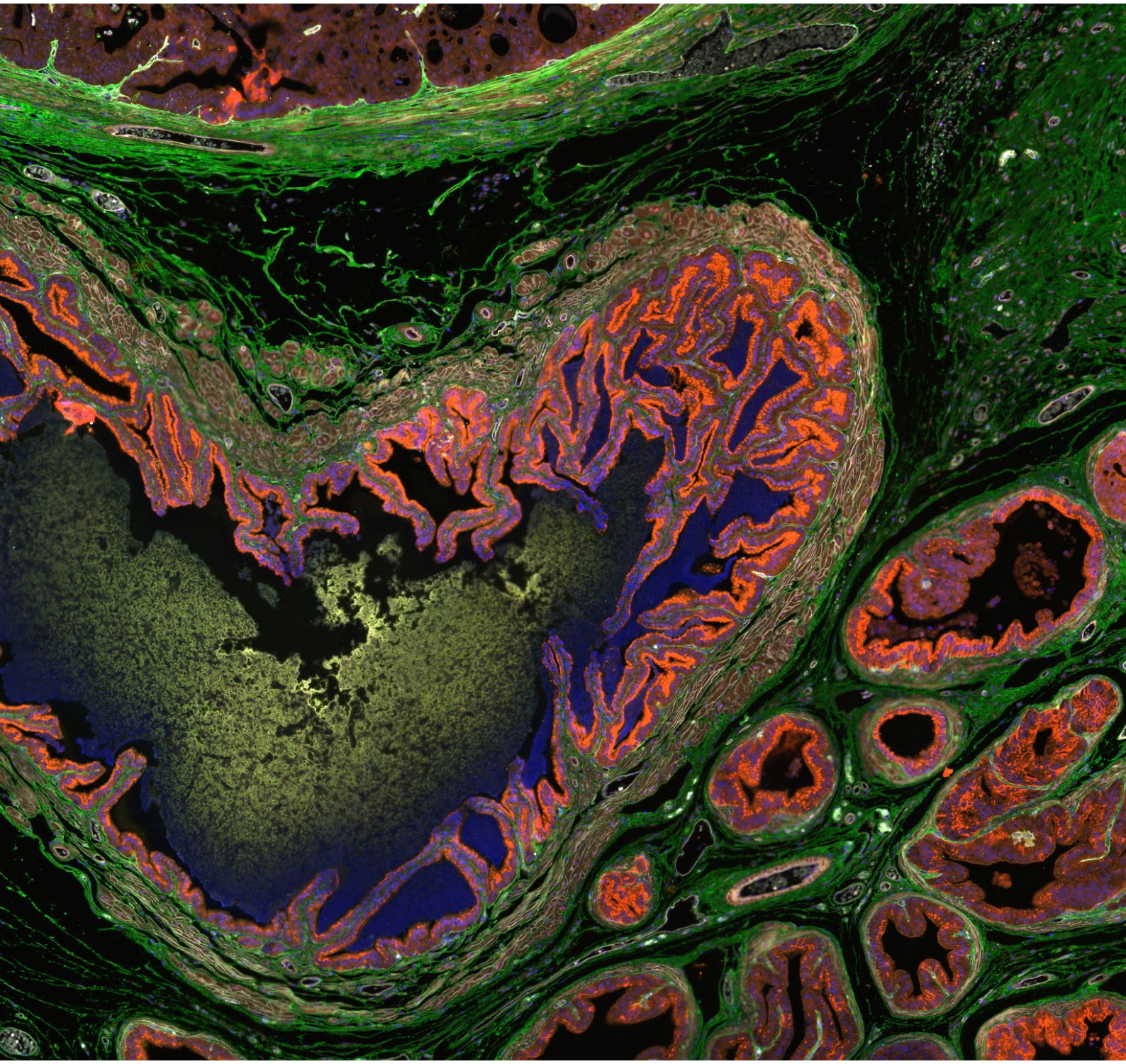
DEPARTMENT FOR BIOMEDICAL RESEARCH
www.dbmr.unibe.ch

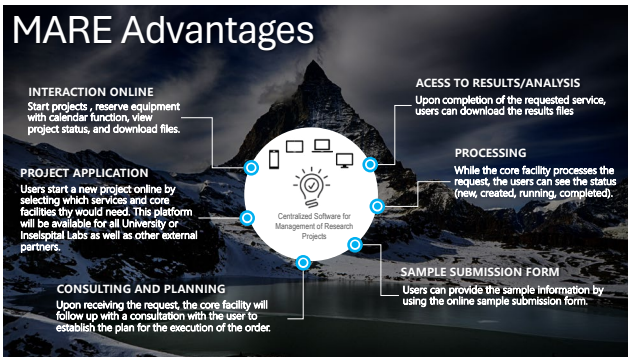
UNIVERSITÄT
BERN

Annual Report
2023



Content

Foreword
Director's Report



MARE System-a new system to help drive biomedical science forward

As part of an important University of Bern Initiative toward digitalization, the DBMR will introduce a new web-based system to order services. This innovation should help us manage projects and resources more efficiently.

As part of the DBMR re-organization, we identified critical inefficiencies within our operational framework as a biomedical research community, primarily stemming from the absence of a unified software infrastructure for managing orders, reservations, data exchange, and billing. This led to reliance on manual, paper-based processes that are not only time-intensive but also impose a financial burden due to the replication of efforts.

Our IT team, working with leadership, core directors, and members of the DBMR community, defined a plan to implement an improved process. The overarching objective of this initiative was to significantly enhance the operational efficiency and cost-effectiveness of the interactions between the Core Facilities and their user base. This entailed formulating and adopting standardized strategic processes, optimizing resource allocation, reducing redundant activities, and streamlining the streamlined execution of billing operations. The result of this 18-month project is MARE, a centralized software platform designed to facilitate a comprehensive suite of functionalities, including user management, administrative handling of offers, order processing, equipment reservation, and efficient data transfer mechanisms.

Scientific and Operational Advantages

- → Project Application Platform: Facilitates the digital initiation of research projects, ensuring accessibility for both internal and external stakeholders.
- → Consultation and Planning Mechanism: Ensures a systematic approach to project planning through direct consultation, thereby aligning user needs with facility capabilities.
- → Digital Sample Submission: Introduces an efficient, paperless process for sample information submission, enhancing the accuracy and traceability of submissions.
- → Secure Results Access: Provides a secure, digital mechanism for retrieving results, streamlining the dissemination of scientific findings.
- → Integrated Online Interaction: A unified platform for project initiation, equipment reservation, and data management is offered.

Modular Components

1. Mare Software Core System: The solution's backbone, offering centralized service management across all modules in early 2024.
2. Proteomics & Mass Spectrometry (PMS): Incorporates detailed project workflow management, including sample submission, SOPs, and result dissemination in early 2024.
3. Live Cell Imaging (LCI): Supports online reservations and course bookings, with a launch anticipated mid-2024.
4. Flow Cytometry and Cell Sorting Facility (FCCS): Includes features for equipment reservation and educational offerings, set for a mid-2024 rollout.
5. Translational Organoid Resource (TOR): Implements a streamlined approach to project workflow management by the end of 2024.
6. Biomedical Genomics (BMG): Provides a comprehensive suite for project management by the end of 2024.

Implementing the MARE System represents a pivotal transformation within the DBMR's operational paradigm. It aims to optimize the efficiency and financial stewardship of research activities and elevate the scientific output by leveraging advanced digital solutions to streamline the management of research orders, equipment reservations, and data exchange. This initiative underscores the DBMR's commitment to advancing biomedical research by integrating innovative technological solutions.

MARE will need your support as well. During the rollout of any new informatics system, problems may be detected. Our IT team hopes to continue working with the DBMR membership to improve this much-needed change.

Contact information for IT related to MARE: Ilker Yegit, Project Manager MARE, ↗ ilker.romann@unibe.ch

(Top) Overview of the capabilities and work flow of the management of research data system (MARE) being implemented by the IT team: (Bottom) Ilker Yegit, Project Manager MARE, Luca Sulmoni, Responsible Support, Michael Ackermann, Head IT.

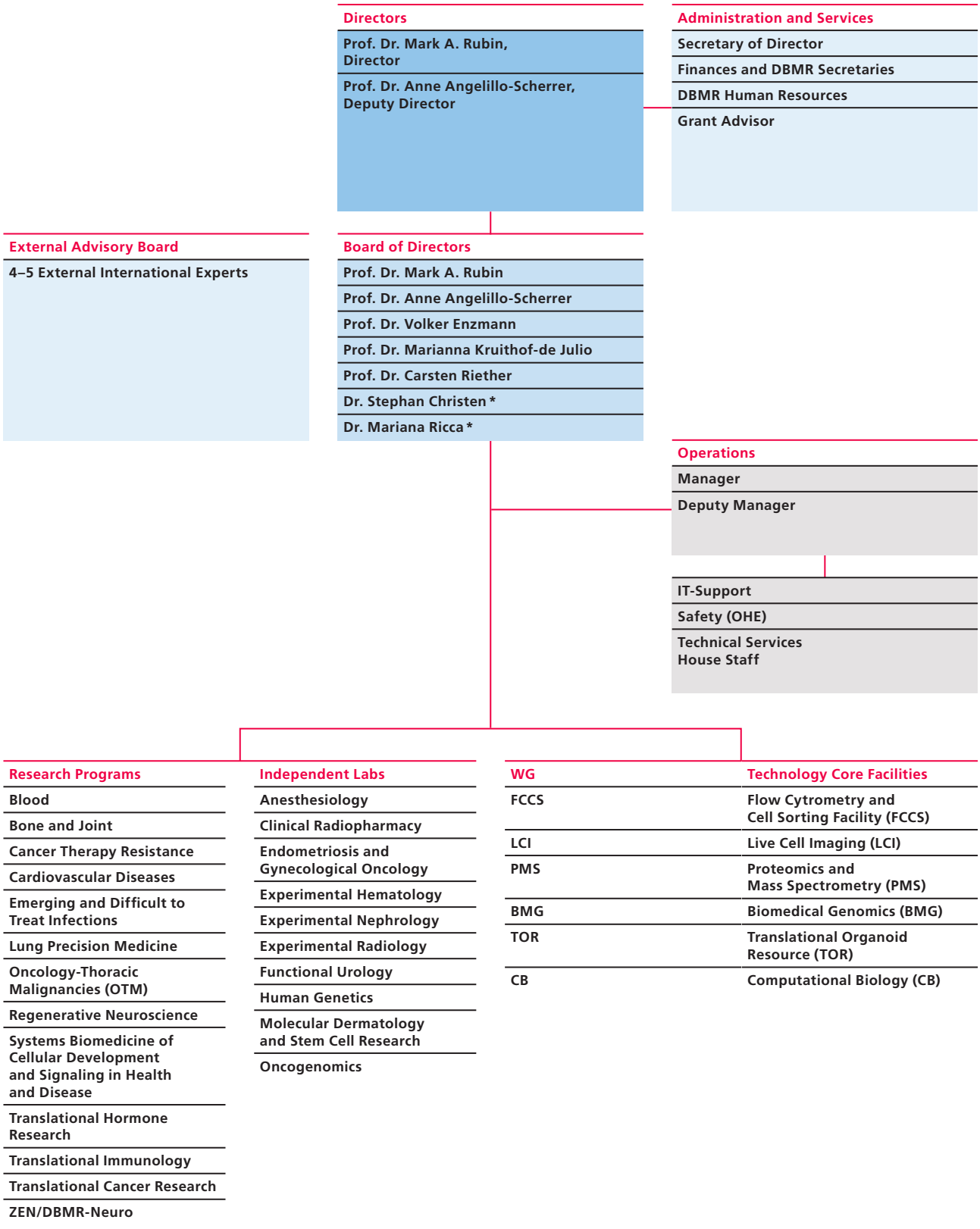
The DBMR at Glance

The Department for BioMedical Research (DBMR) in the Faculty of Medicine at the University of Bern was established in 1994 by the University of Bern and Inselspital (Bern University Hospital). The DBMR has 13 Research Programs with approximately 100 participating individual labs and several independent research labs whose research spans all biomedical fields. To bridge the gap between the bench and bedside, the DBMR promotes an integrative perspective on clinical research with a strong emphasis on the development of translational approaches, the use of omics and other cutting-edge technologies, the operation of core facilities with state-of-the-art technology, and extensive interaction and collaboration between laboratory-based and patient-oriented clinical research.

Organization

The role of the DBMR is to provide optimal infrastructure and scientific support to its affiliated members, comprising labs from the clinics of the Inselspital, Bern University Hospital, and internal DBMR groups. The DBMR also operates six core technological facilities. The research groups are supported by central services responsible for administration, facility management, and technical support, as well as providing informatics and bioinformatics services.

Organigram



* without voting right

Key People

Leadership

Prof. Dr. Mark A. Rubin *
Director

Prof. Dr. Anne Angelillo-Scherrer *
Deputy Director

Board of Directors

Prof. Dr. Volker Enzmann
Member, Board of Directors and
Contact Insel-Uni-Support

PD Dr. Marianna Kruithof-de Julio
Member, Board of Directors and
Gender Equality Representative

Prof. Dr. Carsten Riether
Member, Board of Directors

Dr. Mariana Ricca **
Grant Advisor

Dr. Stephan Christen **
Operations Manager

* Board of Directors
** non-voting members

Management

Dr. Stephan Christen
Operations Manager

Dr. Raschid Setoud
Deputy Operations Manager

Secretary of Director

Franziska Fuchs
Jasmine Stiefel

Administrator / Finances and DBMR Secretaries

Lutz Hempel
Head of Finance

Marla Rittiner
Secretary (until Apr)

Daniela Scherer-Jendly
Human Resources Assistant

Martine Marianne Kaufmann
Secretary (starting Feb)

Jasmine Brühlmann
Secretary (starting May)

Dr. Mariana Ricca
Grant Advisor

Trân Vu
Event Coordinator & DBMR Support

Occupational Safety, Health Protection and Environmental Safety (OHE)

François Achermann

IT-Support

Michael Ackermann
Head of IT

Ilker Romann
Informatician

Luca Sulmoni
Informatician

Technical Services & House Staff

Patrick Furer
Head Technical Services & House Staff

Lucille Wotzkow
Deputy Head Technical Services & House Staff

Ricardo Filipe
Technician

Kaba Sidikiba
House Staff

Monica Straub
House Staff

Susanne Widmer
House Staff

Klaus Ferro
House Staff (starting Aug)

Supply Center

Corinne Hug
Supply Center Manager

Alain Despont
Deputy Supply Center Manager

Scarlet Kohler
Deputy Supply Center Manager

Heads of Core Facilities

PD Dr. phil. nat. Fabian Blank
Live Cell Imaging (LCI)

Prof. Dr. phil. nat. Manfred Heller
Mass Spectrometry and Proteomics Laboratory (PMS)

Dr. phil. nat. Stefan Müller
Flow Cytometry and Cell Sorting FCCS)

Prof. Dr. Marianna Kruithof-de Julio
Translational Organoid Resource (TOR)

Prof. Dr. phil. nat. Ursula Amstutz
Biomedical Genomics (BMG)

Dr. Kiu Yan Charlotte Ng
Computational Biology (CP)

DBMR Research Programs / Independent Research Labs

Research Programs

Blood
Allam Lab
Angelillo-Scherrer Lab
Bacher Lab
Bonadies Lab
Daskalakis Lab
Kremer Hovinga Lab
Meyer Lab
Oppliger Leibundgut Lab
Rovó Lab
Schaller Tschan Lab
Schroeder Lab

Bone & Joint
Gantenbein Lab
Saulacic Lab

Cancer Therapy Resistance (CTR)
Kruithof-de Julio Lab
Rottenberg Lab
Rubin Lab

Cardiovascular Diseases (CVD)
Döring Lab
Heller Lab
Longnus Lab
Mercader Lab
Odening Lab
Osterwalder Lab
Rexhaj Lab
Rieben Lab
Zuppinger Lab

Emerging and Difficult to Treat Infections
Furrer Lab
Leib Lab
Que Lab
Schefold Lab

Lung Precision Medicine (LPM)
Blank Lab
Das Sudip Lab
Eggel Lab
Funke-Chambour Lab
Gazdhar Lab
Geiser Lab
Gote-Schniering Lab
Klein Lab
Mauer Lab
Müller Loretta Lab
Seydoux Lab

Oncology-Thoracic Malignancies (OTM)
Marti Lab
Peng Lab

Regenerative Neuroscience
Enzmann Lab
Escher Pascal Lab
Leib Lab
Marbacher Lab
Mure Lab
Schoeberlein & Surbek Lab
Zandi Lab
Zinkernagel Lab
Zysset Lab

Systems biomedicine of cellular development and signaling in health and disease
Al Nabhani Lab
Balmer Lab
Beldi Lab
Berzigotti Lab
Candinas Lab
Ganal-Vonarburg Lab
Stroka Lab
Macpherson Lab
Misselwitz Lab
Wiest Lab
Yilmaz Lab

Translational Cancer Research
Bernasconi & Rössler Lab
Berger Lab
Cerciello Lab
Häfliger Lab
Medova Lab
Novak Lab
Ochsenbein Lab
Pabst & Seipel Lab
Riether Lab
Wehrli Lab
Zimmer & Medo Lab

Translational Hormone Research
Bally Lab
Escher Lab
Flück Lab
Hediger Lab
Pandey Lab
Vögel Lab
Vogt Lab

Translational Immunology
Bachmann & Vogel Lab
Eggel Lab
Schlapbach Lab

ZEN/DBMR-Neuro
Adamantidis Lab
Baud Lab
Chan Lab
Guttierez Herrera Lab
Pernet Lab
Hoepner Lab
Schmidt Lab
Tinkhauser Lab
Tzovara Lab

Independent Research Labs

Anesthesiology
Stueber & Hedinger Lab

Clinical Radiopharmacy
Rominger Lab

Endometriosis & Gynecological Oncology
Mueller & Andrieu Lab

Experimental Nephrology
Fuster Lab
Huynh-Do Lab
Sidler Lab

Experimental Radiology
Tengg-Kobligk

Functional Urology
Monastyrskaya Lab

Human Genetics
Zweier Lab

Molecular Dermatology & Stem Cell Research
Müller E. Lab

Oncogenomics
Ng Lab

Blood

Participating Labs

- **Allam Lab**
  Inflammation & hematopoiesis
- **Angelillo-Scherrer Lab**
  Hemostasis, thrombosis, inflammation & hematopoiesis/myeloproliferative neoplasms
- **Bacher Lab**
  Targeted diagnostics in hematological malignancies
- **Bonadies Lab**
  Personalized treatment for patients with myeloid malignancies
- **Daskalakis Lab**
  Mechanisms of epigenetic regulation
- **Kremer Hovinga Strebel Lab**
  ADAMTS13, Von Willebrand Factor and thrombotic thrombocytopenic purpura/ thrombotic microangiopathy
- **Meyer Lab**
  Myeloid Malignancies
- **Oppliger Leibundgut Lab**
  Hematopoiesis & molecular genetics
- **Rovó Lab**
  Myeloproliferative Neoplasms, Long term survivorship after Stem Cell Transplantation & Bone marrow failures and cytopenias
- **Schaller Tschan Lab**
  Thrombotic autoimmune diseases
- **Schroeder Lab**
  Experimental hemostasis

Program Contact

Prof. Dr. med. Anne Angelillo-Scherrer
anne.angelillo-scherrer@insel.ch
Link to research program

Selected Collaborators

Batta K. University of Manchester, Manchester (UK)
Casini A. Geneva University Hospitals and Faculty of Medicine, Geneva (CH)
Levine R. L. Memorial Sloan Kettering Cancer Center, New York (US)
Pimanda J. Lowy Cancer Research Centre, University of New South Wales, Sidney, New South Wales (AU)

Hematology is a comprehensive specialty dedicated to the epidemiology, diagnosis, prognosis, treatment, and research of all types of blood-related disorders. Hematological research activities include the investigation of blood production, blood function, and blood-related diseases. The mission of the BLOOD research program is to develop a competitive research program for basic, translational, and clinical research in all areas of hematology. The BLOOD research program comprises projects aimed at investigating epidemiological and pathophysiological processes as well as the diagnosis, prognosis, and therapeutic approaches to all blood-related disorders, as well as pathophysiological processes that contribute to inflammation, thrombosis, and hemato-oncological diseases.

Research Highlights 2023 / Outlook 2024

In 2023, significant progress has been achieved in understanding diverse blood disorders.

The impact of mutant hematopoietic stem cells (HSCs) on myelodysplastic neoplasms (MDS) and chronic myelomonocytic leukemia (CMML) has been a key focus. Hypomethylating agents (HMAs), including azacitidine (AZA), are effective in altering the course of these disorders. Notably, clinical improvement with HMAs does not necessarily eliminate the mutated cells; rather, it enhances the differentiation capacity of mutated HSCs. AZA therapy correlates with improved hematopoiesis, indicating heightened clonal output from mutant progenitors to mature cells (A. Schnegg-Kauffman et al., Blood (2023) 141: 1243–1245).

The investigation into endogenous retroviral element (ERVs) reactivation upon epigenetic drug treatment in an MDS patient cohort aimed to analyze ERV expression using qRT-PCR and ddPCR. This research, led by M. Dehbi in collaboration with A. Goyal and M. Daskalakis, explored new genes of interest and followed a recently published study (A. Goyal et al. Nat Commun (2023), 14:6731).

Another notable finding was the link between increased inflammasome activation, aging, and CMML disease severity. Aging heightens sensitivity to NLRP3 inflammasome activation, contributing to increased inflammation and immune dysregulation in older individuals. Dysregulation of NLRP3 inflammasome activation was identified in a CMML patient cohort and positively correlated with disease severity (N. Andina et al. J Immunol (2023) 2105:580-589).

Advancements have been made in the understanding of myeloproliferative neoplasms (MPN), particularly regarding their resistance to JAK2 inhibitors. The research revealed that changes in histone occupancy lead to the upregulation of AXL tyrosine kinase and subsequent activation of the MAPK pathway, causing resistance to novel JAK2 inhibitors. Translational studies have validated AXL or MAPK pathway inhibition as innovative therapeutic approaches to enhance the sustainability of JAK2 inhibitor treatment (T. Codilupi et al., Clin Cancer Res (2024) 30:586-99).

Another project aims to establish human renal erythropoietin-producing cells (REPC) for cell therapy for chronic kidney disease and anemia. Challenges include the lack of specific markers for REPCs and understanding the molecular mechanisms responsible for erythropoietin downregulation in chronic inflammatory kidney disease and renal anemia. The goal of this study is to establish a human REPC line from nephrectomy kidneys using tumor-free renal tissue for primary cell culture, single-cell culture, and fluorescence-activated cell sorting.

In the context of COVID-19, research has emphasized the significance of neutrophil and complement activation, elevated D-dimer, and cell-free DNA as potential biomarkers for assessing disease severity and predicting fatality (T. Ruggeri et al., J Innate Immunity (2023) 15:850-864).

The background and rationale of hemophilia A (HA) and B (HB) highlight the global impact of these rare bleeding disorders. Despite these advancements, safer and more efficient treatments are still needed. This study explores SLN140, a small interfering RNA (siRNA) targeting protein S (PS), demonstrating promising results in rebalancing hemostasis safely and durably. Preclinical data have confirmed its efficacy in mice and non-human primates, with three patent families granted and ongoing nationalization in multiple countries.

Another study focused on the role of autophagy in autoimmunity, specifically in immune-mediated thrombotic thrombocytopenic purpura (iTTP). Upregulation of ATG5, ATG7, and MTOR, along with significantly elevated BECN1 levels, were observed in spleen-derived B cells from patients with iTTP. The increased autophagic flux activity in iTTP-derived B and T cells compared to that in cells from healthy donors suggests its potential as a biomarker. Additionally, significantly upregulated levels of ATG5 and ATG7 proteins in the serum of patients with systemic lupus erythematosus (SLE) and the plasma of patients with iTTP could serve as biomarkers of autoimmune conditions (Presented at AAI Conference in May 2023).

Selected Publications

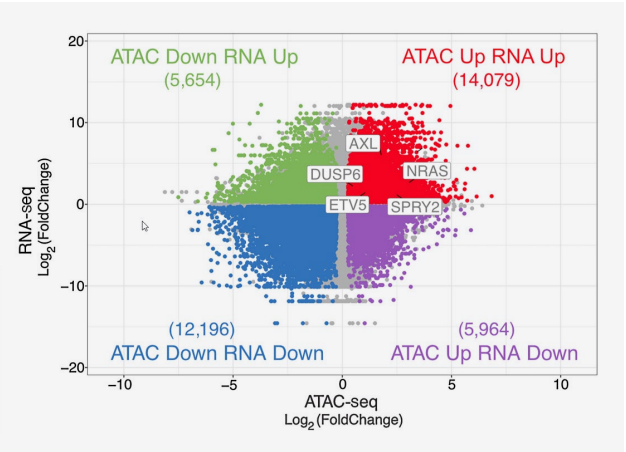
Andina N, de Meuron L, Schnegg-Kaufmann AS, Sarangdhar MA, Ansermet C, Bombaci G, Batta K, Keller N, Porret NA, Angelillo-Scherrer A, Bonadies N, Allam R. I (2023). ↗ *Increased Inflammasome Activation Is Associated with Aging and Chronic Myelomonocytic Leukemia Disease Severity.* Journal of immunology, 210(5), pp. 580-589. ↗ 10.4049/jimmunol.2200412

Codilupi T, Szybinski J, Arunasalam S, Jungius S, Dunbar AC, Stivala S, Brkic S, Albrecht C, Vokalova L, Yang JL, Buczak K, Ghosh N, Passweg JR, Rovo A, Angelillo-Scherrer A, Pankov D, Dirnhofer S, Levine RL, Koche R, Meyer SC (2024). ↗ *Development of resistance to type II JAK2 inhibitors in MPN depends on AXL kinase and is targetable.* Clinical Cancer Research, 30(3), pp. 586-599. ↗ 10.1158/1078-0432.CCR-23-0163

Golomingi M, Kohler J, Lamers C, Pouw RB, Ricklin D, Dobo J, Gal P, Pal G, Kiss B, Dopler A, Schmidt CQ, Hardy ET, Lam W, Schroeder V (2023). ↗ *Complement inhibition can decrease the haemostatic response in a microvascular bleeding model at multiple levels*. Frontiers in Immunology, 14(1226832), p. 1226832. ↗ 10.3389/fimmu.2023.1226832

Ruggeri T, De Wit Y, Scharz N, van Mierlo G, Angelillo-Scherrer A, Brodard J, Schefold JC, Hirzel C, Jongerius I, Zeerleder S (2023). ↗ *Immunothrombosis and complement activation contribute to disease severity and adverse outcome in COVID-19*. Journal of Innate Immunity, 15(1), pp. 850-864. Karger ↗ 10.1159/000533339

Schnegg-Kaufmann AS, Thoms JAI, Bhuyan GS, Hampton HR, Vaughan L, Rutherford K, Kakadia PM, Lee HM, Johansson EMV, Failes TW, Arndt GM, Koval J, Lindeman R, Warburton P, Rodriguez-Meira A, Mead AJ, Unnikrishnan A, Davidson S, Polizzotto MN, Hertzberg M, Papaemmanuil E, Bohlander SK, Faridani OR, Jolly CJ, Zanini F, Pimanda JE (2023). ↗ *Contribution of mutant HSC clones to immature and mature cells in MDS and CMML, and variations with AZA therapy*. Blood, 141(11), pp. 1316-1321. ↗ 10.1182/blood.2022018602



Targeting resistance to JAK2 inhibitors in myeloproliferative neoplasms

Bone & Joint

Participating Labs

- **Gantenbein-Lab**
  Tissue Engineering for Orthopedics & Mechanobiology (TOM)
- **Saulacic-Lab**
  Cranio-Maxillofacial Surgery (CMF)

Program Contact

Prof. Dr. Benjamin Gantenbein
benjamin.gantenbein@unibe.ch
Link to research program

Selected Collaborators

Noailly J. Pompeu Fabra University, Barcelona, Spain
Wöltje M. Dresden University of Technology, Dresden, Germany
Ile F. Lucerne University of Applied Sciences and Arts, Lucerne, Switzerland
Le Maitre C. Sheffield Hallam University, Sheffield, United Kingdom
Ferrari S. L. Geneva University Hospital and Faculty of Medicine, Geneva, Switzerland

The skeletal system is subject to traumatic conditions (fractures and large bone defects) and pathologies due to degeneration (osteoporosis, osteoarthritis, and intervertebral disc [IVD] degeneration). The demand for improved and efficient treatments is increasing as the population of older adults grows and wants to stay physically active. However, surgical procedures for repairing large bone defects or degenerated spinal discs still require significant improvement. The regeneration of skeletal tissues is the focus of the Bone & Joint Research Program. To this aim, strategies based on cells, materials, and growth factors are currently employed, ex vivo (2D/3D cell cultures and bioreactors) and in vivo. Translational orthopaedic research, which has been a long tradition in Bern, requires interactions between surgeons and scientists. The Bone & Joint Research Program will continue to extend this tradition and provide clinicians with tools to improve patient treatment.

Research Highlights 2023 / Outlook 2024

The tissue engineering for orthopedics (TOM) lab has successfully acquired competitive funding for translational and cellular therapies in two main areas. The first focus area is joint research in the field of intervertebral disc regeneration of the spine. The ongoing Marie Skłodowska Curie International Training Network (ITN) "disc4all" (↗ disc4all.upf.edu) with two early-stage researchers (ESRS) and three visiting ESRs continued to train young researchers in the field of wet ab techniques in 2D and 3D cell culturing models in combination with computational simulations and predictions of mechanical loading and mimicking inflammation and cell signaling. A second milestone was the successful completion of the "Silkodisk" project, a tissue engineering project that utilizes silk to repair IVDs. This is an active collaboration with Dr. Michael Wöltje of the Dresden University of Technology (TUD). In this framework, the TOM lab was honored with the best Master's thesis award of Janine Fuhrer, MSc, for her valuable lab work at the Biomedical Sciences and the successful PhD defense of Dr. Andreas Croft, which is nominated for the best PhD thesis at the GCB.

Furthermore, the TOM lab has received a bridge discovery research project (budget 1.3 M CHF for four years) on label-free cell sorting based on electrical impedance to "fish" for rare type of progenitor cells of the IVD. This project is a collaboration with Prof. Patric Eberle and Prof. Fabian Ile, both from the Lucerne University of Applied Sciences. This project is based on cell sorting of a rare stem cell population from the IVD.

Further progress can be made in the second focus field of improved spinal fusion. In this study, an in vivo rat model was established using bone morphogenic protein (BMP) 2 and specific mixtures of a BMP2 analog (L51P) to accelerate spinal fusion to maximum speed, while maintaining concentrations at a low dose close to physiological levels. Future research is foreseen to investigate the role of rheumatoid

arthritis using an identical approach of fixator extern as well as investigate the role of disease-modifying antirheumatic drugs (DMARDs) in patients undergoing treatment for rheumatoid arthritis (RA). In the near future, these drugs will be tested for their effects on healing of impaired spinal fusion.

In collaboration with the Clinic for Radiology at the Inselspital (PD Dr. Rainer Egli), the possible effects of gadolinium-containing contrast agents on bone cell lineages were investigated in vitro. The data demonstrated that both the differentiation and activity of osteoblast and osteoclast lineage cells were inhibited upon exposure to gadolinium, suggesting that long-term exposure to gadolinium-containing contrast agents may affect bone metabolism, which requires further study. Franziska Strunz, the first author of this study, successfully completed her PhD thesis during this reporting period.

The Saulacic lab (CMF) assessed the sequence of osseointegration in 3D-printed titanium implants with a trabecular structure without (R1) or with (R2) an acid-pickled surface in comparison to commercially available titanium implants, in collaboration with the Department of Periodontology, School of Dental Medicine, University of Bern. The 3D-printed implants have been shown to maintain crestal bone height and successfully osseointegrate with adequate fractions of newly mineralized bone formation.

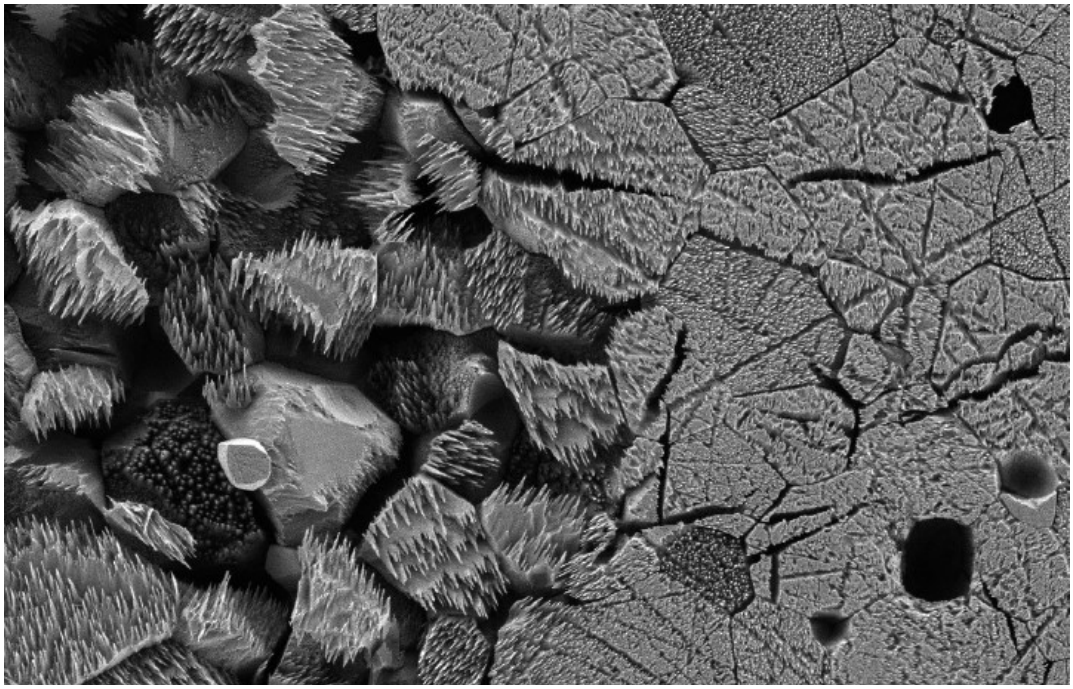
Selected Publications

Croft, AS; Fuhrer, J; Wöltje, M.; Gantenbein, B (2023). ↗ *Creating tissue with intervertebral disc-like characteristics using gdf5 functionalized silk scaffolds and human mesenchymal stromal cells*. European Cells & Materials eCM, 46, pp. 1-23. ↗ 10.22203/eCM.v046a01

Crump KB, Alminnawi A, Bermudez-Lekerika P, Compte R, Gualdi F, McSweeney T, Munoz-Moya E, Nuesch A, Geris L, Dudli S, Karppinen J, Noailly J, Le Maitre C, Gantenbein B (2023). ↗ *Cartilaginous endplates: A comprehensive review on a neglected structure in intervertebral disc research*. JOR Spine, 6(4), e1294. ↗ 10.1002/jsp2.1294

Croft AS, Corluka S, Fuhrer J, Woltje M, Silva-Correia J, Oliveira JM, Erbach GF, Reis RL, Gantenbein B (2023). ↗ *Repairing Annulus Fibrosus Fissures Using Methacrylated Gellan Gum Combined with Novel Silk*. Materials, 16(8), p. 3173. ↗ 10.3390/ma16083173

Lang NP, Imber JC, Lang KN, Schmid B, Munoz F, Bosshardt DD, Saulacic N (2023). ↗ *Sequential osseointegration of a novel implant system based on 3D printing in comparison with conventional titanium implants*. Clinical Oral Implants Research, 34(6), pp. 627-638. ↗ 10.1111/clr.14072



Scanning electron microscope image of the surface of a ß-TCP cylinder after 24 h resorption by *in vitro* generated osteoclasts (from: LeGars Santoni B et al. (2023) Acta Biomaterialia 169:566-578. PMID: 37595772)

Cancer Therapy Resistance (CTR)

Participating Labs

- **Kruithof-de Julio Lab**
  Urology Research Laboratory
- **Rottenberg Lab**
  Therapy Escape of Cancer
- **Rubin Lab**
  Precision Oncology

Contact

Prof. Dr. Marianna Kruithof-de Julio
- marianna.kruithofdejulio@unibe.ch
- Link to research program

Selected Collaborators

Emerling B. Sanford Burnham Prebys Medical Discovery Institute, La Jolla CA (US)
Jonkers J. The Netherlands Cancer Institute, Amsterdam (NL)
Kanadia R. University of Connecticut, Storrs CT (US)
Lord C. J. The Institute of Cancer Research, London (UK)
Rapsomaniki M. University of Lausanne (UNIL), Lausanne (CH)

Research Highlights 2023 / Outlook 2024

We have continued our efforts to identify new vulnerabilities in androgen receptor-resistant prostate cancer (PCa) and to develop therapies to combat the most aggressive forms of PCa by studying *in vivo* and *in vitro* models and performing functional screens. In 2023, we have: 1. Shown that the minor spliceosome is a strong therapeutic target for lethal PCa (PMID: 37295433) 2. Demonstrated that the lipid kinase isoform, PI5P4Kα, influences androgen receptor signaling which supports PCa cell survival. This nominates PI5P4Kα as a target to disrupt PCa metabolic adaptation to cancer resistance (PMID: 36724278). 3. Worked on identifying genes, which in combination with loss of function of RB1 and TP53, have clinical relevance. 4. Studied the underlying mechanisms through which the SWI/SNF complex regulates lineage plasticity and therapy resistance to identify novel therapeutic strategies for neuroendocrine PCa 5. Targeted non-BRCA DNA repair deficient PCa to uncover novel genotype-specific therapeutic vulnerabilities for ATM-, FANCA- and CHek2-deficient PCa. New research support was received from the US Department of Defense, Swiss Cancer Research, and the Swiss Institute for Experimental Cancer Research (ISREC) foundation.

We also made substantial progress in understanding the mechanisms of resistance to anticancer therapy using genetically engineered mouse models of *BRCA1/2*-mutated breast cancer. Major findings in 2023 include: 1. The meiotic proteins MND1 and PSMC3IP control PARP (poly ADP ribose polymerase) inhibitor sensitivity in mitotic cancer cells. Our data suggests that meiotic proteins play a significant role in mitotic DNA repair. 2. MDC1 counteracts restrained replication fork restart and its loss causes chemoresistance in BRCA1/2-deficient mammary tumors. Our results show a role for MDC1 in replication fork progression, which mediates PARPi- and cisplatin-induced DNA damage, in addition to its role in DSB repair. 3. Moreover, we found that H2AX promotes replication fork degradation and chemosensitivity in BRCA-deficient tumors. Our results demonstrate a novel role of H2AX in replication fork biology in BRCA-deficient tumors and establish a function of H2AX separable from its classical role in DNA damage signaling and DSB repair 4. PARG loss is a main mechanism of PARPi resistance in BRCA2; p53-deficient mouse mammary tumors and PARG-deficient cells have an increased dependence on EXO1/FEN1-mediated DNA repair. 5. Regarding LRRC8A- and LRRC8D-mediated platinum drug uptake via volume-regulated anion channels, we found that the N-terminal acetylation of LRRC8A/D is critical for proper drug uptake. 6. For her studies on understanding radiotherapy resistance, Lea Lingg, a PhD student in the Rottenberg group, received the best poster prize for her poster presentation on DNA repair at the International Wolfsberg Meeting on Molecular Radiation Biology/ Oncology in Oslo.

Selected Publications

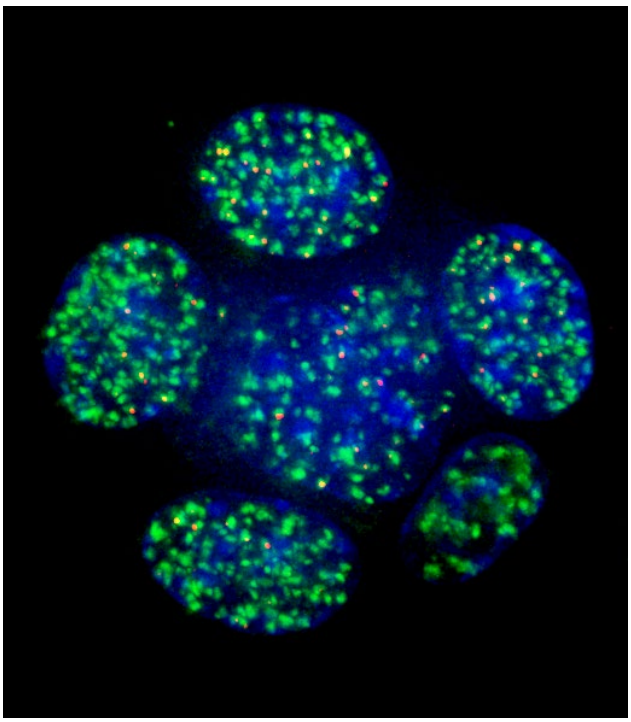
Augspach A, Drake KD, Roma L, Qian E, Lee SR, Clarke D, Kumar S, Jaquet M, Gallon J, Bolis M, Triscott J, Galván JA, Chen Y, Thalmann GN, Kruithof-de Julio M, Theurillat J-PP, Wuchty S, Gerstein M, Piscuoglio S, Kanadia RN, Rubin MA (2023). *Minor intron splicing is critical for survival of lethal prostate cancer*. Molecular Cell, 83(12), 1983-2002.e11. 10.1016/j.molcel.2023.05.017

Minoli M, Cantore T, Hanhart D, Kiener M, Fedrizzi T, La Manna F, Karkampouna S, Chouvardas P, Genitsch V, Rodriguez-Calero A, Comperat E, Klima I, Gasperini P, Kiss B, Seiler R, Demichelis F, Thalmann GN, Kruithof-de Julio M (2023). *Bladder cancer organoids as a functional system to model different disease stages and therapy response*. Nature Communications, 14(1), p. 2214. 10.1038/s41467-023-37696-2

Triscott J, Reist M, Kung L, Moselle FC, Lehner M, Gallon J, Ravi A, Arora GK, de Brot S, Lundquist M, Gallart-Ayala H, Ivanisevic J, Piscuoglio S, Cantley LC, Emerling BM, Rubin MA (2023). *PI5P4Kα supports prostate cancer metabolism and exposes a survival vulnerability during androgen receptor inhibition*. Science Advances, 9(5), eade8641. 10.1126/sciadv.ade8641

Zelceski A, Francica P, Lingg L, Mutlu M, Stok C, Liptay M, Alexander J, Baxter JS, Brough R, Gulati A, Haider S, Raghunandan M, Song F, Sridhar S, Forment JV, O'Connor MJ, Davies BR, van Vugt M, Krastev DB, Pettitt SJ, Tutt ANJ, Rottenberg S, Lord CJ (2023). *MND1 and PSMC3IP control PARP inhibitor sensitivity in mitotic cells*. Cell Reports, 42(5), p. 112484. 10.1016/j.celrep.2023.112484

Bhin J, Paes Dias M, Gogola E, Rolfs F, Piersma SR, de Bruijn R, de Ruiter JR, van den Broek B, Duarte AA, Sol W, van der Heijden I, Andronikou C, Kaiponen TS, Bakker L, Lieftink C, Morris B, Beijersbergen RL, van de Ven M, Jimenez CR, Wessels LFA, Rottenberg S, Jonkers J (2023). *Multi-omics analysis reveals distinct non-reversion mechanisms of PARPi resistance in BRCA1- versus BRCA2-deficient mammary tumors*. Cell Reports, 42(5), p. 112538. 10.1016/j.celrep.2023.112538



Drug-resistant BRCA1/p53-deficient mammary tumoroids show restored RAD51 foci formation in response to IR-induced DNA damage. Blue=DNA, green=γH2AX, red=RAD51. Courtesy of Anna Moyseos.

Cardiovascular Diseases

Participating Labs

- **Döring Lab**
  Atherosclerosis, vascular inflammation & lower extremity arterial disease
- **Heller Lab**
  Mass spectrometry-based methods to characterize circulating extracellular vesicles and system-wide protein regulation
- **Longnus Lab**
  Cardioprotection following ischemia, cardiac metabolism & signaling, heart transplantation
- **Mercader Lab**
  Heart development and regeneration
- **Odening Lab**
  Cardiac electrophysiology & arrhythmogenic mechanisms in inherited rhythm disorders
- **Osterwalder Lab**
  Gene regulatory mechanisms underlying cardiac development, disease and reprogramming
- **Rexhaj Lab**
  Fetal programming of metabolic and cardiovascular function/dysfunction later in life
- **Rieben Lab**
  Ischemia/reperfusion injury, xenotransplantation, vascularized composite allotransplantation
- **Zuppinger Lab**
  Mechanisms of adverse effects of cancer therapies on the cardiovascular system (Cardio-Oncology)

Contact

Prof. Dr. Yvonne Döring
- yvonne.doering@unibe.ch
- Link to research program

Selected Collaborators

Enriquez J. A. and Torres M. Cardiovascular Regeneration Program, Spanish National Center for Cardiovascular Research (CNIC), Madrid (ES)

Marsano A. Basel University, Biomedicine/ Cardiac Surgery, Basel (CH)

Soehnlein O. Institute of Experimental Pathology, University of Münster (WWU), Münster (DE)

Wolf E. Gene Center and Department of Biochemistry, Ludwig-Maximilians University of Munich (LMU), Munich (DE)

Büttner F. Hannover Medical University, Institute for Clinical Biochemistry, Hannover (DE)

Tight spatiotemporal control of cardiac gene expression and a functional cardiovascular system are crucial for both embryonic development and lifelong maintenance, ensuring adequate blood supply throughout the body. In healthy adults, blood vessels remain in a quiescent state with a non-proliferating, anti-thrombotic, anti-inflammatory, and non-angiogenic endothelial and smooth muscle cell phenotype. Cardiomyocytes ensure proper electrical and contractile function in the heart.

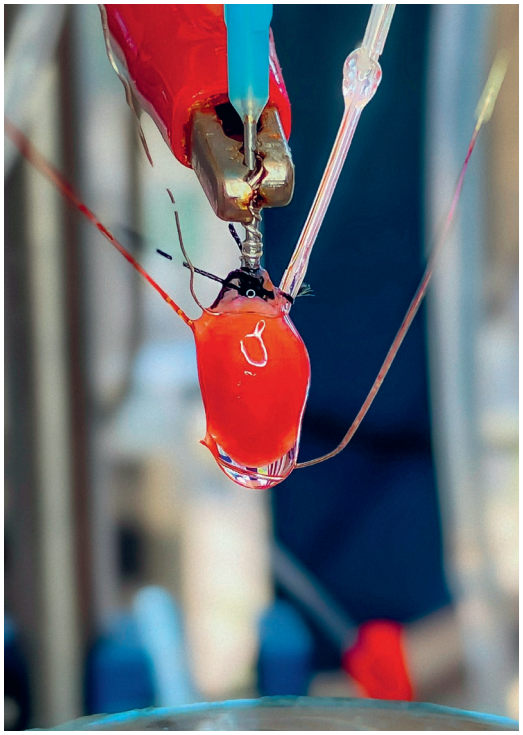
Focusing on human cardiovascular diseases (CVDs), the DBMR CVD research program covers all aspects of cardiac development, vascular and injury responses: we analyze molecular, epigenetic, and physiological mechanisms underlying heart formation, regeneration and injury responses after tissue damage (inflammation, ischemia/reperfusion injury, cancer treatment). We aim to dissect cardiac gene regulatory networks and fibrotic repair mechanisms, and investigate the long-term consequences of injury (e.g., arrhythmias and heart failure). Furthermore, we examine the vascular biology (e.g., role of the glycocalyx), chronic inflammation (e.g., atherosclerosis), and immune mechanisms (e.g., complement or NETs) affecting vascular health and disease.

Research Highlights 2023 / Outlook 2024

This year, Katia Odening (Contact Investigator), Nadia Mercader (co-investigator) and Marco Osterwalder (young investigator), as members of the CVD program, together with Christiane Zweier and Jean-Louis Reymond (co-investigators), successfully applied for the BCPM Lighthouse Project Award worth CHF 1,000,000 for 3 years "Precision Diagnosis and Therapy in Cardiac Channelopathies (PACE)". Moreover, Katia Odening and Sarah Longnus (co-directors) together with Prof. Matthias Siepe (director) were granted the "Faculty of Medicine Strategic Funding Board Grant" to investigate "Ex-vivo Heart Perfusion – Technology that innovates cardiac transplantation and precision therapies" (CHF 750'000 for 3 years). In addition, the SNSF NRP78 (4078P0_198297, Program PIs: Yvonne Döring, Nadia Mercader, Robert Rieben; Associated PI: Sarah Longnus, Katia Odening.; External PI: Britta Engelhardt) was successfully completed in June 2023, and results were presented, for example, at the CVRC Annual Meeting (18.01.2023), the DBMR Day of Biomedical Research (05.07.2023), and the SNSF Corona Research Conference (21.03.2023). Through a grant from the Swiss-European Mobility Programme, Agnieszka Olejnik joined the CVD Program to work on the CoVasc Study. The SNF NRP79 (407940_206520) "HeartX: Decoding cardiac regulatory landscapes in an all-human model for cardiogenesis" with CVD-PIs Marco Osterwalder (main applicant), Christian Zuppinger (co-applicant), Iros Barozzi (external PI, co-applicant), Nadia Mercader (project partner), Katia Odening and Yvonne Döring (collaborators) will continue until 2026. In line, joint SNF project (310030_205073), "Cardiac metabolism

as a basis for sex differences in ischemic tolerance and a target for reperfusion therapy in heart transplantation with donation after circulatory death" from Program PI Sarah Longnus with program collaboration from Manfred Heller continues.

The CVD Program has continued its contribution to the Cardiovascular Research Cluster supporting the PhD Specialization Program "Cardiovascular Research" which was newly established in 2023 to enable additional courses for mandatory (e.g. CV Technologies Course, Annual Meetings) and elective requirements (e.g. CVD Program Monthly Meeting, Wahlpraktikum (Elective Internship): Cellular and Translational Cardiac Electrophysiology, Journal Club – Cardiac Surgery). In addition, students from Bern will be able to attend established lecture series and courses from partner programs/universities (USI, Lausanne, Munich) and obtain ECTS credits for their doctoral program. Through a collaboration within the PhD Specialized Program (partner Università della Svizzera Italiana), Manuel Egle (Longnus lab) was able to obtain an MD PhD grant. Awards of CVD program members: Nick Kirschke (Mercader lab) was awarded the "Best Project by a Medical Student Poster Prize" by the DBMR and "Best Master Thesis" by the Swiss Society of Anatomy, Histology, and Embryology. At the CVRC Annual Meeting 2023 Anaïs Yerly (Döring lab) won the "Best Poster Prize" and Anastasia Milusev (Rieben lab) gave "Best Flash Presentation" in the category fundamental research. Anastasia also won "Best Poster" in the category "cardiovascular biology" at the LS2 Annual Meeting 2023 in Zürich and Valentina Zollet (Rieben lab) received the "Life Science Award" for the 2nd best presentation at the LS2 Cardiovascular Research Meeting 2023 in Bern and Saranda Nimani and Lucilla Giammarino (both Odening lab) received the "Young Investigator Award" for the best and 2nd best oral presentations and Andras Horvath (Odening lab) the "Postdoc Award" for the best oral presentation at the LS2 Physiology/Ion channel meeting 2023 in Bern. Manovriti Thakur (Döring lab) received the "Best Free Communication Award" at the 23rd Union Congress of Swiss Vascular Societies and Bryce Evans (Döring lab) received the "2nd Best Flash Poster Talk Award". Théo Meister (Rexhaj lab) won the best poster presentation prize at the CVRC Annual Meeting 2023. E. Rexhaj was recognized on the Albinfo platform as "Medical Personality in Switzerland" of the year 2023. Finally, Yvonne Döring was awarded the "Outstanding Achievement Award 2023" by the Basic Cardiovascular Science Cluster of the European Society of Cardiology.



Isolated, perfused mouse heart instrumented for simultaneous assessment of mechanical and electrical function

Selected Publications

Ernst A, Piragyte I, Mp AM, Le ND, Grandgirard D, Leib SL, Oates A, Mercader N (2023). *Identification of side effects of COVID-19 drug candidates on embryogenesis using an integrated zebrafish screening platform*. Scientific Reports, 13(1), p. 17037. 10.1038/s41598-023-43911-3

George RM, Firulli BA, Podicheti R, Rusch DB, Mannion BJ, Pennacchio LA, Osterwalder M, Firulli AB (2023). *Single cell evaluation of endocardial HAND2 gene regulatory networks reveals critical HAND2 dependent pathways impacting cardiac morphogenesis*. Development, 150(3): dev201341. 10.1242/dev.201341

Milusev A, Ren J, Despont A, Shaw J, Langin M, Bender M, Abicht JM, Mokelke M, Radan J, Neumann E, Kemter E, Klymiuk N, Ayares D, Wolf E, Reichart B, Sorvillo N, Rieben R (2023). *Glycocalyx dynamics and the inflammatory response of genetically modified porcine endothelial cells*. Xenotransplantation, 30(5), e12820. 10.1111/xen.12820

Odening KE, Gomez AM, Dobrev D, Fabritz L, Heinzel FR, Mangoni ME, Molina CE, Sacconi L, Smith G, Stengl M, Thomas D, Zaza A, Remme CA, Heijman J (2021). *ESC working group on cardiac cellular electrophysiology position paper: relevance, opportunities, and limitations of experimental models for cardiac electrophysiology research*. EP Europace, 23(11), pp. 1795-1814. 10.1093/europace/euab142

Thakur M, Junho CVC, Bernhard SM, Schindewolf M, Noels H, Doring Y (2023). *NETs-Induced Thrombosis Impacts on Cardiovascular and Chronic Kidney Disease*. Circulation Research, 132(8), pp. 933-949. 10.1161/CIRCRESAHA.123.321750

Emerging and Difficult to Treat Infections

Participating Labs

- **Leib Lab**
  Neuroinfection laboratory
- **Que Lab**
  Critical Care Microbiology
- **Schefold Lab**
  Immunosuppression in Critical Illness
- **Furrer Lab**
  Infectious diseases

Contact

Prof. Dr. Yok-Ai Que
- yok-Ai.Que@insel.ch
- Link to Research Program

Selected Collaborators

Egli A. Institute for Medical Microbiology, University of Zurich, Zürich (CH)
Fürholz M. Department of Cardiology, Bern University Hospital, Inselspital, University of Bern, Bern (CH)
Jutzler C. Department of Health Sciences and Technology, Institute for Translational Medicine, ETH Zurich, Zurich (CH)
Resch G. Center for Research and Innovation in Clinical Pharmaceutical Sciences CHUV, Lausanne University Hospital, Lausanne (CH)
Wolf H. Department of Emergency Medicine, Bern University Hospital, Inselspital, University of Bern, Bern (CH)

The incidence of infectious diseases has increased worldwide. Not only are new infectious diseases caused by recently characterized pathogens emerging, but old and previously curable infectious syndromes are also becoming more difficult to treat. Therapeutic options specifically targeting emerging infectious threats are scarce despite public and private initiatives; only a few new anti-infective molecules are reaching the market, and the drug development process has become disappointingly slow. Innovative diagnostic and therapeutic approaches are urgently required to bring novel management strategies for infections to the bedside.

Using a translational and collaborative approach, the program addresses novel diagnostic and therapeutic strategies to combat emerging and hard-to-treat infections in critically ill patients. Research projects include the identification and validation of novel digital and biological biomarkers to identify patients with infections and prognosticate their outcome, the evaluation of innovative anti-infectives (e.g. bacteriophages) both *in vitro* and *in vivo* in various animal models of infections and the development of novel microbiological diagnostic tools.

Research Highlights 2023 / Outlook 2024

Phage therapy projects (SNF#310030_212584, Bangerter-Rhyner & Herz Stiftungen)

The use of bacterial viruses to kill bacteria, referred to as phage therapy, is increasingly considered a valuable approach for overcoming the antimicrobial resistance crisis. The long-term goal of phage therapy projects is to address the knowledge gaps that prevent the immediate use this therapy in human patients, focusing on new methods to isolate phages and phage pharmacology. (1) We validated a new phage-hunting pipeline in which phages intended for therapy are isolated from the individuals' own skin microbiota in patients with end-stage heart failure using a left ventricular assist device (LVAD). We found new phages in 8 of the 32 patients. One phage was able to significantly reduce S. *epidermidis* bacterial loads in both exponentially growing and in stationary phase cultures, as well as in ex vivo biofilms formed on explanted drivelines. (2) To provide a rationale for the optimal dose selection and dose schedule of phage therapy and guidance for phage-antibiotic combinations, we developed a new platform for the study of phage pharmacology, implementing a hollow fiber infection model in vitro and a new tissue cage infection model in rodents.

Biomarkers projects

(PSP Projects) Triaging patients with infections admitted to emergency rooms or intensive care units is highly challenging. Current biomarkers, such as C-reactive protein (CRP) and procalcitonin, have suboptimal accuracy. Pancreatic stone protein (PSP) is increasingly used in acute settings to diagnose infections. Several studies have suggested that PSP might also discriminate patients with severe infection and/or

poor prognosis. We performed an individual patient-level meta-analysis, and confirmed the ability of PSP to discriminate between patients with poor outcomes and/or severe disease, and proposed threshold values for that purpose.

(SPHN-NDS-IICU) Infections account for a substantial number of deaths among critically ill patients admitted to intensive care units. Infections show a wide range of phenotypes that affect clinical course and patient outcomes. The aim of this collaborative project is to build a national infrastructure for clinical and microbiological data exchange to facilitate the study and prediction of personalized health in intensive care in general and in patients with infections in particular. Specifically, the project will investigate various phenotypes among critically ill patients treated for infection in one of the five Swiss University ICUs using a combined data- and clinical-driven approach to improve personalized assessment, characterization, and outcome prediction. As an innovative approach, we will collect contextual data in addition to standard monitoring information, especially data related to clinical reasoning and interpretation when decisions are made, procedures are performed, and treatments are initiated or changed.

Genomic-based Method for Bacterial Pathogen Characterization in Patients with Sepsis (BCPM-BRIDGE)

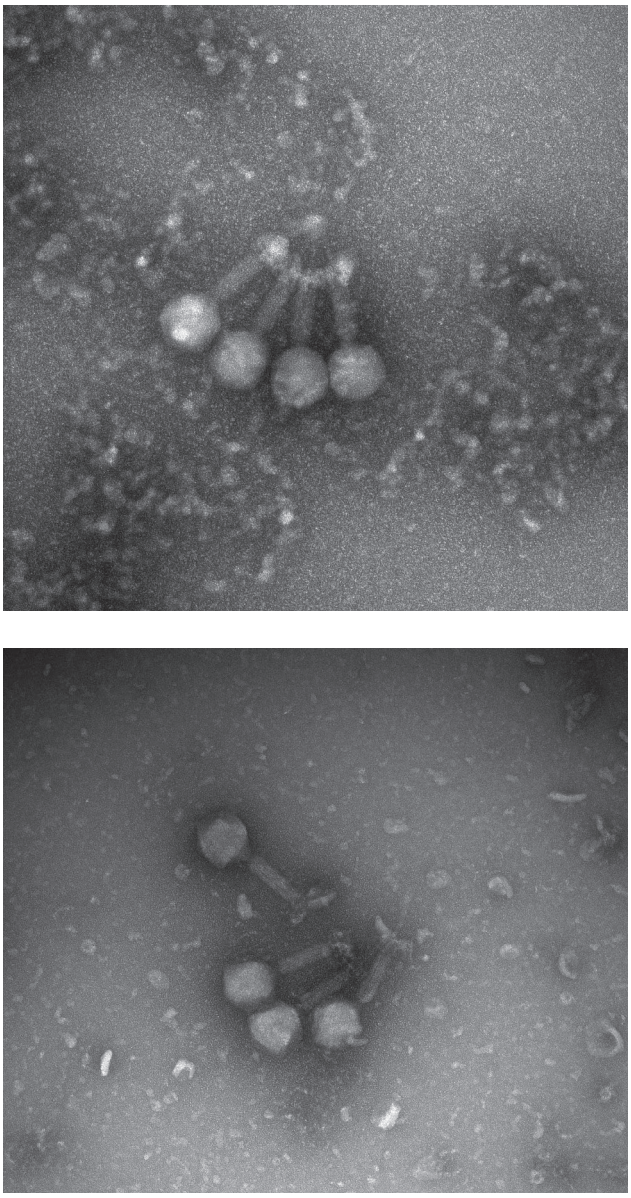
Next-generation sequencing (NGS) technologies may represent an attractive solution to overcome the limitations of conventional microbiological diagnostic methods. They are sensitive, quick, and may be applied as soon as blood samples are available, without the need for bacterial culture. The overarching goal of this project, led by PD Dr. Alban Ramette, is to improve the development and to validate metagenomic protocols for the rapid detection and characterization of bacterial pathogens present in clinical native blood samples from critically ill patients sent for routine blood cultures and compare these NGS approaches to standard care methods based on conventional diagnostic approaches.

Selected Publications

Pitton M, Valente LG, Oberhaensli S, Casanova C, Sendi P, Schnegg B, Jakob SM, Cameron DR, Que YA, Furholz M (2023). ↗ *Dynamics of bacterial pathogens at the driveline exit site in patients with ventricular assist devices: a prospective, observational, single-centre cohort study.* The Journal of heart and lung transplantation, 42(10), pp. 1445-1454. ↗ 10.1016/j.healun.2023.05.016

Zuercher P, Moser A, Garcia de Guadiana-Romualdo L, Llewelyn MJ, Graf R, Reding T, Eggimann P, Que YA, Prazak J (2023). ↗ Discriminative performance of pancreatic stone proteins in predicting ICU mortality and infection severity in adult patients with infection: a systematic review and individual patient level meta-analysis. Infection, 51(6), pp. 1797-1807. ↗ 10.1007/s15010-023-02093-w

Zuercher P, Moser A, Frey MC, Pagani JL, Buetti N, Eggimann P, Daneman N, Fowler R, Que YA, Prazak J (2023). ↗ *The effect of duration of antimicrobial treatment for bacteremia in critically ill patients on in-hospital mortality – Retrospective double center analysis*. Journal of Critical Care, 74, p. 154257. ↗ 10.1016/j.jcrc.2023.154257



Electron microscopy of bacteriophages active against Staphylococcus epidermidis isolated from a patient with a left-ventricular assist device.

Lung Precision Medicine

Participating Labs

- **Blank lab**
  interaction between (nano) particles and the respiratory tract
- **Das Sudip lab**
  Role of the Microbiome in the human distal lung
- **Eggel lab**
  Type-2 immunity in health an disease with specific focus on allergies
- **Funke-Chambour lab**
  exacerbations in fibrotic lung diseases – immunological mechanisms
- **Gazdhar lab**
  stem cells in lung regeneration and fibrosis, novel treatment approaches in lung cancer
- **Geiser lab**
  Inflammation, injury and fibrosis in lung diseases, nanoplastic particles in the respiratory tract
- **Gote-Schniering lab**
  Integrative lung biology and imaging
- **Klein lab**
  Multiomics in Sjögren's disease
- **Maurer lab**
  Multiomics in connective tissue-associated lung diseases
- **Müller Loretta/Latzin lab**
  disease mechanisms on primary ciliary dyskinesia, immunity, and air pollution
- **Seydoux/Kopp lab**
  lung disease prevention through novel vaccination technologies

Contact

Prof. Thomas Geiser
thomas.geiser@insel.ch
loretta.mueller@insel.ch
Link to Research Program

Selected Collaborators

Guenat O. ARTORG, University of Bern, Bern (CH)
Rutishauser Rothen B. Merckle Institute, Fribourg (CH)
Herbert S. Helmholtz Munich, Munich (DE)
Hansbro P. Centenary Institute, Sydney (AU)
Jardetzky T./ Wyss-Coray T. Stanford School of Medicine, Stanford (US)
Tschanz S. Institute of Anatomy, University of Bern, Bern (CH)
Frenz M. Institute of Applied Physics, University of Bern, Bern (CH)

The interdisciplinary Lung Precision Medicine Program brings together clinicians, biologists, physicists, and engineers of the University of Bern and the University Hospital of Bern. The aim of the program is to address unmet clinical needs by focusing on acute and chronic lung diseases of different origins and infectious, immunological, and environmental etiologies. We aim to combine profound knowledge of inflammatory and fibrotic lung diseases and lung regeneration for precision and regenerative medicine, which are closely linked to current clinical needs. We are running a basic research platform to investigate the key mechanisms driving respiratory diseases and develop novel technologies such as precision-cut lung slices, distal lung organoids, and sophisticated cell culture models that mimic functional healthy and/or diseased lung tissues based on patient cells or patient-derived induced pluripotent stem cells. Novel personalized in vitro disease models will allow the development of novel therapeutic strategies for lung infection and immunity, lung fibrosis, lung repair, and regeneration.

Research Highlights 2023 / Outlook 2024

With the new lab space at Murtenstrasse 24-28, the Lung Precision Medicine Program (LPM) intensified scientific collaborations between the different groups. Several in vitro/ex vivo technologies that are used now by several labs of LPM were developed. In particular, lung stem cell methodologies have been established (lung alveolar/bronchial epithelial cells, macrophages, lung endothelial cells, and induced pluripotent stem cells) and further developed for lung organoids, ex vivo lung tissue culture slices, differentiated primary nasal epithelial cells, and cilia biology. We employed cutting-edge methods including single-cell genomics, spatial transcriptomics, and highly multiplexed immunofluorescence imaging. Based on these technologies, common research projects are in development and have been successfully funded, including one SNF grant (Prof. A. Eggel), one SNF Spark (PD K. Klein), and two SF Board calls (PD K. Klein; Prof. B. Maurer).

We welcomed two additional groups in the program that fit very well with the scientific interests of the LPM: Prof. Alex Eggel (Rheumatology/Immunology/Allergology) and Dr. Janine Gote-Schniering (Rheumatology/Immunology) joined the LPM with their groups and were very well integrated in a short period.

We run common lab meetings every week with progress update on individual projects and

Last but not least, to ensure a good coordination and organization within the LPM program, we count with the help of Loretta Müller, LPM Coordinator, and of the lab technicians that contributed to all the common tasks of the program.

Selected Publications

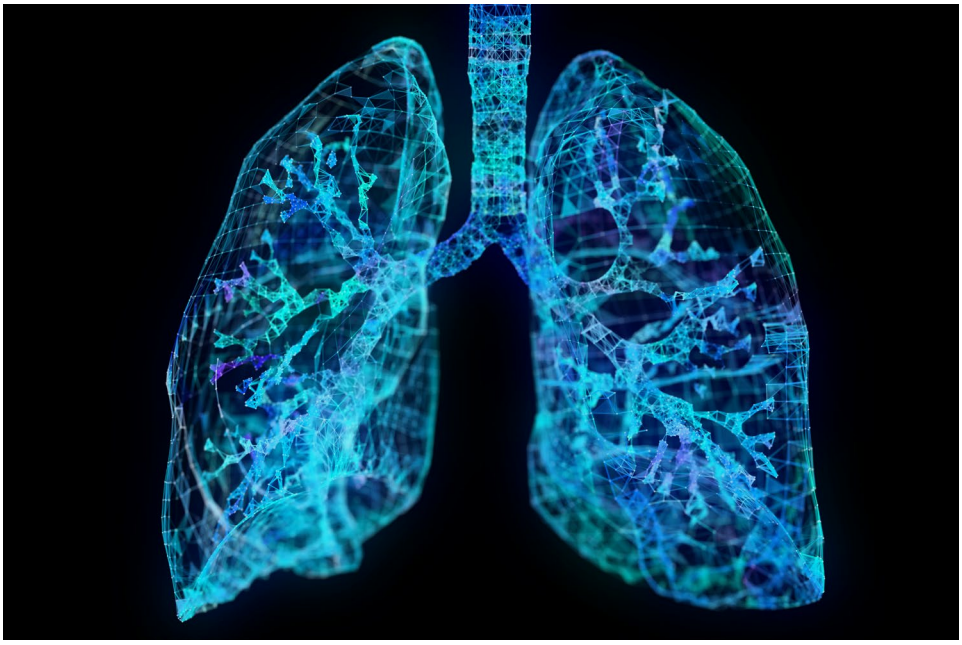
Abu Hussein N, Machahua C, Ruchti SC, Horn MP, Piquilloud L, Prella M, Geiser TK, von Garnier C, Funke-Chambour M (2023). *Circulating calprotectin levels four months after severe and non-severe COVID-19*. BMC Infectious Diseases, 23(1), p. 650. 10.1186/s12879-023-08653-7

Brigger D, Guntern P, Jonsdottir HR, Pennington LF, Weber B, Taddeo A, Zimmer G, Leborgne NGF, Benarafa C, Jardetzky TS, Eggel A (2023). *Sex-specific differences in immune response to SARS-CoV-2 vaccination vanish with age*. Allergy, 78(6), pp. 1683-1686. 10.1111/all.15652

Escher A, Kieninger E, Groof S, Savas ST, Schneiter M, Tschanz SA, Frenz M, Latzin P, Casaulta C, Muller L (2023). *In Vitro Effect of Combined Hypertonic Saline and Salbutamol on Ciliary Beating Frequency and Mucociliary Transport in Human Nasal Epithelial Cells of Healthy Volunteers and Patients with Cystic Fibrosis*. Journal of Aerosol Medicine and Pulmonary Drug Delivery 36(4), pp. 171-180. 10.1089/jamp.2022.0026

Guler S, Sarbu AC, Stalder O, Allanore Y, Bernardino V, Distler J, Gabrielli A, Hoffmann-Vold AM, Matucci-Cerinic M, Muller-Ladner U, Ortiz-Santamaria V, Rednic S, Riccieri V, Smith V, Ullman S, Walker UA, Geiser TK, Distler O, Maurer B, Kollert F (2023). *Phenotyping by persistent inflammation in systemic sclerosisassociated interstitial lung disease: a EUSTAR database analysis*. Thorax, 78(12), pp. 1188-1196. 10.1136/thorax-2023-220541

Lang NJ, Gote-Schniering J, Porras-Gonzalez D, Yang L, De Sadeleer LJ, Jentzsch RC, Shitov VA, Zhou S, Ansari M, Agami A, Mayr CH, Hooshiar Kashani B, Chen Y, Heumos L, Pestoni JC, Molnar ES, Geeraerts E, Anquetil V, Saniere L, Wograth M, Gerckens M, Lehmann M, Yildirim AO, Hatz R, Kneidinger N, Behr J, Wuyts WA, Stoleriu MG, Luecken MD, Theis FJ, Burgstaller G, Schiller HB (2023). *Ex vivo tissue perturbations coupled to single-cell RNA-seq reveal multilineage cell circuit dynamics in human lung fibrogenesis*. Science Translational Medicine, 15(725), eadh0908. 10.1126/scitranslmed.adh0908



Experimental Radiology

For several decades, metal-based drugs have been used in cancer treatment and as contrast agents in imaging. Nevertheless, several questions remain unanswered, particularly regarding their effects at the cellular level. For example, the development of cisplatin resistance, which is the first-line treatment for lung cancer chemotherapy, is still largely unknown. The latter also applies to contrast agents containing gadolinium, especially since reports of gadolinium deposits in the brain have been published. There are still many unanswered questions that govern our research. A variety of methods are used to approach them, ranging from classical biochemical and cell biology methods to modern analytical methods, e.g. single-cell ICP-MS and bioinformatics.

Research Highlights 2023 / Outlook 2024

Gadolinium based contrast agents (GBCA): GBCA are used to enhance MRI examinations. Despite being well tolerated by most patients, gadolinium accumulates in various compartments of the body after multiple administrations, including the brain. The specific chemical form and exact location of the gadolinium deposits within the body are currently unknown. However, the cellular-level interactions of GBCA have not yet been investigated. Hence, our current research focuses on understanding the general interaction between GBCA and cells with a specific emphasis on white blood cells and components of the blood-brain barrier.

A recent study demonstrated the uptake of GBCA by white blood cells in patients undergoing contrast-enhanced MRI. Another study investigated GBCA permeability across the blood-brain barrier (BBB). It was shown that GBCA cannot freely pass through the BBB. However, peripheral blood mononuclear cells (PBMCs) can take up GBCA and migrate across the BBB in vitro, suggesting that GBCA-loaded PBMCs cross the brain barrier in vivo and contribute to the permanent deposition of GBCA in the brain.

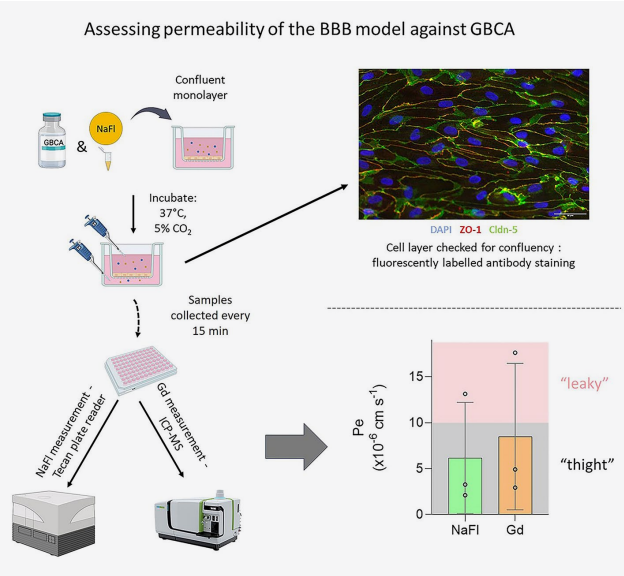
Cisplatin Resistance in Lung Cancer: Therapeutically induced cisplatin resistance develops regularly following platinum-based combination chemotherapy. To circumvent cisplatin resistance, it is necessary to understand the mechanisms underlying resistance development and/or develop alternative drugs. Both are the focus of our research, with the latter being in close collaboration with external experts in chemistry, biochemistry, and pharmacology.

Selected Publications

Ruprecht N, Parakkattel D, Hofmann L, Broekmann P, Ludi N, Kempf C, Heverhagen JT, von Tengg-Kobligk H (2023). ↗ *Uptake of Gadolinium-Based Contrast Agents by Blood Cells During Contrast-Enhanced MRI Examination*. Investigative Radiology. ↗ 10.1097/RLI.0000000000001029

Ruprecht N, Hofmann L, Hungerbuhler MN, Kempf C, Heverhagen JT, von Tengg-Kobligk H (2020). ↗ *Generation of Stable cisPt Resistant Lung Adenocarcinoma Cells*. Pharmaceuticals, 13(6), p. 109. ↗ 10.3390/ph13060109

Galé A, Hofmann L, Ludi N, Hungerbuhler MN, Kempf C, Heverhagen JT, von Tengg-Kobligk H, Broekmann P, Ruprecht N (2021). ↗ *Beyond Single-Cell Analysis of Metallodrugs by ICP-MS: Targeting Cellular Substructures*. International Journal of Molecular Sciences, 22(17), p. 9468. ↗ 10.3390/ijms22179468



Workflow for the determination of the BBB permeability and a representative experimental result (NaFl: sodium fluoresceine; Gd: Gadoteric acid)

Program Contact

Nico Ruprecht

↗ nico.ruprecht@unibe.ch

↗ Link to Independent Lab

Selected Collaborators

Broekmann P. Department of Chemistry, Biochemistry and Pharmaceutical Sciences, University of Bern, Bern (CH)

Engelhardt B. Theodor Kocher Institute, University of Bern, Bern (CH)

Furrer J. Department of Chemistry, Biochemistry and Pharmaceutical Sciences, University of Bern, Bern (CH)

Hofmann L. Department of Chemistry, Faculty of Exact Sciences and Institute of Nanotechnology and Advanced Materials, Bar Ilan University Ramat-Gan (IL)

Schürch S. Department of Chemistry, Biochemistry and Pharmaceutical Sciences, University of Bern, Bern (CH)

Experimental Nephrology

About a tenth of the world's population has impaired kidney function. However, most people do not notice it, and the disease only becomes apparent as kidney function declines with age or because of other severe, more acute events. If left untreated, these often progress to chronic kidney disease (CDK), which in its final stages can only be treated with dialysis or organ transplantation, and is a major financial burden on the healthcare system. In the Experimental Nephrology lab, we study how to ameliorate acute kidney injury or prevent the transition to CKD. In addition to these injury-related kidney disease mechanisms, other foci of the lab include acid/base transporters and their influence on kidney stone formation, genetic kidney diseases (ADPKD), and the study of nephrotoxic side effects of immunosuppressants. Furthermore, the lab has recently focused on developing innovative tools for studying kidney regeneration. Overall, the main goals of the Experimental Nephrology Laboratory are to uncover the mechanisms underlying kidney disease and develop individualized treatment methods for women and men that protect against kidney damage and maintain kidney function in the long term.

Research Highlights 2023 / Outlook 2024

Contribution of acid/base transporters to human disease: Thiazides, which are widely prescribed diuretic drugs, are linked to glucose intolerance and new-onset diabetes with an unclear pathogenesis. In 2023, we published our recent findings demonstrating that thiazides attenuate insulin secretion in pancreatic β-cells by inhibiting mitochondrial carbonic anhydrase (CA) type 5b. We furthermore discovered that pancreatic β-cells express only one functional CA isoform, CA5b, which exerts a critical function in replenishing the mitochondrial tricarboxylic acid cycle with oxaloacetate (anaplerosis). Together, our results offer a mechanistic explanation for thiazide-induced glucose intolerance, and reveal a fundamental role of CA5b in tricarboxylic acid cycle anaplerosis and insulin secretion in β-cells.).

Factors safeguarding kidney function: In collaboration with CSL Behring, we are currently investigating the tissue-protective functions of plasma glycoprotein fetuin-A, which attenuates the transition from acute to chronic kidney disease in mice. In 2024, we will conduct the PEAK study (PrEcision medicine) in the management of cardiovascular surgery-associated AKI, an investigator-initiated clinical prospective observational cohort study. Furthermore, in a French/Swiss collaboration, we will study how Maged-d2 protects the kidneys against ER stress and hypoxia.

Novel tissue sorting method for nephron segment: We developed a simple, straightforward, inexpensive, and widely applicable research tool using fluorophore-labeled lectins that yielded large amounts of pure and morphologically intact renal tubules. In 2024, we will use this method as a basis for establishing innovative 3D cultures of sorted nephron segments, with the long-term aim of promoting drug screening and renal regenerative research.

Selected Publications

Kucharczyk P, Albano G, Deisl C, Ho TM, Bargagli M, Anderegg M, Wueest S, Konrad D, Fuster DG (2023). ↗ *Thiazides Attenuate Insulin Secretion Through Inhibition of Mitochondrial Carbonic Anhydrase 5b in β-Islet Cells in Mice*. J Am Soc Nephrol. Jul 1;34(7), pp. 1179-1190. ↗ 10.1681/ASN.0000000000000122

Roskosch J, Huynh-Do U, Rudloff S (2024). ↗ *Lectin-mediated, time-efficient, and high-yield sorting of different morphologically intact nephron segments*. Pflügers Archiv – European Journal of Physiology 476(3), pp.379-393. ↗ 10.1007/s00424-023-02894-w [Epub 2023/12/13]

Rudloff S, Jahnen-Dechent W, Huynh-Do U (2022). ↗ *Tissue chaperoning-the expanded functions of fetuin-A beyond inhibition of systemic calcification*. Pflügers Archiv – European Journal of Physiology, 474(8), pp. 949-962. ↗ 10.1007/s00424-022-02688-6

Rudloff S, Janot M, Rodriguez S, Dessalle K, Jahnen-Dechent W, Huynh-Do U (2021). ↗ *Fetuin-A is a HIF target that safeguards tissue integrity during hypoxic stress*. Nature Communications 12(1), p. 549. ↗ 10.1038/s41467-020-20832-7

Ho TM, Berger S, Muller P, Simonin C, Reymond JL, Von Ballmoos C, Fuster DG (2022). ↗ *Physiological and Molecular Function of the Sodium/Hydrogen Exchanger NHA2 (SLC9B2)*. CHIMIA, 76(12), pp. 1019-1024. ↗ 10.2533/chimia.2022.1019

Program Contact

Prof. Dr. Daniel Fuster
↗ daniel.fuster@unibe.ch
Prof. Dr. Uyen Huynh-Do
↗ uyen.huynh-do@insel.ch
Prof. Dr. Daniel Sidler
↗ daniel.sidler@insel.ch

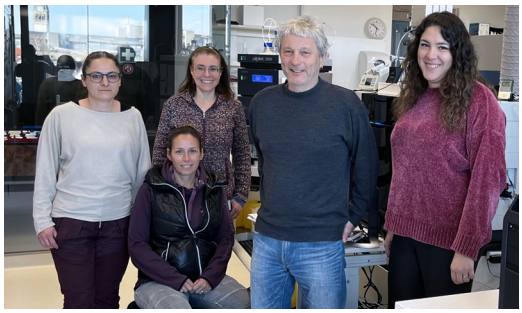
↗ Link to Independent Lab

Selected Collaborators

von Ballmoos C. University of Bern. Bern (CH)
Drew D. Stockholm University, Stockholm (SE)
Laghmani K. Sorbonne University, Paris (FR)
Jahnen-Dechent W. Rheinisch-Westfälische Technical University Aachen (RWTH), Aachen (DE)
Moe O. UT Southwestern Medical Center, Dallas, TX (US)

Technology Core Facilities

Proteomics & Mass Spectrometry (PMS CF)



Achievements 2023

Our services have experienced a noticeable surge in demand. In February, we successfully launched a second Bruker timsTOF system accompanied by a newly designed nano-ultra-performance liquid chromatography (UPLC) system. Challenges emerged with the nano-UPLC, leading to unforeseen issues, which were resolved in the fall with the support of Bruker. We introduced the new instrument for the production of advanced blood plasma proteomic workflows. High-pH reverse-phase fractionation was implemented on the MAP BRAVO robot, and a streamlined pipeline was established for the isolation and validation of immunopeptides bound to MHC-I complexes.

Performance report 2023

We processed 1983 samples submitted by laboratories from the Faculty of Medicine (59.5 %), Faculty of Science (15.7 %), Vetsuisse Faculty (21.4 %), and external institutions (3.4 %), resulting in a total injection count of 9258 nano-LC-MS/MS runs, including publishable data, development, QC, and blanks, which relate to approximately 8030 hours of machine time (335 days).

Outlook 2024

We are in the process of securing finances to replace an instrument that turns 10 this year. The development of single-cell proteomics is being planned.

Publications

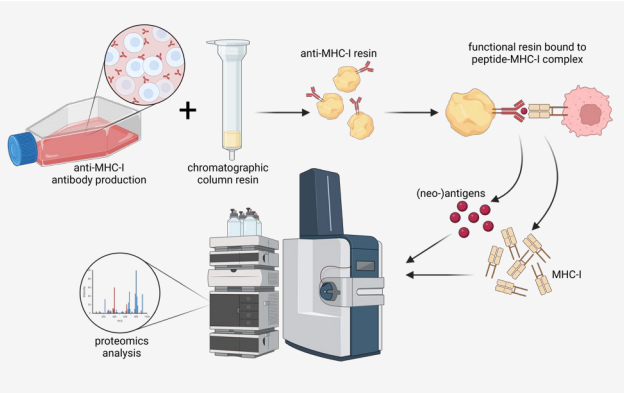
Hänggeli KPA, Hemphill A, Muller N, Heller M, Uldry AC, Braga-Lagache S, Muller J, Boubaker G. (2023). ↗ *Comparative Proteomic Analysis of Toxoplasma gondii RH Wild-Type and Four SRS29B (SAG1) Knock-Out Clones Reveals Significant Differences between Individual Strains*. International Journal of Molecular Sciences, 24(13), p. 10454. ↗ 10.3390/ijms241310454

Pilotto F, Douthwaite C, Diab R, Ye X, Al Qassab Z, Tietje C, Mounassir M, Odriozola A, Thapa A, Buijsen RAM, Lagache S, Uldry AC, Heller M, Muller S, van Roon-Mom WMC, Zuber B, Liebscher S, Saxena S (2023). ↗ *Early molecular layer interneuron hyperactivity triggers Purkinje neuron degeneration in SCA1*. Neuron, 111(16), pp. 2523-2543.e10. ↗ 10.1016/j.neuron.2023.05.016

Müller J, Preza M, Kaethner M, Rufener R, Braga S, Uldry AC, Heller M, Lundstrom-Stadelmann B (2023). ↗ *Targeted and non-targeted proteomics to characterize the parasite proteins of Echinococcus multilocularis metacestodes*. Frontiers in Cellular and Infection Microbiology, 13, p. 1170763. ↗ 10.3389/fcimb.2023.1170763

Nasif S, Colombo M, Uldry AC, Schroder MS, de Brot S, Mühlemann O (2023). ↗ *Inhibition of nonsense-mediated mRNA decay reduces the tumorigenicity of human fibrosarcoma cells*. NAR Cancer, 5(3), zcad048. ↗ 10.1093/narcan/zcad048

Timpanaro A, Piccand C, Uldry AC, Bode PK, Dzhumashev D, Sala R, Heller M, Rössler J, Bernasconi M (2023). ↗ *Surfaceome Profiling of Cell Lines and Patient-Derived Xenografts Confirm FGFR4, NCAM1, CD276, and Highlight AGRL2, JAM3, and L1CAM as Surface Targets for Rhabdomyosarcoma*. International Journal of Molecular Sciences, 24(3), p. 2601 ↗ 10.3390/ijms24032601



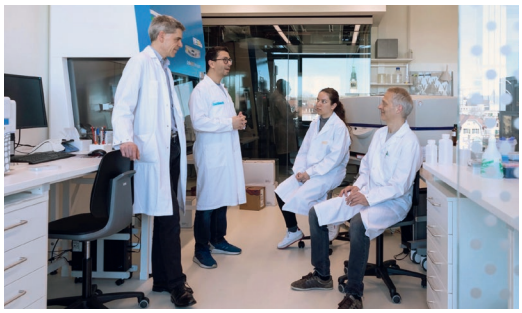
Pipeline for the isolation and identification of MHC-I bound immunopeptides

Head of PMS Core Facility
Prof. Dr. phil. nat. Manfred Heller
↗ manfred.heller@unibe.ch
↗ Link to Core Facility

Core Facility Members

Anne-Christine Uldry PhD, Computational Scientist
Sophie Braga Lagache MSc, Senior Assistant
Natasha Buchs Laboratory Assistant
Alexandra Emanuela Burger MSc, PhD student
Giselle Franca Oliveira visiting fellow, PhD student (Sep.-Dec.)

Flow Cytometry and Cell Sorting (FCCS)



Achievements 2023

Our application to purchase a BD FACS Discover S8 with a CellView cell sorter has been approved and the instrument was installed in December. Its image-supported sorting decisions expand the power of cell analysis and sorting into new dimensions by combining spectral flow cytometry with real-time spatial and morphological insights.

Bundled with the S8 and in cooperation with the next-generation sequencing platform, the BD Rhapsody Single Cell Analysis System was purchased and installed in the Biomedical Genomics CF of the DBMR. The BD Rhapsody system allows visual inspection during the processing of single cells to cDNA and represents a very useful alternative to the established 10X system, especially for delicate cell types such as granulocytes.

The long-awaited upgrade of our imaging flow cytometer, ImageStreamX Mk II, has also been approved, and our instrument was upgraded with a 2nd camera and a 96-well auto-loader. With two cameras, both of which now have high gain capability for improved measurements of extracellular vesicles, there is now, apart from additional channels, greater flexibility for designing staining panels.

Viorel Walther, our BMA-student in 2023, successfully established Fluorescence In Situ Hybridization in flow (Flow-FISH) on the ImageStreamX Mk II.

Lorenzo Raeli regrettably left the team, but the FCCS CF was lucky to hire, with Janine Bögli, an equally experienced person, instead.

Performance report 2023

2023 saw a small increase in demand of our services compared to 2022. Self-operated measurements on our instruments increased by 0.8 % and, with a total of 4838.6 hours, reached the second highest usage after 2018 (5104.9 hrs).

Cell sorting services increased by 2.2 % (1639.6 hrs) compared to 2022 (1605.0 hrs). This is 25 % below the maximum observed in 2018 (2182.0 hrs).

Self-operated measurements were performed at 75.7% by researchers from Inselspital clinics and 24.3% by institutes at the University of Bern. Measurements by external parties comprise 0.04 %.

89.2 % of cell sorting were performed for Inselspital clinics and 10.3 % for institutes at the University of Bern, while 0.5 % were performed for external parties.

78.1 % of the measurements and 93.2 % of cell sorting were performed by or for DBMR groups.

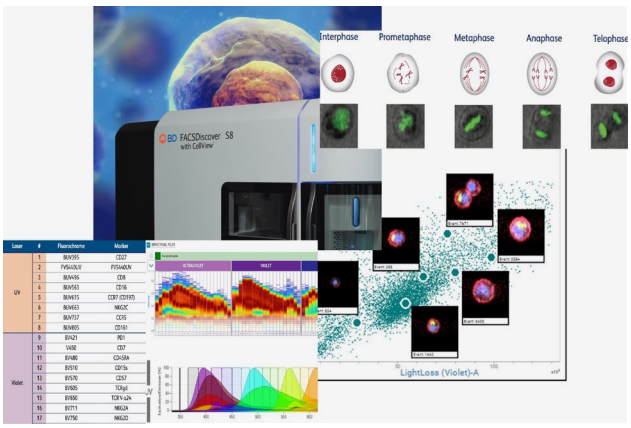
Outlook 2024

After training the new cell sorter, we are currently promoting cell sorting with extended capabilities and improved QC.

A new BMA-student, Adena Lack, is establishing a protocol for single cell RNA sequencing with sorted human granulocytes, using the new cell sorter and the Rhapsody system.

A new round of our FACS course has begun and we expect two more rounds in the course of 2024.

A collaboration with the Proteomics and Mass Spectrometry CF to establish single-cell proteomic measurements is planned.



BD FACSDiscover S8 with CellView technology

Head of FCCS Core Facility

Dr. phil. nat. Stefan Müller, PhD

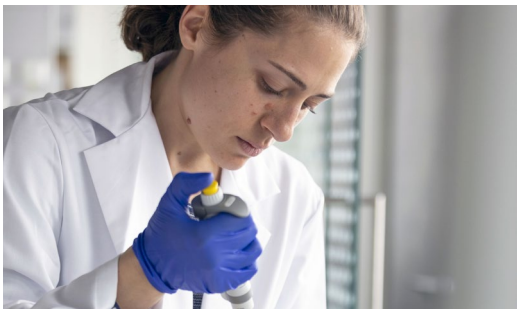
↗ stefan.mueller@unibe.ch

↗ Link to Core Facility

Core Facility Members

Dr. Thomas Schaffer PhD
Dr. Lorenzo Raeli PhD (until Aug.)
Dr. Fiona Appiah PhD
Janine Bögli, MSc (since Aug.)
Dr. Malgorzata Sobota, PhD (since Apr.)

Biomedical Genomics (BMG)



Achievements 2023

In spring 2023, we were able to test a NanoDrop One and DeNovix spectrophotometer in parallel. A DeNovix DS-11 FX was then purchased, which contains a spectrophotometer and a fluorometer for nucleic acid and protein quantification in one device.

In addition, a new QuantStudio Absolute Q digital PCR System was installed in the BMG post PCR lab and started operation. This dPCR system is based on microfluidic array plate technology and performs all the dPCR steps, from compartmentalization and thermal cycling to data acquisition, on a single instrument.

The BMG core facility was involved in organizing a seminar about PCR vs. NGS by Thermo Fisher and one about the MGI sequencing technology by Witec.

Performance report 2023

The total number of hours booked for using qPCR instruments (ViiA7 and QuantStudio) amounted to 1030 in 2023 and the BMG staff gave 33 introductions on PCR and QC instruments. Furthermore, a digital PCR training course by Thermo Fisher was organized for the new QuantStudio Absolute Q, which was attended by members from various labs. Additionally, we provided some technical support for gene expression and targeted sequencing projects.

Outlook 2024

We are looking forward to giving more introductory trainings for instruments and supporting projects.

Selected Publications

Gallon J, Rodriguez-Calero A, Benjak A, Akhoundova D, Maletti S, Amstutz U, Hewer E, Genitsch V, Fleischmann A, Rushing EJ, Grobholz R, Fischer I, Jochum W, Cathomas G, Osunkoya AO, Bubendorf L, Moch H, Thalmann G, Feng FY, Gillessen S, Ng CKY, Rubin MA, Piscuoglio S (2023). ↗ *DNA methylation landscapes of prostate cancer brain metastasis are shaped by early driver genetic alterations*. Cancer Research, 83(8), pp. 1203-1213. The American Association for Cancer Research AACR ↗ 10.1158/0008-5472.CAN-22-2236

Head of BMG Core Facility
Prof. Dr. phil. nat. Ursula Amstutz
↗ ursula.amstutz@insel.ch
↗ Link to Core Facility

Core Facility Members
Sina Maletti Lab Manager

Live Cell Imaging (LCI)

Achievements 2023

After receiving generous financial support from the Faculty of Medicine in early 2023, LCI coordinated the purchase, installation, and usage of new histology equipment to allow researchers of the DBMR the access to perform complete state-of-the-art histology at Murtenstrasse 24 and Murtenstrasse 35. Following new instruments are available (reservation via OpenIris after introduction training): Two embedding stations, four microtomes, two cryostats, and an automated infiltration system.

Performance report 2023

The total booked hours for using LCI equipment decreased to 5259 in 2023 (8475 in 2022). These do not include systems, which have to be booked on a daily basis, such as the Incucyte microscopes. In 2023, the LCI staff spent a total of 128 hours for introduction training on LCI microscopes (131 hours in 2022). Working hours spent collaborating with research groups from the DBMR and other institutes increased slightly to 329 (307 hours in 2022). During this period, the LCI supported students from a 29 individual research groups. The number of hours spent on technical assistance declined to 143 (2022:262). Like every year, the Facility contributed to the advanced microscopy lectures and practical modules organized with the MIC. More than 20 students were trained in practical modules with the involvement of LCI in 2023.

Outlook 2024

In 2024, the LCI will finalize the installation and coordination of new histology equipment at Mu24 and Mu35 and continue to focus on the improvement of its digital infrastructure, such as a network-based data storage and digital archive for common protocols for imaging and histology.

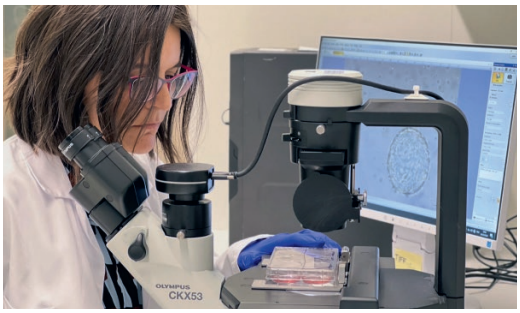
Publications

Seyran M, Melanie S, Philip S, Amiq G, Fabian B (2023). ↗ *Allies or enemies? The effect of regulatory T cells and related T lymphocytes on the profibrotic environment in bleomycin-injured lung mouse models*. Clinical and Experimental Medicine, 23(4), pp. 1075-1088. Springer ↗ 10.1007/s10238-022-00945-7

Head of LCI Core Facility
PD. Dr. phil. nat. Fabian Blank
↗ fabian.blank@unibe.ch
↗ Link to Core Facility

Core Facility Members
Carlos Wotzkow Lab Technician
Selina Steiner Lab Technician

Translational Organoid Resource (TOR)



Achievements 2023

The CORE has been set up at a new location. A state-of-the-art CQ1 confocal microscope with a live imaging option has been acquired, and the automated pipetting robot Assist Plus has been acquired and installed. The CORE has acquired a W8 for organoid mass imaging.

Performance report 2023

The Translational Organoid Resource (TOR) core is committed to streamlining the accessibility, creation, storage, and application of organoids and primary cells sourced from patients and model organisms. Startup quality checks for the protocol were performed. Within the domain of cancer research, TOR has dedicated efforts to produce and examine organoids from various cancer types, such as pancreatic, bladder, prostate, colon, and more, with the intent of employing these as preclinical models across diverse experimental scenarios. As part of a clinical feasibility trial in partnership with the Hirslanden Clinic in Zurich, TOR has successfully developed patient-derived pancreatic ductal adenocarcinoma (PDAC) organoids that have undergone preliminary assessments of their response to therapeutic interventions and are poised for utilization within the framework of several projects.

TOR is currently involved in the GAIN-INST Phase II trial, a collaboration with the Urology Department of the Spitalzentrum in Biel (Central Hospital in Biel), which uses non-muscle invasive bladder cancer patient-derived organoids to screen the standard of care treatments and select the most effective treatment for the patient.

In collaboration with the Ophthalmology Department at the Inselspital in Bern, TOR is working on culturing human ipSC-derived retina organoids.

Outlook 2024

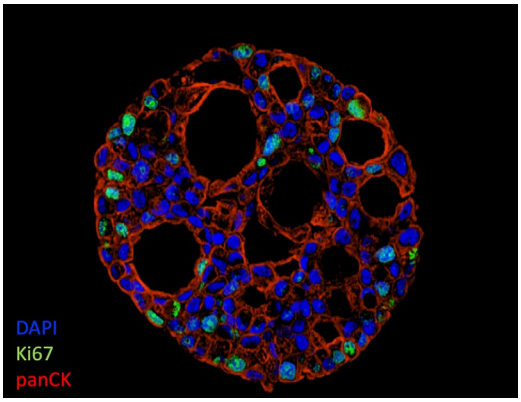
The CORE will expand and initiate funded projects.

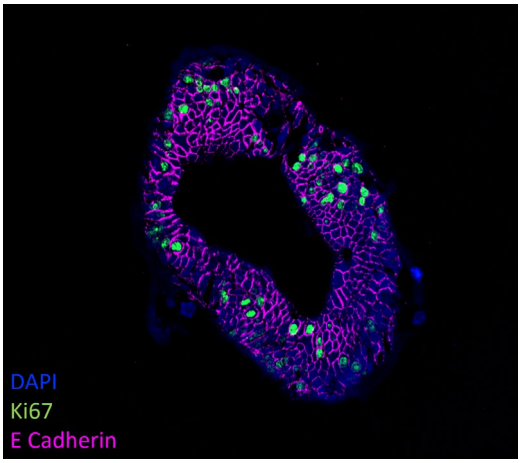
Publications

Karkampouna S, La Manna F, Benjak A, Kiener M, De Menna M, Zoni E, Grosjean J, Klima I, Garofoli A, Bolis M, Vallerga A, Theurillat JP, De Filippo MR, Genitsch V, Keller D, Booij TH, Stirnimann CU, Eng K, Sboner A, Ng CKY, Piscuoglio S, Gray PC, Spahn M, Rubin MA, Thalmann GN, Kruithof-de Julio M (2021). ↗ *Patient-derived xenografts and organoids model therapy response in prostate cancer.* Nature Communications., 12(1), p.1117 ↗ 10.1038/s41467-021-21300-6

Kiener M, Roldan N, Machahua C, Sengupta A, Geiser T, Guenat OT, Funke-Chambour M, Hobi N, Kruithof-de Julio M (2021). ↗ *Human-Based Advanced in vitro Approaches to Investigate Lung Fibrosis and Pulmonary Effects of COVID-19*. Frontiers in Medicine, 8(644678), p. 644678. ↗ 10.3389/fmed.2021.644678

Seiler R, Egger M, De Menna M, Wehrli S, Minoli M, Radic M, Lyatoshinsky P, Hosli R, Blarer J, Abt D, Kruithof-de Julio M (2023). ↗ *Guidance of adjuvant instillation in intermediate-risk non-muscle invasive bladder cancer by drug screens in patient derived organoids: a single center, open-label, phase II trial*. BMC Urology, 23(1), p. 89. ↗ 10.1186/s12894-023-01262-1





Patient Derived Organoid

Head of FCCS Core Facility
Prof. Dr. Marianna Kruithof-de Julio
↗ marianna.kruithofdejulio@unibe.ch

Core Facility Members
Dr. Marta De Menna Deputy Director
Dr. Sofia Karkampouna Affiliated member
Dr. Panagiotis Chouvardas Affiliated member
Dr. Federico La Manna Affiliated member

Johanna Dürmüller-Bol DBMR Research Award

Bio-sketch

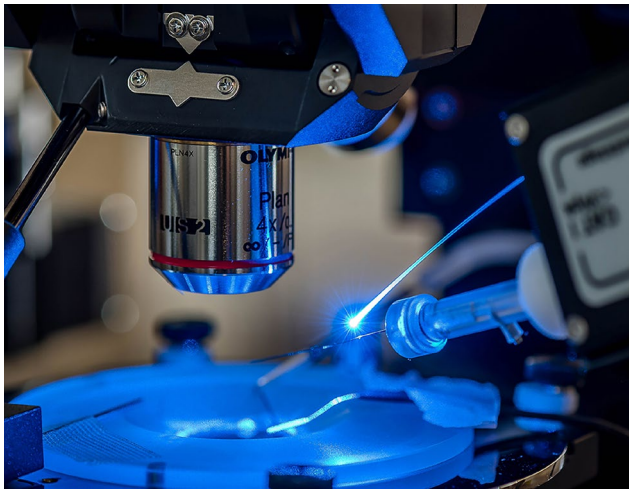
Dr. Mattia Aime

PhD in Neurosciences at the University of Bordeaux (France) (2017). Since 2018 Postdoctoral Researcher at the University of Bern in the Lab of Prof. Adamantidis (Zentrum für Experimentelle Neurologie).

Project summary and outlook 2024

Rapid eye movement (REM) sleep is a critical sleep stage, characterized by vivid dreams and high emotional content. Over the years, researchers have been intrigued by the relationship between REM sleep and emotions. During this sleep state, the brain processes emotional experiences, consolidates associated memories, and eliminates negative emotions linked to traumatic events. Additionally, the amygdala, a brain region associated with emotional processing, is highly active during REM sleep. Abnormalities in REM sleep have been linked to several psychiatric disorders, such as depression, anxiety, and post-traumatic stress disorder (PTSD). Hence, understanding the link between REM sleep and emotions is of great interest and relevant to understanding the worldwide prevalence of this neuropsychiatric condition.

Building upon these findings, the preliminary results of this project revealed that during REM sleep, long-range projections from the amygdala instruct the prefrontal cortex, a region with high cognitive functions, about the emotional valence of events encountered during the day. This mechanism is orchestrated by the basal forebrain, a region involved in sleep regulation that is highly active during REM sleep. In the next steps, I will investigate how amygdala neurons adapt their activity during REM sleep and store emotional information before transferring it to the prefrontal cortex.



A technique called Optogenetics can be used to study brain activity during REM sleep". Credits: @Pascal Gugler, InselGruppe.

Selected Publications

Aime M (2023). ↗ *To "feel" better, sleep on it!* Science, 382(6670), p. 528. ↗ 10.1126/science.adk3894

Aime M, Calcini N, Borsa M, Campelo T, Rusterholz T, Sattin A, Fellin T, Adamantidis A (2022). *Paradoxical somatodendritic decoupling supports cortical plasticity during REM sleep*. Science, 376(6594):724-730. ↗ 10.1126/science.abk2734

Aime M, Calcini N, Borsa M, Campelo T, Rusterholz T, Sattin A, Fellin T, Adamantidis A (2022). ↗ *Paradoxical somatodendritic decoupling supports cortical plasticity during REM sleep*. Science, 376(6594), pp. 724-730. ↗ 10.1126/science.abk2734

Contact

Dr. Mattia Aime

↗ mattia.aime@unibe.ch

↗ ZEN/DBMR-Neuro, Department for BioMedical Research, University of Bern

↗ Experimental Neurology Center (ZEN), Department of Neurology, Inselspital, Bern University Hospital

Supervisor

Prof. Antoine Adamantidis PhD

↗ Link to the lab

Selected Collaborators

Fellin T. Italian Institute of Technology, Genova (IT)

Tzovara A. University of Bern, Bern (CH)

Key Events

Study Week Biology & Medicine

In collaboration with the Swiss Youth in Science, the DBMR hosted 8 high school and vocational students from Switzerland for the Swiss Study Week of Biology and Medicine, March 13 – 17, 2023. During the week, students had the chance to gain insight into the real research environment in the fields of biology and medicine.

TOR Symposium

The recently established Translational Organoid Resource (TOR) Core Facility organized its first symposium in May 2023, with Professor Matthias Lütolf, Scientific Director of the Roche Institute for Translational Bioengineering, Basel, and Professor Helmuth Gehart, Department of Biology, ETH Zurich, as keynote speakers. Other highlights included the announcement of the three winners of the TOR-DBMR Best Organoid Picture Awards: Arnal Fahmi and Isabel Schultze-Pernice (Institute of Virology and Immunology), Dr. Martin Sadowski (Experimental Pathology), and Jan Schulte (ARTORG Center).

DBMR Research Conference 2023

6 February 2023
Prof. François R. Jornayvaz, MD
Department of Endocrinology, Diabetes, Nutrition and Therapeutic Patient Education, Geneva University Hospital (CH)
"NAFLD and insulin resistance: from bench to bedside"

6 March 2023
Prof. Mauricio Rojas, MD
Department of Internal Medicine, The Ohio State University (USA)
"Making sense of senescence in aging"

3 April 2023
Prof. Chantal Pauli, MD
Department of Pathology and Molecular Pathology, University of Zurich (CH)
"Patient – derived EX Vivo Models for Functional Tumor Profiling"

1 May 2023
Prof. Dr. Joel Zindel – The Awardee of the Johanna Dürmüller – Bol DBMR Research Award 2021
Visceral and Transplantation Surgery (DBMR) and Department of Visceral Surgery and Medicine, Inselspital (CH)
"Immune-Mediated Methothelial Cell Recruitment in Serosal Repair"

5 June 2023
Prof. Dr. Jerome Guicheux
The Regenerative Medicine and Skeleton Research, ISERM & Nantes University Hospital (FR)
"4R medicine for diseased joints: Replace, Repair, Regenerate & Reprogram"

2 October 2023
Prof. Maria Luz Martinez Chantar, PhD
Professor University of Deusto, School of Medicine, CIC bioGUNE CIBERehd – Spanish Carlos III Health Institute (ES)
"Searching for New Mechanisms of Liver Disease with Therapeutic Potential. Is Magnesium a New Hepatic Player?"

6 November 2023
Jacco van Rheenen, PhD
Group leader Intravital Cancer Imaging Professor Intravital Microscopy, Molecular Pathology, Netherlands (NL) Cancer Institute and Oncode Institute
"Filming the fate of cells that carry mutations in oncogenic driver genes"

Day of BioMedical Research, Wednesday, July 5, 2023

Highlights of the event included the lecture of the keynote speaker Prof. Hans Clevers, Head of pharma Research & Early Development (pRED), Roche, and the announcement of several Poster Prizes, of the Best DBMR Publication 2022, and of Dr. Mattia Aime as the winner of the Johanna Dürmüller-Bol DBMR Research Award 2023 for his project on investigating the impacts of REM sleep and emotions on quality of life. Additionally, the DBMR Best Innovative Research Idea Prize was presented for the first time.

Johanna Dürmüller-Bol Research Award 2023

Mattia Aime, PhD
Department for BioMedical Research, University of Bern
Department of Neurology, Inselspital, Bern University Hospital
"REM sleep and emotions: the missing link for a better life quality"

Poster Prizes of the Day of BioMedical Research 2023

Best Preclinical Project
Fabian Luther
Department of Dermatology, Inselspital, Bern University Hospital, University of Bern
"PPAR-γ regulates the effector function of human TH9 cells by promoting glycolysis"

Best Clinical Project
Matteo Bargagli
Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern
"Selective V2 vasopressin receptor blockade with tolvaptan increases urinary exosome pendrin expression in patients with Autosomal Dominant Polycystic Kidney Disease"

Best Medical Project of a Medical Student
Nick Kirschke
Institute of Anatomy, University of Bern
"Influence of macronutrients on heart regeneration in zebrafish"

Research Prize Alumni MedBern 2023

Nic Krummenacher
Gerontechnology & Rehabilitation Group, ARTORG Center for Biomedical Engineering Research, University of Bern
"Validation of the usability of a new interactive and sensor-based hand trainer, the Smart Sensor Egg, for training hand coordination and dexterity"

SCRM Poster Prize for Best Stem Cell Project 2023

Ines de Paula Costa Monteiro
Tumor Immunology, Department for BioMedical Research, University of Bern
Department of Medical Oncology, Inselspital, Bern University Hospital
"Role of ILC2s in the regulation of colorectal cancer stem cells"

DBMR Prize for Innovative Research Idea 2023

Christa König
Division of Pediatric Hematology/ Oncology, Department of Pediatrics Inselspital, Bern University Hospital
"When time matters: Association of time to antibiotics (TTA) with outcome in children undergoing chemotherapy for cancer with fever in neutropenia (FN) – an international individual patient data (IPD) Meta-analysis"

Federico La Manna
Department for BioMedical Research, University of Bern
"A cross-omic toolkit to approach residual disease in prostate cancer"

Mattia Aime
Department for BioMedical Research, University of Bern
Department of Neurology, Inselspital, Bern University Hospital
"REM sleep and emotions: the missing link for a better life quality"

Prize for Best DBMR Publication 2022

Dr. Jakob Zimmermann
Systems Biomedicine of Cellular Development and Signaling in Health and Disease, Department for BioMedical Research
"Noninvasive assessment of gut function using transcriptional recording sentinel cells"
Published on 05.2022, Science

Benoit Pochon Prize 2022

Dr. Jana Remlinger
Supervisor: PD Dr. med. Anke Salmen, Co-advisor Prof. Dr. Volker Enzmann.
"Investigation of Antibody-driven Central Nervous System Autoimmunity with Focus on Involvement of the Visual Pathway"

Personnel Update

Academic Degrees

Full Professor

Prof. Dr. med. Annalisa Berzigotti
Systems Biomedicine of Cellular Development and Signaling in Health and Disease

PhD (Supervisor in parentheses)

Chantal Lea Bachmann, PhD in Immunology, (Prof. Dr. med. Adrian Ochsenbein)
"Immune-Checkpoints in the Regulation of Leukemia and Cancer Stem Cells"

Ida Luisa Boccalaro, PhD in Neurosciences, (Prof. Dr. Antoine Roger Adamantidis)
"A role for the medio-dorsal thalamus in sensory discrimination during sleep"

Andreas Shaun Croft, PhD in Biomedical Sciences, (Prof. Dr. Benjamin Gantenbein)
"Fibre-based 3D silk fibroin scaffolds for intervertebral disc regeneration"

Murielle Koni-Kepo Golomingi, PhD in Biomedical Sciences, (Prof. Dr. Verena Schröder)
"Interactions between the complement system and Blood coagulation: a potential role of complement Components and activation during haemostasis"

Martin Gonzalez Fernandez,
PhD in Biochemistry and Molecular Biology, (Prof. Dr. Sven Rottenberg)
Charting the Chemogenetic Landscape of Taxane Response in BRCA1-Deficient Mammary Tumors"

Pascal Martin Guntern, PhD in Immunology, (Prof. Dr. Alexander Eggel)
"Assessment of multifunctional anti-IgE molecules and their modes of action for the treatment of allergic disorders"

Lusine Hovhannisyan, PhD in Biomedical Sciences, (Prof. Dr. Yitzhak Zimmer)
"Combining Radiation with MET-targeted CAR T-cell Therapy for Enhanced Glioblastoma Treatment"

Cristina Lisa Kalbermatter, PhD in Immunology (Prof. Andrew Macpherson, Prof. Dr. Stephanie Chrisitne Ganal-Vonarburg)
"The role of maternal microbiota in shaping intestinal immunity and gene expression in the offspring through epigenetic mechanisms"

Harpreet Kaur Mandhair, PhD in Biomedical Sciences, (Prof. Dr. Urban Novak)
"Subtype-specific role of autophagy associated protein ULK1 in Diffuse Large B-cell Lymphomas"

Martina Minoli, PhD in Biomedical Sciences, (Prof. Dr. Roland Seiler Blarer, Prof. Dr. Marianna Kruithof-de Julio)
"Developing new Tools for Precision Medicine in Bladder Cancer"

Carmen Muñoz Maldonado, PhD in Cell Biology, (PD Dr. Michaela Medova)
"Understanding the DNA damage response and uncovering synthetic interactions in CHK2-deficient cancers"

Anastasia Milusev, PhD in Biomedical Sciences, (Prof. Dr. Robert Rieben, Dr. Nicoletta Sorvillo)
"Distinct arterial and venous glycocalyx dynamics impact endothelial function"

Seyran Mathilde Mutlu, PhD in Biomedical Sciences (April 26), (PD. Dr. Fabian Blank and PD. Dr. med. Amiq Gazdhar)
"Adoptive transfer of HGF overexpressing T cells as a potential therapeutic approach in the bleomycin injured mouse lung"

Damian Tobias Nydegger, PhD in Biochemistry and Molecular Biology, (Prof. Dr. Matthias Hediger)
"The impact of amino acid transporters in diseases: COVID-19 and Colon cancer"

Kevin Plattner, PhD in Immunology, (Prof. Monique Vogel)
"On the role of IgE glycosylation in the protection against anaphylaxis by IgG anti-IgE antibodies"

Rudy Rizzo, PhD in Biomedical Engineering, (Prof. Dr. Roland Kreis)
"Multiparametric MR Spectroscopy: evaluation of quantitative frameworks based on modeling and deep learning"

Bianca Viberti, PhD in Neuroscience, (PD Dr. Markus Helmut Schmidt)
"The role of MCH neurons in gating REM sleep and cataplexy in narcolepsy"

Simon Zinkhan, PhD in Immunology, (Prof. Dr. Monique Vogel)
"On the role of antigen conformation in the regulation of immune responses and allergic disease"

MD, PhD (Supervisor in parentheses)

Juening Kang, MD PhD, (Prof. Dr. Marianna Kruithof-de Julio, Dr. Sofia Karkampouna)
"Identifying drug sensitivity of multifocal primary prostate cancer towards personalized screens and treatment decision"

Sonia Selicean, MD PhD, (Prof. Dr. med. Annalisa Berzigotti, Dr. Jordi Gracia-Sancho)
"Role of the stiffness-derived molecular axis in liver cirrhosis and portal hypertension"

Cong Wang, MD PhD, (Prof. Dr. med.Annalisa Berzigotti, Dr. med. Jordi Sergio Gracia Sancho)
"Role of liver stiffness in the pathophysiology of portal hypertension"

Liang Zhao, MD PhD, (Prof. Dr. med. Ralph Schmid, Prof. Dr. Ren-Wang Peng)
"A non-canonical function of LDHB promotes glutathione metabolism and protects against ferroptosis in KRAS-driven lung cancer"

Staff Changes

New Staff

Martine Kaufmann, Secretary
DBMR Secretaries (since Feb.)

Jasmine Brühlmann, Secretary
DBMR Secretaries (since May.)

Klaus Ferro, House Staff
Technical Services & House Staff (since Aug.)

Lisa Conrad, PhD, Osterwalder Lab
Cardiovascular Diseases (since May)

Pragya Nagar, Functional Urology
PhD Student (since May)

Chaimae Bahou, Functional Urology
PhD Student (since May)

Resignation

Alina Naveed, Cancer Therapy Resistance
Postdoc (until Feb)

Alison Ferguson, Cancer Therapy Resistance
Postdoc (until Jun)

Gabriele Chiffi, Cardiovascular Diseases
Early Postdoc (until Mar)

Jianfang Ren, Cardiovascular Diseases
PhD Student (until Aug)

Valentina Zollet, Cardiovascular Diseases
PhD Student (until Oct)

Lei Zhang, Cardiovascular
MD Fellowship (until Apr)

Short Employment

Chiara Parodi, Cardiovascular Diseases
Vet. med. Internship (Jan – Dec)

Awards/Grants

PD. Dr. med. Patrick Dom
Co-PI: PD. Dr. Thomas Michael Marti
Oncology – Thoracic Malignancies
Stiftung zur Krebsbekämpfung (Foundation for flight against cancer)
"Malignant pleural mesothelioma: spatial RNA expression profile on the single cell level"

Prof. Dr. Ren-Wang Peng (PI)
Co-PIs: PD. Dr. med. Patrick Dorn, Prof. Dr. Erik Vassella (Institute of Tissue Medicine and Pathology, IGMP)
Oncology – Thoracic Malignancies
Bern Center for Precision Medicine (BCPM)
"Towards precision medicine for malignant pleural mesothelioma"

Prof. Dr. Ren-Wang Peng (PI)
Oncology – Thoracic Malignancies
Novartis Foundation for medical-biological Research
"Unlocking subtype-specific mechanisms to overcome heterogeneity and therapy resistance in KRAS-mutant lung adenocarcinoma"

PD. Dr. Thomas Michael Marti
Co-PI: PD. Dr. med. Patrick Dorn
Oncology – Thoracic Malignancies
Swiss National Science Foundation
"Modulate cellular plasticity and lactate metabolism to augment lung cancer therapy"

Prof. Dr. Katja Elisabeth Odening
Co-PIs: Christiane Zweier, Prof. Dr. Nadia Mercader, SNSF Assistant Prof. Marco Osterwalder
Prof. Dr. Jean-Louis Reymond
Cardiovascular Diseases
Bern Center for Precision Medicine (BCPM)-Lighthouse Project Award
"Precision Diagnosis and Therapy in Cardiac Channelopathies (PACE)"

SNSF Assistant Prof. Marco Osterwalder
Cardiovascular Diseases
Swiss National Science Foundation
Flexibility Grant (related to the NRP79 grant started in 2022)

Prof. Dr. Sarah Longnus
Collaborator: Manfred Heller
Cardiovascular Diseases
Swiss National Science Foundation
"Cardiac metabolism as a basis for sex differences in ischemic tolerance and a target for reperfusion therapy in heart transplantation with donation after circulatory death"

Prof. Dr. Mark A. Rubin
Cancer Therapy Resistance
Swiss Cancer Research
"Towards a novel theranostics approach for AR-negative castration-resistant prostate cancer"

Prof. Dr. Mark A. Rubin
Co- PI: Prof. Dr. Silke Sillessen Sommer (Institute of Oncology of Southern Switzerland)
Cancer Therapy Resistance
Fondation Recherche Cancer (ISREC)
"Novel therapies for PSMA non-eligible and non-responsive metastatic prostate cancer"

Prof. Dr. Mark A. Rubin
Cancer Therapy Resistance
US Department of Defense
"Defining the role of the SWI/SNF chromatin remodeling complex in advanced metastatic castration-resistant prostate cancer therapy resistance."

Prof. Dr. Marianna Kruithof-de Julio
Dr. Nina Hobi (AlveoliX)
Cancer Therapy Resistance
Innosuisse project
"iBloC: a ground-breaking translational bladder cancer-on-chip model to empower development of novel immune-oncology drugs"

Prof. Dr. Marianna Kruithof-de Julio, Dr. Sofia, Karkampouna, Dr. Panagiotis Chouvardas
Cancer Therapy Resistance
Wilheim Sander Foundation
"Identification of a spatial single-cell proteome atlas of bladder cancer to characterize disease heterogeneity by imaging mass cytometry"

Dr. med. Dilara Akhoundova
Cancer Therapy Resistance
Stiftung für klinisch-experimentelle Tumorforschung
(Foundation for Clinical-Experimental Cancer Research)
"Deciphering novel treatment strategies for DNA repair deficient prostate cancer"

Lea Lingg
Cancer Therapy Resistance
Best Poster Prize for poster on DNA repair at the International Wolfsberg Meeting on Molecular Radiation Biology/Oncology in Oslo.
"TAOK1 facilitates IR and PARPi response in BRCA1/2-deficient mammary tumors"

Dr. Federico La Manna
Cancer Therapy Resistance
Best Project on Prostate Cancer
4th Swiss SAKK Translational Urogenital Cancer Network Meeting
"A cross-omic toolkit to approach residual disease in prostate cancer"

Dr. med. Antonio Rodriguez Calero
Cancer Therapy Resistance
Benjamin Castleman Award 2023
Massachusetts General Hospital and United States and Canadian Academy of Pathology

Dr. Anke Augspach
Cancer Therapy Resistance
Artwork "Lineage plasticity" was selected for the collection of the 2023 edition
Promega Art Contest for Creative Scientists

Dr. Anastasia Milusev
Cardiovascular Diseases
AdipoGen Life Sciences Award
Best poster in the category cardiovascular biology at the LS2 meeting, Zurich
"Differential glycocalyx dynamics of arterial and venous endothelial
cells under inflammatory conditions"

Dr. Anastasia Milusev
Cardiovascular Diseases
Best flash presentation in the category fundamental research
Cardiovascular Research Cluster (CVRC)
Annual Meeting, Bern
"Arterial and venous endothelial cells show differential glycocalyx dynamics under inflammatory conditions"

Anaïs Yerly
Cardiovascular Diseases
Best Poster Prize for Fundamental Category
Cardiovascular Research Cluster (CVRC)
Annual Meeting, Bern
"Examining the role of ACKR3 expression on B cells in atherosclerosis"

Valentina Zollet
Cardiovascular Diseases
Life Sciences Award for the 2nd best oral presentation in the category cardiovascular biology
LS2 Cardiovascular Research Meeting 2023, Bern
"Elevated citrullinated fibrinogen delays fibrinolysis in a porcine model of limb ischemia reperfusion injury, contributing to the development of thrombo-inflammatory events"

Prof. Dr. Katia Odening, Prof. Dr. Sarah Longnus, Prof. Matthias Siepe
Cardiovascular Diseases
UniBE Strategic Funding Board Call
"Ex-vivo Heart Perfusion – Technology that innovates cardiac transplantation and precision therapies"

Nick Kirschke
Cardiovascular Diseases
Best Master Thesis by the Swiss Society of Anatomy, Histology and Embryology
"Influence of macronutrients on heart regeneration in zebrafish"

Emrush Rexhaj
Cardiovascular Diseases
Medical Personality in Switzerland
Albinfo Platform

Prof. Dr. Yvonne Döring
Cardiovascular Diseases
Outstanding Achievement Award 2023
Basic Cardiovascular Science Cluster of the European Society of Cardiology

PD Dr. rer. nat. Kerstin Klein
Co-PIs: Prof. Dr. med. Britta Maurer, Prof. Dr. med. Dr. nat. phil. Nasser Semmo, PD Dr. med. Urs Borner
Collaboration partner: PD Dr. Rémy Bruggmann
Lung Precision Medicine
UniBE Strategic Funding Board Call 2023
"Functional impact of environmental factors on Sjögren's syndrome and primary biliary cholangitis"

Prof. Dr. Andreina Schoeberlein
Regenerative Neuroscience
Co-PIs: Prof. Dr. Katia Monastyrskaya, PD Dr. Amiq Gazdhar, Prof. Dr. Deborah Stroka, Prof. Dr. Benjamin Gantenbein

Strategic Funding (SF) Board Medical Faculty, University of Bern
"Harnessing extracellular vesicles for cell-based therapies"

Prof. Dr. med. Annalisa Berzigotti
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Prof. Paola Luciani (Department of Chemistry, Biochemistry and Pharmaceutical Sciences)
UniBE ID Grants 2023
"Antifibrotic effects of phospholipid-based drug formulations in experimental liver cirrhosis"

Dr. Eric Felli
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
UniBE Initiator Grants 2023
"The myth of Argo in mechanobiology: Nuclear mechano-protective surveillance in liver fibrosis"

Dr. Yuly P. Mendoza
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
UniBE Protected Research Time Grant
"Role of Hippo signaling pathway in fibrosis regression of advanced chronic liver disease"

Prof. Dr. med. Joel Zindel
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Swiss National Foundation Starting Grant
"Macrophage Aggregation Control against Scarring (MACScar)"

Dr. Jakob Zimmermann
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Swiss National Foundation Starting Grant
"Engineered symbionts elucidate gut T-cell memory and its (dys)regulation"

Prof. Dr. Deborah Stroka
Co-PI: Prof. Daniel Candinas
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
SAMW (Swiss Academies of Arts and Sciences)
"Role of biliary microbiota in biliary injury and the development of cholangiopathy"

PD. Dr. Daniel Sanchez Taltavull
Co-PIs: Dr. Tess Brodie, Ass. Prof. Pilar Guerrero (Universidad Carlos III), Dr. Ruben Perez-Carrasco (Imperial College London).
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Krebsliga Bern (Cancer League Bern)
"Multidimensional imaging to identify the role of JunB and novel cell communities driving colorectal liver metastasis progression"

Dr. Nicolas Melin
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
UniBE Venture Fellowship
"Liver tumor-specific anti-CD47 therapy: Decreasing systemic toxicity, increasing therapeutic potential"

Dr. Felix Alexander Baier
Co-PI: Prof. Dr. Deborah Stroka
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Innosuisse
"CALDRE. Cholestasis And Liver Disease Resolved"

Dr. Felix Alexander Baier
Co-PI: Prof. Dr. Deborah Stroka
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Ruth and Arthur Scherbarth Foundation
"Selection and validation of a new therapeutic for the treatment of cholestatic liver diseases"

Prof. Ziad Al Nadhani
Prof. Thomas A. Lutz (University of Zurich)
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
Swiss National Foundation Sinergia
"Understanding the role of immuno-metabolic imprinting for sustainable weight loss"

Dr. med. Jordi Sebastian
Systems Biomedicine of Cellular Development and Signaling in Health and Disease
National MD-PhD Grants Program (Swiss Academy of Medical Sciences (SAMS))
"Metabolic dynamics of the small intestinal microbiota upon nutritional challenges"

Dr. med. Damian Bürgin
Translational Cancer Research
National MD-PhD Grants Program (Swiss Cancer Research (KFS))
"The functional role of CD93 in multiple myeloma"

Prof. Dr. Alexander Eggel
Translational Immunology & Lung Precision Medicine
Swiss National Foundation
"Multifunctional IgE inhibitors: Deciphering their therapeutic modes-of-action in allergic disease"

Prof. Dr. Antoine Adamantidis
Co-PIs: Ass. Prof. Athina Tzovara, PD Dr. Carolina Gutierrez Herrera
Collaborator: PD Dr. Markus Schmidt
ZEN/DBMR Neuroscience
Swiss National Foundation BRIDGE Discovery Grant
"Translational predictive tools for improved drug screening for insomnia"

Prof. Dr. Katia Monastyrskaya
Functional Urology
IRP – International Foundation for Research in Paraplegia
"Effect of early treatment with Onabotulinumtoxin A on the bladder function of patients with acute SCI in single cell resolution"

Publications

Ali S, Abrar M, Hussain I, Batool F, Raza RZ, Khatoon H, Zoia M, Visel A, Shubin NH, Osterwalder M, Abbasi AA (2023). *Identification of ancestral gnathostome Gli3 enhancers with activity in mammals.* Development, growth & differentiation, 66(1), pp. 75-88. 10.1111/dgd.12901

Akhoundova D, Francica P, Rottenberg S, Rubin MA (2024). *DNA Damage Response and Mismatch Repair Gene Defects in Advanced and Metastatic Prostate Cancer.* Advances in anatomic pathology, 31(2), pp. 61-69. 10.1097/PAP.0000000000000422 [Epub 2023/11/07]

Akshay A, Katoch M, Abedi M, Besic M, Shekarchizadeh N, Burkhard FC, Bigger-Allen A, Adam RM, Monastyrskaya K, Gheinani AH (2023). *SpheroScan: A User-Friendly Deep Learning Tool for Spheroid Image Analysis.* bioRxiv. 10.1101/2023.06.28.533479

Akshay A, Abedi M, Shekarchizadeh N, Burkhard FC, Katoch M, Bigger-Allen A, Adam RM, Monastyrskaya K, Gheinani AH (2023). *MLcps: machine learning cumulative performance score for classification problems.* GigaScience, 12. 10.1093/gigascience/giad108

Augspach A, Drake KD, Roma L, Qian E, Lee SR, Clarke D, Kumar S, Jaquet M, Gallon J, Bolis M, Triscott J, Galván JA, Chen Y, Thalmann GN, Kruithof-de Julio M, Theurillat J-PP, Wuchty S, Gerstein M, Piscuoglio S, Kanadia RN, Rubin MA (2023). *Minor intron splicing is critical for survival of lethal prostate cancer.* Molecular cell, 83(12), pp. 1983-2002.e11. 10.1016/j.molcel.2023.05.017

Benito-Villalvilla C, de la Rocha-Munoz A, Lopez-Abente J, Eggel A, Bottoli I, Severin T, Woisetschlager M, Palomares O (2023). *Ligelizumab impairs IgE-binding to plasmacytoid dendritic cells more potently than omalizumab and restores IFN-α production and FOXP3+ Treg generation.* Allergy, 78(4), pp. 1060-1072. 10.1111/all.15567

Brigger D, Guntern P, Jonsdottir HR, Pennington LF, Weber B, Taddeo A, Zimmer G, Leborgne NGF, Benarafa C, Jardetzky TS, Eggel A (2023). *Sex-specific differences in immune response to SARS-CoV-2 vaccination vanish with age.* Allergy, 78(6), pp. 1683-1686. 10.1111/all.15652

Deng H, Ge H, Dubey C, Losmanova T, Medova M, Konstantinidou G, Mutlu SM, Birrer FE, Brodie TM, Stroka D, Wang W, Peng RW, Dorn P, Marti TM (2023). *An optimized protocol for the generation and monitoring of conditional orthotopic lung cancer in the KP mouse model using an adeno-associated virus vector compatible with biosafety level 1.* Cancer Immunology, Immunotherapy, 2(12), pp. 4457-4470. 10.1007/s00262-023-03542-z

Esposito R, Lanzos A, Uroda T, Ramnarayanan S, Buchi I, Polidori T, Guillen-Ramirez H, Mihaljevic A, Merlin BM, Mela L, Zoni E, Hovhannisyan L, McCluggage F, Medo M, Basile G, Meise DF, Zwyssig S, Wenger C, Schwarz K, Vancura A, Bosch-Guiteras N, Andrades A, Tham AM, Roemmele M, Medina PP, Ochsenbein AF, Riether C, Kruithof-de Julio M, Zimmer Y, Medova M, Stroka D, Fox A, Johnson R. (2023). *Tumour mutations in long noncoding RNAs enhance cell fitness.* Nature communications, 14(1), p. 3342. 10.1038/s41467-023-39160-7

Felli E, Selicean S, Guixe-Muntet S, Wang C, Bosch J, Berzigotti A, Gracia-Sancho J. (2023). *Mechanobiology of portal hypertension.* JHEP reports, 5(11), p. 100869. 10.1016/j.jhepr.2023.100869

Ferguson CA, Firulli BA, Zoia M, Osterwalder M, Firulli AB (2024). *Identification and characterization of Hand2 upstream genomic enhancers active in developing stomach and limbs.* Developmental dynamics, 253(2), pp. 215-232. 10.1002/dvdy.646 [Epub 2023/08/08]

Gallon J, Rodriguez-Calero A, Benjak A, Akhoundova D, Maletti S, Amstutz U, Hewer E, Genitsch V, Fleischmann A, Rushing EJ, Grobholz R, Fischer I, Jochum W, Cathomas G, Osunkoya AO, Bubendorf L, Moch H, Thalmann G, Feng FY, Gillessen S, Ng CKY, Rubin MA, Piscuoglio S (2023). *DNA methylation landscapes of prostate cancer brain metastasis are shaped by early driver genetic alterations.* Cancer research, 83(8), pp. 1203-1213. 10.1158/0008-5472.CAN-22-2236

Jakob MO, Spari D, Sanchez Taltavull D, Salm L, Yilmaz B, Doucet Ladeveze R, Mooser C, Pereyra D, Ouyang Y, Schmidt T, Mattiola I, Starlinger P, Stroka D, Tschan F, Candinas D, Gasteiger G, Klose CSN, Diefenbach A, Gomez de Aguero M, Beldi G (2023). *ILC3s restrict the dissemination of intestinal bacteria to safeguard liver regeneration after surgery.* Cell reports, 42(3), p. 112269. 10.1016/j.celrep.2023.112269

Koch JP, Roth SM, Quintin A, Gavini J, Orlando E, Riedo R, Pozzato C, Hayrapetyan L, Aebersold R, Stroka DM, Aebersold DM, Medo M, Zimmer Y, Medova M (2023). *A DNA-PK phosphorylation site on MET regulates its signaling interface with the DNA damage response.* Oncogene, 42(26), pp. 2113-2125. 10.1038/s41388-023-02714-6

Loste A, Clement M, Delbosc S, Guedj K, Senemaud J, Gaston AT, Morvan M, Even G, Gautier G, Eggel A, Arock M, Procopio E, Deschildre C, Louedec L, Michel JB, Deschamps L, Castier Y, Coscas R, Alsac JM, Launay P, Caligiuri G, Nicoletti A, Le Borgne M (2023). *Involvement of an IgE/Mast cell/B cell amplification loop in abdominal aortic aneurysm progression.* PLoS ONE, 18(12), e0295408. 10.1371/journal.pone.0295408

Kemmler CL, Smolikova J, Moran HR, Mannion BJ, Knapp D, Lim F, Czarkwiani A, Hermosilla Aguayo V, Rapp V, Fitch OE, Botschi S, Selleri L, Farley E, Braasch I, Yun M, Visel A, Osterwalder M, Mosimann C, Kozmik Z, Burger A. (2023). *Conserved enhancers control notochord expression of vertebrate Brachyury.* Nature communications, 14(1), p. 6594. 10.1038/s41467-023-42151-3

Milusev A, Rieben R, Sorvillo N (2022). *The Endothelial Glycocalyx: A Possible Therapeutic Target in Cardiovascular Disorders.* Frontiers in cardiovascular medicine, 9, p. 897087. 10.3389/fcvm.2022.897087

Milusev A, Despont A, Shaw J, Rieben R, Sorvillo N (2023). *Inflammatory stimuli induce shedding of heparan sulfate from arterial but not venous porcine endothelial cells leading to differential proinflammatory and procoagulant responses.* Scientific Reports, 13(1), p. 4483. 10.1038/s41598-023-31396-z

Felli E, Felli E, Muttillo EM, Urade T, Laracca GG, Giannelli V, Famularo S, Geny B, Ettorre GM, Rombouts K, Pinzani M, Diana M, Gracia-Sancho J. (2023). *Liver ischemia-reperfusion injury: From trigger loading to shot firing.* Liver Transplantation Society, 29(11), pp. 1226-1233. 10.1097/LVT.0000000000000252

Orlando E, Medo M, Bensimon A, Quintin A, Riedo R, Roth SM, Riether C, Marti TM, Aebersold DM, Medova M, Aebersold R, Zimmer Y (2023). *An oncogene addiction phosphorylation signature and its derived scores inform tumor responsiveness to targeted therapies.* Cellular and Molecular Life Sciences, 80(1):6. 10.1007/s00018-022-04634-2

Peiseler M, Araujo David B, Zindel J, Surewaard BGJ, Lee WY, Heymann F, Nusse Y, Castanheira FVS, Shim R, Guillot A, Bruneau A, Atif J, Perciani C, Ohland C, Ganguli Mukherjee P, Niehrs A, Thuenauer R, Altfeld M, Amrein M, Liu Z, Gordon PMK, McCoy K, Deniset J, MacParland S, Ginhoux F, Tacke F, Kubes P (2023). *Kupffer cell-like syncytia replenish resident macrophage function in the fibrotic liver.* Science, 381(6662), pp. 1-16. 10.1126/science.abq5202

Schindler M, Osterwalder M, Harabula I, Wittler L, Tzika AC, Dechmann DKN, Vingron M, Visel A, Haas SA, Real FM (2023). *Induction of kidney-related gene programs through co-option of SALL1 in mole ovotestes.* Development, 150(17) 10.1242/dev.201562

Sengupta A, Dorn A, Jamshidi M, Schwob M, Hassan W, De Maddalena LL, Hugi A, Stucki AO, Dorn P, Marti TM, Wisser O, Stucki JD, Krebs T, Hobi N, Guenat OT. (2023). *A multiplex inhalation platform to model in situ like aerosol delivery in a breathing lung-on-chip.* Frontiers in Pharmacology, 14, p.1114739. 10.3389/fphar.2023.1114739

Skorup I, Valentino G, Aleandri S, Gelli R, Ganguin AA, Felli E, Selicean SE, Marxer RA, Teworte S, Lucic A, Gracia-Sancho J, Berzigotti A, Ridi F, Luciani P (2023). *Polyenylphosphatidylcholines as bioactive excipient in tablets for the treatment of liver fibrosis.* International Journal of Pharmaceutics, 646, p. 123473. Elsevier 10.1016/j.ijpharm.2023.123473

Sobczak JM, Krenger PS, Storni F, Mohsen MO, Balke I, Resevica G, Heath MD, Carreno Velazquez TL, Kramer MF, Scott CJW, Skinner MA, Zeltins A, Kundig TM, Vogel M, Bachmann MF (2023). ↗*The next generation virus-like particle platform for the treatment of peanut allergy.* Allergy, 78(7), pp. 1980-1996. ↗10.1111/all.15704

Triscott J, Reist M, Kung L, Moselle FC, Lehner M, Gallon J, Ravi A, Arora GK, de Brot S, Lundquist M, Gallart-Ayala H, Ivanisevic J, Piscuoglio S, Cantley LC, Emerling BM, Rubin MA (2023). ↗*PI5P4Kα supports prostate cancer metabolism and exposes a survival vulnerability during androgen receptor inhibition.* Science Advances, 9(5), eade8641. ↗10.1126/sciadv.ade8641

Vali Y, Lee J, Boursier J, Petta S, Wonders K, Tiniakos D, Bedossa P, Geier A, Francque S, Allison M, Papatheodoridis G, Cortez-Pinto H, Pais R, Dufour JF, Leeming DJ, Harrison SA, Chen Y, Cobbold JF, Pavlides M, Holleboom AG, Yki-Jarvinen H, Crespo J, Karsdal M, Ostroff R, Zafarmand MH, Torstenson R, Duffin K, Yunis C, Brass C, Ekstedt M, Aithal GP, Schattenberg JM, Bugianesi E, Romero-Gomez M, Ratziu V, Anstee QM, Bossuyt PM (2023). ↗*Biomarkers for staging fibrosis and non-alcoholic steatohepatitis in non-alcoholic fatty liver disease (the LITMUS project): a comparative diagnostic accuracy study.* The Lancet Gastroenterology & Hepatology, 8(8), pp. 714-725. ↗10.1016/S2468-1253(23)00017-1

von Siebenthal M, Akshay A, Besic M, Schneider MP, Hashemi Gheinani A, Burkhard FC, Monastyrskaya K (2023). ↗*Molecular Characterization of Non-Neurogenic and Neurogenic Lower Urinary Tract Dysfunction (LUTD) in SCI-Induced and Partial Bladder Outlet Obstruction Mouse Models*. International journal of molecular sciences, 24(3) MDPI ↗10.3390/ijms24032451

Xu K, Ma J, Hall SRR, Peng RW, Yang H, Yao F (2023). ↗*Battles against aberrant KEAP1-NRF2 signaling in lung cancer: intertwined metabolic and immune networks.* Theranostics, 13(2), pp. 704-723. ↗10.7150/thno.80184

Yang H, Gao Y, Xu D, Xu K, Liang SQ, Yang Z, Scherz A, Hall SRR, Forster S, Berezowska S, Yao F, Ochsenbein AF, Marti TM, Kocher GJ, Schmid RA, Dorn P, Peng RW (2023). ↗*MEK1 drives oncogenic signaling and interacts with PARP1 for genomic and metabolic homeostasis in malignant pleural mesothelioma.* Cell Death Discovery, 9(1), p. 55. ↗10.1038/s41420-023-01307-2

Zhang L, Hoyos IA, Zubler C, Rieben R, Constantinescu M, Olariu R. (2023). ↗*Challenges and opportunities in vascularized composite allotransplantation of joints: a systematic literature review.* Frontiers in Immunology, 14:1179195. ↗10.3389/fimmu.2023.1179195

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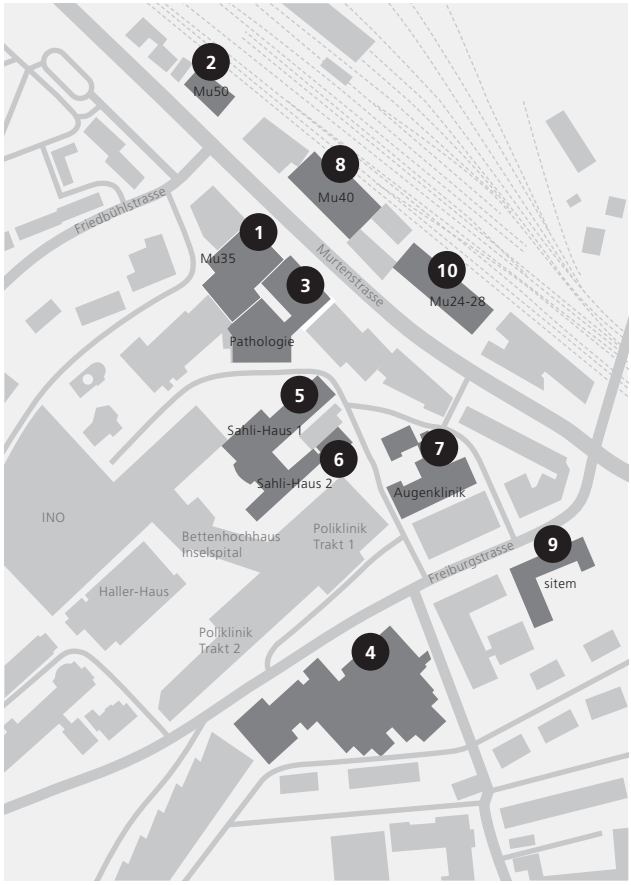

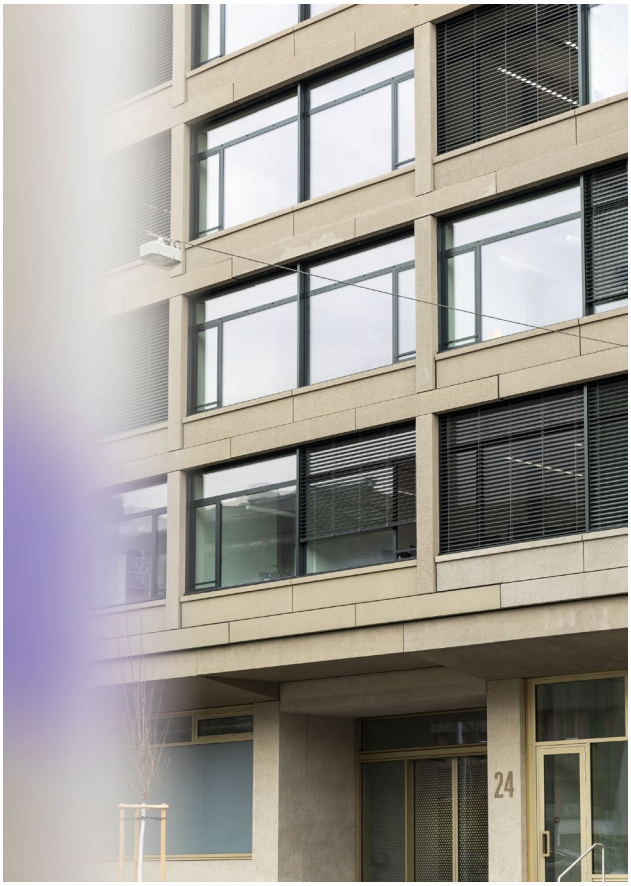

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Contact
Department for BioMedical Research DBMR
University of Bern
Murtenstrasse 24–28
3008 Bern, Switzerland
www.dbmr.unibe.ch

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Elisa Rodrigues Sousa and Boudewijn Kruithof,
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