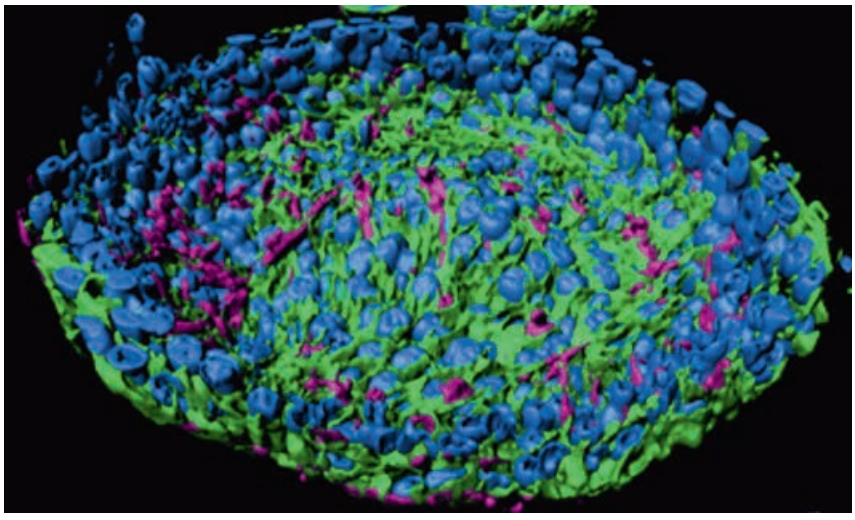
Human graft-derived mesenchymal stromal cells potently suppress alloreactive T-cell responses. de Mare-Bredemeijer, EL; Mancham, S; Verstegen, MM; de Ruiter, PE; van, GR; O'Neill, D; Tilanus, HW; Metselaar, HJ; de, JJ; Kwekkeboom, J; Hall, SR; van der Laan, LJ (2015) in: Stem Cells Dev, 24(12), p. 1436-1447.

The Topoisomerase I Inhibitor Irinotecan and the Tyrosyl-DNA Phosphodiesterase 1 Inhibitor Furamidine Synergistically Suppress Murine Lupus Nephritis. Keil, A; Frese-Schaper, M; Steiner, SK; Korner, M; Schmid, RA; Frese, S (2015) in: Arthritis Rheumatol, 67(7), p. 1858-1867.

The importance of phrenic nerve preservation and its effect on long-term postoperative lung function after pneumonectomy. Kocher, GJ; Poulson, JL; Blichfeldt-Eckhardt, MR; Elle, B; Schmid, RA; Licht, PB (2015) in: Eur J Cardiothorac Surg, e-pub ahead of print.

Is clipping the preferable technique to perform sympathicotomy? A retrospective study and review of the literature. Kocher, GJ; Taha, A; Ahler, M; Schmid, RA (2015) in: Langenbecks Arch Surg, 400(1), p. 107-112.

Blocking the epithelial-to-mesenchymal transition pathway abrogates resistance to anti-folate chemotherapy in lung cancer. Liang, SQ; Marti, TM; Dorn, P; Froment, L; Hall, SR; Berezowska, S; Kocher, G; Schmid, RA; Peng, RW (2015) in: Cell Death Dis, 6, p. e1824.



Key Events

Swiss Youth in Science: "Biology and Medicine" Study Week
16-21 Mar.

Welcome Events 2015
27 May and 21 Oct.
Around 35 interested DCR newcomers attended each of these events. The next Welcome Event will take place on 13 April 2016.

Day of Clinical Research 2015
3-4 Nov.
A large and interested audience followed the presentations of **Prof. Dr. Silvestro Micera** (Bertarelli Foundation Chair in Translational Neuroengineering, EPF Lausanne) entitled "The quest for a bionic hand: recent achievements and future perspectives" and **Prof. Dr. Christian Leumann** (Vice-Rector for Research and Rector-Designate, University of Bern) entitled "Research at UniBE: challenges and opportunities".

Four candidates applied for the Johanna Dürmüller-Bol DCR Research Prize 2015 (funded by the Johanna Dürmüller-Bol Foundation) and 145 abstracts were submitted for the Poster Prizes of the DCR and the Research Prize Alumni MedBern. The winners were (left to right in photo below): Juan Antonio Delgado Rodríguez, Dr. Federica Moalli, Selina Crippa, Paola Francica, Eleanore Young.

Johanna Dürmüller-Bol DCR Research Award 2015
Dr. Federica Moalli
Theodor Kocher Institute (TKI), University of Bern

Poster Prizes of the DCR for
- *best preclinical project*
  Paola Francica
  Radiation Oncology, DCR and Department of Radio-Oncology, Inselspital
- *best clinical project*
  Juan Antonio Delgado Rodríguez
  Department of Paediatrics, Division of Neuropaediatrics, Inselspital
- *best project by a medical student*
  Selina Crippa
  Department of Neurology, Inselspital and Neurology, DCR

Research Prize Alumni MedBern
Eleanore Young
Gerontechnology and Rehabilitation, ARTORG Center for Biomedical Engineering Research; Department of Old Age Psychiatry, University Hospital of Psychiatry Bern and Division of Cognitive and Restorative Neurology, Department of Neurology, Inselspital

The next Day of Clinical Research will be held 1-2 November 2016.

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

DKF Research Conferences 2015

With an average of 50 visitors each month, the DKF Research Conferences continue to be successful. In 2015, we were pleased to present the following speakers:

2 Feb. – Dr. Maaike Pols
Faculty of 1000, London (UK)
F1000 – a new way of writing, discovering and sharing science

2 Mar. – Prof. Dr. Thierry Pedrazzini
Experimental Cardiology Unit, University of Lausanne (CH)
Long noncoding RNAs in cardiac homeostasis and regeneration

13 Apr. – Dr. Alessandra Piersigilli and Prof. Dr. Inti Zlobec
Institute of Animal Pathology and Institute of Pathology, University of Bern (CH)
COMPATH: one medicine, one pathology, one platform

4 May – Dr. Eli C. Lewis
Ben-Gurion University of the Negev, Beer-Sheva (IL)
Alpha1-Antitrypsin: Evolution of a unique endogenous protein towards treating cell injury-related diseases

1 June – Prof. Dr. Pierre Fontana
University Hospitals of Geneva and Geneva Platelet Group (CH)
Dissecting modulators of platelet reactivity: towards personalized medicine

6 July – Prof. Dr. Rita Bernhardt
Saarland University, Saarbrücken (DE)
Cytochromes P450 and their importance for medicine and biotechnology

7 Sep. – Prof. Dr. Alain Doucet
Centre de Recherche des Cordeliers, Paris (FR)
Hydro-electrolytical disorders in experimental nephrotic syndrome stemming for edema and ascites

5 Oct. – Prof. Dr. Bernard Ducommun
University of Toulouse (FR)
Multicellular tumor spheroid 3D models for cancer cell biology studies and anticancer drugs evaluation

7 Dec. – Prof. Dr. Raimund Dutzler
University of Zurich (CH)
Structural basis for cellular iron uptake by the SLC11/NRAMP family of transport proteins

In 2016, the DKF Research Conferences will once again present fascinating speakers who will talk about their outstanding, clinically relevant research. The Conferences will take place as usual every first Monday of the month from 5-6 pm, followed by an apéro.

Personnel Update

Academic Degrees

The following academic degrees where awarded to DCR group members:

Full Professor

Prof. Dr. Stephan Windecker
Cardiology

Professor

Prof. Dr. Urs Fischer
Neurology

Associate Professor

Prof. Dr. Daniel G. Fuster
Nephrology and Hypertension

Prof. Dr. Johanna A. Kremer Hovinga
Hematology (Adults)

Prof. Dr. Arto C. Nirkko
Neurology

Prof. Dr. Thomas Pilgrim
Cardiology

Prof. Dr. Ulrike Stamer
Anaesthesiology

Prof. Dr. Christophe von Garnier
Pulmonary Medicine (Adults)

Titular Professor

Prof. Dr. Klemens Gutbrod
Neurology

Lecturer (Privatdozent)

PD Dr. Vanessa Banz Wüthrich
Visceral and Transplantation Surgery

PD Dr. Marc Ulrich Baumann
Prenatal Medicine

PD Dr. Sarah Henning Longnus
Cardiovascular Surgery

PD Dr. Pascal Juillerat
Gastroenterology / Mucosal Immunology

PD Dr. Marie-Luise Mono
Neurology

PD Dr. Henriette Most
Cardiovascular Surgery

PD Dr. Carsten Riether
Tumor-Immunology

PD Dr. Monika Schaller Tschan
Hematology (Adults)

PD Dr. Joerg Schefold
Intensive Care Medicine

PD Dr. Andreina Schoeberlein
Prenatal Medicine

PD Dr. Florian Schönhoff
Cardiovascular Surgery

PD Dr. Stefan Stortecky
Cardiology

PD Dr. Sven Trelle
Clinical Trials Unit (CTU) Bern

PhD

(supervisors in brackets)

Guiseppe Albano
(Prof. Dr. Daniel Fuster)
Calcium and phosphate transport by osteoclasts: In vitro and in vivo studies

John Choy
(Prof. Dr. Willy Hofstetter)
Biofunctionalisation of beta-tricalcium phosphate ceramic bone substitute materials

Christine Deisl
(Prof. Dr. Daniel Fuster)
The role of the sodium/hydrogen exchanger NHA2 in the endocrine pancreas

Valeriya Dimitrova
(PD Dr. Alexandre Arcaro)
c-Myc network in medulloblastoma

Nicole Eisele
(Prof. Dr. Markus G. Mohaupt)
Aldosterone and salt availability in pregnancy

Stefan Hahnewald
(PD Dr. Pascal Senn)
Development of an in vitro bioassay to study response profiles of auditory neurons

Ali Hashemi Gheinani
(Prof. Dr. Katia Monastyrskaya)
The role of microRNAs in organ remodeling in lower urinary tract dysfunction

Yasmin Köller
(Prof. Dr. Kathy McCoy, Prof. Dr. Andrew J. Macpherson)
Microbial education of the immune system

Cheong K.C. Kwong Chung
(Prof. Dr. Kathy McCoy, Prof. Dr. Andrew J. Macpherson)
Role of antigen-specific antimicrobial $CD4^+$ T cell responses in host-microbial mutualism

Zaira Leni
(PD Dr. Alexandre Arcaro)
Novel targeted therapies in childhood cancer – from metabolism to drug therapy

Giulio Loforese
(PD Dr. Deborah Stroka)
Hippo in the regenerating liver

Thi Ngoc Thao (Anna) Pham
(PD Dr. Elisabeth Oppliger Leibundgut)
Role of endothelial cells and mutational status in patients with polycythemia vera

Aline Schögler
(Dr. Marco Alves, Prof. Dr. Thomas Geiser)
Mechanisms and modulation of the antiviral response in the cystic fibrosis airway epithelium

Maryam Seif
(Prof. Dr. Peter Vermathen)
Advanced multi-modal MR imaging methods and analysis tools for reliable determination of renal function in native and transplanted kidneys

Stefanie Seiler
(Prof. Dr. Hans Rudolf Widmer)
The potential of Nogo-A neutralization as a novel treatment strategy for Parkinson's disease

Stefania Sgroi
(Prof. Dr. Alain Kaelin)
Role of striatal opioidergic neuropeptides on locomotor hypersensitivity and dyskinesia in Parkinsonian rats

Diana Amy Shy
(Prof. Dr. Hugues Abriel)
Nav1.5 regulation via interacting proteins and subcellular localization

Valentin Sottas
(Prof. Dr. Hugues Abriel)
Characterization of Nav1.5 genetic variants leading to different cardiac arrhythmias

Wilhelm Wimmer
(Prof. Dr. Martin Kompis)
Multidisciplinary approaches toward an improved efficacy of cochlear implants

MD, PhD

(supervisor in brackets)

Sophie Yammine
(PD Dr. Philipp Latzin)
Transition of inert gas washout measurements from research into clinics

Awards

The following DCR group members received awards in 2015:

Prof. Dr. Ramanjaneyulu Allam
Hematology (Adults)
SNF professorship: "Role of ribonuclease inhibitor (RNH1) in hematopoiesis and inflammation"

Dr. Julia Cahenzli, Dr. Yasmin Köller
Gastroenterology / Mucosal Immunology
Research Prize for Infectious Diseases, Rheumatology and Immunology, Pfizer Foundation: "Intestinal microbial diversity during early-life colonization shapes long-term IgE levels"

Selina Crippa
Neurology
Poster Prize of the DCR for Best Project by a Medical Student: "Transcranial direct current stimulation effects on cognitive control in high versus low conflict situations"

Paola Francica
Radiation Oncology
Poster Prize of the DCR for Best Preclinical Project: "FOXM1 is a critical mediator of DNA damage-induced senescence in gastric cancer models following targeting the MET receptor tyrosine kinase"

Dr. Thusitha Gajanayake, Prof. Dr. Robert Rieben
Hand Surgery
Swiss Transplant Research Award 2015 (2nd prize for research), Swiss Transplantation Society: "A single localized dose of enzyme-responsive hydrogel improves long-term survival of a vascularized composite allograft"

Dr. Morteza Jafari
Dermatology
Poster Prize for Excellent Clinical Research Project in Dermatology, Swiss Society of Dermatology and Venereology (SGDV): "One versus two cm excision margins for cutaneous malignant melanomas thicker than 2 mm"

Prof. Dr. Johanna A. Kremer Hovinga
Hematology (Adults)
Ellerman Prize and Lecture, Morgens and Wilhelm Ellermann-Foundation and Swiss Society of Hematology: "Acquired TTP – insights into the autoimmmune response against ADAMTS13"

Shun-Qing Liang, Dr. Thomas M. Marti, Dr. Patrick Dom, Laurène Froment, Dr. Sean R.R. Hall, Dr. Sabina Berezowska, Dr. Gregor Kocher, Prof. Dr. Ralph A. Schmid, Dr. Ren-Wang Peng
Thoracic Surgery
Best Experimental Publication, Swiss Society of Thoracic Surgery: "Blocking the epithelial-to-mesenchymal transition pathway abrogates resistance to anti-folate chemotherapy in lung cancer"

Dr. Sheida Moghadamrad
Hepatology
Benoît Pochon Prize: "HEP-14-1526.R1 attenuated portal hypertension in germ-free mice: function of bacterial flora on the development of mesenteric lymphatic and blood vessels"

Prof. Dr. Adrian Ochsenbein
Tumor-Immunology
Swiss Bridge Award for the project "Targeting TNF receptor TNIK signalling to eliminate cancer stem cells", and SAKK/RTFCCR/Gateway-Research Prize: "Phase I/II study of ARGX-110 in patients with relapsed/refractory acute myeloid leukemia"

Dr. Christoph Schlapbach
Dermatology
Peter Hans Hofschneider Professorship for Molecular Medicine, Foundation of Experimental Biomedicine: "Characterizing human IL-9 producing T helper cells and their role in human anti-melanoma immunity"

Dr. Christian Schürch, PD Dr. Carsten Riether
Tumor-Immunology
Young Investigator Award, Charles Rodolphe Brupbacher Foundation: "CD70/CD27-signaling is an independent adverse prognostic marker and novel therapeutic target for acute myelogenous leukemia"

Magdalena Skowronska, PD Dr. Monica Schaller Tschan, Irmela Sulzer, Prof. Dr. Johanna A. Kremer Hovinga
Hematology (Adults)
Best Abstract Award and Presidential Symposium Lecture, 59th Annual Meeting, Society of Thrombosis and Hemostasis Research (GTH), and Roche Hemostasis Research Award 2015, 83rd Annual Meeting, Swiss Society of Hematology: "Characterization of single sorted anti-ADAMTS13 specific B cells from the spleen of aTTP patients"

Staff Changes

New Staff

Claudia Güttinger
Laboratory Technician (80%),
Research Division MEM (since Sep.)

Dr. Thomas Schaffer
Scientific Assistant (30%),
Cytometry Laboratory / FACSlab
(since Jan.)

Nathalie Schuster
Laboratory Technician (100%),
Genomics and Molecular Biology
(since June)

Sarah Helena Vermij
Doctoral Student (100%),
Ion Channels and Channelopathies
(since Aug.)

Retirements

Andreas Furer
Laboratory Technician (80%),
Research Division MEM (until June)

Cynthia Furer
Laboratory Technician (20%),
Research Division MEM (until June)

Anton Strahm
House Staff (100%),
Research Division MEM (until Sep.)

Resignations

Dr. Jörg Arnoldi
Head of Laboratory (50%),
Plastic and Hand Surgery (until Apr.)

Luca Bologna
Doctoral Student (100%),
Hematology (Adults) (until July)

Raja El Adnani Prince
Doctoral Student (100%),
Hematology (Adults) (until July)

Muriel Fragnière
Laboratory Technician (90%),
Genomics and Molecular Biology
(until Feb.)

Claudia Quarroz
Laboratory Technician (100%),
Hematology (Adults) (until Jan.)

Diana Shy
Doctoral Student (100%),
Ion Channels and Channelopathies
(until Sep.)

Valentin Sottas
Doctoral Student (100%),
Ion Channels and Channelopathies
(until Sep.)

DCR Director: Prof. Dr. Hugues Abriel
Coordination: Verena Frazao
Editing: Leah Witton, wordsmith.ch@gmail.com
Photos: DCR; Susanne Bürki, Bern; Pascal Gugler, Inselspital
Typesetting: Nadine Wüthrich
Print: Geiger AG Bern

Contact
Basak Ginsbourger
Administrator
Department of Clinical Research
University of Bern
Murtenstrasse 35
3008 Bern
Switzerland

Phone: +41 31 632 3552
Fax: +41 31 632 0946
Email: basak.ginsbourger@dkf.unibe.ch

Members of the University of Bern and Inselspital can obtain a copy of this report online at: www.dkf.unibe.ch

Cover:
The building at Murtenstrasse 50, a DCR Research Division.
Image: Susanne Bürki, Bern