

## Bone & Joint

The skeletal system is subject to traumatic conditions, including fractures and large bone defects, and pathologies due to degeneration, such as osteoporosis, osteoarthritis, and intervertebral disc degeneration. The demand for improved and efficient treatments is increasing as the proportion of the elderly in societal populations increases, with many desiring to stay physically active. However, surgical procedures for the repair of large bone defects or degenerated spinal discs need to be improved. The regeneration of skeletal tissues is the focus of the Bone & Joint Research Program. To this end, strategies based on cells, materials, and growth factors are being used *ex vivo* (2D/3D cell cultures and bioreactors) and *in vivo*. Pioneering orthopedic surgery, which has been a longstanding tradition in Bern, requires interaction between surgeons and scientists. The Bone & Joint Research Program will continue and extend this tradition and provide clinicians with tools to improve the treatment of patients.

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### Participating Labs

- **Gantenbein & Hofstetter Lab**  
Orthopedic Research
- **Saulacic Lab**  
Cranio-Maxillofacial Surgery

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### Program Contact

**Prof. Dr. Benjamin Gantenbein**

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### Selected Collaborators

- Albers C** Department of Orthopaedics & Traumatology, Bern University Hospital (CH)
- Bohner M** Robert Mathys Foundation, Bettlach, Switzerland
- Ferrari S. L.** Division of Bone Diseases, Department of Internal Medicine Specialties, Faculty of Medicine, Geneva University Hospital (CH)
- Krebs P** Institute of Pathology, University of Bern
- Le Maitre C** Biomolecular Sciences Research Centre, Sheffield Hallam University (UK)
- Noailly J** Department of Information and Communication Technologies, University Pompeu Fabra (ES)
- Schär M** Department of Orthopaedics & Traumatology, Bern University Hospital (CH)
- Tryfonidou M** Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University (NL)

### Research Highlights 2021 / Outlook 2022

As of 2021, there are four competitively funded research projects actively concerning intervertebral disc regeneration and improved spinal fusion, long bone repair, osteoimmunology (interaction of immune system and skeleton). Two of these research projects were funded by the EU Horizon 2020 framework, one by the Swiss National Science Foundation, and one by the Center of Applied Science and Molecular Medicine (CABMM).

The first highlight is the iSpine research project on progenitor cells. iSpine is an international consortium led by Prof. Marianna Tryfonidou, a leading veterinarian from the University Medical Center Utrecht & University Utrecht. The consortium includes both universities and companies and received 16 million euros from EU funding (➤ <https://cordis.europa.eu/project/id/825925>). The consortium was established in January 2019 to begin researching a new advanced therapy for the treatment of LBP caused by disc deterioration. The aim of this project is to investigate and develop a new advanced biological therapy using induced pluripotent stem cells (iPSCs) (➤ <https://ipspine.eu>). iPSCs are created by reprogramming fully mature cells, such as cells from the blood or skin, into spine-specific cells. Over the next five years, the goal of the iSpine partners is to demonstrate the success of iPSCs as a therapeutic strategy. By the end of the project, the therapy should be ready for the first clinical trial. Within this highly cross-disciplinary consortium, our group was able to isolate primary cells from human trauma intervertebral discs (IVDs) with written consent from patients. These cells were then delivered to the consortium partners at INSERM in Montpellier and Nantes, France. These partners were able to produce novel iPSC cell lines that can be used in future cell therapies to cure degenerated IVDs.

A second highlight is the investigation of engineered silk scaffolds for IVD repair. A new project funded by the Swiss National Science has been initiated that targets regeneration of the IVD by using “cross-linked growth factors and engineered” silk fibers and knitting techniques developed by Dr. Michael Wöltje at the Dresden University of Technology, Institute of Textile Machinery and High Performance Material Technology, Dresden, Germany.

A third key highlight is a project that began in Nov 2020. The project involves artificial intelligence, statistical shape and finite element modelling, and organ culture models for IVD regeneration. The €4M-funded Disc4All project aims to tackle this issue through collaborative expertise of clinicians, computational physicists and biologists, geneticists, computer scientists, cell and molecular biologists, microbiologists, bioinformaticians, and industrial partners (➤ <https://cordis.europa.eu/project/id/955735>). The project provides interdisciplinary training in data curation and integration, experimental and theoretical/computational modelling, computer algorithm development, tool generation, and model and simulation platforms to transparently integrate primary data

for enhanced clinical interpretations through models and simulations. The consortium is led by biomedical engineer Prof. Jérôme Noailly, Universitat Pompeu Fabra, Barcelona, Spain (<https://www.upf.edu/web/disc4all>). The Disc4All early-stage researchers will provide a new generation of internationally mobile professionals with unique skill sets for the development of thriving careers in translational research applied to multifactorial disorders.

Finally, the fourth highlight is the development of a coccygeal rat non-fusion model for IVDs. In collaboration with the RMS foundation (Bettlach, SO), porous ceramic implants are currently being tested in an *in vivo* rat animal model for spinal fusion. This project was awarded in Dec 2021 with the Best Poster Award at the German Spine Society Conference.

Another topic of interest in orthopedics is the healing of osteoporotic bone treated with bisphosphonates (BP), a class of drugs that inhibit osteoclastic bone resorption. In the past year, a mouse model of ovariectomized (OVX) and  $\beta$ -tricalcium phosphate (BTCP)-filled femoral critical-size defects was used to investigate whether treatment with BP affects defect healing and impairs biomaterial turnover. After harvesting all the tissue samples and preparing the RNA, the outcomes were assessed by histomorphometry and second-generation sequencing. The research was performed by PhD student Franziska Strunz and was supported by a grant from the Alfred & Anneliese Sutter-Stöttner Foundation.

Regeneration of extended bone deficiencies is one of the most challenging goals in the field of Cranio-Maxillofacial Surgery. A standardized critical-size bone defect calvarial model was used to assess the rate of bone formation and resorption of the biphasic calcium phosphates (BCP) and collagen-based bone substitute materials. Lowering the level of biomimetic hydroxyapatite coating induced higher rate of bone formation concomitant with the higher degradation rate of BCP. Cross-linking of the collagen-based matrices (CM) induced significantly greater total tissue volume in the middle area of the defects compared to non-cross-linked CM, concomitant with a thicker connective tissues regeneration. Mineralization of CM further contributed to the new bone formation and a shift from M1 to M2 macrophages.

Another key research focus in bone research is to identify the regulatory mechanism of supraosteal bone formation induced by mechanical manipulation of periosteum. Reciprocal interactions between the bone and the periosteum are most important for *de novo* bone formation. Research project supported by SNF aimed to assess the mechanobiological principles governing hard tissue formation. Results indicated that an alternated activation and relaxation of periosteum (periosteal pumping) enhanced modelling and remodeling of the calvarial bone. Gadolinium (Gd) is a component of contrast agents and is frequently used in clinical practice. Despite its common application, it is not clear whether the incorporation of Gd into tissues causes negative long-term effects. In this study, the effects of ionized Gd and complexed Gd on the development

and activation of bone cell lineages were investigated. This work was also performed by Franziska Strunz in collaboration with Dr. Rainer Egli (Clinic of Diagnostic and Interventional Radiology) and supported by a grant from Inselspital.

In collaboration with Dr. Philippe Krebs (Institute of Pathology, University of Bern), the effects of a deficiency in inositol-polyphosphate-5-phosphatase (SHIP1) on osteoclast development and activity were assessed. SHIP1-deficient Styx mice are characterized by a low bone mass phenotype. The cellular basis for this phenotype was analyzed *in vitro* and *in vivo*.

### Selected Publications

- Gantenbein, B., S. Tang, J. Guerrero, N. Higuera-Castro, A. I. Salazar-Puerta, A. S. Croft, A. Gazdhar, and D. Purmesur. "Non-Viral Gene Delivery Methods for Bone and Joints." *Front Bioeng Biotechnol* 8 (2020): 598466.
- Croft, A. S., Y. Roth, K. A. C. Oswald, S. Corluka, P. Bermudez-Lekerika, and B. Gantenbein. "In Situ Cell Signalling of the Hippo-Yap/Taz Pathway in Reaction to Complex Dynamic Loading in an Intervertebral Disc Organ Culture." *Int J Mol Sci* 22, no. 24 (Dec 20 2021).
- Zhang, X., J. Guerrero, A. S. Croft, C. E. Albers, S. Hackel, and B. Gantenbein. "Spheroid-Like Cultures for Expanding Angiopoietin Receptor-1 (Aka. Tie2) Positive Cells from the Human Intervertebral Disc." *Int J Mol Sci* 21, no. 24 (Dec 10 2020).
- Saulacic, N., F. Munoz, E. Kobayashi, V. Chappuis, A. Gonzales-Cantalapiedra, and W. Hofstetter. "Effects of Local Application of Alendronate on Early Healing of Extraction Socket in Dogs." *Clin Oral Investig* 24, no. 4 (Apr 2020): 1579-89.
- Schnyder, D., G. Albano, P. Kucharczyk, S. Dolder, M. Siegrist, M. Anderegg, G. Pathare, et al. "Deletion of the Sodium/Hydrogen Exchanger 6 Causes Low Bone Volume in Adult Mice." *Bone* 153 (Dec 2021): 116178



X-ray of a fixed bone fracture in a large bone defect model in black six mice 12-week post-operation.

# Cancer Therapy Resistance

We studied therapy resistance using matched patient samples before and after treatment, state-of-the-art *in vivo*, *ex vivo*, and *in vitro* models, and functional screens to identify new vulnerabilities in resistant tumors. We hope to elucidate the basic mechanisms of therapy resistance by combining the power of next-generation sequencing with functional genomic screens. This is an additional validation of patient-derived samples, organoids, three-dimensional cultures, and realistic animal models that provide a unique opportunity. The added value created by the CTR cluster comes from an interdisciplinary team with extensive experience in basic, translational, and clinical research. We aimed to identify novel genomic alterations associated with treatment resistance and new therapeutic targets to restore treatment sensitivity. CTR principal investigators have established collaborations with other leading scientists abroad (e.g., SU2C-PCF Prostate, SPORE, SNF Sinergia, KWF, ITN, FWF, The Netherlands Cancer Institute). CTR is active internationally, and we are convinced that it will provide more visibility for the University of Bern and Switzerland in the field of precision oncology.

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## Participating Labs

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

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## Program Contact

### Prof. Dr. Marianna Kruithof-de Julio

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## Selected Collaborators

- Demichelis F** University of Trento (IT)
- Emerling B** Sanford Burnham Prebys Medical Discovery Institute (USA) ➤
- Jonkers J** The Netherlands Cancer Institute, Amsterdam (NL)
- Lunardi A** University of Trento (IT)
- Piscuoglio S** University of Basel (CH)

## Research Highlights 2021 / Outlook 2022

Research highlights in the Kruithof-de Julio laboratory include the following:

1. Generated patient-derived xenografts (PDX) and patient-derived organoids (PDO) from biopsies of prostate and bladder cancer (Karkampouna et al. 2021).
2. In collaboration with NEXUS and ETH, a new medium composition was developed that allows culture of PDO matrix-free and medium throughput on the PDOs.
3. Developed and implemented a clinically relevant culture system for studying tumor tissues *ex vivo* (patent pending).
4. We have previously shown that the effects of drug treatment in this system are consistent with those observed in organoids (*in vitro*) and PDXs (*in vivo*) (Karkampouna et al. 2021). Presently, we customized a microvasculature-on-chip device to mimic the bone microenvironment.
5. Generated and fully characterized a unique PDX *BRCA2* mutant (Karkampouna et al. 2021).
6. A medium throughput screen with NEXUS was used to identify 16 compounds that are in current use in PDO (Karkampouna et al. 2021; LaManna 2021 FrOnc).
7. Demonstrated that the CRIPTO cell surface protein drives bone metastatic progression and plays a novel role in fibrosis (Karkampouna et al. 2021).

New support has been received for several research projects (SNSF Sinergia, Swiss Cancer League, Bernese Cancer League, PHRT and Innosuisse).

Precision oncology applies precision medicine approaches to understand the mechanisms of prostate cancer (Pca) progression and therapy resistance. Related highlights in the Rubin laboratory include the following:

1. Validation of findings from multi-omic datasets that characterize changes in cell metabolism using P15P4K-depleted systems and continued characterization of the first prostate cell type-specific mouse models to target expression *in vivo* (PMID: 33984270).
2. Determination of the role of reduced METTL3 expression and resistance to androgen-targeted therapy (PMID: 34088870).
3. Development of *in vitro* models to elucidate the biological processes underlying metastases, including organoid models of the brain and liver.
4. Demonstration that the minor spliceosome is a strong therapeutic target for lethal PCa (manuscript under review).
5. Clarification of the underlying mechanisms of how the SWI/SNF complex regulates lineage plasticity and therapy resistance to identify novel therapeutic strategies for neuroendocrine Pca.
6. Continued development of new therapeutic strategies that exploit vulnerabilities in the TC-NER pathway of Pca patients.

7. Defined tumor heterogeneity and its molecular landscape from matched samples of primary and brain metastatic PCa (PMID: 35504881).

New support has been received for several research projects (Fond'Action, Engelhorn Foundation, Swiss Government, ISREC, Berger-Janser Foundation, Hermann Foundation, and Fondation Nuovo-Soldati).

In the Rottenberg lab, we have continued our efforts to understand the mechanisms of anti-CTR using genetically engineered mouse models for BRCA1/2-mutated breast cancer, as well as genome-wide functional CRISPR/Cas9 screens. Highlights in 2021 include the following:

1. Validated that MDC1 counteracts restrained replication fork restart, and that its loss causes poly (ADP-ribose) polymerase (PARP) inhibitor resistance in BRCA1/2-deficient tumors (manuscript in revision).
2. Demonstration that the loss of nuclear DNA ligase III reverts PARP inhibitor resistance in BRCA1/53BP1-deficient cells by exposing ssDNA gaps (PMID: 34555355).
3. Investigated the essentialome of p53 and BRCA1 in p53-deficient human cells exposed to ionizing radiation (IR).
4. Identified genes that promote IR resistance when depleted for further validation.
5. Confirmed that the loss of the volume-regulated anion channel components, LRRC8A and LRRC8D, limits platinum drug uptake and efficacy.
6. Identified a posttranslational modification that is essential for LRRC8A/D-mediated platinum drug uptake was identified.
7. Demonstrated that the cellular receptor of a canine distemper virus strain might be useful for oncolytic immunotherapy.

In 2021, this research was supported by the EU (ERC-AdG 883877, ERC-CoG-681572), SNSF (310030\_179360, 31BL30\_189698, MD-PhD 02/21), Swiss Cancer League (KLS-4282-08-2017), Wilhelm Sander Foundation (no. 2019.069.1), and Foundation for Clinical-Experimental Cancer Research.

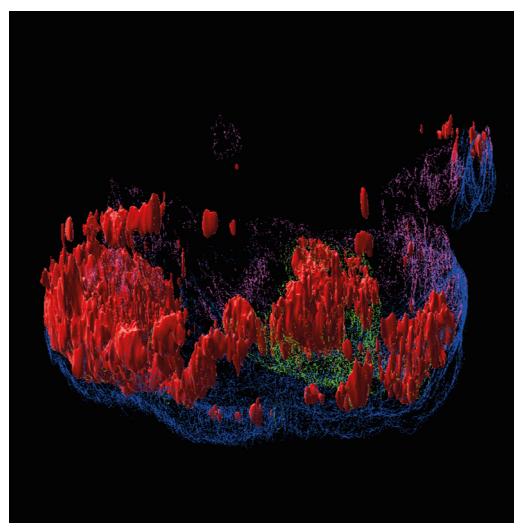
### Selected Publications

- Cotter, K. A., J. Gallon, N. Uebersax, P. Rubin, K. D. Meyer, S. Piscuoglio, S. R. Jaffrey, and M. A. Rubin. "Mapping of M(6)a and Its Regulatory Targets in Prostate Cancer Reveals a Mettl3-Low Induction of Therapy Resistance." *Mol Cancer Res* 19, no. 8 (Aug 2021): 1398-411.
- Ravi, A., L. Palamiuc, R. M. Loughran, J. Triscott, G. K. Arora, A. Kumar, V. Tieu, et al. "Pi5p4ks Drive Metabolic Homeostasis through Peroxisome-Mitochondria Interplay." *Dev Cell* 56, no. 11 (Jun 7 2021): 1661-76 e10.
- Karkampouna, S., D. van der Helm, M. Scarpa, B. van Hoek, H. W. Verspaget, M. J. Goumans, M. J. Coenraad, B. P. T. Kruihof, and M. Kruihof-de Julio. "Oncofetal Protein

- Cripto Is Involved in Wound Healing and Fibrogenesis in the Regenerating Liver and Is Associated with the Initial Stages of Cardiac Fibrosis." *Cells* 10, no. 12 (Nov 26 2021).
- Karkampouna, S., F. La Manna, A. Benjak, M. Kiener, M. De Menna, E. Zoni, J. Grosjean, et al. "Patient-Derived Xenografts and Organoids Model Therapy Response in Prostate Cancer." *Nat Commun* 12, no. 1 (Feb 18 2021): 1117.
- Rottenberg, S., C. Disler, and P. Perego. "The Rediscovery of Platinum-Based Cancer Therapy." *Nat Rev Cancer* 21, no. 1 (Jan 2021): 37-50.

### Link to publication list

- [www.ncbi.nlm.nih.gov/myncbi/1tchmU-55LZ5H8/bibliography/public/](http://www.ncbi.nlm.nih.gov/myncbi/1tchmU-55LZ5H8/bibliography/public/)
- [www.ncbi.nlm.nih.gov/myncbi/mark.rubin.1/bibliography/public/](http://www.ncbi.nlm.nih.gov/myncbi/mark.rubin.1/bibliography/public/)
- [www.ncbi.nlm.nih.gov/myncbi/sven.rottenberg.1/bibliography/public/](http://www.ncbi.nlm.nih.gov/myncbi/sven.rottenberg.1/bibliography/public/)



Tumour cells (red) colonise the brain milieu and expand among the cortical plate (green) and neurons (magenta) of the mini-brain after co-culture. 5x magnification, scale bar = 200µm.

# Cardiovascular Diseases

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## Participating Labs

- **Döring Lab – Yvonne Döring (Y.D.)**  
Atherosclerosis, vascular inflammation, and lower extremity arterial disease
- **Heller Lab – Manfred Heller (M.H.)**  
Mass spectrometry-based methods to characterize circulating extracellular vesicles and system-wide protein regulation
- **Longnus Lab – Sarah Longnus (S.L.)**  
Cardiac metabolism and signalling, and heart transplantation
- **Mercader Lab – Nadia Mercader (N.M.)**  
Heart development and regeneration
- **Odening Lab – Katja Odening (K.O.)**  
Cardiac electrophysiology and arrhythmogenic mechanisms in inherited rhythm disorders
- **Osterwalder Lab – Marco Osterwalder (M.O.)**  
Gene regulatory mechanisms underlying cardiac development, disease, and reprogramming
- **Rexhaj Lab – Emrush Rexhaj (E.R.)**  
Fetal programming of metabolic and cardiovascular function/dysfunction later in life
- **Rieben Lab – Robert Rieben (R.R.)**  
Ischemia/reperfusion injury, xenotransplantation, vascularized composite allotransplantation
- **Zuppinger Lab – Christian Zuppinger (C.Z.)**  
Mechanisms of adverse effects of cancer therapies on the cardiovascular system (Cardio-Oncology)

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## Program Contact

### Prof. Dr. Yvonne Döring

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## Selected Collaborators

- Enriquez JA** Cardiovascular Regeneration Program of The National Centre for Cardiovascular Research, Madrid, (ES)
- Torres M** Cardiovascular Regeneration Program of The National Centre for Cardiovascular Research CNIC, Madrid, (ES)
- Marsano A** Basel University, Biomedicine/Cardiac Surgery, Basel (CH)
- Weber C** IPEK, LMU Munich, Munich (DE)
- Söhnlein O** Institute of Experimental Pathology at the WWU, Münster (DE)
- Eckhard Wolf** Gene Center and Department of Biochemistry, LMU, Munich (DE)

Tight spatiotemporal control of cardiac gene expression and a functional cardiovascular system is essential for embryonic development and during the entire lifespan, ensuring blood supply throughout the body. In healthy adults, blood vessels remain in a quiescent state with nonproliferating, antithrombotic, anti-inflammatory, and nonangiogenic endothelial and smooth muscle cell phenotypes. 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 and vascular and injury responses. We analyze molecular, epigenetic, and physiologic 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 to investigate the long-term consequences of injury (e.g., arrhythmias and heart failure). Furthermore, we examine vascular biology (e.g., role of glycocalyx), chronic inflammation (e.g., atherosclerosis), and immune mechanisms (e.g., complement or neutrophil extracellular traps) affecting vascular health and disease.

## Research Highlights 2021

In 2021, we moved into our new laboratory and office spaces in Murtenstrasse 24. This spatial consolidation of CVD program groups fosters joint meetings, get-togethers, and group discussions. All members greatly appreciate the new lab space and proximity to the core facilities. Beginning in November 2021, a monthly CVD program meeting has focused on exchanging information with the DBMR management team and presentation of the latest scientific findings and our own data. This platform provides younger scientists the opportunity to present their data in a protective and supportive setting to the larger group.

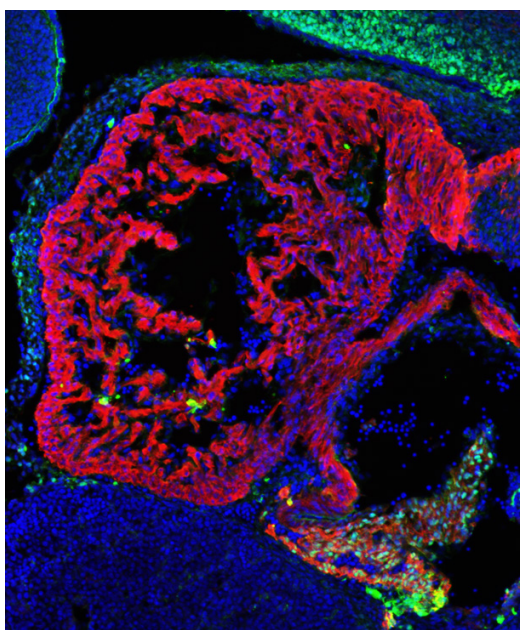
In 2021, successful scientific collaborations involving the CVD program resulted in several joint efforts to raise third-party funding:

1. We were successful in obtaining funding from the SNSF NRP78 (4078P0\_198297) to study the effects of SARS-CoV-2 on the cardiovascular system (Program PIs: Y.D., N.M., R.R.; Associated: S.L., K.O.; External PI: B.Engelhardt).
2. In a joint application involving CVD-PIs M. O. (main applicant), C. Z. (co-applicant), Iros Barozzi (external PI, co-applicant), N. M. (project partner), K. O. (collaborator/implementation partner), and Y. D. (collaborator), we applied for a NRP79 (407940\_206520) "Advancing 3R – Animals, Research and Society" grant, termed HeartX. We also have focused on establishing a novel type of cardiac organoids, which we intend to leverage as a mouse replacement model recapitulating in vivo cardiac chamber formation. The outcome decision is scheduled for May 18, 2022.
3. We were awarded an SNSF project grant (310030\_205073) to investigate energy metabolism as a basis for

sex differences in cardiac tolerance to ischemia and reperfusion (Program PI: S.L., Program Partner: M.H.).

4. Since March 2021, a state-of-the-art cardiac catheterization lab for large animals has become available. This lab is essential for translational projects in CVD research. An example is the ongoing Innosuisse project 2155005728 from R.R. together with HAYA Therapeutics, Lausanne.
5. Y.D. and K.O., together with cooperation partners from the CVD cluster, also applied for a grant in the framework of the newly launched fields of competence of the medical faculty of Bern. The grant, titled "Cardiovascular rare disease – to establish personalized diagnostic and therapeutic approaches", did not receive initial funding within the scope of the Competence Fields initiative. Nonetheless, it will continue to be pursued thematically in the Medizinbereich Herz/Gefäss.

S.L. and K.O. are coordinators and Y.D., N.M., M.O., and R.R. are board members of the CV Research Cluster Bern. This cluster promotes research collaborations among fundamental and clinical researchers, raises visibility and awareness of CVD research in Bern, enriches the training environment of junior researchers, and provides a framework for multi-team and/or interdisciplinary projects. Cluster activities include regular seminar series with internal and external speakers, student research events, and annual networking meetings.



Marco Osterwalder group. Cross-section of the mouse embryonic heart (red) at gestation day 11.5. The SHOX2 transcription factor (green) is essential for cardiac pacemaker differentiation in the sinus venosus.

### Outlook 2022

A research article by N.M. and M.O. has been very recently published in the scientific journal "Development" (DOI: 10.1242/dev.200375). C.Z. published a paper titled "Supplementing soy-based diet with creatine in rats: implications for cardiac cell signaling and response to doxorubicin" in *Nutrients*. Y.D., N.M., R.R., and colleagues had a review article titled "COVID-19 and the vasculature: current aspects and long-term consequences" accepted for publication in *Frontiers of Cell and Developmental Biology*.

The following CVD Program researchers received funding: Individual funding to Y.D. (SNSF project grant 310030\_197655), N.M. (ERC Consolidator grant 819717 and SNSF Project ForcelnRegeneration 310030L\_182575), K.O. (SNSF project grant 310030\_197595, NIH joint-grant 2R01HL131461-05, and EJP-RD grant 31ER30\_194836), M.O. (SNSF Eccellenza Professorial Fellowship PCEFP3\_186993), E.R. (SNF project grant 320030\_185023/1), and R.R. (SNSF Sinergia CRSII5\_198577, SNSF project grant 310030\_182264, US DoD project W81XWH1910714).

Finally, we are proud that the PI N.M. was nominated as an individual member of the Swiss Academy of Medical Sciences in 2021.

### Selected Publications

- Thakur, M., B. Evans, M. Schindewolf, I. Baumgartner, and Y. Doring. "Neutrophil Extracellular Traps Affecting Cardiovascular Health in Infectious and Inflammatory Diseases." *Cells* 10, no. 7 (Jul 4 2021).
- Bonetti, N. R., T. A. Meister, R. Soria, A. Akhmedov, L. Liberale, S. Ministrini, A. Dogar, et al. "In Vitro Fertilization Exacerbates Stroke Size and Neurological Disability in Wildtype Mice." *Int J Cardiol* 343 (Nov 15 2021): 92-101.
- Marques, I. J., A. Sanz-Morejon, and N. Mercader. "Ventricular Cryoinjury as a Model to Study Heart Regeneration in Zebrafish." *Methods Mol Biol* 2158 (2021): 51-62.
- Mendez-Carmona, N., R. K. Wyss, M. Arnold, A. Segiser, N. Kalbermatter, A. Joachimbauer, T. P. Carrel, and S. L. Longnus. "Effects of Graft Preservation Conditions on Coronary Endothelium and Cardiac Functional Recovery in a Rat Model of Donation after Circulatory Death." *J Heart Lung Transplant* 40, no. 11 (Nov 2021): 1396-407.
- Tokarska-Schlattner, M., L. Kay, P. Perret, R. Isola, S. Attia, F. Lamarche, C. Tellier, et al. "Role of Cardiac AMP-Activated Protein Kinase in a Non-Pathological Setting: Evidence from Cardiomyocyte-Specific, Inducible AMP-Activated Protein Kinase Alpha1alpha2-Knockout Mice." *Front Cell Dev Biol* 9 (2021): 731015.
- Olariu, R., C. Tsai, M. Abd El Hafez, A. Milusev, Y. Banz, I. Lese, J. I. Leckenby, et al. "Presence of Donor Lymph Nodes within Vascularized Composite Allotransplantation Ameliorates VEGF-C-Mediated Lymphangiogenesis and Delays the Onset of Acute Rejection." *Transplantation* 105, no. 8 (Aug 1 2021): 1747-59.



# Anesthesiology

## Stueber & Hedinger Lab

Research in macro-physiology-embracing dimensions such as respiration and hemodynamics has shaped research in anesthesia over decades. Looking ahead, further discoveries and deepened understanding of molecular biology offer tremendous opportunities to advance perioperative care. With anesthesiology and surgery evolving interdependently and given the nature of anesthesiology as a collaborative aspect of perioperative medicine, we aim to understand the molecular risks and responses of anesthetized patients to surgical interventions. Our goal is to define the best practices for personalized perioperative patient care.

Our group focuses on the anesthesia-induced neurotoxicity and the genetic predisposition for perioperative morbidity and mortality. Our special interests include inflammation/immunology, cardiovascular system, pharmacokinetics and pharmacodynamics of general anesthetics, pharmacogenetics, and pain medicine. With basic science as our foundation and translational medicine as our vision, our goal is to contribute significantly to precision medicine in anesthesiology and perioperative care both nationally and internationally.

In our lab, we apply a broad spectrum of state-of-the-art molecular and cell biology methods, including *in vitro*, *ex vivo*, and *in vivo* models, linking basic science with clinical phenotypes to enhance recovery after surgery through personalized medicine.

### Research Highlights 2021 / Outlook 2022

1. Flow cytometry-based RNA interference high-throughput screening RNAi HTS in human melanoma cells for either up- or down-regulation of microRNAs (miRNAs) of surface human leucocyte antigen HLA-DR expression has been conducted. *In silico* approaches have been applied to functional miRNA-mRNA interaction prediction. The potential underlying gene regulation by different miRNAs has been proposed. The manuscript summarizing this study is currently under revision. Individual miRNA candidates will be further tested in monocytic and primary cell lines. Our results will promote the study of miRNA-mediated HLA-DR regulation under both physiological and pathological conditions and may pave the way for potential clinical applications.
2. We established behavior-based HTS assays for testing established and widely used anesthetic and sedative compounds in a novel zebrafish *in vivo* model. The goal is to identify drug-specific neurotoxicity endpoints and discover new anesthetic adjuvants and target-specific neuroprotective agents that can enhance anesthetic safety and management.
3. Human THP-1 cells were used to investigate regulatory mechanisms of the nociceptin system. The expression of nociceptin, nociceptin opioid receptor, and Toll-like receptors (TLRs) in response to different stimulations was analyzed. The study outcomes were presented at the SGAR Congress 2021. The manuscript on the

interactions between nociceptin and the TLR system has been accepted for publication. Further studies on the mechanisms underlying nociception/TLR regulation will be conducted.

### Selected Publications

- Ropelato S, Menozzi M, Huang MY. Hyper reoriented walking in minimal space. *Virtual Reality* (2021). <https://doi.org/10.1007/s10055-021-00608-0>
- Spinetti, T., C. Hirzel, M. Fux, L. N. Walti, P. Schober, F. Stueber, M. M. Luedi, and J. C. Schefold. "Reduced Monocytic Human Leukocyte Antigen-Dr Expression Indicates Immunosuppression in Critically Ill Covid-19 Patients." *Anesth Analg* 131, no. 4 (Oct 2020): 993-99.
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### Program Contact

#### Melody Ying-Yu Hedinger

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- ✉ [www.dbmr.unibe.ch](http://www.dbmr.unibe.ch) → Research → Independent Research Labs

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### Selected Collaborators

- Leib S & Grandgirard D** Institute for Infectious Diseases, University of Bern, Switzerland
- Mercader Huber N** Institute of Anatomy, University of Bern, Switzerland
- Menozzi M** Department of Health Sciences and Technology D-HEST, ETH Zurich, Switzerland
- Cullen K** Department of Biomedical Engineering, Johns Hopkins University, USA
- Chacron M** Department of Physiology, McGill University, Canada



# Technology Core Facilities



# Proteomics and Mass Spectrometry Core Facility (PMS)



## Achievements 2021

The demand for proteomics services continues to be very high. This has slowed the delivery of results due to the saturation of work capacity by the researchers and instrument capacities. We were able to quantify several hundred proteins from only 10–20,000 sorted small cells, in collaboration with Prof. S. Saxena (DBMR). The facility is now accompanied by a working group consisting of members from all three life sciences faculties. The laboratory was moved to the 4th floor of the new research building at Murtenstrasse 24. A business plan for PMS CF was written, which included ideas on how the university could deal with core facilities. We take this opportunity to thank all our customers for their trust in our services.

## Performance report 2021

We processed 1830 samples submitted by laboratories from the Faculty of Medicine (50.2%), Faculty of Science (27.4%), Vetsuisse Faculty (21.9%), and external institutions (0.5%). This produced 3679 LC-MS/MS runs for the generation of publishable data. This number was supplemented by 209 runs for development, 896 standards, and 4981 blanks for quality assurance. The 3-week lab shutdown due to the move and the use of the new timsTOF™ instrument decreased the average up-time from 43 weeks at a 69% time occupancy rate to 42 weeks at 64% on the three orbitraps.

## Finances 2021

Our financial situation remains sound, mainly due to substantial support from the NCCR RNA & Disease and DBMR.

## Outlook 2022

Our CF business plan will be discussed with the new vice-rector for research. Our oldest instrument will be replaced using investment funds from the university rectorate. We intend to equip the laboratory with a liquid-handling robot for reproducible sample preparation if funding is available.

## Selected Publications

- Hill, V., H. Akarsu, R. S. Barbarroja, V. L. Cippa, P. Kuhnert, M. Heller, L. Falquet, et al. "Minimalistic Mycoplasmas Harbor Different Functional Toxin-Antitoxin Systems." *PLoS Genet* 17, no. 10 (Oct 2021): e1009365.
- Anghel, N., J. Muller, M. Serricchio, J. Jelk, P. Butikofer, G. Boubaker, D. Imhof, et al. "Cellular and Molecular Targets of Nucleotide-Tagged Trithiolato-Bridged Arene Ruthenium Complexes in the Protozoan Parasites *Toxoplasma Gondii* and *Trypanosoma Brucei*." *Int J Mol Sci* 22, no. 19 (Oct 5 2021).
- Schniering, J., M. Maciukiewicz, H. S. Gabrys, M. Brunner, C. Bluthgen, C. Meier, S. Braga-Lagache, et al. "Computed Tomography-Based Radiomics Decodes Prognostic and Molecular Differences in Interstitial Lung Disease Related to Systemic Sclerosis." *Eur Respir J* (Oct 14 2021).
- Hallal, M., S. Braga-Lagache, J. Jankovic, C. Simillion, R. Bruggmann, A. C. Uldry, R. Allam, M. Heller, and N. Bonadies. "Inference of Kinase-Signaling Networks in Human Myeloid Cell Line Models by Phosphoproteomics Using Kinase Activity Enrichment Analysis (Kaea)." *BMC Cancer* 21, no. 1 (Jul 8 2021): 789.
- Contu, L., G. Balistreri, M. Domanski, A. C. Uldry, and O. Muhlemann. "Characterisation of the Semliki Forest Virus-Host Cell Interactome Reveals the Viral Capsid Protein as an Inhibitor of Nonsense-Mediated Mrna Decay." *PLoS Pathog* 17, no. 5 (May 2021): e1009603.

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### Head of PMS Facility

**Ass. Prof. Dr. phil. nat. Manfred Heller**

✉ [manfred.heller@dbmr.unibe.ch](mailto:manfred.heller@dbmr.unibe.ch)

✉ [www.pmscf.dbmr.unibe.ch](http://www.pmscf.dbmr.unibe.ch)

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### Core Facility Members

**Anne-Christine Uldry**

PhD, Computational Scientist

**Sophie Braga-Lagache**

MSc, Senior Assistant

**Natasha Buchs**

Laboratory Assistant

## Live Cell Imaging Core Facility (LCI)



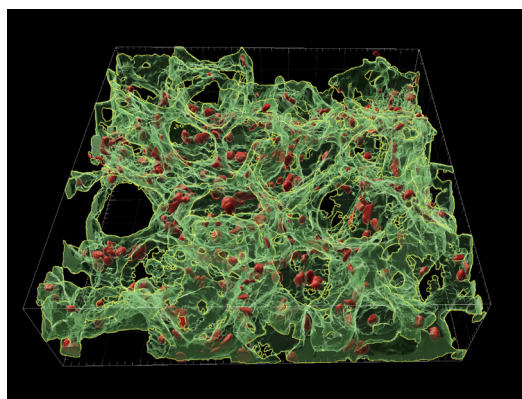
### Achievements 2021

The DBMR LCI Core Facility successfully moved its major equipment to the new DBMR Research Building at Murtenstrasse 24 and started operations on the 4th floor. In addition to the existing equipment, a new single-point Zeiss LSM980 confocal microscope equipped with an Airyscan 2 unit and near-infrared detection (total cost approximately CHF 600'000) was installed and began operation. The core facility has also started to manage and take care of histology equipment that includes a new cryostat, microtome, and 3D Histech Slide Scanner in the new histology lab, which are accessible to all users.

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

### Performance report 2021

The total number of booked hours for using LCI microscopes in 2021 was 4752, an increase from 4073 hours in 2020. These figures do not include systems that have to be booked on a daily basis, such as the InCuCyte S3 system. In 2021, LCI staff spent 117 hours on introductory training on LCI microscopes (91 hours in 2020). Working hours spent collaborating with other research groups from the DBMR increased to 257 in 2021 from 61 hours in 2020. The hours spent on technical assistance remained constant (182 hours in 2021, 185.5 in 2020). Every year, the facility contributes to 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 2021.



### Finances 2021

Owing to the recovery of research activities in the course of the pandemic in 2021, revenue is recovering to pre-pandemic levels and even increasing slightly. As in previous years, most expenses consisted of costs for repairs and maintenance contracts. The MIC kindly supported LCI with CHF 3,000 for general maintenance and repair.

### Outlook 2022

The LCI is closely collaborating with its working group to extend and improve services for the DBMR. A great focus will be on equipping the new histology laboratory at Murtenstrasse 24 and providing extended support for users dealing with sample processing.

### Selected Publications

- Fahmi, A., M. Brugger, T. Demoulins, B. Zumkehr, B. I. Oliveira Esteves, L. Bracher, C. Wotzkow, et al. "Sars-Cov-2 Can Infect and Propagate in Human Placenta Explants." *Cell Rep Med* 2, no. 12 (Dec 21 2021): 100456.
- Wang, L., H. Yang, P. Dorn, S. Berezowska, F. Blank, C. Wotzkow, T. M. Marti, et al. "Peritumoral Cd90+Cd73+ Cells Possess Immunosuppressive Features in Human Non-Small Cell Lung Cancer." *EBioMedicine* 73 (Nov 2021) 103664.

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### Head of LCI Facility

**PD. Dr. phil. nat. Fabian Blank**

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✉ [www.dbmr.unibe.ch](http://www.dbmr.unibe.ch) → Services → Core facilities → Live Cell Imaging

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### Core Facility Members

**Carlos Wotzkow**

Lab Technician

**Selina Steiner**

Lab Technician

# Flow Cytometry and Cell Sorting Core Facility (FCCS)



## Achievements 2021

We successfully completed our last round of the fluorescence-activated cell sorting (FACS) course after interruptions caused by the COVID-19 lockdown and subsequent related restrictions.

An FCCS CF working group was established. Under the direction of the selected PI, the working group aims to support the FCCS CF in terms of strategic development and implementation.

Two members of our team left the FCCS CF. Lab technician Isabelle Gsponer, who took the chance for a new challenge at Lonza, and Claudio Vallan, who had a long-standing, half-day per week appointment as a course administrator. They were replaced by Lorenzo Raeli, who has many years of experience in flow cytometry, cell sorting, and teaching.

Finally, we were able to purchase a new cytometer to replace one of the old instruments. The Cytek Aurora instrument adds innovative value to the FCCS CF with its novel technology of full spectrum analysis.

Moving to the new labs at Murtenstrasse 24 on October 20th and 21st occurred without notable problems, and all services were available one day later.

## Performance report 2021

Self-operated measurements increased by 10.9% compared to 2020, and were, thus, half-way to the pre-pandemic level. Cell sorting services increased by 31.8% compared to 2020, reaching a level between the peak year 2018 and 2019.

Self-operated measurements were performed to 60.9% by researchers from Inselspital clinics and to 37.9% from unibe institutes. Measurements by external parties made up 1.2%. 75.6% of cell sorts were performed for Inselspital clinics and 22.6% for unibe institutes, while 1.8% were performed for external parties. 61.2% of measurements and 75.3% of cell sorts were performed by or for DBMR groups.

More than 50 students, postdocs, and lab techs successfully registered for the new round of our FACS course and attended the kick-off seminar and training offered by FlowJo analysis software company.

## Finances 2021

Income: CHF 253,000.–

Expenses: CHF 203,000.–

## Outlook 2022

The current round of our 5-day FACS course with more than 50 participants will be completed. This course is worth two European Credit Transfer System Points for members of the Graduate School of Cellular and Biomedical Sciences, and the list of future participants for the next round planned for late fall in 2022 is already growing.

Interested users will receive training for the self-operated usage of the new Cytek Aurora full spectrum flow cytometer.

The FCCS CF coordinates and supports a full SNF R'Equip application to purchase a NanoFCM NanoAnalyzer, planned to replace the NanoSight NS300.

## Selected Publications

Lipp, J. J., L. Wang, H. Yang, F. Yao, N. Harrer, S. Muller, S. Berezowska, et al. "Functional and Molecular Characterization of Pd1(+) Tumor-Infiltrating Lymphocytes from Lung Cancer Patients." *Oncoimmunology* 11, no. 1 (2022), 2019466.

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### Head of LCI Facility

**Dr. phil. nat. Stefan Müller, PhD**

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✉ www.dbmr.unibe.ch → Services →

Core facilities → Flow Cytometry and Cell Sorting

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### Core Facility Members

**Dr. Fiona Augsburg** PhD, Technical Assistant (since Oct.)

**Isabelle Gsponer** Lab Technician (until June)

**Bernadette Nyfeler** Lab Technician

**Dr. Thomas Schaffer** PhD, Senior Assistant

**Dr. Lorenzo Raeli** PhD, Scientific Assistant (since Oct.)

**Dr. Claudio Vallan** Scientific and Educational Support (until July)



# Johanna Dürmüller-Bol DBMR Research Award



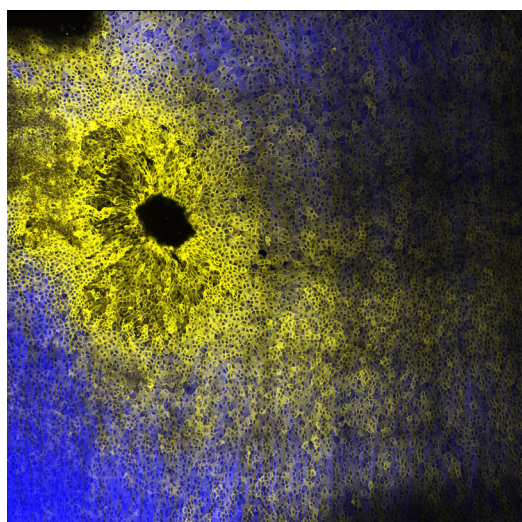
## Dr. med Dr. sc. nat. Joel Zindel Systems biomedicine of cellular development and signaling in health and disease

Abdominal surgeries can save lives as they allow surgeons to remove malignant tumors or fight abdominal infections. However, these surgeries can also lead to fibrotic complications called peritoneal adhesions. Adhesions are internal scars that result in significant suffering and high health costs; they have no cure at present.

Collagen deposition by fibroblasts is a critical step in adhesion formation. Our published data (Zindel et. al. Nature Communications 2021) indicate that fibroblasts are recruited from distant mesothelium. However, the mechanism of cell migration remains largely unknown.

In 2022, we aim to introduce a new multi-photon intravital microscopy (IVM) model to Bern. This model will allow us to image the abdominal cavity in real time with subcellular resolution (Zindel et al. Science 2021). We will leverage this model with our fluorescent reporter system that fate-maps mesothelial cells. Mesothelial cells and mesothelium-derived fibroblasts can be tracked over time to describe when and how they migrate in response to injury. We will also investigate the potential molecular mechanisms underlying mesothelial cell migration using single-cell RNA-Seq.

These studies will allow us to identify mechanisms that could be targeted in future studies to inhibit mesothelial cell migration in injury repair and to investigate the effect on adhesion formation.



Mesothelial cells (yellow) grow over focal peritoneal injury (black circle) where they heal the lesion by depositing collagen (blue)

## Biosketch

### Dr. med Dr. sc. nat. Joel Zindel

MD at the University of Bern (2011). Residents in general surgery and visceral and transplantation surgery, General Surgery Tiefenausspital (Prof. Dr. Daniel Inderbitzin), Visceral Surgery and Medicine, Inselspital (Prof. Dr. Daniel Candinas) 2012–2017. FMH Certification in Surgery, 2018. Clinical Research Fellowship Visceral Surgery and Medicine (Supervisors: Prof. Dr. Daniel Candinas, Prof. Dr. Deborah Keogh-Stroka, Co-Advisor: Prof. Dr. Andrew J. Macpherson) 2017–2018. Research Fellowship in Calgary, Canada (Supervisor: Prof. Dr. Paul Kubes) 2018–2020. PhD in Immunology 2021. Since 2022, Staff Surgeon and Junior Group Leader Visceral Surgery and Medicine, Inselspital Bern, University of Bern.

## Selected Publications

- Zindel, J., J. Mittner, J. Bayer, S. L. April-Monn, A. Kohler, Y. Nusse, M. Dosch, et al. "Intraperitoneal Microbial Contamination Drives Post-Surgical Peritoneal Adhesions by Mesothelial Egfr-Signaling." *Nat Commun* 12, no. 1 (Dec 16 2021): 7316.
- Zwicky, S. N., Stroka, D., and Zindel, J. "Sterile injury repair and adhesion formation at the serosal surfaces *Front Immunol* 12 (2021) 684967.
- Zindel, J., M. Peiseler, M. Hossain, C. Deppermann, W. Y. Lee, B. Haenni, B. Zuber, et al. "Primordial Gata6 Macrophages Function as Extravascular Platelets in Sterile Injury." *Science* 371, no. 6533 (Mar 5 2021).
- Deppermann, C., R. M. Kratofil, M. Peiseler, B. A. David, J. Zindel, Fves Castanheira, F. van der Wal, et al. "Macrophage Galactose Lectin Is Critical for Kupffer Cells to Clear Aged Platelets." *J Exp Med* 217, no. 4 (Apr 6 2020).
- Zindel, J., and P. Kubes. "Damps, Pamps, and Lamps in Immunity and Sterile Inflammation." *Annu Rev Pathol* 15 (Jan 24 2020): 493-518.

## Contact

### Dr. med Dr. sc. nat. Joel Zindel

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- ➔ [www.dbmr.unibe.ch](http://www.dbmr.unibe.ch) → Research → Research Programs → Keogh-Stroka Lab

## Selected Collaborators

- Macpherson AJ** University of Bern (CH)
- Kubes P** University of Calgary (CA)
- Kopf M** ETH Zürich (CH)
- Castagner Bastien** McGill University (CA)
- Deppermann C** Johannes Gutenberg University Mainz (GE)

## Key Events

### Johanna Dürmüller-Bol DBMR Research Prize 2021

21 candidates submitted applications for the 2021 Johanna Dürmüller-Bol DBMR Research Prize, funded by Johanna Dürmüller-Bol Foundation. The winner of the Johanna Dürmüller-Bol DBMR Research Award 2021 was Dr. med. Dr. sc. n. Joel Zindel, Systems Biomedicine of Cellular Development and Signaling in Health and Disease, Keogh-Stroka Lab Department for BioMedical Research, for his project on "Defining macrophage-dependent mesothelial cell recruitment in peritoneal injury repair and adhesion formation."

### DBMR Research Conferences 2021

In 2021, we were pleased to host the following speakers:

#### 01 Feb.: Dr. Paul Krimpenfort

Division of Molecular Genetics, Netherlands Cancer Institute, Amsterdam (NL)  
*Animal Model Generation Facility at The Netherlands Cancer Institute*

#### 01 Mar.: Prof. Dr. Wilhelm E. Jahnen-Dechent

Helmholtz-Institute for Biomedical Engineering, RWTH Aachen University (DE)  
*Mud in the blood: The role of fetuin, a protein-mineral complex, in mineral metabolism*

#### 12 Apr.: Prof. Dr. Oliver Söhnlein

Ludwig-Maximilians-University (LMU) Munich (DE)  
*Neutrophils in chronic inflammation – from physiology to therapeutic intervention*

#### 03 May: Prof. Robert Bristow

University of Manchester (UK)  
*The effect of hypoxia on the genomic architecture of human tumours*

#### 07 June: Prof. Dr. Larry J. Suva

Veterinary Physiology and Pharmacology, Texas A&M University, Galveston (USA)  
*Large animals in biomedical research: CRISPR, bisphosphonates and beyond*

#### 06 Sep.: Prof. Michal Schwartz

Department of Neurobiology, Weizmann Institute of Science, Rehovot (ISR)  
*A novel approach to defeat Alzheimer's disease: Empowering the immune system to mobilize monocyte-derived macrophages*

#### 04 Oct.: Prof. Dr. Anna Greka

Center for Kidney Disease and Novel Experimental Therapeutics, Harvard Institutes of Medicine, Brigham and Women's Hospital, Boston MA (USA)  
*The arc of discovery: From genes to mechanisms to therapies for kidney diseases and beyond*

#### 06 Dec.: Prof. Dr. Anna Köttgen

Institute of Genetic Epidemiology, Albert Ludwig University of Freiburg, Freiburg (DE)  
*Understanding kidney function through population-based genetic studies*



The winner and the jury committee of the Johanna Dürmüller-Bol DBMR Research Award 2021:  
Dr. med Dr. sc. nat. Joel Zindel  
Prof. Dr. Mark A. Rubin  
Prof. Dr. Anne Angelillo-Scherrer  
Prof. Dr. Marianna Kruithof-de Julio  
Ass. Prof. Dr. Volker Enzmann  
Ass. Prof. Dr. Carsten Riether (not in picture)



# Personnel Update

## Academic Degrees

### Full Professor

**Prof. Dr. Britta Maurer**  
Lung Precision Medicine

### Full Professor (Extraordinus)

**Prof. Dr. Benoît Schaller**  
Bone & Joint

### Assistant Professor

**Prof. Dr. Ziad Al Nabhani**  
Systems biomedicine of cellular development and signaling in health and disease

### Associate Professor

**Prof. Dr. Ursula Amstutz**  
BMG, Biomedical Genomics

**Prof. Dr. Alexander Eggel**  
Translational Immunology

**Prof. Dr. Marianna Kruihof-de Julio**  
Cancer Therapy Resistance

**Prof. Dr. Ren-Wang Peng**  
Oncology-Thoracic Malignancies

**Prof. Dr. Carsten Riether**  
Translational Cancer Research

**Prof. Dr. Nikola Saulacic**  
Bone & Joint

**Prof. Dr. Christoph Schlapbach**  
Translational Immunology

### Lecturer

**PD Dr. Carolina Gutierrez Herrera**  
ZEN/DBMR-Neuro

**PD Dr. Ramin Radpour**  
Translational Cancer Research

### PhD (Supervisor in parentheses)

**Ivan Bozic**  
(Prof. Dr. Antoine Roger Adamantidis)  
Coordination of sleep oscillations amongst cortical, thalamic and hippocampal structures – Relevance to sleep structure and function

**Maud Bagnoud**  
(Prof. Dr. Andrew Hao-Kuang Chan)  
Mechanisms to improve glucocorticosteroid efficacy in multiple sclerosis

**Emmanuele Giuseppe Bulla**  
(Prof. Pascal Escher)  
Molecular mechanisms of photoreceptor differentiation

**Martina Calió**  
(Prof. Benjamin Gantenbein)  
Intervertebral disc disease and osteoarthritis: approaching the research needs using RNA sequencing and mechanical unloading

**Kathrin Chiffi**  
(Prof. Dr. René Müri)  
Cognitive processes in healthy and stroke subjects, methodological considerations and the relation to sleep

**Noëlle Dommann**  
(Prof. Dr. Deborah Stroka)  
Unraveling proliferation by mapping origins of replication and the function of Ajuba

**Silvan Rolf Heeb**  
(Prof. Dr. Johanna Anna Kremer Hovinga)  
Novel insights into the immune response in immune-mediated and hereditary Thrombotic Thrombocytopenic Purpura

**Lijuan Ma**  
(Prof. Christoph Müller)  
The Role of EMT in the Alteration of Hormone Response in Endometriotic Lesions and its Contribution to the Recurrence of Endometriosis

**Pascal Näf**  
(Prof. Adrian Ochsenbein)  
The role of IL-33/ST2 signaling in hematopoiesis and myeloid leukemia

**Carlos Pulido Quetglas**  
(Prof. Rory Johnson)  
Accurate candidate selection for improved CRISPR library designs of long noncoding RNAs

**Yannick Raphael Suter**  
(Prof. Dr. Mauricio Reyes)  
Multiforme

**Anna Silvia Wenning**  
(Prof. Andrew MacPherson, Dr. Mercedes Gomez de Agüero)  
The maternal microbiota drives embryonic epidermal development and configures neonatal skin barriers

**Xingshuo Zhang**  
(Prof. Benjamin Gantenbein)  
Tissue-specific progenitor cells of the intervertebral disc – rare cells with big potential for the cure of low back pain?

**Joel Zindel**  
(Prof. Daniel Candinas and Prof. Deborah Keogh-Stroka)  
Peritoneal macrophage aggregation and EGFR-dependent mesothelial to mesenchymal transition: novel therapeutic avenues for peritoneal adhesions

### MD, PhD (Supervisor in parentheses)

**Sophie Manon Cottagnoud**  
(Dr. Marianne Jörger-Messerli and Prof. Dr. Andreina Schoeberlein)  
Isolation of Wharton's Jelly-derived small extracellular vesicles and analysis of their microRNA cargo

**Haibin Deng**  
(Prof. Ralph Schmid)  
Lactate dehydrogenase B (LDHB) and its involvement in mitochondrial metabolism in lung cancer

**Judith Gili-Kovács**  
(Prof. Dr. Andrew Chan and Dr. med. Myriam Sandra Briner)  
An algorithm using clinical data to predict the optimal individual glucocorticoid dosage to treat multiple sclerosis relapses

**Mirjam Nussbaumer**  
(PD Dr. Loretta Müller)  
Diagnosis of primary ciliary dyskinesia: discrepancy according to different algorithms

**Katharina AC Oswald**  
(PD Dr. Christoph Albers)  
Neisseria meningitidis-induced discitis at L5-S1 mimics lumbar disc herniation, accepted for publication in The Lancet Infectious Diseases

**Maximilian Pistor**  
(Prof. Dr. Andrew Chan and PD Dr. Med. Robert Hoepner)  
Immunotherapies and COVID-19 mortality: A multidisciplinary open data analysis based on FDA's Adverse Event Reporting System

**Irina Schlegel**  
(Prof. Dr. Martin S. Zinkernagel and Dr. Denise C. Zysset-Burri)  
Identification of the ocular microbiome and its role on dry eye disease

**Alexander Joseph Schmitz**  
(Prof. Dr. Smita Saxena)  
Emerging Perspectives on Dipeptide Repeat Proteins in C9ORF72 ALS/FTD

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**Staff changes**
**New Staff****Dr. med. Dilara Akhoundova Sanoyan**

Early Postdoc (80 %)  
Rubin Lab (since Apr.)

**Fiona Estelle Augsburg**

Lab Technician (80 %)  
FCCS (since Oct.)

**Gabriela Maria Bäerlocher**

Scientific Assistant (5 %)  
Baerlocher Lab (since May)

**Carole Gygax**

Lab Technician (20 %)  
Rieben Lab (since Aug.)

**Monika Haubitz**

Scientific Assistant (100 %)  
Baerlocher Lab (since May)

**Ingrid Helsen**

Lab Technician (100 %)  
Baerlocher Lab (since Apr.)

**Dr. Melle Holwerda**

Early Postdoc (100 %)  
Rieben Lab (since Mar.)

**Corinne Nicole Hug**

Lab Technician (100 %)  
DBMR Services (since Oct.)

**Kirsten Ina Irmiler**

Lab Technician (25 %)  
Rieben Lab (since June)

**Dr. Alina Naveed**

Early Postdoc (100 %)  
Rubin Lab (since Mar.)

**Saskia Perret-Gentil-dit-Maillard**

Scientific Assistant (20 %)  
Hofstetter Lab (since Oct.)

**Lorenzo Raeli**

Scientific Assistant (100 %)  
FCCS (since Oct.)

**Vincent Lucien Paul Rapp**

PhD Student (75 %)  
Osterwalder Lab (since Dec.)

**Neda Salimi Afjani**

PhD Student (70 %)  
Rieben Lab (since Jan.)

**Thi Bao Trân Vu**

Secretary (60 %)  
Administration (since Sep.)

**Junhua Wang**

Scientific Assistant (50 %)  
Rieben Lab (since Feb.)

**Lucille Wotzkow Alvarez**

Polymechanic (100 %)  
DBMR Services (since Sep.)

**Sigrid Zimmermann**

Human resources assistant (90 %)  
Administration (since Dec.)

**Resignations****Basak Ginsbourger**

Administrator (80 %)  
Administration (until Dec.)

**Claudia Güttinger**

Lab Technician (100 %)  
DBMR Services (until June)

**Matthias Reist**

Lab Technician (20 %)  
Rubin Lab (CTR)

**Mark Siegrist**

Lab Technician (50 %)  
Hofstetter Lab (until Mar.)

**Rahel Tschudi**

Human resources assistant (90 %)  
Administration (until Dec.)

**Claudio Vallan**

Scientific Assistant (10 %)  
FCCS (until July)

**Song Xue**

PhD Student (75 %)  
Clinical Radiopharmacy (until Mar.)

**Short employment****Ahmed Fahiem Abdelsalam**

Hilfsassistent (50 %)  
Rieben Lab (Mar. – Mar.)

**Anaïs Elodie Yerly**

Hilfsassistentin (50 %)  
Rieben Lab (Mar. – Mar.)

**Retirements****Silvia Dolder**

Lab Technician (90 %)  
Hofstetter Lab (until June)

**We mourn****Yvonne Roschi**

House Staff Manager (80 %)  
DBMR Services (until Mar.)

# Awards/Grants

## Prof. Dr. Ziad Al Nabhani

*Systems Biomedicine of Cellular Development and Signaling in Health and Disease*  
Helmut Horten Foundation's Grant for "How child intestinal microbiota influence lifelong immunity."

## Prof. Dr. Ziad Al Nabhani

*Systems Biomedicine of Cellular Development and Signaling in Health and Disease*  
Swiss Immunology Early Career Award 2021 by the Swiss Society for Allergology and Immunology and Sanofi Genzyme Switzerland Pasteur Institute Young Scientist Award 2021 by the Pasteur Institute, Paris, France

## Dr. Anke Augspach

*Cancer Therapy Resistance*  
Fond'ation contre le cancer Young Investigator Grant 2021 for "Towards understanding the role of the minor spliceosome in advanced cancer"

## Dr. Maxime Baud, Timothée Priox (UniGE)

*ZEN/DBMR-Neuro*  
Schweizerische Epilepsie Liga-Alfred-Hauptmann-Preis 2021 for publication: "Forecasting seizure risk in adults with focal epilepsy: a development and validation study"

## Dr. Maxime Baud

*ZEN/DBMR-Neuro*  
SNSF Eccellenza Professorial Fellowship for "Dynamical Control of Seizures"

## Dr. Daniel Brigger,

## Prof. Dr. Alexander Eggel

*Translational Immunology*  
Vontobel Award for Research on Age(ing) 2021, Center for Gerontology of the University of Zurich (endowed by the Vontobel Foundation), Project: "Eosinophils regulate adipose tissue inflammation and sustain physical and immunological fitness in old age."

## Dr. Daniel Brigger

## Prof. Dr. Alexander Eggel

*Dr. Mario Noti*  
*Translational Immunology*  
Vontobel-Preis für Alter(n)sforschung 2021 for the publication "Eosinophils Regulate Adipose Tissue Inflammation and Sustain Physical and Immunological Fitness in Old Age", published on Nature Metabolism, 6, 2020.

## Dr. Pauline Challande

*Regenerative Neuroscience*  
Manegold-Brauer G, Ardabili S, Hösli I, Schönberger H, Amyli-Mohr S, Kohl J, Hodel M, Surbek D, Raio L, Mosimann B. IPSISS—Implementing preeclampsia screening in a Switzerland Pilot study. Annual Congress Gynécologie Suisse-Swiss Society for Gynecology and Obstetrics, June 24–26, Interlaken, Switzerland. 1st Prize Free Communication.

## Dr. Noëlle A. Dommann

*Systems Biomedicine of Cellular Development and Signaling in Health and Disease*  
Benoit Pochon Prize 2021: "Unraveling proliferation by mapping origins of replication and the function of Ajuba"

## Dr. Therina du Toit

*Experimental Nephrology*  
H2020 MSCA IF for "Tracing novel androgen pathways: deciphering the role of 16 $\alpha$ -hydroxylation in human fetal biology."

## Prof. Dr. Alexander Eggel

*Translational Immunology*  
Theodor-Kocher-Preis (2021), University of Bern, Project: "From Innovation to Application: Putting Immunology Research into Use."

## Manuel Egle

*Cardiovascular Diseases*  
The Swiss National Science Foundation awarded the MD-PhD Grant for "Cardiac graft preservation and evaluation in transplantation with donation after circulatory death."

## Prof. Dr. Benjamin Gantenbein

*Bone & Joint*  
Best Poster award: Verbesserung der spinalen Fusion mittels BMP2 und L51P in einem spinalen Fusionsmodell der Ratte in vivo K. A. C. Oswald, S. F. Bigdon, A. S. Croft, P. Bermudez-Lekerika, B. Gantenbein, C. E. Albers (Bern/Schweiz) presented at the 16. Jahrestagung der Deutschen Wirbelsäulengesellschaft, Münster, 9.–11. Dezember 2021

## Liana Hayrapetyan

*Translational Cancer Research*  
Best Poster Award of the 2nd AACR-KCA Joint Conference on Precision Medicine in Solid Tumors, held on November 12, 2021.

## Liana Hayrapetyan

*Translational Cancer Research*  
Best Academic Presentation Award, Scientific Association of Swiss Radiation Oncology (SASRO), 25th Annual SASRO Meeting (Rorschach, Switzerland). Project title: "HPV and p53 status determine irradiation-related responses to a selective DNA-PK inhibitor in head and neck squamous cell carcinoma models"

## Liana Hayrapetyan

*Translational Cancer Research*  
Best Poster Award, 2nd AACR-KCA Joint Conference on Precision Medicine in Solid Tumors (Seoul, Korea and virtual). Title of the project: "HPV and p53 status determine irradiation-related responses to a selective DNA-PK inhibitor in head and neck squamous cell carcinoma models"

## Prof. Dr. Marianna Kruthof-de Julio

*Cancer Therapy Resistance*  
InnoSuisse Grant for "AlvireX: A game-changing translational drug screening platform to revolutionize drug development against respiratory viral infections"

## Dr. Niran Maharjan,

## Prof. Dr. Smita Saxena

*ZEN/DBMR-Neuro*  
FSRMM annual meeting 1st poster prize for "Seeding and spreading of dipeptide repeat proteins in C9ORF72 linked ALS"

## Harpreet Kaur Mandhair

*Translational Cancer Research*  
Short oral and poster presentation, 11th Swiss Apoptosis and Autophagy Meeting (SA2M) 2021 (Bern, Switzerland), awarded by the French Autophagy Society CFATG. Title of the project: "ULK complex blockade elicits NF- $\kappa$ B activation in GCB-DLBCL whilst augmenting cytotoxicity of Ibrutinib"

## Prof. Dr. Britta Maurer

*Lung Precision Medicine*  
Paul Klee Research Award, Boehringer Ingelheim, "HRCT-based radiomics for drug response reduction in progressive fibrosis interstitial lung disease"

## Prof. Dr. Eliane Jasmin Müller

*Molecular Dermatology & Stem Cell Research*  
Prof. Dr. Marianna Kruthof-de Julio Cancer Therapy Resistance SNF Sinergia Grant for "PROMETEX: Metabolically-instructed personalized therapy selection for prostate cancer."

## PD Dr. Loretta Müller

*Lung Precision Medicine*  
SAG Award (2021) for the publication "Diesel exposure increases susceptibility of primary human nasal epithelial cells to rhinovirus infection"

## Dr. Charlotte Ng

*Oncogenomics*  
Bern Center for Precision Medicine Young Investigators Projects: "Towards translating hepatocellular carcinoma cellular interactions into biomarkers"

## Dr. Anda-Petronela Radan

*Regenerative Neuroscience*  
Fluri M, Schlatter B, Raio L, et al.. Gestational diabetes is associated with SARSCoV-2 infection during pregnancy. Annual Congress Gynécologie Suisse-Swiss Society for Gynecology and Obstetrics, June 24–26, Interlaken, Switzerland. 2nd Prize Poster.

## Patricia Verena Renz

*Regenerative Neuroscience*  
Deciphering astrocyte polarization in acute perinatal white matter injury and its contribution to disease outcomes. European Neuroscience Conference by Doctoral Students (ENCODS), June 4–6, 2021. Online. Short presentation.

**Patricia Verena Renz***Regenerative Neuroscience*

Tscherrig V, Haesler V, Liddelow S, Schoeberlein A, Surbek D, Brosius Lutz A. Understanding the role of inflammatory reactive astrocytes in acute perinatal white matter injury. Stem Cell Community Day, Nov 3, 2021, Cologne, Germany. Short presentation

**Ass. Prof. Dr. Carsten Riether***Translational Cancer Research*

Pfizer Research Prize (Oncology)

**Prof. Dr. Mark A. Rubin***Cancer Therapy Resistance*

Werner und Hedy Berger-Janser Foundation: "Molecular characterization, in vitro modelling and therapeutic targeting of prostate cancer liver metastases"

**Prof. Dr. Mark A. Rubin***Cancer Therapy Resistance*

Fondation ISREC Translational Project:

"Advanced in vitro models of prostate cancer metastases: unravelling and overcoming ARSI resistance"

**Dr. Markus Schmidt***ZEN/DBMR-Neuro*

SNSF Project Funding for "Hypothalamic regulations of REM sleep"

**Dr. Gerd Tinkhauser***ZEN/DBMR-Neuro*

SNSF Ambizione Grant for "Adaptive neuromodulation in movement disorders – a precision medicine approach"

**Ioanna Tsioti***Regenerative Neuroscience*

XIXth International Symposium on Retinal Degenerations (RD2021) and the BrightFocus Macular Fast TrackSM awarded a virtual travel fellowship for the project: "Systemic lipopolysaccharide exposure triggers Tlr4-dependent inflammatory responses in the mouse retina in vivo."

**Dr. Nicoletta Sorvillo***Blood*

Prof. Dr. Uyen Huynh-Do

Experimental Nephrology

CSL Research Acceleration Initiative Funding.

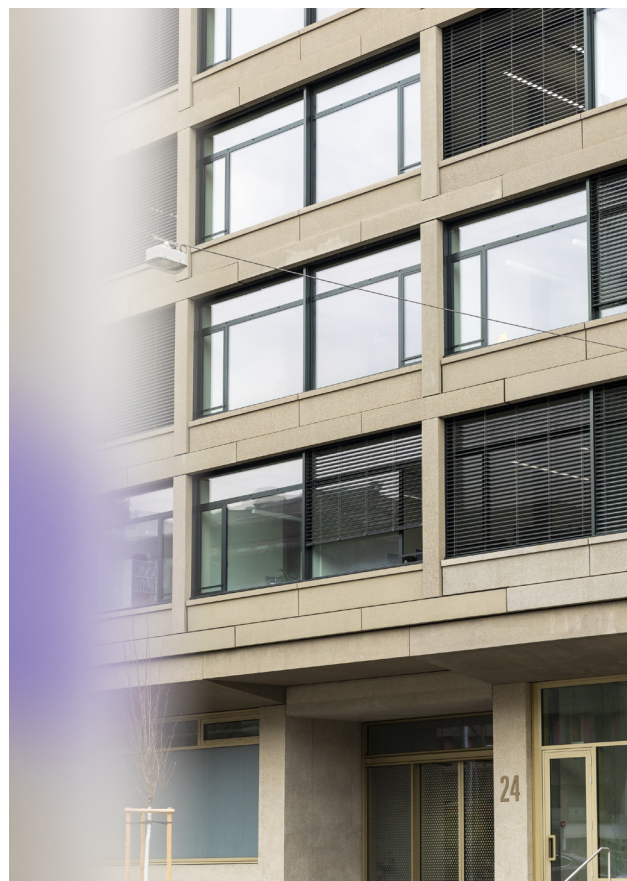
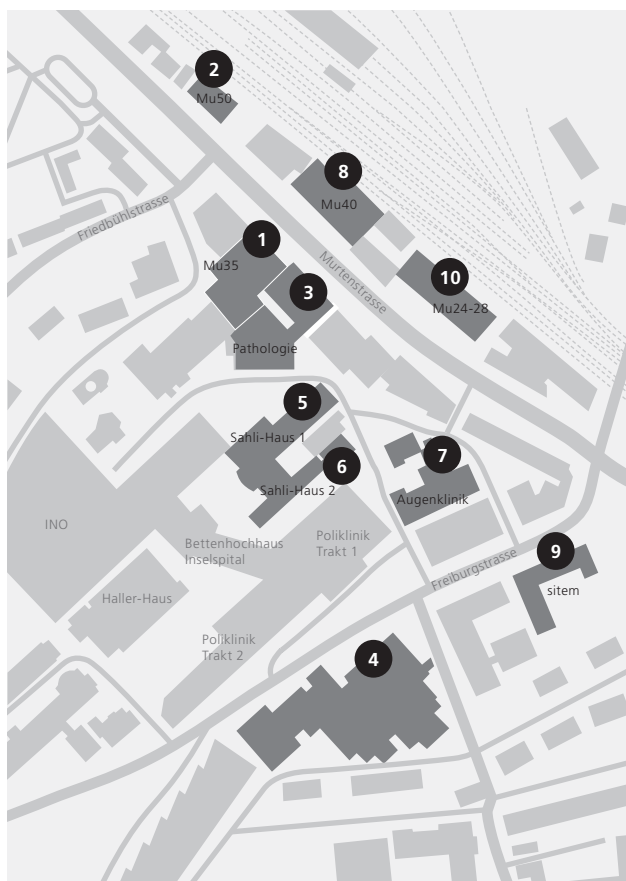
**Dr. Bahtiyar Yilmaz***Systems Biomedicine of Cellular Development and Signaling in Health and Disease*

Bern Center for Precision Medicine Young Investigators Projects: "Targeting D-lactate producing gut microbial strains in pediatric IBD patients"

**Dr. Jakob Zimmermann***Systems Biomedicine of Cellular Development and Signaling in Health and Disease*

Bern Center for Precision Medicine Young Investigators Projects: Transcriptional recording sentinel cells as living diagnostics of the human gastrointestinal tract"

# DBMR Locations



- |   |   |
|---|---|
| <b>1 Murtenstrasse 35</b>   | <b>6 Sahli-Haus 2</b><br>Freiburgstrasse 14                               |
| <b>2 Murtenstrasse 50</b>   | <b>7 Augenklinik</b><br>(Ophthalmology – Eye Clinic)<br>Freiburgstrasse 8 |
| <b>3 Pathologie</b><br>(Institute of Pathology)   | <b>8 Murtenstrasse 40</b>   |
| <b>4 Kinderklinik</b><br>(Children's University<br>Hospital Bern)<br>Freiburgstrasse 15 | <b>9 sitem</b><br>Freiburgstrasse 3                                       |
| <b>5 Sahli-Haus 1</b><br>Freiburgstrasse 14a  | <b>10 Murtenstrasse 24–28</b>   |

#### **Imprint**

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Cellular Development and Signaling in Health and Disease

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