Regenerative Medicine and Medical Imaging

Symposium Program **11.12.2023**

10:00-10:15 Welcome at UMR1260 CRBS (Centre de Recherche en Biomédecine de Strasbourg, 1 Rue Eugene Boeckel, Strasbourg)
10:15-11:15 Guided tour of the UMR1260 CRBS
11:15-12:45 Lunch (CRBS 2nd floor)

Oral presentations (12' plus 3' discussion)

12:45-13:00 **Willy Kuo**: Micrometer resolution computed tomography of mouse brain cerebrospinal fluid spaces *in vivo* at the synchrotron SPring-8
13:00-13:15 **Pierre-Yves Gegout**: Porphyromonas gingivalis promotes the secretion of pro-inflammatory extracellular vesicles by oral keratinocytes
13:15-13:30 **Hans Deyhle**: Challenges in imaging the entire human brain at cellular resolution
13:30-13:45 **Guoqiang Hua**: Mechanistic illustration: How newly-formed blood vessels stopped by the mineral blocks of bone substitutes can be avoided by using innovative combined therapeutics
13:45-14:00 **Christine Tanner**: Nondestructive analysis of annual layers in archeological teeth cementum based on synchrotron radiation microtomography
14:00-14:15 **Florence Toti**: Microvesicles in organ transplantation and shock
14:15-15:15 Flash poster session and coffee break (CRBS 2nd floor)

Oral presentations (12' plus 3' discussion)

15:15-15:30 **Guido R. Sigron**: Combining high-resolution hard X-ray tomography and histology to evaluate stem cell-mediated distraction osteogenesis
15:30-15:45 **Rana Smaida**: Lamina Therapeutics: Development of a combined advanced therapy medicinal product for regenerative medicine
15:45-16:00 **Georg Schulz**: Micro- and Nanotomography Core Facility: Next-generation X-ray microCTs (Exciscope Polaris & Zeiss xradia 610 Versa) in comparison to the state of the art (phoenix|xray nanotom m & Bruker Skyscan 1275)
16:00-16:15 **Thierry Vandamme**: Biogalenic and therapeutic innovation
16:15-16:30 **Griffin Rodgers**: Personalized non-invasive neuromodulation for treatment at home
16:30-16:45 **Canan G. Nebigil**: Follow your cardiac spheroids: Tackling cardiotoxicity by finding an early biomarker

Micrometer resolution computed tomography of mouse brain cerebrospinal fluid spaces *in vivo* at the synchrotron SPring-8

Willy Kuo,[1] Marta Girona Alarcón,[1] Britta Bausch,[1] Irene Spera,[2] Mattia Humbel,[3] Hans Deyhle,[3] Britta Engelhardt,[2] Steven Proulx,[2] Bert Müller,[3] Vartan Kurtcuoglu[1]

[1]*The Interface Group, Institute of Physiology, University of Zurich, Switzerland*

[2]*Theodor Kocher Institute, University of Bern, Bern, Switzerland*

[3]*Biomaterials Science Center, Department of Biomedical Engineering / Department of Clinical Research, University of Basel, Switzerland*

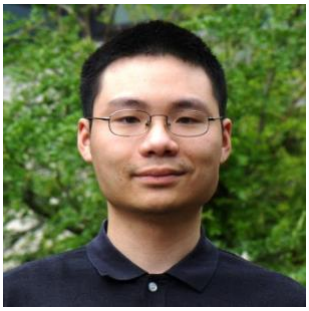
The blood-brain barrier limits the entry of immune cells from the blood into the central nervous system. Immune cells are, however, also present in the cerebrospinal fluid (CSF), the liquid surrounding the brain. Autoimmune diseases such as multiple sclerosis are characterized by a breakdown of the brain-CSF-barrier, allowing immune cells to enter the brain from the CSF. We aim to better understand this disease mechanism by reconstructing immune cell paths via capturing time-resolved μCT images of contrast agent distribution in the CSF and combining these data with in vivo microscopy images and computational fluid dynamics models. We will present the first *in vivo* imaging experiments at the synchrotron SPring-8 in Japan.

[1] B. Engelhardt and C. Coisne: *Fluids and barriers of the CNS establish immune privilege by confining immune surveillance to a two-walled castle moat surrounding the CNS castle*, Fluids Barriers CNS, **8** (2011) 4, doi:10.1186/2045-8118-8-4

[2] M. Asgari, D. A. de Zélicourt, and V. Kurtcuoglu: *Barrier dysfunction or drainage reduction: differentiating causes of CSF protein increase*, Fluids and Barriers of the CNS, **14** (2017) 14, doi:10.1186/s12987-017-0063-4

[3] G. Rodgers et al., *Virtual histology of an entire mouse brain from formalin fixation to paraffin embedding. Part 1: Data acquisition, anatomical feature segmentation, tracking global volume and density changes*, Journal of Neuroscience Methods, **364** (2021) 109354, doi:10.1016/j.jneumeth.2021.109354.

[4] W. Kuo et al., *Simultaneous Three-Dimensional Vascular and Tubular Imaging of Whole Mouse Kidneys With X-ray μCT*, Microsc Microanal, **26** (2020) 731–740, doi:10.1017/S1431927620001725.



Willy Kuo is a senior scientist at the University of Zurich. He received his BS and MS degrees in Interdisciplinary Sciences from the ETH Zürich. He received his PhD degree in Integrative Molecular Medicine at the University of Zurich, working on micrometer resolution imaging of whole mouse kidneys with synchrotron X-ray tomography and 3D light microscopy methods. Current research activities include development of custom-designed X-ray contrast agent and *in vivo* imaging at synchrotron radiation facilities.

Porphyromonas gingivalis promotes the secretion of pro-inflammatory extracellular vesicles by oral keratinocytes

Pierre-Yves Gegout, Benjamin Mary, Céline Stutz, Vincent Hyenne, Hadar Zigdon-Giladi, Olivier Huck

French National Institute of Health and Medical Research (INSERM), UMR 1260, Regenerative Nanomedicine (RNM), Strasbourg, France

Extracellular vesicles (EVs) are recognized as important cellular mediators involved in significant biological processes such as maintaining homeostasis, inflammation response, or wound healing. Recently, it has been observed that EVs could play a paracrine or autocrine role in the development of periodontal or peri-implantitis lesions, especially when responding to periodontal pathogens. This study aimed to isolate EVs released by oral epithelial cells in response to Porphyromonas gingivalis and ascertain their pro-inflammatory impact when introduced to naïve epithelial cells. Another focus was to identify EVs' miRNA content changes.

[1] P.-Y. Gegout et al.: *Interests of Exosomes in Bone and Periodontal Regeneration: A Systematic Review*, Cell Biology and Translational Medicine, **13** (2020), doi:10.1007/5584_2020_593.

[2] P. D. Stahl, and G. Raposo: *Extracellular Vesicles: Exosomes and Microvesicles, Integrators of Homeostasis*, Physiology, **34** (2019) 3, doi:10.1152/physiol.00045.2018.

[3] R. Wang. et al.: *Role of gingival mesenchymal stem cell exosomes in macrophage polarization under inflammatory conditions*, International Immunopharmacology, **81** (2020), doi:10.1016/j.intimp.2019.106030.

Pierre-Yves Gegout is a PhD student at the INSERM UMR1260, and an assistant professor at the Department of Periodontology of Strasbourg. He received his DDS degrees and obtained his specialization in Periodontology from the University Strasbourg in 2019 and 2022. His current research interests include periodontal diseases and bone regeneration.

Challenges in imaging the entire human brain at cellular resolution

Hans Deyhle,[1] Griffin Rodgers,[1] Mattia Humbel,[1] Christine Tanner,[1] Georg Schulz,[1] Felix Beckmann,[2] Julian Moosmann,[2] Bert Müller[1]

[1]*Biomaterials Science Center, Department of Biomedical Engineering, Medical Faculty, University of Basel, Switzerland*

[2]*X-ray Imaging with Synchrotron Radiation, Hereon Outstation at DESY in Hamburg, Germany*

The human brain is a complex organ that coordinates essential human abilities such as memory, vision, respiration, and body temperature regulation. Its diameter is on the order of 10 cm, whereas cells are on the order of micrometers. Thus, obtaining images of the entire brain at cellular resolution poses a significant challenge, as one finds a trade-off between imaged volume and spatial resolution. Currently, visualization of the anatomical features on the micrometer or even nanometer level is only obtained after physical sectioning that leads to severe artefacts and, generally, a reduction of spatial resolution in one of the three orthogonal directions. Synchrotron radiation-based micro computed tomography takes advantage of the penetration power of hard X-rays to circumvent physical sectioning. The talk covers some technical challenges involved in imaging cm-sized objects with micrometer resolution and presents preliminary results obtained at the beamline p07 at the DESY in Germany.

Hans Deyhle is a research associate at the Biomaterials Science Center at the University of Basel. He received his diploma in experimental physics from the Swiss Federal Institute of Technology Zürich in 2007, respectively, and his PhD degree in experimental physics from the University of Basel in 2012. His current research interests include advanced multimodal synchrotron imaging techniques, with application in biomedical science.

Mechanistic illustration: How newly-formed blood vessels stopped by the mineral blocks of bone substitutes can be avoided by using innovative combined therapeutics

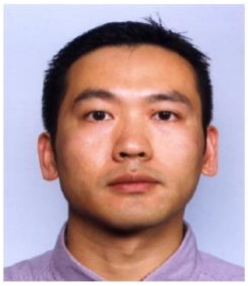
Guoqiang Hua,[1] Fabien Bornert,[1] François Clauss,[1] Ysia Idoux-Gillet,[1] Laetitia Keller,[1] Gabriel Fernandez De Grado,[1] Damien Offner,[1] Rana Smaida,[1] Quentin Wagner,[1] Florence Fioretti,[1] Sabine Kuchler-Bopp,[1] Georg Schulz,[2] Wolfgang Wenzel,[1] Luca Gentile,[1] Laurent Risser,[1] Bert Müller,[2] Olivier Huck,[1] Nadia Benkirane-Jessel[1]

[1]*French National Institute of Health and Medical Research (INSERM), UMR 1260, Regenerative Nanomedicine (RNM), Strasbourg, France*

[2]*Biomaterials Science Center, Department of Biomedical Engineering, Medical Faculty, University of Basel, Switzerland*

One major limitation for the vascularization of bone substitutes used for filling is the presence of mineral blocks. The newly-formed blood vessels are stopped or have to circumvent the mineral blocks, resulting in inefficient delivery of oxygen and nutrients to the implant. This leads to necrosis within the implant and to poor engraftment of the bone substitute. The aim of the present study is to provide a bone substitute currently used in the clinic with suitably guided vascularization properties. This therapeutic hybrid bone filling, containing a mineral and a polymeric component, is fortified with pro-angiogenic smart nano-therapeutics that allow the release of angiogenic molecules. Our data showed that the improved vasculature within the implant promoted new bone formation and that the newly-formed bone swapped the mineral blocks of the bone substitutes much more efficiently than in non-functionalized bone substitutes. Therefore, we demonstrated that our therapeutic bone substitute is an advanced therapeutical medicinal product, with great potential to recuperate and guide vascularization that is stopped by mineral blocks, and can improve the regeneration of critical-sized bone defects. We have also elucidated the mechanism to understand how the newly-formed vessels can no longer encounter mineral blocks and pursue their course of vasculature, giving our advanced therapeutical bone filling great potential to be used in many applications, by combining filling and nano-regenerative medicine that currently fall short because of problems related to the lack of oxygen and nutrients.

[1] G. Fernandez de Grado, L. Keller, Y. Idoux-Gillet, Q. Wagner, A.-M. Musset, N. Benkirane-Jessel, F. Bornert, D. Offner: *Bone Substitutes: A Review of Their Characteristics, Clinical Use, and Perspectives for Large Bone Defects Management*, Journal of Tissue Engineering, **9** (2018), doi:10.1177/2041731418776819.



First Author is an associated professor at the University of Strasbourg. He received his MS and Ph.D degrees in Immunology from the University of Aix-Marseille in 2005 and 2009, respectively. He is the author of more than 30 international peer-reviewed research papers with more than 1000 citations. His current research interests include tissue engineering, bone/cartilage regeneration, patient-derived organoids formation for precision medicine, stem cell production/ reprogramming/differentiation.

Nondestructive analysis of annual layers in archeological teeth cementum based on synchrotron radiation microtomography

Christine Tanner,[1] Muriel Stiefel,[1] Georg Schulz,[1,2] Griffin Rodgers,[1] Gabriela Mani-Caplazi,[3] J. A. von Jackowski,[1] Gerhard Hotz,[3,4] Mario Scheel,[5] Timm Weitkamp,[5] Bert Müller[1]

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[3]*Integrative Prehistory and Archaeological Science, University of Basel, Basel, Switzerland;*

[4]*Natural History Museum of Basel, Anthropological Collection, Basel, Switzerland;*

[5]*Synchrotron Soleil, 91192 Gif-sur-Yvette, France*

Human tooth cementum can exhibit yearly deposited incremental layers, which traditionally are visualized using optical microscopy, *e.g.* [1]. Synchrotron radiation microtomography (SRμCT) enables nondestructive analysis of the layers in three dimensions due to the layers' density variations and relatively high spatial resolution of SRμCT [2,3]. This study presents an automatic method to increase the contrast of incremental layers in SRμCT [3]. We show that the resulting enhancement facilitates the determination of incremental layer distances and the comparison of layer appearance with optical microscopy for archeological human teeth [3,4].

[1] G. Mani-Caplazi, G. Hotz, U. Wittwer-Backofen, W. Vach: *Measuring incremental line width and appearance in the tooth cementum of recent and archaeological human teeth to identify irregularities: First insights using a standardized protocol*, International Journal of Paleopathology, **27** (2019) 24-37, doi:10.1016/j.ijpp.2019.07.003

[2] G. Mani-Caplazi, G. Schulz., H. Deyhle, G. Hotz, W. Vach, U. Wittwer-Backofen, B. Müller: *Imaging of the human tooth cementum ultrastructure of archeological teeth, using hard X-ray microtomography to determine age-at-death and stress periods*, Proceedings of SPIE, **10391** (2017) 103911C, doi:10.1117/12.2276148

[3] C. Tanner, G. Rodgers, G. Schulz, M. Osterwalder, G. Mani-Caplazi, G. Hotz, M. Scheel, T. Weitkamp, B. Müller: *Extended-field synchrotron microtomography for non-destructive analysis of incremental lines in archeological human teeth cementum*, Proceedings of SPIE, **11840** (2021) 1184019, doi:10.1117/12.2595180

[4] B. Müller, M. Stiefel, G. Rodgers, M. Humbel, M. Osterwalder, J. A. von Jackowski, G. Hotz, A. A. Velasco Guadarrama, H. T. Bunn, M. Scheel, T. Weitkamp, G. Schulz, C. Tanner: *Three-dimensional imaging and analysis of annual layers in tree trunk and tooth cementum*. Proceedings of SPIE, **12041** (2022) 120410C, doi:10.1117/12.2615148

Christine Tanner is senior scientist in medical image processing and data analysis. She worked for Siemens AG in Munich, Germany, as a software engineer for 12 years. In 1998, she graduated from the University of Edinburgh, United Kingdom, with a degree in artificial intelligence and mathematics. After a research MSc on radar target classification, she completed her part-time PhD at King's College London, United Kingdom, in 2005 on registration and lesion classification of magnetic resonance breast images. She then was a research fellow and lecturer at University College London, United Kingdom, and the ETH Zürich, Switzerland, in the field of medical image analysis. In 2020, she joined the Biomaterials Science Center at the University of Basel, Switzerland, for support it in all aspects of quantitative information extraction from images.

Microvesicles in organ transplantation and shock

Florence Toti, Laurence Kessler, Julie Helms, Ferhat Meziani

French National Institute of Health and Medical Research (INSERM), UMR 1260, Regenerative Nanomedicine (RNM), Strasbourg, France

Microvesicles (MVs) are plasma membrane fragments shed by stimulated cells that circulate as makers of cell damage and remote cell effectors. Using 2D and spheroids 3D coculture, animal models, and clinical trials, we showed the endothelium as key for the pharmacological control of the coupling between inflammatory and procoagulant responses, in sterile inflammation (pancreatic islet transplantation), or infection-driven inflammatory responses (sepsis). We identified MVs released in both situations, their cellular and molecular partners and how drugs interfere. In islet models, MVs are paracrine and autocrine mediators of the mesenchymal transition that can be pharmacologically repurposed.

[1] D. B. da Cruz, J. Helms, L. R. Aquino, et al.: *DNA-bound elastase of neutrophil extracellular traps degrades plasminogen, reduces plasmin formation, and decreases fibrinolysis: proof of concept in septic shock plasma*, FASEB Journal, **33** (2019) 12 14270-14280. doi:10.1096/fj.201901363RRR.

[2] A. Van der Heyden, P. Chanthavong, E. Angles-Cano, et al.: *Grafted dinuclear zinc complexes for selective recognition of phosphatidylserine: Application to the capture of extracellular membrane microvesicles*, Journal of Inorganic Biochemistry, **239** (2023) 112065. doi:10.1016/j.jinorgbio.2022.112065.

[3] H. Merdji, M. Kassem, L. Chomel, et al.: *Septic shock as a trigger of arterial stress-induced premature senescence: A new pathway involved in the post sepsis long-term cardiovascular complications*, Vascular Pharmacology, **141** (2021) 106922. doi:10.1016/j.vph.2021.106922.

[4] L. Amoura, F. Z. El-Ghazouani, M. Kassem, et al.: *Assessment of plasma microvesicles to monitor pancreatic islet graft dysfunction: Beta cell- and leukocyte-derived microvesicles as specific features in a pilot longitudinal study*, American Journal of Transplantation, **20** (2020) 1 40-51. doi:10.1111/ajt.15534.

First Author is a professor of pharmacology at the Faculty of Pharmacy of Strasbourg and the co-founder the International Master of Biomedicine. She received her Maîtrise in Biochemistry from the University Pierre et Marie Curie (Paris VI), her DEA in Molecular and cellular biology (equivalent to the current M2 master degree) from the University of Strasbourg as well as her PhD degree in Biosciences (1990). Her field of expertise includes blood products, cellular hemostasis and tissue remodeling, and the mechanisms of microvesicle release from cells. She is the co-author of more than 109 manuscripts or book chapters and the co-author of 3 patents. Her current research spans from cellular approaches (2D and spheroids) to animal models and clinical investigation. She focusses on the deciphering of the role of microvesicles as biomarkers and effectors of cell responses, especially in hemostasis, diabetes, bronchiolitis obliterans and cystic fibrosis, shock, and transplantation.

Combining high-resolution hard X-ray tomography and histology to evaluate stem cell-mediated distraction osteogenesis

Guido R. Sigron,[1] Griffin Rodgers,[1] Christine Tanner,[1] Simone E. Hieber,[1] Felix Beckmann,[2] Georg Schulz,[1] Arnaud Scherberich,[3] Claude Jaquiéry,[4] Christoph Kunz,[4] Bert Müller[1]

[1]*Biomaterials Science Center, Department of Biomedical Engineering, Medical Faculty, University of Basel, Switzerland*

[2]*X-ray Imaging with Synchrotron Radiation, Hereon Outstation at DESY in Hamburg, Germany*

[3]*Bone Regeneration, Department of Biomedicine, University of Basel, Basel, Switzerland*

[4]*Clinic of Oral and Cranio-Maxillofacial Surgery, Department of Surgery, University Hospital of Basel, Basel, Switzerland*

Distraction osteogenesis mainly relies on a limited number of histological slices comprising only about 1% of the volume of interest. In order to analyze the entire rat jaw, we combined micro computed tomography (μCT) with histology. The μCT data acquired before and after decalcification were registered to determine the local tissue shrinkage. Identification of the location of the hematoxylin-and-eosin-stained slices within the synchrotron radiation-based μCT data was achieved via non-rigid slice-to-volume registration. The resulting bi- and tri-variate histograms divided into clusters related to anatomical features led to the hypothesis that the multimodal imaging could be used to discriminate between collagen types [1].

[1] G. Rodgers, G. R. Sigron, C. Tanner, S. E. Hieber, F. Beckmann, G. Schulz, A. Scherberich, C. Jaquiéry, C. Kunz, B. Müller: *Combining high-resolution hard X-ray tomography and histology for stem cell-mediated distraction osteogenesis*, Applied Sciences **12** (2022) 6286, doi:10.3390/app12126286

Guido Remigius Sigron is a cranio-maxillo-facial surgeon working at public hospital Kantonsspital Aarau and the private company Zahnchirurgie Zürich AG. He earned a doctoral degree in dentistry from the University of Zurich in 2010 and a doctoral degree in medicine from the University of Basel in 2015. For his research, he was awarded with two grants. Dr. Dr. Sigron teaches at the Master courses of the University of Basel and had co-supervised several thesis projects. His research interests covers a wide variety of subjects including biomedical imaging and biomaterials for the oral cavity. He has been an entrepreneur being shareholder of several companies including Bottmedical AG and Bottneuro AG both located in Basel, Switzerland.

Lamina Therapeutics: Development of a combined advanced therapy medicinal product for regenerative medicine

Rana Smaida,[1] Morgane Meyer,[1,2] Guoqiang Hua,[1,2] Nadia Benkirane-Jessel,[1,3]

[1]*Lamina Therapeutics, Strasbourg, France*

[2]*Université de Strasbourg, (Faculté de Médecine, Faculté de Chirurgie Dentaire, Faculté de Pharmacie), Strasbourg, France*

[3]*French National Institute of Health and Medical Research (INSERM), UMR 1260, Regenerative Nanomedicine (RNM), Strasbourg, France*

Over recent years, breakthroughs in regenerative medicine and tissue engineering have reshaped healthcare. These innovative techniques target the intrinsic repair constraints of human tissues, notably in cartilage and bone, leveraging advanced implantable medical device designs, and advanced therapy medicinal products. However, despite these advancements, significant challenges remain in achieving comprehensive tissue regeneration. Our team developed a combined advanced therapy medicinal product by integrating a polymeric electrospun implantable device for subchondral bone regeneration with a hydrogel containing mesenchymal stem cells for cartilage regeneration to treat advanced osteoarthritis. The creation of the spin-off Lamina Therapeutics underscores our dedication to translating laboratory discoveries into practical clinical applications.

[1] L. Keller, L. Pijnenburg, Y. Idoux-Gillet, F. Bornert, L. Benameur, M. Tabrizian, P. Auvray, P. Rosset, R. María Gonzalo-Daganzo,E. Gómez Barrena, L. Gentile, N. Benkirane-Jessel: *Preclinical safety study of a combined therapeutic bone wound dressing for osteoarticular regeneration*. Nature Commununications, **10** (2019) 2156, doi:10.1038/s41467-019-10165-5

[2] R. Smaida, L. Pijnenburg, S. Irusta, E. Himawan, G. Mendoza, E. Harmouch, Y. Idoux-Gillet, S. Kuchler-Bopp, N. Benkirane-Jessel, G. Hua: *Potential Implantable Nanofibrous Biomaterials Combined with Stem Cells for Subchondral Bone Regeneration*. Materials, **13** (2020) 14 3087, doi:10.3390/ma13143087

[3] H. Favreau, L. Pijnenburg, J. Seitlinger, F. Fioretti, L. Keller, D. Scipioni, H. Adriaensen, S. Kuchler-Bopp, M. Ehlinger, D. Mainard, P. Rosset, G. Hua, L. Gentile, N. Benkirane-Jessel: *Osteochondral repair combining therapeutics implant with mesenchymal stem cells spheroids*, Nanomedicine: Nanotechnology, Biology and Medicine, **29** (2020) 102253, doi:10.1016/j.nano.2020.102253

Rana Smaida is currently a Project Manager at Lamina Therapeutics. She received her MS degree in Biomaterials for Health from the University of Strasbourg in 2020 and her PhD degree in Biotechnology of her work at the Regenerative Nanomedicine laboratory from the University of Strasbourg in 2023. Her current research interests include advanced therapy medicinal products and implantable medical devices.

Micro- and Nanotomography Core Facility: Next-generation X-ray microCTs (Exciscope Polaris & Zeiss xradia 610 Versa) in comparison to the state of the art (phoenix|xray nanotom m & Bruker Skyscan 1275)

Georg Schulz, Alexandra Migga, Christine Tanner, Bert Müller

BMC & MiNa, DBE, University of Basel, Allschwil, Switzerland

The laboratory-based microtomography activities at the Biomaterials Science Center began in 2008 with the acquisition of a Skyscan 1174 (Bruker, Kontich Belgium) and were expanded in 2011 with the nanotom® m (Waygate Technologies, Wunstorf, Germany). Following the replacement of the Skyscan 1174 with a Skyscan 1275 in 2016, the Micro- and Nanotomography Core Facility was officially put into service. With a spatial resolution between ≲1 µm and 75 µm, the two state-of-the-art devices are used to investigate internal structures for a range of sample classes, including biomedical samples, composite materials, electronic devices and palaeontological objects. Inline phase tomography using synchrotron radiation with voxel sizes in the sub-micrometre range is now the gold standard for the examination of soft and hard tissues with a resolution in the micrometer range. Recent developments in detectors and X-ray sources have made it possible to transfer the method to the laboratory environment. Three manufacturers were compared in order to equip the Core Facility with such a device [1]. Since October 2023, the Core Facility has been expanded with a xradia 610 Versa (Zeiss, Oberkochen, Germany) and a Polaris (Exciscope, Kista, Sweden). Next-generation microtomography systems have the potential to study epilepsy mouse models, which was previously done with synchrotron radiation [2].

[1] A. Migga, *et al.*: *Comparative hard x-ray tomography for virtual histology of zebrafish larva, human tooth cementum, and porcine nerve*, Journal of Medical Imaging **9** (2022) 3 031507, doi:10.1117/1.JMI.9.3.031507

[2] G. Rodgers, C. Bikis, P. Janz, C. Tanner, G. Schulz, P. Thalmann, C. A. Haas, B. Müller: *3D X-ray histology for the investigation of temporal lobe epilepsy in a mouse model,* Microscopy and Microanalysis **00** (2023) 1-16, doi:10.1093/micmic/ozad082

Georg Schulz is a senior scientist in the high-resolution X-ray imaging group at the Biomaterials Science Center, University of Basel. Since 2017 he is the scientific and technical leader of the 'Micro- and Nanotomography' Core Facility of the Department of Biomedical Engineering. His current research topics include laboratory- and synchrotron radiation-based high-resolution X-ray microtomography using absorption- and phase-contrast modes. He graduated 2008 in theoretical physics (diploma) at University of Freiburg i. Br., Germany and received 2012 his Ph.D. in applied physics at the University of Basel.

Biogalenic and therapeutic innovation

Thierry Vandamme**,** Nicolas Anton, Guillaume Conzatti

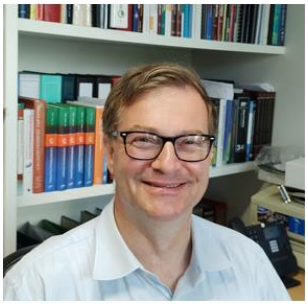
French National Institute of Health and Medical Research (INSERM), UMR 1260, Regenerative Nanomedicine (RNM), Strasbourg, France

The general objective of the Biogalenic and Therapeutic Innovations team is to develop new systems both for therapy or tissue engineering and for diagnosis, achieved through different techniques and innovative formulations containing molecules of interest, or the development of functional systems. Multidisciplinary, the Biogalenic and Therapeutic Innovations team covers many scientific fields such as formulation, chemical modification, processes, nanosciences, and the science of semi-solid and solid materials [1-3]. It also benefits from the know-how of the other teams of the Regenerative Nanomedicine laboratory as well as the CRBS technology platforms.

[1] G. Conzatti, D. Faucon, M. Castel, F. Ayadi, S. Cavalie, A. Tourrette: *Alginate/chitosan polyelectrolyte complexes : A comparative study of the influence of the drying step on physicochemical properties*, Carbohydrate Polymers **172** (2017) 142-151, doi:10.1016/j.carbpol.2017.05.023

[2] R. Pedron, T. Vandamme, V. A. Luchnikov: *Programming of drug release via rolling-up of patterned biopolymer films*, Nano Select, **2** (2021) 5 948-957, doi:10.1002/nano.202000126

[3] S. Ding, B. Mustafa, N. Anton, C. A. Serra, D. Chan-Seng, T. F. Vandamme: *Production of lipophilic nanogels by spontaneous emulsification*, International Journal of Pharmaceutics, **585** (2020) 119481, doi:10.1016/j.ijpharm.2020.119481



T. Vandamme perform with his research team the design, the formulation and pharmacokinetic studies of innovative therapeutic tools. He conducted and participated to several public-private consortia, several of them resulting in developments of new marketed drug delivery systems. He carried out and he is carrying on an important activity of scientific management of several projects (more than 20), both at the European and National levels.

Personalized non-invasive neuromodulation for treatment at home

Griffin Rodgers, Mahyar Joodaki, Bekim Osmani

Bottneuro AG, Basel, Switzerland

Transcranial alternating current stimulation (tACS) is a non-invasive brain stimulation technique that could potentially serve as a therapy for several brain disorders [1,2]. Inter-patient anatomical variations require personalized planning to deliver accurate and focal tACS [3]. Therefore, Bottneuro creates personalized head models [4] and electrode positioning systems for customized neurostimulator caps based on patient MRIs. We optimize electric field distribution to propose a tACS montage for each physician-prescribed anatomical target. The trade-offs and limitations in montage selection will be discussed, with an outlook towards future developments in non-invasive brain stimulation.

[1] H. Hampel, *et al.*: *Revolution of Alzheimer Precision Neurology. Passageway of Systems Biology and Neurophysiology*, Journal of Alzheimer's Disease, **64(s1)** (2018) S47-S105, doi:10.3233/JAD-179932

[2] A. Menardi, S. Rossi, G. Koch, H. Hampel, A. Vergallo, M. A. Nitsche, Y. Stern, B. Borroni, S. F. Cappa, M. Cotelli, G. Ruffini, G. El-Fakhri, P. M. Rossini, B. Dickerson, A. Antal, C. Babiloni, J.-P. Lefaucheur, B. Dubois, G. Deco, U. Ziemann, A. Pascual-Leone, E. Santarnecchi: *Toward noninvasive brain stimulation 2.0 in Alzheimer's disease,* Ageing Research Reviews, **75** (2022) 10155, doi:10.1016/j.arr.2021.101555

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Follow your cardiac spheroids: Tackling cardiotoxicity by finding an early biomarker

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Cardiotoxicity is one of the main adverse effects of cancer treatment, affecting completion of treatment and quality of life among the survivals [1]. No reliable early marker of cardiotoxicity has not yet been identified. We aim at identifying a biomarker candidate of cardiotoxicity induced by anti-cancer drug, doxorubicin (DOX) in breast cancer patients (BCPs). We found an increased level of prokinetin-2 (PROK2), a cytokine [2], in the serum of the BCPs primarily treated with DOX. To study the molecular and cellular mechanism of PROK2 release we used human cardiac spheroids (hCSs). Our study demonstrated that hCS models are relevant for studying DOX-mediated cardiotoxicity, and identified PROK2 as an early biomarker of cardiotoxicity.

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List of flash presentations

Amira Saidi: Strategy for preserving pancreatic islet vascularization during transplantation: A spheroid model composed of endothelial and insulin cells; *INSERM Strasbourg*
Alexandra Migga: Virtual X-ray histology of the entire facial nerve; *University of Basel*
Aurélien Lagarde: Development of a bio device for lung cancer personalized therapy; *INSERM Strasbourg*
Beate Lyko: Adaptive artificial muscles for treating incontinence; *University of Basel*
Julien Demisell: A Matrigel-free protocol for patient's derived lung organoids: another tool to study lung infectious disease?; *INSERM Strasbourg*
Mattia Humbel: The chameleon effect in dental fillings illuminated with nanotomography; *University of Basel*
Elise Pérennes: Bioactive membrane for rare disease bone defect; *INSERM Strasbourg*
Marta Girona: Comparison of the mouse cerebral ventricular geometry: in vivo and post-mortem; *University of Zurich*
Ali Imran Abid: Formulation of stem cells for advanced delivery; *INSERM Strasbourg*
Morgane Meyer : Development and optimization of a preventive combined therapeutical medical product for early osteoarthritis; *Lamina Therapeutics*

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