UNIVERSITÄT BERN

DEPARTMENT FOR BIOMEDICAL RESEARCH
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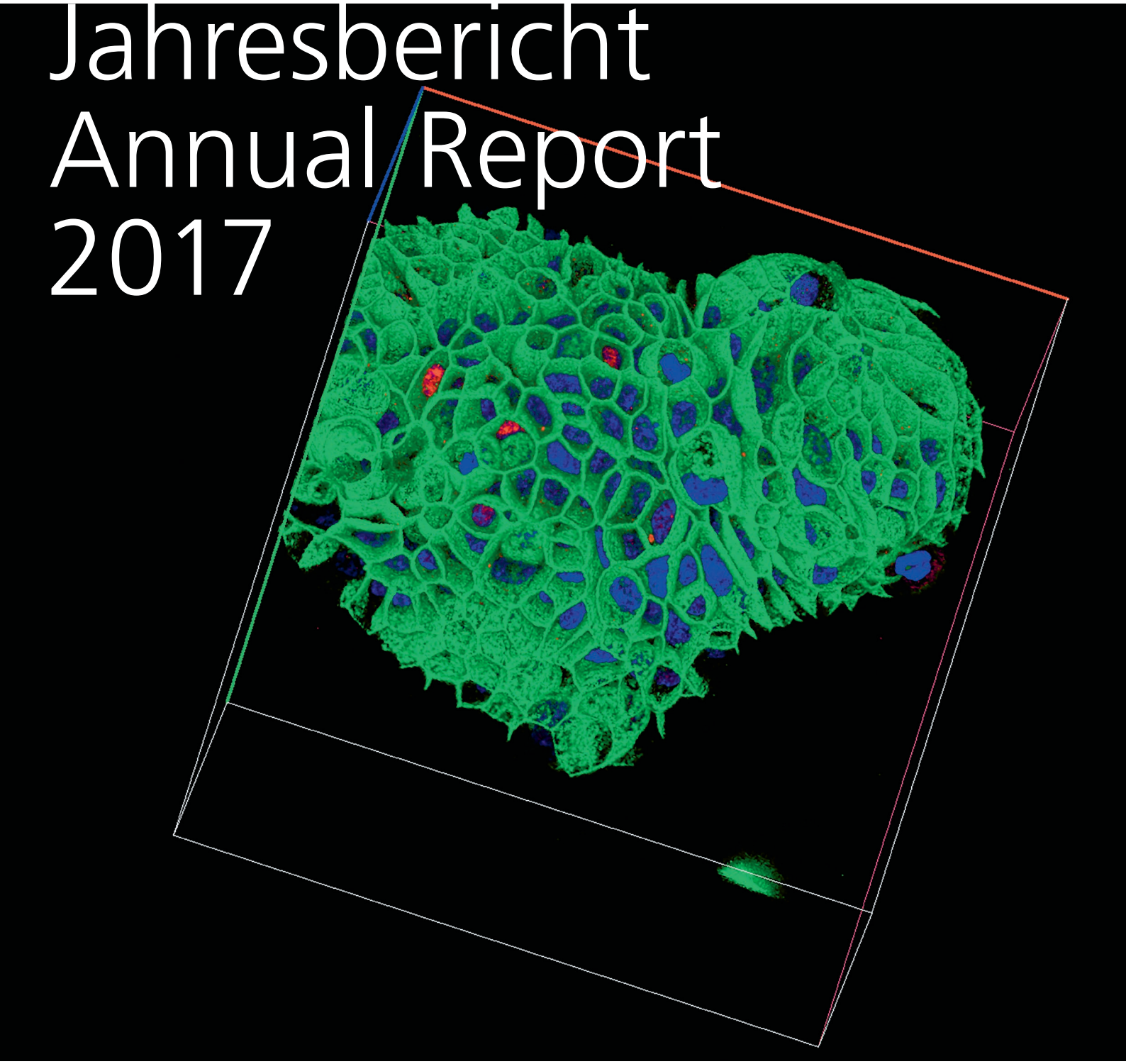
Jahresbericht Annual Report 2017



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A copy of this report can be obtained online at:
www.dbmr.unibe.ch

Cover:
3D projection of Breast Cancer Bone Metastasis organoid stained for E-Cadherin (green), Estrogen Receptor (red) and DAPI (blue)
Image: PD Dr. Marianna Kruithof-de Julio (Urology, DBMR, Inselspital)

Contents

Foreword – Director's Report

This past year has been one of change for the Department. The Department took on a new name, *Department for BioMedical Research*, to better reflect the type of work that we support. As the new Director, I also have the opportunity to re-evaluate and re-shape the Department with a strong focus on translational biomedical research. We have retired the DKF newsletter and have replaced this with a commitment to provide a more active and informative website (see figure). The new website now features three key areas for news, events and social media (@DBMR_UniBe). We hope that the new format will provide information at a glance as to what is happening at the DBMR. The social media feed should allow us to develop a presence within and outside of Bern. We hope to highlight our investigator's achievements, here and at the new website. (Note: Please make sure to tell us about your events and achievements so we can share the news!).

The DBMR is also exploring new ways to provide more technical support at the already excellent core facilities. One way will require a careful re-evaluation of costs and service fees. We believe that this will be needed to maintain the highest level of technical quality. We look forward to working with group leaders to explore other means of supporting the DBMR over the coming year, in close collaboration with the Dean's office.

We are also working on structural changes and strategic planning around moving into a new facility at Murtenstrasse 24 in 2021 (see figures).

While still a few years away, we still need to plan carefully how to best use the new space, and importantly, re-vitalize space that will be made available as research groups in such areas as cardiology, neurology and oncology move to the new facility. One key principle of our mission will be to develop new synergies in both existing and new space. We hope this greatly needed expansion will also lead to more thematic research initiatives, enabling more collaboration both in Bern and beyond. Perhaps one of the most important new synergies will be our ability to consolidate all of the technology core facilities on one floor. We hope that this will lead to a better user experience and workflow. We are excited that the Next Generation Sequencing Platform facility lead by Tosso Leeb (Director Institute of Genetics, University of Bern) and Rémy Bruggmann (Head of Interfaculty Bioinformatics Unit, University of Bern) will join the existing cores (see figures, Tosso Leeb left, Rémy Bruggmann right). We are also establishing a new core facility to help develop patient-derived organoid models. This state-of-the-art facility will already take root in Murtenstrasse 35 and will expand in the new core facility. We are happy to announce that Marianna de Julio will be our faculty leader for this critical, new translational research activity.

I want to extend my thanks to all of those members of the administrative and technical staff that have done a great job over the past year working to support DBMR research. They maintain a wonderful facility and atmosphere for our trainees and researchers. Finally, a special thanks goes to Willy and Robert for serving the department so well over the past year, and enabling most of the changes that I have just described.

Together, we are happy to share with you in this Annual Report some of the DBMR highlights for 2017.

Prof. Dr. Mark A. Rubin, Director

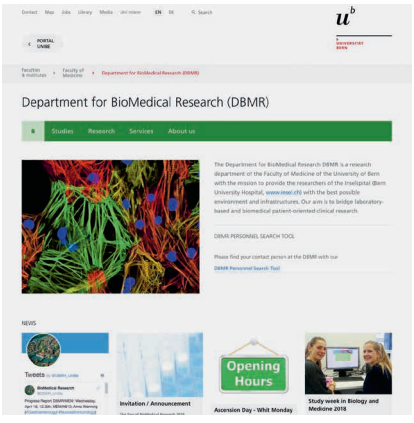
Vorwort – Bericht des Direktors

Das vergangene Jahr stand im Zeichen der Veränderung für das Departement. Es wurde neu zu Department for BioMedical Research umbenannt, um im Namen die im Departement geleistete Arbeit besser abzudecken. Als dem neuen Direktor bietet sich mir die Möglichkeit, die Forschung im Departement zu evaluieren und neu auszurichten. Dabei wird das Schwergewicht auf die translationale, biomedizinische Forschung gelegt. Als eine der ersten Neuerungen haben wir den DKF Newsletter eingestellt. Dieser wurde ersetzt durch eine neue, aktivere und informativere Webseite (siehe Abbild). Die neue Webseite enthält nun drei Schlüsselbereiche für News, Events und soziale Medien (@DBMR_UniBe). Das neue Format wird auf einen Blick Informationen zum Geschehen am DBMR vermitteln und stellt unser wichtigstes Werkzeug zur Kommunikation dar. Der Twitter Feed sollte uns eine Präsenzerweiterung in- und ausserhalb von Bern ermöglichen. Hier, sowie auf der neuen Webseite, möchten wir auf die Erfolge unserer Forscher hinweisen. (Hinweis: stellt bitte sicher, dass ihr uns über eure Anlässe und Erfolge informiert, damit wir diese Informationen publizieren können!).

Das DBMR denkt ferner über neue Wege nach, den technischen Support durch die bereits hervorragenden Core Facilities zu erweitern. Eine Möglichkeit dazu bedingt eine wohlüberlegte Neueinschätzung und Anpassung der Kosten und der Servicegebühren. Dies wird unserer Meinung nach nötig sein, um den höchsten technischen Qualitätsstandard aufrecht zu erhalten. Wir freuen uns mit den Gruppenleitern zusammen zu arbeiten, um in enger Kollaboration mit dem Dekanat zusätzliche Wege zu finden, um das DBMR im kommenden Jahr zu unterstützen.

Wir arbeiten zudem an Änderungen in der Infrastruktur sowie an der strategischen Planung für den Umzug im 2021 in das neue Forschungsgebäude an der Murtenstrasse 24 (siehe Abbildungen). Auch wenn dies erst in ein paar Jahren geschehen wird, muss jetzt mit der Planung begonnen werden, wie diese neuen Flächen optimal genutzt werden können. Ebenso wichtig ist die Planung der neuen Nutzung der Flächen, die in den bestehenden Räumlichkeiten des DBMR durch den Umzug der Gruppen in Bereichen wie Kardiologie, Neurologie und Onkologie an die Murtenstrasse 24 frei werden. Das Augenmerk wird auf der Schaffung von neuen Synergien zwischen den existierenden und den neuen Infrastrukturen liegen. Wir hoffen, dass diese dringend benötigte Erweiterung auch zu mehr thematischen Forschungsinitiativen führen wird, um sowohl in Bern, wie auch ausserhalb, vermehrte Kooperation zu ermöglichen. Wir versprechen uns auch viel von der Möglichkeit, alle Technologie Core Facilities des DBMR auf einem Stockwerk an der Murtenstrasse 24 zusammen zu bringen. Dadurch werden wir eine Verbesserung der Benutzerzufriedenheit sowie eine Effizienzsteigerung im Workflow erreichen. Wir freuen uns, dass der Next Generation Sequencing Platform, geleitet von Tosso Leeb (Leiter Institut für Genetik, Universität Bern) und Rémy Bruggmann (Leiter Einheit Bioinformatik und computerbasierte Biologie, Universität Bern), sich zu den bestehenden Core Facilities gesellen wird. Wir kreieren zudem eine neue Core Facility, um die Entwicklung von Organoidmodellen aus Geweben von PatientInnen zu unterstützen. Diese hochmoderne Einrichtung wird bereits an der Murtenstrasse 35 etabliert, und danach in der neuen Core Facility an der Murtenstrasse 24 erweitert. Es freut uns mitzuteilen, dass Marianna de Julio die Leitung dieser wesentlichen, neuen translationalen Forschungstätigkeit übernehmen wird.

Ich möchte mich bei allen administrativen und technischen Mitarbeiterinnen und Mitarbeitern bedanken, welche im letzten Jahr grossartige Arbeit geleistet haben, um die Forschung im DBMR zu unterstützen. Sie verwalten eine wundervolle Einrichtung und fördern eine positive Atmosphäre für unsere Auszubildenden (Studierenden) und Forscherinnen und Forschern. Und zum Schluss geht mein ganz besonderer Dank an Willy und Robert für ihren bemerkenswerten Dienst an das Departement im vergangenen Jahr, und dass sie die meisten Änderungen, die ich erwähnt habe, ermöglicht haben. Zusammen freuen wir uns, durch diesen Jahresbericht einige der DBMR Höhepunkte im 2017 mit Euch teilen zu können.



The DBMR at a Glance

The Department for BioMedical Research (DBMR, formerly 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 2017, 48 independent research groups, covering almost all fields of biomedical research, were affiliated with the DBMR.

The DBMR aims to bridge laboratory-based biomedical and patient-oriented clinical research through 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 DBMR auf einen Blick

Das Department for BioMedical Research (DBMR, früher 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 2017 waren 48 unabhängige Forschungsgruppen dem DBMR angeschlossen, die zusammen fast alle Bereiche der biomedizinischen Forschung abdecken.

Ziel vom DBMR 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 DBMR angegliedert. Ausserdem wird ein starkes Gewicht auf die Entwicklung von translationellen Ansätzen und der Anwendung von Omics-Technologien gelegt.

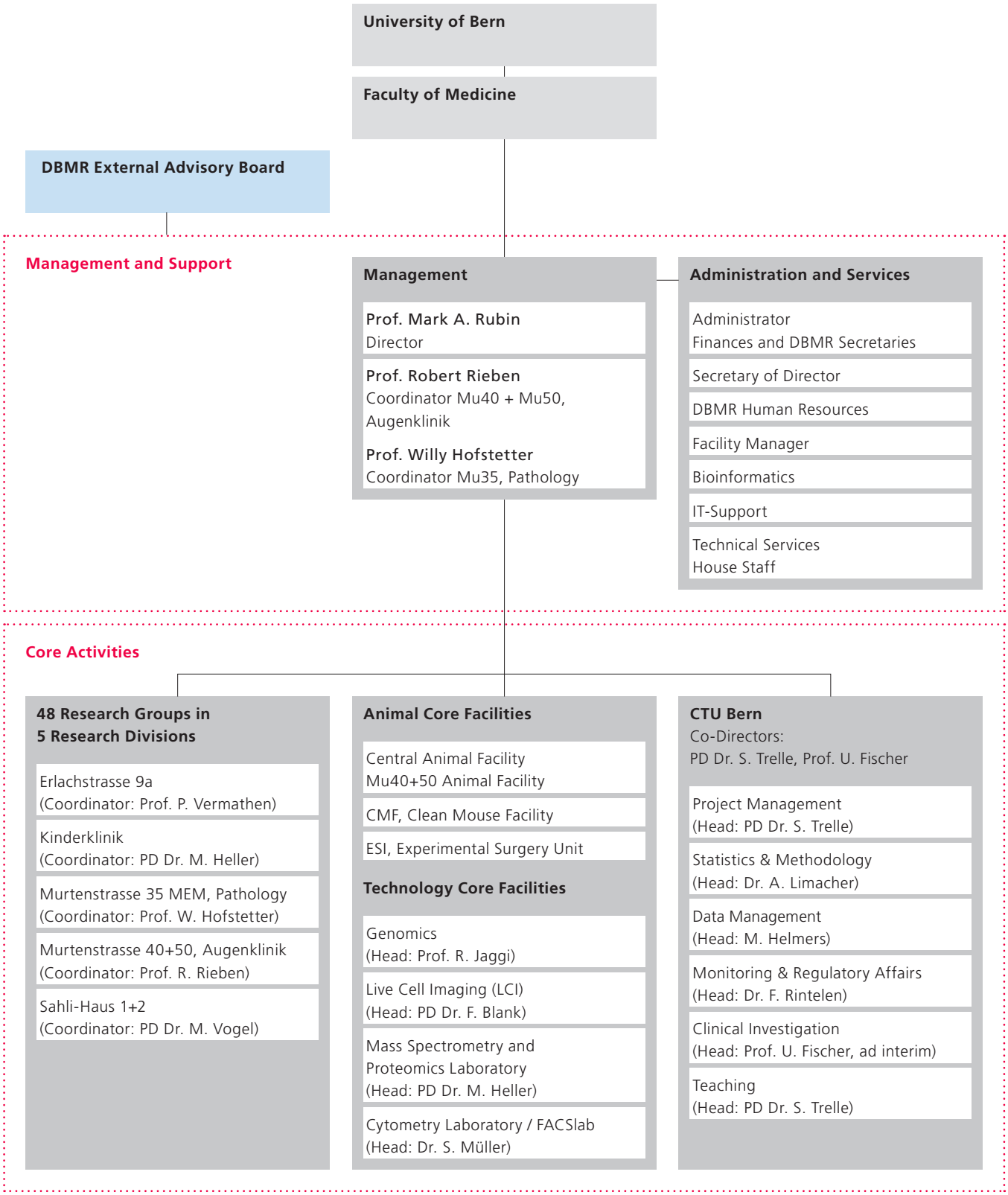
Organisation

The role of the DBMR is to provide optimal infrastructure and scientific support to its research groups, of which there were 48 at the end of 2017. The vast majority (43) of these groups are from clinics of the Inselspital, Bern University Hospital. The remainder (5) are internal DBMR groups, involved in the scientific support and coordination of equipment and infrastructure on a daily basis. The 48 groups are divided into 5 Research Divisions. Equally important, the DBMR is responsible for operating Technology and Animal Core Facilities. It also hosts the Clinical Trials Unit (CTU) Bern. Furthermore, the groups of the department are supported by central services responsible for administration, facility management, technical support, informatics and bioinformatics.

The External Advisory Board evaluates the overall strategies and operation of the DBMR.

Organigram

Department for BioMedical Research



1

M.E. Müller-Haus
Murtenstrasse 35

2

Murtenstrasse 50

3

Pathologie
Murtenstrasse 31

4

Kinderklinik
Freiburgstrasse 15

5

Sahli-Haus 1
Freiburgstrasse 14a

6

Sahli-Haus 2
Freiburgstrasse 14

7

Augenklinik
Freiburgstrasse 8

8

Murtenstrasse 40

9

Erlachstrasse 9a

10 Murtenstrasse 24
(under construction)

Key People

Management

Prof. Dr. Mark A. Rubin
Director (since Feb.)

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

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

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 DBMR Secretaries

Basak Ginsbourger, Administrator
Deborah Re, Secretary
Marla Rittiner, Secretary (since Oct.)
Beatrix Stalder, Secretary
Uyen Vo, Secretary

Secretary of Director

Verena Frazao (until June)
Peggy Kübler (until June)
Claudia Requeta (since May)
Jasmine Stiefel (since Sep.)

DBMR Human Resources

Silvia Rösselet
Marla Rittiner (since Oct.)

Facility Manager

Bernhard Grossniklaus

Occupational Safety, Health Protection and Environmental Safety (OHE)

François Achermann

IT-Support

Michael Ackermann
Thomas Späti
Luca Sulmoni (since July)

Bioinformatics

Dr. Irene Keller
Dr. Cedric Simillion (until Nov.)
Ilker Romann

Technical Services

Patrick Furer, Head DBMR Maintenance

Coordinators of Research Divisions

PD Dr. Manfred Heller
Kinderklinik

Prof. Dr. Willy Hofstetter
Murtenstrasse 35 MEM, Pathology

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

Prof. Dr. Peter Vermathen
Erlachstrasse 9a

PD Dr. Monique Vogel
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

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

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

Achievements 2017

A consortium of all academic clinical trial units in Switzerland under the auspices of the Swiss Clinical Trial Organization got an infrastructure grant approved by the State Secretariat for Education and Research of more than CHF 10m overall for the next 4 years. The grant will help to establish Switzerland-wide competency platforms that will help to increase the quality of academic clinical research in the country. CTU Bern is responsible for the work package on statistics and methodology.

In 2017, the first trials receiving funding by the Investigator-Initiated Clinical Trials (IICT) program of the Swiss National Science Foundation (SNSF) started enrolment: NOSTONE, SERVE, and SIMPL'HIV. Two other trials that were approved in the same program in May 2017 started planning with support from CTU Bern. In 2017, CTU Bern's involvement in large international trials further expanded: two European stroke trials coordinated by the Department of Neurology at Inselspital (ELAN and SWIFT-DIRECT) started recruitment and CTU is responsible for the data management, monitoring, and statistical analysis.

Besides planning, several projects were completed and published in 2017 with support of CTU Bern. For example, final results of a trial comparing symptomatic therapy with antibiotic treatment in female patients with uncomplicated urinary tract infection were published. The trial is the first supported by CTU Bern that was solely conducted in a general practice setting. SPIRIT, a trial evaluating a modified enteral formulation in intensive care medicine patients found no effect of this diet on diarrhoea.

Performance Report 2017

Our consulting service remains one of the most important tasks. Overall, 265 consultancy activities were performed in 2017. Statistical and methodological support for study design, as well as questions regarding data management, were the hot consulting topics. Since we had contact with almost all clinical and non-clinical institutions of the Faculty of Medicine, we consider this support not only essential, but also well established.

Overall, 157 research projects were supported by CTU Bern in 2017 (with at least 8 hours of support). In 58 of these, more than one division of CTU Bern provided services, and in 20 projects all major divisions were involved. Overall, 51 projects were clinical trials, i.e. studies that evaluated the effect of a health-care intervention. Of these, 32 were conducted as multicenter trials and 17 included non-Swiss study sites. Cardiovascular projects remained the main focus. However, other disciplines such as neurology (stroke) or general internal medicine have become more and more important.

We were once again active in teaching. For the first time, CTU Bern was the main institution responsible for a week-long teaching activity dedicated to clinical epidemiology for third year medical students. GCP course activity remained high and we conducted 5 basic courses, 3 advanced courses and 1 refresher course. A monthly CTU lecture covering current topics has now been fully established.

www.ctu.unibe.ch

Finances 2017

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

Outlook 2018

From January 1st onwards, CTU Bern will be an independent institute of the Faculty of Medicine of the University of Bern. We leave the Department for BioMedical Research with mixed feelings, but are nevertheless looking forward to this independence.

Several new teaching activities will start in 2018: the new CAS in Clinical Research primarily organized by the Institute of Social and Preventive Medicine, but with major contributions by CTU Bern and the clinical trial module – for which CTU Bern is responsible – within the MAS in Translational and Entrepreneurship Medicine. We are awaiting feedback on several exciting grant proposals. Finally, the Safer Cannabis – Research in Pharmacies Trial (SCRIPT) is expected to start at the end of 2018.

Staff Members

PD Dr. Sven Trelle, Co-Director (methodological)
Prof. Dr. Urs Fischer, Co-Director (medical)
Hafeezul Adnan, Clinical Data Manager
Dr. Poorya Amini, Project Manager (since June)
Appadoo Sheila, Clinical Data Manager (since Nov.)
Sereina Battaglia, Central Data Monitor (since May)
Dr. Steve Berger, Data Manager (since June)
Sarah Berner, Quality Manager
Anna Blättler, Assistant
Yves Bochud, Data Manager (since Mar.)
Renata Bünter, Clinical Research Coordinator
Dr. Lukas Bütikofer, Senior Statistician
Madeleine Dähler, Study Coordinator
Gian-Andrea Degen, Junior Clinical Data Manager (since Jan.)
Dr. Niklaus Fankhauser, Statistician
Dr. Enrico Frigoli, Project Manager
Brigitta Gahl, Project Coordinator (since June)
Dr. Alan Haynes, Senior Statistician
Dr. Dik Heg, Head, Cardiovascular Health
Muriel Helmers, Head, Clinical Data Management
Sybille Horat, Clinical Trial Monitor (since Oct.)
Stefanie Hossmann, Project Manager
Christina Huf, Quality Manager (since Nov.)
Yanika Jäger, Junior Research Assistant (since Oct.)
Regula Jaeggi, Clinical Research Coordinator
Lucia Kacina, Clinical Trial Monitor
Dr. Alex Karagiannis, Senior Statistician
Stefan Künzler, Junior Research Assistant (since May)
Dr. Armando Lenz, Statistician (since Jan.)
Dr. Andreas Limacher, Head Statistics and Methodology
Dr. Pia Massatsch, Clinical Trial Monitor (since Apr.)
Lena Maurer, Junior Research Assistant (until July)
Julie Rat-Wirtzler, Clinical Data Manager
Dr. Felix Rintelen, Head, Monitoring and Regulatory Affairs
Martina Rothenbühler, Statistician
Dr. Marie Roumet, Senior Statistician
Dominique Rubi, Clinical Data Manager
Ursina Sager, Clinical Research Coordinator (until Dec.)
Dr. Georgia Salanti, Senior Statistical Consultant
Nathalie Schwab, Clinical Trial Monitor (until Oct.)
Odile Stalder, Statistician
Dr. Luca Tamó, Project Manager
Markus van Oosterhout, Junior Research Assistant (since Aug.)
Simona Wanner, Assistant
Miriam Wegmann, Clinical Data Manager
Selina Wegmüller, Junior Research Assistant
Priska Wölfli, Clinical Data Manager
Adrian Wyss, Clinical Data Manager (until Feb.)
Katrin Ziegler, Clinical Data Manager

Acknowledgements in publications

A. Kronenberg, L. Butikofer, A. Odutayo, K. Muhlemann, B.R. da Costa, M. Battaglia, D.N. Meli, P. Frey, A. Limacher, S. Reichenbach, P. Juni, Symptomatic treatment of uncomplicated lower urinary tract infections in the ambulatory setting: randomised, double blind trial, BMJ 359 (2017) j4784.

H. Sekhar, M. Zwahlen, S. Trelle, L. Malcomson, R. Kochhar, M.P. Saunders, M. Sperrin, M. van Herk, D. Sebag-Montefiore, M. Egger, A.G. Renehan, Nodal stage migration and prognosis in anal cancer: a systematic review, meta-regression, and simulation study, Lancet Oncol 18(10) (2017) 1348-1359.

N. Faller, A. Limacher, M. Mean, M. Righini, M. Aschwanden, J.H. Beer, B. Frauchiger, J. Osterwalder, N. Kucher, B. Lammle, J. Cornuz, A. Angelillo-Scherrer, C.M. Matter, M. Husmann, M. Banyai, D. Staub, L. Mazzolai, O. Hugli, N. Rodondi, D. Aujesky, Predictors and Causes of Long-Term Mortality in Elderly Patients with Acute Venous Thromboembolism: A Prospective Cohort Study, Am J Med 130(2) (2017) 198-206.

S.M. Jakob, L. Butikofer, D. Berger, M. Coslovsky, J. Takala, A randomized controlled pilot study to evaluate the effect of an enteral formulation designed to improve gastrointestinal tolerance in the critically ill patient-the SPIRIT trial, Crit Care 21(1) (2017) 140.

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

Cytometry Laboratory / FACSlab

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

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 DBMR. Since 2010, Head, DMBR Cytometry Laboratory / FACSlab Core Facility.

Achievements 2017

The staff of the FACSlab received training to operate the new MoFlo ASTRIOS^{EQ} high-speed cell sorter, and already faced a remarkable request for 6-way or biosafety level II sorts.

Due to the enhanced usage of BUV-labelled antibodies, a third detector for the UV-laser was added to both of our state-of-the-art BD FACS LSR II cytometers.

We held the first Swiss Flow Cytometry Core Facility Managers Meeting to exchange experiences and discuss important issues, such as billing users in view of the new SNSF regulations.

Performance Report 2017

Compared to 2016, both FACS measurements and cell sorting increased by 25 %, and 23 %, respectively!

47.1 % of the FACS measurements were performed by researchers from Inselspital clinics and 52.6 % by researchers from University of Bern institutes. Measurements for external parties made up only 0.3 %. Cell sorting numbers were 40.9 % and 59.0 %, respectively, with only one single sort for an external party. 49.6 % of measurements and 60.3 % of cell sorts were performed by/for DBMR groups.

In 2017, four 2-ECTS-points-worth FACS courses for 12 participants each were successfully carried through.

On the downside, due to unchanged workforce and concurrent decrease of financial support by the Faculty of Medicine, the FACSlab faced increasing difficulties to appropriately meet important criteria for a technical core facility of its size and demand, such as QC, collaboration, user support, or strategic planning and development.

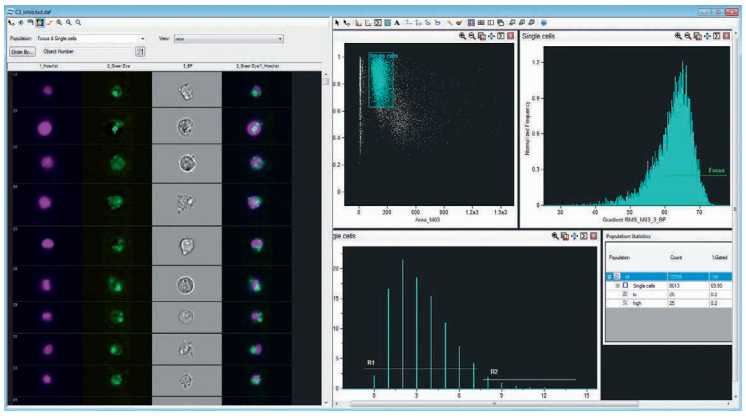
Finances 2017

While enhanced usage of our instruments resulted in a corresponding increase in revenue, the heavily increased bill for the yearly FlowJo software licence, and the expensive replacement of a broken UV-laser, for which financial support by the Faculty of Medicine had unexpectedly been withdrawn, led to a deficit of roughly CHF 50,000!

Outlook 2018

We will continue to plead for the purchase of the previously top-prioritized "MultiMag" and "Enhanced Depth of Field Module" upgrades for our Imaging Flow Cytometer. These are crucial upgrades for cutting-edge research experiments with innovative methods, such as Flow-Fluorescence-In-Situ-Hybridization or asymmetric cell division measurements.

A thorough work-over of our severely outdated website is an urgent project for 2018. Furthermore, we plan to offer individual course modules in collaboration with other Swiss FACS core facilities in place of our hitherto existing 5-day FACS course. However, for this to happen, as well as to prevent painful decreases in technical, methodological and scientific support for our users, the staff and financial situation needs to be urgently and substantially improved.



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

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Live Cell Imaging (LCI)

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

MSc in Cell Biology (2003) and PhD in Structural Biology (2006) at 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), DBMR; since 2010, Commission Member, Microscopy Imaging Centre. Since 2012, Head, Live Cell Imaging (LCI) Core Facility, DBMR. Venia docendi (2016).

Achievements 2017

In 2017 the LCI Core Facility was busy with establishing new histological techniques in order to provide more services for users involved in projects dealing with histology and imaging. In particular, a specific technique for embedding samples in stereology has been established in our histo-lab. This method allows the embedding of tissue samples for sectioning, avoiding non-homogenous shrinkage artefacts, and is essential for accurate morphometric measurements (Schneider & Ochs; Am J Physiol Lung Cell Mol Physiol. 2014 Feb 15; 306(4): L341-50). In addition to Technovit embedding, the histo-lab has provided service in histological processing. Please contact Fabian Blank (fabian.blank@dbmr.unibe.ch) or Carlos Wotzkow (carlos.wotzkow@dbmr.unibe.ch) for more information regarding specific service and pricing.

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 members of the University of Bern.

Performance Report 2017

Booked hours for LCI equipment have increased significantly compared to the previous year (6,782 in 2017 vs. 4,433 in 2016) due to the use of additional microscopes introduced in 2016. In 2017, LCI staff has spent a total of 170 hours on introduction trainings for LCI microscopes. Working hours spent for collaborations with other research groups from the DBMR have increased to 424 (2016: 372), hours spent on technical assistance dropped to 195 (2016: 279). As in previous years, the Facility contributed to cutting-edge lectures and practical modules organised by the MIC. A total of 18 students were trained in practical modules of the LCI in 2017.

Finances 2017

Revenue increased slightly compared to 2016 due to increased usage of the LSM710. The Facility has received a working credit of CHF 4,000 from the DBMR for general maintenance and repairs. The LCI Core Facility has also covered the yearly IMARIS software license fee for three floating licenses. The software is available free for users of the Facility and installed on the workstations available for booking.

Outlook 2018

Selina Steiner is joining the LCI Core Facility as a lab technician as of March 2018. With her help, we will be able to support more research groups in their projects. Furthermore, a brand new IncuCyte Live Cell Analysis System will be installed soon in our Facility, allowing users to monitor the growth of organoids and similar 3D cultures in real-time over a long period.

Staff Members

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

www.lci.dkf.unibe.ch

Genomics (Core Facility) / Molecular Biology (Research Group)

Prof. Dr. Rolf Jaggi
rolf.jaggi@dbmr.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, DBMR and since 2011, Head of Genomics Core Facility.

Achievements 2017 / Outlook 2018

Molecular Biology

We generated several CRISPR/Cas9 constructs targeting exon1 of the progesterone receptor (PR). Pools of 2, 3 or 5 different sgRNA constructs were transfected into PR-expressing T47D breast cancer cells and 3 pools of transfected cells were isolated by FACS. The T47D cells have more than two copies of the PR gene and transfected cells were not PR-negative but still expressed reduced levels of PR (PR-low). Reference cells transfected with an unrelated CRISPR construct (directed against the luciferase gene) were studied in parallel. RNA-seq data were generated from untreated (no hormone), progesterone-treated (P4) and P4 + estrogen (E2)-treated cells. Differentially expressed genes (between PR-low and reference cells and between untreated and treated cells) and pathways (over- or under-represented between groups of cells) were identified. The results may be clinically relevant as PR-positive breast cancer has a better prognosis than PR-negative, but the underlying biology is only poorly understood at this time. The data from the cell culture model are compared to observation from PR-positive and -negative breast cancer specimens. The results are being prepared for the thesis of a PhD student. They shall be documented in a manuscript (in preparation).

The second research project is conducted in collaboration with three Departments of the Inselspital, Bern University Hospital – Frauenklinik, Oncology, and Pathology. Archival material from 132 human breast cancer specimens was characterized histologically and immuno-histochemically; 87 samples were derived of primary tumours, 20 of local recurrences and 25 of brain metastases. Primary breast cancer and recurrence material from the same patient was available for 16 local recurrences and 19 brain metastases. Clinical and histological data was systematically assembled from each patient, and tumour RNA was isolated and gene expression measured using the nCounter system (Nanostring). The 55 genes of PAM50 (including 5 control/reference genes) were measured in parallel with 28 genes of RISK (own score), 21 genes for RS (recurrence score), 12 genes of EP (EndoPredict) and ROR (Risk of recurrence, proliferation-related genes of PAM50). All four scores are prognostic for ER-positive breast cancer of postmenopausal patients. The aim of our study was to compare the different scores with the intrinsic subtypes generated with PAM50 and against each other. The four scores performed similarly with respect to risk of recurrence. This was in agreement with the good correlation of the different genes related to proliferation. Interestingly, the variation is considerably higher when other genes present in the scores are compared, especially genes related to the response to ER and PR. The four scores failed to be prognostic in primary breast cancer that progress and form local recurrences, although it is well-documented that patients with such tumours have a poorer prognosis than patients with primary breast cancer remaining recurrence-free.

www.gcf.dkf.unibe.ch
www.molbiol.dkf.unibe.ch

Performance Report 2017 / Outlook 2018

Genomics Platform

The Genomics Core Facility offers support mainly to individuals or groups of the Faculty of Medicine who are planning studies on the basis of next generation sequencing or other RNA and DNA technologies (e.g. Nanostring, digital PCR, real-time PCR). Our team has been involved with several clinical projects mainly by providing technical support during sample preparation (RNA/DNA isolation, quantitation, quality control) from small and/or archival samples (e.g. from formalin-fixed, paraffin-embedded tissue), or from Laser Capture Microdissection. In addition, our team provided protocols and novel reagents for RNA isolation. Reagents were tested with respect to recovery from archival material and with respect to feasibility for sequencing on an Illumina HiSeq instrument. Another area of support was to provide basic analysis of raw data.

Finances 2017

Genomics

The Genomics Core Facility has a working credit of CHF 4,000 from the DBMR, which is used for maintenance of equipment.

Staff Members

Prof. Dr. Rolf Jaggi, Group Leader and Head of Genomics Core Facility
PD Dr. Heinz Keller, Neurologist (Inselspital)
Dr. Irene Keller, Bioinformatician (Core Facility)
Nathalie Schuster, Laboratory Technician (Research Group & Core Facility)
Mariana Bustamante, PhD Student (Research Group)

Collaborators

Aebi S, Günthert A, Lucerne Cantonal Hospital (CH)
Centeno Ramos I, Hewer E, University of Bern (CH)
Imboden S, Inselspital (CH)
Popovici V, Masaryk University (CZ)
Rothschild S, University Hospital Basel (CH)

Mass Spectrometry and Proteomics Laboratory (Core Facility)

Protein and Cell Biology (Research Group)

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

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

Achievements 2017

Mass Spectrometry and Proteomics

As in 2016, the demand for our service was constantly high during the entire year, with many exciting projects of larger sample sets. Of note was an extraordinary increase of instrument usage time by NCCR RNA & Disease group members, from 13 % in 2016, to 44 % in 2017, also due to the affiliation of new principal investigators to this research project. As a consequence of heavy use, instruments were spoiled at a faster rate. Cleaning interventions were necessary, which specifically led to some longer downtimes at the end of summer. As every year, we would like to thank all users for their trust in our service and patience while waiting for results.

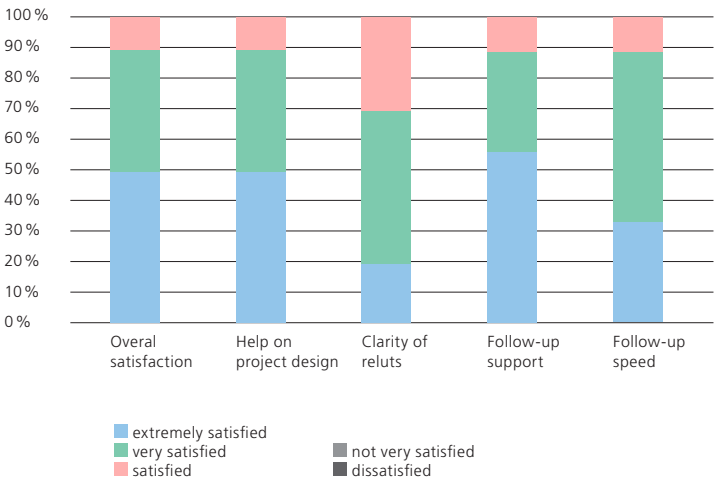
We launched a short questionnaire at the end of the year and have received ten responses to date, indicating that scientists were very satisfied with our work (see figure below) and that all would recommend our service to others. We were also able to complete the set-up of a new, automated software pipeline for the interpretation of LC-MS/MS data.

Protein and Cell Biology

We could establish a protein extraction protocol for grapevine leaf petioles, and finalize the data acquisition on leaf and petiole proteomes of healthy and grapevine red blotch virus (GRBV) infected plants (a total of six datasets). GRBV is a widespread virus in red cultivars in North America with a significant commercial impact on wine production. Despite the fact that the virus is known since 2012, we are the first researchers able to show the physical existence of GRBV in infected plants at the protein level. In addition, we absolutely quantified the GRBV coat protein load in petioles of three plants, and by way of label-free shotgun proteomics identified an upregulation of flavonoid biosynthesis as a defence mechanism of the plants against viral infection. The data will be presented at a plant conference in Chile and a mass spectrometry conference in the US (manuscript in preparation).

Furthermore, we worked on a project to determine the effect of blood transportation on extracellular vesicles. We had access to MDS patients at the

Questionnaire summary



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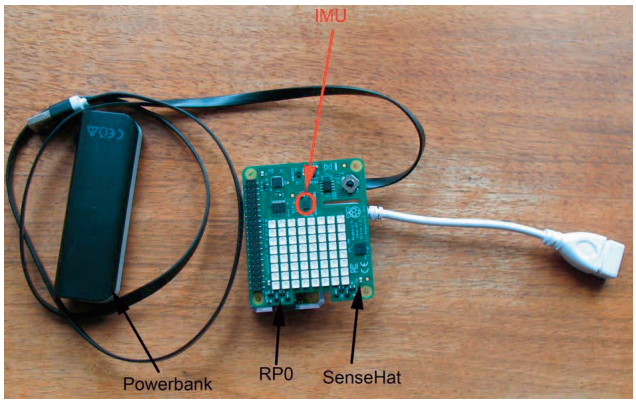

Department of Hematology for this study. With an inertial measurement unit bearing an accelerometer, gyroscope and magnetometer, we measured the forces impacting blood tubes during the pneumatic tube system and human carrier transport together with vesicle size and proteome composition changes (work in progress). In relation to this project, M. Heller was invited to two liquid biopsy workshops in Tutzing (DGKL, Germany) and Helse Bergen (Norway).

Plans for 2018

We aim to 1) publish the two above-mentioned manuscripts; 2) extend the automated pipeline for the interpretation of LC-MS/MS data with quantification tools and a GUI; 3) continue to develop further methods for the analysis of extracellular vesicles and analyse collected MDS samples; 4) hyphenate the automated sample processing station (RTC PAL) with a nano-UPLC.

Performance Report 2017

Mass Spectrometry and Proteomics

We processed almost 2,400 samples during the year (+500 compared with 2016), submitted by laboratories from the Vetsuisse Faculty (2 %), external institutions (1 %), Faculty of Medicine (38 %), Faculty of Science (45 %), and from our own developments, collaborations, and the grapevine project (14 %). This relates to about 3,600 LC-MS/MS runs, not including the 850 QC standards and 3,900 blanks.

Finances 2017

Mass Spectrometry and Proteomics

Our financial situation profited from the fact that we often do maintenance work ourselves. Several of the bills for service engineer interventions at the end of 2017 will stress the balance of 2018. Profits from 2017 will be invested in a software upgrade on the Fusion Lumos instrument and above mentioned nano-UPLC for the RTC-PAL workstation.

The Facility received a working credit of CHF 8,000 from the DBMR 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), DBMR Head of Occupational Safety, Health Protection and Environmental Safety (OHE)
Sophie Braga, Laboratory Assistant (Core Facility & Research Group)
Natasha Buchs, Laboratory Technician (Core Facility & Research Group)
Ilker Romann, IT Specialist (Core Facility)
Dr. Anne-Christine Uldry, Computational Scientist (Core Facility)

Collaborators

Böhm G, CTC Analytics AG (CH)
Bonadies N, University Hospital of Bern (CH)
Burgener M, Geistlich AG (CH)
Debonneville C, Bioreba AG (CH)
Reynard JS, Agroscope, Nyon (CH)

Teaching activities

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

Publications

A. Gazdhar, P. Ravikumar, J. Pastor, M. Heller, J. Ye, J. Zhang, O.W. Moe, T. Geiser, C.C.W. Hsia, Alpha-Klotho Enrichment in Induced Pluripotent Stem Cell Secretome Contributes to Antioxidative Protection in Acute Lung Injury, Stem Cells 36(4) (2018) 616-625.

N. Langenegger, D. Koua, S. Schurch, M. Heller, W. Nentwig, L. Kuhn-Nentwig, Identification of a precursor processing protease from the spider Cupiennius salei essential for venom neurotoxin maturation, J Biol Chem 293(6) (2018) 2079-2090.

N. Meneses, H. Taboada, M.F. Dunn, M.D.C. Vargas, N. Buchs, M. Heller, S. Encarnacion, The naringenin-induced exoproteome of Rhizobium etli CE3, Arch Microbiol 199(5) (2017) 737-755.

V. Brügger, M. Duman, M. Bochud, E. Münger, M. Heller, S. Ruff, C. Jacob, Delaying histone deacetylase response to injury accelerates conversion into repair Schwann cells and nerve regeneration, Nat Commun 8 (2017) 14272.

Link to publication list:
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Bone Biology & Orthopaedic Research

Prof. Dr. Willy Hofstetter
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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, DBMR.

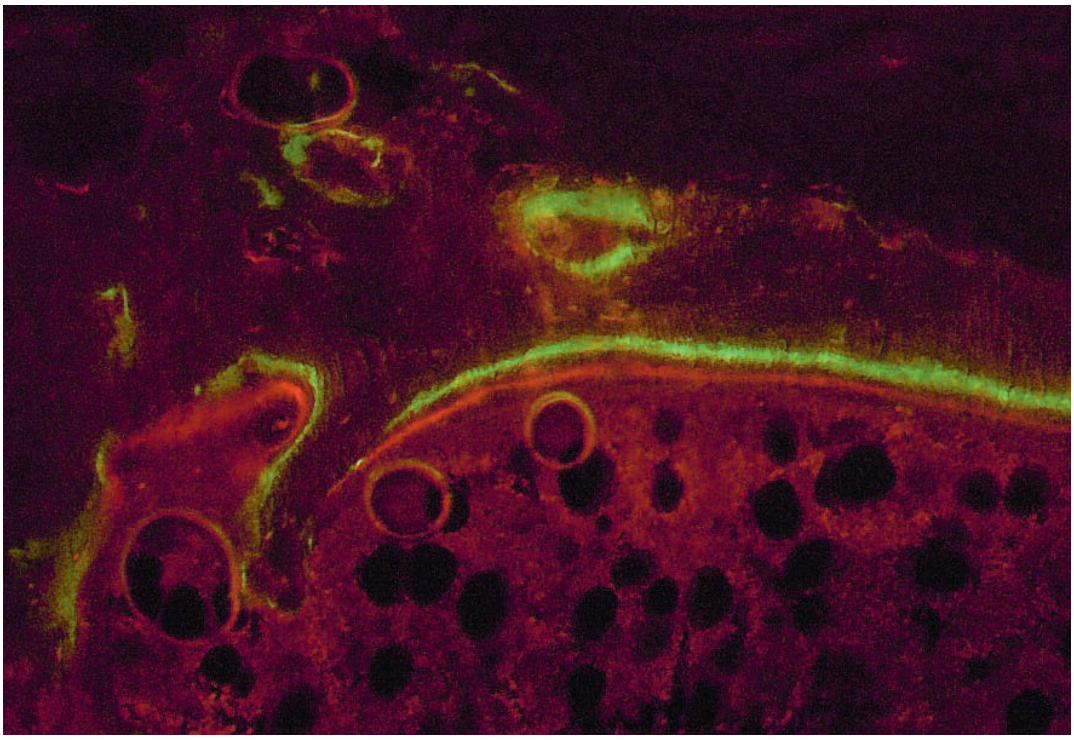
Research Highlights 2017 / Outlook 2018

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. The plasticity of differentiation and function of haematopoietic cells is of particular interest. The data obtained in this project demonstrate that even after differentiation, haematopoietic cells require a specific microenvironment to maintain phenotype and function. Changes in the microenvironment will lead to redifferentiation with acquisition of new phenotypic and functional characteristics. (Alfred and Anneliese Sutter-Stöttner Foundation, PhD Thesis N. Ruef).
- The role of iron, the body's major trace element, in bone cell biology was further investigated. For this purpose, iron uptake assays and osteoclast-specific ko mice for DMT1 were established. While iron uptake by bone cells was found to be modulated by exogenous iron levels, osteoclast-directed deficiency in DMT1 (divalent metal ion transporter) did not affect development and activity of this cell lineage. Due to the critical role of iron in oxidative phosphorylation, the dependence of cell biology on iron in low oxygen conditions will be further studied (NCCR TransCure, PhD project R. Cabra).
- A main topic in the group's research was bone healing in osteoporotic individuals treated with the anti-resorptive bisphosphonate alendronate (ALN). Applying a model for repair of small defects in mice, the impairment of an efficient bone healing process by ALN was demonstrated under conditions of non-rigid fixation of the defect. Subsequently, in a rat critical size model, it was found that treatment with ALN resulted in a delayed turnover of calcium phosphate ceramics used to fill the defect. In a next step, transcriptome analysis will be performed on a mouse femoral critical size defect model (Alfred and Anneliese Sutter-Stöttner Foundation, PhD project M. Hauser).
- With a new PhD student in the group (F. Safari), the investigation on the modulation of osteoclastogenesis by antagonists of bone morphogenetic proteins (BMP) will be resumed. BMP antagonists are well known regulators of the activity of this family of growth factors. It has not been known, however, for the antagonists to exert direct, receptor mediated effects of their own. This new aspect in BMP biology will be the focus of this program (RMS Foundation and Clinic of Orthopaedic Surgery, PhD project F. Safari).
- The roles of GDF10 and FRZB in the development of chondroblast lineage cells were assessed by gain of function / loss of function experiments. Despite hard work and many different approaches, the data have not been promising and the project will be discontinued. (Robert Mathys Foundation, R. Egli, D. Nesic).

www.bonebiology.dbmr.unibe.ch



Group Members

Bone Biology & Orthopaedic Research Group
Prof. Dr. Willy Hofstetter, Group Leader
PD Dr. Dobrila Nesic, Project Leader
Silvia Dolder, Laboratory Technician
Mark Siegrist, Laboratory Technician
Romina Cabra, PhD Student
Michel Hauser, PhD Student
Nina Ruef, PhD Student (until Feb.)

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

Collaborators

Aeberli D, Inselspital (CH)
Bohner M, RMS Foundation (CH)
Fuster D, Inselspital (CH)
Iizuka T, Inselspital (CH)
Luginbuehl R, RMS Foundation (CH)
Saulacic N, Inselspital (CH)
Seitz M, Inselspital (CH)
Siebenrock KA, Inselspital (CH)
Zumstein M, Inselspital (CH)

Teaching Activities

- 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

B. Schaller, N. Saulacic, S. Beck, T. Imwinkelried, E.W.Y. Liu, K. Nakahara, W. Hofstetter, T. Iizuka, Osteosynthesis of partial rib osteotomy in a miniature pig model using human standard-sized magnesium plate/screw systems: Effect of cyclic deformation on implant integrity and bone healing, J Craniomaxillofac Surg 45(6) (2017) 862-871.

N. Ruef, S. Dolder, D. Aeberli, M. Seitz, D. Balani, W. Hofstetter, Granulocyte-macrophage colony-stimulating factor-dependent CD11c-positive cells differentiate into active osteoclasts, Bone 97 (2017) 267-277.

S. Zhang, C. Wotzkow, A.K. Bongoni, J. Shaw-Boden, M. Siegrist, A. Taddeo, F. Blank, W. Hofstetter, R. Rieben, Role of the plasma cascade systems in ischemia/reperfusion injury of bone, Bone 97 (2017) 278-286.

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

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

Cardiovascular Research

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

Studies in biology at the University of Bern; PhD in Immunology (1992). SNSF 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, DBMR.

Research Highlights 2017 / Outlook 2018

In healthy blood vessels the inner surface, made up of endothelial cells, is covered by a layer of sulfated proteoglycans, mostly heparan sulfates. This layer – the glycocalyx – is crucial for the natural, anti-coagulant and anti-inflammatory properties of the endothelium. If a blood vessel is injured, the endothelial cells become activated, they partly shed their glycocalyx and the endothelial surface becomes pro-coagulant and pro-inflammatory. This makes sense in case of an injury to stop bleeding and fight microorganisms which could infect the wound. However, endothelial cell activation also occurs after prolonged ischemia followed by reperfusion, for example in case of a myocardial infarction treated by peripheral coronary intervention (PCI), or because of the binding of natural antibodies in xenotransplantation. In these cases, the ensuing thrombus formation is detrimental. It will dramatically reduce tissue survival after PCI-treated myocardial infarction or lead to vascular rejection of discordant xenografts.

We and others have shown before that the complement system is crucially involved in endothelial cell activation. In 2017, we performed two studies to increase our understanding of the pathophysiology of reperfusion injury on one hand, and pave the way to clinical xenotransplantation, on the other.

Thanks to our collaboration with the group of Eckhard Wolf in Munich, we were able to obtain piglets which were transgenic for the human complement regulatory protein CD46. The use of these transgenic pigs, overexpressing the complement regulator CD46, allowed us to study the effect of physiological complement regulation in an established model of acute myocardial ischemia and reperfusion in pigs. Our data show that the CD46-overexpressing pigs had smaller infarct sizes than the non-transgenic ones, supporting the hypothesis that the complement system is crucially involved in ischemia/reperfusion injury.

In the context of xenotransplantation, use of the human CD46 transgene alone is not sufficient to prevent rejection. In addition to CD46, also CD55 and CD59, thrombomodulin, HO-1, HLA-E, and several other transgenes might be needed to prevent endothelial cell activation. Testing combinations of currently up to 12 – and in the future maybe many more – transgenes is pretty much impossible if all has to be done in pigs, for example by perfusion of pig organs with human blood. We have therefore established a novel in vitro system in which we can grow porcine endothelial cells under physiological, pulsatile flow. The system is based on microfluidic chips and has round channels of 100-550 µm diameter, in which the endothelial cells form a monolayer just as in a natural blood vessel. In collaboration with our partners from the German xenotransplantation consortium TR127, we have been testing transgenic porcine endothelial cells, as well as fibroblasts, in our microfluidic system. These experiments are currently ongoing and it is our ambition to establish the microfluidic in vitro model as a reliable standard to test transgene combinations for xenotransplantation.

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

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
Marla Rittiner, Secretary (since Oct.)
Mai Abdelhafez, PhD Student (until Nov.)
Dzhuliya Dzhonova, PhD Student
Riccardo Sfriso, PhD Student

Collaborators

Ayares D, Revivicor Inc (US)
Bovin N, Korchagina E, Russian Academy of Sciences, Moscow (RU)
Constantinescu MA, Olariu R, Inselspital (CH)
Cowan P, Bongoni A, St. Vincent's Hospital, Melbourne (AU)
Garweg J, Zandi S, Berner Augenklinik am Lindenhofspital, Bern (CH)
Guenat O, University of Bern (CH)
Heinis Ch, EPFL, Lausanne (CH)
Hofstetter W, University of Bern (CH)
Jenni HJ, Inselspital (CH)
Langelé B, Duisit J, Université Catholique de Louvain, Brussels (BE)
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)
Schnieke A, Fischer K, Technical 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)
von Gunten S, Frias Boligan K, University of Bern (CH)
Wolf E, Klymiuk N, Bähr A, Ludwig Maximilian University of Munich (DE)

Teaching Activities

- MSc in Biomedical Sciences: Elective modules, 2 Master students (6 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

G. Puga Yung, A.K. Bongoni, A. Pradier, N. Madelon, M. Papaserafeim, R. Sfriso, D.L. Ayares, E. Wolf, N. Klymiuk, A. Bahr, M.A. Constantinescu, E. Voegelin, D. Kiermeir, H. Jenni, R. Rieben, J.D. Seebach, Release of pig leukocytes and reduced human NK cell recruitment during ex vivo perfusion of HLA-E/human CD46 double-transgenic pig limbs with human blood, Xenotransplantation 25(1) (2018).

R. Sfriso, A. Bongoni, Y. Banz, N. Klymiuk, E. Wolf, R. Rieben, Assessment of the Anticoagulant and Anti-inflammatory Properties of Endothelial Cells Using 3D Cell Culture and Non-anticoagulated Whole Blood, J Vis Exp (127) (2017).

R. Olariu, J. Denoyelle, F.M. Leclere, D.V. Dzhonova, T. Gajanayake, Y. Banz, M. Hayoz, M. Constantinescu, R. Rieben, E. Vogelin, A. Taddeo, Intra-graft injection of tacrolimus promotes survival of vascularized composite allotransplantation, J Surg Res 218 (2017) 49-57.

J. Duisit, L. Maistriaux, A. Taddeo, G. Orlando, V. Joris, E. Coche, C. Behets, J. Lerut, C. Dessy, G. Cossu, E. Vogelin, R. Rieben, P. Gianello, B. Lengele, Bioengineering a Human Face Graft: The Matrix of Identity, Ann Surg 266(5) (2017) 754-764.

A.K. Bongoni, E. Salvaris, S. Nordling, N. Klymiuk, E. Wolf, D.L. Ayares, R. Rieben, P.U. Magnusson, P.J. Cowan, Surface modification of pig endothelial cells with a branched heparin conjugate improves their compatibility with human blood, Sci Rep 7(1) (2017) 4450.

M.M. Abdelhafez, J. Shaw, D. Sutter, J. Schnider, Y. Banz, H. Jenni, E. Voegelin, M.A. Constantinescu, R. Rieben, Effect of C1-INH on ischemia/reperfusion injury in a porcine limb ex vivo perfusion model, Mol Immunol 88 (2017) 116-124.

S.E. Pischke, A. Gustavsen, H.L. Orrem, K.H. Egge, F. Courivaud, H. Fontenelle, A. Despont, A.K. Bongoni, R. Rieben, T.I. Tonnessen, M.A. Nunn, H. Scott, H. Skulstad, A. Barratt-Due, T.E. Mollnes, Complement factor 5 blockade reduces porcine myocardial infarction size and improves immediate cardiac function, Basic Res Cardiol 112(3) (2017) 20.

S. Zhang, C. Wotzkow, A.K. Bongoni, J. Shaw-Boden, M. Siegrist, A. Taddeo, F. Blank, W. Hofstetter, R. Rieben, Role of the plasma cascade systems in ischemia/reperfusion injury of bone, Bone 97 (2017) 278-286.

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

Precision Oncology

Prof. Dr. Mark A. Rubin
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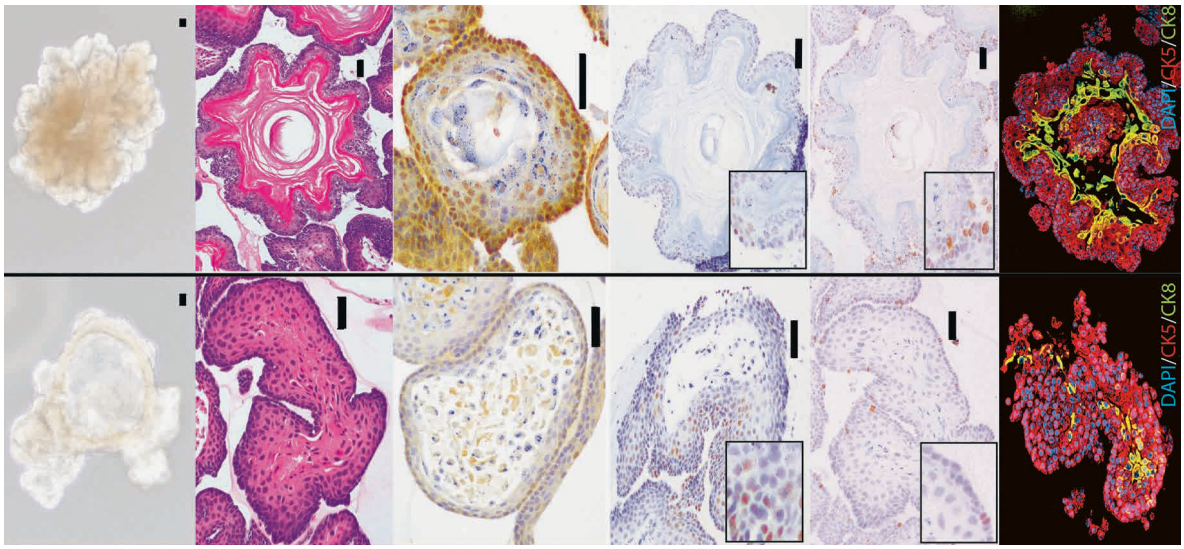
Prof. Mark Rubin is a leader in the fields of prostate cancer biology and precision medicine as it applies to all cancers. Prof. Rubin's laboratory has led a series of landmark studies defining distinct molecular features of prostate cancer, and revealing pathways that are perturbed and which drive the different prostate cancer subtypes. Prof. Rubin has translated many of his genomic discoveries into clinical tests that are currently patented and are standardly used in the diagnosis and treatment of prostate cancer. In May 2017, Prof. Rubin joined the University of Bern as Professor and Director of the Department for Biomedical Research and also as Project Leader for Precision Medicine at the University Hospital of Bern.

Research Highlights 2017 / Outlook 2018

Prof. Rubin established his Precision Oncology research group in Bern. The focus of the lab is on utilizing Precision Medicine approaches to oncology research in order to understand the mechanisms of prostate cancer disease progression and therapy resistance. The research is centered around the questions of how deregulation of signaling pathways in response to oncogene activation promotes cancer, downstream effectors of such pathways facilitate cell transformation, and genomic characteristics of a patient's tumor can be matched to an efficacious treatment. Prof. Rubin is the PI of a multi-institutional National Cancer Institute (NCI)-funded Specialized Program of Research Excellence (SPORE) based at Weill Cornell Medicine focused on Prostate Cancer. Since May 2017, the group has managed to acquire and initiate several major projects.

1) **Swiss Oncology and Cancer Immunology Breakthrough Platform (SOCIBP) for Precision Oncology.** Prof. Rubin leads an SPHN-PHRT program with co-leads Holger Moch (UHZ), George Coukos (CHUV/UNIL), and Gunnar Rätsch (ETHZ), in collaboration with Olivier Elemento (Englander Institute for Precision Medicine). This Swiss Federal Government-funded project addresses a critical scientific gap in immuno-oncology, while simultaneously developing important molecular oncology tools. Despite the rapid acceleration of novel targeted and immunology-based therapies for cancer, tumor cell resistance remains one of the greatest unmet challenges. SOCIBP will both provide important new tools for the Swiss and international research community, and give insight into the mechanism of resistance for immuno-oncology.
2) **Understanding non-canonical phosphatidylinositol kinases in the maintenance of prostate metabolism.** Unlike other tissue types, prostate cell growth and development is heavily dependent on the androgen receptor (AR) signaling pathway. However, other effectors work in conjunction with AR to coordinate key alterations to androgen-dependent tumor biology. In this SNSF-funded project, we are exploring the function of a family of poorly understood lipid kinases called the type II phosphatidylinositol-5-phosphate 4-kinases (PI5P4Ks), and posit that the PI5P4Ks have roles in the control of cellular metabolism that could be pivotal in the regulation of AR in prostate tissue. We are the first group to profile the type II PIP kinases in prostate cancer and will thus establish the foundation for understanding the roles of PI5P4K isoforms in prostate cell biology.
3) **Towards a precision therapy for Speckle-type POZ protein (SPOP) mutant prostate cancer.** This project is funded by the Swiss Krebsliga Association in collaboration with Ruedi Aebersold's laboratory (ETHZ). The focus of this study is to understand the downstream effectors of SPOP, recurrently mutated in 10 % of primary prostate cancer patients, through targeted proteomics, and to help develop clinical biomarkers. Our overarching hypothesis is that SPOP mutant prostate cancer will respond distinctly to targeted therapy due to its inherent vulnerabilities. Other areas of SPOP biology are supported by an NCI grant in its 9th year.
4) **Towards understanding and modulating neuroendocrine transdifferentiation in prostate cancer.** This project seeks to understand the underlying biology of neuroendocrine prostate cancer (NEPC), which will help create therapeutic approaches that can delay or inhibit this terminal form of prostate cancer and lead to earlier co-targeted therapies prior to disease progression.

www.rubinlab.unibe.ch



Group Members

Prof. Dr. Mark A. Rubin, Group Leader
Sandra Cohen, Technician (Weill Cornell Medicine)
Dr. Anke Augspach, Postdoctoral Fellow (since Nov.)
Dr. Laura Patricia Brandt, Postdoctoral Fellow (since May)
Dr. Kellie Anne Cotter, Postdoctoral Fellow (since Oct.)
Dr. Joanna Triscott, Postdoctoral Fellow (since Dec.)

Collaborators

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Emerling B, Sanford Burnham Prebys Medical Discovery Institute (US)
Demichelis F, University of Trento (IT)
Elemento O, Weill Cornell Medicine (US)
Aebersold R, ETH Zurich (CH)
Moch H, University of Zurich (CH)
Coukos G, University of Lausanne (CH)
Rätsch G, ETH Zurich (CH)

Publications

F.W. Huang, J.M. Mosquera, A. Garofalo, C. Oh, M. Baco, A. Amin-Mansour, B. Rabasha, S. Bahl, S.A. Mullane, B.D. Robinson, S. Aldubayan, F. Khani, B. Karir, E. Kim, J. Chimene-Weiss, M. Hofree, A. Romanel, J.R. Osborne, J.W. Kim, G. Azabdaftari, A. Woloszynska-Read, K. Sfanos, A.M. De Marzo, F. Demichelis, S. Gabriel, E.M. Van Allen, J. Mesirov, P. Tamayo, M.A. Rubin*, I.J. Powell, L.A. Garraway, Exome Sequencing of African-American Prostate Cancer Reveals Loss-of-Function ERF Mutations, **Cancer Discov** 7(9) (2017) 973-983. * Co-senior author

M. Zou, R. Toivanen, A. Mitrofanova, N. Floch, S. Hayati, Y. Sun, C. Le Magnen, D. Chester, E.A. Mostaghel, A. Califano, M.A. Rubin, M.M. Shen, C. Abate-Shen, Transdifferentiation as a Mechanism of Treatment Resistance in a Mouse Model of Castration-Resistant Prostate Cancer, **Cancer Discov** 7(7) (2017) 736-749.

C. Pauli, B.D. Hopkins, D. Prandi, R. Shaw, T. Fedrizzi, A. Sboner, V. Sailer, M. Augello, L. Puca, R. Rosati, T.J. McNary, Y. Churakova, C. Cheung, J. Triscott, D. Pisapia, R. Rao, J.M. Mosquera, B. Robinson, B.M. Faltas, B.E. Emerling, V.K. Gadi, B. Bernard, O. Elemento, H. Beltran, F. Demichelis, C.J. Kemp, C. Grandori, L.C. Cantley, M.A. Rubin, Personalized In Vitro and In Vivo Cancer Models to Guide Precision Medicine, **Cancer Discov** 7(5) (2017) 462-477.

M. Blattner, D. Liu, B.D. Robinson, D. Huang, A. Poliakov, D. Gao, S. Nataraj, L.D. Deonarine, M.A. Augello, V. Sailer, L. Ponnala, M. Ittmann, A.M. Chinnaiyan, A. Sboner, Y. Chen, M.A. Rubin*, C.E. Barbieri, SPOP Mutation Drives Prostate Tumorigenesis In Vivo through Coordinate Regulation of PI3K/mTOR and AR Signaling, **Cancer Cell** 31(3) (2017) 436-451. * Co-corresponding author

P. Mu, Z. Zhang, M. Benelli, W.R. Karthaus, E. Hoover, C.C. Chen, J. Wongvipat, S.Y. Ku, D. Gao, Z. Cao, N. Shah, E.J. Adams, W. Abida, P.A. Watson, D. Prandi, C.H. Huang, E. de Stanchina, S.W. Lowe, L. Ellis, H. Beltran, M.A. Rubin, D.W. Goodrich, F. Demichelis, C.L. Sawyers, SOX2 promotes lineage plasticity and antiandrogen resistance in TP53- and RB1-deficient prostate cancer, **Science** 355(6320) (2017) 84-88.

DBMR Research Groups from the Inselspital

Forty-two research groups from departments of the Inselspital and other clinics were affiliated with the DBMR at the end of 2017. Below is a list of the groups. Five of the groups are featured on the following pages.

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

Cardiology: Prof. Dr. Stephan Windecker, Prof. Dr. Paul Mohacsi, Prof. Dr. Christian Seiler, Prof. Dr. Stefano Rimoldi, 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, 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 / Diabetology (Adults): Prof. Dr. Christoph Stettler

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

Endocrinology of the Breast: Prof. Dr. Petra Stute

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

Endometrium & Ovary: Prof. Dr. Michael von Wolff

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

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

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

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

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

Hematology / Oncology (Paediatrics): Prof. Dr. Jochen Rössler

Hepatology: Prof. Dr. Jean-François Dufour, Prof. Dr. Annalisa Berzigotti, Prof. Dr. Andrea De Gottardi, Prof. 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. 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 Basseti, Prof. Dr. Antoine Adamantidis, Prof. Dr. Kaspar Schindler, Prof. Dr. Arnold Marcel, Prof. Dr. Urs Fischer, PD Dr. Simon Jung, PD Dr. Michael Schüpbach, Prof. Dr. Matthias Sturzenegger, Prof. Dr. René Müri, Prof. Dr. Kai Rösler, Prof. Dr. Werner Z'Graggen, Prof. Dr. Kalla Roger, Prof. Dr. Andrew Chan, Prof. Dr. Roland von Känel, Prof. Dr. Saxena Smita

Neurosurgery: Prof. Dr. Hans-Rudolf Widmer

Oncology / Haematology (Adults): Prof. Dr. Thomas Pabst, PD Dr. Katja Seipel

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

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

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

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, Prof. Dr. Christophe von Garnier, Dr. Manuela Funke-Chambour

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

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

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

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

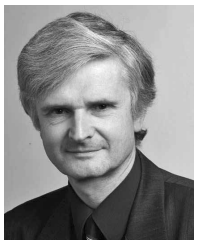
Thoracic Surgery: Prof. Dr. Ralph A. Schmid, Dr. Sean R.R. Hall, Dr. Thomas Marti, PD Dr. Ren-Wang Peng

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

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

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

Gastroenterology / Mucosal Immunology



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

Dr. Mercedes Gomez de Agüero
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Studied Biology (MSc, 2007) at the University of Madrid (ESP) and the University of Lyon (FR), and Immunology (PhD, 2011) at the University of Lyon (FR). Postdoc at DBMR at the University of Bern (2012-2016). Since July 2016, Clean Mouse Facility Manager at the University of Bern and Group Leader at the DBMR since January 2017.

Research Highlights 2017 / Outlook 2018

Microbiome Composition and Function of Inflammatory Bowel Disease (IBD) Patients

In a large translational project we study the mucosa-associated microbiome in a large number of IBD patients. Biopsy samples are obtained from the Swiss Inflammatory Bowel Disease Cohort (SIBDC) and from the Endoscopy Unit of the Department of Gastroenterology at the Inselspital. We have deeply characterized these cohorts consisting of more than 2500 biopsies from over 550 IBD patients/250 Non-IBD subjects, thus building one of the largest cohorts covering sequence data for IBD. Our goal is to associate the clinical variable with observed microbial dysbiosis in these patients by combining metabolomic, metagenomic, and immunological approaches. We also used computational machine learning to characterize potential microbial biomarkers for the identification of therapeutic responses and disease activity status in IBD patients.

Intestinal Antibodies Limit Microbial Metabolite Exposure and the Resulting Immune Response of the Host

Using a system of transient colonisation to pre-induce bacterial-specific IgA followed by colonisation with metabolically-labelled bacteria coupled to high-resolution mass spectrometry, we showed that hundreds of microbial metabolites penetrated 23 host tissues and fluids within hours after intestinal exposure. Mucosal maturation through transient colonization increased the clearing rate via the urine of bacterial metabolites entering the body, independent of pre-induced antibodies. Antibodies, however, increased intestinal transit time, thereby limiting small intestinal mucosal exposure to microbial products and subsequent systemic cytokine release.

The Role of Commensal Microbiota in Disease Protection

A dysregulated microbiota can promote diseases through various non-antigen-specific effects on both pathogenic and regulatory lymphocytes. Together with collaborators from the University of Calgary (CA), we have identified a specific antigen expressed by several species of the human and murine gut microbial genus Bacteroides, which mimics a mammamlian host antigen, a self-reactive pancreatic antigen. This molecular mimicry was able to shape and educate the host intestinal immune response towards protection from intestinal disease in a mouse model, suggesting a powerful role of the microbiota in maintaining host homeostasis and protection from autoinflammatory diseases.

Role of Maternal Microbiota in Shaping Immune System Development in the Offspring

Although colonization of the intestine of newborns occurs only after birth, we showed that pre- and postnatal exposure of the offspring to maternal microbial metabolites extensively shapes the immune system of the offspring with alterations in innate lymphoid and mononuclear cells and extensive reprogramming of intestinal transcriptional profiles. We are currently extending this study by further characterizing the mechanisms by which this early innate education occurs, by testing if maternal microbial products can alter disease susceptibility in the offspring, and by determining the effect on other organs in the offspring, such as the skin and the liver.

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Studied Molecular Medicine (MSc, 2009) at Albert-Ludwigs-University of Freiburg (DE) and at the University of British Columbia (CA), and Immunology (PhD, 2013) at Albert-Ludwigs-University of Freiburg (DE). Postdoc at DBMR, University of Bern (2013-2016). Since September 2016, Group Leader at the DBMR and since July 2016, Clean Mouse Facility Manager at the University of Bern.

Group Members

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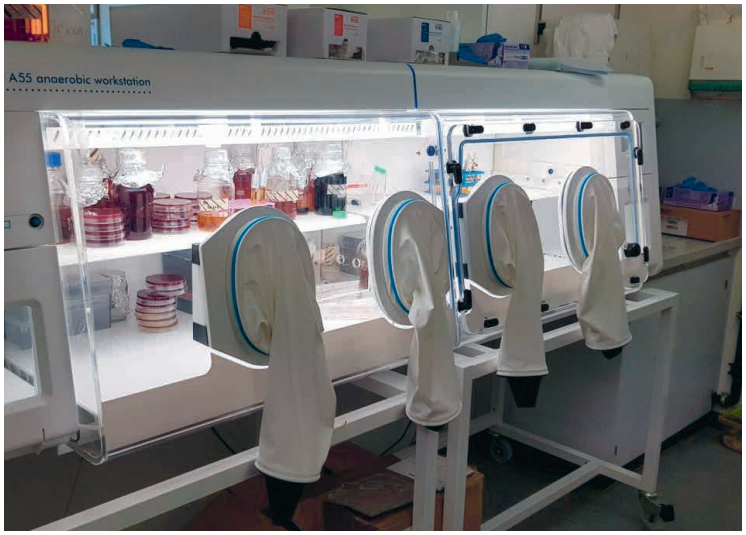
Dr. Stephanie Ganal-Vonarburg, Senior Teaching and Research Assistant
Dr. Mercedes Gomez de Agüero, Senior Teaching and Research Assistant
Prof. Dr. Reiner Wiest, Senior Consultant, Lead Physician Gastroenterology
PD Dr. Pascal Juillert, Consultant, Physician Gastroenterology
Dr. Hai Li, Postdoctoral Fellow
Dr. Julien Limenitakis, Postdoctoral Fellow
Dr. Francesca Ronchi, Postdoctoral Fellow
Dr. Yasuhiro Uchimura, Postdoctoral Fellow (until Apr.)
Dr. Bahtiyar Yilmaz, Postdoctoral Fellow
Dr. Jakob Zimmermann, Postdoctoral Fellow
Beatrice Flogerzi, Lab Technician
Geraldine Käslin, Lab Technician
Terry Müller, Lab Technician (from Sept.)
Karin Stettler, Lab Technician
Dr. Catherine Mooser, MD-PhD Student
Marcel Sorribas, PhD Student
Dr. Anna Wenning, MD-PhD Student
Madeleine Wyss, PhD Student (until Jan.)



Selected Collaborators

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Santamaria P, University of Calgary (CA)
Sauer U, ETH Zurich (CH)
Vivier E, Centre d'Immunology de Marseille-Luminy (FR)

Selected Publications

A.J. Macpherson, M.G. de Aguero, S.C. Ganal-Vonarburg, How nutrition and the maternal microbiota shape the neonatal immune system, Nat Rev Immunol 17(8) (2017) 508-517.

R. Hebbandi Nanjundappa, F. Ronchi, J. Wang, X. Clemente-Casares, J. Yamanouchi, C. Sokke Umeshappa, Y. Yang, J. Blanco, H. Bassolas-Molina, A. Salas, H. Khan, R.M. Slattery, M. Wyss, C. Mooser, A.J. Macpherson, L.K. Sycuro, P. Serra, D.M. McKay, K.D. McCoy, P. Santamaria, A Gut Microbial Mimic that Hijacks Diabetogenic Autoreactivity to Suppress Colitis, Cell 171(3) (2017) 655-667 e17.

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

Laboratory on Sleep Structures & Functions

Prof. Dr. Antoine Adamantidis
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PhD (2005) at University of Liege (BE). Postdoc (2006–2010) at Stanford University School of Medicine (US). Assistant Professor (2010–2014), Department of Psychiatry, McGill University (CA). Assistant Professor (2014–2017), Department of Neurology, Inselspital. Director, Zentrum für Experimentelle Neurologie, ZEN (2014–Present). Associate Professor, Department of Neurology, Inselspital (2017).

Research Highlights 2017 / Outlook 2018

Sleep, or sleep-like states occurring during the rest period, is an evolutionarily conserved biological phenomenon across species, yet its mechanisms and functions remain a mystery. Sleep is essential for proper functioning of the brain, the body and the mind. Indeed, growing clinical evidence emphasizes the prevalence of sleep-related disorders in our society and their dramatic impact on health, performance, productivity, and overall quality of life.

In mammals, the sleep electroencephalogram (EEG) is used to distinguish non-rapid-eye movement (NREM, 3 stages in humans, 1 in rodents) from rapid-eye-movement (REM) sleep and reflects the activity of distinct oscillatory neuronal networks distributed across the brain. For instance, NREM slow waves or spindles and REM theta oscillations originate from neural circuits located in the thalamo-cortical structures and the hippocampus, respectively (see figure). In this context, my research interest aims at understanding the neurobiological nature of sleep and sleep oscillations. Our recent work on brain oscillations during REM sleep has unlocked new experimental ways to probe their role in sleep-dependent memory consolidation.

Ten years ago, together with my colleagues a Stanford University School of Medicine, we pioneered the use of *in vivo* optogenetics to dissect the sleep-wake circuits of the brain. Using millisecond flashes of 473-nm blue light, we were able to selectively induce action potentials in neurons expressing channelrhodopsin-2 (ChR2), a light-activatable non-selective ion channel. We established for the first time a causal link between the optogenetic activation of hypothalamic hypocretins/orexins neurons and sleep-to-wake transitions (Adamantidis et al., 2007). Since then, we (Jego et al., 2013) and others (Weber and Dan, 2016) have pursued the dissection of neural circuits controlling sleep-wake states, as well as sleep-dependent brain function including memory consolidation.

Following two unexpected discoveries in the laboratory, we refined the way we look at sleep by investigating the network mechanism underlying the generation and function(s) of single sleep oscillations, including slow wave, delta, spindle oscillations during NREM and theta, gamma rhythms during REM sleep. In a first study, we found that the inhibitory neurons of the medial septum (MS_{GABA}) are essential to "drive" theta rhythm in the hippocampus (Boyce et al., 2016), a key structure contributing to the "GPS" ability of the brain (Nobel Prize for Physiology & Medicine, 2014). In fact, their optogenetic silencing completely abolished theta rhythm during REM sleep. This opened new perspectives in the experimental probing of the role of sleep in brain functioning. Indeed, we demonstrated that the activity of this theta rhythm generator during REM sleep is necessary for the consolidation of (hippocampal) contextual memory, but not for the amygdala-encoded conditioned stimulus during a fear-conditioning task (see figure) (Boyce et al., 2016). These results strongly suggest that local network oscillation during sleep is essential for the consolidation of a distinct set of information during sleep.

In a more recent study, we identified an arousal circuit between the hypothalamus – thalamus – cortex (Herrera et al., 2016). Following this discovery, we are investigating the dual role of the thalamus, and the medio-dorsal thalamus in particular – e.g. the centro-medial thalamic (CMT) neuron – in controlling either the onset of wakefulness or the depth of NREM sleep. Our unpublished work suggests that tuning of CMT neurone firing supports a dual control of sleep

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slow waves and wakefulness through wide-scale cortical propagation of slow waves. These findings provide a circuit mechanism for thalamo-cortical synchrony during sleep that is essential for sleep recovery.

Finally, our research activities also reflect scientific interactions within the Zentrum für Experimentelle Neurologie (ZEN) and the Department of Neurology, focused on the contribution of sleep to brain plasticity after stroke (Prof. C. Bassetti), epilepsy (Prof. K. Schindler/Dr M. Baud), modulation of cellular and organism metabolism (Dr. C. Gutierrez Herrera; Dr. M. Schmidt) and neurodegeneration (Dr. S. Saxena).

Group Members

Prof. Dr. Antoine Adamantidis, Group Leader
Dr. Markus Schmidt, Research Associate & Clinician
Dr. Mattia Aime, Postdoctoral Fellow
Dr. Mary Gazea, Postdoctoral Fellow
Dr. Thomas Gent, Postdoctoral Fellow
Dr. Cornelia Schöne, Postdoctoral Fellow
Andrea Oberli, Lab Manager and Technician
Lea Normand, Lab and Animal Technician
Claudia Wille, Secretary
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Selected Collaborators

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Jones B, Williams S, McGill University (CA)

Selected Publications

R. Boyce, S.D. Glasgow, S. Williams, A. Adamantidis, Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation, Science 352(6287) (2016) 812-6.

C.G. Herrera, M.C. Cadavieco, S. Jego, A. Ponomarenko, T. Korotkova, A. Adamantidis, Hypothalamic feedforward inhibition of thalamocortical network controls arousal and consciousness, Nat Neurosci 19(2) (2016) 290-8.

S. Jego, S.D. Glasgow, C.G. Herrera, M. Ekstrand, S.J. Reed, R. Boyce, J. Friedman, D. Burdakov, A.R. Adamantidis, Optogenetic identification of a rapid eye movement sleep modulatory circuit in the hypothalamus, Nat Neurosci 16(11) (2013) 1637-43.

L. de Lecea, M.E. Carter, A. Adamantidis, Shining light on wakefulness and arousal, Biol Psychiatry 71(12) (2012) 1046-52.

A.R. Adamantidis, F. Zhang, A.M. Aravanis, K. Deisseroth, L. de Lecea, Neural substrates of awakening probed with optogenetic control of hypocretin neurons, Nature 450(7168) (2007) 420-4.

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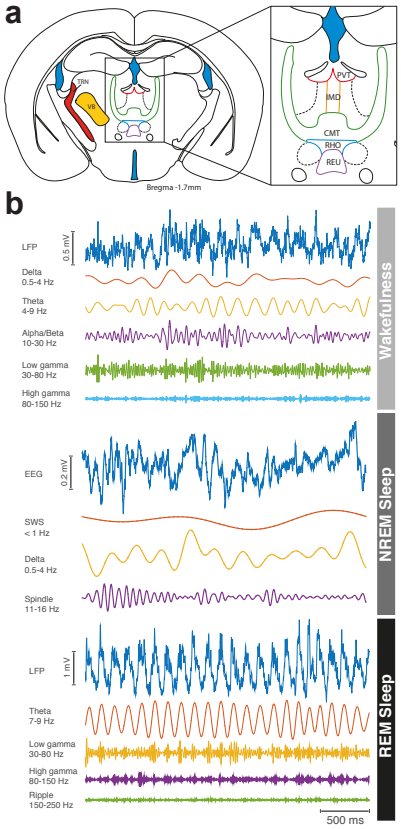

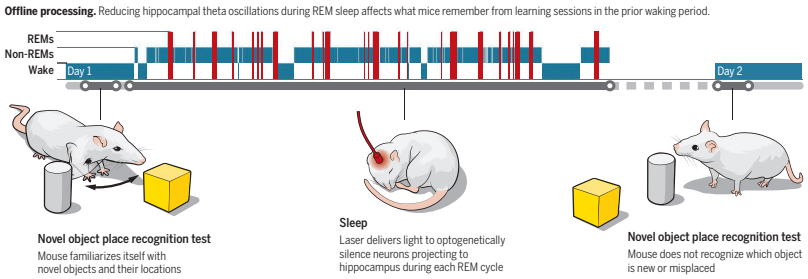

Laboratory of Neurodegeneration

Prof. Dr. Smita Saxena
smita.saxena@dbmr.unibe.ch

PhD in Cell Biology at the Institute of Pathology, University of Bern (2004); Postdoc at Friedrich Miescher Institute for Biomedical Research, University of Basel (2004–2010). SNSF Professor at the Institute of Cell Biology, University of Bern (2010–2016). Since 2017, Professor and Group Leader at the Center for Experimental Neurology, Department of Neurology, Inselspital.

Research Highlights 2017 / Outlook 2018

Neurodegenerative diseases remain an incurable, ever-increasing burden to our aging society. In these diseases specific neuronal populations within defined regions of the central nervous system degenerate. An enigmatic but uniform finding in patients and in murine models of neurodegeneration is the early and selective alteration in intrinsic excitability properties of vulnerable neurons, as well as changes in its neuronal circuitry. The precise cause of these alterations and whether these modifications regulate degenerative pathomechanisms or whether they are complex compensatory responses occurring during disease, remains intriguing and unknown.

Investigating the Connectivity Correlate of Molecular Pathology in Neurodegeneration

In a project funded by the European Research Council Consolidator Grant, we investigate how molecular alterations occurring at the level of neuronal circuits impair normal neuronal activity, thereby leading to the development of symptoms. To this end, we employ a combination of orthogonal pharmacogenetics, transcriptomics, proteomics, connectomics, virus-mediated gene therapy, behaviour paradigms and *in vivo* imaging in preclinical models of neurodegenerative disease: Amyotrophic Lateral Sclerosis (ALS), Fronto-Temporal Dementia (FTD) and Spinocerebellar Ataxia type 1 (SCA1).

The Effect of CDNF in ALS and ER Stress

In a transnational collaborative effort funded by an E-RARE grant, we aim to investigate the neuroprotective properties of a novel factor: Cerebral Dopamine Neurotrophic Factor (CDNF). CDNF is mainly endoplasmic reticulum (ER) located in the neurons and functions as a secreted growth factor having a unique mode of action on neurons. The objective of this proposal is to perform preclinical experiments using rodent models of ALS and patient-derived induced pluripotent stem cells, in order to decipher the neuroprotective action of CDNF and to test the benefits, as well as the feasibility of CDNF treatment in patients living with ALS. See http://www.erare.eu/node/1369

Characterizing the Role of Cell Stress in C9orf72-linked ALS – FTD Pathology

The hexanucleotide G4C2 repeat expansions in the intronic region of C9orf72 is a common genetic cause of ALS and FTD. Studies in iPS cell-derived motoneurons from C9orf72 and sporadic ALS patients show that ER stress is a major pathological feature triggering defects in neuronal connectivity and excitability. In this project funded by the Swiss Foundation for Research in Muscle Diseases, we will focus on identifying and characterizing the mechanism behind repeat expansion induced ER stress in motoneurons and test at preclinical level therapeutic targets to alleviate ALS-associated symptoms.

In 2017, my group relocated to the Center for Experimental Neurology, Inselspital. I would like to thank all my colleagues at the DBMR and the Dept. of Neurology for making our move a smooth one. Special thanks to the Cluster for Regenerative Neuroscience for accommodating our lab needs and to Prof. Willy Hofstetter for helping us with our animal holding necessities.

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Group Members

Prof. Dr. Smita Saxena, Group Leader
Dr. Grace Iyirhiaro, Senior Scientist
Federica Pilotto, PhD Student

Selected Collaborators

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Zuber B, Institute of Anatomy, University of Bern (CH)
Saarma M, Institute of Biotechnology, University of Helsinki (FI)
Trottier Y, Institut de Génétique et de Biologie Moléculaire et Cellulaire, Strasbourg (FR)

Selected Publications

C. Hetz, S. Saxena, ER stress and the unfolded protein response in neurodegeneration, Nat Rev Neurol 13(8) (2017) 477-491.

N. Maharjan, C. Kunzli, K. Buthey, S. Saxena, C9ORF72 Regulates Stress Granule Formation and Its Deficiency Impairs Stress Granule Assembly, Hypersensitizing Cells to Stress, Mol Neurobiol 54(4) (2017) 3062-3077.

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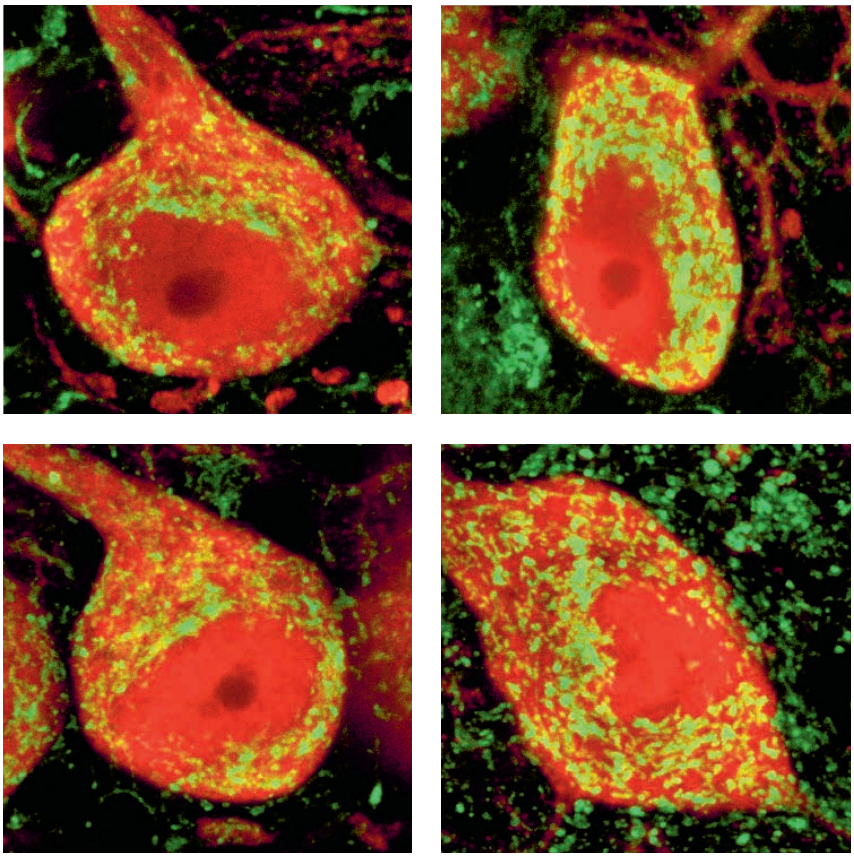

RNA & Cancer

Prof. Dr. Rory Johnson
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MSci in Physics at Imperial College, London; Wellcome Trust 4-Year PhD in Molecular Genetics at University of Leeds (UK) with N. J. Buckley (2002–2007). Postdoc at Genome Institute of Singapore with L. J. Stanton (2007–2010). Ramón y Cajal Researcher and Staff Scientist at Centre for Genomic Regulation (ES) with R. Guigó (2010–2016). Since 2016, Group Leader at NCCR "RNA & Disease"; Assistant Professor at Department of Medical Oncology, Inselspital.

Research Highlights 2017 / Outlook 2018

Our objective is to understand the role of long noncoding RNAs (lncRNAs) in human diseases. LncRNAs are extremely numerous genes, easily outnumbering their protein-coding cousins. They represent a promising source of new therapeutic targets and biomarkers. However, our understanding of how lncRNAs work at a mechanistic level is highly incomplete, and so far <1 % have been characterised. In our lab, we use a combination of bioinformatic and genome-engineering approaches to screen for promising lncRNAs in disease models.

Bioinformatic prediction of cancer driver lncRNAs: A major focus of the International Cancer Genome Consortium (ICGC) is to identify cancer-driver mutations and elements genome-wide. Andrés Lanzós has developed a pipeline called *ExInAtor* to predict driver lncRNAs using somatic mutational burden (Lanzós et al). ExInAtor has been used alongside other methods by the ICGC to make consensus predictions of driver lncRNAs.

LncRNA annotation: The GENCODE Consortium produces the "official" annotation of coding and lncRNA genes. In 2017, together with my former mentor Roderic Guigó and colleagues, we published a new method for mapping lncRNA genes, based on third-generation long-read sequencing coupled to cDNA capture: "Capture LongSeq" (CLS) (Lagarde et al).

CRISPR-Cas9 for discovering cancer lncRNAs: We develop tools for knocking out lncRNAs, in order to investigate their roles in cancer cells. In 2017, Carlos Pulido published the first bioinformatic server for designing such experiments, called "CRISPETa" (Pulido-Quetglas et al). Núria Bosch, Taisia Polidori and Roberta Esposito are working on applying these tools to cancer models along with collaborators at DBMR.

LncRNAs in cardiac disease: Together with collaborator Thierry Pedrazzini, we have begun to investigate the role of lncRNAs in pathogenic processes underlying heart disease. Panagiotis Chouvardas and Carlos Pulido are developing bioinformatic pipelines to identify candidate lncRNAs by means of RNA sequencing data.

LncRNA localisation: We believe that the location of lncRNsA in the cell is a powerful clue about their molecular functions. Joana Carlevaro-Fita presented LncATLAS, a webserver designed to enable researchers to access quantitative localisation data for their lncRNA of interest (Mas-Ponte, Carlevaro-Fita et al). Joana also completed, alongside Taisia Polidori and Monalisa Das, a study implicating transposable elements in lncRNA localisation (in review).

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

Group Members

Prof. Dr. Rory Johnson, Group Leader
Panagiotis Chouvardas, Postdoctoral Fellow (since Oct.)
Roberta Esposito, Postdoctoral Fellow (since Aug.)
Núria Bosch, PhD Student
Joana Carlevaro-Fita, PhD Student
Taisia Polidori, PhD Student
Carlos Pulido, PhD Student (since Mar.)

Selected Collaborators

Ochsenbein A, University of Bern (CH)
Riether C, University of Bern (CH)
Marti T, University of Bern (CH)
Pedrazzini T, CHUV, Lausanne (CH)
GENCODE, European Bioinformatics Institute, Hinxton (UK)
International Cancer Genome Consortium (Various)

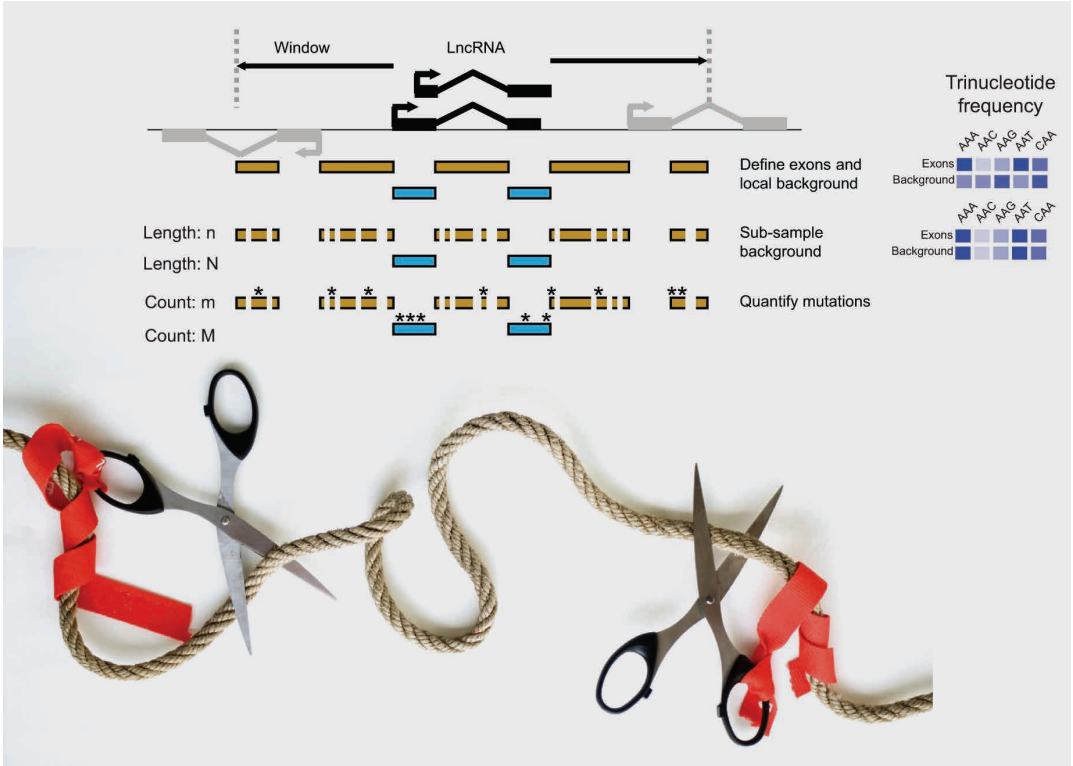
Selected Publications

J. Lagarde, B. Uszczynska-Ratajczak, S. Carbonell, S. Perez-Lluch, A. Abad, C. Davis, T.R. Gingeras, A. Frankish, J. Harrow, R. Guigo, R. Johnson, High-throughput annotation of full-length long noncoding RNAs with capture long-read sequencing, Nat Genet 49(12) (2017) 1731-1740.

D. Mas-Ponte, J. Carlevaro-Fita, E. Palumbo, T. Hermoso Pulido, R. Guigo, R. Johnson, LncATLAS database for subcellular localization of long noncoding RNAs, RNA 23(7) (2017) 1080-1087.

C. Pulido-Quetglas, E. Aparicio-Prat, C. Arnan, T. Polidori, T. Hermoso, E. Palumbo, J. Ponomarenko, R. Guigo, R. Johnson, Scalable Design of Paired CRISPR Guide RNAs for Genomic Deletion, PLoS Comput Biol 13(3) (2017) e1005341.

A. Lanzós, J. Carlevaro-Fita, L. Mularoni, F. Reverter, E. Palumbo, R. Guigo, R. Johnson, Discovery of Cancer Driver Long Noncoding RNAs across 1112 Tumour Genomes: New Candidates and Distinguishing Features, Sci Rep 7 (2017) 41544.



Tumor-Immunology

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). SNSF Professorship (2003) at the DBMR. Chief Physician at the Department of Medical Oncology, Inselspital, Bern (2011–2017). Since 2017, Chair of the Department of Medical Oncology, Inselspital, Bern. Member of the Research Council of the SNSF since 2016.

PD Dr. Carsten Riether, PhD
carsten.riether@dbmr.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. Habilitation (Venia Docendi), Faculty of Medicine, University of Bern, (2015) (CH). Since 2014, group leader at the Department of Medical Oncology, Inselspital and DBMR.

Research Highlights 2017 / Outlook 2018

Our laboratory has been investigating for several years the interplay between hematopoietic stem cells (HSCs) / cancer stem cells (CSCs) and cells of the adaptive immune system. We aim to understand the mechanisms by which HSCs and CSCs are regulated and to find new therapeutic targets for effective immunotherapies against CSCs.

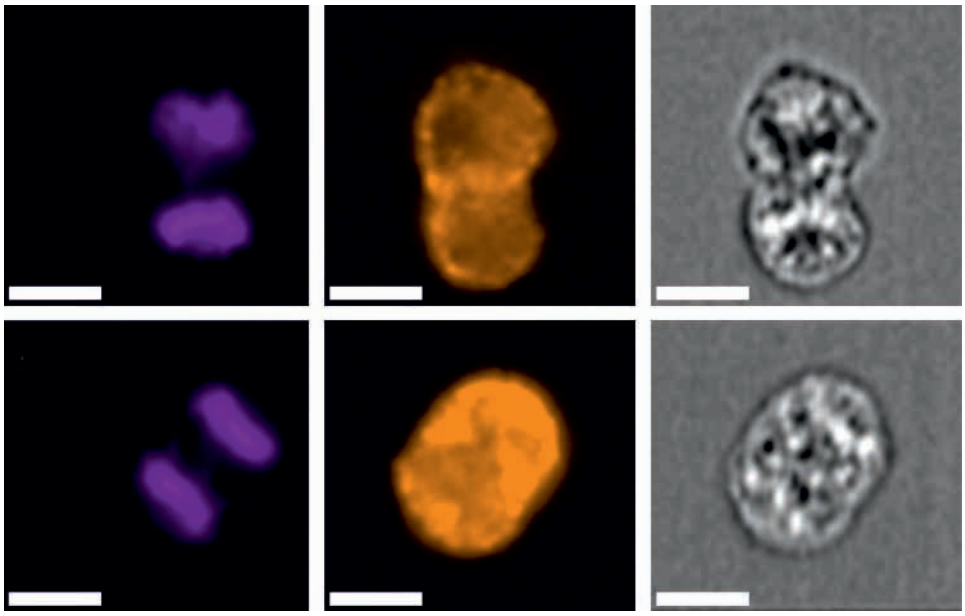
We were able to demonstrate that HSCs and leukemia stem cells (LSCs) interact directly and indirectly with defined immune cells / immune-related factors (e.g. IL-6 and IFN-γ) in the bone marrow (BM) niche. Additionally, we defined a new mechanism by which cells of the adaptive immune system regulate demand-adapted hematopoiesis and could show that these pathways are hijacked by LSC to propagate the disease.

Furthermore, a special interest of our group is related to TRAF2- mediated TNF receptors (TNFR) and their role in normal and malignant hematopoiesis. So far, the main focus was on the interaction between TNFR CD27 with its unique ligand CD70. The interaction of TNFR CD27 with CD70 is an emerging target to treat cancer. In myeloid leukemia, CD27 signaling induces "stemness" in LSC and leads to a more aggressive disease. We demonstrated that blocking the CD70/CD27 interaction effectively eradicates LSCs. Based on these preclinical results, we developed a phase I study to test the human anti-CD70 antibody (ARGX-110), in combination with azacytidine in acute myelogenous leukemia (AML) patients.

Furthermore, we could show that the interaction of CD70 on NK cells with CD27 on B-cell lymphoma cells induces CD70 reverse signaling in NK cells, thereby contributing to the immune control of CD27-expressing lymphomas and leukemia.

The network and functionality of other TRAF2-mediated TNF receptors in HSCs and CSCs in solid tumors and leukemia are currently under detailed investigation. A main focus is to understand the role of TNFR signaling in murine models and patients with lung cancer, colon cancer and myeloid leukemia.

www.ochsenbeinlab.ch
www.rietherlab.ch



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
Dr. Carla Jaeger-Ruckstuhl, Postdoctoral Fellow
Ursina Lüthi, Laboratory Technician
Tanja Chiorazzo, Laboratory Technician
Dr. Michael A. Amrein, MD-PhD Student
Dr. Elias D. Bührer, MD-PhD Student
Magdalena Hinterbrandner, PhD Student
Pascal Näf, PhD Student
Viviana Rubino, PhD Student

Selected Collaborators

Macpherson A, University of Bern (CH)
Nombela-Arrieta C, University Hospital Zurich (CH)
Pinschewer DD, University of Basel (CH)
Von Gunten S, University of Bern (CH)

Selected Publications

T. Hilmenyuk, C.A. Ruckstuhl, M. Hayoz, C. Berchtold, J.M. Nuoffer, S. Solanki, H.C. Keun, P.A. Beavis, C. Riether, A.F. Ochsenbein, T cell inhibitory mechanisms in a model of aggressive Non-Hodgkin's Lymphoma, Oncoimmunology 7(1) (2017) e1365997.

M.F. Al Sayed, C.A. Ruckstuhl, T. Hilmenyuk, C. Claus, J.P. Bourquin, B.C. Bornhauser, R. Radpour, C. Riether, A.F. Ochsenbein, CD70 reverse signaling enhances NK cell function and immunosurveillance in CD27-expressing B-cell malignancies, Blood 130(3) (2017) 297-309.

C. Riether, C.M. Schurch, E.D. Buhrer, M. Hinterbrandner, A.L. Huguenin, S. Hoepner, I. Zlobec, T. Pabst, R. Radpour, A.F. Ochsenbein, CD70/CD27 signaling promotes blast stemness and is a viable therapeutic target in acute myeloid leukemia, J Exp Med 214(2) (2017) 359-380.

M. Murone, R. Radpour, A. Attinger, A.V. Chessex, A.L. Huguenin, C.M. Schurch, Y. Banz, S. Sengupta, M. Aguet, S. Rigotti, Y. Bachhav, F. Massiere, M. Ramachandra, A. McAllister, C. Riether, The Multi-kinase Inhibitor Debio 0617B Reduces Maintenance and Self-renewal of Primary Human AML CD34(+) Stem/Progenitor Cells, Mol Cancer Ther 16(8) (2017) 1497-1510.

Key Events

Swiss Youth in Science: "Biology and Medicine" Study Week
12–18 Mar.

Info Events DBMR 2017
12 Apr. and 11 Oct.
Around 25 interested DBMR newcomers attended each of these events. The next Info Events will take place in April and October 2018.

Day of Clinical Research 2017
30–31 Oct.
As usual, a large and interested audience followed the presentations of **Prof. Gary Koretzky** (Weill Cornell Medicine, Graduate School of Medical Sciences, New York, US) entitled "Insights into Hematopoietic Cell Development & Function through Targeted Mutation of an Adapter Protein", and **Prof. Mark A. Rubin** (Department for BioMedical Research, University of Bern, Bern, Switzerland) entitled "Precision Medicine: Mapping Switzerland".

Five candidates applied for the Johanna Dürmüller-Bol DBMR Research Prize 2017 (funded by the Johanna Dürmüller-Bol Foundation) and 132 abstracts were submitted for the Poster Prizes of the DBMR and the Research Prize Alumni MedBern. The winners were (left to right in photo below): Prof. Robert Rieben (Coordinator DBMR), Cornelia Schmid, Dr. med. Manuela Funke-Chambour, Martina Stilinovic, Manuel Keller, Sebastian Bellwald.

Johanna Dürmüller-Bol DBMR Research Award 2017
Dr. med. Manuela Funke-Chambour
Department of Pulmonary Medicine, Inselspital; Pulmonary Medicine (Adults), Department for BioMedical Research, University of Bern

Poster Prizes of the DBMR for:
- *best preclinical project*
  Martina Stilinovic
  Department for BioMedical Research, University of Bern,
  Research Group Hematology (Adults) and Department of Hematology and Central Hematology Laboratory, Inselspital, Bern University Hospital, University of Bern
- *best clinical project*
  Sebastian Bellwald
  Department of Neurology, ZEN, Inselspital, Bern University Hospital, University of Bern
- *best project by a medical student*
  Manuel Keller
  Institute of Pathology, University of Bern

Research Prize Alumni MedBern
Cornelia Schmid
Department of Pulmonary Medicine, Inselspital

The next Day of BioMedical Research will be held on 7 November 2018.

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

DBMR Research Conferences 2017

With an average of 54 visitors each month, the DBMR Research Conferences continue to be successful. In 2017, we were pleased to present the following speakers:

6 Feb. – Prof. Dr. Jason Rock
Department of Anatomy, Cardiovascular Research Institute, University of California (US)
Myeloid regulation of adult lung regeneration post-pneumonectomy

6 Mar. – Prof. Dr. Andreas Papassotiropoulos
University of Basel (CH)
Epigenetic signatures of brain aging

3 Apr. – Prof. Dr. Pascal O. Zinn
Department of Neurosurgery Baylor College of Medicine, Houston, Texas (US)
The making of human brain – A novel paradigm for personalized patient care

5 May – 100th DBMR Research Conference
Prof. Dr. Francesca Demichelis, Centre for Integrative Biology, University of Trento (IT)
Biology and evolution of poorly differentiated neuroendocrine tumors

Prof. Dr. Bernhard Küster, Chair of Proteomics and Bioanalytics, Technische Universität München, Freising (DE)
Chemical proteomics reveals the target landscape of clinical kinase drugs

Prof. Dr. Elaine Holmes, Head of Division of Computational and Systems Medicine, Imperial College London (UK)
Metabolic phenotyping in precision medicine and population screening

12 June – Dr. Tobias Fuhrer
Department of Biology, Institute of Molecular Systems Biology, ETH Zurich (CH)
Biological insights from untargeted metabolomics: discovering enzymatic activities of non-annotated genes

3 July – Dr. Chevrier Stéphane
Institute of Molecular Life Sciences, University of Zurich (CH)
Characterization of immune infiltrating cells in human cancer using mass cytometry

4 Sep. – Prof. Dr. Fredric P. Manfredsson
Department of Translational Science & Molecular Medicine, College of Human Medicine, Michigan State University (US)
Alpha-synuclein: The role of this ubiquitous protein in neuronal (dys) function and disease

2 Oct. – Prof. Dr. Sadis Matalon
University of Birmingham, Alabama (US)
Publishing in scientific journals: An Editor's Perspective

4 Dec. – Prof. Dr. Ralph Müller
Institute for Biomechanics, ETH Zurich (CH)
Bone LivE Imaging – from systems mechanobiology to personalized medicine


H2O

Personnel Update

Academic Degrees

The following academic degrees where awarded to DBMR group members:

Full Professor

Prof. Dr. Christa Flück
Endocrinology / Diabetology / Metabolism (Paediatrics)

Prof. Dr. Stephan Jakob
Intensive Care Medicine

Prof. Dr. Adrian Ochsenbein
Tumor-Immunology

Prof. Dr. Mark A. Rubin
Precision Oncology

Prof. Dr. Roland von Känel
Neurology

Full Professor (Extraordinus)

Prof. Dr. Antoine Adamantidis
Neurology

Prof. Dr. Guido Beldi
Visceral and Transplantation Surgery

Associate Professor

Prof. Dr. Ulrike Bacher
Hematology

Prof. Dr. Lorenz Räber
Cardiology

Prof. Dr. Nasser Semmo
Hepatology

Lecturer (Privatdozent)

PD Dr. Lukas Andereggen
Neurosurgery

PD Dr. Nicolas Bonadies
Hematology (Adults)

PD Dr. Alexander Eggel
Rheumatology

PD Dr. Niklaus Egloff
Neurology

PD Dr. Manfred Heller
Protein- and Cellbiology

PD Dr. Roger Kalla
Neurology

PD Dr. Gregor Kocher
Thoracic Surgery

PD Dr. Emrush Rexhaj
Cardiology

PD Dr. Marta Roccio
Audiology

PD Dr. Christoph Schankin
Neurology

PD Dr. Julian Schardt
Oncology / Haematology (Adults)

PD Dr. Ren-Wang Peng
Thoracic Surgery

PD Dr. Tim Vanbellingen
Neurology

PD Dr. Monique Vogel
Rheumatology

PD Dr. Bernhard Winkler
Cardiovascular Surgery

PD Dr. Mathias Matthias Worni
Visceral and Transplantation Surgery

PhD

(supervisors in brackets)

Mai Moustafa Ahmed Abd El Hafez
(Prof. Dr. Robert Rieben)
Role of complement and coagulation in ischemia/reperfusion injury

Victor Javier Adalid López
(Prof. Dr. Roland Kreis)
Generalizing the modeling of interrelated datasets in magnetic resonance spectroscopy

Emilie Farine
(PD Dr. Sarah Longnus,
Prof. Dr. Hendrik Tevaearai Stahel)
Cardioprotective reperfusion strategies and recovery monitoring in donation after circulatory death: Studies in the isolated working rat heart

Nicole Damara Fichtner
(Prof. Dr. Roland Kreis)
Effects of exchange in magnetic resonance spectroscopy and imaging at ultra-high fields

Astrid Andreina Glück
(PD Dr. Yitzhak Zimmer)
Investigations over the role of MET signaling in the HIF-1α pathway and in H2AX-related ubiquitinations

Agata Górecka
(Dr. Lukas Brügger)
Adipose derived stem cells for skeletal muscle regeneration

Andreas Keil
(PD Dr. Steffen Frese)
The mechanism of topoisomerase I inhibition in the treatment of lupus nephritis

Sreenath Pruthviray Kyathanahally
(Prof. Dr. Roland Kreis)
Quality aspects of clinical magnetic resonance spectroscopy: Quantification issues, quality prediction, and quality assessment by machine learning

Shun-Qing Liang
(Prof. Dr. Ralph A. Schmid, PD Dr. Ren-Wang Peng)
Targeting chemoresistance in non-small cell lung cancer

Dr. Nesa Magdalena Marti
(Prof. Dr. Christa E. Flück)
Pathways and mechanisms of androgen biosynthesis

Petra Niederberger
(PD Dr. Sarah Longnus, Prof. Dr. Hendrik Tevaearai Stahel)
Metabolic-based strategies to improve cardiac recovery after ischemia in an isolated rat heart model of donation after circulatory death

Bertrand Pouymayou
(Prof. Dr. Chris Boesch)
Multi-Nuclear MRS for the elucidation of insulin resistance (IR) in humans: Lipid characterization and magnetization transfer (MT) methods

Maria Christina Precht
(Prof. Dr. Peter Vermathen)
Magnetic resonance imaging and spectroscopy in small ruminants affected by listeria rhombencephalitis

Carla A. Ruckstuhl
(Prof. Dr. Adrian Ochsenbein)
Regulation of "stemness" in immune cells and leukemia stem cells

Nina Ruef
(Prof. Dr. Willy Hofstetter)
Inflammatory cytokines in the modulation of osteoclastogenesis and bone resorption

Magdalena Skowrońska
(Prof. Dr. Johanna A. Kremer Hovinga, PD Dr. Monica Schaller Tschan)
Antibody repertoire of immune mediated thrombotic thrombocytopenic purpura (iTTP) – towards the development of a targeted therapy

Rahel Thomi
(Prof. Dr. Robert Hunger)
Interleukin-32, Interleukin-36 and LL-37 in the pathogenesis of hidradenitis suppurativa

Colin Charles Tièche
(Prof. Dr. Ralph Schmid, Dr. Thomas Marti)
Discovery and characterization of plastic subpopulations associated with distinct hallmarks of cancer in the NSCLC cell line A549

MD, PhD
(supervisor in brackets)

Elias Bührer
(Prof. Dr. Adrian Ochsenbein)
CD70/CD27 signaling promotes blast stemness and is a viable therapeutic target in acute myeloid leukemia

Chantal-Simone Dysli
(Prof. Dr. Martin Zinkernagel)
Fluorescence-lifetime imaging ophthalmoscopy (FLO) from bench to bedside

Martin Müller
(Prof. Dr. Boris W. Kramer, Prof. Dr. Daniel Surbek)
Pregnancy derived product for treatment of perinatal brain injuries

Lluís Nisa
(PD Dr. Yitzhak Zimmer)
Mechanisms of invasion and therapeutic resistance in head and neck cancer: Emphasis on MET signaling

Seyed Morteza Seyed Jafari
(Prof. Dr. Robert Hunger)
Efficacy of electroporation-mediated gene delivery on survival of skin flaps

Awards

The following DBMR group members received awards in 2017:

Mai Moustafa Ahmed Abd El Hafez
Cardiovascular Research
Outstanding abstract award at the European Meeting on Complement in Human Disease (EMCHD), Copenhagen, Denmark: "Reduction of myocardial ischemia reperfusion injury in pigs by (over) expression of human membrane co-factor protein"

Dr. Petra Arendt
Ophthalmology
SWISS RetinAWARD 2017 Project with most clinical relevance from the Swiss VitreoRetinal Group (SVRG) Fluorescence Lifetimes in Stargardt Disease: "Potential marker for disease progression"

Maria Arnold
Cardiovascular Research
Cardiovascular and Metabolic Research Meeting 2017: Best poster prize, 2nd place

Dr. Mojtaba Bandarabadi
Neurology
International diversity travel award to attend the ICTALS2017 conference, Minnesota, USA

Dr. Mojtaba Bandarabadi
Neurology
Travel award from the Blue Brain Project to attend the NM2 conference, Lausanne, Switzerland

Dr. Daniel Becker
Cardiovascular Surgery
Union Schweizerischer Gesellschaft für Gefässkrankheiten (USGG) Award for best poster: "Mycotic pseudoaneurysm in the groin due to injection drug abuse"

Colette Bichsel
Thoracic Surgery
Award for the best experimental publication from the Swiss Society for Thoracic Surgery: "Increased PD-L1 expression and IL-6 secretion characterize human lung tumor-derived perivascular-like cells that promote vascular leakage in microvasculature model"

Elias Bührer
Tumor-Immunology
ASH Abstract Achievement Award, Annual Meeting of the American Society of Hematology, ASH, 2017, Atlanta, USA: "Splenic red pulp macrophages provide a secondary stem cell niche for chronic myeloid leukemia stem cells"

Dr. Gaëlle Diserens
AMSM
Benoît-Pochon Prize: "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"

Emilie Farine
Cardiovascular Surgery
Swiss Transplantation Society Award: Best Article – Fundamental Research section, 2nd place

Dr. Sean Hall
Thoracic Surgery
Award for the best scientific poster from the Swiss Society for Thoracic Surgery: "Identifying rare lineage negative epithelial progenitor cells in the early postnatal human lung"

Silvan Jungi
Cardiovascular Surgery
Schweizerische Gesellschaft für Gefässchirurgie (SGG) Award for Best poster: "Isolated mesenteric artery dissection – a case series"

Rahel Klossner
Nephrology
Deutscher Gestose Kongress 2017: "Cultured trophoboblasts are salt-sensititive with Na+ and Cl- transporters differentially expressed in placenta and kidney of rats upon salt exposure"

Dr. Sofia Karkampouna
Urology
Marie Curie Award MSCA-IF-EF-ST (Standard EF), STOPCa: "The cryptic path of tumor-microenvironment interactions in prostate cancer"

Dr. Thomas Marti
Thoracic Surgery
Award for the best scientific presentation from the Swiss Society for Thoracic Surgery: "Prognostic significance of glycine decarboxylase and HIF-1α expression in early stage non-small cell lung cancer"

Dr. Martin Müller
Prenatal Medicine
SRI President's Presenter's Award (Society for Reproductive Investigation), Orlando, USA: "Synthetic PreImplantation Factor (PIF) prevents fetal loss by modulating LPS induced inflammatory response"

Petra Niederberger
Cardiovascular Surgery
Swiss Experimental Surgery: Best Poster Prize

Dr. Radu Olariu
Plastic Surgery
Best oral presentation at the Congress of the European Plastic Surgery Research Council: "Intra-graft injection of tacrolimus may modulate local immune response promoting long-term acceptance of VCA in a modified Brown Norway-to-Lewis transplantation model"

Dr. Byron Oppliger
Prenatal Medicine
Benoît-Pochon Prize: "Wharton's jelly mesenchymal stem cells as a treatment for preterm brain injury"

PD Dr. Carsten Riether
Tumor-Immunology
Theodor-Kocher Prize 2017

PD Dr. Carsten Riether
Tumor-Immunology
Stiftung Pfizer Forschungspreis 2017 (Oncology / Basic research) awarded project: "Tyrosine kinase inhibitor–induced CD70 expression mediates drug resistance in leukemia stem cells by activating Wnt signaling"

Nina Ruef, Silvia Dolder, Daniel Aeberli, Deepak Balani, Dr. Willy Hofstetter
Bone Biology and Orthopaedic Research
SBMS President Award, 2017 "Granulocyte-macrophage colony-stimulating factor-dependent CD11c-positive cells differentiate into active osteoclasts"

PD Dr. Verena Schröder
Experimental Haemostasis
Invitation Fellowship for Research in Japan (for a research stay from 1st–15th March 2017), Japan Society for the Promotion of Science JPSP: "Function and role of the activation peptide of coagulation factor XIII"

Riccardo Sfriso
Cardiovascular Research
Young Investigators Award at the Meeting of the International Xenotransplantation Association (IXA) in Baltimore, MD, USA: "Evaluation of innate immune activation after ex vivo xenoperfusion of GTKO/Hcd46/HLA-E transgenic pig hearts with human blood"

Dr. Damian Sutter
Hand Surgery
Greatest Future Clinical Application Award (GFCA): "In situ forming implant with rapamycin prolongs survival of vascularized composite allograft"

Gerd Tinkhauser
Neurology
Poster Award (cat. clinical research) from the 12th Annual Meeting Clinical Neuroscience Bern: "Brain signals to optimise directional DBS programming in Parkinson's disease"

Gerd Tinkhauser
Neurology
Prize for best oral presentation from the 8th Symposium Graduate School for Health Sciences Bern: "Deep brain signals to optimise deep brain stimulation"

Dr. Adrian Zehnder
Thoracic Surgery
Award for the best video presentation from the Swiss Society for Thoracic Surgery: "Robotic first rib resection for thoracic outlet syndrome: The DaVinici-assisted minimally invasive approach"

Dr. Eugenio Zoni
Urology
EMBO Short-Term Fellowship Award: "Identification of the metabolic signature for high risk and lethal prostate cancer"

Staff Changes

New Staff

Anke Ausgpach
Research Assistant (100 %),
Precision Oncology (since Nov.)

Laura Patricia Brandt
Research Assistant (100 %),
Precision Oncology (since May)

Kellie Cotter
Research Assistant (100 %),
Precision Oncology (since Oct.)

Claudia Requeta Rull-Herold
Directorate Secretary (70 %),
Directorate (since May)

Marla Rittiner
Secretary (60 %),
Administration (since Oct.)

Prof. Dr. Mark A. Rubin
Director (70 %),
Directorate (since Feb.)

Jasmine Stiefel
Directorate Secretary (40 %),
Directorate (since Sep.)

Luca Sulmoni
Practical Student (100 %),
IT-Support (since July)

Joanna Triscott
Research Assistant (100 %),
Precision Oncology (since Dec.)

Murteza Volina
House Staff (20 %),
Administration

Retirements

Walter Hutzli
House Staff (60 %),
DBMR Services (until June)

Short employment

Romina Frey
Assistant (40 %),
Cardiovascular Surgery (July–Dec.)

Desiré von Alpen
Research Assistant (100 %),
Precision Oncology (Apr.–Oct.)

Resignations

Nicolai Grimm
Apprentice (100 %),
DBMR Services (until Aug.)

Peggy Kübel
Directorate Secretary (70 %),
Directorate (until June)

Oliver Steck
Lab Technician (55 %),
Cardiovascular Research (until Dec.)

Reallocations to the Inselspital

PD Dr. Siamak Djafarzadeh
Research Assistant (60 %),
Intensive Care Medicine (until Dec.)

Sandra Nansoz
Lab Technician (55 %),
Intensive Care Medicine (until Aug.)


H20

DBMR Director: Prof. Dr. Mark A. Rubin
Coordination: Basak Ginsbourger, Marla Rittiner
Editing: Patricia Teixidor Monsell, motuproprioeditions@gmail.com
Photos: DBMR; Susanne Bürki, Bern; Pascal Gugler, Inselspital
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