

DEPARTMENT OF CLINICAL RESEARCH
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Jahresbericht Annual Report 2016



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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 2016, 45 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 2016 waren 45 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 translationellen Ansätzen und der Anwendung von Omics-Technologien gelegt.



Foreword – Report of the Directorate

When the DCR was founded in 1994 it was nothing more than a virtual roof over the various research groups of the clinics of the Inselspital, Bern University Hospital. These groups took care of themselves, they had their own infrastructure and staff, supported by the Inselspital and their own research grants. Over the last 22 years we have built walls under the roof and the DCR has become a solid house and home for its research units. In part this is still a virtual house, because the groups are scattered over 11 different locations, but with the Murtenstrasse 50 building (opened in 2010) and the new labs at Murtenstrasse 40 (opened in 2016) we have been able to create new, state-of-the-art research laboratories. Today, the research groups are supported with everything they need and all of them can safely affirm in their grant applications: "As a research group of the Department of Clinical Research of the University of Bern we have access to all the necessary equipment and Core Facilities for the proposed project." This support, however, comes at a cost: For each and every person working in one of the DCR laboratories, the University of Bern spends between CHF 30,000 and CHF 50,000 per year to provide infrastructure and permanent staff. And while the number of DCR collaborators continues to grow, just like the number of laminar flows, incubators, freezers, FACS machines, etc., the financial resources available to the DCR do not. This is particularly difficult in a situation in which the DCR should – and wants to – improve its services for the research groups, for example because of increasing quality control requirements. We need to be creative, but we clearly want to continue to provide the best possible conditions for the research groups from the clinics of the Inselspital.

The past year was the beginning of a transition phase for the DCR, which will continue until mid-2017. Our Director, Prof. Hugues Abriel, stepped down in April 2016 to focus on his job as Director of the NCCR TransCure. Since October, he is also Director of the Institute of Biochemistry and Molecular Medicine (IBMM) and his research group 'Channelopathies' will leave the DCR and take over new labs and offices in the IBMM around mid-2017. Hugues was our Director for 7 years and much of the current structure of the DCR was developed under his guidance. He was a strong supporter of the concept of Core Facilities, which today are a key element of the DCR. In April 2016 the current Interim Directorate took over and in May 2017 we will have a new Director, Prof. Mark Rubin, who will also bring in a whole new field of research: Precision Medicine. We welcome our new Director already (he started to work 20 % in February 2017) and look forward to transforming the DCR into the DBMR (Department of Biomedical Research), which will be our new name as of mid-2017.

In 2016 we also experienced important changes with respect to laboratory space. The Haller-/Ludwig-Haus was demolished to make space for other buildings in the heart of the Insel campus. The groups with laboratories in these buildings had to move, as did the groups on the 6th floor of the Pathology building. The latter was renovated and now is used by the Institute of Pathology. In the research division Murtenstrasse 50, the DCR had to empty labs, to provide space for the ARTORG groups. As a (partial) compensation for the loss of lab space, the DCR got new laboratories at Murtenstrasse 40, which made it possible to finally bring the Hematology groups together at a single location, joined by the stem cell researchers



(Cluster for Regenerative Neuroscience and Dermatology Research), as well as the Genomics Core Facility.

In 2017 the management of laboratory space will continue to be extremely difficult in the DCR/DBMR and until 2020, when we will be able to move into our new building at Murtenstrasse 24, no relief is in sight. While the DCR will do its best to accommodate the needs of each group, in the future compromises will also be necessary.

This review of 2016 would not be complete without thanking all the collaborators who contributed enormously to the success of the DCR. First of all, we thank and congratulate the researchers who with their high quality and successful work make the DCR one of the places in which to be. Furthermore, special thanks go to the Coordinators of the DCR Research Divisions, the Heads of the Technology and Animal Core Facilities, the numerous members that contribute to daily DCR life in their many different functions, and to the DCR administration team.

Prof. Robert Rieben
Interim Director

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

Vorwort – Bericht der Direktion

Als das DKF 1994 gegründet wurde, war es nichts weiter als ein virtuelles Dach über den verschiedenen Forschungsgruppen der Kliniken des Inselspitals, Universitätsspital Bern. Die Gruppen kümmerten sich um sich selbst, sie verfügten über eigene Infrastruktur und Mitarbeitende, finanziert vom Inselspital und aus eigenen Forschungsmitteln. In den letzten 22 Jahren haben wir Wände unter das Dach gebaut, und aus dem DKF ist ein massives Haus und eine Heimat für seine Forschungsgruppen geworden. Teilweise ist es nach wie vor ein virtuelles Haus, da die Gruppen auf 11 verschiedene Standorte verstreut sind. Mit dem Gebäude Murtenstrasse 50 (eröffnet 2010) und den neuen Labors an der Murtenstrasse 40 (eröffnet 2016) konnten wir jedoch neue, dem heutigen Stand der Technik entsprechende Laborräumlichkeiten schaffen. Gegenwärtig werden die Gruppen mit allem was sie benötigen unterstützt und können in ihren Förderanträgen unbesorgt schreiben: "Als Forschungsgruppe des Departements Klinische Forschung der Universität Bern haben wir Zugang zu allen notwendigen Geräten und Core Facilities, die für das vorgeschlagene Projekt notwendig sind." Diese Unterstützung hat jedoch ihren Preis: Für jede einzelne Person, die in einem der DKF Labors arbeitet, wendet die Universität CHF 30,000 bis CHF 50,000 pro Jahr auf für die Bereitstellung von Infrastruktur und Personalkosten. Und während die Zahl sowohl der DKF Mitarbeitenden wie auch der Laminar Flows, Inkubatoren, Gefrierschränke, FACS-Geräte, usw. immer noch wächst, ist dies bei den finanziellen Ressourcen, die dem DKF zur Verfügung stehen, nicht der Fall. Dies ist besonders schwierig in einer Situation, in der das DKF seine Leistungen für die Forschungsgruppen verbessern sollte – und möchte – beispielsweise durch steigende Anforderungen

an die Qualitätskontrolle. Wir müssen kreativ sein, aber wir wollen auch weiterhin die bestmöglichen Bedingungen für die Forschungsgruppen aus den Kliniken des Inselspitals bereitstellen.

Das vergangene Jahr war der Beginn einer Übergangsphase, die bis Mitte 2017 dauern wird. Unser Direktor, Prof. Hugues Abriel, trat im April 2016 zurück, um sich auf seine Funktion als Direktor von NCCR TransCure zu konzentrieren. Seit Oktober ist er zudem Geschäftsführender Direktor des Instituts für Biochemie und Molekulare Medizin (IBMM). Seine Forschungsgruppe 'Channelopathies' wird das DKF Mitte 2017 verlassen und im IBMM neue Labors und Büros beziehen. Hugues war 7 Jahre unser Direktor, und ein Grossteil der aktuellen Struktur des DKF ist unter seiner Leitung entstanden. Er war ein starker Befürworter des Konzepts der Core Facilities, die heute ein Schlüsselement des DKF sind. Im April 2016 hat die derzeitige Interimsdirektion übernommen, und ab Mai 2017 werden wir einen neuen Direktor haben, Prof. Mark Rubin, der auch ein ganz neues Forschungsgebiet einbringen wird: Präzisionsmedizin. Wir begrüßen unseren neuen Direktor (im Februar 2017 hat er seine Tätigkeit mit 20% aufgenommen) und freuen uns, das DKF in das DBMF (Departement für Biomedizinische Forschung) über zu führen. Dies wird ab Mitte 2017 unser neuer Name sein.

Im Jahr 2016 hatten wir wichtige Veränderungen im Hinblick auf Laborflächen. Das Haller-/Ludwig-Haus wurde abgerissen, um Platz für andere Gebäude im Herzen des Inselcampus zu schaffen. Die Gruppen mit Labors in diesen Gebäuden mussten umziehen, ebenso die Gruppen im 6. Stock des Pathologiegebäudes. Letzteres wurde renoviert und wird heute vom Institut für Pathologie genutzt. Im Forschungsbereich Murtenstrasse 50 musste das DKF Raumflächen frei geben, um Platz

für ARTORG-Gruppen zu schaffen. Als (Teil-)Kompensation für den Verlust von Laborräumlichkeiten erhielt das DKF in der Murtenstrasse 40 neue Labors, die es endlich ermöglichten, die Hämatologie-Gruppen an einem Standort unterzubringen, zusammen mit den Stammzellenforschenden (Cluster für Regenerative Neurowissenschaft und Forschungsgruppe Dermatologie) sowie der Genomics Core Facility.

Auch im Jahr 2017 wird die Bereitstellung von genügend Laborfläche im DKF/DBMF extrem schwierig sein, und bis 2020, wenn wir in unseren Neubau Murtenstrasse 24 einziehen können, ist keine Entlastung in Sicht. Obschon das DKF sein Bestes tun wird, um den Bedürfnissen der einzelnen Gruppen nachzukommen, werden auch in Zukunft Kompromisse notwendig sein.

Dieser Rückblick auf 2016 wäre unvollständig, ohne unseren Dank an alle Mitarbeitenden, die enorm zum Erfolg des DKF beigetragen haben. Zuerst danken und gratulieren wir den Forschenden, die mit der ausgezeichneten Qualität ihrer Arbeit dafür sorgen, dass das DKF ein begehrter Platz für herausragende Forschende ist und bleibt. Ein besonderer Dank gilt den Koordinierenden der DKF Forschungsbereiche, den Leitenden der Technologie und Tier Core Facilities, den vielen Mitarbeitenden, die in verschiedenen Funktionen zum täglichen DKF-Leben beitragen, und dem Team der DKF Administration.



Prof. Robert Rieben
Direktor ad interim



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

Organisation

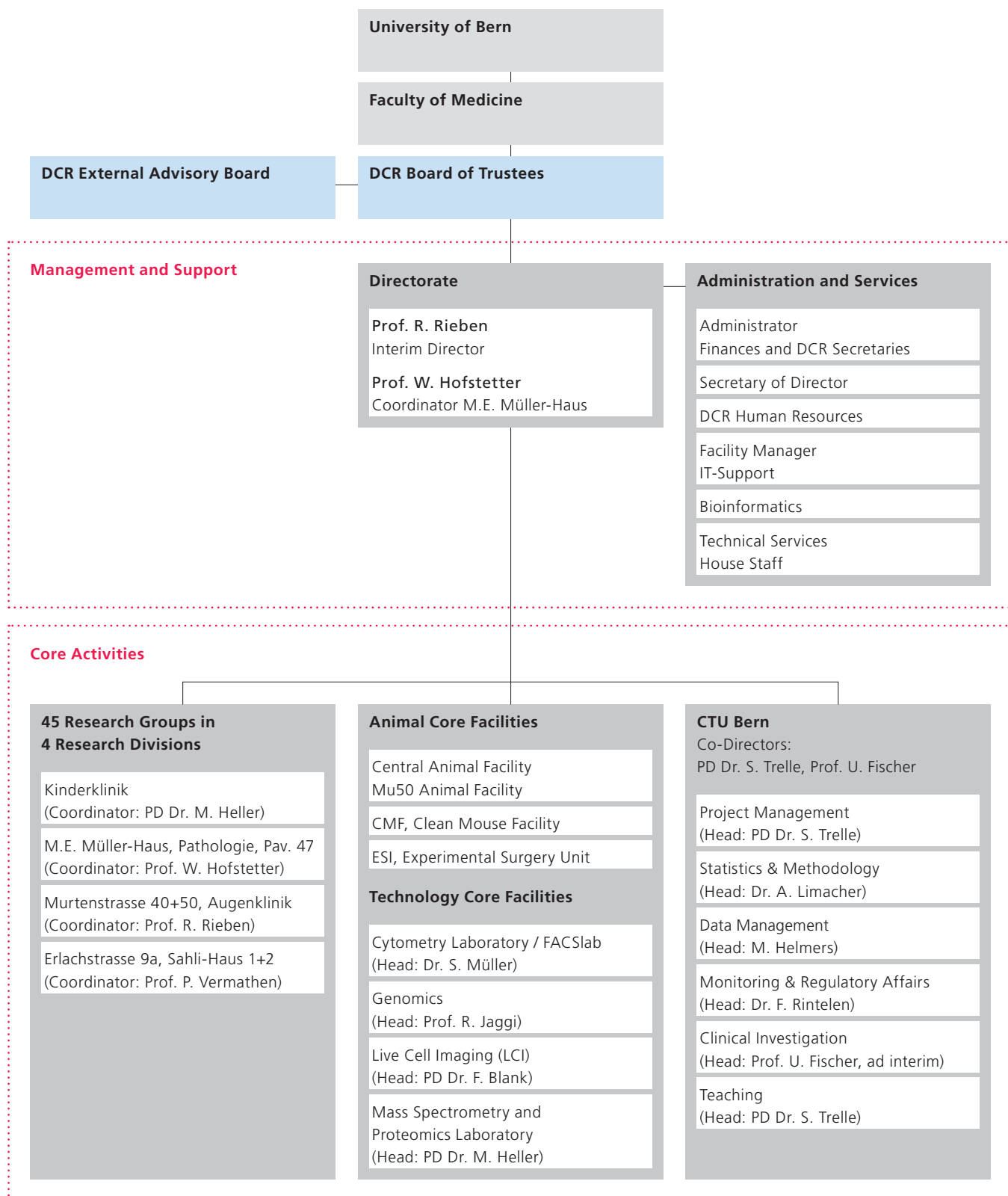
The role of the DCR is to provide optimal infrastructure and scientific support to its research groups, of which there were 45 at the end of 2016. The vast majority (41) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainder (4) are internal DCR groups, involved in the scientific support and coordination of equipment and infrastructure on a daily basis. The 45 groups are divided into 4 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 Interim Director and the responsible of the Research Division M.E. Müller-Haus, is supported by a Facility Manager. The External Advisory Board evaluates the overall strategies and operation of the DCR.



Organigram

December 2016





1
M.E. Müller-Haus
Murtenstrasse 35



2
Murtenstrasse 50



3
Pathologie
Murtenstrasse 31



4
Pavillon 52 (until Aug.)
Freiburgstrasse 3



5
Kinderklinik
Freiburgstrasse 15



6
Sahli-Haus 1
Freiburgstrasse 14a



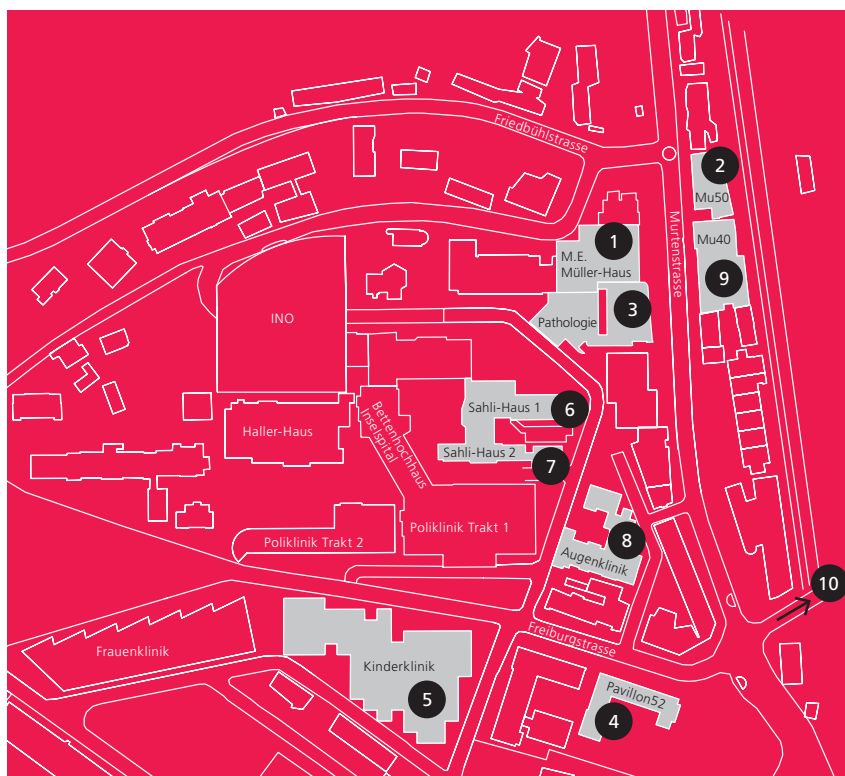
7
Sahli-Haus 2
Freiburgstrasse 14



8
Augenklinik
Freiburgstrasse 8



9
Murtenstrasse 40
(since Feb.)



10
Erlachstrasse 9a
(since Sept.)

Key People

DCR Board of Trustees (until Aug.)



Prof. Dr. Hans-Uwe Simon
Chair

Members

Prof. Dr. Hugues Abriel
Prof. Dr. Claudio Bassetti
Prof. Dr. Daniel Candinas
Prof. Dr. Marcel Egger
Prof. Dr. Peter Eggli
Prof. Dr. Sabina Gallati
Prof. Dr. Matthias Gugger
Prof. Dr. Christoph Müller
Prof. Dr. Lutz-Peter Nolte

Prof. Dr. Anton Sculean
Prof. Dr. Christian Seiler
Dr. Katharina Stegmayer

Advisory Members

Dr. Lukas Stalder

Directorate (until Mar.)

Prof. Dr. Hugues Abriel
Director

Prof. Dr. Willy Hofstetter
Managing Director

Directorate (since Apr.)



Prof. Dr. Robert Rieben
Interim Director



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

External Advisory Board

Prof. Dr. Gisou van der Goot
EPF Lausanne (CH)

Prof. Dr. Paul Klenerman
University of Oxford (UK)

Prof. Dr. Karl Schaller
University of Geneva (CH)

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

Administration and Central Services

Administrator / Finances and DCR Secretaries

Basak Ginsbourger, Administrator
Deborah Re, Secretary
Beatrix Stalder, Secretary
Uyen Vo, Secretary

Secretary of Director

Verena Frazao
Peggy Kübler (since Dec.)

DCR Human Resources

Silvia Rösselet

Facility Manager

Bernhard Grossniklaus

Occupational Safety, Health Protection and Environmental Safety (OHE)

Dr. Antoinette Wetterwald
(until Apr.)
François Achermann (since May)

IT-Support

Michael Ackermann
David Schär
Thomas Späti

Bioinformatics

Dr. Irene Keller
Dr. Cedric Simillion
Ilker Romann

Technical Services

Otto Aeby, Head DCR Maintenance
(until June)
Patrick Furer, Head DCR
Maintenance (since May)

Coordinators of Research Divisions



PD Dr. Manfred Heller
Kinderklinik



Prof. Dr. Willy Hofstetter
M. E. Müller-Haus,
Pathologie, Pav. 47



Prof. Dr. Robert Rieben
Murtenstrasse 40
(since Feb.) +50, Augenklinik



Prof. Dr. Peter Vermathen
Pavillon 52 (until Aug.),
Erlachstrasse 9a (since Sept.),
Sahli-Haus 1+2

Heads of Core Facilities



PD 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

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Achievements 2016

In autumn 2015, the Swiss National Science Foundation (SNSF) initiated a new funding program dedicated to investigator-initiated trials (IICT). We supported several researchers in submitting a grant. Eventually, nine out of 75 proposals have received funding and CTU is involved in three of these multicentric projects:

- NOSTONE, a placebo-controlled randomized trial evaluating the value of different doses of hydrochlorothiazide to prevent recurrent kidney stones (D. Fuster, Department of Nephrology, Inselspital).
- SERVE, a randomized placebo-controlled trial that evaluates the effects of the phosphodiesterase-5 inhibitor tadalafil on systemic right ventricular size and function in adult patients with a systemic right ventricle, a congenital heart disease (M. Schwerzmann, Department of Cardiology, Inselspital).
- SIMPL'HIV, a randomized non-inferiority trial evaluating a simplified strategy for the long-term management of HIV infection (A. Calmy, Department of Infectious Disease, HUG Geneva).

In addition to these three trials, preparatory work also started for several other trials in which CTU Bern contributes significantly. Two of these deserve special attention:

- The OPERAM trial is an international randomized-controlled trial in four European countries evaluating the effects of structured drug review in multimorbid elderly patients with polypharmacy. The trial is part of the OPERAM project, which is funded by the European Commission within the HORIZON 2020 programme. CTU Bern is responsible for coordination of the trial, data management, monitoring, and statistics.

- The MASTER DAPT trial is a global trial that will be conducted in more than 100 sites worldwide. The trial evaluates different anticoagulation strategies in patients who received a stent and who are at high risk of bleeding. CTU Bern is responsible for the data management, central data monitoring, and statistics.

Furthermore, several projects were completed and published in 2016 with support of CTU Bern. For example, final results of the Ebola Ça Suffit! trial, which was the first trial to evaluate the efficacy of a vaccine against Ebola virus disease, were presented. A randomized-controlled phase II trial comparing placebo with tocilizumab as induction and maintenance therapy in patients with giant cell arteritis was completed and published. The trial showed for the first time that tocilizumab is highly effective in this indication.

Performance Report 2016

Our consulting service remains one of the most important tasks. Overall, 244 consultancy activities were performed in 2016. Statistical and methodological support for study design, as well as questions regarding data management, were the most popular requests. Since we had contact with almost all clinical and non-clinical institutions of the faculty, we consider this support not only essential, but also well established.

Overall, 158 research projects were supported by CTU Bern in 2016 (with at least 8 hours of support). Of these, 50 were clinical trial projects, i.e. studies that evaluated the effect of a health-care intervention. Cardiovascular projects remained the main focus. However, other disciplines such as general internal medicine, gynecology, rheumatology, or paediatrics



PD Dr. Sven Trelle
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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, methodological Co-Director, 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. Professor for Acute Neurology and Stroke (Extraordinarius, 2015), University of Bern. Since 2015, medical Co-Director, CTU Bern.

have gained importance. We also increased our teaching activities. In 2016 we provided specific GCP and research ethics courses for dentists and, in collaboration with the Berner Fachhochschule (BFH), courses for master students in nursing and physiotherapy. Overall, seven basic and five advanced courses were taught, with more than 300 participants. We also completed a certificate of advanced studies course for Clinical Research Coordinators with 21 participants. This CAS is offered in collaboration with the BFH.

Finances 2016

Inselspital continues to provide core funding to support basic services and core positions at CTU. Project funds and service charges remain very important as they cover more than two thirds of the budget.

Outlook 2017

Several large-scale trials will start patient recruitment (see above). We are especially excited about this as these trials show that it is possible to get competitive funding for large-scale clinical trial projects in Switzerland. The SNF had issued a second IICT call in autumn 2016. We were again involved in several applications. Results of the review process of this highly competitive call are expected to be communicated in the spring.

Staff Members

PD Dr. Sven Trelle, Co-Director (methodological)

Prof. Dr. Urs Fischer, Co-Director (medical)

Hafeezul Adnan, Clinical Data Manager

Sarah Berner, Quality Manager

Anna Blättler, Assistant (since Sept.)

Renata Bünter, Clinical Research Coordinator

Dr. Lukas Bütikofer, Senior Statistician

Madeleine Dähler, Study Coordinator

Ibrahima Dina Diatta, Statistical Data Manager (until Feb.)

Dr. Niklaus Fankhauser, Statistician

Dr. Enrico Frigoli, Project Manager (since Dec.)

Dr. Alan Haynes, Senior Statistician

Dr. Dik Heg, Head, Cardiovascular Health

Sarah Heldner, Research Fellow (until Jan.)

Muriel Helmers, Head, Clinical Data Management

Stefanie Hossmann, Project Manager

Regula Jaeggi, Clinical Research Coordinator

Lucia Kacina, Clinical Trial Monitor

Dr. Alex Karagiannis, Senior Statistician (since Mar.)

Dr. Andreas Limacher, Head, Statistics and Methodology

Lena Maurer, Junior Research Assistant

Julie Rat-Wirtzler, Clinical Data Manager

Dr. Felix Rintelen, Head, Monitoring and Regulatory Affairs

Martina Rothenbühler, Statistician

Dr. Marie Roumet, Senior Statistician (since Nov.)

Dominique Rubi, Clinical Data Manager

Ursina Sager, Clinical Research Coordinator (since Apr.)

Dr. Georgia Salanti, Senior Statistical Consultant

Magdalena Sánchez, Clinical Trial Monitor (until Nov.)

Dr. Roger Schürch, Senior Statistician (until Nov.)

Nathalie Schwab, Clinical Trial Monitor

Odile Stalder, Statistician (since May)

Dr. Luca Tamó, Project Manager

Brigitte Wanner, Head, Quality Management (until Jan.)

Simona Wanner, Assistant

Miriam Wegmann, Clinical Data Manager

Selina Wegmüller, Junior Research Assistant

Priska Wölfli, Clinical Data Manager

Janine Wyniger, Clinical Trial Monitor (until July)

Adrian Wyss, Clinical Data Manager

Serge Zaugg, Statistician (until Mar.)

Katrin Ziegler, Clinical Data Manager

Acknowledgements in publications

Efficacy and effectiveness of an rVSV-vectored vaccine in preventing Ebola virus disease: final results from the Guinea ring vaccination, open-label, cluster-randomised trial (Ebola Ça Suffit!). Henao-Restrepo, AM; Camacho, A; Longini, IM; Watson, CH; Edmunds, WJ; Egger, M; Carroll, MW; Dean, NE; Diatta, I; Doumbia, M; Drugeuz, B; Duraffour, S; Enwere, G; Grais, R; Gunther, S; Gsell, PS; Hossmann, S; Watle, SV; Konde, MK; Keita, S; Kone, S; Kuisma, E; Levine, MM; Mandal, S; Maugot, T; Norheim, G; Riveros, X; Soumah, A; Trelle, S; Vicari, AS; Rottingen, JA; Kiény, MP (2017) in: *Lancet*, 389(10068), p. 505-518.

Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Villiger, PM; Adler, S; Kuchen, S; Wermelinger, F; Dan, D; Fiege, V; Bütikofer, L; Seitz, M; Reichenbach, S (2016) in: *Lancet*, 387(10031), p. 1921-1927.

Effectiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in knee and hip osteoarthritis: a network meta-analysis. da Costa, BR; Reichenbach, S; Keller, N; Nartey, L; Wandel, S; Juni, P; Trelle, S (2016) in: *Lancet*, 387(10033), p. 2093-2105.

Link to publication list:

www.ctu.unibe.ch/research/publications/index_eng.html



Cytometry Laboratory / FACSlab

www.facslab.unibe.ch

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



Dr. Stefan Müller
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Studies in microbiology at University of Bern; PhD (1996). Postdoc (2000–2001) in intestinal mucosal immunology 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 2016

The new UNICARD-controlled access system replaced the key deposit at the Emergency head office and allows to keep the doors to the facility locked for unauthorized persons at all times.

The FACSlab now hosts a Malvern NanoSight 300 instrument which is designed to quantify and characterize nano-/microparticles, such as exosomes or microvesicles.

A new high-speed cell sorter placed in a specifically designed biosafety class II hood was installed. It allows uncompromised sterile handling and sorting, as well as biosafety level 2 work. In addition, it is equipped with a UV-laser to meet the demand for sorting cells stained with novel brilliant ultraviolet fluorochrome-conjugated antibodies, together with the live-cell DNA dye Hoechst.

In addition, a new 4-laser, 13-color plate loader-equipped flow cytometer was installed under a cooperation contract with the company. On the long run, it will replace the BD FACS Array for which replacement parts supply will end in 2018.

Performance Report 2016

Compared to 2015, FACS measurements slightly decreased (-6.2 %), while sorting again increased by 33.6%! Decreased use of FACS analyzers was expected because of the availability of a new BD FACS LSR II Fortessa not hosted by the FACSlab.

42.5 % of the FACS measurements were performed by researchers from Inselspital clinics and 57.5 % by researchers from University of Bern institutes. Cell sorting numbers were 62.8 % and 35.5 %, respectively. Sorting for external parties made up 1.8 %, whereas 41.3 % of acquisitions and 63.2 % of cell sorting were performed by DCR groups.

A high interest in using the NanoSight 300 was observed: during the subsequent 6 months since its inclusion in the DCR Reservations-System, it was already booked for more than 500 hours (not included in the statistics above)!

Finances 2016

Software and hardware upgrades for BD instruments were exceptionally expensive items in 2016. Together with the increased costs for the FlowJo analysis software licences, offered to registered DCR FACS users by the FACSlab, expenses surpassed the revenues in 2016.

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

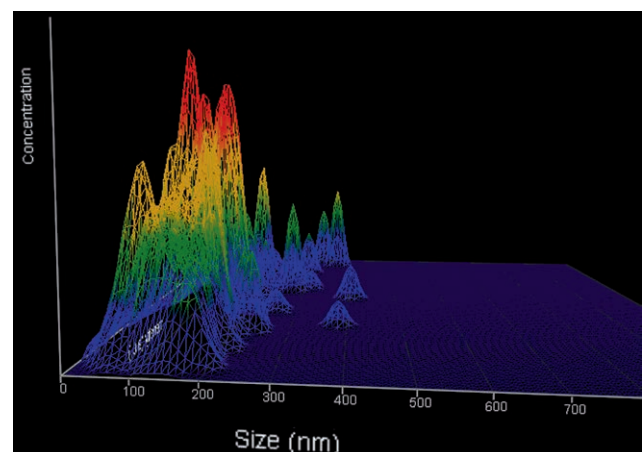
Outlook 2017

With the NanoSight, a new cell sorter and a new flow cytometer, the FACSlab now offers a wider range of FACS-related methodological options and will focus more than ever on technical, methodological and scientific support. In that respect, we hope to be able to upgrade the ImageStream imaging

flow cytometer with a 60x objective and “Enhanced Depth of Field Module”, to allow image-based FISH-analysis, as well as microparticle measurements with high statistical power.

Staff Members

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



Live Cell Imaging (LCI)

www.lci.dkf.unibe.ch/

www.dkf.unibe.ch/services/core_facilities/live_cell_imaging_lci



PD 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. Venia docendi (2016).

Achievements 2016

The equipment of the facility has been expanded again. A newly inverted Nikon-Eclipse brightfield/fluorescence microscope has been installed at Murtenstrasse 40 (U116). Two high-end computers have been installed in the same room for image processing with IMARIS or other applications. First users looking for imaging with enhanced resolution have been introduced to the AiryScan unit of the LSM710. Furthermore, users in need of fast 3D imaging have started to receive training at the Nikon-Eclipse spinning disk confocal System.

The histology lab of the LCI Core Facility was relocated from Murtenstrasse 50 to the MEM building (G809). At the new location there is more space and more equipment available to perform specific applications of histology. Please contact Carlos Wotzkow (carlos.wotzkow@dkf.unibe.ch) for more information.

Since its launch in 2012, the LCI Core Facility is supported by the Microscopy Imaging Centre (MIC), 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 2016

A total of 95 users (2015: 72) from 39 different research groups (2015: 30) acquired microscopy data with the help of the Facility and spent a total of 4,433 booked hours (2015: 5,144) using its equipment during the last year. As in previous years, the Facility contributed to cutting-edge lectures and practical modules organised by the MIC. In addition, the Facility is continuously advising, supporting and collaborating with a number of research groups from the DCR and from other institutions. This resulted in 372 hours

of technical work for collaborations and 279 hours of technical assistance for support in 2016.

Finances 2016

Revenue remained at the level of the previous year. The Facility received a working credit of CHF 6,000 from the DCR for general maintenance and repairs. The yearly IMARIS software license fee was no longer covered by the "Ressourcenausschuss" of the Faculty of Medicine. However, the Facility has paid CHF 2,426 to cover the costs for three IMARIS licenses, which are available for users in the Facility for free.

Outlook 2017

The LCI Core Facility will put special effort in training more users to become familiar with the latest technology acquired. In this regard, the Facility is organizing courses in laser scanning microscopy, spinning disk microscopy and in the use of IMARIS together with the MIC.

Staff Members

PD Dr. Fabian Blank, Head
Carlos Wotzkow, Laboratory Technician

Genomics (Core Facility)

www.gcf.dkf.unibe.ch/
www.dkf.unibe.ch/services/core_facilities/genomics

Molecular Biology (Research Group)

www.molbiol.dkf.unibe.ch/
www.dkf.unibe.ch/research/research_groups/molecular_biology

Achievements 2016 / Outlook 2017 Molecular Biology

Our research has been focused on the role of steroid hormone receptors (glucocorticoid receptor, GR; oestrogen receptor, ER; progesterone receptor, PR) during normal development of the breast and during breast cancer. In general, steroid hormone receptors are activated upon binding of their respective receptors. Active receptors translocate to the nucleus of the cells where they directly act as transcription factors by binding to specific elements in the DNA, thereby activating or repressing multiple genes in responsive cells. Importantly, target genes may vary from cell type to cell type and depending on the activity of other regulatory elements. About 70 % of breast cancer cells express the ER. Following oestrogen binding, the ER stimulates proliferation in breast cancer cells. Growth promotion can be blocked in a majority of patients with anti-oestrogens (e.g. tamoxifen), or inhibitors of oestrogen synthesis (e.g. aromatase inhibitors). The PR is often expressed together with the ER. Independent studies from various groups have documented that PR expression correlates with reduced risk of recurrence in ER-positive breast cancers. PR expression is often limited to a subset of cancer cells and it remains unclear whether PR-positive and -negative cells exert a similar risk of recurrence for the patient.

We developed several "CRISPR/Cas9" constructs. These are small and efficient molecular scissors which bind and cleave genomic DNA in a highly specific way. Single genes in the genome can be targeted and disrupted leading to the elimination of functional genes. We used the system to destroy the PR gene in breast cancer cells *in vitro* in order to generate PR-deficient cells from PR-expressing cells. The transcriptome of starting and knockout

cells will be compared using RNA-seq and the role of differentially expressed genes will be studied in cultured cells and also in human breast cancers. This will hopefully lead to a more detailed understanding of PR as a transcription factor and to targets of PR. Hopefully, our work will contribute to the development of novel approaches to control proliferation of human breast cancer cells.

Performance Report 2016 / Outlook 2017

Genomics

The Genomics Core Facility has supported several users of the Faculty of Medicine with either next generation sequencing (both, on the Ion Torrent PGM and the Illumina Hi-Seq), gene expression measurement using Nanostring technology (two groups), digital PCR (two groups) or real-time PCR. Our group has been involved to various degrees with several clinical projects which started in 2016 by providing technical and experimental support during sample preparation (RNA isolation, quantitation and quality control), special issues related to low or very low recoveries from very small amounts of clinical material, e.g. we isolated RNA from a few thousand cells sorted by FACS (collaboration with Dr. S. Rothschild, Basel); we isolated cells from histologically well-defined brain areas from formalin-fixed, paraffin-embedded hippocampus tissue using Laser Capture Microdissection (collaboration with PD Dr. H. Krestel, Neurology, Inselspital, Dr. I. Centeno Ramos and Dr. E. Hewer, Institute of Pathology); and we provided specialised protocols and reagents for RNA isolation and optimal recovery. In many cases the RNAs were further analysed by Next Generation Sequencing on an Illumina HiSeq machine. Additionally, the results generated in these



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.

collaborations were analysed by the bioinformatics team of the DCR. In every case, the support provided by our group was adjusted to the specific needs of the external groups.

Finances 2016

Genomics

The Genomics Core Facility received a working credit of CHF 4,000 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)

Nathalie Schuster, Laboratory Technician (Research Group & Core Facility)

Collaborators

Aebi S, Gautschi O, Günthert A, Lucerne Cantonal Hospital (CH)

Centeno Ramos I, Hewer E, University of Bern (CH)

Krestel H, Inselspital (CH)

Ochsenbein A, Inselspital (CH)

Popovici V, Masaryk University (CZ)

Rothschild S, University Hospital Basel (CH)

Schlapbach R, Inselspital (CH)

von Tengg H, Granzow C, Inselspital and DCR (CH)

Zweifel M, Inselspital (CH)

Teaching activities

- Selected topics in molecular pathology: Molecular Processes of Disease lecture

Publication

Molecular Biology

Joint analysis of histopathology image features and gene expression in breast cancer. Popovici, V; Budinska, E; Capkova, L; Schwarz, D; Dusek, L; Feit, J; Jaggi, R (2016) in: BMC Bioinformatics, 17(1), p. 209.

Grants

Amounts allocated for 2016:

Molecular Biology

- W.+H. Berger-Janser Foundation: Characterization of ER-negative cancer cells in ER-positive breast cancer (R. Jaggi) CHF 61,300
- S. Rothschild: Deciphering mechanisms of resistance to PD-1 blockade in patients with non-small cell lung cancer (Nanostring analyses) (R. Jaggi) CHF 17,200
- Various donors: (R. Jaggi) CHF 7,000

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

Achievements 2016 / Outlook 2017

Mass Spectrometry and Proteomics & Protein and Cell Biology

It was with great fortune that we were able to acquire two cutting-edge new instruments last year. It would have been impossible to process all the service requests without the new equipment. At this point, we would like to thank all those researchers for their trust in us and patience while waiting for results. We saw many exciting projects this year and can state that proteome science has finally reached a wider community at the University of Bern. We burned about 1mg of proteases, which relates to about 100mg of proteins digested during this year!

Our highlight was the publishing of our research results on circulating extracellular vesicles from human blood plasma in the December issue of *Molecular & Cellular Proteomics*. Other achievements were:

- 1) The automated protein sample processing for LC-MS/MS on a PAL RTC liquid handling robot from CTC Analytics (Zwingen) was accomplished and presented at the International Mass Spectrometry Conference in Toronto.
- 2) We established a robust protocol for deep phosphoproteome sequencing with a simple shotgun approach. With this protocol, we participated in a pan-European study with 23 other laboratories. We were the winner in terms of numbers of identified phosphopeptides.
- 3) We managed to implement an isobaric tag-based workflow for comparative, quantitative proteomics.
- 4) In collaboration with Sohvi Blatter (Animal Pathology at Vetsuisse Faculty), and Dr. Stefan Müller (FACSlab), we were able to establish general guidelines for working

with sorted cells. The issue was that samples with an apparently equal number of sorted cells resulted in variable protein yields and irreproducible proteomics results. It turned out that the surface of vials for collecting cells had to be saturated with protein first, otherwise cells would stick to the vial walls and be lost for down-stream analysis. Cell size dependent, 0.1 to 0.5 Mio cells should be provided for a comprehensive proteomics analysis.

- 5) We established a reproducible protocol for protein extraction from grapevine leaves, but now need to do the same for leaf petioles, as it turned out that the virus we aim to quantify in leaves is only weakly expressed there.
- 6) In collaboration with Geistlich AG (Wolhusen), we performed the absolute quantification of three collagen chains in a medical specimen using heavily labelled peptide standards and a targeted mass spectrometry approach.

Last but not least, Dr. Anne-Christine Uldry (Computational Scientist in support of the Core Facility) and Dr. Anabel Maciel Dominguez (Post-doctoral Fellow, Research Group) joined us in September.

Plans for 2017

We aim to 1) produce preliminary results showing the involvement of extracellular vesicles in Myelodysplastic Syndrome (A. Maciel in collaboration with N. Bonadies, Hematology); 2) set-up a new, automated pipeline for the interpretation of LC-MS/MS data (A-C. Uldry); 3) submit grant proposals to funding agencies, in order to fund contract extensions of our two new team members; and 4) develop a new software for the interpretation of fragment spectra of cross-linked

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. Nineteen years of experience in mass spectrometry, proteomics and bioinformatics.

peptides (Bioinformatic Masters student with A-C. Uldry in collaboration with M. Müller, SIB).

Müller M, Swiss Institute of Bioinformatics (CH)

Stiefel N, Geistlich AG (CH)

Zlobec I, University of Bern (CH)

Performance Report 2016

Mass Spectrometry and Proteomics

We processed approximately 1,900 samples during the year, submitted by laboratories from the Vetsuisse Faculty (21.1 %), external institutions (2.0 %), Faculty of Medicine (28.1 %), Faculty of Science (28.8 %), and from our own developments and collaborations with other groups (20.0 %). This relates to about 3,600 LC-MS/MS runs, not including the 712 QC standards and 3,540 blanks.

Finances 2016

Mass Spectrometry and Proteomics

Our financial situation profited from the fact that two of the three mass spectrometers were under warranty, saving repair costs. We had a positive balance of around CHF 7,000.

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. Anabel Maciel Dominguez, Postdoctoral Fellow (Research Group)

Ilker Romann, IT Specialist (Core Facility)

Dr. Cedric Similion, Bioinformatician (Core Facility)

Dr. Anne-Christine Uldry, Computational Scientist (Core Facility)

Collaborators

Böhm G, CTC Analytics AG (CH)

Bonadies N, University of Bern (CH)

Debonneville C, Bioreba AG (CH)

Reynard JS, Agroscope, Nyon (CH)

Grants

Amounts allocated for 2016:

Protein and Cell Biology

- CTI Grant 18393: 1PFLS-LS (M. Heller) CHF 45,200

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

Robust Label-free, Quantitative Profiling of Circulating Plasma Microparticle Associated Proteins. Braga-Lagache, S; Buchs, N; Iacovache, MI; Zuber, B; Jackson, CB; Heller, M (2016) in: Mol Cell Proteomics, 15(12), p. 3640-3652.

Aberrant association of misfolded SOD1 with Na(+)/K(+)-ATPase- α 3 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 (2016) in: Acta Neuropathol, 131(3), p. 427-451.

Bone Biology & Orthopaedic Research

www.bonebiology.dkf.unibe.ch

www.dkf.unibe.ch/research/research_groups/bone_biology_amp_orthopaedic_research/index_eng.html



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 the University of Georgia (US). Then joined the Institute of Pathophysiology, University of Bern. Since 1997, Head, Bone Biology & Orthopaedic Research Group, DCR.

Research Highlights 2016 / Outlook 2017

Bone Biology & Orthopaedic Research Group

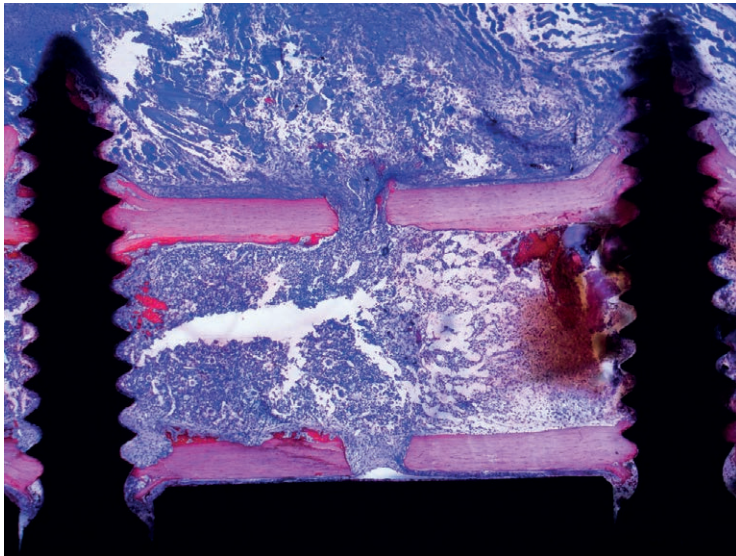
Highlights of our research on bone cell biology, inflammatory diseases and molecular transport systems include the projects described below:

- Inflammatory cytokines exert profound effects on the development and activation of bone cell lineages. In particular, we are interested in the plasticity of haematopoietic phenotypes that are developing under the control of haematopoietic growth factors and cytokines (NFP64 / Alfred and Anneliese Sutter-Stöttner Foundation, PhD project N. Ruef).
- The research on iron as a modulator of bone metabolism was carried on. Osteoclast-specific knock out (KO) mice for ferroportin and DMT1 were established. Neither of these KO mice expressed an obvious phenotype and they are presently being further investigated to assess the consequences of a loss of DMT1 and ferroportin in osteoclasts. (NCCR TransCure, PhD project R. Cabra).
- Bone healing in osteoporotic bones treated with the bisphosphonate alendronate (Ale) was followed under rigid and non-rigid fixation. Transcriptome analysis was performed to elucidate the healing pathways for a small bone defect in dependence of stability of fixation and therapeutic treatment. The analysis of the data is presently in progress (Alfred and Anneliese Sutter-Stöttner Foundation, PhD project M. Hauser).
- Transcriptome data of bovine articular chondrocytes were confirmed for 10 genes differentially expressed in two different monolayer and two different high-density pellet cell cultures. GDF10 and FRZB were selected for further analysis. Silencing or over-expression of each or both genes will demonstrate their potential role for neochondrogenesis in vitro. (Robert Mathys Foundation, R. Egli, D. Nestic).
- We have found the BMP antagonist Noggin to exert BMP-independent effects on bone cell lineages. At least parts of these effects are mediated indirectly through an activation of TGF β signalling. (ITI Foundation, E. Hartmann; PI: F. Klenke).

Osteo-Articular Research Group

The aim of the research includes:

- Investigation of the putative correlation between the presence of SNPs in VEGFA and VEGF Receptor 2 (KDR) and the predisposition for the post-operative shoulder stiffness (a pilot study with the Department of Orthopaedic Surgery and Traumatology, Inselspital).



Group Members

Bone Biology & Orthopaedic Research Group

Prof. Dr. Willy Hofstetter, Group Leader

Dr. Antoinette Wetterwald, Senior Scientist (until Apr.)

Eliza Hartmann, Research Assistant (until Sept.)

Silvia Dolder, Laboratory Technician

Mark Siegrist, Laboratory Technician

Romina Cabra, PhD Student

Michel Hauser, PhD Student

Nina Ruef, PhD Student

Osteo-Articular Research Group

PD Dr. Dobrila Nestic, Group Leader

Clinicians with projects in the group

Dr. Rainer Egli, Project Leader

PD Dr. Frank Klenke, Project Leader

Collaborators

Aeberli D, Inselspital (CH)

Fuster D, Inselspital (CH)

Iizuka T, Inselspital (CH)

Kohl S, Inselspital (CH)

Luginbuehl R, RMS Foundation (CH)

Saulacic N, Inselspital (CH)

Seitz M, Inselspital (CH)

Siebenrock KA, Inselspital (CH)

Zumstein M, Inselspital (CH)

Grants

Amounts allocated for 2016:

Bone Biology & Orthopaedic Research

- SNF: NCCR TransCure sub-project: Role of ion transporters in bone

homeostasis (W. Hofstetter)
CHF 75,000

- Alfred und Anneliese Sutter-Stöttner Foundation: Heilung von Frakturen in osteoporotischen Knochen (W. Hofstetter) CHF 87,000
- Alfred und Anneliese Sutter-Stöttner Foundation: Faser-verstärkte Knochenersatzmaterialien – Verbesserung der Biokompatibilität und des Umbaus (W. Hofstetter) CHF 85,000
- Robert Mathys Foundation Research Support (W. Hofstetter) CHF 54,000

Teaching Activities

- MSc Biomedical Engineering: Tissue Engineering course (Nestic)
- 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

Regulation of peripheral classical and non-classical monocytes on infliximab treatment in patients with rheumatoid arthritis and ankylosing spondylitis. Aeberli, D; Kamgang, R; Balani, D; Hofstetter, W; Villiger, PM; Seitz, M (2016) in: *RMD Open*, 2(1), p. e000079.

Increased bone resorption by osteoclast-specific deletion of the sodium/calcium exchanger isoform 1 (NCX1). Albano, G; Dolder, S; Siegrist, M; Mercier-Zuber, A; Auberson, M; Stoudmann, C; Hofstetter, W; Bonny, O; Fuster, DG (2017) in: *Pflügers Arch*, 469(2), p. 225-233.

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 (2016) in: *J Biomed Mater Res B Appl Biomater*, 104(6), p. 1121-1131.

In vivo degradation of a new concept of magnesium-based rivet-screws in the minipig mandibular bone. Schaller, B; Saulacic, N; Beck, S; Imwinkelried, T; Goh, BT; Nakahara, K; Hofstetter, W; Iizuka, T (2016) in: *Mater Sci Eng C Mater Biol Appl*, 69, p. 247-254.

In vivo degradation of magnesium plate/screw osteosynthesis implant systems: Soft and hard tissue response in a calvarial model in miniature pigs. Schaller, B; Saulacic, N; Imwinkelried, T; Beck, S; Liu, EW; Gralla, J; Nakahara, K; Hofstetter, W; Iizuka, T (2016) in: *J Craniomaxillofac Surg*, 44(3), p. 309-317.

Three-Dimensional Quantitative Morphometric Analysis (QMA) for In Situ Joint and Tissue Assessment of Osteoarthritis in a Preclinical Rabbit Disease Model. Stok, KS; Besler, BA; Steiner, TH; Villarreal Escudero, AV; Zulliger, MA; Wilke, M; Atal, K; Quintin, A; Koller, B; Muller, R; Nestic, D (2016) in: *PLoS One*, 11(1), p. e0147564.

Glutamate Receptor Agonists and Glutamate Transporter Antagonists Regulate Differentiation of Osteoblast Lineage Cells. Xie, W; Dolder, S; Siegrist, M; Wetterwald, A; Hofstetter, W (2016) in: *Calcif Tissue Int*, 99(2), p. 142-154.

Extracellular Iron is a Modulator of the Differentiation of Osteoclast Lineage Cells. Xie, W; Lorenz, S; Dolder, S; Hofstetter, W (2016) in: *Calcif Tissue Int*, 98(3), p. 275-283.

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

Cardiovascular Research

www.cvrc.unibe.ch/research/ischemia___reperfusion/
www.dkf.unibe.ch/research/research_groups/cardiovascular_research



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 (1995–1997) in Leiden (NL). Return to Bern in 1997 to establish a research group. Habilitation (2002); Associate Professor (2007). Sabbatical in Melbourne (AU) in autumn/winter 2015/2016. Since 2005, Group Leader, Cardiovascular Research, DCR. Since April 2016, DCR Interim Director.

Research Highlights 2016 / Outlook 2017

In this yearly report I would like to highlight just a few of the many different collaborations on which much of the research activities of our group rely and which are absolutely crucial for the success of basic and translational research in general.

Since 2009 our group has been collaborating with the Institute of Molecular Animal Breeding and Biotechnology at the Ludwig Maximilian University in Munich (DE). Eckhard Wolf, the director of this institute, and his team have been pioneers in the genetic manipulation of pigs. We have been using genetically modified porcine cells and also whole pigs in the context of our research on xenotransplantation and ischemia / reperfusion injury. Bruno Reichart, a cardiac surgeon from Munich, has initiated the German Transregio DFG Project 127 on xenotransplantation, which started its second 4-year term in April 2016. Our group is currently collaborating with several of the TRR 127 members, and while they profit from our knowhow on complement and coagulation and our whole blood in vitro models, we benefit from their genetically modified pigs and their non-human primate transplantation models.

Thanks to my sabbatical in Australia, which ended in January 2016, I was able to build up a collaboration with Peter Cowan and his group at the St. Vincent's Hospital in Melbourne (AU). Like us, Peter has been working both on xenotransplantation and ischemia / reperfusion injury and through him I got in touch with Petra Magnusson from Uppsala (SE), who is closely collaborating with the Swedish company Corline. Corline produces a heparin-conjugate which can be used to coat plastic or metal surfaces to make them perfectly compatible with human blood, or alternatively to protect endothelial cells from attack by the innate immunity and the plasma cascade systems. Based on this collaboration spanning half of the globe we want to develop a novel in vitro system in which endothelial cells are cultured under pulsatile flow and then exposed to non-anti-coagulated whole blood. At the same time this collaboration will boost the development and testing of endothelial cell protectants and hopefully pave their way into clinical application for the prevention of reperfusion injury and early graft damage in transplantation.

A very recent collaboration is the one with Christian Heinis from the EPFL in Lausanne. Christian and his team synthesize bicyclic peptides and among others they have designed a specific inhibitor of coagulation factor XII, which is crucial in thrombus formation due to endothelial damage. We are currently testing a bicyclic FXII inhibitor in our closed-chest pig model of acute myocardial infarction, hoping that this inhibitor can reduce necrosis due to reperfusion injury. An efficient reduction of reperfusion injury related to treatment of myocardial infarction by balloon catheter intervention would clearly improve the heart function of patients suffering from acute myocardial infarction.

Group Members

Prof. Dr. Robert Rieben, Group Leader
Alain Despont, Laboratory Technician
Jane Shaw-Boden, Laboratory Technician
Oliver Steck, Laboratory Technician
Uyen Vo, Secretary and Web Administrator
Mai Abdelhafez, PhD Student
Dzhuliya Dzhonova, PhD Student
Riccardo Sfriso, PhD Student
Shengye Zhang, PhD Student (until July)
Pavan Garimella, Research Assistant (until Feb.)

Collaborators

Ayares D, Revivacor Inc (US)
Bovin N, Korchagina E, Titov A, Russian Academy of Sciences, Moscow (RU)
Constantinescu MA, Olariu R, Inselspital (CH)
Cowan P, Bongoni A, St. Vincent's Hospital, Melbourne (AU)
Guenat O, University of Bern (CH)
Heinis Ch, EPFL, Lausanne (CH)
Hofstetter W, University of Bern (CH)
Jenni HJ, Inselspital (CH)
Mollnes T, Pischke S, Oslo University Hospital (NO)
Niemann H, Friedrich Loeffler Institut, Neustadt (DE)
Reichart B, Abicht J, Ludwig Maximilian University of Munich (DE)
Seebach J, Geneva University Hospital (CH)
Spirig R, CSL Behring AG (CH)
Vemula P, inStem (IN)
Vögelin E, Taddeo A, Inselspital (CH)
Wolf E, Klymiuk N, Wünsch A, Ludwig Maximilian University of Munich (DE)

Grants

Amounts allocated for 2016:

- 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 159,000
- 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 87,000

- CSL Behring AG: Reperfusionsschaden im Zuge von Knieersatzoperationen (R. Rieben) CHF 33,000

Teaching Activities

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

Publications

Endothelial- and Platelet-Derived Microparticles Are Generated During Liver Resection in Humans. Banz, Y; Item, GM; Vogt, A; Rieben, R; Candinas, D; Beldi, G (2016) in: *J Invest Surg*, 29(1), p. 20-31.

Transgenic Expression of Human Thrombomodulin Inhibits HMGB1-Induced Porcine Aortic Endothelial Cell Activation. Bongoni, AK; Klymiuk, N; Wolf, E; Ayares, D; Rieben, R; Cowan, PJ (2016) in: *Transplantation*, 100(9), p. 1871-1879.

Modifying the Glycome in Pigs for Xenotransplantation. Cowan, PJ and Rieben, R (2016) in: *Transplantation*, 100(3), p. 485-486.

Dexrazoxane Shows No Protective Effect in the Acute Phase of Reperfusion during Myocardial Infarction in Pigs. Kamat, P; Vandenberghe, S; Christen, S; Bongoni, AK; Meier, B; Rieben, R; Khattab, AA (2016) in: *PLoS One*, 11(12), p. e0168541.

Correlation Between Sonographic and In Vivo Measurement of A1 Pulleys

in Trigger Fingers. Spirig, A; Juon, B; Banz, Y; Rieben, R; Vogelin, E (2016) in: *Ultrasound Med Biol*, 42(7), p. 1482-1490.

Vitreous Cytokine Profile Differences Between Eyes With Epiretinal Membranes or Macular Holes. Zandi, S; Tappeiner, C; Pfister, IB; Despont, A; Rieben, R; Garweg, JG (2016) in: *Invest Ophthalmol Vis Sci*, 57(14), p. 6320-6326.

Inhalation anesthesia of rats: influence of the fraction of inspired oxygen on limb ischemia/reperfusion injury. Zhang, S; Duehrkop, C; Plock, JA; Rieben, R (2016) in: *Lab Anim*, 50(3), p. 185-197.

Higher macrophage superoxide anion production in coronary artery disease (CAD) patients with Type D personality. Zuccarella-Hackl, C; von Känel, R; Thomas, L; Kuebler, P; Schmid, JP; Mattle, HP; Mono, ML; Rieben, R; Wiest, R; Wirtz, PH (2016) in: *Psychoneuroendocrinology*, 68, p. 186-193.

Link to publication list:

www.cvrc.unibe.ch/research/ischemia___reperfusion/publications/

Ion Channels and Channelopathies

www.ibmm.unibe.ch/research/group_abriel/index_eng.html



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

Research Highlights 2016 / Outlook 2017

Our research group focusses on the roles of ion channels in human diseases, so-called 'channelopathies'. We are interested in the dysfunction of ion channels expressed in heart and nervous system cells, which can lead to diseases such as cardiac arrhythmias or multiple sclerosis. To investigate this, we are both studying mutant ion-channel genes found in patients with pathological phenotypes and looking for novel molecular and cellular mechanisms regulating the function of these ion channels.

During the past year, we continued our work on the roles of proteins interacting with the cardiac sodium channel Nav1.5. In an article published in *Circulation Research* – a joint collaboration with Hatem and Balse's group in Paris (FR) – we showed that the protein CASK is a negative regulator of the pool of Nav1.5 channels expressed at the lateral membrane of cardiomyocytes. Morgan Chevalier and Sarah Vermij are currently investigating the molecular mechanisms underlying this phenomenon. Jean-Sébastien Rougier also demonstrated – in his first study as senior author – that CASK is able to modify the biophysical properties of the cardiac calcium channel Cav1.2.

The ion channel TRPM4 is another focus of our group and the resultant projects are part of the NCCR TransCure. Two studies on TRPM4 were published in 2016, demonstrating the pathogenic role of several mutations in the gene coding for TRPM4 found in patients with either congenital atrio-ventricular block or progressive conduction cardiac disorder. These investigations were performed with our collaborators from Nantes (FR). Beatrice Bianchi is currently studying more TRPM4 genetic variants causing cardiac disorders. Another important TransCure project is the one with the Department of Chemistry and Biochemistry (Groups of Reymond and Lochner). Lijo Ozhatil, in collaboration with the chemists, has found and characterised new small molecular weight inhibitors of TRPM4 that are more potent than the current ones used for research purposes (to be submitted in 2017).

Lastly, we submitted two studies in the frame of the SNSF-funded interdisciplinary project with the Swiss Institute of Bioinformatics group headed by Pascale Gaudet (University of Geneva). The first paper reported a new description (called ontology) on how to collect electrophysiological data from the literature, an important aspect for the future database that is currently being built with all the known genetic variants and their consequences found in ion channel genes. The second study presents the first online version of all the published variants found in the 9 genes coding for the voltage-gated sodium channel. This NavMut Portal database will serve as a starting point for future developments.

Since October 2016, our group is affiliated to the Institute of Biochemistry and Molecular Medicine (IBMM), University of Bern, and will be relocating to its premises during 2017. We are looking forward to collaborating with our new IBMM colleagues.

Training both as a biologist at ETH Zurich and as a 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. Professor at University of Bern and DCR Director (2009–2016). Since 2012, Member, SNF National Research Council. Since 2015, Director, NCCR TransCure. Since October 2016, Managing Director, Institute of Biochemistry and Molecular Medicine and Professor of Molecular Medicine, University of Bern.

Group Members

Prof. Dr. Hugues Abriel, Group Leader

Dr. Jean-Sébastien Rougier, Research Assistant, Senior Teaching Assistant

Dr. Lijo Ozhatil, Postdoctoral Fellow

Dr. Urs Thomet, Postdoctoral Fellow (since May)

Maria Essers, Laboratory Technician

Sabrina Guichard, Laboratory Technician

Verena Frazao, Secretary

Beatrice Bianchi, PhD Student

Morgan Chevalier, PhD Student

Sarah Vermij, PhD Student

Zizun Wang, PhD Student (since Sept.)

Collaborators

Bairoch A, SIB Swiss Institute of Bioinformatics (CH)

Balse E, Pierre and Marie Curie University, Paris (FR)

Decosterd I, University of Lausanne (CH)

Gaudet P, SIB Swiss Institute of Bioinformatics (CH)

Gertsch J, NCCR TransCure (CH)

Hatem SN, Pierre and Marie Curie University, Paris (FR)

Kucera JP, University of Bern (CH)

Lochner M, NCCR TransCure (CH)

Medeiros Domingo A, Inselspital (CH)

Reymond JL, NCCR TransCure (CH)

Schott JJ, University of Nantes (FR)

Zambelli T, ETH Zurich (CH)

Grants

Amounts allocated for 2016 (until Sept.):

- SNF: Molecular determinants of Nav1.5 multiprotein complexes in cardiac cells (H. Abriel) CHF 14,000
- SNF: Multiple Nav1.5 pools in cardiac cells: molecular determinants and functional roles (H. Abriel) CHF 154,000
- SNF: NCCR TransCure subproject: Physiology, pharmacology and pathophysiology of the calcium-activated non-selective cation TRPM4 channel (H. Abriel) CHF 202,800
- SNF: NavMutPredict, an interdisciplinary project to assess the severity of patients mutations with sodium channel channelopathies (A. Bairoch, H. Abriel) CHF 53,900

- Jubiläumsstiftung der Schweizerischen Mobiliar Genossenschaft: Regulation of L-type voltage-gated cardiac calcium channel Cav1.2 via a “new partner”: CASK (J.-S. Rougier) CHF 40,000

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

Antiarrhythmic Action of Flecainide in Polymorphic Ventricular Arrhythmias Caused by a Gain-of-Function Mutation in the Nav 1.5 Sodium Channel. Amarouch, MY; Swan, H; Leinonen, J; Marjamaa, A; Lahtinen, AM; Kontula, K; Toivonen, L; Widen, E; Abriel, H (2016) in: *Ann Noninvasive Electrocardiol*, 21(4), p. 343-351.

Targeted resequencing identifies TRPM4 as a major gene predisposing to progressive familial heart block type I. Daumy, X; Amarouch, MY; Lindenbaum, P; Bonnaud, S; Charpentier, E; Bianchi, B; Nafzger, S; Baron, E; Fouchard, S; Thollet, A; Kyndt, F; Barc, J; Le, SS; Makita, N; Le, MH; Dina, C; Gourraud, JB; Probst, V; Abriel, H; Redon, R; Schott, JJ (2016) in: *Int J Cardiol*, 207, p. 349-358.

Lateral Membrane-Specific MAGUK CASK Down-Regulates Nav1.5 Channel in Cardiac Myocytes. Eichel, CA; Beuriot, A; Chevalier, MY; Rougier, JS; Louault, F; Dilanian, G; Amour, J; Coulombe, A; Abriel, H; Hatem, SN; Balse, E (2016) in: *Circ Res*, 119(4), p. 544-556.

ICEPO: the ion channel electrophysiology ontology. Hinard, V; Britan, A; Rougier, JS; Bairoch, A; Abriel, H; Gaudet, P (2016) in: *Database (Oxford)*, 2016, p. baw017.

Calcium/calmodulin-dependent serine protein kinase CASK modulates the L-type calcium current. Nafzger, S and Rougier, JS (2016) in: *Cell Calcium*, e-pub ahead of print.

Variants of Transient Receptor Potential Melastatin Member 4 in

Childhood Atrioventricular Block. Syam, N; Chatel, S; Ozhatil, LC; Sottas, V; Rougier, JS; Baruteau, A; Baron, E; Amarouch, MY; Daumy, X; Probst, V; Schott, JJ; Abriel, H (2016) in: *J Am Heart Assoc*, 5(5), p. e001625.

DCR Research Groups from the Inselspital

Forty-one research groups from departments of the Inselspital were affiliated with the DCR at the end of 2016. Below is a list of the groups and the names of the Chairs of Department, Heads of Research/Laboratory and/or Group Leaders. Eight 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, Prof. 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, PD Dr. Sarah Longnus, PD Dr. Henriette Most

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

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

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

Endocrinology of the Breast: Prof. Dr. Petra Stute

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

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

Endometriosis and Gynaecological Oncology: Prof. Dr. Michel D. Müller, Prof. Dr. Nick A. Bersinger

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

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

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

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

Hepatology: Prof. Dr. Jean-François Dufour, Prof. Dr. Annalisa Berzigotti, Dr. Diren Beyoglu, Prof. 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, PD Dr. Selma Aybek, Prof. Dr. Andrew Chan, Prof. Dr. Urs Fischer, Prof. Dr. René Müri, PD Dr. Michael Schüpbach, Prof. Dr. Roland von Känel, Prof. Dr. Werner Z'Graggen

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, Prof. Dr. Volker Enzmann, Prof. Dr. Martin Zinkernagel

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

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

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

Plastic Surgery: Prof. Dr. Mihai Constantinescu

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

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

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

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

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

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

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

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

Urology: Prof. Dr. George Thalmann, Dr. Marianna Kruthof-de Julio, 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

Experimental Haemostasis

www.dkf.unibe.ch/research/research_groups/experimental_haemostasis



Prof. Dr. Hans-Peter Kohler
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Research Highlights 2016 / Outlook 2017

Our group investigates factors that influence thrombus formation and have implications for cardiovascular and thromboembolic diseases. One focus of our research is coagulation factor XIII (FXIII), while another is on interactions between the complement system – a part of innate immunity – and the coagulation system.

We have recently set up a microvascular flow model that combines the following features: endothelial cells, whole blood, vessel structure with a diameter of around 50 µm (similar to human arterioles), and blood flow leading to physiological shear rates. It allows to study clot formation and vessel occlusion in realtime under the microscope under nearly physiological conditions. This model is a major part of our current and future research on coagulation FXIII and the effects of the complement system on thrombus formation, which is funded by two novel SNF project grants awarded to us in 2016.

The action of FXIII made visible in a microvascular flow model

During clot formation, FXIII is activated by thrombin and crosslinks fibrin fibres. We have made the action of activated FXIII visible by adding a monoclonal antibody that specifically detects fibrin crosslinks together with a fluorescent secondary antibody in a whole blood perfusion experiment. The fibrin formation and crosslinking by FXIII can be observed in realtime. Details in clot structure, as well as the breakdown of the clot by the fibrinolytic system, can also be detected.

Structural aspects of coagulation FXIII

We have recently shown that the FXIII activation peptide (AP-FXIII) plays a crucial role in stabilising the FXIII A-subunit dimer. We are now studying the contribution of amino acids located at the interface between two A-subunits and also between A- and B-subunits. Our results will contribute to a better understanding of the molecular structure of this important coagulation factor.

Complement MASP-1 accelerates vessel occlusion in a microvascular flow model

We have previously shown that MASP-1, a serine protease of the complement lectin pathway, is able to directly induce fibrin formation by activating several coagulation factors including prothrombin. We can now show that MASP-1 also accelerates vessel occlusion in our microvascular flow model. This mechanism may be one explanation for the increased risk of thrombosis in inflammatory conditions.

Effects of MASP-1 on fibrinolysis

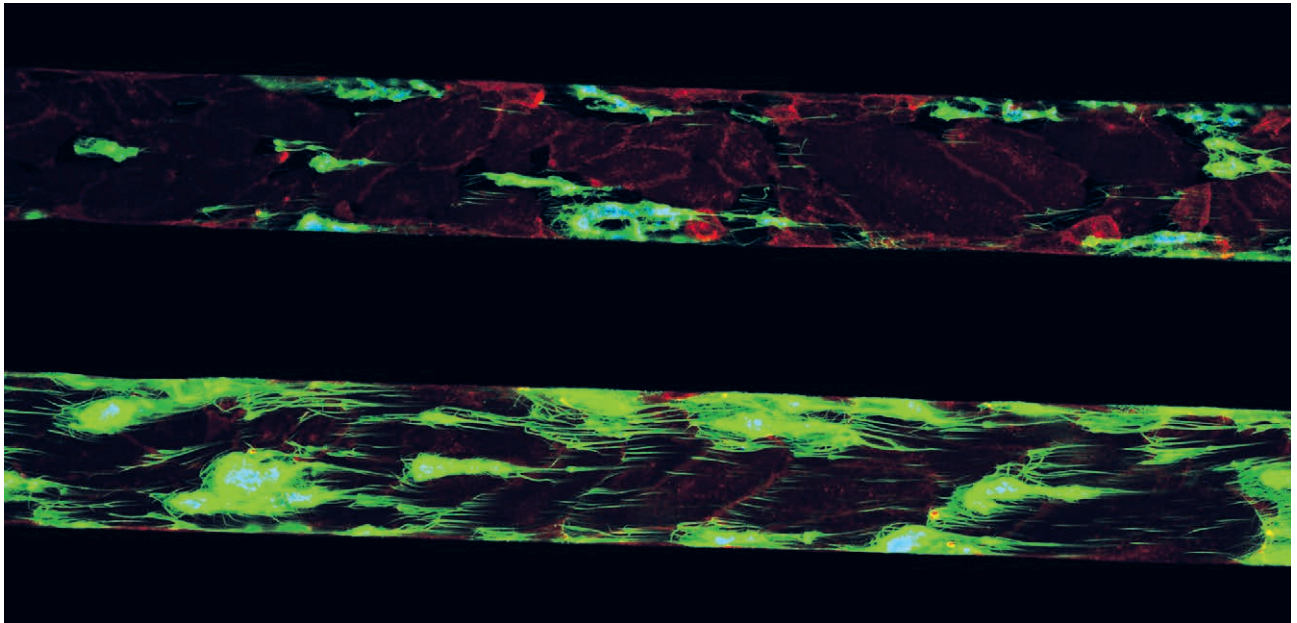
We have presented evidence in the past that MASP-1 affects fibrin structure, which is an important determinant of fibrinolysis. Currently, we study the effects of MASP-1 on fibrinolysis in whole blood using thromboelastometry and the Chandler loop system.

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. Head of Internal Medicine (2008–2015), Spital Netz Bern Hospitals Tiefenau and Ziegler. Since 2016, Head of Internal Medicine and Head of Division Stadtspital, Tiefenau Spital, Insel Gruppe.



PD Dr. Verena Schröder
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MSc in Pharmacy (1999) at University of Basel; PhD (2003) at University of Basel performed at Laboratory for Thrombosis Research, DCR (2000–2003). 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).



Group Members

Prof. Dr. Hans-Peter Kohler,
Group Leader

PD Dr. Verena Schröder,
Group Leader

Dr. Lorenz Jenny, Postdoctoral
Fellow

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)

Grants

Amounts allocated for 2016:

- SNF: Interactions between comple-
ment and coagulation in cardio-
and cerebrovascular diseases: Role
of MASP-1 in thrombus formation
and diabetes (V. Schröder)
CHF 64,058
- OPO-Foundation: A novel microvas-
cular flow system to study the
role of coagulation FXIII and com-
plement activation in thrombus
formation in a physiological environ-
ment (V. Schröder, H.-P Kohler)
CHF 52,267

Selected Publications

Factor XIII: Structure and Function.
Schröder, V and Kohler, HP (2016) in:
Semin Thromb Hemost, 42(4),
p. 422-428.

Magnetic Resonance Spectroscopy and Methodology (AMSM)

www.amsm.dkf.unibe.ch

www.dkf.unibe.ch/research/research_groups/magnetic_resonance_spectroscopy_and_methodology_amsm

Research Highlights 2016 / Outlook 2017

Magnetic resonance imaging (MRI) and spectroscopy (MRS) are extremely versatile methods for non-invasive studies and diagnostic examinations. 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. Two SNF grants with Pls in our group, five SNF grants in collaboration with other groups, one UniBE ID Grant 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 at the development of MR acquisition and synergistic post-processing methods that are tailored to the observation of brain metabolism, yet are also transferrable to other organs. In collaboration with the ETH and University of Zurich, as well as the MPI in Tübingen (DE), exchange processes between amide protons and water, diffusion-weighted MRS as well as functional MRS at very high fields were studied in the human brain, liver and skeletal muscle. Four PhD students are working in this area.

We are investigating renal function in kidneys by multi-modal MRI and MRS in a UniBE ID Grant in collaboration with the Department of Nephrology. A fast MR measurement protocol was developed in preparation of the protocol for the Bernese renal biopsy registry. In collaboration with groups from the ISTB, image post processing was developed (PhD projects M.Seif and Postdoctoral position G. Diserens).

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

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 using machine learning tools so that radiologists are better able to routinely use MRS (one PhD student funded).



Prof. Dr. Chris Boesch
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Studied Physics at ETH Zurich; PhD with Kurt Wüthrich. Studies in Medicine, 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

Studied Chemistry at ETH Zurich; PhD with Richard Ernst. Postdoc and Boswell Fellow at Caltech and HMRI (1989–1992) (US). 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

Studied Chemistry at University of Münster (DE); PhD in Physical Chemistry with Prof. Müller-Warmuth. 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).

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 (until Oct.)
 Dr. Gaëlle Diserens, Postdoctoral Fellow
 Karin Zwygart-Brügger, Technician
 Aline Kreis, Research Assistant
 Victor Adalid, PhD Student
 Sila Dokumaci, PhD Student (until June)
 André Döring, PhD Student
 Nicole Fichtner, PhD Student
 Maike Höfemann, PhD Student (since Oct.)
 Bertrand Pouymayou, PhD Student
 Sreenath Pruthviraj Kyathanahally, PhD Student
 Marc Stadelmann, PhD Student

Selected Collaborators

Henning A, MPI for Biological Cybernetics, Tübingen (DE)
 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 2016:

- SNF: Multi-nuclear magnetic resonance spectroscopy (MRS) and imaging (MRI) on a clinical whole-body MR-system: Lipid organelles and mitochondria (C. Boesch) CHF 115,868
- SNF: Magnetic resonance techniques to determine metabolite levels: extending scope and clinical robustness (R. Kreis) CHF 195,000
- UniBe ID: Comprehensive assessment of renal function, metabolites and lipids in kidneys by in vivo and ex vivo NMR methods for determining disease biomarkers (P. Vermathen) CHF 58,962

Selected Publications

Direct determination of phosphate sugars in biological material by $(1)H$ high-resolution magic-angle-spinning NMR spectroscopy. Diserens, G; Vermathen, M; Gjuroski, I; Eggimann, S; Precht, C; Boesch, C; Vermathen, P (2016) in: Anal Bioanal Chem, 408(20), p. 5651-5656.

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 (2016) in: Magn Reson Med, 75(5), p. 1867-1874.

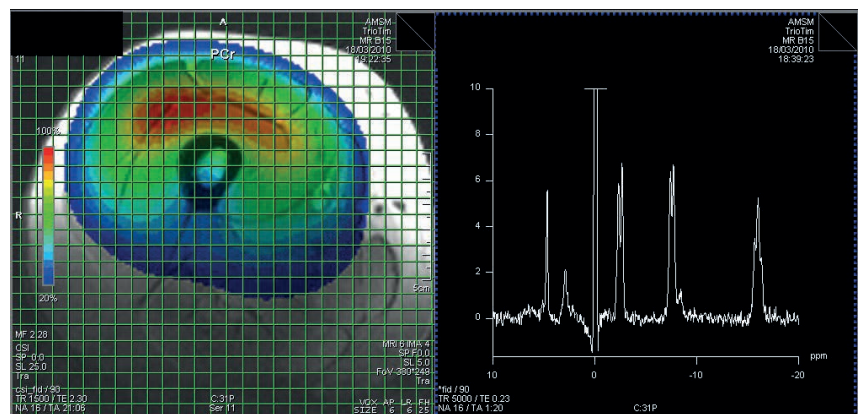
Elucidation of the downfield spectrum of human brain at 7 T using multiple inversion recovery delays and echo times. Fichtner, ND; Henning, A; Zoelch, N; Boesch, C; Kreis, R (2016) in: Magn Reson Med, e-pub ahead of print.

Renal Blood Oxygenation Level-dependent Imaging in Longitudinal Follow-up of Donated and Remaining Kidneys. Seif, M; Eisenberger, U; Binser, T; Thoeny, HC; Krauer, F; Rusch, A; Boesch, C; Vogt, B; Vermathen, P (2016) in: Radiology, 279(3), p. 795-804.

Influence of muscle fiber orientation on water and metabolite relaxation times, magnetization transfer, and visibility in human skeletal muscle. MacMillan, EL; Bolliger, CS; Boesch, C; Kreis, R (2016) in: Magn Reson Med, 75(4), p. 1764-1770.

Link to publication list:

www.amsm.dkf.unibe.ch



Neurology

www.neuro-bern.ch

www.dkf.unibe.ch/research/research_groups/neurology

Research Highlights 2016 / Outlook 2017

In 2016, Prof. Chan, head of the Multiple Sclerosis/Neuroimmunology research group, and PD Aybek arrived in Bern. Also, Clinical Neuroscience Bern (CNB) underwent structural reorganization and Profs. Fischer and Adamantidis were elected to its executive committee. We look back at successful grant acquisitions: SNF IICT program (Prof. Bassetti), SNF project funding (Profs. Fischer & Schindler), and ERC consolidator grant (Prof. Adamantidis). Furthermore, Prof. Adamantidis and Dr. Gutierrez received the 2017 Pfizer-Prize in neurosciences/disease of the neurosystem. A total of 12 SNF grants were running in our department. We published 86 original publications, including the 'highlight' paper on the role of REM sleep theta rhythm in contextual memory consolidation (Science, 2016).

Stroke Group

We published a matched pair analysis of patients with a large artery anterior circulation stroke treated with mechanical thrombectomy \pm prior intravenous and found no difference (Stroke, 2016). This is the rationale for a clinical trial starting in 2017. Further, we showed that obesity is a risk factor for cerebral venous thrombosis especially when oral contraceptives are used (JAMA Neurology, 2016). We received 2 grants (SNF, Swiss Heart Foundation) for a randomized controlled trial (ELAN safety). Two group members achieved the habilitation (PD Dr. Mono, PD Dr. Goeggel-Simonetti) and two a MD degree.

Sleep-Wake Mechanisms / Disorders and Epilepsy Group

In rodents, we identified a new arousal circuit using a combination of high-density electrophysiology and optogenetics (Nat Neurosci, 2016).

Further, we probed the function of sleep in memory consolidation and demonstrated causal evidence for a role of REM sleep theta rhythms (Science, 2016). In humans, we investigated the time-irreversibility of iEEG signal as an important and efficiently computable marker of epileptogenic brain areas (Clin Neurophysiol, 2016). Our international multicenter study on the role of sleep disordered breathing on the acute evolution of stroke was supported by an SNF IICT grant (PI: Prof. Bassetti).

Movement / Motor Disorders Group

In 2016 we focused on several projects related to clinical and electrophysiological aspects of the new technology of directional deep brain stimulation with segmented electrodes.

Neuromuscular Group

In 2016 we received a SNF grant on Muscle Diseases and we started a project on neuromuscular imaging in development of MR-based methods for nerve diagnostics.

Multiple Sclerosis / Neuroimmunology Group

Our translational research group started in 2016 in Bern, currently focusing on treatment optimization of acute MS-relapses, regulation of multi-drug resistance transporters and neuroprotective autoimmunity in an animal model of stroke. Most recently published studies in Bern include the validation of a biomarker approach for risk stratification under immunotherapy or the role of immunotherapy on cognition in late MS stages.

Neurorehabilitation / Cognitive Disorders Group

In 2016, we received a collaborative SNF research project with Prof. Nyffeler (Luzern). Furthermore, 5 PhD students successfully finished their thesis:



Prof. Dr. Claudio L. Bassetti
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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), University Hospital Zurich. Director (2009–2011), Neurocenter of Southern Switzerland. Since 2012, Full Professor of Neurology; Chair, Department of Neurology, Inselspital.
Clinical and animal research, sleep, stroke.



Prof. Dr. Urs Fischer
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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 2014, Associate Professor; since 2015, Professor for Acute Neurology and Stroke (Extraordinarius), Co-Chair Stroke Centre, Department of Neurology, Inselspital and Co-Director Clinical Trials Unit, University of Bern. General Secretary European Stroke Organisation.
Clinical research, acute neurology, stroke.



Prof. Dr. Marcel Arnold
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MD (1994) at University of Bern; Neurology residency in Bern; FMH certification (2000). Research fellowships in clinical neurology (2005) at Lariboisiere Hospital, University of Paris 7 (FR). Venia docendi (2007). Since 2010, Associate Professor of Neurology. Currently Chair, Stroke Center, Department of Neurology, Inselspital. President Swiss Stroke Society.
Clinical research, 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, Assistant Professor, Department of Neurology, Inselspital. *Animal research, sleep.*



Prof. Dr. Andrew Chan
andrew.chan@insel.ch

MD (1997) at University of Hamburg (DE); Consultant in Neurology (2004). *Venia legendi/Privatdozent* (2006), University of Göttingen (DE). Professor of Neurology (2012), Ruhr-University Bochum (DE). Associate Professor (2016), University of Bern. Since 2016 Head, Ambulantes Neurozentrum, 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.*

Hopfner, Preisig, De Leon Rodriguez, Eggenberger, Schumacher. Finally, Dr. Maalouli-Hartmann received an Ambizione Fellowship.

Neuropsychosomatic Group

The Functional Neurological Disorder (FND) group investigates the links between stress regulation and FND (e.g. movement disorders, non-epileptic attacks). We confirmed a dissociation between perceived subjective stress and objective cortisol levels in patients during a social stress task, suggesting an impairment in bodily awareness in FND.

The Psychosomatics Group published several experimental and observational studies on how stress and other psychological factors affect physiology, including immune system function, and health outcomes of patients with cardiovascular disease, inflammatory bowel disease and chronic pain.

Group Members

Stroke Group

Prof. Dr. Marcel Arnold, Group Leader

Prof. Dr. Urs Fischer, Group Leader

PD Dr. Simon Jung, Group Leader

PD Dr. Marie-Luise Mono, Group Leader

Prof. Dr. Werner Z'Graggen, Group Leader

Prof. Dr. Claudio L. Bassetti, Head of Department

Prof. Dr. Heinrich Mattle, Senior Consultant

Dr. Aikaterini Galimanis, Consultant

PD Dr. Barbara Goeggel-Simonetti, Consultant

Dr. Mirjam Heldner, Consultant

Dr. Thomas Horvath, Consultant

PD Dr. Christoph Schankin, Consultant

PD Dr. Hakan Sarikaya, Consultant
Dr. Sebastian Bellwald, Research Fellow

Dr. Rebekka Kurmann, Research Fellow

Dr. Rascha von Martial, Research Fellow

Marianne Kormann, Study Nurse

Andrea Surtmann, Study Nurse

Sleep-Wake Mechanisms / Disorders and Epilepsy Group

Prof. Dr. Claudio L. Bassetti, Group Leader

Prof. Dr. Antoine Adamantidis, Group Leader (ZEN)

Prof. Dr. Kaspar Schindler, Consultant, Group Leader

Prof. Dr. Johannes Mathis, Senior Consultant

Dr. Heidemarie Gast, Consultant

Dr. Markus Schmidt, Consultant

Dr. Panagiotis Bargiotas, Research Fellow

Dr. Corina Gorban, Research Fellow

Dr. Doris Kuen, Research Fellow

Dr. Mojtaba Bandarabadi, Postdoctoral Fellow (ZEN)

Dr. Simone Duss, Postdoctoral Fellow

Dr. Mary Gazea, Postdoctoral Fellow (ZEN)

Dr. Thomas Gent, Postdoctoral Fellow (ZEN)

Dr. Cornelia Schöne, Postdoctoral Fellow (ZEN)

Dr. Andreas Steimer, Postdoctoral Fellow

Dr. Carolina Gutierrez Herrera, Research Associate (ZEN)

Laura Facchin, PhD Student (ZEN)

Lukas Oesch, PhD Student (ZEN)

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

Gerd Tinkhäuser, PhD Student

Multiple Sclerosis / Neuroimmunology

Prof. Dr. Andrew Chan, Group Leader

Dr. Sandra Bigi, Consultant

Dr. Anke Salmen, Consultant

Kirsten Guse, PhD Student

Lisa Schrewe, PhD Student

Nicole Kamber, Clinical Fellow

Saskia Steinheimer, Research Fellow

Dr. Monika Käser, Study Nurse and Coordinator

Margit Kälin, Study Nurse (until Nov.)

Karin Streit, Study Nurse (from Dec.)

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
Dr. Matthias Maalouli-Hartmann, Ambizione Fellow
Aleksandra Eberhard-Moscicka, Postdoctoral Fellow
Dr. Jurka R. Meichtry, Postdoctoral Fellow
Dr. Tim Vanbellingen, Postdoctoral Fellow
Noëmi Eggenberger, PhD Student
Simone Hopfner, PhD Student
Basil Preisig, PhD Student
Rahel Schumacher, PhD Student
Denise de Jong, Research Assistant
Diana Lorenzo, Research Assistant

Neuro CTU Group

Prof. Dr. Urs Fischer, Medical Chair
PD Dr. Michael Schüpbach, Medical Vice Chair
Dr. Stefanie Lerch, Managing Chair
Jenny Bressan, Managing Vice Chair
Dr. Corrado Bernasconi, Head Statistics
Lena Burkhardt, Trial Coordinator
Marianne Kormann, Lead Study Nurse
Dr. Monika Käser, Study Nurse
Prof. Dr. Claudio L. Bassetti, Head of Department
Prof. Dr. Marcel Arnold, Group Leader, Stroke Group
Prof. Dr. Andrew Chan, Group Leader, Multiple Sclerosis / Neuroimmunology Group
Prof. Dr. René M. Müri, Group Leader, Neurorehabilitation/Cognitive Disorder Group
Prof. Dr. Kaspar Schindler, Group Leader, Sleep-Wake Mechanisms / Disorders and Epilepsy Group
Dr. Anke Salmen, Group Member, Multiple Sclerosis / Neuroimmunology Group

Neuropsychosomatic Group

PD Dr. Selma Aybek, Group Leader
Ninon Horié, Clinical Research Associate
Dr. Viridiana Mazzola, Postdoctoral Fellow
Dr. Kalliopi Apazoglou, Postdoctoral Fellow
Dr. Jennifer Wegrzyk, Postdoctoral Fellow
Dimitri Horn, MD Student
Dr. Silvio Galli, MD, PhD Student
Dr. Anita Barbey, Consultant

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

Neuromuscular Group

Prof. Dr. Kai Rösler, Group Leader
Dr. Olivier Scheidegger, Group Leader
Dr. Waldo Valenzuela, Postdoctoral Fellow

Selected Collaborators

Annoni J-M, University of Fribourg (CH)
Gralla J, Inselspital (CH)
Herrmann D, University of Essen (DE)
Burdakov D, National Institute for Medical Research (UK)
Massimini M, University of Milan (IT)

Selected Grants

Amounts above CHF 50,000 allocated for 2016:

- SNF: A Bayesian Inference Approach to intracranial EEG Seizure dynamics (K. Schindler) CHF 112,292
- SNF: Optogenetic dissection of hypothalamic regulation of sleep-wake states (A. Adamantidis) CHF 120,000
- SNF: Swiss study of initial decompressive craniectomy versus best medical treatment of spontaneous supratentorial intracerebral hemorrhage (switch): a randomized controlled trial (U. Fischer) CHF 127,597
- SNF: Sleep loss and sleep disorders and their impact on the short and long term in outcome of stroke (C. Bassetti) CHF 251,127
- SNF Sinergia: Sleep as a model to understand and manipulate cortical activity in order to promote neuroplasticity and functional recovery after stroke (C. Bassetti, A. Adamantidis; Co-Applicants: R. Huber, M. Massimini) CHF 260,369
- SNF: Etiopathogenesis, Diagnosis, Imaging and Treatment of Cervicocerebral Artery Dissections: A Multifactorial, Multidisciplinary



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, Director of Sleep-Wake-Epilepsy Center, Department of Neurology, Inselspital.
Clinical research, epilepsy.



PD Dr. Michael Schüpbach
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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. Since 2016, Extraordinary Professor.
Clinical and Stress Research, Psychosomatics.



PD. Dr. Selma Aybek
selma.aybek@insel.ch

MD (1998) at University of Lausanne; Board Certification in Neurology; FMH certification (2006), Postdoctoral fellowship (2007–2010) at the Institute of Psychiatry, King's College, London (UK); Venia docendi (2014) at University of Lausanne; Venia docendi (2015) at University of Geneva; FNS Ambizione Fellow (2013–2017) at University of Geneva. Since 2016, Senior Attending in Neuropsychosomatik, Department of Neurology, Inselspital. *Clinical research, functional neurological disorders.*

- and Translational Approach (EDIT-CAD-II-Study) (M. Arnold; Co-Applicant: U. Fischer) CHF 426,202
- 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 65,548
- CTU-Research grant: The International PFO consortium Secondary Stroke Prevention In Patients With Patent Foramen Ovale (M.-L. Mono) CHF 54,276
- CTU-Research grant: The Impact of Deep Brain Stimulation on Sleep-Wake Function in Patients with Parkinson's Disease (P. Bargiotas) CHF 69,300
- CTU-Research grant: Enhancing MR Neurography using diffusion-relaxation correlation spectroscopy (DRCOSY) for the assessment of axonal versus demyelinating neuropathies (O. Scheidegger) CHF 79,331
- Human Frontiers Science program (HFSP): Neural basis of behavioral multitasking and coordination by hypothalamic circuit (A. Adamantidis) CHF 94,541
- Jazz Pharmaceuticals: Swiss Narcolepsy Scale (C. Bassetti) CHF 85,185
- Kommission für Technologie und Innovation: DRIVE – Development of a Fatigue- and Sleepiness-Prediction-Device for use in Vehicles and Clinical Environments (D. Schreier; J. Mathis) CHF 86,146
- Swiss Heart Foundation: Sleep loss and sleep disorders and their impact on the short- and long-term outcome of ischemic stroke and transient ischemic attacks – a multi-centered cohort study (C. Bassetti) CHF 50,451

- UCB Biopharma: Preclinical studies on FcRn blockade in a Neuromyelitis optica model (A. Chan; Co-Applicant: A. Salmen) CHF 140,000

Selected Publications

Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation. Boyce, R; Glasgow, SD; Williams, S; Adamantidis, A (2016) in: *Science*, 352(6287), p. 812-816.

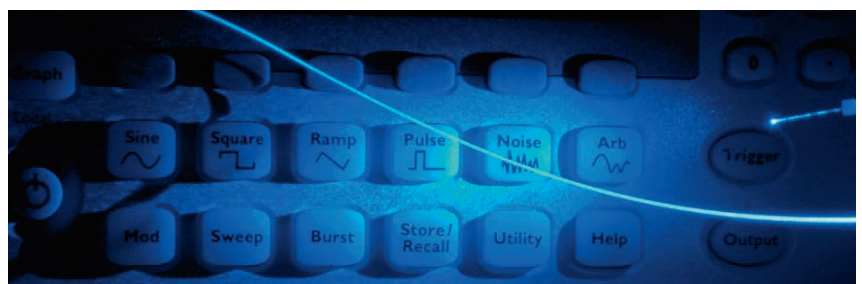
Direct Mechanical Intervention Versus Combined Intravenous and Mechanical Intervention in Large Artery Anterior Circulation Stroke: A Matched-Pairs Analysis. Broeg-Morway, A; Mordasini, P; Bernasconi, C; Buhlmann, M; Pult, F; Arnold, M; Schroth, G; Jung, S; Mattle, HP; Gralla, J; Fischer, U (2016) in: *Stroke*, 47(4), p. 1037-1044.

Hypothalamic feedforward inhibition of thalamocortical network controls arousal and consciousness. Herrera, CG; Cadavieco, MC; Jago, S; Ponomarenko, A; Korotkova, T; Adamantidis, A (2016) in: *Nat Neurosci*, 19(2), p. 290-298.

Eye Gaze Behavior at Turn Transition: How Aphasic Patients Process Speakers' Turns during Video Observation. Preisig, BC; Eggenberger, N; Zito, G; Vanbellingen, T; Schumacher, R; Hopfner, S; Gutbrod, K; Nyffeler, T; Cazzoli, D; Annoni, JM; Bohlhalter, S; Muri, RM (2016) in: *J Cogn Neurosci*, 28(10), p. 1613-1624.

Ictal time-irreversible intracranial EEG signals as markers of the epileptogenic zone. Schindler, K; Rummel, C; Andrzejak, RG; Goodfellow, M; Zubler, F; Abela, E; Wiest, R; Pollo, C; Steimer, A; Gast, H (2016) in: *Clin Neurophysiol*, 127(9), p. 3051-3058.

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



Prenatal Medicine

www.dkf.unibe.ch/research/research_groups/prenatal_medicine

Research Highlights 2016 / Outlook 2017

Stem cell-derived therapies for perinatal brain injury

Peripartum brain damage due to hypoxia or preterm birth is a major cause of neonatal death and long-term disability, such as cerebral palsy. Today's therapeutic approaches have very limited success. The aim of our research is to explore neuroregenerative therapies that have the potential to become off-the-shelf treatments for affected neonates at the time of diagnosis. We have shown in a newborn rat model that intracranioventricularly transplanted umbilical cord tissue-derived mesenchymal stem cells (Wharton's jelly MSC, WJ-MSc) reduced myelin loss and astroglial activation, both considered hallmarks of the injury. In search of a non-invasive method of stem cell transplantation, we confirmed these results with the intranasal delivery of the WJ-MSc. In addition, we further explored the neuroprotective property of a synthetic peptide analogous to the mammalian embryo-derived pre-implantation factor (sPIF). Exosomes are small vesicles that are secreted by cells and serve as vehicles for intercellular communication by transferring molecules, such as proteins or non-coding RNAs, into recipient cells. The therapeutic potential of MSC-derived exosomes has been widely recognized, however, exosomes from WJ-MSc have not been used yet in the treatment of neurodegenerative diseases. Our working hypothesis is that therapy of the peripartum brain damage with WJ-MSc-derived exosomes leads to neuroregeneration through the modulatory properties of their non-coding RNA cargo. We have started applying exosomes to neural cell lines (neural progenitor cells, N2a neuroblastoma cells, astrocytes) that were subjected to an in vitro oxygen/glucose-deprivation brain injury model. Preliminary data indicated that WJ-MSc-derived exosomes had a neuroprotective role.

Preeclampsia Research

Uric acid is increased in women with pre-eclampsia – a pregnancy-specific disease characterized by hypertension and proteinuria – and is believed to play a significant role in its pathogenesis. Hyperuricemia originates from renal and placental dysregulation of uric acid transport and may lead to long-term maternal cardiovascular risk and alterations in fetal programming. Our focus is on the glucose transporter 9 (GLUT9/LC2A9) isoforms in placenta. GLUT9 belongs to the glucose transporter family, but transports uric acid. It is the major transporter regulating uric acid homeostasis in humans. Currently, we have two transgenic GLUT9-knock out (KO) mouse models to further examine mechanistic issues. With a systemic GLUT9 KO model, we showed that fetal hyperuricemia leads to a reduced growth phenotype in the offspring and a chronic kidney inflammation resulting in necrosis later in life. We further used an inducible liver-specific KO mouse model to assess maternal hyperuricemia during pregnancy. Our goal is to show that hyperuricemia leads to elevated blood pressure, characteristic of preeclamptic pregnancies, and to identify new targets for therapy.



Prof. Dr. Daniel Surbek
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MD (1988) at University of Basel. FMH obstetrics and gynecology (1996). Research Fellow at Johns Hopkins University, Baltimore, Children's Hospital, Philadelphia (US) (1996), Kings College Hospital London (UK) (2000). Venia docendi (2002). Since 2005, Co-Chair and Full Professor of Obstetrics and Gynecology, Head of Obstetrics and Feto-Maternal Medicine, Inselspital.



PD Dr. Andreina Schoeberlein
andreina.schoeberlein@dkf.unibe.ch

MSc in agriculture (1990), PhD in animal genomics (1993) at ETH Zurich. Postdocs at University of Liège (BE) (1994–1996), University Hospital Zurich (1996–2001). Research scientist at University Hospital Basel (2001–2005), Inselspital (2005–2009). Venia docendi (2015). Since 2009, Co-Head Laboratory for Prenatal Medicine, DCR.



PD Dr. Marc Baumann
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MD at University of Geneva and Bern (1996). Research Fellow (2000–2002) at Perinatal Biology Group, University of Medicine and Dentistry, New Jersey (US). Specialist in obstetrics and gynecology, Inselspital (2010). Venia docendi (2016). Currently Senior Fellow at Department of Obstetrics and Gynecology, Inselspital and Co-PI NCCR TransCure.



PD Dr. Martin Müller
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MD (2002) at University Wroclaw (PL).
FMH Obstetrics and Gynecology (2007). FMH
Feto-Maternal Medicine (2013). Research
Fellow (2013-2014), Yale University School of
Medicine, New Haven (US). Since 2015, Visiting
Assistant Professor Yale University School of
Medicine. Venia docendi (2016). Since 2016,
Medical Director, Department of Gynaecology
and Obstetrics, Inselspital.

Group Members

Prof. Dr. Daniel Surbek, Co-Chair,
Head of Research
PD Dr. Andreina Schoeberlein,
Co-Head of Research, Group Leader
PD Dr. Marc Baumann, Group Leader,
Senior Fellow
PD Dr. Martin Müller, Group Leader,
Senior Fellow
Prof. Dr. Luigi Raio, Research
Associate, Senior Consultant
Dr. Marianne Jörgen-Messerli,
Postdoctoral Fellow
Dr. Benjamin Lüscher, Postdoctoral
Fellow
Dr. Byron Oppliger, Postdoctoral
Fellow
Annina Etter, Research Midwife
(from Nov.)
Judith Herbst, Research Midwife
(until Nov.)
Valérie Haesler, Laboratory Technician
(since Sept.)
Ursula Reinhart, Laboratory
Technician (until June)
Philipp Schneider, Laboratory
Technician
Camilla Marini, PhD Student
(until July)
Dr. Marialuigia Spinelli, PhD Student
Gierin Thomi, PhD Student (since June)

Selected Collaborators

Barnea E, BioIncept, LLC Cherry
Hill (US)
Bordey A, Yale University,
New Haven (US)
Paidas M, Yale University,
New Haven (US)

Selected Grants

Amounts allocated for 2016:

- Cryo-Save Stem cell research
(D. Surbek) CHF 112,000
- SNF: ABCA1 in the placenta
(C. Albrecht, D. Surbek)
CHF 90,000
- SNF: Fetal programming
(S. Rimoldi, L. Raio) CHF 120,000
- SNF: Salt and preeclampsia
(M. Mohaupt, D. Surbek)
CHF 120,000
- NIH/STTR: sPIF as immune modula-
tor (M. Paidas, M. Müller)
CHF 110,000

Selected Publications

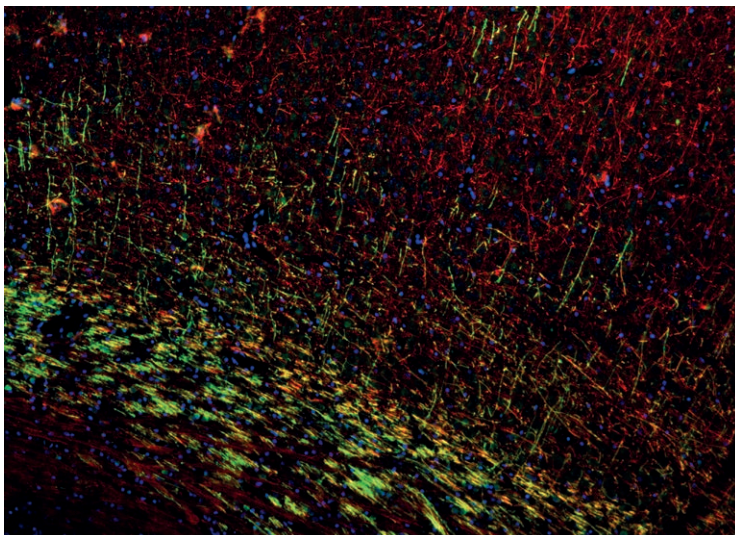
Placental expression of the angiogenic
placental growth factor is stimulated by
both aldosterone and simulated star-
vation. Eisele, N; Albrecht, C; Mistry,
HD; Dick, B; Baumann, M; Surbek, D;
Currie, G; Delles, C; Mohaupt, MG;
Escher, G; Gennari-Moser, C (2016) in:
Placenta, 40, p. 18-24.

Establishment of a confluent
monolayer model with human primary
trophoblast cells: novel insights into
placental glucose transport. Huang, X;
Luthi, M; Ontsouka, EC; Kallol, S;
Baumann, MU; Surbek, DV; Albrecht,
C (2016) in: Mol Hum Reprod, 22(6),
p. 442-456.

Wharton's Jelly Mesenchymal Stem
Cells Protect the Immature Brain in
Rats and Modulate Cell Fate. Mueller,
M; Oppliger, B; Joerger-Messerli, M;
Reinhart, U; Barnea, E; Paidas, M;
Kramer, BW; Surbek, DV; Schoeberlein,
A (2017) in: Stem Cells Dev, 26(4),
p. 239-248.

Intranasal Delivery of Umbilical
Cord-Derived Mesenchymal Stem
Cells Preserves Myelination in Perina-
tal Brain Damage. Oppliger, B;
Joerger-Messerli, M; Mueller, M;
Reinhart, U; Schneider, P; Surbek, DV;
Schoeberlein, A (2016) in: Stem Cells
Dev, 25(16), p. 1234-1242.

A novel, bedside technique to
rapidly identify umbilical cord blood
units with high total nucleated cell
numbers. Wagner, AM; Krenger, W;
Stettler, S; Beutler, E; Herbst, J;
Surbek, DV; Baerlocher, GM (2016) in:
Transfusion, 56(6), p. 1406-1412.



Thoracic Surgery

www.dkf.unibe.ch/research/research_groups/thoracic_surgery/

Research Highlights 2016 / Outlook 2017

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. These cells may act as key effectors in regulating the composition and function of infiltrating lymphocytes within the tumour microenvironment, tipping the balance towards immunosuppression. 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 tumour-derived mesenchymal cells 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. In NSCLC, high mitochondrial activity correlated with sphere formation capacity and increased tumour growth, which is in agreement with the findings in pancreatic cancer. 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 based on the expression of a mitochondrial marker 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 constitutes the rationale for our research, which is mainly oriented towards identification of therapy-resistant tumour cells and the underlying molecular mechanisms accounting for the resistance phenomenon. We focus on cancer stem cells in the resistance of lung cancer and malignant pleural mesothelioma (MPM) to standard therapies currently used in the clinic, with the ultimate goal of unravelling the vulnerabilities – the 'Achilles' heel' – of therapy-resistant cells, and developing new and more effective therapeutic strategies for the treatment of patients with lung cancer and MPM.



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, Division of Surgery, University Hospital Zurich (1996–1999). 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.



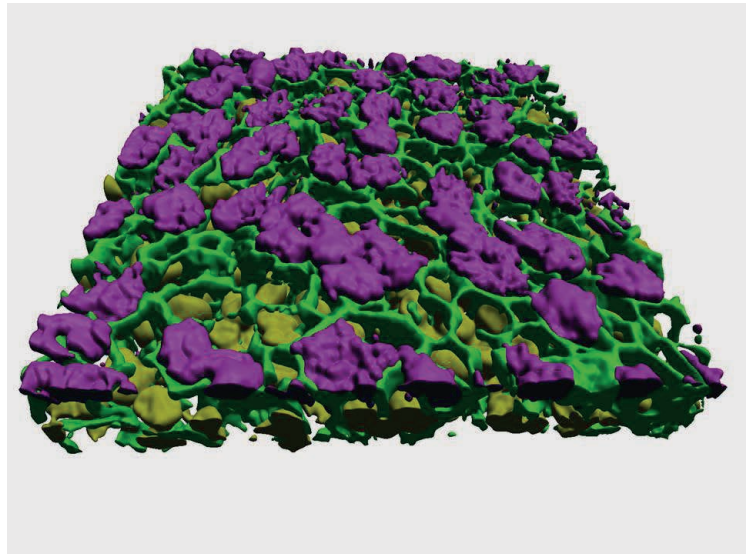
Dr. Thomas M. Marti
thomas.marti@insel.ch

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.



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
Dr. Duo Li, Postdoctoral Fellow
Yanyun Gao, PhD Student
Liang Shunqing, PhD Student
Colin Tièche, PhD Student
Limei Wang, PhD Student
Duo Xu, MD, PhD Student (since Aug.)
Haitang Yang, MD, PhD Student

Selected Collaborators

Galetta, D, European Institute of Oncology (IT)
Möhrle, U, University Children's Hospital Zurich (CH)
Sommergruber, W, Boehringer Ingelheim (AU)
Qian, C, Third Military Medical University (CN)
Zhao, H, Shanghai Jiaotong University (CN)

Selected Grants

Amounts allocated for 2016:

- Cancer League Bern: Role of PD-1/PD-L1 in NSCLC (S.R.R. Hall) CHF 60,000

- Cancer League Bern: Functional identification and molecular targeting of human lung cancer stem cells (R.-W. Peng) CHF 72,000
- Cancer League Bern: Characterization and therapeutic targeting of chemoresistance-driving pathways in lung cancer (R.-W. Peng) CHF 60,000
- Swiss Cancer League: Characterization and Targeting of Cancer Initiating Cells in Lung Cancer (T. Marti) CHF 84,616
- Swiss Cancer League: Unravelling and reversing drug resistance of human lung cancer (R.-W. Peng) CHF 80,000
- Boehringer Ingelheim: Analysis of the transcriptome of matched NSCLC patient samples and establishment of pathophysiologically relevant organoid models. (SRR Hall) CHF 60,834

Selected Publications

Schedule-dependent increased efficiency of pemetrexed-ionizing radiation combination therapy elicits a differential DNA damage response in lung cancer cells. Dorn, P; Tieche, CC; Peng, RW; Froment, L; Schmid, RA; Marti, TM (2016) in: *Cancer Cell Int*, 16(1), p. 66.

Nuss procedure for repair of pectus excavatum after failed Ravitch procedure in adults: indications

and caveats. Kocher, GJ; Gstrein, N; Jaroszewski, DE; Ewais, MM; Schmid, RA (2016) in: *J Thorac Dis*, 8(8), p. 1981-1985.

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 (2016) in: *Eur J Cardiothorac Surg*, 49(4), p. 1059-1062.

Completely Thoracoscopic Diaphragmatic Plication. Kocher, GJ; Zehnder, A; Schmid, RA (2016) in: *World J Surg*, e-pub ahead of print.

Prolonged pemetrexed pretreatment augments persistence of cisplatin-induced DNA damage and eliminates resistant lung cancer stem-like cells associated with EMT. Tieche, CC; Peng, RW; Dorn, P; Froment, L; Schmid, RA; Marti, TM (2016) in: *BMC Cancer*, 16, p. 125.

Link to publication list:

www.thoraxchirurgie.insel.ch/de/forschung-und-studien-aus-dem-labor/

Tumor-Immunology

www.ochsenbeinlab.ch

www.dkf.unibe.ch/research/research_groups/tumor_immunology

Research Highlights 2016 / Outlook 2017

For several years, our laboratory has been investigating the interplay between hematopoietic stem cells (HSCs) / cancer stem cells (CSCs) and adaptive immune cells. Our aim is twofold: understanding the mechanisms by which HSCs and CSCs are regulated and finding new therapeutic targets for effective immunotherapies against CSCs.

We were able to demonstrate that HSCs and leukemic stem cells (LSCs) interact directly or indirectly with certain adaptive immune cells and immune regulating factors within the bone marrow (BM) niche. By using a mouse model of viral infection we showed that secretion of IFN- γ by activated cytotoxic CD8 T cells (CTLs) stimulated BM mesenchymal stromal cells (MSCs) to secrete the hematopoietic cytokine IL-6. This induced the expansion of HSCs and myeloid differentiation. Thus, we defined a new mechanism by which adaptive immune cells regulate demand-adapted hematopoiesis. In addition, our group demonstrated in a chronic myelogenous leukemia (CML) mouse model and in CML patient samples, that IFN- γ secretion by CTLs induced LSC proliferation and differentiation. Therefore, similar mechanisms that are crucial for demand-adapted hematopoiesis induce the expansion of LSCs and leukemia progression.

Moreover, our group focuses on TRAF2- mediated TNF receptors (TNFR) and their signaling pathways in the hematopoietic system. So far, we have mainly focused on the interaction between the TNF receptor CD27 with its ligand CD70. CD27 signaling induces "stemness" in leukemic cells and leads to a more aggressive disease. We demonstrated that blocking the CD27/CD70 interaction effectively eradicates LSCs. Related to this, a phase I clinical trial with α CD70 monoclonal antibody was recently initiated in acute myelogenous leukemia (AML) patients.

The network and functionality of other TRAF2-mediated TNF receptors in HSCs and CSCs are presently under detailed investigation. We currently examine the role of TNFR signaling in murine models and samples from patients with lung and colon cancer.



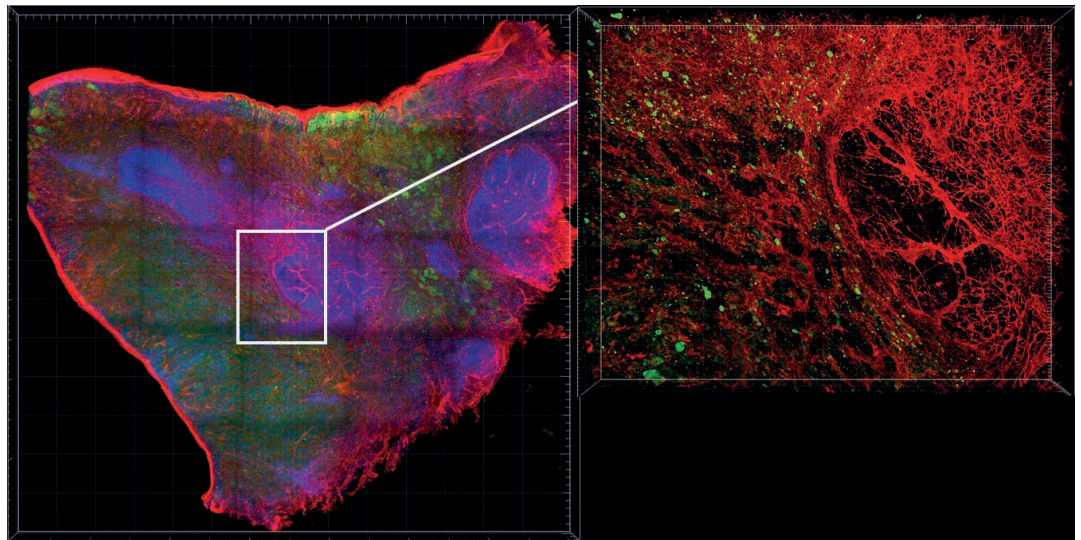
Prof. Dr. Adrian F. Ochsenbein
adrian.ochsenbein@insel.ch

MD (1992) at University of Bern; Postgraduate education in internal medicine and medical oncology in Solothurn and Bern. Research Fellow (1996–1999), Institute for Experimental Immunology, University of Zurich. Postdoc (2001–2002) at Fred Hutchinson Cancer Research Center, Seattle (US). SNF Professorship (2003) at the DCR. Since 2011, Chief Physician at Department of Medical Oncology, Inselspital.



PD Dr. Carsten Riether
carsten.riether@dkf.unibe.ch

Master in Biotechnology (2005) at ESBS Strasbourg (FR). PhD in Immunology (2008) at ETH Zurich; Postdoctoral Research Fellow (2009–2012) and since 2013 Principal Investigator at the Tumor-Immunology Lab, Department of Medical Oncology, Inselspital.



Group Members

Prof. Dr. Adrian F. Ochsenbein,
Group Head
PD Dr. Carsten Riether, Group Leader
Dr. Sabine Höpner, Postdoctoral
Fellow
Dr. Ramin Radpour, Postdoctoral
Fellow
Ursina Lüthi, Laboratory Technician
Dr. Michael A. Amrein, PhD Student
Elias D. Bühner, PhD Student
Magdalena Hinterbrandner,
PhD Student
Pascal Näf, PhD Student (since Aug.)
Carla Ruckstuhl, PhD Student
Mohamad Al Sayed, PhD Student
(until Sept.)

Selected Collaborators

Krebs P, University of Bern (CH)
Macpherson A, University of Bern (CH)
Pinschewer DD, University of
Basel (CH)
Reya T, University of California (US)
Nombela Arrieta C, University
Hospital Zurich (CH)

Selected Grants

Amounts allocated for 2016:
 – Otto Naegeli Prize for Medical
Research 2016 (A. F. Ochsenbein)
CHF 100,000
 – SAKK/RTFCCR/Gateway Research
Grant Award: New combination
therapy for elderly and frail patients
with newly diagnosed acute

myeloid leukemia (A. F. Ochsenbein)
CHF 300,000
 – SNF: Targeting TNF Receptor
TNIK signaling to eliminate cancer
stem cells (A. F. Ochsenbein)
CHF 190,333
 – Werner and Hedy Berger-Janser
Foundation: Targeting tumor necro-
sis factor receptor (TNFR) signaling
to treat leukemia (A. F. Ochsenbein)
CHF 106,604
 – Krebsliga: Targeting CD70 in chron-
ic and acute myeloid leukemia
(C. Riether) CHF 118,900
 – Krebsliga: IL33/ST2 signaling in
leukemia (A. F. Ochsenbein)
CHF 124,902

Selected Publications

143PD: Bevacizumab and pemetrexed
versus pemetrexed alone as mainte-
nance therapy for patients with
advanced nonsquamous NSCLC: Results
of the expanded SAKK19/09 trial.
Gautschi, O; Li, Q; Matter-Walstra, K;
Betticher, D; Frueh, M; Rauch, D; Pless,
M; Froesch, P; Mach, N; Ochsenbein, A
(2016) in: J Thorac Oncol, 11(4 Suppl),
p. S120.
 CD70/CD27 signaling promotes
blast stemness and is a viable thera-
peutic target in acute myeloid leu-
kemia. Riether, C; Schurch, CM; Buhrer,
ED; Hinterbrandner, M; Huguenin, AL;
Hoepner, S; Zlobec, I; Pabst, T;
Radpour, R; Ochsenbein, AF (2017) in:
J Exp Med, 214(2), p. 359-380.

Regulation of hematopoietic and
leukemic stem cells by the immune
system. Riether, C; Schurch, CM;
Ochsenbein, AF (2015) in: Cell Death
Differ, 22(2), p. 187-198.

Blocking programmed cell death 1
in combination with adoptive cyto-
toxic T-cell transfer eradicates chronic
myelogenous leukemia stem cells.
Riether, C; Gschwend, T; Huguenin, AL;
Schurch, CM; Ochsenbein, AF (2015)
in: Leukemia, 29(8), p. 1781-1785.

Tyrosine kinase inhibitor-induced
CD70 expression mediates drug
resistance in leukemia stem cells by
activating Wnt signaling. Riether, C;
Schurch, CM; Flury, C; Hinterbrandner,
M; Druck, L; Huguenin, AL; Baerlocher,
GM; Radpour, R; Ochsenbein, AF
(2015) in: Sci Transl Med, 7(298),
p. 298ra119.

Link to publication list:
[www.ochsenbeinlab.ch/publications.
htm](http://www.ochsenbeinlab.ch/publications.htm)

Urology

www.urologie.insel.ch/en/

www.dkf.unibe.ch/research/research_groups/urology

Research Highlights 2016 / Outlook 2017

Genital-Urothelial (GU) Cancer Research Group

Our research focusses on the role of cancer stem cells and the supportive stroma in the progressive and metastatic GU cancers. The process of metastasis depends on the cancer cell of the primary tumour, as well as on the host micro-environment. Increasing experimental evidence indicates that the cell population in the primary tumour capable of metastasising has a stem/progenitor cell phenotype, as it has been shown for prostate cancer by our group and others. We have analysed the stromal-epithelial (cancer) interaction of prostate cancer with the bone/bone marrow microenvironment by means of an experimental model using next-generation sequencing. At the moment, we are establishing a personalised GU platform that will integrate effective therapeutic treatments for individual patients, testing not only in vitro, but also ex vivo and in vivo. This platform consists of 1. tumour organoids/canceroids, which facilitate the integration of genomic, transcriptomic, proteomic and metabolomic data, combined with drug screening of patients' tumour samples; 2. patient derived xenografts (PDX), that allow the growth of tumour material for further testing, and 3. zebrafish high-throughput model system that allows the (fast) assessment of the metastatic potential of the individual canceroid lines.

Bladder Dysfunction Research Group

Lower urinary tract dysfunction – characterized by urgency, frequency and incomplete emptying – has multiple causes, including bladder outlet obstruction and neurological diseases such as spinal cord injury. The consequences of both obstructive and neurogenic bladder dysfunction are believed to share molecular mechanisms. Small regulatory microRNA molecules, affecting protein synthesis, are quickly winning recognition as potential therapeutic agents. Our group has pioneered the study of the role of miRNAs in the pathogenesis of lower urinary tract diseases. Our experimental approach combines the analysis of human biopsy material with in vitro cell-based models to elucidate the impact of myogenic and neurogenic components postulated to be involved in the development of these disorders. We have established miRNA and mRNA expression profiles of several defined states of lower urinary tract dysfunction and identified signalling pathways activated in obstructed bladders. Altered miRNAs serve as biomarkers and might be used to optimise the timing of treatment. We determined combinations of 3 mRNAs and 3 miRNAs sufficient to discriminate between bladder functional states. We are currently quantifying these miRNAs in urinary exosomes with the aim of developing a non-invasive tool for reliable diagnosis of bladder dysfunction. Modulation of the key pathways activated in disease states using miRNAs might help avoiding irreparable changes to the bladder and associated organs.



Prof. Dr. George N. Thalmann
george.thalmann@insel.ch

Postdoc (1993-1995) at MD Anderson Cancer Center Houston Texas (US). Urology Consultant (1996–2000). Fellow of European Board of Urology (1997). Habilitation (2000). Senior Attending and Deputy Physician-in-Chief (2000–2005); Physician-in-Chief “ad personam” (2005–2010), and since 2010, Chair, Department of Urology, Inselspital.



Dr. Marianna Kruihof-de Julio
marianna.kruihofdejulio@dkf.unibe.ch

PhD in Medicine (2004) at University of Amsterdam (NL). Postdoc (2004–2011) at Columbia University (US). Senior Scientist (2011–2015) at Leiden University Medical Center (NL). Joined the Department of Urology, Inselspital as a Principal Investigator (2016). Since September 2016, Group Leader in the same department.



Prof. Dr. Katia Monastyrskaya
katia.monastyrskaia@dkf.unibe.ch

DPhil in Biochemistry (1995), Wadham College, University of Oxford (UK). Postdoc (1994–1997) at NERC Institute of Virology, Oxford (UK). Senior Scientist (1997–2001) at H. Hoffmann-La Roche/Givaudan AG. Senior Research Associate (2001–2011), University of Bern. Habilitation (2007), Associate Professor (2014) at University of Bern. Since 2011, Group Leader, Urology Research Laboratory, Department of Urology, Inselspital.

Group Members

Prof. Dr. George Thalmann, Chair and Group Leader

Dr. Marianna Kruithof-de Julio, Group Leader

Prof. Dr. Katia Monastyrskaya, Group Leader

Dr. Marco Cecchini, Group Leader

Dr. Antoinette Wetterwald, Senior Scientist (until Apr.)

Dr. Letizia Astrologo, Postdoctoral Fellow

Dr. Hashemi Gheinani Ali, Postdoctoral Fellow

Dr. Janine Hensel, Postdoctoral Fellow (until July)

Dr. Sofia Karkampouna, Postdoctoral Fellow

Dr. Eugenio Zoni, Postdoctoral Fellow

Irena Klima, Laboratory Technician, Laboratory Manager

Joël Grosjean, Laboratory Technician

Prof. Dr. Fiona Burkhard, Clinical Partner

Prof. Dr. Martin Spahn, Clinical Partner

Ivonne Koeck, PhD Student

Federico La Manna, PhD Student

Selected Collaborators

Carbone, P, Catapano, C, IOR, Bellinzona (CH)

Gray P, Salk Institute, La Jolla (US)

Henry, M, Iowa Cancer Center (US)

Jenster, G, Erasmus Medical Center, Rotterdam (NL)

Shen, M, Columbia University, New York City (US)

Selected Grants

Amounts allocated for 2016:

- SNF: Haematopoietic Stem Cell (HSC) niches as biomarker and therapeutic target in prostate cancer bone metastasis (G. Thalmann) CHF 125,000

- SNF: Gene expression regulation by miR-221: A novel mechanism in prostate cancer progression (M. Spahn, B. Kneitz) CHF 67,000
- SNF: Phenotypic and genomic characterization of stem-like cancer cells surviving castration in human prostate cancer (M. Kruithof-de Julio, M. Cecchini, C. Rentsch) CHF 189,000
- SNF: Changes of miRNA expression in obstructive and neurogenic bladder dysfunction reveal common signalling pathways relevant for disease progression and recovery (K. Monastyrskaya, F. C. Burkhard, J. Pannek) CHF 129,000
- SNF R'Equip: Nanoparticle Tracking Analysis using NanoSight NS300 instrument (K. Monastyrskaya (main applicant), E. Vassella, A. Draeger, H. Tevaeearai Stahel) CHF 147,000
- EuroStar: The development of a novel medicine for advanced prostate cancer (G. Thalmann, M. Cecchini) CHF 120,000
- KWF: Decrypting Cripto in PCa (M. Kruithof-de Julio) CHF 135,000
- Velux Foundation: Diagnostic and therapeutic potential of microRNAs for prevention of bladder outlet obstruction-induced irreversible changes in bladder function in elderly men (K. Monastyrskaya) CHF 133,000

Selected Publications

Mouse models for studying prostate cancer bone metastasis. Dai, J; Hensel, J; Wang, N; Kruithof-de Julio, JM; Shiozawa, Y (2016) in: Bonekey Rep, 5, p. 777.

MicroRNA-424 impairs ubiquitination to activate STAT3 and promote prostate tumor progression. Dallavalle, C; Albino, D; Civenni, G; Merulla, J; Ostano, P; Mello-Grand, M; Rossi, S;

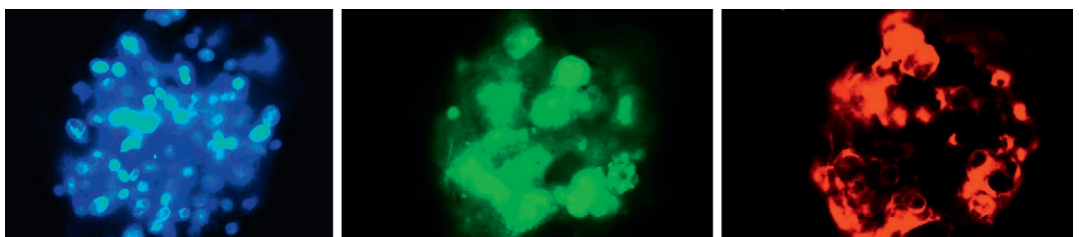
Losa, M; D'Ambrosio, G; Sessa, F; Thalmann, GN; Garcia-Escudero, R; Zitella, A; Chiorino, G; Catapano, CV; Carbone, GM (2016) in: J Clin Invest, 126(12), p. 4585-4602.

Importance and outcome relevance of central pathology review in prostatectomy specimens: data from the SAKK 09/10 randomized trial on prostate cancer. Ghadjar, P; Hayoz, S; Genitsch, V; Zwahlen, DR; Holscher, T; Gut, P; Guckenberger, M; Hildebrandt, G; Muller, AC; Putora, MP; Papachristofilou, A; Stalder, L; Biaggi-Rudolf, C; Sumila, M; Kranzbuhler, H; Najafi, Y; Ost, P; Azinwi, NC; Reuter, C; Bodis, S; Khanfir, K; Budach, V; Aebersold, DM; Thalmann, GN (2016) in: BJU Int, e-pub ahead of print.

Activin Receptor-like Kinase 1 Ligand Trap Reduces Microvascular Density and Improves Chemotherapy Efficiency to Various Solid Tumors. Hawinkels, LJ; de Vinuesa, AG; Paauwe, M; Kruithof-de Julio, JM; Wiercinska, E; Pardali, E; Mezzanotte, L; Keereweer, S; Braumuller, TM; Heijkants, RC; Jonkers, J; Lowik, CW; Goumans, MJ; ten Hagen, TL; ten, DP (2016) in: Clin Cancer Res, 22(1), p. 96-106.

Activation of common signaling pathways during remodeling of the heart and the bladder. Koeck, I; Burkhard, FC; Monastyrskaya, K (2016) in: Biochem Pharmacol, 102, p. 7-19.

It is with great sadness that we inform you of the death of Dr. Marco G. Cecchini. He passed away in August 2016.



Visceral and Transplantation Surgery

www.dkf.unibe.ch/research/research_groups/visceral_and_transplantation_surgery

Research Highlights 2016 / Outlook 2017

Liver regeneration

The adult liver has the ability to self-maintain its optimal mass in response to injury or resection. Nevertheless, in some patients the liver fails to regenerate thus leading to organ failure. Our research focuses on improving liver regeneration following several lines of investigation:

- Immune mediated modulation of liver regeneration via components of the innate immune system (Beldi).
- The impact of gut bacteria on liver regeneration (Beldi/Candinas).
- Inhibition of the Hippo core kinases MST1 and MST2 with siRNA for the improvement of liver regeneration in age-related non-regenerative disorders (Stroka/Candinas).
- Isolating liver-derived Lgr5+ stem cells for reconstitution of diseased liver tissue (Stroka/Keogh/Candinas).

Sphincter muscle regeneration

Adipocyte-Derived Stem Cells (ADSCs) are being studied for the functional improvement of sphincter muscle contraction; the exact mechanism of improving muscular healing by ADSCs is being investigated (Brügger).

Gastrointestinal tumours

New targets for the treatment of hepatocellular carcinoma are being investigated. For example, targeting YAP1 of the Hippo Pathway is being investigated in models of hepatocellular carcinoma (Banz Wüthrich).

Pathophysiology of radiation-induced liver disease (RILD), a limiting factor for the use of ionising radiation to treat liver tumours is being studied (Stroka / Radiation Oncology Group) (Aebersold/Hermann/Zimmer).

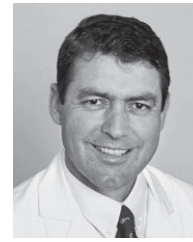
On-going studies bridging clinical and basic research

A prospective randomised trial exploring the impact of modulation of intestinal hemodynamics by Terlipressin on postoperative morbidity after major hepatic resection (Beldi).

In collaboration with psychologists from the University of Neuchatel, our study "communication in the operating room" has shown that case-relevant communication protects from deep surgical site infections. The consequence of this finding is a large prospective multicentre trial to improve intraoperative communication, which has started in 2015 and is funded by the Swiss National Foundation (Beldi).

In collaboration with the Biomaterial Science Center, Basel, the Institute for Surgical Technology & Biomechanics, Bern, the Swiss Federal Laboratories for Materials Science and Technology (EMPA) and the Cantonal Hospital Schaffhausen prototype devices are being developed using novel technologies to treat patients with severe faecal incontinence. A pilot study to assess anatomic, physiologic and biomechanical characteristics of the pelvic floor was conducted (Brügger). A follow-up study in patients with incontinence is foreseen for 2017. We are further planning to investigate transcutaneous energy transfer to charge batteries in an animal model.

With the ARTORG, we are exploring the applicability of computer-assisted, navigated liver surgery in patients undergoing hepatic interventions (Banz Wüthrich/Tinguely/ Weber ARTORG).



Prof. Dr. Daniel Candinas
daniel.candinas@insel.ch

Board examination (1987) and MD (1991) at University of Zurich. Fellowships in Birmingham (UK) (1993–1994) and Harvard Medical School, Boston (US) (1994–1995). Staff Surgeon at University Hospital Zurich (1996–1999) and Queen Elizabeth Hospital, Birmingham (1999–2002). Venia docendi (1997) at University of Zurich. Since 2002, Chair, Department of Visceral and Transplantation Surgery, Inselspital.



PD Dr. Deborah Keogh-Stroka
deborah.stroka@dkf.unibe.ch

Studied biology at Harvard University, Boston (US), MSc (1996) and natural sciences/genetics at University of Vienna (AT), PhD (1998). Post-docs at Institute of Physiology, University of Zurich (1998–1999) and Department of Surgery, University of Birmingham (UK) (1999–2002). Since 2002, Laboratory Head, Visceral and Transplantation Surgery, DCR. Venia docendi (2011).



PD Dr. Vanessa Banz Wüthrich
vanessa.banzwuehtrich@insel.ch

Board examination (2001) and MD (2005) at University of Basel. Fellowships at HPB and Liver Transplant Unit, Queen Elizabeth Hospital and Centre for Liver Research, IBR, Birmingham (UK) (2008–2010). FMH certification in Surgery (2008). Since 2010, Staff Surgeon, Department of Visceral and Transplantation Surgery, Inselspital. PhD (2012), Graduate School for Cellular and Biomedical Sciences, Bern. Venia docendi (2016).



Prof. Dr. Guido Beldi
guido.beldi@insel.ch

Board examination (1998) and MD (2000) at University of Bern. Fellowships in Berlin (DE) (2004) and at Liver Center, Beth Israel Deaconess, Harvard Medical School Boston (US) (2006–2007). FMH certification in Surgery (2005). Since 2008, Staff Surgeon, Department of Visceral and Transplantation Surgery, Inselspital. Venia docendi (2009), Associate Professor (2012).



PD Dr. Lukas Brügger
lukas.bruegger@insel.ch

MD (1992) at University of Bern; FMH certification in Surgery (2001). Research Fellowship on stem cell therapy for (sphincter) muscle regeneration at Laboratory for Stem Cell Therapy and Tissue Engineering, Urology, University Hospital Zurich (2010–2012). Joined Coloproctology Division, Inselspital in 2006; Senior Attending since 2013. Principle Investigator, Nano-Tera project on smart muscles for incontinence treatment. Venia docendi (2016).

Group Members

Prof. Dr. Daniel Candinas, Director
PD Dr. Deborah Stroka, Laboratory Head, Group Leader
PD Dr. Vanessa Banz Wüthrich, Group Leader
Prof. Dr. Guido Beldi, Group Leader
Dr. Lukas Brügger, Group Leader

Dr. Manuel Jakob, Staff Surgeon
Dr. Corina Kim, Staff Surgeon
Dr. Andreas Kohler, Staff Surgeon
Dr. Peter Studer, Staff Surgeon
Dr. Pascale Tinguely, Staff Surgeon

Dr. Adrian Keogh, Research Assistant
Dr. Fadi Jebbawi, Postdoctoral Fellow (since Aug.)
Dr. Giulio Loforese, Postdoctoral Fellow

Isabel Büchi, Laboratory Technician (since Feb.)
Sarah Overney, Laboratory Technician
Riccardo Tombolini, Laboratory Technician
Lilian Smith, Administrator

Felix Baier, PhD Student
Noëlle Dommann, PhD Student (since Apr.)
Michel Dosch, MD-PhD Student
Jacopo Gavini, PhD Student
Agata Gorecka, PhD Student
Ramesh Kudira, PhD Student (until Apr.)
Nicolas Melin, PhD Student

Selected Collaborators

Eberli D, University Hospital Zurich (CH)
Halazonetis T, University of Geneva (CH)
Starlinger P, Brostjan C, Vienna General Hospital (AT)
Tschan F, University of Neuchatel (CH)
Vozenin MC, Lausanne University Hospital (CH)

Selected Grants

Amounts allocated for 2016:

- SNF: Purinergic control of innate lymphoid cells in liver injury and repair (G. Beldi)
- Bernese Cancer League: Targeting YAP for the treatment of hepatocellular carcinoma using small molecule inhibitors: a promising new strategy (V. Banz Wüthrich)

- Strauss Foundation: Adult Stem Cells for Regenerative Medicine (D. Stroka)
- Stiftung für klinisch-experimentelle Tumorforschung: IL-33 signaling in hepatocarcinogenesis (D. Stroka)

Selected Publications

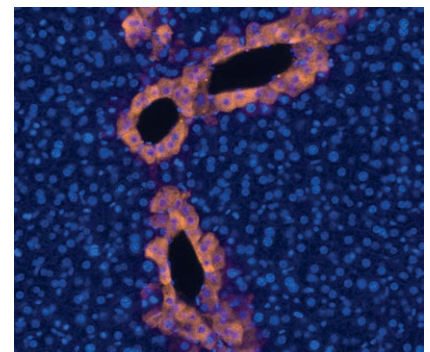
Impact of case-relevant and case-irrelevant communication within the surgical team on surgical-site infection. Tschan, F; Seelandt, JC; Keller, S; Semmer, NK; Kurmann, A; Candinas, D; Beldi, G (2015) in: Br J Surg, 102(13), p. 1718-1725.

Intraoperative image-guided navigation system: development and applicability in 65 patients undergoing liver surgery. Banz, VM; Muller, PC; Tinguely, P; Inderbitzin, D; Ribes, D; Peterhans, M; Candinas, D; Weber, S (2016) in: Langenbecks Arch Surg, 401(4), p. 495-502.

P2X1-regulated IL-22 secretion by innate lymphoid cells is required for efficient liver regeneration. Kudira, R; Malinka, T; Kohler, A; Dosch, M; de Agüero, MG; Melin, N; Haegele, S; Starlinger, P; Maharjan, N; Saxena, S; Keogh, A; Stroka, D; Candinas, D; Beldi, G (2016) in: Hepatology, 63(6), p. 2004-2017.

R-spondin 1 and noggin facilitate expansion of resident stem cells from non-damaged gallbladders. Lugli, N; Kamileri, I; Keogh, A; Malinka, T; Sarris, ME; Talianidis, I; Schaad, O; Candinas, D; Stroka, D; Halazonetis, TD (2016) in: EMBO Rep, 17(5), p. 769-779.

Impaired liver regeneration in aged mice can be rescued by silencing Hippo core kinases MST1 and MST2. Loforese, G; Malinka, T; Keogh, A; Baier, F; Simillion, C; Montani, M; Halazonetis, TD; Candinas, D; Stroka, D (2017) in: EMBO Mol Med, 9(1), p. 46-60.



Key Events

**Swiss Youth in Science:
"Biology and Medicine" Study
Week
13-19 Mar.**

**Welcome Events 2016
13 Apr. and 12 Oct.**

Around 20 interested DCR newcomers attended each of these events. The next Welcome Event will take place on 12 April 2017.

**DKF Info-Veranstaltung,
InselNord, Murtenstrasse 24
28 June**

The construction project, as well as the occupancy plan, were presented. About 50 people attended this event.

**Day of Clinical Research 2016
1-2 Nov.**

As usual, a large and interested audience followed the presentations of Prof. Dr. Martin Jinek (Department of Biochemistry, University of Zurich) entitled "CRISPR-Cas genome editing:

from molecular insights into clinical applications", and Prof. Dr. Lawrence Rajendran (Systems and Cell Biology of Neurodegeneration, University of Zurich) entitled "ScienceMatters – the next-gen science journal for publishing single observations".

Six candidates applied for the Johanna Dürmüller-Bol DCR Research Prize 2016 (funded by the Johanna Dürmüller-Bol Foundation) and 156 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): Prof. Robert Rieben (DCR ad interim Director), Dr. Markus Lüdi, Anna Maria Peter, Dr. Andrea Grotzky, Seid Hamzic, Dr. Michael Amrein.

*Johanna Dürmüller-Bol DCR Research
Award 2016*

Dr. Markus Lüdi
Anaesthesiology, DCR and Department of Anaesthesiology and Pain Medicine, Inselspital

Poster Prizes of the DCR for:

- *best preclinical project*
Andrea Grotzky
Clinical Radiopharmacy, DCR and Department of Nuclear Medicine, Inselspital
- *best clinical project*
Seid Hamzic
Department of Clinical Chemistry, Inselspital
- *best project by a medical student*
Anna Maria Peter
Department of Paediatrics and Department of Clinical Chemistry, Inselspital

Research Prize Alumni MedBern

Dr. Michael Amrein
Tumor-Immunology, DCR and Department of Medical Oncology, Inselspital

The next Day of Clinical Research will be held 30-31 October 2017.

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



DKF Research Conferences 2016

With an average of 40 visitors each month, the DKF Research Conferences continue to be successful. In 2016, we were pleased to present the following speakers:

18 Jan. – Prof. Dr. Mauricio Rojas
University of Pittsburgh (US)
Mesenchymal stem cells, lessons learned in our route from bench to bedside

1 Feb. – Prof. Dr. Suchitra Sumitran-Holgersson
University of Gothenburg (SE)
Tissue-engineering of organs: A new frontier in regenerative medicine

7 Mar. – Prof. Dr. Marten Trendelenburg
Division of Internal Medicine and Department of Biomedicine, University Hospital Basel (CH)
Autoimmunity, infection, ischemia: It's all about complement

4 Apr. – Prof. Dr. Marc Solioz
Tomsk State University (RU)
Antimicrobial copper materials for hygiene and infection prevention – Too good to be true?

2 May – Prof. Dr. C. Roland Wolf
University of Dundee (UK)
Humanised mouse models for targeted anticancer therapy

6 June – Prof. Dr. Christian Heinis
Institute of Chemical Sciences and Engineering, EPFL, Lausanne (CH)
Towards the development of peptide therapeutics: phage display selection of bicyclic peptides to disease targets

4 July – Prof. Dr. W. Jonathan Lederer
University of Maryland School of Medicine, Baltimore (US)
Tugging at the heartstrings: Surprising heart discoveries

5 Sept. – Prof. Dr. Marcelo Rivolta
University of Sheffield (UK)
Repairing the ear with stem cells

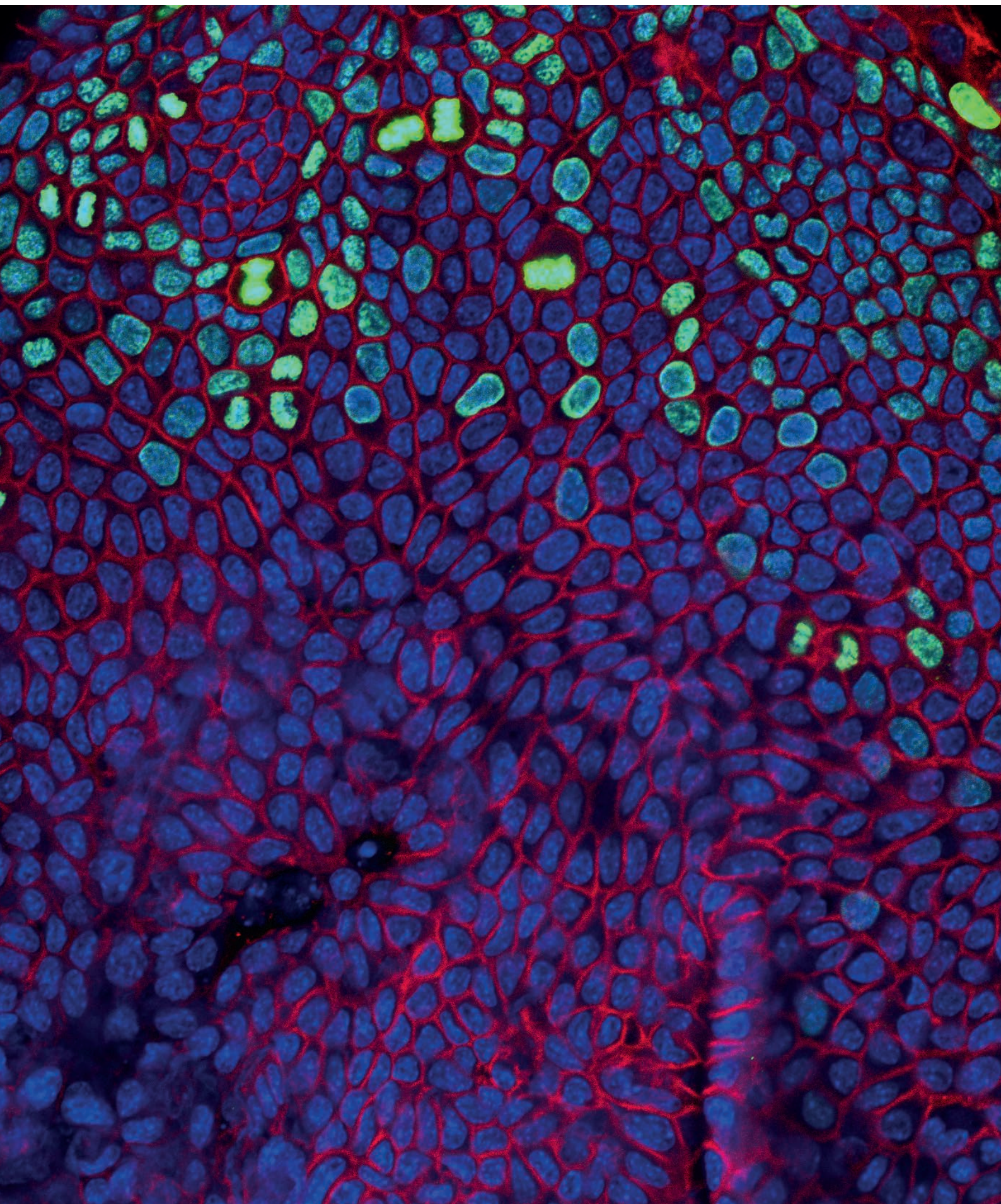
3 Oct. – Prof. Dr. Eric Leguern
Hôpital Pitié-Salpêtrière, Paris (FR)
Advances in genetics of epilepsy

5 Dec. – Dr. Michaela Kneissel
Novartis Institutes for Biomedical Research, Basel (CH)
WNT Signaling in Bone – A brief personal history of time

In 2017, 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.

In addition, we will have the great pleasure to celebrate the 100th DKF Research Conference on 5 May 2017.





Personnel Update

Academic Degrees

The following academic degrees were awarded to DCR group members:

Professor

Prof. Dr. Urs Fischer
Neurology

Prof. Dr. Philipp Latzin
Pulmonary Medicine (Paediatrics)

Associate Professor

Prof. Dr. Annalise Berzigotti
Hepatology

Prof. Dr. Andrew Chan
Neurology

Prof. Dr. Volker Enzmann
Ophthalmology

Prof. Dr. Stefano Rimoldi
Cardiology

Prof. Dr. Joerg C. Schefold
Intensive Care Medicine

Prof. Dr. Martin Spahn
Urology

Prof. Dr. Petra Stute
Endocrinology of the Breast

Prof. Dr. Hendrik von Tengg-Kobligk
Radiology

Prof. Dr. Martin A. Walter
Clinical Radiopharmacy

Prof. Dr. Martin Zinkernagel
Ophthalmology

Lecturer (Privatdozent)

PD Dr. Marc Ulrich Baumann
Prenatal Medicine

PD Dr. Fabian Blank
Pulmonary Medicine (Adults)

PD Dr. Andreas Ebnetter
Ophthalmology

PD Dr. Elizaveta Fasler-Kan
Pediatric Surgery

PD Dr. Barbara Goeggel-Simonetti
Neurology

PD Dr. Stefano de Marchi
Cardiology

PD Dr. Pascal Juillerat
Gastroenterology /
Mucosal Immunology

PD Dr. Christian P. Kamm
Neurology

PD Dr. Marie-Luise Mono
Neurology

PD Dr. Martin Müller
Prenatal Medicine

PD Dr. Benoît Schaller
Cranio-Maxillofacial Surgery

PhD

(supervisors in brackets)

Parisa Aghagolzadeh
(PD Dr. Andreas Pasch)
Cellular and molecular mechanisms of calcification, induction and prevention in human vascular smooth muscle cells

Mohamad F. Al Sayed

(Prof. Dr. Adrian F. Ochsenbein)
Lymphocytes in cancer:
a double-edged sword

Rebecca Blom

(Prof. Dr. Christophe von Garnier)
Pulmonary immune responses to
bio-mimetic antigen carriers for novel
therapeutic approaches

Ramona Bolognini

(PD Dr. André Schaller)
Characterization of molecular patho-
mechanisms in mitochondrial disorders

Gaëlle Diserens

(Prof. Dr. Peter Vermathen)
In vivo and ex vivo investigations of
ectopic lipids in renal and other tissues
by magnetic resonance imaging and
spectroscopy: method establishment
and first applications for determining
disease biomarkers

Ayse Sila Dokumaci

(Prof. Dr. Chris Boesch)
Development and application of
non-invasive MR spectroscopy
methods for studies of insulin resis-
tance in humans

Simone Ebener

(Prof. Dr. Thomas Geiser,
Dr. Manuela Funke-Chambour)
Toll-like receptor 4 in idiopathic
pulmonary fibrosis

Noëmi Anne Eggenberger

(Prof. Dr. René Müri)
Perception and production of
co-speech gestures in aphasic patients

Paola Francica

(PD Dr. Yitzhak Zimmer,
Dr. Michaela Medová)
Depletion of FOXM1 via MET target-
ing underlies establishment of a
DNA damage-induced senescence
program in gastric cancer

Simone Hopfner

(Prof. Dr. Thomas Nyffeler)
Spatial neglect and motion: the influence of directionally non-specific and directionally specific motion on neglect behaviour

Lorenz Jenny

(PD Dr. Verena Schröder)
Complement protease MASP-1 – a major link between the complement and the coagulation system

Ramesh Kudira

(Prof. Dr. Guido Beldi)
Purinergic modulation of innate lymphoid cells during liver regeneration

Camilla Marini

(Prof. Dr. Daniel V. Surbek,
PD Dr. Marc U. Baumann)
Placental transport systems and their impact on fetal programming

Byron Oppliger

(Prof. Dr. Daniel Surbek,
PD Dr. Andreina Schoberlein)
Wharton's jelly mesenchymal stem cells as a treatment for preterm brain injury

Marta Pace

(Prof. Dr. Claudio L. Bassetti,
Prof. Dr. Antoine Adamantidis)
Role of REM sleep, melanin concentrating hormone and orexin systems in ischemic stroke

Basil Christoph Preisig

(Prof. Dr. René Müri)
Aphasia and dialogue: what eye movements reveal about the processing of co-speech gestures and the prediction of turn transitions

Miriam Helen Reisenhofer

(Prof. Dr. Volker Enzmann)
Cellular responses in MNU-induced retinal degeneration

Sandra Rupp

(Prof. Dr. Kathy McCoy)
Microbial impact on B cell development and regulation

Rahel Schuhmacher

(Prof. Dr. René Müri)
Exploring and influencing language processing in the intact and damaged brain

Luca Tamò

(Prof. Dr. Thomas Geiser)
The role of induced pluripotent stem cells (iPSC) in lung repair and regeneration

Manuela Tham

(PD Dr. Frauke Förger)
Regulatory role of $\gamma\delta$ T cell subpopulations in pregnancy induced remission of rheumatic disease

Stephanie Sarah Uster

(Prof. Dr. Michael Seitz)
Effects of anti-TNF α therapy on the distribution of osteoclast precursors in a murine antigen induced arthritis model

MD, PhD

(supervisor in brackets)

Shengye Zhang

(Prof. Dr. Robert Rieben)
Role of the plasma cascade systems in endothelial cell activation induced by peripheral ischemia/reperfusion injury

Awards

The following DCR group members received awards in 2016:

Prof. Dr. Antoine Adamantidis,**Dr. Carolina Gutierrez**

Neurology
Research Prize for Neurosciences and Diseases of the Neurosystem, Pfizer Foundation: "Hypothalamusthalamic networks on sleep, arousal, and consciousness"

Dr. Michael Amrein

Tumor-Immunology
Research Prize Alumni MedBern: "CML progression in the bone marrow is fuelled by spleen resident leukemia stem and progenitor cells"

Maria Arnold

Cardiovascular Surgery
1st Prize of the PhD student competition, Cardiovascular Research Cluster's Networking Symposium: "Molecular mechanisms of cardioprotective reperfusion strategies in an isolated rat

heart model of donation after circulatory death"

Luca Bologna, Raja Prince

Hematology (Adults)
Hämostase Award 2016, Swiss Society of Hematology: "Targeting anticoagulant protein S to achieve hemostasis in hemophilia"

Dr. Chantal Dysli

Ophthalmology
Swiss RetinAWARD 2016 for the best project with the most clinical relevance, Swiss VitreoRetinal Group: "Fluorescence lifetimes in Stargardt Disease: potential marker for disease progression"

PD Dr. Andreas Ebnetter

Ophthalmology
Prix Retina 2016 for the best clinical research project, Swiss VitreoRetinal Group: "Prognostic significance of foveal capillary drop-out and previous panretinal photocoagulation for diabetic macular oedema treated with ranibizumab"

Dr. Stephanie Ganal-Vonarburg,**Dr. Mercedes Gomez de Agüero**

Gastroenterology / Mucosal Immunology
Gastroenterology-Prize 2016, Swiss Society of Gastroenterology: "The maternal microbiota drives early post-natal innate immune development"

Dr. Ali Hashemi Gheinani

Urology
Senior Citizens' University Prize for Aging Research, Dies academicus 2016: "The role of microRNAs in organ remodelling in lower urinary tract"

Dr. Ludovic Gillet

Ion Channels and Channelopathies (until July 2015)
Outstanding Publication Award for Young Electrophysiologists in the area of basic research 2016, HeartRhythm Journal: "Cardiac-specific ablation of synapse-associated protein SAP97 in mice decreases potassium currents but not sodium current"

Andrea Grotzky

Clinical Radiopharmacy
Poster Prize of the DCR for the Best Preclinical Project: "Imaging-guided

development of nanoparticles for tissue-activated drug delivery"

Dr. Lorenz Jenny

Experimental Haemostasis
Travel Award, 26th International Complement Workshop: "MASP-1 enhances clot formation in a microvascular flow model"

Dr. Despina Kokona

Ophthalmology
Swiss RetinAWARD 2016 for the best experimental project, Swiss VitreoRetinal Group: "Role of differentially activated macrophages in the course of a murine model of Branch Retinal Vein Occlusion"

Prof. Dr. Johanna A. Kremer

Hovinga Strebel
Hematology (Adults)
Thrombosis and Hemostasis Award 2016, ISTH 2007 Presidential Fund: "Characterization of the splenic autoantibody repertoire in additional acquired TTP patients by single cell sorting and deep sequencing of B-cells and generation of full anti-ADAMTS13 antibodies by cloning of obtained immunoglobulin sequences"

Dr. Christoph Lippuner

Anaesthesiology
Poster Prize (2nd prize), Annual Meeting, Swiss Society of Anaesthesiology and Reanimation and Schweizerische Interessengemeinschaft für Anästhesiepflege: "Functional analysis of beta-defensin 2 gene copy number variations in monocytes"

Dr. Markus Lüdi

Anaesthesiology
Johanna-Dürmüller-Bol DCR Research Price 2016: "Clinically well tolerated low dose camptothecin as a counter to dexamethasone induced microvascularization in glioblastoma", and John D. Michenfelder New Investigator Award 2016, 44th Annual Meeting, Society for Neuroscience in Anesthesiology and Critical Care: "A dexamethasone-regulated gene signature is prognostic for poor survival in glioblastoma patients"

Prof. Dr. Heinrich Mattle

Neurology
Presidential Award, European Stroke

Organisation (ESO): "Ausserordentlichen Leistungen in Forschung und Klinik auf dem Gebiet des Hirnschlags"

Dr. Théo Meister

Cardiology
1st Prize of the Post-Graduate competition, Cardiovascular Research Cluster's Networking Symposium: "Assisted reproductive technology increases the vasoconstrictor responsiveness to angiotensin II in the aorta"

PD Dr. Marie-Luise Mono

Neurology
Swiss Stroke Society Research Prize: "Repeated intravenous thrombolysis for early recurrent stroke"

Dr. Michael Nagler

Hematology (Adults)
Viollier Prize 2016: "Diagnostic value of immunoassays for heparin-induced thrombocytopenia: a systematic review and meta-analysis"

Prof. Dr. Adrian F. Ochsenbein

Tumor-Immunology
Otto Naegeli Prize for Medical Research 2016

Dr. Marta Pace

Neurology
EAN-Runner-up Prize: "Role of REM sleep and melanin concentrating hormone in the neuroprotective effect of sleep deprivation preischemia preconditioning"

Michael Perny

Audiology
Poster Prize for the Best Stem Cell Project, Platform for Stem Cell Research in Regenerative Medicine: "Intracochlear transplantation of neuronal progenitors to replenish spiral ganglion neurons lost after experimental bacterial meningitis"

Anna Maria Peter

Poster Prize of the DCR for Best Project by a Medical Student: "Diagnostic and prognostic value of autoantibodies against gastric goblet cells in paediatric and adolescent inflammatory bowel disease patients"

**Michaela Poliaková,
Prof. Dr. Daniel Aebbersold,**

**PD Dr. Yitzhak Zimmer,
Dr. Michaela Medová,**
Radiation Oncology
Aegean Conference Award, 4th International Conference on Tumor Microenvironment and Cellular Stress: "A metabolomics discovery approach for identification of metabolic changes associated with MET-addicted and non-MET-addicted cellular systems"

PD Dr. Monica Schaller

Hematology (Adults)
Klinische Hämatologie Award 2016, Swiss Society of Hematology: "Anti-idiotypic therapy in acquired TTP – optimizing the amount and variety of DARPins (Designed-Ankyrin-Repeat proteins) for maximal autoantibody neutralization in a large patient cohort"

Dr. Aline Schögler

Pulmonary Medicine (Paediatrics)
Benoît Pochon Prize: "Mechanisms and modulation of the antiviral response in the cystic fibrosis airway epithelium"

PD Dr. Michael Schüpbach

Neurology
Bruno Speck Award 2016 for Clinical Research: "Allogeneic haematopoietic stem cell transplantation for mitochondrial neurogastrointestinal encephalomyopathy"

Dr. Stefanie Seiler

Neurosurgery
Benoît Pochon Prize: "The potential of Nogo-A neutralization as a novel treatment strategy for Parkinson's disease"; and Synapsis Best Poster Prize in the category "neurodegenerative diseases", Swiss Society for Neuroscience (SSN) and Synapsis Foundation: "Nogo-A neutralization improves engraftment of dopaminergic neurons in a rat model of Parkinson's disease"

Riccardo Sfriso

Cardiovascular Research
Poster Award, 26th International Complement Workshop: "Activation of complement and coagulation in xenotransplantation: effect of growth hormone receptor knockout on porcine aortic endothelial cells"

Staff Changes

New Staff

Patrick Furer

Head DCR Maintenance (100 %),
DCR Services (since May)

Peggy Kübler

Directorate Secretary (70 %),
Administration (since Dec.)

Susanne Widmer

House Staff (40 %),
Research Division Mu40 (since Aug.)

Retirements

Otto Aeby

Head DCR Maintenance (100%),
DCR Services (until June)

Dr. Antoinette Wetterwald

Occupational Safety, Health
Protection and Environmental Safety
(OHE) (40),
OHE DCR (until Apr.);
Senior Scientist (40%),
Bone Biology & Orthopaedic Research
and Urology (until Apr.)

Resignations

Prof. Dr. Hugues Abriel

DCR Director (50 %),
Administration (until Mar.);
Group Leader (50 %),
Ion Channels and Channelopathies
(until Sept.)

Maria Essers

Laboratory Technician (100 %),
Ion Channels and Channelopathies
(until Sept.)

Prof. Dr. Kathy McCoy

Head of Research (100 %),
Gastroenterology / Mucosal Immunol-
ogy (until Aug.)

Dr. Jean-Sebastien Rougier

Research Assistant (100 %),
Ion Channels and Channelopathies
(until Sept.)

David Schär

IT-Support (60 %),
Administration (until Dec.)

