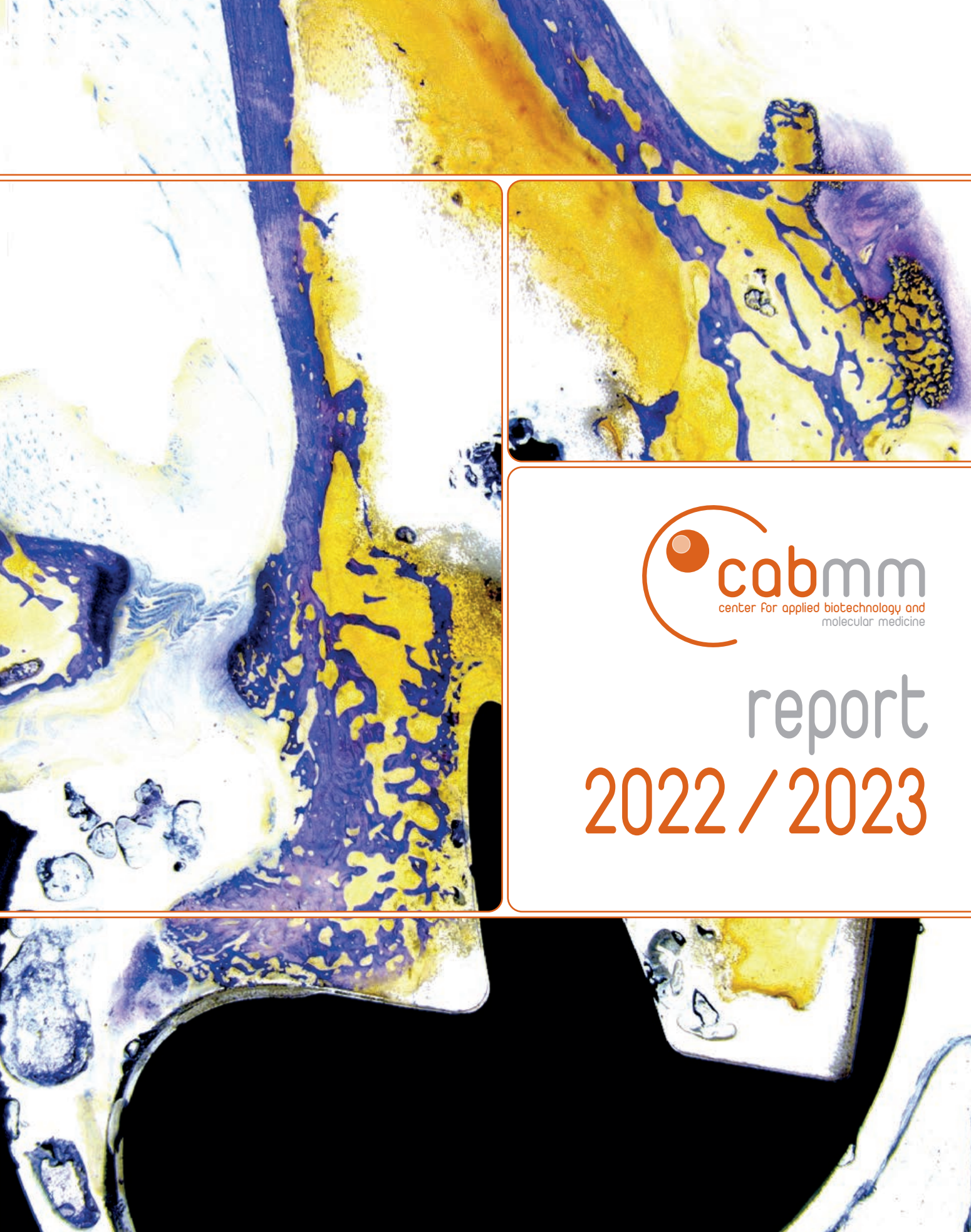
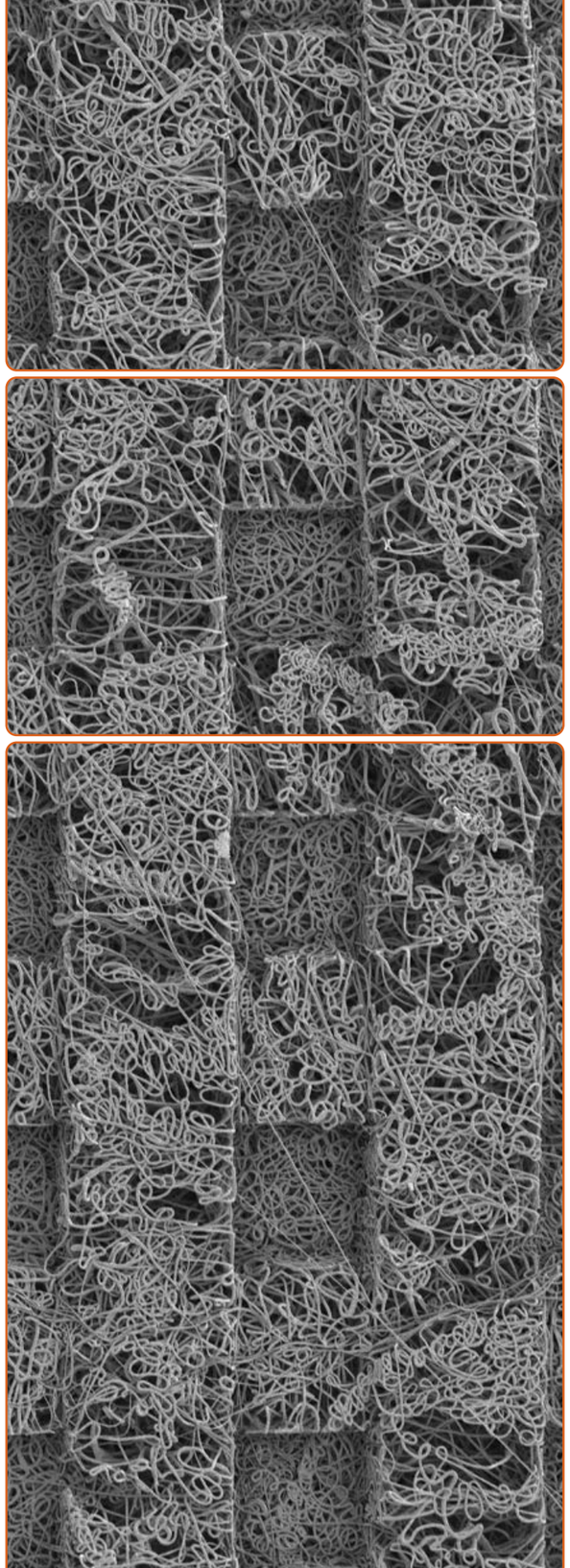


cabmm
center for applied biotechnology and molecular medicine

report 2022 / 2023

cabmm report
2022 / 2023



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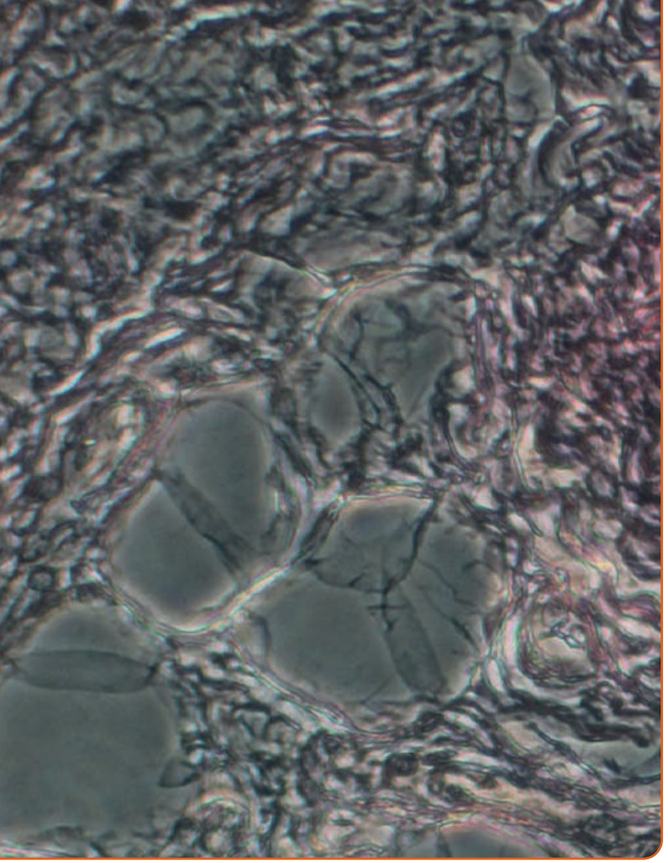

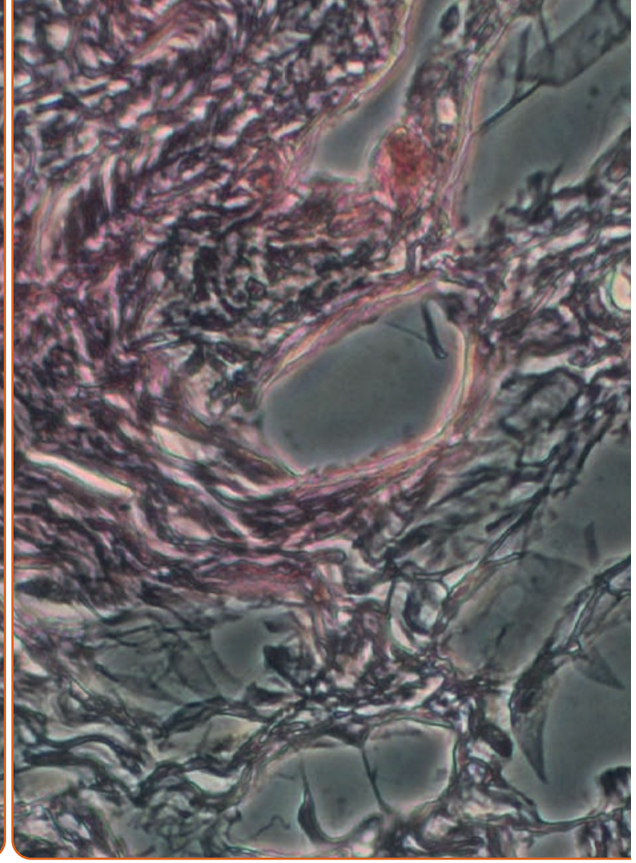

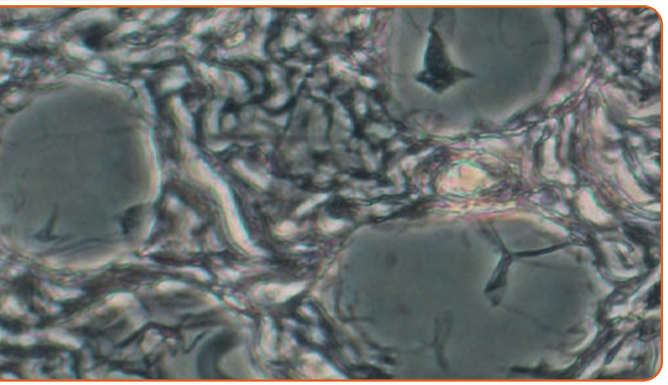

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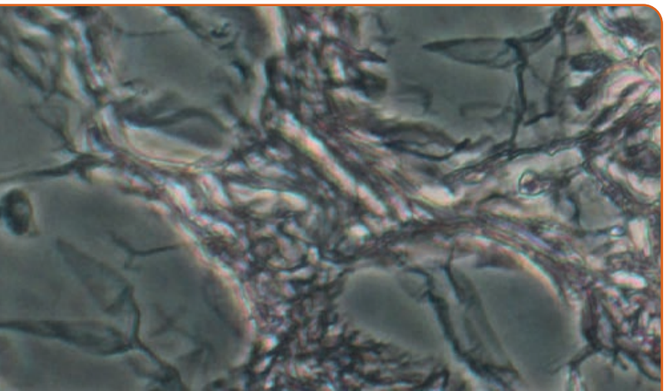
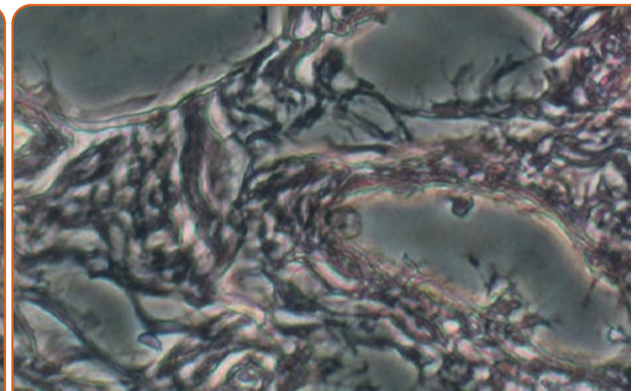




Liebe Leserin, lieber Leser,

„Gesundheit ist nicht alles,
aber ohne Gesundheit ist alles nichts.“
Arthur Schopenhauer

Was ist für Sie das Wichtigste im Leben? Bei Umfragen nimmt hier neben Familie und Freunden die Gesundheit einen Spitzenplatz ein. Nicht umsonst wird die Gesundheit auch als höchstes Gut bezeichnet.

Das CABMM hat zum Ziel, die translationale Forschung zu fördern und damit auch einen Beitrag zum Wohlbefinden und zur Gesundheit von Mensch und Tier zu leisten. Ein hehres Ziel, welches wir mit viel Elan und Motivation verfolgen.

Einen kleinen Einblick in unsere vielfältige Arbeit in den Jahren 2022/2023 gibt Ihnen der vorliegende CABMM Report. Er enthält Hintergrundinformationen, Interessantes aus unserer aktuellen Forschung und erlaubt mit persönlichen Porträts von Personen aus dem CABMM Netzwerk auch wieder einen Blick hinter die (Arbeits-)Kulissen.

Viel Spass beim Lesen!

Dr. Silke Kalchofner-Mark
Geschäftsführerin CABMM

Dear reader,

„Health is not everything,
but without health everything is nothing.”
Arthur Schopenhauer

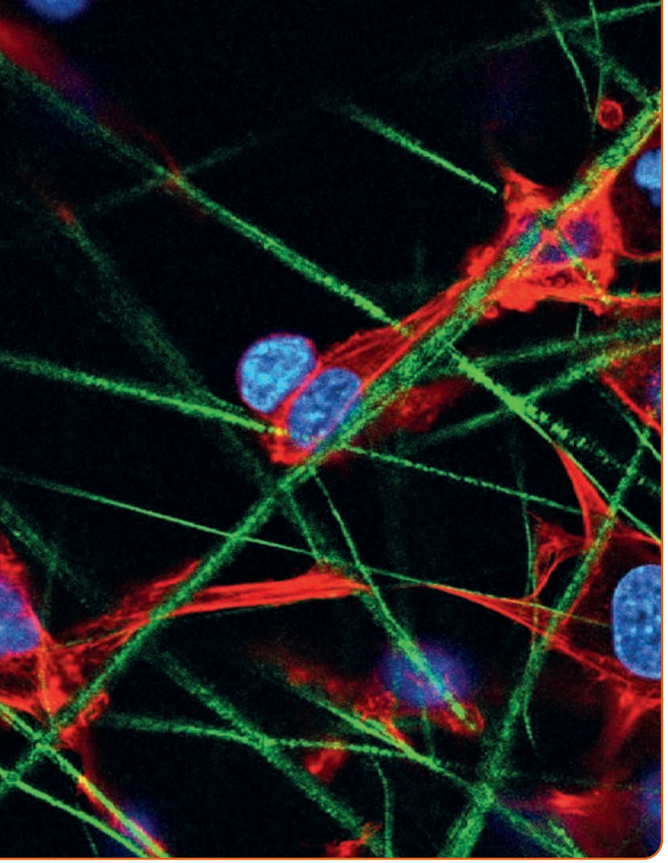
What is the most important thing for you? In surveys, health usually takes a top place alongside family and friends. It is not for nothing that health is also referred to as the greatest good.

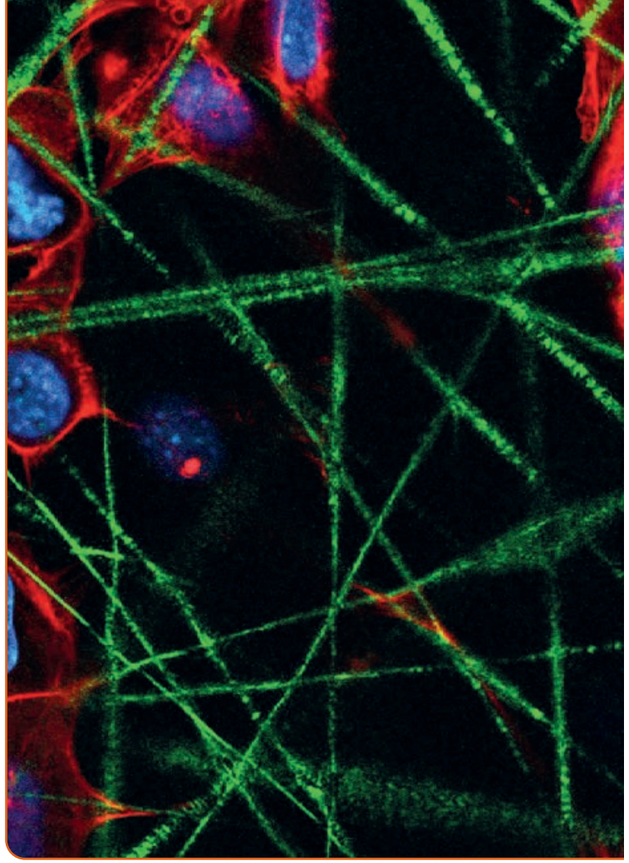
The CABMM aims to promote translational research and thus to contribute to the well-being and health of humans and animals. A noble goal, which we pursue with drive and motivation.

This CABMM Report gives you an insight into our multifaceted work in 2022/2023. It contains background information, interesting articles from our current research, and, with personal portraits of people connected to the CABMM network, also allows again a look behind the (working-)scene.

Enjoy reading!

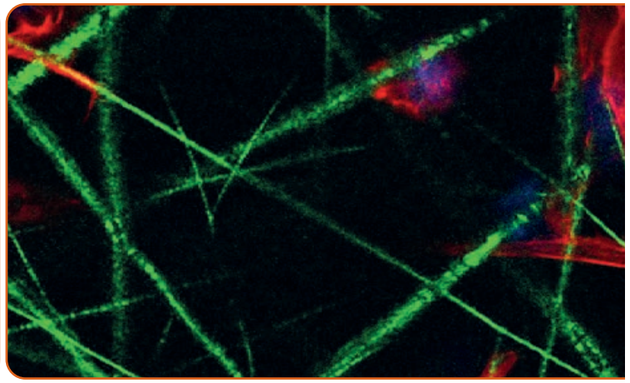
Dr. Silke Kalchofner-Mark
Managing Director CABMM

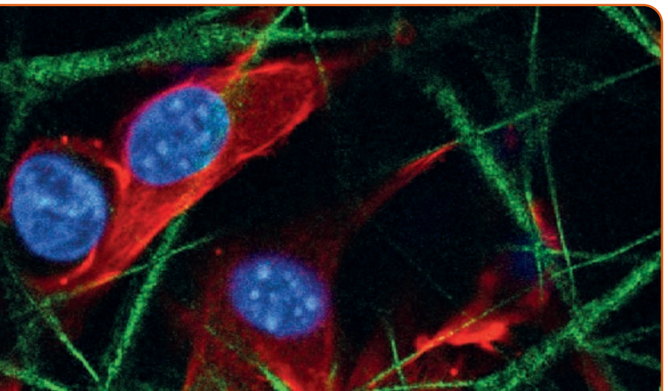


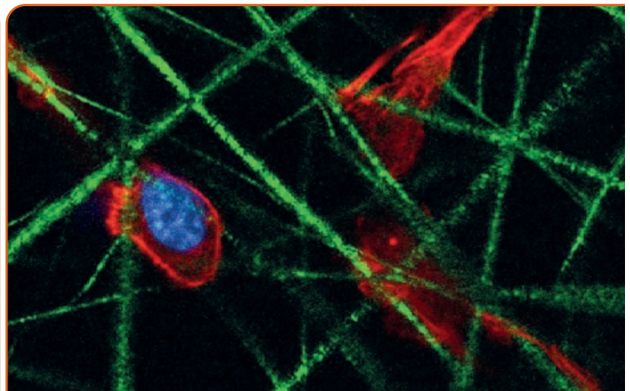


about us

cabmm bodies and events







The “Center for Applied Biotechnology and Molecular Medicine (CABMM)” is an official competence center of the University of Zurich and was founded in 2008 by a small group of highly motivated and successful scientists, namely Prof. em. Dr. Brigitte von Rechenberg, Prof. Dr. Dr. Simon P. Hoerstrup, and Prof. Dr. Dr. Michael O. Hottiger. With the creation of the CABMM, they gave rise to a stimulating environment for interdisciplinary and translational research, promoting scientific exchange and collaborations between basic and clinical researchers.

Administratively, the CABMM is assigned to the Vetsuisse Faculty of the University of Zurich and consists of the Plenum as highest decision-making body, the Steering Committee as operating body and the Managing Director heading both the Coordinating Office as central contact and coordination point and the Platform Organization Team dealing with all aspects connected to the CABMM Research Platform. Additionally, a Scientific Advisory Board was established as controlling body.

The CABMM demonstrates a unique structure, in that it combines (1) a network of existing research groups interested in exchanging scientific information and creating collaborations and (2) a working platform for collaborative research, where basic scientists, clinicians and veterinarians are able to work together shoulder to shoulder for the purpose of developing novel therapeutic approaches for the treatment of dysfunctional and diseased tissues.

Another special feature of the CABMM is the fact that we do not focus on one particular medical field, but rather on translational and interdisciplinary aspects. Thus, under the slogan “From bench to bedside … and back”, the CABMM is dedicated to fostering advances in applied, clinically oriented research in the fields of (A) experimental medicine and surgery, (B) molecular medicine, (C) regenerative medicine, and (D) applied biotechnology.

Furthermore, the CABMM offers expertise in regulatory affairs: Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP) were established through two founding members of the CABMM, Prof. Dr. Dr. Simon P. Hoerstrup and Prof. em. Dr. Brigitte von Rechenberg, respectively. As Good Clinical Practice (GCP) has already been running at the University Hospital for several years, the University of Zurich now combines all regulatory requirements for the development, production and first clinical trials of new drugs and therapies. The CABMM continues its efforts in regulatory affairs by providing a platform that allows for intensifying the interaction between the three responsible groups, e.g., by promoting the exchange of ideas and discussions about the interfaces of their regulatory fields.

In order to strengthen the CABMM network and enhance collaborations between CABMM members from a variety of research disciplines, the CABMM pursues different approaches. Every year, two major events are organized: the CABMM Winter Colloquium and the CABMM Symposium. Unfortunately, the event at the very beginning of the reporting period had to be cancelled due to the COVID-19 pandemic, but we are very happy that everything turned to be back to normal and all other events could take place. We are further delighted to report that the Swiss federal authorities have recognized all our events as continuing education for animal experimentation. This is not only considered to be very helpful in extending our member network, but it also follows a great interest expressed by our members and is well in line with the CABMM’s focus on animal welfare. Furthermore, the CABMM Coordinating Office organizes the CABMM Scientific Seminar, a lecture series held in an online format. This way, also CABMM member groups from outside Zurich are able to participate, allowing for a lively exchange within the CABMM member network and beyond.

On the following pages, the Steering Committee represented by Dr. Silke Kalchofner-Mark and the Scientific Advisory Board represented by Prof. em. Brigitte von Rechenberg are looking back on the achievements within the reporting period. Additionally, summaries about our main events, a tabular summary of the CABMM Scientific Seminar, and an article of the CABMM’s exhibition at the OLMA St. Gallen can be found.

from the cabmm steering committee

from left to right: Prof. Dr. Dr. Michael O. Hottiger, Prof. Dr. Dr. Simon P. Hoerstrup, Prof. Dr. Annette Liesegang, Prof. Dr. Janine Reichenbach, Prof. Dr. Marcy Zenobi-Wong, Dr. Katja Nuss, Dr. Silke Kalchofner-Mark

Founded in 2008, the CABMM celebrated its 15th birthday at the end of the 2022/2023 reporting period. Our goal of promoting interdisciplinary, clinically oriented, translational research has lost none of its relevance, and we are very proud of the highly **active network** of members we have built up over the past few years. The many collaborations between basic researchers and veterinary and human physicians in our network are illustrated in Figure 1. Each line corresponds to a collaboration so that we can once again look back on an impressive number of 220 collaborations during the reporting period. And we will continue to do our best to strengthen the network and advance translational research forward!

As a translational center, the CABMM continued to pursue its strategy of promoting **regulatory affairs** during the reporting period. We are pleased to report further positive news from our member network in this area:
The Musculoskeletal Research Unit (MSRU), as one of the core groups of the CABMM network, received renewed accreditation from Swissmedic to test the biocompatibility and efficacy of medical devices and medicinal products (including advanced therapy medicinal products/gene therapy) in compliance with the principles of Good Laboratory Practice (GLP), and is now also accredited to perform toxicity studies. Congratulations!

Moreover, building on the existing GLP infrastructure of the MSRU, the GLP Research Center UZH (GLP-RCU) is currently being established with the aim of advancing biomedical discovery and innovation even further by centralizing all GLP quality assurance activities at the UZH. This unified GLP compliance monitoring program will not only ensure the highest ethical and legal standards but will also allow and facilitate the expansion of the UZH GLP framework through the integration of further units, such as the Clinical Laboratory and the Center for Preclinical Development, led by two CABMM members, Prof. Dr. Regina Hofmann-Lehmann and PD Dr. Paolo Cinelli, respectively. We look forward to their successful future GLP accreditation and further GxP-related expansion within the CABMM network.

We are also pleased to report that the **CABMM events** (pages 14-25) were able to resume during the reporting period after the Corona pandemic. All events, as well as three mini-series of our lecture series, the **CABMM Scientific Seminar** (pages 26-31), were approved for continuing education credits by the Swiss federal authorities, in keeping with the CABMM's focus on **animal welfare**. Our events not only served to consolidate the network but also to improve collaborations between human and veterinary medicine through comprehensive sessions focusing on specific medical topics. These efforts will be intensified in the future, with a particular focus on strengthening and expanding the existing links between the Vetsuisse Faculty and the Medical Faculty of the UZH.

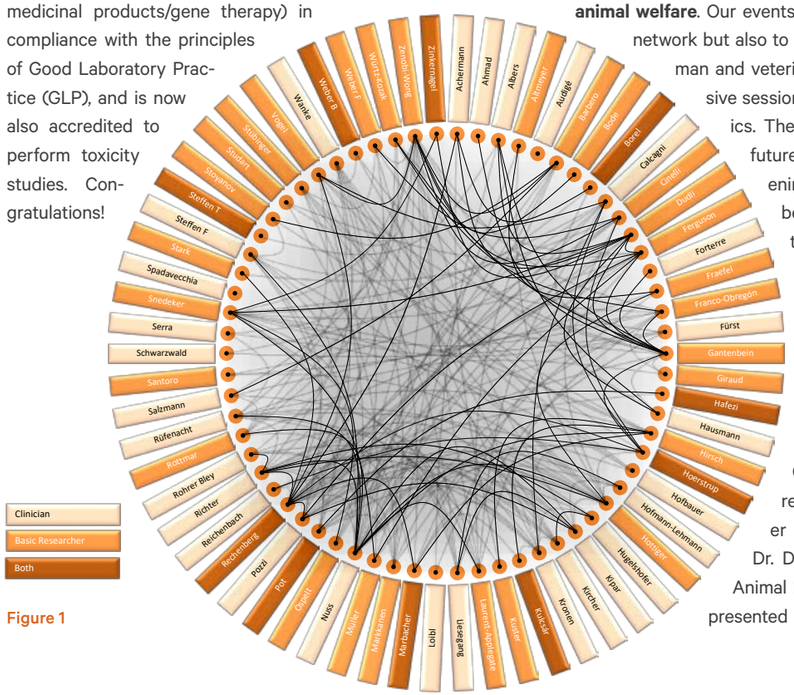


Figure 1

A highlight of the reporting period was certainly the participation of the CABMM at the **OLMA 2023 in St. Gallen** (pages 32-33), the largest Swiss trade fair for agriculture and nutrition, where the CABMM was selected as one of two representatives of the UZH. Together with Prof. Annette Liesegang and Dr. Daniel Brugger from the Institute of Animal Nutrition and Dietetics, the CABMM presented an exciting research project in the field of "Food Innovation" to a broad public audience. Many exciting discussions took place, and the participation was very successful. Our special thanks go to Annette and Daniel for their excellent partnership and scientific leadership.

There have been some personnel changes in the **CABMM Steering Committee** during the reporting period. We are very pleased to welcome Dr. Katja Nuss, co-director of the MSRU, as a new member of the CABMM Steering Committee. Her involvement will further strengthen the long-standing close collaboration between the CABMM and the MSRU.
There has also been a change in the Chairmanship of the CABMM Steering Committee: Prof. Simon P. Hoerstrup handed over the Chairmanship to Prof. Michael O. Hottiger in June 2023. We would like to express our sincere thanks to Simon for his many years of service to the CABMM, and we would also like to thank Michael for taking over the Chairmanship and for his tireless support of the CABMM since its foundation.

Finally, we would like to thank everyone who has supported the CABMM and made it what it is today. We look forward to continuing the CABMM's success story with all of you in the next reporting period.

Zurich, November 2024
Dr. Silke Kalchofner-Mark, Managing Director of the CABMM

cabmm steering committee

Name and affiliation	Application field
Prof. Dr. med. vet. Dr. phil. II Michael O. Hottiger (chairman), Vetsuisse Faculty and Faculty of Science, University of Zurich	B – Molecular Medicine
Prof. Dr. med. Simon P. Hoerstrup, PhD Medical Faculty, University of Zurich	C – Regenerative Medicine
Prof. Dr. med. vet. Annette Liesegang Vetsuisse Faculty, University of Zurich	A – Experimental Medicine and Surgery
Prof. Dr. med. Janine Reichenbach Medical Faculty, University of Zurich and University Children's Hospital Zurich	B – Molecular Medicine
Prof. Dr. Marcy Zenobi-Wong (PhD) ETH Zurich	C – Regenerative Medicine
Dr. med. vet. Katja Nuss Vetsuisse Faculty, University of Zurich	A – Experimental Medicine and Surgery
Dr. Silke Kalchofner-Mark (PhD) Vetsuisse Faculty, University of Zurich	Managing Director

the scientific advisory board of the cabmm

The aim of the Scientific Advisory Board (SAB) is to critically evaluate the quality of the CABMM and to review the grant applications for a CABMM Start-up Grant. Furthermore, all SAB members offer general support in all scientific questions and participate in the training and promotion of young academics. The participation in the yearly CABMM events like the CABMM Winter Colloquium and the CABMM Symposium allows the SAB to get insights into the quality of the network and to contribute to fruitful discussions. The SAB represents various scientific disciplines and fields of medical practice and is supported by the Deans of the Medical and the Vetsuisse Faculty of the University of Zurich who are *ex officio* members.

cabmm scientific advisory board

Name and affiliation	Representing
Prof. em. Dr. med. vet. Brigitte von Rechenberg (chairwoman) University of Zurich	Application field A – Experimental Medicine and Surgery
Prof. em. Dr. Walter Schaffner (PhD) University of Zurich	Application field B – Molecular Medicine
Prof. em. Dr. med. Dr. med. dent. Dr. h. c. Hans-Florian Zeilhofer University Hospital Basel	Application field C – Regenerative Medicine
Prof. em. Dr. Markus Aebi (PhD) ETH Zurich	Application field B – Molecular Medicine
Prof. Dr. med., Frank Rühli, PhD Dean of the Medical Faculty, University of Zurich	*(ex officio)*
Prof. Dr. med. vet. Dr. h. c. Roger Stephan Dean of the Vetsuisse Faculty, University of Zurich	*(ex officio)*

There were no personnel changes in the reporting period, so that the CABMM Scientific Advisory Board still consists of four members and the Deans of the Medical and Vetsuisse Faculty of the University of Zurich, Prof. Frank Rühli and Prof. Roger Stephan, respectively. Prof. em. Brigitte von Rechenberg chairs the Board, Prof. em. Walter Schaffner, Prof. em. Markus Aebi, and Prof. em. Hans-Florian Zeilhofer act as members at large, such that the Board represents a diverse expertise in basic, clinical, and experimental research.

In the reporting period, the Board evaluated and supported the future structural changes of the CABMM as proposed by the CABMM Steering Committee and is convinced that this strategy leads the CABMM to a prosperous future. Both Deans also participated in this important meeting to set the future direction of the CABMM, and we would like to thank them for their time and committment, as we consider their input of crucial importance.

Furthermore, efforts have been directed into finding new money for seeding grants, the CABMM Start-up Grant, but at this point, unfortunately, without success. After the funding from the Mäxi Foundation expired, no new sponsor for open-seeding grants could be found. Probably also here, the CABMM needs to change its strategy. This will be discussed in the next Scientific Advisory Board meeting and, hopefully, a new successful strategy can be developed that allows CABMM members to get seed money for more high risk grants again.

But there is also good news: The new building Y80 at the Irchel Campus for animal experimental surgery has been finished providing very modern surgery and diagnostic equipment as well as laboratories for histology, cell biology, and fundamental biomedical research. It is the new homebase of two CABMM member groups, the Musculoskeletal Research Unit (MSRU) from the Vetsuisse Faculty and the Center for Preclinical Development (CPD) from the Medical Faculty. Finally, the original goal of the CABMM, namely that human and veterinary forces should be united for optimal translational research, has thus been achieved. We wish a prosperous future research for all groups of the CABMM taking advantage of these new facilities and possibilities for fulfilling regulatory requirements under one roof at the UZH.

Zurich, December 2024
Prof. em. Dr. med. vet. Brigitte von Rechenberg
Chairwoman of the CABMM Scientific Advisory Board

from left to right: Prof. em. Dr. Brigitte von Rechenberg, Prof. em. Dr. Dr. Dr. Hans-Florian Zeilhofer, Prof. em. Walter Schaffner, Prof. em. Dr. Markus Aebi

11th symposium of the center for applied biotechnology and molecular medicine

After a long break due to the coronavirus pandemic, we could successfully restart with the organization of our events in 2022. The 11th CABMM Symposium took place on June 16th, 2022, at the University of Zurich and was completely dedicated to “One Health”, giving a comprehensive overview of the field. Aside from the keynote lecture given by Prof. Jakob Zinsstag from the Swiss Tropical and Public Health (TPH) Institute, several aspects of One Health were presented, including zoonosis, antibiotic resistance, comparative medicine in cancer therapy, and human-animal interactions.

Prof. Michael O. Hottiger, vice chairman of the CABMM Steering Committee, opened the meeting, welcomed the audience, and highlighted the importance of One Health as an approach to balance and optimize the health of people, animals, and the environment.

Prof. Zinsstag from the Swiss TPH Institute started the meeting with a comprehensive lecture about the development of the One Health approach, that started in the 1960’s with the term “One Medicine” coined by Calvin Schwabe and referring to similarities between animal and human medicine. Nowadays, many more disciplines are part of the approach and transdisciplinarity is a key factor for its further development. He furthermore showed numerous transcontinental studies that improved the health of people and animals in Africa and Asia. The subsequent coffee break provided a first opportunity to bring people together who work on different fields of One Health.

Representing the important field of zoonoses, Prof. Nicole Borel from the University of Zurich talked about chlamydia, a genus of pathogenic bacteria, and the direct link between human and animal infections. A study performed by the group showed that up to 90 % of pigs are positive and that infected pigs can be found on all Swiss fattening pig farms involved in the study. Resistances against special antibiotics aggravate the treatment and containment. The next presentation given by PD Dr. Walter Zingg from the University Hospital Zurich dealt with the increasing mortality due to antimicrobial resistance, that is expected to affect up to ten million people in 2050. Antimicrobial resistance is driven by hospital transmission and selection of resistant microorganisms and resistance genes due to breaches in infection prevention and control practices, limited diagnostic capacity, and prescription behaviour. Additionally, antibiotics usage in animals aggravate the problem.

Subsequently, Prof. Enni Markkanen from the Vetsuisse Faculty Zurich talked about naturally occurring tumors in pets as models for human cancers. There are similarities in cancer development, clinical presentations, and equivalent genetic aberrations, e.g., canine mammary carcinoma shows high grade molecular homology in cancer-associated stroma. Cross-species analysis of stromal reprogramming has the potential to identify novel therapeutic targets. Lively discussions took place on what has been heard in the following coffee break.

11. symposium des zentrums für angewandte biotechnologie und molekulare medizin

Nach einer langen Pause aufgrund der Corona-Pandemie, konnten wir 2022 endlich wieder mit der Ausrichtung unserer Events und der damit verbundenen Stärkung der Zusammenarbeit innerhalb unseres Netzwerkes starten. Das 11. CABMM Symposium war dem Thema „One Health“ gewidmet und fand am 16. Juni 2022 an der Universität Zürich statt. Neben einem Übersichtsvortrag von Prof. Zinsstag vom Schweizerischen Tropen- und Public Health-Institut wurden verschiedene One Health-Aspekte, einschliesslich Zoonosen, Antibiotika-Resistenzen, komparativer Medizin in der Krebsbehandlung und der Interaktion zwischen Mensch und Tier, präsentiert.

Prof. Michael O. Hottiger, stellvertretender Vorsitzender des CABMM Leitungsausschusses, eröffnete das Meeting und hiess die Teilnehmenden willkommen. Er betonte die Bedeutung von One Health als wichtige Möglichkeit, die Gesundheit von Mensch, Tier und Umwelt ins Gleichgewicht zu bringen und zu optimieren.

Prof. Zinsstag startete mit einer umfassenden Vorlesung über die Entwicklung des One Health-Ansatzes. Bereits in den sechziger Jahren prägte der Tierarzt Calvin Schwabe den Begriff „One Medicine“ und betonte Ähnlichkeiten zwischen Tier- und Humanmedizin. Mittlerweile sind einige weitere Disziplinen involviert und diese Transdisziplinarität ist ein wesentliches Element der weiteren Entwicklung. Prof. Zinsstag zeigte zudem zahlreiche transkontinentale Projekte, welche die Gesundheit von Menschen und Tieren in Afrika und Asien verbesserten. Die nachfolgende Kaffeepause bot eine erste Gelegenheit, Forschende der unterschiedlichen Bereiche von One Health zum persönlichen Austausch zusammenzubringen.

Zu Beginn der zweiten Session verdeutlichte Prof. Nicole Borel von der Universität Zürich den wichtigen Aspekt von Zoonosen und sprach über Chlamydien, einer Gattung pathogener Bakterien, deren Infektionen in Menschen und Tieren in direktem Zusammenhang stehen. Eine Studie zur Prävalenz chlamydialer Infektionen von Schweinen in Schweizer Mastbetrieben zeigte positiv getestete Schweine auf allen Höfen und bis zu 90 % infizierte Schweine. Resistenzen gegen bestimmte Antibiotika erschweren zudem die Behandlung und Eindämmung. Die darauffolgende Präsentation von PD Dr. Walter Zingg vom Universitätsspital Zürich behandelte die zunehmende Sterblichkeit aufgrund antimikrobieller Resistenzen, die im Jahr 2050 voraussichtlich zehn Millionen Menschen betreffen wird. Antibiotikaresistenzen werden durch die Übertragung von im Krankenhaus erworbenen Erregern und der damit verbundenen Selektion von Resistenzgenen, den limitierenden diagnostischen Möglichkeiten und dem Verschreibungs- und Abgabeverhalten vorangetrieben. Die übermässige Anwendung von Antibiotika in der Tierhaltung begünstigt zusätzlich die Verbreitung von Antiobiotikaresistenzen.

Im Anschluss sprach Prof. Enni Markkanen von der Vetsuisse Fakultät Zürich über natürlich vorkommende Tumore in Haustieren als Modell für menschliche Krebserkrankungen. Es gibt Ähnlichkeiten in der Krebsentwicklung, der klinischen Präsentation und vergleichbare genetische Veränderungen. Zum Beispiel zeigt das tumorumgebende Gewebe bei Brustkrebs in Hunden signifikante Homologien zum Menschen. Eine artübergreifende Analyse der Stromaveränderungen hat das Potential, neue therapeutische Ansatzpunkte zu identifizieren. In der darauffolgenden Kaffeepause wurden weitere rege Diskussionen über das Gehörte geführt.

The next presentation by PD Dr. Mirja Nolff from the Vetsuisse Faculty continued the previous topic on dogs as models for human cancer focusing on soft tissue sarcoma. One of the main challenges during tumor resection is that tumor margins are difficult to identify and thus tumors recurrence. The group uses and improves the methodology of targeted near infrared real-time tumor imaging during surgery to differentiate between healthy and diseased tissue. The last presentation highlighted a completely different aspect of One Health: Prof. em. Brigitte von Rechenberg presented a project focusing on strengthening self-competence, self-perception, and empathy of children through working and interacting with horses. Results have been very positive and showed favorable benefits for both, humans, and animals: e.g., teenagers learned non-violent communication, responsibility, and concentration.

In his concluding remarks, the chairman of the CABMM Steering Committee, Prof. Simon Hoerstrup, thanked all speakers for their valuable contributions and mentioned that the diversity within the One Health approach needs interdisciplinary exchange of involved parties further on. During the final Apéro, all participants engaged in stimulating discussions in a relaxed atmosphere.

Die nächste Präsentation von PD Dr. Mirja Nolff von der Vetsuisse Fakultät führte das vorige Thema über Hunde als Modell für Krebserkrankungen fort und fokussierte auf Weichteilsarkome. Eine wesentliche Herausforderung der Tumorresektion ist die Identifizierung der Tumorränder, um einem Krankheitsrückfall entgegenzuwirken. Die Gruppe nutzt und optimiert eine operative Methode zur gezielten Bildgebung mit Nahinfrarot, um zwischen gesundem und erkranktem Gewebe zu unterscheiden. Die letzte Präsentation beleuchtete einen völlig anderen Aspekt von One Health: Prof. em. Brigitte von Rechenberg präsentierte ein Projekt, welches auf die Stärkung von Selbstkompetenz, Selbstwahrnehmung und Empathie von Jugendlichen fokussiert, ermöglicht durch die Arbeit und Interaktion mit Pferden. Die Ergebnisse zeigten positive Nutzen für Menschen und Tiere. So konnten die Teenager zum Beispiel in gewaltfreier Kommunikation, Verantwortung und Konzentration geschult werden.

In seinen abschliessenden Worten dankte der Vorsitzende des CABMM Leitungsausschusses, Prof. Simon Hoerstrup, allen Rednern für ihren wertvollen Beitrag und erwähnte, dass die Diversität innerhalb des One Health-Ansatzes den weiteren interdisziplinären Austausch aller involvierter Parteien benötigt. Während des abschliessenden Apéros beteiligten sich alle Teilnehmer an stimulierenden Diskussionen in einer angenehmen Atmosphäre.

1st winter colloquium of the center for applied biotechnology and molecular medicine

As follow-up event of our annual CABMM Seminar, the 1st CABMM Winter Colloquium took place at the University of Zurich on February 2nd, 2023. Well in line with the intention to foster relationships within our network, the first session offered the opportunity to get to know research interests of newer members from various fields. During the second session, the speakers could impressively demonstrate the One Medicine concept, e.g., joint promotion of human and animal healthcare, by means of new advances in ophthalmology.

As the representative of the CABMM Steering Committee, Prof. Michael O. Hottiger welcomed all participants and reiterated the fundamental idea behind the CABMM: fostering advances in interdisciplinary and translational research, with scientific exchange during our events being of great importance for its implementation. Subsequently, Dr. Salim Darwiche, scientific coordinator of the CABMM, moderated the colloquium and guided through the program.

The first speaker, Dr. Katja Nuss, gave an overview of the diversity of research projects of the UZH's Musculoskeletal Research Unit: from bone and cartilage regeneration to wound healing to aneurysms. The implementation of GLP standards and the successful education of 100 veterinarians to date demonstrate further competencies of the group. In the following talk, Dr. Markus Rottmar, Empa St. Gallen, talked about the interaction of human cells and tissues with different materials. Thus, for example, biological interaction of metallic glasses was tested concerning their suitability as implant materials. Another focus was the development of a 3D polymer to treat skin wounds. Prof. Andrea Barbero from the University of Basel and University Hospital Basel completed the session with a talk about the implantation of nasal chondrocytes including surrounding matrix in cartilage defects in knee joints. To further improve clinical outcomes, new surgical technologies were investigated, and the use of biochemical factors were tested using a cartilage-on-a-chip, specifically developed for this purpose.

At the beginning of the second session, Prof. Farhad Hafezi from the University of Zurich gave a keynote speech about cross-linking technology (CXL) for the treatment of corneal diseases that he co-developed two decades ago. This method uses UV light, oxygen, and vitamin B2 to strengthen the cornea and was constantly optimized by means of experimental settings in the laboratory. CXL has developed to become the gold standard treatment of keratoconus, a potentially sight threatening corneal disease. Moreover, the technology is successfully used to combat bacterial infections of the cornea. To making the method more available to responsible medical professionals, a new device was developed. The following talk by Enes Aydemir, employee at the ELZA institute in Dietikon, made the importance of keratoconus early detection a subject of discussion to prevent loss of sight. The corneal disease is detected using modern diagnostic imaging that is not widely available. Therefore, a smartphone-based keratograph project comprised the development of an inexpensive, simple to operate and portable screening device.

1. winter colloquium des zentrums für angewandte biotechnologie und molekulare medizin

Als Nachfolger des jährlich stattfindenden CABMM Seminars, wurde am 2. Februar 2023 das erste CABMM Winter Colloquium an der Universität Zürich abgehalten. Entsprechend der Intention, die Beziehungen innerhalb unseres Netzwerkes zu stärken, bot sich während der ersten Session die Gelegenheit, die Forschungsschwerpunkte von neueren Mitgliedern aus verschiedenen Bereichen kennenzulernen. Während der zweiten Session konnten die Redner eindrucksvoll das Konzept von One Medicine, die gemeinsame Förderung der Gesundheit von Mensch und Tier, anhand neuer Entwicklungen im Bereich der Ophthalmologie verdeutlichen.

Als Vertreter des Leitungsausschusses des CABMM übernahm Prof. Michael O. Hottiger die Begrüssung der Teilnehmenden und erinnerte an den Grundgedanken des CABMM: die Förderung von interdisziplinärer und translationaler Forschung, für dessen Umsetzung der wissenschaftliche Austausch während unserer Events von grosser Bedeutung ist. Anschliessend führte Dr. Salim Darwiche, wissenschaftlicher Koordinator des CABMM, durch das Programm.

Die erste Rednerin, Dr. Katja Nuss, gab eine Übersicht über die vielfältigen Forschungsprojekte der Musculoskeletal Research Unit der UZH: Von Knochen- und Knorpelregeneration über Wundheilung bis hin zu Aneurysmen. Die Implementierung von GLP-Standards und die erfolgreiche Ausbildung von bislang 100 Veterinärmedizinern belegen weitere Kompetenzen der Gruppe. Im Anschluss sprach Dr. Markus Rottmar, Empa St. Gallen, über die Interaktion von humanen Zellen und Geweben mit verschiedenen Materialien. So werden zum Beispiel metallische Gläser auf ihre biologische Wechselwirkung mit Zellen untersucht, um deren Eignung als potenzielles Implantat-Material zu prüfen. Ein weiterer Fokus ist die Entwicklung eines 3D-Polymers für die Behandlung chronischer Wunden. Prof. Andrea Barbero von der Universität und dem Universitätsspital Basel komplettierte die erste Session mit einem Vortrag über die Implantation von nasalen Knorpelzellen und ihrer umgebenden Matrix in Kniegelenksdefekte. Um die klinischen Ergebnisse weiter zu verbessern, wurden neue chirurgische Technologien und der Einsatz von biochemischen Faktoren in einem Knorpel-Biochip getestet.

Prof. Farhad Hafezi von der Universität Zürich gab zu Beginn der zweiten Session den Hauptvortrag über die von ihm mitentwickelte Cross-Linking (CXL)-Methode zur Behandlung verschiedener Erkrankungen der Hornhaut. Die Technologie, die UV-Licht, Sauerstoff und Vitamin B2 benötigt, konnte durch Untersuchungen im Labor stetig optimiert werden und hat sich zum weltweiten Standard in der Behandlung von Keratokonus, einer degenerativen Augenerkrankung, die unbehandelt zu Erblindung führen kann, entwickelt. CXL wird ebenfalls erfolgreich zur Bekämpfung bakterieller Hornhautinfektionen angewendet. Um die Vernetzungstechnologie vielseitig und umfassend zugänglich zu machen, wurde eigens ein Gerät hierfür entwickelt. Der anschliessende Vortrag von Enes Aydemir, Mitarbeiter am ELZA Institut in Dietikon, thematisierte die frühzeitige Erkennung von Keratokonus, um Erblindung vorzubeugen. Die Hornhauterkrankung wird in modernen Arztpraxen mittels bildgebender Diagnostik detektiert. Da der Zugang zu dieser Technik mancherorts limitiert ist, wurde ein Smartphone-basierter Keratograph entwickelt, der kostengünstig, tragbar und einfach zu bedienen ist.

Finally, Prof. Simon Pot from the Vetsuisse Faculty Zurich gave a lecture on the use of corneal cross-linking in veterinary medicine. Infectious keratitis is quite common in various animal patients. As an alternative to conventional treatment (e.g., medication), the group investigated effects of PACK-CXL (photoactivated chromophore for infectious keratitis) in cats and dogs in clinical studies and optimized the treatment protocols based on the research results.

At the end of the event, a lively and lasting discussion was held focusing on the presented topics, highlighting several connections and collaborations amongst our CABMM member network. In the closing remarks, the colloquium moderator Dr. Salim Darwiche and the managing director of the CABMM, Dr. Silke Kalchofner-Mark, reflected on key features of the talks, and how throughout the various topics, the unexpected findings became the basis for innovation. Subsequently, they invited the audience to enjoy some food and drinks in a relaxing atmosphere, affording an opportunity for further scientific exchange.

Abschliessend referierte Prof. Simon Pot von der Vetsuisse Fakultät Zürich über die Verwendung der Cross-Linking Technologie in der Veterinärmedizin. Infektionen der Hornhaut sind in verschiedenen Spezies recht verbreitet. Als Alternative zur herkömmlichen, medikamentösen Behandlung wurde und wird in klinischen Studien der Effekt von PACK-CXL (photoactivated chromophore for infectious keratitis) in Katzen und Hunden untersucht und das Behandlungsprotokoll optimiert.

Am Ende der Veranstaltung gab es eine lebhafte und ausdauernde Diskussion über die gehörten Vorträge, in deren Verlauf zahlreiche Vernetzungen und Kollaborationen unserer Mitglieder zur Sprache kamen. In ihren abschliessenden Worten fassten Dr. Salim Darwiche und Geschäftsführerin des CABMM, Dr. Silke Kalchofner-Mark, die gewonnenen Erkenntnisse anschaulich zusammen und entliessen das Publikum in einen gemütlichen Apéro, der zu weiterem Austausch einlud.

12th symposium of the center for applied biotechnology and molecular medicine

The 12th CABMM Symposium gave a comprehensive overview in the field of tendon repair and regeneration. The event took place on June 29th, 2023, at the University of Zurich and showed perspectives from human and veterinary medicine, *in vitro* basic research, new treatment options, industry developments, and regulatory aspects, and thus, showcasing the complete range of applied, translational research performed at the CABMM. Additionally, projects funded by CABMM Start-up Grants in the field of musculoskeletal research were presented.

The meeting was opened by the managing director of the CABMM, Dr. Silke Kalchofner-Mark, who welcomed a big audience from a variety of research disciplines. She announced that participation in the symposium is again recognized as continuing education for animal experimentation by the Swiss federal authorities, reflecting once more the successful effort of our center in promoting education and animal welfare. The moderation of the event was subsequently performed by Dr. Kalchofner-Mark and Dr. Salim Darwiche, scientific coordinator of the CABMM.

At first, a keynote lecture presenting current concepts and future expectations of rotator cuff repair in humans was given by Prof. Karl Wieser from the Balgrist University Hospital. He talked about risk factors and symptoms of tendon injuries in the shoulder. Numerous factors must be considered to decide on a conservative or surgical treatment. Current biological and structural tools for surgery (i.e., bone marrow aspirates or synthetic patches, respectively) need further improvement, for example to strengthen the patch-tendon interface. At this point, he referred to a new technology developed by ZuriMED Technologies. Prof. Wieser also mentioned numerous collaborative projects with CABMM member groups. Thereafter, Prof. Anton Fürst from the Vetsuisse Faculty Zurich looked at tendon injuries from the animal perspective, where up to 43 % of sport horses are affected. Classical treatment strategies include cooling, anti-inflammatory drugs, and box rest, but unfortunately end up in reduced biomechanical properties and risk of recurrence. Regenerative treatments like platelet-rich plasma or mesenchymal stem cells are not satisfactory. An alternative approach with genipin, a naturally occurring collagen cross-linking agent, showed mechanical augmentation of treated lesions.

After a relaxing coffee break that was used to exchange ideas, Elias Bachmann, co-founder and CTO of ZuriMED Technologies, presented the development of an innovative tendon repair technology, which was inspired by the textile industry, specifically how felt is stitched to other textiles. He walked the audience through the process of innovation in developing a medical device and highlighted the necessary balancing act between meeting regulatory requirements of safety and efficacy while highlighting the novelty of a new technology.



12. symposium des zentrums für angewandte biotechnologie und molekulare medizin

Das 12. CABMM Symposium fand am 29. Juni 2023 an der Universität Zürich statt und gab einen umfassenden Überblick über die Forschung im Bereich der Sehnenreparatur und -regeneration: Sichtweisen aus der Human- und Veterinärmedizin, Ansätze in der Grundlagenforschung, neue Therapiemöglichkeiten, Entwicklungen in der Industrie und regulatorische Aspekte wurden beleuchtet. Auf diese Weise konnte die gesamte Bandbreite angewandter, translationaler Forschung am CABMM gezeigt werden. Darüber hinaus wurden CABMM Start-up Grant-Projekte im Bereich des Bewegungsapparats präsentiert.

Die Geschäftsführerin des CABMM, Dr. Silke Kalchofner-Mark, eröffnete das Meeting und begrüsste ein grosses Publikum aus verschiedenen Forschungsdisziplinen. Sie gab bekannt, dass der Besuch des Symposiums von den schweizer Behörden erneut als Weiterbildung für Tierversuche anerkannt wurde, was einmal mehr unsere erfolgreichen Bemühungen in den Bereichen Lehre und Tierwohl zeigt. Dr. Kalchofner-Mark und der wissenschaftliche Koordinator des CABMM, Dr. Salim Darwiche, moderierten anschliessend das Event.

Zunächst hielt Prof. Karl Wieser von der Universitätsklinik Balgrist einen Hauptvortrag über derzeitige Ansätze und künftige Erwartungen bei der Reparatur der Rotatorenmanschette im Menschen. Er sprach über Risikofaktoren und Symptome von Sehnenverletzungen der Schulter. Zahlreiche Faktoren müssen berücksichtigt werden, um über eine konservative oder operative Behandlung zu entscheiden. Derzeitige biologische und strukturelle Mittel (z.B. Knochenmarksaspirate oder künstliche Pflaster) benötigen weitere Optimierung, um zum Beispiel die Pflaster-Sehnen-Schnittstelle zu verstärken. An dieser Stelle verwies er auf eine neuartige Technologie, die von ZuriMED entwickelt wurde, und Thema eines späteren Vortrags war. Prof. Wieser brachte ausserdem zahlreiche kollaborative Projekte mit CABMM-Mitgliedergruppen zur Sprache. Prof. Anton Fürst von der Vetsuisse Fakultät Zürich betrachtete danach Sehnenverletzungen in tierischen Patienten: mehr als 40 % der Sportpferde sind hiervon betroffen. Die klassische Behandlung umfasst Kühlung, antientzündliche Medikamente und Stallruhe, geht schlussendlich jedoch mit reduzierten biomechanischen Eigenschaften und einem hohen Rückfallrisiko einher. Regenerative Behandlungen wie zum Beispiel Thrombozyten-reiches Plasma oder mesenchymale Stammzellen sind zudem nicht zufriedenstellend. Ein alternativer Ansatz mit Genipin, einem natürlich vorkommenden Wirkstoff, der Kollagen vernetzten kann, zeigte eine erhöhte mechanische Stabilität der behandelten Läsionen.

Nach einer erholsamen Kaffeepause, die für wissenschaftlichen Austausch genutzt wurde, präsentierte Elias Bachmann, Mitbegründer und Technischer Direktor von ZuriMED Technologies, die Entwicklung einer innovativen Technologie für die Sehnenreparatur. Die Methode wurde durch die Textilindustrie inspiriert, vor allem dadurch, wie Filz an andere Stoffe angeheftet wird. Er nahm die Zuhörer mit auf die Entwicklungsreise eines Medizinprodukts und betonte die dazugehörige Gratwanderung zwischen der Erfüllung regulatorischer Anforderungen wie Sicherheit und Wirksamkeit und der Promotion des neuartigen Produkts.







The next presentation from network members of the University of Lausanne focused on cell therapies from a regulatory and technological perspective. Regulatory aspects of tendon repair approaches were presented by Prof. Lee Ann Applegate who spoke about the development of more strict regulatory requirements during the last decades. The presence of various authorities in different countries complicates the translation of promising treatments. Alexis Laurent talked about the use of cell therapies for tendon repair. Different cell formulations are an active field of research, e.g., biologic supplementation with primary progenitor tenocytes or bio-enhanced solid devices as tendon tissue replacement. He also highlighted the importance of scalability when developing cell therapies and the infrastructure needed to ensure a reliable production chain. Dr. Salim Darwiche then spoke on the preclinical *in vivo* testing of novel tendon repair devices in compliance with Good Laboratory Practices (GLP). He showed how an agile approach is compatible with a GLP framework in *in vivo* study design and implementation. This allows the research question to drive study design, and not existing standard operating procedure. He then showed highlights from two *in vivo* preclinical ovine studies testing tendon repair technologies in GLP at the Musculoskeletal Research Unit (UZH), which were part of 510(k) submission processes for the USFDA.

Another coffee break allowed for fruitful discussions and commonalities could be recognized and strengthened. The last session served the purpose of presenting results from two successful CABMM Start-up Grant-funded studies. Prof. Antonio Pozzi from the Vetsuisse Faculty Zurich discussed the potential of canine meniscal degeneration as suitable model for translational medicine. The study confirmed that biological changes in spontaneous meniscal pathology in dogs partially correspond to alterations documented in humans. Finally, PD Dr. Stefan Dudli from Balgrist University Hospital Zurich talked about painful vertebral bone marrow lesions termed Modic changes resulting from increased nerve fiber density. Bone marrow stromal cells provide pro-neurotrophic cues and could be a relevant disease-modifying treatment target.

In his concluding remarks, Prof. Michael O. Hottiger, vice chairman of the CABMM Steering Committee, thanked the organizers of the event. Intriguing presentations made the 12th Symposium a successful event that showed the importance of scientific exchange and collaborations. At the end of the event, an Apéro offered the opportunity for further personal talks in a cozy atmosphere.

Die nächste Präsentation von Partnern der Universität Lausanne fokussierte auf Zelltherapien aus regulatorischer und technologischer Sicht. Regulatorische Aspekte bei der Entwicklung neuer Ansätze zur Sehnenreparatur wurden von Prof. Lee Ann Applegate thematisiert. Sie sprach über die Implementierung strengerer regulatorischer Anforderungen während der letzten Jahrzehnte, wobei die Zuständigkeit verschiedener Behörden in unterschiedlichen Ländern die Translation vielversprechender Ergebnisse erschwert. Alexis Laurent sprach über die Nutzung von Zelltherapien für die Sehnenreparatur. Unterschiedliche Zellformulierungen sind Gegenstand aktueller Forschung, so z. B. biologische Supplementierung mit primären Vorläuferzellen oder feste Materialien mit erhöhter biologischer Wirksamkeit als Sehnenersatz. Bei der Entwicklung von Zelltherapien seien zudem die Skalierbarkeit sowie die Infrastruktur, welche eine zuverlässige Produktionskette sichert, von Bedeutung. Dr. Salim Darwiche sprach danach über die präklinische Testung von neuen Sehnenreparaturansätzen in vitro gemäss den Bedingungen der guten Laborpraxis (GLP). Er zeigte, wie eine agile Vorgehensweise mit einem GLP-Rahmen für die Planung und Durchführung von in vivo Studien vereinbar ist. So kann die Forschungsfrage das Studiendesign bestimmen und nicht die bestehenden Standardarbeitsanweisungen. Dann präsentierte Dr. Darwiche zwei präklinische in vivo-Studien der Musculoskeletal Research Unit der UZH, in welchen Sehnenreparaturtechnologien unter GLP-Bedingungen in Schafen getestet werden. Diese Studien sind Teil eines Antrages zur Markteinführung bei der US-amerikanischen FDA.

Eine weitere Kaffeepause gab Raum für angeregte Diskussionen, und gemeinsame Forschungsinhalte konnten erkannt und ausgebaut werden. Die letzte Session diente dem Zweck, die Ergebnisse zweier CABMM Start-up Grant-Studien zu präsentieren. Prof. Antonio Pozzi von der Vetsuisse Fakultät Zürich diskutierte das Potential des Hundes als geeignetes Modell für Meniskuserkrankungen. Die Studie bestätigte, dass biologische Veränderungen in spontanen Meniskuserkrankungen in Hunden denen im Menschen ähneln. Zum Schluss sprach PD Dr. Stefan Dudli vom Universitätsklinikum Balgrist über schmerzhafte Knochenmarksläsionen der Wirbelkörperknochen, sogenannte Modic changes, die aus einer erhöhten Nervenfaserdichte resultieren. Knochenmarkzellen sekretieren pro-neurotrophe Signale und könnten ein relevantes Ziel für krankheitsmodulierende Therapien sein.

In seinen abschliessenden Bemerkungen dankte der stellvertretende Vorsitzende Prof. Michael O. Hottiger den Organisatoren des Events. Beeindruckende Präsentationen machten das 12. Symposium zu einem erfolgreichen Event, welches die Bedeutung von wissenschaftlichem Austausch und Kollaborationen hervorhob. Am Ende des Events bot ein Apéro die Möglichkeit für weitere persönliche Gespräche in gemütlicher Atmosphäre.

cabmm scientific seminar

The CABMM Scientific Seminar is a lecture series organized by the CABMM that is held each spring and autumn semester.

It has a special structure consisting of different mini-series, each of which representing a specific research group of the CABMM network or highlighting a collaborative project or a special topic in the field of translational research that is considered to be of importance to our network.

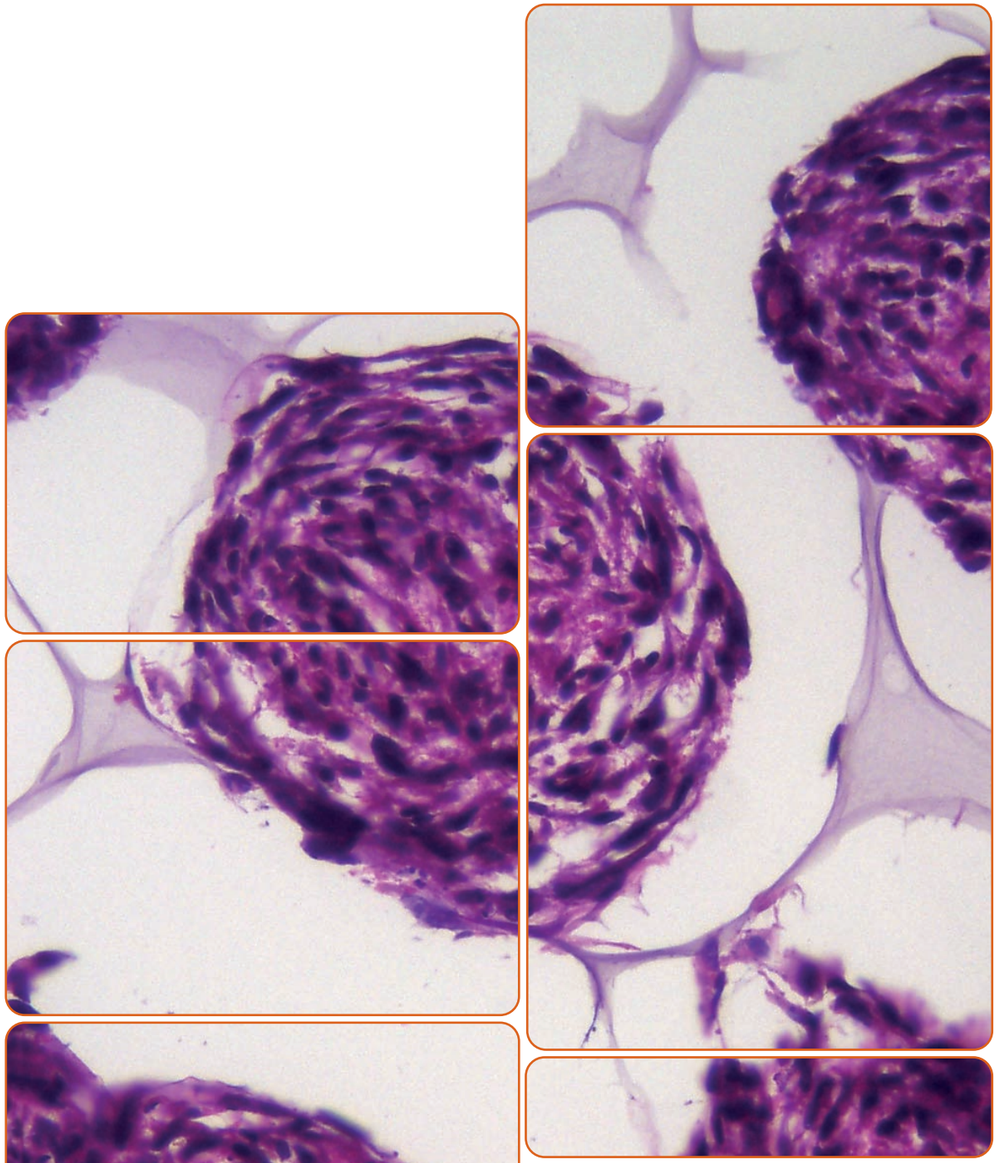
In general, every mini-series starts with an overview talk given by the principal investigator that is followed by presentations of research projects or topic-related articles by group members. After each presentation, a discussion takes place that encourages scientific brainstorming.

The lectures are integral part of the University's course catalogue (05VLFWB82).

We would like to highlight that, well in line with the CABMM's commitment to animal welfare, the following three mini-series were recognized as continuing education by the Veterinary Office of the Canton of Zurich and the Association of Swiss Cantonal Veterinarians in this reporting period:
(1) "The pig as experimental model: are we ensuring animal welfare during anaesthesia?" given by the group of CABMM member Prof. Claudia Spadavecchia from the Section of Veterinary Anaesthesiology and Pain Therapy, Vetsuisse Faculty Bern, in the autumn semester of 2022 dealing with special aspects of anaesthesia and analgesia in laboratory animals;
(2) "Swiss 3R Competence Centre (3RCC)" held by the 3RCC in the spring semester of 2023 introducing their compentence center and presenting different topics related to the 3R concept; and
(3) "Changes and new guidelines for animal experimentation – updates by the AWO" given by the Office for Animal Welfare and 3R, University of Zurich, in the spring semester of 2023 highlighting changes and adaptions related to animal experimentation.

All topics attracted a large audience, also from outside of the CABMM and from outside Zurich.

A tabular summary of all mini-series given during the reporting period can be found on the following pages.



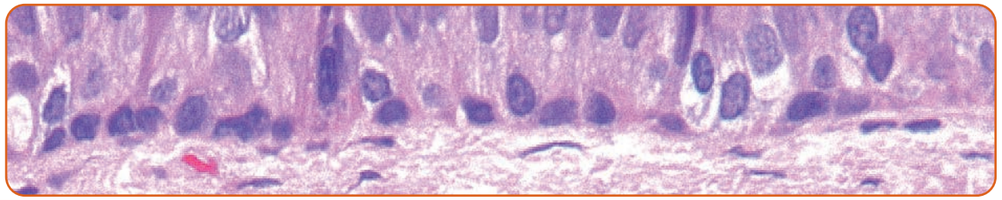
spring semester 2022

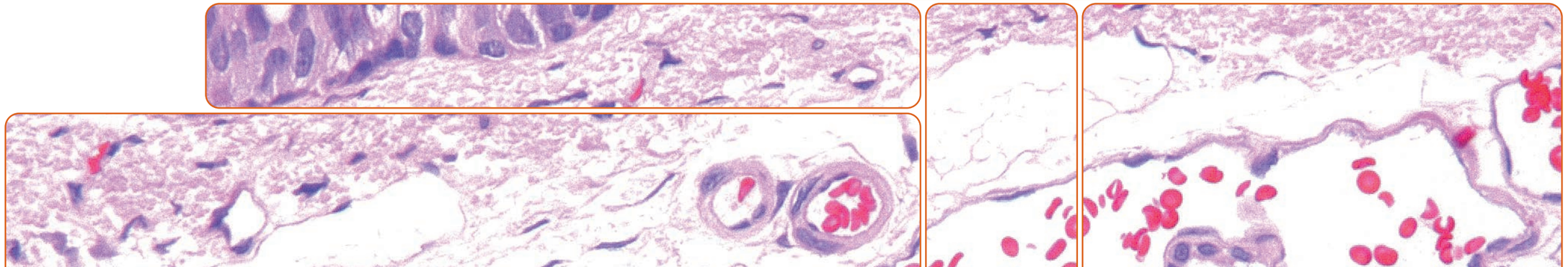
Title	Speaker	Title
Mechanobiology in Health and Disease *Laboratory of Applied Mechanobiology, ETH Zurich*	Prof. Dr. Viola Vogel (PhD)	Introduction and case studies: mechanisms how forces regulate the functions of molecules, cells, and tissues
	Dr. Sebastian Lickert (PhD)	Mechanobiology of platelets and how it regulates thrombus formation
	Prof. Simon Pot (DVM)	Mechanobiology of corneal wound healing
	Dr. med. vet. Mario Benn, PhD	Mechanobiology as forceful player in tissue growth processes
Translational Research for Health Maintenance After Spinal Cord Injury *SCI Population Biobanking & Translational Medicine, Swiss Paraplegic Research, Nottwil*	Prof. Dr. Jivko Stoyanov (PhD)	Spinal Cord Injury Population Biobanking and Translational Medicine
	PD Dr. Marija Glisic (MD, PhD)	Cardiometabolic Health after Spinal Cord Injury
	Dr. Alessandro Bertolo (PhD)	Stem Cells Application to Accelerate and Improve Pressure Injury Healing after Surgery
iPSC Research in Zurich *Institute for Regenerative Medicine, University of Zurich*	PD Dr. Marta Roccio (PhD)	Step-wise differentiation of inner ear sensory cell types from hiPSC in 3D organoids
	Matthew C.S. Denley, MSc	Mitochondrial dysfunction drives iPSC-derived neuronal pathology in methylmalonic aciduria
	Melanie Eschment, MSc	Generation of a human 3D brain model for the ciliopathy Joubert Syndrome
	Dr. Joana Figueiro da Silva (PhD)	Modeling ciliopathies with iPSC-derived kidney organoids
	Dr. Melanie Generali (PhD)	Mending broken hearts using iPSC

autumn semester 2022

Title	Speaker	Title
Fostering preclinical research: the Center for Surgical Research *Center for Surgical Research, University of Zurich & University Hospital Zurich*	PD Dr. Paolo Cinelli (PhD)	Dissecting Mesenchymal Stromal Cell heterogeneity for improved bone bioengineering
	Dr. med. vet. Miriam Weisskopf	The sheep as an experimental model in preclinical research
	Dr. Christian Stoeck (PhD)	Experimental imaging in large animal models – Insights from the pig's heart
	Dr. med. vet. Nina Trimmel	The sheep chair – multiparameter analysis of stress response in sheep during deck chair restraint
The pig as experimental model: are we ensuring animal welfare during anaesthesia? * *Section of Veterinary Anaesthesiology and Pain Therapy, Vetsuisse Faculty, University of Bern*	Prof. Dr. med. vet. Claudia Spadavecchia, PhD	Pigs, anaesthesia and welfare: highlighting the gaps
	Dr. med. vet. Alessandro Mirra, DVM	Depth of anaesthesia in experimental pigs: where are we now?
	Dr. med. vet. Alessandro Mirra, DVM	Depth of anaesthesia in experimental pigs: future opportunities
	Dr. med. vet. Daniela Casoni, DVM, PhD	Knowns and unknowns in diagnosing and handling intraoperative nociception

* Participation was recognized as continuing education credits for animal experimentation by the Association of Swiss Cantonal Veterinarians.





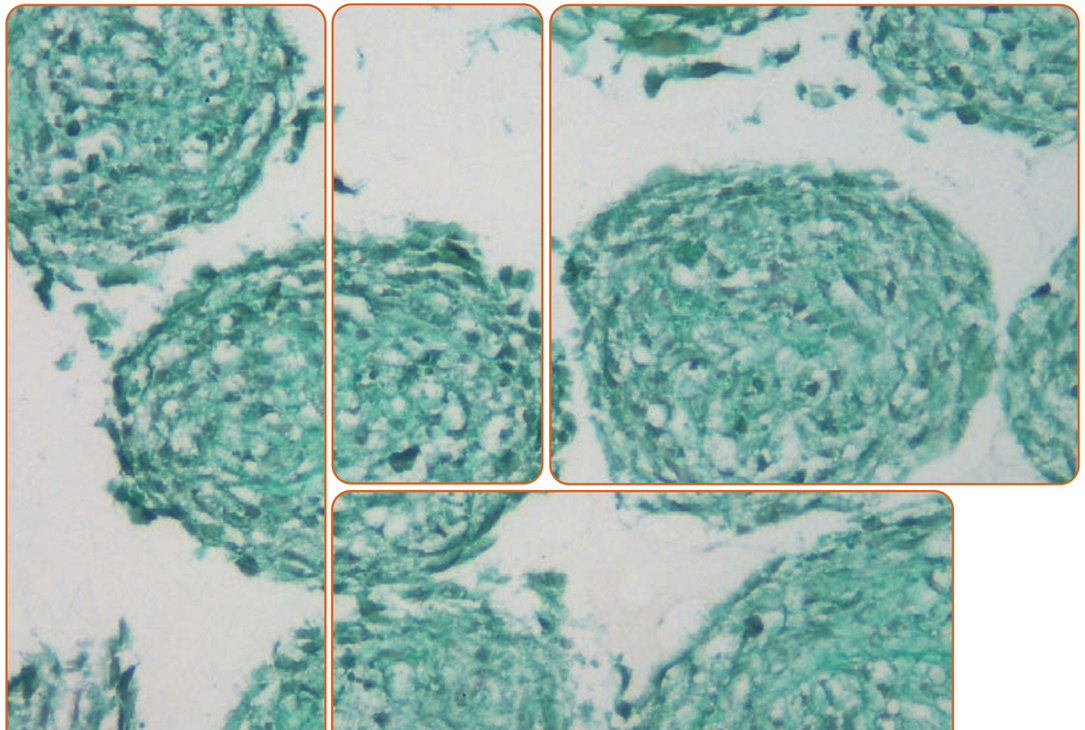
spring semester 2023

Title	Speaker(s)	Title
Changes and new guidelines for animal experimentation – updates by the AWO * *Office for Animal Welfare and 3R, University of Zurich*	Dr. Michaela Thallmair (PhD)	Applications for animal experiments – new guidance from the cantonal veterinary office Zurich
	Dr. Bernadetta Tarigan (PhD)	Good Statistical Practice in Animal Research
	Dr. med. vet. Melania Osto, Dr. Nicole Wildner (PhD)	Of Scoring and Caring
	Dr. med. vet. Corina Berset	What to expect when your experiments are inspected
Advanced imaging of occlusive thrombus in acute ischemic stroke *Department of Neuroradiology, University Hospital Zurich*	Dr. Gergely Bertalan (PhD)	A novel imaging biomarker of thrombus composition
	Dr. Gergely Bertalan (PhD)	Quantitative MRI in brain tumor imaging
Swiss 3R Competence Centre * *Swiss 3R Competence Centre*	Dr. Armand Mensen (PhD)	What is the 3Rs Principle in 2023?
	Dr. Armand Mensen (PhD)	How to obtain funding for your 3Rs project
	Dr. Jessica Lampe (PhD)	Scientific Engagement: Communicating Science
	Dr. Antoine Champetier (PhD)	Monitoring the 3Rs in Switzerland

* Participation was recognized as continuing education credits for animal experimentation by the Association of Swiss Cantonal Veterinarians.

autumn semester 2023

Title	Speaker	Title
Hematopoietic stem cell-directed gene therapy for genetic disorders *Institute for Regenerative Medicine, University of Zurich*	Dr. Panagiotis Tsapogas (PhD)	Gene therapy for immunodeficiencies: clinical and preclinical aspects
	PD Dr. Ute Modlich (DVM, PhD)	Preclinical *in vivo* and *in vitro* models to assess safety of HSC-directed gene therapy
	Dr. Kah Mun Siow (PhD)	Genome editing of hematopoietic stem cells for therapeutic applications
Cartilage tissue engineering *Tissue Engineering and Biofabrication laboratory, ETH Zurich*	Prof. Dr. Marcy Zenobi-Wong (PhD)	Introduction and light-based printing
	Maryam Asadikorayem, MSc, Patrick Weber, MSc	Injectable zwitterionic materials for treatment of osteoarthritis
	Dr. Philipp Fisch (PhD), Dr. Anna Puiggali-Jou	Osteochondral tissue engineering
	Prof. Dr. Hala Zreiqat (PhD)	3D printed ceramics for osteochondral grafts



OLMA 2023

The Canton of Zurich was guest canton at the OLMA St. Gallen 2023, the largest Swiss trade fair for agriculture and food. In this context, the UZH's Institute of Animal Nutrition and Dietetics and the CABMM presented an exciting research project in the field of food innovation. Project leader Dr. Daniel Brugger was responsible for the scientific supervision and the CABMM coordinating office supported the design and supervision of the exhibition stand.

The project "More from the sea: macroalgae for healthy and sustainable nutrition" investigated the effects of seaweed on porcine nutrition. Feeding trials were conducted to investigate the effects of whole plant brown algae *(Laminaria japonica)* supplementation to piglets. The findings of the studies were promising: Algae-fed animals needed significantly less feed amount to gain the same growth performance as control animals. It was shown that algae serve as food source for natural intestinal bacteria, which in turn help to suppress diarrhea pathogens. The intestinal immune system saves energy that can be used for growth.

Besides the improvement of intestinal health, the feed saving also reduces the agricultural area required for wheat cultivation. This effect is further increased as algae are aquatic plants and do not need arable land.

Additionally, positive effects on sustainability should be noted: Algae are a large biomass with high capacities to remove carbon dioxide from the environment. Moreover, they can also bind nutrients like iodine and selenium, trace elements that are usually supplemented to basal diets in pig breeding.

The OLMA trade fair 2023 attracted more than 330'000 people over a period of 11 days. The special exhibition "Familie Zürchers Garten" was well attended, and we are pleased to have engaged in many conversations, heard ideas or concerns, and had a good time in and outside the academic environment.

OLMA 2023

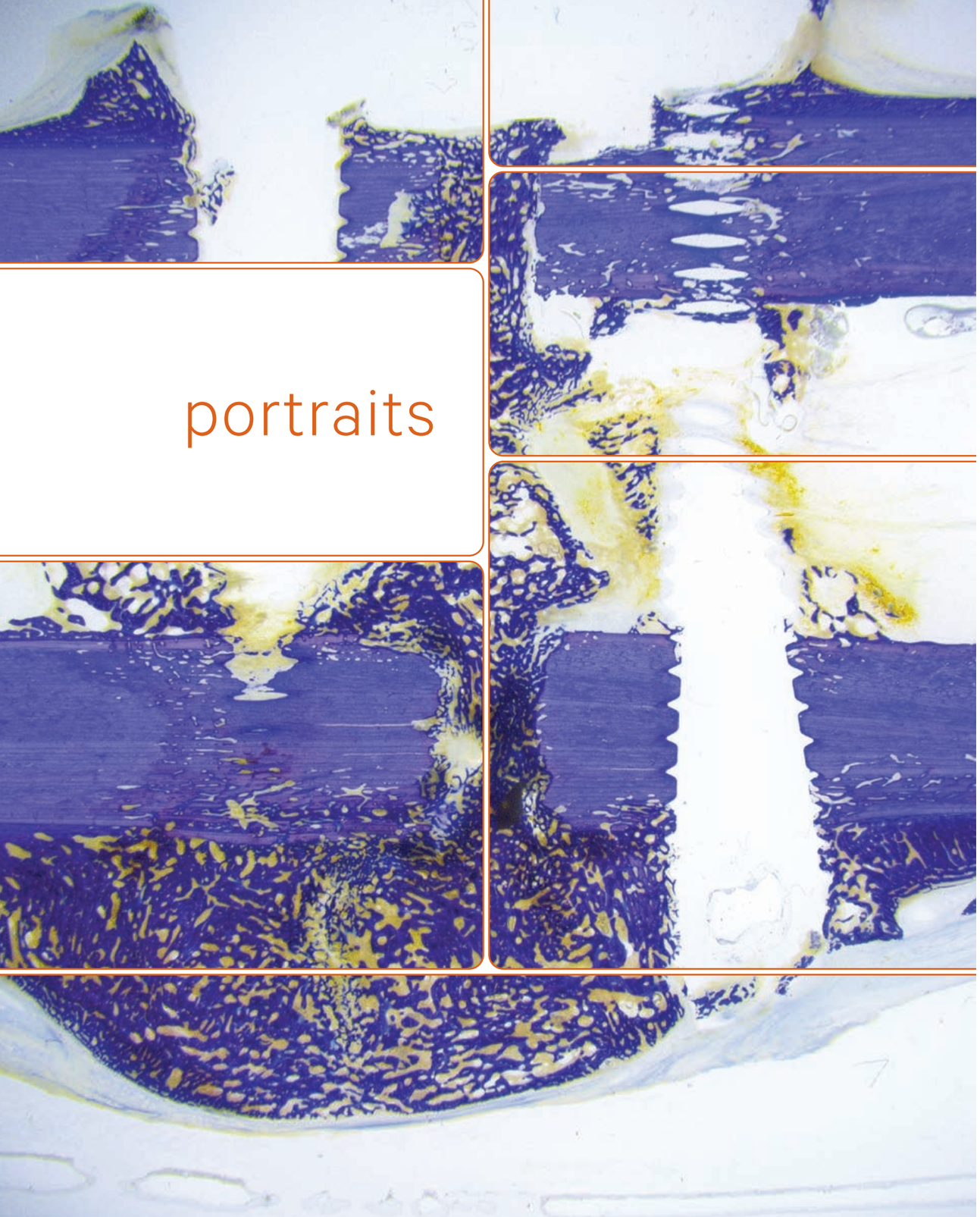
Der Kanton Zürich war 2023 zu Gast an der OLMA in St. Gallen, der grössten Schweizer Messe für Landwirtschaft und Ernährung. In diesem Rahmen präsentierte das Institut für Tierernährung und Diätetik der UZH in Zusammenarbeit mit dem CABMM ein spannendes Forschungsprojekt im Bereich „Food Innovation". Die wissenschaftliche Begleitung übernahm Projektleiter Dr. Daniel Brugger, das CABMM unterstützte bei der Gestaltung und Betreuung des Messestandes.

Das Projekt „Mehr aus dem Meer: Makroalgen für eine gesunde und nachhaltige Ernährung" untersuchte die Auswirkungen von Makroalgen auf die Ernährung von Schweinen. Anhand verschiedener Fütterungsversuche wurden die Effekte der Supplementierung mit Braunalgenextrakt (Laminaria japonica) untersucht. Die Resultate der Studie sind vielversprechend: Tiere, deren Futter mit Algen versetzt war, benötigten signifikant weniger Futter, um dieselbe Wachstumsleistung zu erreichen wie die Kontrolltiere. Es konnte gezeigt werden, dass die Algen als Energiequelle für nicht-pathogene Darmbakterien dienen, die wiederum Durchfallerreger im Darm verdrängen. Auf diese Weise spart das Immunsystem Energie, die für das Wachstum der Tiere genutzt werden kann.

Neben den positiven Effekten auf die Darmgesundheit, könnte die Futterersparnis zudem die benötigte Getreideanbaufläche für die Futtermittelproduktion reduzieren. Da Algen aquatische Pflanzen sind und selbst keine Anbaufläche benötigen, wird dieser Effekt nochmals verstärkt.

Zusätzlich sind positive Auswirkungen auf eine nachhaltige Kreislaufwirtschaft zu erwähnen: Algen stellen eine grosse Biomasse dar, die erhebliche Mengen an CO_2 aus der Umwelt aufnehmen kann. Ausserdem binden sie Spurenelemente wie Jod und Selen, welche normalerweise zum Basisfutter hinzugefügt werden müssen.

Die OLMA 2023 lockte über einen Zeitraum von 11 Tagen mehr als 330'000 Besucher an. Die Sonderausstellung „Familie Zürchers Garten" war gut besucht. Wir freuen uns über die vielen interessanten Gespräche, die wir geführt haben, und die Ideen und Bedenken, die geäussert wurden. Es war nicht nur aus wissenschaftlicher Sicht eine gute Zeit.



portraits

Behind every person there is also a personal story, but in the demanding business environment of daily work there is often not much time left to get to know each other very well on a private level. However, private and work life are always connected, and one influences the other. That is why we decided to introduce some people connected to the CABMM network with a personal portrait in every CABMM Report, describing not only their scientific interests, but also some private aspects of their life.

Paula Lanfranconi, free journalist, interviewed the following people for this CABMM Report:

Dr. med. vet. Katja Nuss

- Co-leader of the Musculoskeletal Research Unit
- Member of the CABMM Steering Committee
- Family and doctoral students' manager
- Dog and nature lover
- Sports fan and avid reader

Prof. Dr. em. Markus Aebi (PhD)

- Professor emeritus of mycology at ETH Zurich
- Member of the CABMM Scientific Advisory Board
- Pioneer in glycobiology
- Passionate teacher
- Enthusiastic traveler and photographer

Prof. Dr. med. vet. Antonio Pozzi

- Head of the Clinic for Small Animal Surgery
- Supporter of translational research
- Lecturer with a great sense of humor
- Father of three teenage daughters
- Passionate climber and outdoor lover

For those who are not yet familiar with the portrayed people, this may be a good opportunity to gain insight into their research and also to learn about their private life and personality. For those who already know these people in person, it may be still possible to learn something new about them. And for all readers, it may be interesting to recognize the parallels between their work and private life.

„meinen doktorierenden soll es gut gehen“

porträt von paula lanfranconi

Tierärztin Dr. Katja Nuss ist Co-Leiterin der MSRU (Musculoskeletal Research Unit) und Mitglied des Leitungsausschusses des CABMM. Sie findet es erfüllend, ihre Doktorierenden an der MSRU mit den Anforderungen wachsen und aufblühen zu sehen. Neben der Arbeit hat sie noch Energie für andere Interessen.

Die Besucherin hat die E-Mail etwas ungenau gelesen und irrt nun suchend auf dem Campus der Universität Zürich-Irchel umher. Also Anruf bei Dr. Katja Nuss – und die reagiert so, wie sie es bei ihren Doktorierenden tut: Fehlerbegrenzung, keine Vorwürfe. Jetzt sagt sie: „Ich komme Ihnen entgegen.“ Danach gibt’s erst mal einen Kaffee.

Sie ist hoch gewachsen, ihr Blick zugewandt, der Schritt ausgreifend. Ihr Büro im umgebauten alten Bauernhaus auf dem Strickhof-Areal teilt sie mit vier Mitarbeitenden. Es ist eng. Zum Glück ragt nebenan ein Kran in die Höhe. Hier entsteht ein geräumiger Neubau mit mehr Platz für die MSRU. 1993, als Prof. em. Brigitte von Rechenberg die MSRU gründete, war diese im Wesentlichen ein Ein-Frau-Betrieb. Heute hat die MSRU 20 Mitarbeitende. Sie testen neue Therapieansätze und Medizinprodukte nach GLP-Standard. Die erfahrene Veterinärchirurgin und -anästhesiologin Katja Nuss hat 2004 in Zürich ihre Arbeit aufgenommen. Es sei eine halb private, halb berufliche Geschichte gewesen: Ihr Mann, Prof. Karl Nuss, war damals für einen dreijährigen Aufenthalt als Veterinärchirurg an die Zürcher Nutztierklinik gekommen. Zur gleichen Zeit suchte Brigitte von Rechenberg eine Person, die mithelfen sollte, die MSRU weiter auszubauen. „Die Chemie hat sofort gestimmt“, erinnert sich Katja Nuss.

Seit 2020 ist sie nun Co-Leiterin der MSRU. Vieles hätten sie unverändert von der Gründerin übernommen. So verlange man, zum Beispiel, von den Doktorierenden nicht, dass sie Dinge tun, die ihnen nicht liegen. „Dafür hat jede Person andere gute Fähigkeiten, die es auszubauen gilt.“ Das schaffe eine Atmosphäre von gegenseitigem Vertrauen. Und da ist eben die Fehlerkultur: Wer einen Fehler gemacht hat, soll dazu stehen. „Es gibt bei uns keine Vorwürfe und kein Geschimpfe.“

Man spürt rasch: Katja Nuss mag Menschen – ihre Neugier, ihr Wissen, ihre Lebensentwürfe. Sie findet es erfüllend zu beobachten, wie ihre Doktorierenden aufblühen, weil sie sich im geschützten Rahmen selbst kennen lernen können, auch in Stresssituationen. Dass sie Anerkennung bekommen und sehen: Ich schaffe das! Die Doktorierenden seien ja gleich alt wie ihre Kinder – das Wichtigste in Katja Nuss‘ Leben. „Ich möchte, dass es ihnen allen gut geht.“

Die Tiermedizinerin arbeitet schon seit 2011 beim CABMM mit; heute sitzt sie im Leitungsausschuss. Die Plattform, sagt sie, ebne den Weg zu Kollaborationen und ermögliche unkompliziert Kontakte zu anderen Forschenden. Ihre Gruppe hat viele Forschungsprojekte mit CABMM-Mitgliedern durchgeführt. „Wir sind ja spezialisiert auf Orthopädie und einige Komponenten der Weichteilchirurgie und haben durch CABMM-Leute viele Einblicke in andere Gebiete erhalten.“ Deren Expertise und Begeisterung seien „total ansteckend“. Auch Katja Nuss brennt spürbar für ihre Arbeit: „Was beispielsweise in einer Aneurysmawand passiert, wie der Körper es schafft, die Schäden in sehr vielen Fällen zu reparieren – das ist total faszinierend“, stellt sie fest.

Foto: Vetsuisse-Fakultät, UZH – Michelle Aimée Oesch

Sie kommt aus einer Kieler Arztfamilie. Schon Grossvater, Vater und Mutter waren Mediziner, medizinische Themen tägliches Tischgespräch in der achtköpfigen Familie. Die junge Katja hatte zudem ein Faible für die Landwirtschaft und arbeitete oft als Erntehelferin. Tiermedizin schien ihr die beste Kombination dieser beiden Welten zu sein. Ihre Eltern fanden indes, für eine Frau sei das körperlich zu schwer. Doch solche Rollenzuschreibungen stachelten die junge Frau an. Sie studierte in München Tiermedizin und arbeitete 20 Jahre an der universitären Tierklinik als Chirurgin. Dort lernte sie auch ihren Mann Karl kennen. Als das erste Kind kam, ein Sohn, fand sie: „Ein Kind ist eine neue Welt, ich widme mich ihm ganz.“ Doch bald vermisste sie ihre Arbeit und begann, wieder kurativ zu arbeiten. Drei Töchter folgten.

Nur: wie bringt man das alles unter einen Hut? Sie habe mit Au Pairs, Tagesmüttern, Kita und Hort gearbeitet. Für vier Kinder, räumt sie ein, sei das schon eine gewisse logistische Herausforderung. In der Schweiz, wo die Kinderbetreuung enorm teuer sei, wäre es gar „ein absolutes Zuschussgeschäft gewesen“. Inzwischen sind alle Kinder aus dem Haus, halten aber immer noch engen Kontakt mit der „Managerin“ der Familie. Auch aus diesen Erfahrungen heraus findet Katja Nuss immer Lösungen, wenn Doktorierende Probleme mit der Vereinbarkeit von Privatleben und Beruf haben.

Sie pendelt täglich von Waldshut-Tiengen nach Zürich. Oft zu viert in einer Fahrgemeinschaft, wegen des ökologischen Fussabdrucks. Mit dabei ist zudem Mia. Die junge Lagottohündin hat die Familie mit sechs Monaten übernommen: Den früheren Besitzern war das Tier zu lebhaft geworden. Nun begleitet Mia ihre Besitzerin auf langen Spaziergängen im nahen Südschwarzwald.

Die 63-Jährige macht viel Sport. Dreimal die Woche Workouts beim ASVZ. „Körperliches Auspowern – danach geht’s mir richtig gut“, sagt sie strahlend. Sie ist auch eine begeisterte Leserin. Wenn die Familie in ihr dänisches Ferienhaus fährt, ist immer eine grosse Büchertasche im Gepäck. Ihre Favoriten seien im Moment Dörte Hansens „Zur See“ und Mariana Lekys „Was man von hier aus sehen kann“.

Schon bald wird Katja Nuss mehr Zeit für sich haben: Ihr Mann wird Anfang 2025 emeritiert, sie selber ein halbes Jahr später. Das Paar hat noch viel vor, Fernwanderungen etwa. Und da ist Katja Nuss’ Wissbegierde. Nach 40 Jahren Medizin möchte sie eintauchen in geisteswissenschaftliche Sphären. Zum Beispiel in die Neuere Deutsche Literaturwissenschaft: „Schauen, was man da in der Tiefe finden kann“. Was sie auch „total interessiert“, sind die Vergleichenden Religionswissenschaften – etwa die Frage, welche Narrative die Menschen brauchen, um ein gemeinsames grosses Projekt zu verfolgen.

Beruflich schaut sie mit Freude auf den Bezug des neuen MSRU-Gebäudes mit seinen grosszügigen Labors und OPs. Im Oktober 2024 wird es so weit sein. Ihre Vision: MSRU und CABMM sollen auch räumlich enger zusammen arbeiten. Zum Beispiel mit WissenschaftlerInnen, die dann hauptsächlich *in vitro* arbeiten – etwa zur Frage, wie Knorpelzellen auf ein bestimmtes Material reagieren. Und dies dann auch *in vivo* testen, damit man es nachher am Menschen anwenden kann.

Es ist Mittag geworden, Zeit für den Workout. Danach geht’s raus zum mittäglichen Spaziergang. Sehr zur Freude von Mia und der anderen bewegungshungrigen MSRU-Bürohunde. „Dabei wird der Kopf wieder frei für neue Ideen und Projekte.“

“my doctoral students should be fine”

portrait by paula lanfranconi
translation by silke kalchofner-mark

The veterinarian Dr. Katja Nuss is co-leader of the MSRU (Musculoskeletal Research Unit) and a member of the CABMM Steering Committee. It is satisfying for her to see her doctoral students blooming and growing along with their tasks. Besides her work, she has also energy for other interests.

The visitor didn’t read the e-mail carefully and is now wandering around on the Irchel Campus of the University of Zurich. Finally, she is giving Dr. Katja Nuss a ring – and she does exactly what she would have done with her doctoral students: error limitation, no criticism. She says: “I am walking towards you.” Then, they are having a cup of coffee first.

She is tall, her look is direct, her strides are long. She shares her office in an old, altered farmhouse at the Strickhof area with four co-workers. Everything is cramped. Luckily, a crane soars just aside. There, a new, spacious building with much more space for the MSRU is constructed. In 1993, when Prof. em. Brigitte von Rechenberg founded the MSRU, it was basically a one-woman operation. Today, the MSRU has 20 employees. They are testing new therapies and medicinal products in compliance with GLP. The experienced veterinary surgeon and anesthesiologist Katja Nuss started her work in Zurich in 2004. It would have been a half-private, half-professional story: Her husband, Prof. Karl Nuss, had just moved for a three-year stay as veterinary surgeon to the Clinic for Farm Animals in Zurich. At the same time, Brigitte von Rechenberg was looking for a person to help her build up the MSRU. “We instantly had a good chemistry”, Katja Nuss remembers.

Since 2020, she has been co-leader of the MSRU. They adopted many things from the founder without any changes. For example, they would not ask any doctoral students to do something they are not able to do well. “Every person has other good abilities, and these have to be strengthened.” This would create an atmosphere of mutual trust. And they would have exactly the above-mentioned culture of failure: Who does a mistake should admit it. “There is no criticism and no accusation.”

It is obvious: Katja Nuss likes people – their curiosity, their knowledge, their lifestyle concepts. It is satisfying for her to see how her doctoral students start blooming because they can learn more about themselves in a protected setting, also in stress situations. That they receive acknowledgement and realize: I can do it! Her doctoral students would be at the same age as her children – the most important thing in Katja Nuss’ life. “I want all of them to be fine.”

The veterinarian has been working with the CABMM since 2011; nowadays, she is a member of its Steering Committee. This platform, she says, would pave the way for new collaborations and would allow to contact other researchers in an easy and uncomplicated way. Her group performed many research projects with other CABMM members. “We are specialized in orthopedics and some parts of soft tissue surgery and gained many insights into other fields through CABMM people. Their expertise and enthusiasm would be “really infectious”. Katja Nuss is also on fire for her work: “What happens in an aneurysm wall, for example, how the body is often able to repair such damages – that’s absolutely fascinating”, she states.

She comes from a family of physicians in Kiel. Already her grandfather, her father and her mother were doctors, medical topics were daily table talk in the family of eight. Young Katja also really liked agriculture and often worked as a harvest hand. For her, veterinary medicine seemed to be the best combination of these two worlds. Whereas her parents thought this to be too physically demanding for a woman. But those gender assignments only spurred the young woman. She studied veterinary medicine in Munich and worked as a surgeon at the University’s animal hospital for 20 years. There, she also met her husband, Karl. After the first child, a son, she thought: “A child is a completely new world, I will thoroughly dedicate myself to him.” But soon, she missed her work and started to work curatively again. Three daughters followed.

But how was she able to manage all that? She worked with au pairs, day nannies, day-care centers, and after-school care facilities. Having four kids, she acknowledges, would be a certain logistic challenge. In Switzerland, where childcare is extremely expensive, it would have been even a “real loss-making deal”. In the meantime, all children have left home, but they all keep close contact to the “family manager”. Also thanks to these experiences, Katja Nuss always finds a solution when her doctoral students have problems with their work-life balance.

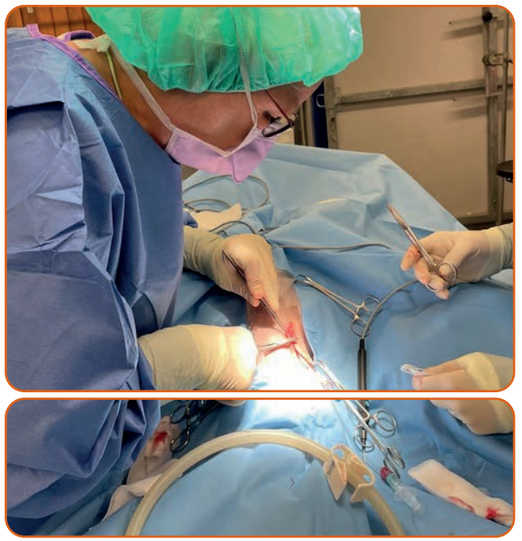
She commutes every day from Waldshut-Tiengen to Zurich. Often in a four-people carpool because of the ecological footprint – and accompanied by Mia. The family adopted the young female Lagotto dog when she was six months old and became too lively for her former owner. Now, she accompanies her new owner on long walks in the nearby Southern Black Forest.

The 63-year-old does a lot of sports. Three times a week, she has workout sessions at the ASVZ. “Physically giving everything – afterwards I feel pretty good”, she says with a bright smile. She is also an enthusiastic reader. Every time, when the family goes to their Danish vacation home, she takes a big bag with books. Currently, her favorites are Dörte Hansen’s “Zur See” (“To the Sea”) and Mariana Leky’s “Was man von hier aus sehen kann” (“What You Can See from Here”).

Soon, Katja Nuss will have more time for herself: Her husband will receive emeritus status at the beginning of 2025, she herself will retire half a year later. The couple has a lot of plans, long-distances hikes, for example. And there is Katja Nuss’ thirst for knowledge. After 40 years in medicine, she would like to dive into humanistic spheres. New German literature, for example: “To see, what can be found in the very depths.” She is also “totally interested” in comparative religious studies – for example, which narratives people need to share a big common purpose.

Professionally, she is really looking forward to moving into the new MSRU building with its spacious labs and surgery suites. The move is scheduled for October 2024. Her vision: a closer collaboration of MSRU and CABMM, also in spatial terms. For example, with scientists focusing on *in vitro* work, e.g., on the question how cartilage cells react to a certain material. Followed by *in vivo* testing, to allow its future use in humans.

It is already noon, time for her workout. Afterwards, she will go out for her midday walk. Much to the delight of Mia and the other active dogs at the MSRU office. “To get my mind cleared for new ideas and projects.”



„an grenzflächen passiert das interessante“

porträt von paula lanfranconi

Prof. em. Markus Aebi ist Mitglied des Wissenschaftlichen Beirats des CABMM. Mit seiner Forschung an Hefen hat der Schweizer Mikrobiologe viel zur N-Glykosylierung von Proteinen und Diagnostik der angeborenen Stoffwechselkrankheit CDG (Congenital Disorders of Glycosylation) beigetragen. Seit seiner Emeritierung reist er zusammen mit seiner Frau öfters auf Darwins Spuren.

Foto: ETH Zürich – Gian Marco Castelberg

Es ist Nikolaustag. Wir treffen uns an der ETH Hönggerberg. Markus Aebi teilt hier ein Büro mit anderen emeritierten Professoren. Die Besucherin hat einen Grittibänz mitgebracht – auch, weil der Hefeteigmann zu Aebis Forschungsgebiet passt. Aebi liebt aktuelle Bezüge. Als Professor für Mykologie passte er seine Krawatte jeweils dem Vorlesungsthema an. Mit der Krawatte, erklärt er, habe er den Studierenden zeigen wollen: Die Vorlesung ist für mich etwas Wichtiges, Festliches. Noch heute kann sich der passionierte Lehrer ärgern über einschläfernde Vorlesungen aus der eigenen Studienzeit. „Das Wichtigste ist doch, seine Begeisterung für das Fach zu zeigen, den Studierenden nie den Rücken zuzukehren – wir sind visuelle Organismen!“

Das Stichwort Interaktion wird sich wie ein roter Faden durch das Gespräch ziehen. Seit seiner Emeritierung 2020 ist Aebi Mitglied des Wissenschaftlichen Beirats des CABMM. Als Grundlagenforscher sei es ihm immer wichtig gewesen, mit seinem Spezialwissen an Grenzflächen heran zu gehen: „Dort passieren die interessanten Entwicklungen.“ Das CABMM – „diese wichtige Initiative“ - ermuntert der renommierte Forscher, noch vermehrt Strukturen für fächerübergreifende Interaktionen bereit zu stellen und auch Forschungsgesuche noch stärker aus diesem Blickwinkel zu beurteilen.

Markus Aebis Faszination für Biologie begann mit Echsen, die er als Bub im Terrarium hielt. Aufgewachsen im schweizerischen Brugg, wusste er schon früh, dass er an der ETHZ studieren wollte. Es wurde Biochemie. „Retrospektiv eine super Studienrichtung.“ Er dissertierte über die Genetik von Hefen. Sein Doktorvater, Ralf Hütter, förderte seine Begeisterung für die Forschung. Eigentlich hätte Aebis akademischer Weg danach in die USA geführt. Doch die Liebe verzögerte dies ein bisschen: Aebi hatte schon im Studium seine künftige Frau Kerstin kennen gelernt und wartete, bis sie ihr Medizinstudium abgeschlossen hatte. „So suchte ich in Zürich jemanden, bei dem ich noch mehr lernen konnte.“

Dieser Jemand war der weltbekannte Molekularbiologe Charles Weissmann, ein äusserst inspirierender, aber auch fordernder Chef. „Ein Glückstreffer, in diesem Toplabor arbeiten zu können“, rühmt Aebi. Solcherart gewappnet und ausgestattet mit einem Stipendium des Schweizerischen Nationalfonds, zog er vier Jahre später mit seiner Frau und dem halbjährigen Sohn ans Caltech. Nach einem Jahr gings zurück nach Zürich: Ein Startstipendium des SNF ermöglichte es ihm, eine unabhängige Forschungsgruppe aufzubauen - wieder ein Glücksfall. Er habe brillante Ideen gehabt, erinnert sich Aebi schmunzelnd. „Bloss funktionierten sie nicht.“ So rutschte der junge Forscher in ein völlig neues Gebiet, die Glyko-Biologie. „Ich betrat einen unbekannten Raum, von dem viele Türen abgingen – was gibt es Besseres für einen Forscher?“ Serendipity, Glück und Zufall hätten ihn in diesen Raum geführt, sagt er mit funkelndem Blick.

Dann ein Durchbruch. Aebi konnte nachweisen, dass die Glykosylierung von Proteinen bei Pflanzen, Tieren und Menschen gleich abläuft. Grund genug, jenen belgischen Pädiater anzurufen, der die komplexe Stoffwechselkrankheit CDG im Jahr 1980 erstmals beschrieben hatte. Mikrobiologe Aebi sagte dem

Mediziner: „Meine Hefezellen zeigen mir, warum deine CDG-Kinder krank sind!“ Nach anfänglichem Unverständnis hätten sie dann zwei Jahre später zusammengearbeitet, erinnert sich Aebi. Es habe auch Treffen mit Patienten gegeben. Einmal sei eine Grossmutter aus der Schweiz dabei gewesen. Auf die Frage, was er denn mache, habe er ihr geantwortet, er arbeite an Hefen. Da habe die Frau ihn gross angeschaut und gefragt: Hefen? Wieso arbeiten Sie nicht daran, dass meine Enkelin geheilt wird? Die Grundlagenforschung zu rechtfertigen, sei nicht immer einfach: „Ich war froh, dass meine Kollegen aus der Medizin den Kontakt zu den direkt Betroffenen übernommen haben.“

Es sind nicht die wissenschaftlichen Entdeckungen, die Markus Aebi im Rückblick am meisten beglücken. Denn ein reines Forscherleben gleiche einer Achterbahnfahrt: „Die euphorische Entdeckerphase dauert fünf Minuten, der Rest des Tages ist geprägt von Normalität und Misserfolg.“ Vielmehr sei es die Interaktion mit den jungen Forschenden, die in Erinnerung bleiben. Mit ihnen zusammenzuarbeiten, ihnen Wissen weiterzugeben und von ihnen zu lernen, sei ein Privileg gewesen.

Seit 2020 ist Markus Aebi emeritiert. Dass er wegen des Corona-Lockdowns keinen richtigen Schlusspunkt hinter diese wichtige Lebensphase setzen konnte, schmerzt ihn: „Das Team zerstreute sich in alle Himmelsrichtungen, ich konnte die Mitarbeitenden nicht verabschieden.“ Aber schon bringt er wieder das Wort Glück ins Spiel: Das Glück, sich für das CABMM engagieren zu können. Und für die ETHZ. Im Rahmen des Projektes rETHink leitete Aebi zusammen mit einer Kollegin ein Projekt zur Neuorganisation von Professuren. Auch hier sei es um mehr Interaktion gegangen. „Spannend!“

Aebi ist Frühaufsteher. Schon um fünf Uhr war er jeweils im Büro, damit die Familie wenigstens abends gemeinsam essen konnte. Den Grossteil der Erziehungsarbeit, lobt Aebi, habe seine Frau geleistet. Da sie ihre Praxis im Familienhaus eingerichtet hatte, konnte sie ihre Behandlungszeiten dem Stundenplan des Sohnes anpassen. Und da waren auch die Grosseltern. Er habe das Glück gehabt, seine Karriere im familiären Umfeld machen zu können. „Ich bin“, scherzt er, „in meinem Leben nicht weit gekommen – bloss von Brugg nach Wettingen.“ Mit einem kleinen Umweg über Pasadena.

Jetzt, wo er mehr Zeit hat, fotografiert Aebi viel. Nein, keine Pilze. Früher habe er mit seinem Sohn öfters Pilze gesammelt. Seine Frau habe ihn aber immer zur Pilzkontrolle geschickt – ihn, den Professor für Mykologie! „Da habe ich aufgehört mit dem Pilzlen“, sagt er und schmunzelt.

Seit seine Frau ihre Praxis geschlossen hat, reist das Paar viel. Gerade waren sie für zweieinhalb Monate in Australien und auf Borneo. Aebi interessierten vor allem die Orang Utans. Und natürlich die Evolution. Auf Borneo wollte er herausfinden, wie der Brite Alfred Russel Wallace zu seiner Evolutionstheorie kam. „Das fasziniert mich extrem, verstanden habe ich es aber noch nicht richtig.“ Im Gegensatz zu Galapagos. Wenn man auf diesen Inseln stehe, sagt Aebi, könne man nachvollziehen, wie Darwin seine bahnbrechenden Erkenntnisse gewann.

Der Grittibänz ist längst aufgegessen. Aebi ist ein inspirierender Gesprächspartner, ein Thema ergibt das nächste – KI, Autismus. Doch nun klopft ein anderer Emeritus an die Bürotüre. Zeit zum Aufbruch.

“interesting things happen at interfaces”

portrait by paula lanfranconi
translation by silke kalchofner-mark

Prof. em. Markus Aebi is a member of the CABMM Scientific Advisory Board. With his research on yeasts, the Swiss microbiologist significantly contributed to the process of N-linked protein glycosylation and diagnostics of the inborn metabolic disease CDG (Congenital Disorders of Glycosylation). Since he was conferred emeritus status, he often travels together with his wife on Darwin’s footsteps.

It’s St. Nicholas’ Day. We meet at ETH Hönggerberg, where Markus Aebi shares an office with other emeriti. The visitor brought a Grittibänz along – also because the yeast dough man fits very well to Aebi’s research field. Aebi loves topical connections. As professor for mycology, he matched his tie with each lecture topic. With the ties, he explains, he wanted to show the students: The lecture is something important, something festive to me. Even nowadays, the passionate lecturer is still annoyed about soporific lectures from his own student days. “It is most important to show one’s passion for the field, never to turn one’s back on the students – we are visual organisms!”

The keyword interaction runs like a golden thread through the interview. Since he was conferred emeritus status in 2020, Aebi has been a member of the CABMM Scientific Advisory Board. As basic researcher, it has always been important to him to approach interfaces with this special knowledge: “The interesting developments happen there.” The renowned researcher encourages the CABMM – “this important initiative” – to provide even more structures for interdisciplinary interactions as well as to evaluate research proposals more from this perspective.

Markus Aebi’s fascination with biology started with lizards that he kept as a child in a terrarium. Growing up in Brugg in Switzerland, he knew very soon that he wanted to study at the ETHZ. It turned out to be biochemistry. “Retrospectively, a great field of study.” He wrote his dissertation on yeast genetics. His PhD supervisor, Ralf Hütter, promoted his passion for research. Actually, his academic path would have led him to the US. But love delayed this a bit: Already as a student, he met his future wife Kerstin and waited until she earned her medical degree. “That is why I was looking for someone in Zurich, where I could learn even more.”

This person was the world-famous molecular biologist Charles Weissmann, a very inspiring but also demanding boss. “A lucky strike to be able to work in this top lab”, Aebi praises. Forearmed in such way and equipped with a grant from the Swiss National Science Foundation, he moved four years later together with his wife and their six-month-old son to Caltech. One year later, they went back to Zurich: A SNSF Starting Grant allowed him to establish an independent research group – once again a lucky strike. He had brilliant ideas, Aebi remembers smiling. “They just didn’t work.” Thus, the young researcher slipped into a completely new field: glycobiology. “I entered an unknow room leading to many doors – is there anything better for a researcher?” Serendipity brought him into this room, he says with a sparkling glance.

Then the breakthrough. Aebi could prove that protein glycosylation is identical in plants, animals, and humans. Reason enough to call the Belgian pediatrician who was the first describing the complex metabolic disease CDG in 1980. The microbiologist Aebi told the physician: “My yeast cells show me why your children are sick.” Two years later, after an initial lack of understanding, they started to work together, Aebi remembers. There were also meetings with patients. Once a grandmother from Switzerland was present. To her question, what he was doing, he answered that he works with yeast. Thereupon the woman looked at him wide-eyed and asked: Yeast? Why are you not working on a therapy for my grandchild? To justify basic research would not always be easy: “I was glad that my medical colleagues were the contact point for the people directly concerned.”

Retrospectively, the scientific discoveries are not the most rewarding for Markus Aebi. The life of a researcher would be like a roller coaster ride: “The euphoric phase of a discovery lasts five minutes, the remaining daytime is characterized by normality and failure.” He would rather treasure the interaction with young researchers. To work with them, to pass on knowledge and to learn from them is a privilege.

In 2020, Markus Aebi was conferred emeritus status. It is painful for him that he couldn’t put a real end to this important stage of life because of the Corona lockdown: “The team scattered in all directions, I couldn’t say goodbye to my coworkers.” But again, he brings the word luck into play: the luck to be able to engage himself for the CABMM. And for the ETHZ. In the project rETHink, Aebi and a colleague were responsible for reorganizing the professorships. Again, it was about more interactions. “Exciting!”

Aebi is an early bird. He was always in the office as early as five o’clock, so the family could at least have dinner together. The main part of raising the child, Aebi complimented, his wife would have taken. As she established her doctor’s practice in the family house, she could adapt her working hours to their son’s timetable. And there were also the grandparents. He was lucky that he could carve out his career in a family environment. “I didn’t get far in my life”, he jokes, “only from Brugg to Wettingen.” With a small detour via Pasadena.

Nowadays, where he has more time, he is photographing a lot. No, not any mushrooms. In the past, he used to collect mushrooms with his son. But his wife always sent him to an official mushroom control – him, the professor of mycology! “After that, I stopped with the mushrooms”, he says smiling.

Since his wife closed her medical practice, the couple has been traveling a lot. They are just back from two and a half months in Australia and Borneo. Aebi was particularly interested in the orangutans. And, of course, in evolution. On Borneo, he wanted to discover how the Briton Alfred Russel Wallace developed his evolutionary theory. “This is extremely fascinating to me, but I haven’t understood it entirely yet.” In opposition to the Galapagos Islands. If you are on these islands, Aebi says, one can easily imagine how Darwin developed his groundbreaking ideas.

The Grittibänz has been finished long ago. Aebi is an inspiring conversational partner, one topic leads to the next – AI, autism. But now, another emeritus is knocking at the door. It is time to leave.

„klettern ist mein wahres selbst“

porträt von paula lanfranconi

Prof. Antonio Pozzi leitet die Klinik für Kleintierchirurgie an der Universität Zürich. Der gebürtige Genuese ist einer der weltbesten Kniechirurgen und CABMM-Mitglied. Forschung und Lehre betrachtet er als Chance zum Wachsen – beruflich, aber auch persönlich. Seine ganz grosse Liebe gilt dem Klettern.

Wie eine Ikone thront das schneebedeckte Matterhorn vor dem stahlblauen Himmel. Jeden Morgen, wenn er ins Büro kommt, schaut Antonio Pozzi auf das riesige Foto. Es erinnert ihn daran, dass es eine Welt ausserhalb des Berufes gibt – die Welt des Kletterns, „mein wahres Selbst“, sagt der 53-Jährige. Der 4478 Meter hohe schweizerisch-italienische Berg gehört zu Pozzis nächsten Kletterzielen. Neben vielen anderen, „too many to list …“. Auf dem Eiger war er bereits. Nordwand, Heckmair-Route. Seine Gipfelgefühle? „Müde, erfüllt, friedvoll.“ Er ist braun gebrannt, sehnig, empathisch. Und sehr humorvoll. Über das Klettern werden wir noch sprechen. Allerdings erst auf ausdrückliche Nachfrage. Antonio Pozzi ist keiner, der seine Leistungen vor sich her trägt.

Heute morgen hat er als Erstes zusammen mit seiner Frau die drei Teenage-Töchter geweckt. Keine einfache Aufgabe, es habe „ein bisschen Yelling gegeben, normal life halt“, sagt er lachend. In der Klinik folgte dann Meeting auf Meeting, Gesuche für wichtige Grants, Clinical Round. Danach, sagt Pozzi, hätten sie auch „über das Leben“ gesprochen – das Leben der jungen Menschen: Ihren Spagat zwischen dem Wunsch, im Job zu brillieren und ihrem persönlichen Alltagsstress. Darum möchte der Professor die jungen Leute auch persönlich kennen lernen. „Wir sind ja vier Jahre zusammen. So kann ich ihnen helfen, mit Stress umzugehen.“

Antonio Pozzi, man merkt es schnell, liebt die Lehre. Zu sehen, wie sich die jungen Menschen entwickeln. Das Teilen seiner Erfahrung mit ihnen. Am liebsten in Kombination mit der Forschung, Pozzis Lieblingstätigkeit. Dabei versteht er Forschung nicht als Ziel an sich. Sondern als Chance, neues Wissen zu entdecken und auszuprobieren. Von anderen Forschenden zu lernen und auch persönlich zu wachsen. Seine Mitgliedschaft beim CABMM komme diesen Zielen ideal entgegen: die translationalen Kooperationen mit anderen Spitzenforschenden, die Option, Tieren zu helfen und diese Erkenntnisse dann auf den Menschen zu übertragen.

Antonio Pozzi hat in Milano Tiermedizin studiert. Mit dem Plan, danach in einem Nationalpark mit Wildtieren zu arbeiten. „Denn was mir wirklich Motivation und Happyness gibt“, sagt er mit Leidenschaft in der Stimme, „ist das Klettern, die Natur.“ Sein Weg führt ihn in die USA, über die Ohio State University an die University of Florida. Dann, 2014, kommt ein Angebot aus Zürich. Die universitäre Klinik für Kleintierchirurgie sucht einen weltweit renommierten Spezialisten für Gelenkchirurgie, Hundesportmedizin, minimalinvasive und regenerative Therapien. Die Entscheidung sei ihm leicht gefallen: „Näher zu meiner Familie in Italien, näher zu den Alpen und eine grosse Jobchance – das waren drei gute Gründe für Zürich.“

Es war dann aber doch ein Nationalpark, wo der passionierte Kletterer ein spezielles Erlebnis hatte: Die italienische Alpinistin Eleonora Delnevo, nach einem Absturz beim Eisklettern querschnittgelähmt, hatte den Traum, den berühmten, fast 1000 Meter hohen Kletterfelsen El Capitan im US-Nationalpark Yosemite zu erklettern. Pozzi und zwei Freunde liessen sich auf das Abenteuer ein, einer Person, die nur die obere Körperhälfte bewegen kann, über überhängende Felsen zu helfen. Und vier Nächte im Hängezelt in der Steilwand zu verbringen. Eigentlich, sagt Pozzi, sei Klettern etwas sehr Egozentrisches. „Aber das hier war etwas, was ich für jemand anderen tun konnte.“ Es wurde dann allerdings richtig gefährlich. Ein Sturm brach aus, die Rettungskräfte waren andernorts engagiert. So musste sich die Gruppe selber in Sicherheit bringen.

Wie geht die Familie mit seiner Kletterleidenschaft um? Seine Frau, sagt Pozzi, kenne ihn und wisse, dass er versuche, vorsichtig zu sein. „Sie lässt mich immer gehen, für zwei, drei Tage.“ Wobei diese Vorsicht relativ ist: Vor kurzem sei er, zum Beispiel, zum Eisklettern an einem Wasserfall gewesen. Gerne hätte er mehr Zeit für die Familie. Und für sich selber. Seine Frau, eine Anästhesistin, war immer Vollzeit für die drei Kinder da. Ihm selber blieben die Wochenenden. Heute, wo die Töchter im Teenageralter sind, geht die Familie gemeinsam Skifahren, Campen. „Einfach Outdoor-Aktivitäten. Das ist, was ich am liebsten mache.“ Er versucht auch, längere Ferien zu nehmen und dann halt ein bisschen zu arbeiten. Aber in seiner Position sei es schwierig, zu verschwinden, relativiert er. Es gebe immer zu tun, „der struggle“ höre nie auf. Wobei er den Begriff nicht negativ verstanden haben möchte. Eher im Sinne von vorwärts kommen, sich entwickeln, beruflich und persönlich. Und doch spürt man die Verantwortung, die er auf seinen Schultern trägt.

Er hat noch einiges vor. Eines seiner Ziele ist, die klinische Forschung am Tierspital zu vergrössern und die verschiedenen Gruppen zu einem Clinical Trial Center zusammen zu führen. „Als veterinärmedizinisches Pendant zum Clinical Trials Center am Universitätsspital Zürich.“ Und auch für sich selber, den Meniskusspezialisten, gibt es eine stimulierende Herausforderung, die er zusammen mit zwei Humanforschenden angeht: den degenerativen Meniskusriss. Er betreffe aktive Leute über 50, „wie mich“, sagt er und deutet lachend auf sein linkes Knie. Für dieses Problem gebe es bisher keine überzeugenden Lösungen. „Die Mechanismen zu verstehen und dann eine Therapie zu finden, das wäre ein Highlight.“

Woher nimmt der 53-Jährige die Kraft für seinen Workload? Die Antwort kommt sofort: Das Klettern, die Natur. Am Berg vergisst Pozzi Klinik und Alltagssorgen, ist ganz im Hier und Jetzt, kommt in einen Flow. Allerdings, räumt er ein, werde er älter und benötige mehr Zeit, um die Batterien wieder aufzuladen.

Auch sein heutiges Programm ist durchgetaktet. Die Kniekoperation eines Sporthundes steht an, eine Patellaluxation. Er und sein Team haben für diese bei Hunden häufige Knieerkrankung eine neue, minimal invasive Operationstechnik entwickelt. Nach der einstündigen OP geht es weiter mit diversen Zoom Meetings, To-do-Listen, Forschungsanträgen. Ob sein Plan aufgeht, um 18 Uhr nach Hause zu fahren und dort an der Kletterwand noch ein wenig Sport zu machen, ist fraglich. Manchmal werde es spät, „you never know“. Eines steht aber fest: Wenn er heim kommt, wird ihn Adoptivhund Rudy, eine Strassenmischung, aufs Überschwänglichste begrüssen. Das passiere ihm mit seinen Töchtern nicht mehr, sagt er lachend. „Aber sie sind nice!“

Von der Bürowand strahlt noch immer magisch das Matterhorn. Wenn die Bedingungen stimmen, will er es im kommenden Winter angehen. „Maybe.“

“climbing is my true self”

portrait by paula lanfranconi
translation by silke kalchofner-mark

Prof. Antonio Pozzi is head of the Clinic for Small Animal Surgery at the University of Zurich. The Genovese-born is one of the world-best knee surgeons and a CABMM member. He considers research and teaching as a chance to grow – professionally as well as personally. His greatest passion is climbing.

Like an icon, the Matterhorn is enthroned in front of a steel blue sky. Every morning, when he enters his office, Antonio Pozzi looks at this huge photograph. It reminds him that there is a world outside of his job – the world of climbing, “my true self”, the 53-year-old says. The 4’478 m high Swiss-Italian mountain is one of Pozzi’s next climbing destinations. Beside many others, “too many to list …”. He has been already on top of the Eiger. North face, Heckmair’s route. His feelings at the peak? “Tired, satisfied, peaceful.” He is tanned, sinewy, empathic. And he has a very good sense of humor. Later, we will talk again about climbing. But only after explicitly asking for it. Antonio Pozzi isn’t a person showcasing his achievements.

This morning, he first got his three teeny daughters up, together with his wife. Not an easy task. There was “a bit of yelling, normal life” he says laughing. Afterwards, in the clinic, one meeting followed another: about important grant applications, and the clinical round. After discussing the clinical cases, Pozzi says, they also talked “about life” – the life of the young people: Their balancing act between the wish to be brilliant at their job and their personal everyday challenges. The professor wants to get known to the young people. “We are working together for four years. I can help them to learn how to handle stress.”

It is obvious that Antonio Pozzi loves teaching. To see how young people develop. To share his knowledge with them. Preferably in combination with research, his favorite activity. He does not see research as a goal per se, but as a chance to try and discover new things. To learn from other researchers and to grow personally. His CABMM membership is well in line with these goals: the translational cooperation with other top researchers, the possibility to help animals and to transfer these findings to humans.

Antonio Pozzi studied veterinary medicine in Milano, with the idea to work with wild animals in a national reserve afterwards. “Because climbing, the nature”, he says with passion in his voice, “is what gives me real motivation and happiness”. His way took him to the US, from the Ohio State University to the University of Florida. Then, in 2014, he got an offer from Zurich. The University’s Clinic for Small Animal Surgery was looking for a renowned specialist in joint surgery, canine sports medicine, as well as minimally invasive and regenerative therapies. It was an easy decision for him: “Being closer to my family in Italy, closer to the Alps and taking a great job opportunity – three good reasons for Zurich.”

But, after all, it was in a national park where the passionate climber had a very special experience: The Italian alpinist Eleonora Delnevo, being paraplegic after an ice climbing accident, had the dream to climb on top of the famous and almost 1’000 m high climbing wall El Capitan in Yosemite National Park. Pozzi and two friends took the plunge to help this person, who was only able to move the upper part of her body, over overhanging cliffs. And to stay four nights in a hanging tent in a steep face. Usually, Pozzi says, climbing would be very egocentric. “But that was something I could do for someone else.” But then it got very dangerous: A storm came, and the rescue teams were engaged somewhere else. Thus, the group had to seek shelter by themselves.

How does his family deal with his climbing passion? His wife, Pozzi says, knows him very well, and she also knows that he tries to be careful. “She always lets me go, for two, three days.” Although this carefulness would be relative: Recently, for example, he was ice climbing on a waterfall. He would love to have more time for his family. And for himself. His wife, an anesthesiologist, has taken care of the kids full-time. His family time has been limited to the weekends. Today, with daughters in the teenage years, the whole family goes skiing or camping together. “Simple outdoor activities. That’s what I like most.” He also tries to take longer holidays and then to work a bit alongside. But in his position, it would be difficult to disappear, he relativizes. There is always something to do, the “struggle” never stops. He doesn’t mean this expression in a negative sense. Rather in the sense of moving forward, developing, professionally as well personally. Nevertheless, the responsibility on his shoulders is noticeable.

He still has a lot of plans. One of his goals is to promote clinical research at the Animal Hospital and to centralize the different groups in a Clinical Trial Center. “As veterinary pendant to the Clinical Trials Center at the University Hospital Zurich.” One of his main research focuses is the degenerative meniscus (tear), a real challenge for sports medicine, which he is tackling together with two human researchers, and which is also personally important to him, the meniscus specialist. It concerns active people older than fifty years, “like me”, he says and points with a smile to his left knee. There isn’t a convincing solution for this problem yet. “To understand the mechanisms and then to find a therapy, that would be a highlight.”

From where does the 53-year-old get the energy for his workload? The answer comes immediately: From climbing, from nature. In the mountains, Pozzi forgets the clinic and his everyday worries, he is completely in the here and now, gets into a flow. However, he admits, he would get older and would need more time to charge his batteries.

Today, his schedule is also extremely tight. A knee surgery of a sports dog is about to start. A patellar luxation. He and his team developed a new, minimally invasive operation technique for this frequently occurring knee problem in dogs. After the one-hour surgery, his day will go on with several zoom meetings, to do-lists, research grants. It is questionable if his plan to go home at 6 pm and to do some sports there at his climbing wall will work out. Sometimes it’s getting late, “you never know”. But one thing is certain: When he will arrive at home, his adopted dog Rudy, a lovable mutt, will welcome him with great excitement. That wouldn’t happen with his daughters anymore, he says laughing. “But they are nice!”

The Matterhorn still shines with some magic from his office wall. If the conditions are good, he will put his plan into action next winter. “Maybe.”

research reports

cabmm research platform

The CABMM Research Platform is a multidisciplinary organisation embedded within the Department of Molecular Mechanisms of Disease (DMMD) at the University of Zurich. Our main objectives are to foster translational, clinically oriented research and to promote scientific collaborations between CABMM members. The CABMM Research Platform is well equipped and offers basic scientists and clinicians the possibility to discuss their research and ideas with each other and work shoulder to shoulder for the purpose of developing novel therapeutic approaches for the treatment of dysfunctional and diseased tissues.

In the reporting period 2022/2023, the following research groups have been continuously using the CABMM Research Platform during the entire period:

1. Musculoskeletal Research Unit
   Group leaders: Katja Nuss, Karina Klein, Salim Darwiche

2. Ocular Cell Biology Group
   Group leader: Farhad Hafezi

3. Skin Engineering Group
   Group leader: Maurizio Calcagni

A short overview of the projects conducted by our platform users is given on the following pages.

Moreover, we present the research of CABMM Steering Committee member Prof. Dr. Marcy Zenobi-Wong, head of the Tissue Engineering and Biofabrication Group at the Institute for Biomechanics of the ETH Zurich, in the field of articular cartilage regeneration.

In her leading article **"Tissue engineering approaches to cartilage regeneration"** she describes the work of her group in cartilage tissue engineering, focusing on biomaterials, cells, and biofabrication techniques such as 3D bioprinting, and finally concludes with summarizing the challenges connected with the *in vivo* translation of such new therapeutical approaches into the clinic.

tissue engineering approaches to cartilage regeneration

Prof. Dr. Marcy Zenobi-Wong (PhD)

Acknowledgements:

I would like to acknowledge the former and current members of the Tissue Engineering and Biofabrication laboratory at ETH Zurich, Dr. Angela Bonato, Dr. Ece Öztürk, Dr. Anna Puiggali-Jou, Dr. Philipp Fisch, Dr. Emma Cavalli, Dr. Parth Chansoria, Dr. Michael Müller, Dr. Frantisek Surman, Simone Ponta and Hao Liu, for their excellent contributions.

Cartilage diseases of the joint present a huge socioeconomic burden, afflicting over 7% of the world's population. Most common is osteoarthritis, a slow and painful degenerative condition which greatly limits the patient's ability to participate in daily activities. Over the past 15 years, my research group has worked on approaches to engineer articular cartilage, both to produce models of disease and to develop therapies which could one day be used in clinics to restore damaged cartilage and alleviate the symptoms of osteoarthritis. Our work on this topic can be divided into three main areas: biomaterials, cells, and the biofabrication strategies that can leverage our tools to recapitulate the organization of adult articular cartilage.

Biomaterial Approaches:

Cartilage is subdivided into the superficial, mid, deep and calcified cartilage layers, and this zonal organization contributes to the load-carrying and lubrication properties of the tissue (Fig. 1). The extracellular matrix of cartilage is composed of collagens and proteoglycans, the most common of which are collagen type II and aggrecan. The aggrecan core protein is post-translationally modified by negatively charged glycosaminoglycans, giving the tissue its high negative fixed charge density. Many tissue engineering approaches have taken a biomimetic strategy, trying to reproduce one or more aspects of the native ECM. For example, Öztürk *et al.* investigated the effect of increasing negative charge of alginates on the process of chondrogenesis by adding sulfate groups [1]. Sulfation promoted the secretion of cartilage-specific collagen type II and aggrecan (Fig. 2). Interestingly, sulfation also promoted the proliferation of chondrocytes without comprising their chondrogenic behavior, suggesting that expansion of cells within a 3D biomimetic environment can prevent the typical loss of phenotype associated with 2D culture. Mechanistically, sulfate alginate has been shown to be important in linking the fibroblast growth factor with its receptor. Additional anti-inflammatory properties of the material [2] suggest it has promise as a scaffold for tissue engineering.

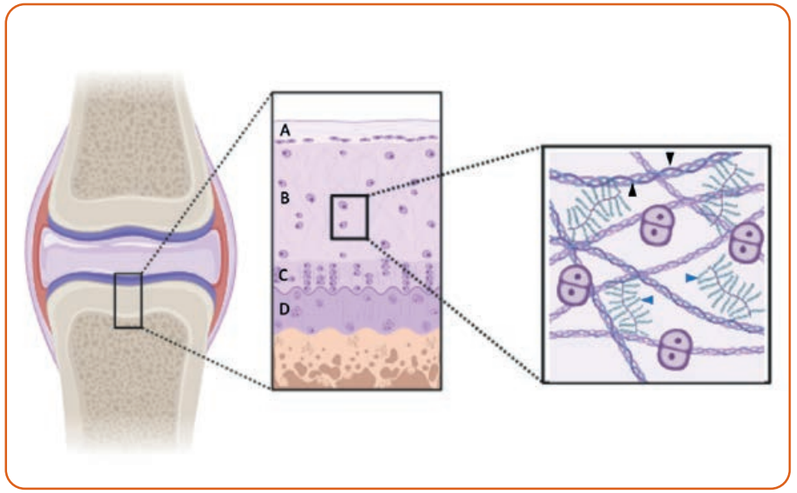


Figure 1: Schematic illustrating the zonal organization of articular cartilage. Middle panel: A – superficial zone, B – mid zone, C – deep zone, D – calcified cartilage. Right panel: chondrocytes and the main extracellular matrix components collagen type II (black arrows) and aggrecan (blue arrows). Figure created in BioRender.

Abbildung 1: *Schematische Darstellung des Aufbaus von Gelenkknorpel. Mitte: A – oberflächliche Schicht, B – mittlere Schicht, C – tiefe Schicht, D – verkalkende Schicht. Rechts: Knorpelzellen und die Hauptbestandteile der extrazellulären Matrix Kollagen Typ II (schwarze Pfeile) und Aggrecan (blaue Pfeile). Abbildung erstellt mit BioRender.*

tissue-engineering zur knorpelregeneration

Übersetzung von
Marina Klawitter & Silke Kalchofner-Mark

Prof. Dr. Marcy Zenobi-Wong (PhD)

Danksagung:

Ich bedanke mich bei den ehemaligen und derzeitigen Mitgliedern des Tissue Engineering and Biofabrication Labors der ETH Zürich für ihre ausgezeichneten Beiträge: Dr. Angela Bonato, Dr. Ece Öztürk, Dr. Anna Puiggali-Jou, Dr. Philipp Fisch, Dr. Emma Cavalli, Dr. Parth Chansoria, Dr. Michael Müller, Dr. Frantisek Surman, Simone Ponta und Hao Liu.

Erkrankungen des Gelenkknorpels betreffen über 7% der Weltbevölkerung und stellen somit eine enorme sozioökonomische Belastung dar. Am weitesten verbreitet ist dabei Osteoarthritis, eine schleichende und schmerzhafte, degenerative Erkrankung, die den Alltag der betroffenen Patienten massiv beeinträchtigt. In den letzten 15 Jahren hat meine Forschungsgruppe verschiedene Ansätze verfolgt, um künstliches Knorpelgewebe herzustellen. Dazu zählen sowohl die Etablierung geeigneter Krankheitsmodelle als auch die Entwicklung von Therapieansätzen, um eines Tages eine klinische Wiederherstellung von beschädigtem Knorpelgewebe zu ermöglichen und so die Symptome von Osteoarthritis zu mildern. Unsere Arbeit auf diesem Gebiet kann in drei Schwerpunktbereiche unterteilt werden: Biomaterialien, Zellen und Strategien der Biofabrikation, bei denen unsere verschiedenen Technologien kombiniert werden, um die Zusammensetzung von erwachsenem Gelenkknorpel zu imitieren.

Ansätze mit Biomaterialien:

Knorpelgewebe wird in vier untergeordnete Schichten unterteilt: die oberflächliche, die mittlere, die tiefe und die verkalkende Schicht (Abb. 1). Dieser geschichtete Aufbau trägt zu den verschiedenen Eigenschaften des Gewebes wie seiner Tragfähigkeit und der Gleitfähigkeit von Gelenken bei. Die extrazelluläre Matrix von Knorpelgewebe besteht aus Kollagenen und Proteoglykanen, darunter vor allem Kollagen Typ II und Aggrecan. Das Aggrecan-Kernprotein wird posttranslational durch negativ geladene Glykosaminoglykane modifiziert, was dem Gewebe seine hohe negative Ladungsdichte verleiht. Viele Ansätze in der Gewebetechnologie verfolgen biomimetische Strategien, bei denen eine oder mehrere Eigenschaften der nativen extrazellulären Matrix nachgeahmt werden. So untersuchten zum Beispiel Öztürk und Kollegen die Effekte zunehmender negativer Ladung auf die Reifung von Knorpelzellen in einem

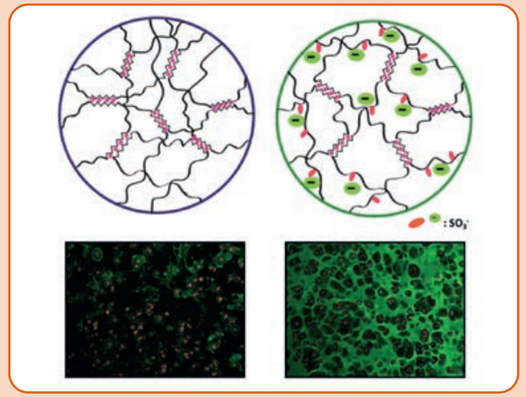


Figure 2: Chemical modification of the marine polysaccharide alginate by sulfate groups (SO_3^-) allowed the formation of hydrogels with tunable degrees of negative fixed charge (top). Bottom left: Bovine chondrocytes seeded onto uncharged alginate hydrogels are viable but produce little type II collagen (green). Bottom right: The production of collagen II is greatly enhanced in the sulfated alginate. Adapted from [1].

Abbildung 2: *Die chemische Modifizierung des marinen Polysaccharids Alginat mit Sulfatgruppen (SO^{3-}) erlaubt die Herstellung von Hydrogelen mit regulierbarer negativer Ladung (oben). Unten links: Knorpelzellen sind auf einem ungeladenen Alginat-Hydrogel lebensfähig, produzieren aber nur sehr wenig Kollagen Typ II (grün). Unten rechts: Die Produktion von Kollagen II ist in sulfatiertem Alginat stark erhöht. Angepasst von [1].*

3D Alginat-Hydrogel [1]. Durch das Anheften negativ geladener Sulfatgruppen (Sulfatierung) konnte die Sekretion von knorpelspezifischem Kollagen Typ II und Aggrecan verstärkt werden (Abb. 2). Interessanterweise begünstigte die Sulfatierung zudem die Proliferation der Knorpelzellen, ohne deren knorpeltypisches Verhalten zu beeinträchtigen. Diese Ergebnisse weisen darauf hin, dass die Vermehrung der Zellen in einem 3D biomimetischen Umfeld dem typischen Verlust des Phänotyps entgegenwirken kann, der unter 2D Kulturbedingungen stattfindet. Bei Untersuchungen zum zugrundeliegenden Mechanismus konnte gezeigt werden, dass das sulfatierte Alginat-Gel eine wichtige Rolle bei der Bindung von FGF (fibroblast growth factor, Fibroblasten-Wachstumsfaktor) an seinen Rezeptor spielt. Darüber hinaus besitzt das Material anti-entzündliche Eigenschaften [2], was sein grosses Potential als vielversprechendes Gerüstmaterial zur Herstellung von künstlichem Knorpelgewebe zusätzlich unterstreicht.

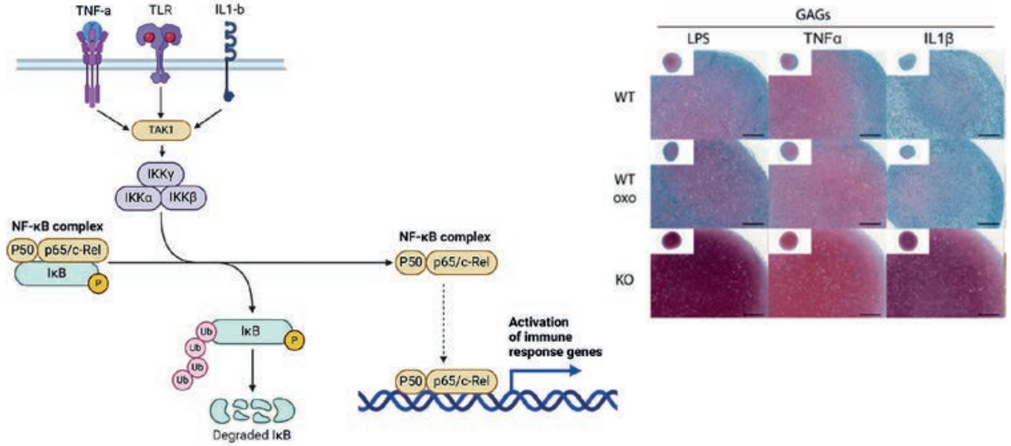


Figure 3: Left: TNF-α, IL-1β, and toll-like receptors (TLR) can activate the inflammatory NF-κB signaling pathway, with TAK1 acting as a centralized hub. Right, lower panel: By knocking out TAK1, it was possible to form cartilage in the presence of pro-inflammatory signals as shown by the production of cartilage specific glycosaminoglycans (GAGs). GAGs are detected by Safranin O staining (red color, adapted from [3]). Figure created in BioRender.

Abbildung 3: *Links: TNF-α , IL-1β und Toll-like-Rezeptoren können die inflammatorische NF-κB Signalkaskade aktivieren, wobei TAK1 als zentrale Drehscheibe agiert. Rechts unten: Wenn das TAK1-Gen ausgeschaltet ist, wird Knorpelgewebe auch in Gegenwart pro-inflammatorischer Signale gebildet, wie anhand der Produktion von knorpel-spezifischen Glycosaminoglykanen (GAGs) gezeigt werden kann. Die Detektion von GAGs erfolgte mittels Safranin O-Färbung (rote Färbung, angepasst von [3]). Abbildung erstellt mit BioRender.*

Cells for Tissue Engineering:

Equally important as the correct selection of the biomaterial scaffolds is the proper sourcing of cells. Current clinical cell-based therapies rely on autologous chondrocytes isolated from biopsies of adult patients. The cells are expanded under GMP (Good Manufacturing Practice) conditions until the number of cells required to treat the lesion is obtained. However, these cells undergo de-differentiation during the expansion process, have lower biosynthetic activity compared to cells from younger patients, and respond poorly to the high mechanical loading and low-grade inflammation of the injured site. To improve the survival chances of engineered tissues in this harsh *in vivo* environment, my lab has recently begun using CRISPR-Cas9 gene editing to render the cells less sensitive to the inflammatory NF-κB signaling pathway. CRISPR-Cas9 uses a guide RNA (gRNA) which recruits the Cas9 protein to the target DNA site where a precise double strand break (DSB) is made. The repair of the DSB by non-homologous end-joining pathway results in the formation of indels and a loss-of-function mutation in the target gene. Using this approach, a functional knockout of the TAK1 gene was performed in chondrocytes, which in turn produced cartilage tissue that was resistant to degradation by pro-inflammatory cytokines [3]. As seen in Figure 3, TAK1 is a central hub in the inflammatory pathway, activated by TNF-α, IL-1β as well as lipopolysaccharide (LPS) from gram-negative bacterial walls. Under inflammatory conditions, cell pellets made from wildtype (WT) chondrocytes showed a significant loss of glycosaminoglycans, as seen by the loss in Safranin O staining (red color). When the TAK1 gene was knocked out, a glycosaminoglycan-rich cartilage could be formed even in the presence of proinflammatory cytokines and LPS.

Zellen für die Gewebetechnologie:

Ebenso wichtig wie die korrekte Wahl des Biomaterials, ist die Verwendung geeigneter Zellen. Derzeit laufende klinische Studien, die auf zell-basierten Therapien beruhen, nutzen autologe Knorpelzellen. Diese werden aus Biopsien von erwachsenen Patienten isoliert und anschliessend unter GMP-Bedingungen (Good Manufacturing Practice) expandiert, bis eine ausreichende Anzahl an Zellen für die Behandlung der Verletzung vorhanden ist. Allerdings kommt es während der Expansion zu einer De-Differenzierung der Zellen, ihre biosynthetische Aktivität ist im Vergleich zu Zellen von jüngeren Patienten geringer und sie reagieren nur unzureichend auf die leichte Entzündung und die hohe mechanische Belastung an der geschädigten Stelle. Um die Überlebenschancen der gezüchteten Gewebe in der rauen in vivo Umgebung zu erhöhen, machen wir uns in meinem Labor seit kurzem die CRISPR-Cas9 Gen-Editierung zu Nutze. Mit dieser Methode konnte die Empfindlichkeit der Zellen gegenüber Entzündungen verringert werden, die über die NF-κB Signalkaskade ausgelöst werden. CRISPR-Cas9 nutzt eine sogenannte Guide RNA (gRNA), die das Cas9 Protein an eine bestimmte Stelle in der DNA lenkt, um dort einen präzisen Doppelstrangbruch (double strand break, DSB) zu verursachen. Die Reparatur des DSB erfolgt über einen spezifischen DNA-Reparaturmechanismus, der als nichthomologe Endverknüpfung (non-homologous end-joining) bezeichnet wird. Dabei entstehen Mutationen im Genom, durch die das Zielgen seine Funktion verliert. Wir konnten auf diese Weise einen funktionellen Knock-out des TAK1 Gens in Knorpelzellen erreichen. Die so modifizierten Zellen stellten anschliessend Knorpelgewebe her, welches dem Abbau durch pro-inflammatorische Zytokine standhielt [3]. Wie in Abbildung 3 zu sehen ist, ist TAK1 eine zentrale Drehscheibe des Entzündungsprozesses und wird durch TNF-α, IL-1β oder von LPS (Lipopolysaccharid), einem Bestandteil der Zellwand Gram-negativer Bakterien, aktiviert. Unter inflammatorischen Bedingungen zeigten Zell-Pellets von Wildtyp-Knorpelzellen (WT) einen signifikanten Verlust an Glykosaminoglykanen, wie die Färbung mit Safranin O (rote Färbung) zeigt. Ohne funktionelles TAK1 konnte Knorpelgewebe reich an Glykosaminoglykanen gebildet werden, sogar in Gegenwart von proinflammatorischen Zytokinen und LPS.

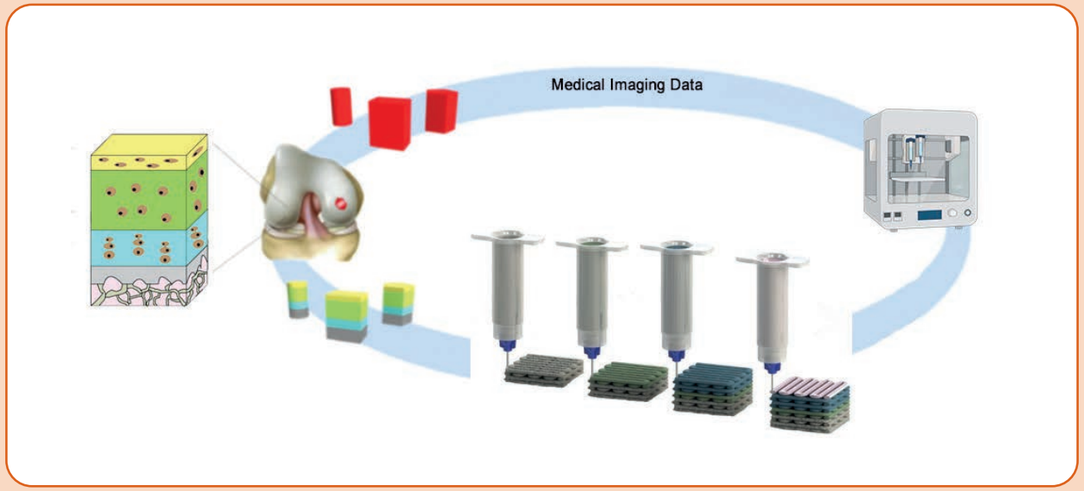


Figure 4: Bioprinting and medical imaging allow the creation of articular cartilage grafts which match the geometry of the patient's specific cartilage lesion. Figure partially created in BioRender.

Abbildung 4: *Bioprinting und medizinische Bildgebung erlauben die Herstellung von Gelenkknorpeltransplantaten, welche die exakte Geometrie der Gelenksverletzung des Patienten aufweisen. Teilweise erstellt mit BioRender.*

Bringing it together with Bioprinting:

Together with cells and biopolymer, it is possible to more closely replicate the structure of articular cartilage using 3D bioprinting technologies (Fig. 4). My laboratory has recently introduced a new light-based Biofabrication technique called Filamented Light (FLight) Biofabrication, which allows rapid printing with micron-level feature size [4].

In FLight Biofabrication, the speckle pattern of the light causes the formation of self-induced wave guides. This projected light crosslinks arrays of fine hydrogel filaments throughout the length of the constructs. These hydrogel filaments can instruct the deposition of collagens in a manner reminiscent of the collagen distribution found in native cartilage (Fig. 5).

Outlook:

The treatment of articular cartilage lesions remains an intractable problem, particularly for large lesions. Although advances in biomaterials and biofabrication have enabled the *in vitro* production of cartilage which is functionally, structurally and compositionally similar to native tissue, challenges remain with *in vivo* translation. In particular, engineered tissues need to integrate into the defect site, which is often inflammed and subjected to high mechanical loading. Furthermore, the high costs and complexity of cell-based therapies have hindered the wide-spread adoption of effective therapies into the clinic. Cost effective solutions in the future may depend on the use of universal donor cells and single step surgical procedures.

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Adv Mater. 2022 Nov;34(45):e2204301

Kombination von Biomaterial und Zellen mit Bioprinting:

Durch die Kombination von Zellen und Biopolymeren mit Bioprinting kann die Struktur von Gelenkknorpel noch präziser nachgebildet werden (Abb. 4). Mein Labor hat kürzlich eine neue, licht-basierte Biofabrikationstechnik eingeführt, die FLight-Biofabrikation (Filamented Light Biofabrication), die einen schnellen Druck im Mikrometer-Bereich ermöglicht [4].

Bei der FLight-Biofabrikation kommt es durch das Specklemuster des Lichts zu einer selbstinduzierten Ausrichtung der Lichtwellen. Das so projizierte Licht vernetzt eine Reihe feiner Hydrogel-Filamente über die gesamte Länge des Konstrukts. An die entstehenden Hydrogel-Filamente kann anschliessend Kollagen derart angelagert werden, dass die Kollagenverteilung der Verteilung in nativem Knorpelgewebe ähnelt (Abb. 5).

Figure 5: Immunohistochemical staining of collagen shows how the FLight scaffold can direction the deposition extracellular matrix components.

Abbildung 5: *Die immunhistochemische Färbung von Kollagen zeigt, wie mittels FLight-Biofabrikation eine gerichtete Anordnung der extrazellulären Matrixkomponenten erreicht werden kann.*

Ausblick:

Die Behandlung von verletztem Gelenkknorpel bleibt ein schwer lösbares Problem, vor allem bei grossen Läsionen. Obwohl Fortschritte in den Bereichen Biomaterial und Biofabrikation die Herstellung von Knorpelgewebe ermöglichen, welches funktionell, strukturell und in seiner Zusammensetzung nativem Gewebe gleicht, bleibt es eine Herausforderung, diese Ergebnisse von einer künstlichen Umgebung in den lebendigen Organismus zu überführen. Dabei kommt erschwerend hinzu, dass das gezüchtete Gewebe in eine verletzte Stelle eingefügt werden muss, die oft Entzündungsprozessen und einer hohen mechanischen Belastung unterliegt. Auch die hohen Kosten und die Komplexität zell-basierter Therapien haben eine weit verbreitete klinische Umsetzung effektiver Therapieansätze bislang verhindert. Für die zukünftige Anwendung ist es dementsprechend ausschlaggebend, kosteneffektivere Lösungen zu finden, wie beispielsweise die Nutzung universeller Spenderzellen und einen Ansatz, der nur einen operativen Eingriff benötigt.

overview cabmm research platform

1. **Musculoskeletal Research Unit (MSRU)**
Group leaders: Dr. med. vet. Katja Nuss, Dr. med. vet. Karina Klein, PhD, Dr. Salim Darwiche (PhD)
Platform users: Dr. Salim E. Darwiche (PhD), med. vet. Mara Heinold, Aymone Lenisa, Prof. em. Dr. med. vet. Brigitte von Rechenberg, Dipl. ECVS

The MSRU is specialized in the design, implementation, and evaluation of *in vivo* preclinical investigations, particularly in large animal models. The areas of investigation are centered on the musculoskeletal system, but also extend to cardiovascular and wound healing applications. It has also established expertise in histology processing and analysis including non-decalcified plastic embedded ground and thin sections, cryosections, paraffin embedded sections as well as immunohistochemistry.

A special feature of the MSRU is its successful implementation of Good Laboratory Practice (GLP). The MSRU facility has received and maintained its GLP accreditation by Swissmedic since 2014. Thus, together with Good Manufacturing Practice (GMP) established at Wyss Zurich and human clinical trials performed under Good Clinical Practice (GCP) at the University Hospital and the close collaboration of the involved institutions, the University of Zurich is able to offer the complete quality chain for research and development of new therapeutics.

Articular Cartilage Tissue Engineering

Restoration of hyaline cartilage after a traumatic or developmental lesion is still one of the most challenging problems in orthopedic surgery. Once a lesion in the hyaline cartilage is present, cartilage matrix degradation is inevitable and in the long term will always result in osteoarthritis of the affected joint. Various surgical interventions have been attempted to repair articular cartilage (e.g., microfracture, osteochondral transplants, mosaicplasty, and autologous chondrocyte implantation). Although acceptable clinical outcomes between 87-90 % are reported initially for some of these technologies, decline of success is also reported after the first 5 years. Limitations are indeed still considerable for all these technologies. Tissue engineered cell-based technologies may provide a solution, but despite recent advances, such technologies are still not widely available clinically. Fundamental aspects to consider for a successful tissue engineering approach are (1) the choice of cell source, (2) the choice of biochemical stimulation, (3) the choice of biomechanical stimulation, if any, and (4) the choice of culture duration, to name a few.

Previous works by our group, in collaboration with LAM Biotechnologies SA, Epalinges, Switzerland, have shown that human chondroprogenitor cells (hCPs, provided by Prof. Lee Ann Laurent-Applegate and LAM Biotechnologies) exhibit the ability to deposit cartilaginous matrix both after a pre-expansion in 2D, or even after thawing them from liquid nitrogen storage and placing them directly in 3D in chondrogenic medium. The cells were also potent up to passages that are higher (up to P7) than those normally used with adult chondrocytes (up to P3-4), without losing potency with expansion rounds. Furthermore, hCPs seeded on non-woven polyester scaffolds (designed, manufactured, and provided by Xiros Ltd., UK) showed good attachment and viability, as well as cartilage-like matrix deposition when cultured in non-loaded and loaded mechanical conditions in a bespoke bioreactor (designed and provided by Xiros Ltd., UK). Although the results were very promising thus far, the mechanical and biochemical properties of the final constructs could still use some improvement and maturation.

During the reporting period, the project was further advanced by improving and testing three fundamental factors: (1) optimizing hCPs seeding on the non-woven scaffolds, (2) testing media formulations using lower concentrations of dexamethasone, and (3) investigating the effect of 3 or 6 weeks of compressive loading on the constructs. To that end, a variety of seeding chambers and dynamic seeding techniques were tested, including sealed chambers versus semi-permeable chambers and varying the rotation axis during seeding. Cell viability and seeding efficiency were tested in all conditions. Of the many methodologies tested, a table-top, temperature-controlled rotator was found to be very reliable in ensuring homogenous cell seeding, excellent cell viability despite the use of sealed chambers, and reliability in the process.

Next, three chondrogenic media formulations were tested, primarily varying the concentration of dexamethasone (0 nM, 10 nM, and 100 nM), a component often used in chondrogenic media formulations for mesenchymal stem cell differentiation. Previous works from our group using 100 nM dexamethasone with hCP-seeded scaffolds showed heterogenous matrix deposition, especially in the center of the scaffolds, as well as compromised glycosaminoglycan deposition on the long run. Testing the three concentrations, we could confirm that after a 4-week construct culture period, high concentrations of dexamethasone were actually detrimental to chondrogenic matrix deposition by hCPs. Instead, low dexamethasone (10 nM) or no dexamethasone showed superior results, prompting the next step of the experiment.

The constructs were then kept in culture for a longer period (6-12 weeks), and the effect of daily biomechanical compressive stimulation was tested (Fig. 1 and 2). This phase of the project aimed to discern advantages of adding low versus no dexamethasone in hCP tissue engineering cultures, when combined with mechanical stimulation and longer culture periods. An experiment was therefore conducted comparing low versus no dexamethasone in culture media formulations and constructs were kept in culture for 6, 9 or 12 weeks. Biomechanical stimulation was applied 5 times per week on half of the constructs which were kept in culture past the 6-week timepoint, specifically 3 weeks of biomechanical stimulation for the 9-week group and 6 weeks of biomechanical stimulation for the 12-week group.

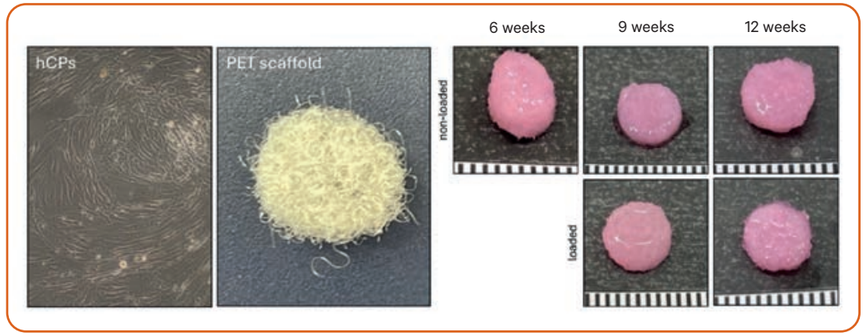


Figure 1: Human chondroprogenitors (hCPs) shown in 2D culture (left panel) were seeded onto non-woven PET scaffold (middle panel) and cultured in chondrogenic conditions for 6, 9 or 12 weeks, with or without biomechanical loading. The constructs shown in the right-side panels are from the low dexamethasone concentration (10 nM) group.

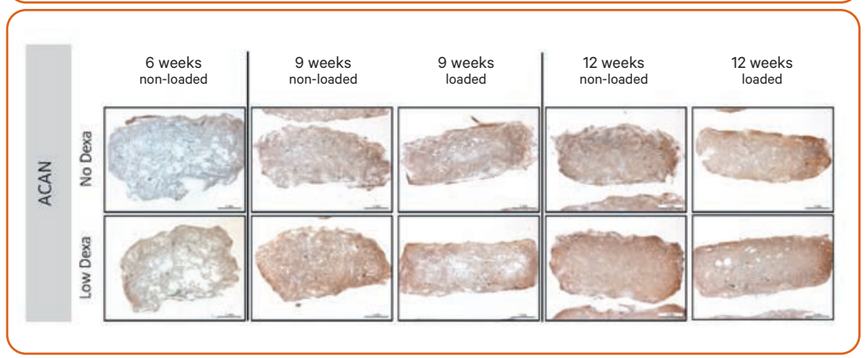


Figure 2: Aggrecan immunohistochemical staining (shown in brown) in histological samples from constructs cultured for 6, 9 or 12 weeks, with (10 nM) or without dexamethasone, with or without biomechanical loading after 6 weeks. The aggrecan increasingly homogenous deposition in this figure matched the glycosaminoglycan deposition.

Overall, constructs showed good, homogenous glycosaminoglycan (Fig. 2) and collagen I deposition after 6 weeks, which would make them good candidates to start biomechanical stimulation. With the addition of biomechanical stimulation, constructs continued to mature and exhibited overall superior mechanical properties. However, and surprisingly, the non-loaded constructs appeared to have matured more than the loaded constructs. Furthermore, biochemical assays quantifying the glycosaminoglycan deposition in the constructs and release in the media (Fig. 3), as well as total protein content and DNA content, indicated a potential protective effect of low dexamethasone supplementation at the 9-week timepoint.

The findings from this experiment highlighted important outcomes: (1) that the choice of media supplementation, even when described as chondrogenic with other cell sources, may not be universally appropriate and needs to be customized to the cell source, (2) and that more stimulation (biomechanical and biochemical) and more time did not necessarily correlate with a linear maturation of tissue engineered constructs. Instead, it is likely that a chondrogenic medium with low dexamethasone is crucial in accelerating early matrix deposition and complementing early mechanotransducive pathways, but at later timepoints, a different set of stimuli may be needed to either further mature the constructs or maintain the constructs in culture until implantation is needed.

The next steps of the project will focus on identifying the optimal windows of biochemical and biomechanical stimulation as well as investigating the conditions required for construct maintenance in culture, in order to assess the potential shelf life of this tissue engineering technology. Finally, *in vivo* implantation will be important in order to test not only the capability of this tissue engineering technology to regenerate cartilage tissue, but also to assess which would be the ideal tissue engineering maturity required *in vitro*, prior to implantation, as the constructs are likely to continue maturing after *in vivo* implantation.

We thank Prof. Lee Ann Laurent-Applegate and the team at LAM Biotechnologies SA (Epalinges, Switzerland) for the fruitful and open collaboration to drive forward this scalable allogenic cell-based cartilage treatment technology. Our thanks also go to Prof. Bahaa Seedhom and the team at Xiros, Ltd. (Leeds, UK) for the funding, guidance, contribution in developing the technology and support throughout the project, and for providing the custom-designed surgical tools, scaffolds, seeding chambers, and bioreactors. We also thank Prof. Marcy Zenobi-Wong and Dr. Philipp Fisch (PhD) from ETH Zurich, for their help in construct mechanical testing.

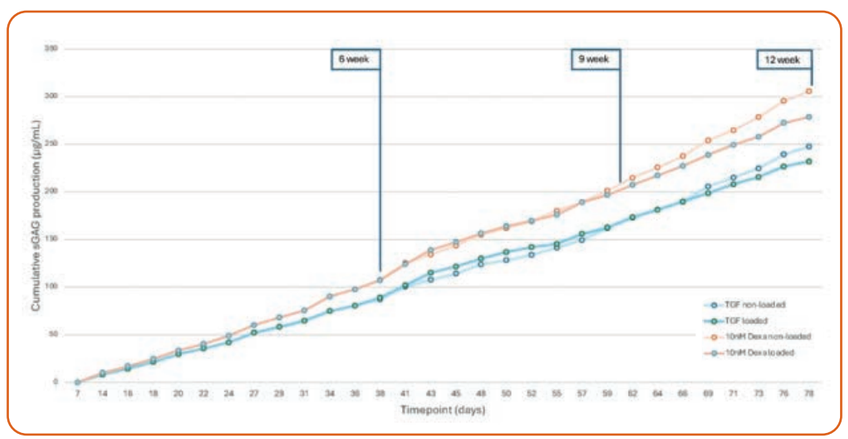


Figure 3: Cumulative soluble glycosaminoglycan (GAG) concentration was quantified at regular intervals throughout the construct culture period. Constructs cultured in low dexamethasone concentration (10nM) appeared to produce more soluble GAG. Biomechanical loading, started after the 6-week timepoint, did not appear to notably change the soluble GAG content, except for the last few days of culture, during which soluble GAGs seem to be more prevalent in non-loaded constructs compared to their counterparts.

2. Ocular Cell Biology Group

Group leader: Prof. Dr. med. Farhad Hafezi, PhD
Platform user: Dr. Dr. Emilio Torres-Netto (MD, PhD)

The Ocular Cell Biology group, headed by Prof. Farhad Hafezi, focuses on developing innovative therapies for ocular diseases, particularly those affecting the cornea. Our research is mainly related to keratoconus, a potentially sight-threatening corneal disease that involves a progressive weakening of the cornea that results in the development of a progressive corneal protrusion, which leads to the development of irregular astigmatism and corneal thinning. Its treatment is corneal cross-linking (CXL): the saturation of the cornea with vitamin B_2 (riboflavin) which is then photoactivated *in situ* with ultraviolet (UV) light to generate reactive oxygen species (ROS). These ROS go on to cross-link together molecules in the main structural layer of the cornea, the stroma, and this strengthens the cornea and counteracts the weakening effect. Members of our team were involved in the initial clinical development of CXL, which occurred nearly a quarter of a century ago. Since then, it has become the global gold standard for treating corneal ectasias.

Our group's key research areas include:

- Diagnosing and treating keratoconus by studying corneal biomechanics,
- Advancing CXL technologies for keratoconus,
- Applying CXL in treating infectious keratitis, and
- Enhancing excimer and femtosecond laser technologies.

During the reporting period, the group's multiple projects led to various peer-reviewed publications, some of which are briefly described:

Effect of repeated application of riboflavin during CXL
(publication 33, page 115)

During CXL, the cornea receives riboflavin eye drops in order to saturate the cornea with riboflavin. This study assessed the effect of repeated riboflavin application during CXL on the biomechanical strength of *ex vivo* porcine corneas.

A total of 66 corneas were divided into three groups: two underwent standard epi-off CXL with UVA irradiation at 3 mW/cm² for 30 minutes, and the third served as a control. One CXL-treated group received repeated riboflavin applications, while the other had repeated iso-osmolar PBS applications. After irradiation was completed, corneal strips were tested for elastic modulus. The results showed no significant difference in biomechanical properties between the two CXL groups, indicating that repeated riboflavin application during UVA irradiation does not enhance corneal stiffening in standard epi-off CXL.

This suggests that the application of riboflavin until saturation has occurred may be sufficient in CXL procedures – rather than requiring repeated administration during irradiation – which may impact how the procedure is currently performed.

Corneal cross-linking with riboflavin using sunlight
(publication 71, page 120)

We investigated the use of sunlight to induce biomechanical stiffening in riboflavin-soaked corneas, similar to conventional CXL.

Using 52 porcine eyes, we estimated the corneal riboflavin concentrations and determined the appropriate sunlight exposure duration to appropriately cross-link them. De-epithelialized corneas were divided into three groups; two were soaked in riboflavin solutions (0.1 % and 0.5 %) and then exposed to sunlight (Fig. 1). The elastic modulus measured corneal stiffness. Sunlight exposure ranged from 16 to 45 minutes, with both treated groups exhibiting significantly increased corneal stiffness compared to the control, but no significant difference between them. Group 1 (0.1 % riboflavin) showed a trend for a greater stiffening effect.

Figure 1: Experimental set-up of outdoor sunlight exposure for porcine corneas.

The study suggests the potential of eventually using oral riboflavin and sunlight for less invasive CXL techniques, offering new possibilities in CXL treatments. A second study *in vivo* was planned to further evaluate this hypothesis.

Mechanical impact of intracorneal ring segment implantation
(publication 19, page 114)

Intracorneal ring segments (ICRSs) are used in ophthalmic surgery to improve the corneal curvature in eyes with keratoconus. Implanted ICRSs are able to selectively flatten the cornea to correct optical errors like myopia, astigmatism, and especially corneal ectatic diseases like keratoconus. Commercially available ICRS are made of polymethylmethacrylate.

We quantified the mechanical impact of varying sizes of ICRS implantations using 30 enucleated porcine eyes. The eyes were categorized into groups for ICRS implantation with varying thicknesses and angles, tunnel creation only, or left as untreated controls. We evaluated the mechanical impact by incrementally increasing intraocular pressure (IOP) and recording optical coherence tomography (OCT) scans, analyzing deformations to derive the effective E-modulus, a measure of global mechanical impact.

Results showed that ICRS implantation increased the effective E-modulus, with the most significant impact observed in smaller optical zones and longer arc lengths of ICRS. The study highlights the importance of considering both geometrical and mechanical aspects in ICRS implantation for treating corneal ectatic diseases, with implications for the optimization of these procedures.

The impact of eye rubbing on corneal biomechanics
(publication 26, page 114)

Eye rubbing is a known risk factor for the progression of keratoconus. Corneas with keratoconus have impaired biomechanics. As the disease's progression is linked with chronic eye rubbing, patients have been correctly told for many years not to rub their eyes. We wished to investigate whether eye rubbing alone could play a central role not in the progression of keratoconus, but rather in keratoconus etiology, as a unique component.

The biomechanical effects of eye rubbing on porcine eyes were investigated to understand its impact on keratoconus. Using an *ex vivo* model, 33 porcine eyes were subjected to 10,500 rub cycles using a custom-built machine (Fig. 2) that mimics human knuckle rubbing, while 37 eyes served as no-rub controls. The rubbing frequency simulated a person with keratoconus rubbing their eyes six times daily for a year. The elastic modulus of 5 mm corneal strips was measured to assess corneal biomechanics.

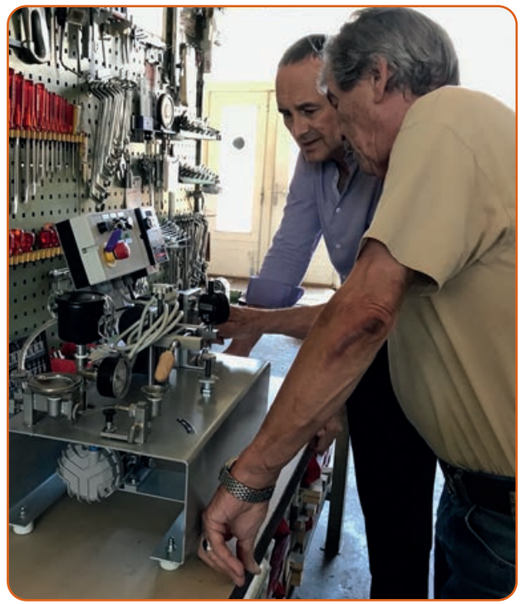


Figure 2: The custom eye-rubbing machine.

Results indicated no significant difference in corneal stiffness between the rubbed and control groups ($p = 0.984$), suggesting that a higher threshold of eye rubbing is required to alter corneal biomechanics. This implies that occasional eye rubbing may not markedly affect corneal biomechanics in normal eyes, and the initial development of keratoconus might be influenced by genetic predisposition or other environmental considerations.

Demarcation line depth in epithelium-off corneal CXL performed at the slit lamp
(publication 30, page 115)

CXL was traditionally performed in a lying position, as it can take over 1 hour to saturate the cornea with riboflavin drops, and up to 30 minutes of UV irradiation. As the CXL procedure has become accelerated since its development, our group introduced the concept of performing the procedure in an upright position at the slit lamp, which might greatly increase the global accessibility to treatment and reduce overall costs related to the procedure.

This study evaluated the depth of the demarcation line following accelerated epithelium-off CXL (A-CXL) performed with patients in an upright position using a CXL device at the slit lamp (Fig. 3). Twenty-three eyes from 20 patients underwent the A-CXL treatment at 9 mW/cm² for 10 minutes. The depth of the demarcation line was measured one month post-procedure using anterior segment optical coherence tomography (AS-OCT). The average postoperative demarcation line depth was 189.4 µm (SD: 58.67 µm), with all surgeries completed without complications.

The findings, showing similar demarcation line depths between upright and traditional supine positions, suggest that CXL effectiveness is independent of patient orientation, offering potential flexibility and convenience in clinical CXL procedures.

Figure 3: CXL being performed at the slit lamp.

Adverse events in corneal cross-linking in an office-based setting
(publication 64, page 119)

CXL treatment is typically performed in an operating room. We analyzed the incidence of infectious keratitis and other complications in 501 epithelium-off CXL (epi-off CXL) procedures performed in an office setting without laminar flow ventilation from November 2015 to October 2021.

Our findings revealed a low complication rate with no infectious keratitis cases. Sterile infiltrates occurred in 2 % of patients, and delayed epithelialization in 2.79 %, all responding well to treatment.

The study concludes that office-based epi-off CXL is as safe as those in operating rooms, supporting its viability in less controlled environments.

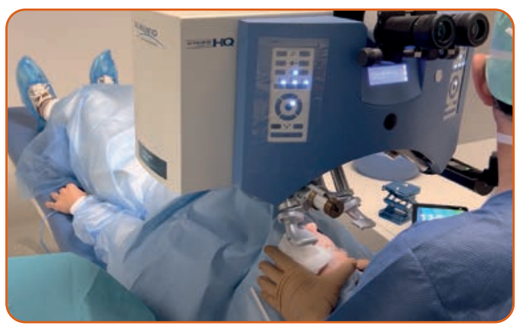


Figure 4: A person undergoing a laser refractive surgery procedure.

Effect of fluence levels on prophylactic corneal cross-linking
(publication 48, page 117)

Prophylactic CXL is a concept in which a CXL is used to improve corneal biomechanics before or during a refractive surgery procedure (Fig. 4). Laser procedures involve the removal of tissue from the structural layer, the stroma, and these weaken the cornea. CXL strengthens this tissue and may enable laser vision correction in eyes that would otherwise have too weak corneas to undergo this procedure.

This study evaluated the effects of different fluence levels in prophylactic CXL for ectasia combined with a femtosecond laser *in situ* keratomileusis (FS-LASIK-Xtra) or transepithelial photorefractive keratectomy (TransPRK-Xtra). It compared low- and high-fluence (LF/HF: 1.8/2.4 J/cm²) CXL protocols in terms of corneal biomechanics, demarcation line (DL) depth, and stromal haze. The study involved 86 eyes from 86 patients, divided into four groups based on the combination of surgical procedure and fluence level. Outcomes measured over six months included Stress-Strain Index (SSI), actual DL depth (ADL), and stromal haze, assessed through OCT and machine learning. Results showed a 15 % increase in SSI across all groups, with similar biomechanical worsening and ADL among groups. However, stromal haze was higher in the TransPRK-Xtra-HF group compared to LF.

The study concluded that both FS-LASIK-Xtra and TransPRK-Xtra yield similar improvements in ADL and SSI, suggesting lower fluence CXL may be preferable, particularly in TransPRK, due to comparable ADL and potentially reduced stromal haze. Further research is needed to determine the clinical relevance of these findings.

Repeatability of a Scheimpflug tonometer to measure biomechanics parameters
(publication 28, page 115)

Corneal biomechanics play a central role in the assessment before and following refractive surgeries. A study using a Scheimpflug tonometer (Corvis ST, Fig. 5) assessed the repeatability of corneal biomechanical parameters in 315 eyes, including 135 myopic and post-refractive surgery (transPRK, SMILE, FS-LASIK) eyes.

Evaluating 40 parameters through three scans, the study found coefficients of variation (CoV) for IOP and biomechanical-corrected IOP (bIOP) ranging from 7.29 % to 9.47 % and 6.11 % to 7.75 %, respectively, with pachymetry CoV under 0.8 %. The intraclass correlation coefficient for the Corvis Biomechanical Index-Laser Vision Correction (LVC) varied post-surgery, and the SSI showed higher CoV, especially after refractive surgeries.

Figure 5: A patient having a biomechanical assessment of the cornea with an Oculus Corvis ST device.

The study concluded that while IOP, bIOP, and pachymetry are highly repeatable, SSI varies more post-LVC, indicating the need for careful assessment in diagnosing iatrogenic ectasia and evaluating biomechanical changes in postoperative refractive corneas.

Progressive keratoconus in patients older than 48 years
(publication 52, page 117)

Progressive forms of keratoconus usually affect adolescents and young adults. This study explored the occurrence of progressive keratoconus in older patients (aged 48 to 54 years) and the efficacy of CXL treatment in these cases, challenging the notion that keratoconus progression halts after the age of 40 years.

The case series included five eyes from four patients, all showing rapid keratoconus progression, monitored using Kmax (keratometry), with increases of up to 14.6 diopters observed. Despite the patients' age, all underwent successful CXL treatment, with one case requiring two procedures for stabilization.

The study concludes that keratoconus progression can occur even after 40, emphasizing the importance of regular corneal tomography examinations in older keratoconus patients. This highlights the need for continued vigilance in keratoconus management across all age groups, especially in older patients.

New keratoconus staging system based on OCT
(publication 74, page 120)

This paper heralded the introduction of a novel keratoconus staging system using spectral-domain ocular coherence tomography (SD-OCT). In this retrospective case-control study, 236 normal eyes and 331 keratoconus eyes were assessed using Scheimpflug tomography, air-puff tonometry, and SD-OCT. The study evaluated SD-OCT-derived corneal epithelium and stroma parameters, focusing on their ability to differentiate between normal and keratoconus eyes using receiver operating characteristic (ROC) curves. Two SD-OCT parameters, stroma overall minimum thickness (ST) and epithelium overall standard deviation (EP), had the highest AUC (area under the curve, i.e., accuracy) ROC values.

These parameters formed the basis of the novel SD-OCT staging system, named STEP, which delineated five stages of keratoconus. The new system, which incorporates epithelium and sublayer stroma information, showed strong agreement with existing staging systems and represents a significant advancement in keratoconus diagnosis and management. The STEP system could improve treatment strategies and follow-up for keratoconus patients in clinical practice.

PACK-CXL for bacterial keratitis using riboflavin/UVA or rose bengal/green
(publication 63, page 119)

We evaluated two different photoactivated chromophores for keratitis cross-linking (PACK-CXL) protocols, riboflavin/UVA light and rose bengal/green light, for treating bacterial keratitis caused by *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Using 117 *ex vivo* porcine corneas inoculated with these bacteria, the corneas were treated with either PACK-CXL protocol or left unirradiated as controls. BKRs (bacterial killing ratios) were calculated by quantifying bacterial colonies post-treatment. Results indicated that riboflavin/UVA light PACK-CXL achieved median BKRs of 52.8 % for *S. aureus* and 45.8 % for *P. aeruginosa,* while rose bengal/green light PACK-CXL showed higher BKRs of 76.7 % for *S. aureus* and 81.0 % for *P. aeruginosa.*

The study concludes that both protocols significantly reduce bacterial loads, but the rose bengal/green light PACK-CXL is more effective. This comparative analysis provides insights for developing strain-specific and depth-dependent PACK-CXL approaches, enhancing treatment for bacterial keratitis. The research's translational relevance lies in its potential to guide future clinical applications of high-fluence accelerated PACK-CXL protocols in human patients.

Acceleration of the antibacterial efficacy of high-fluence PACK-CXL
(publication 44, page 116)

The study assessed the effectiveness of accelerated photoactivated chromophore cross-linking (PACK-CXL) protocols in eliminating bacteria, crucial for optimizing PACK-CXL in treating infectious keratitis.

The study tested nine accelerated PACK-CXL protocols using 365 nm ultraviolet-A irradiation at various intensities (9 to 30 mW/cm²) and fluences (5.4 to 15.0 J/cm²) on bacterial solutions with 0.1 % riboflavin (Fig. 6). The bacterial killing ratios (BKRs) were measured against pathogens like *Staphylococcus aureus* and *Pseudomonas aeruginosa,* with comparisons to unirradiated controls. Additionally, a single accelerated protocol's impact on *Achromobacter xylosoxidans, Staphylococcus epidermidis,* and *Stenotrophomonas maltophilia* was examined. Results showed increased BKRs with higher fluences; e.g., *S. aureus* BKR ranged from 45.78 % to 99.90 %, and *P. aeruginosa* from 69.09 % to 91.44 %.

The study confirmed that high-fluence PACK-CXL can be effectively accelerated while maintaining antibacterial efficacy, that PACK-CXL has species-dependent responses, and indicating its potential for tailored clinical applications in infectious keratitis treatment.

PACK-CXL vs. antimicrobial therapy for bacterial, fungal, and mixed infectious keratitis
(publication 5, page 112)

The efficacy of standalone photoactivated chromophore for keratitis cross-linking (PACK-CXL) was compared with standard antimicrobial treatment as a first-line therapy for early to moderate infectious keratitis. Conducted in Egypt, India, Iran, Israel, and China, the phase 3 randomized controlled trial included participants aged ≥18 years with infectious keratitis of presumed bacterial, fungal, or mixed origin. They were randomly assigned to receive either PACK-CXL or standard antimicrobial therapy based on American Academy of Ophthalmology guidelines. Primary outcomes were time to corneal re-epithelialization, absence of anterior chamber inflammation, and clearance of stromal infiltrates. From July 21, 2016, to March 4, 2020, 18 participants received PACK-CXL, and 21 received antimicrobial therapy. Success rates were 88.9 % for PACK-CXL and 90.5 % for antimicrobial therapy, with no significant difference in corneal re-epithelialization time.

PACK-CXL can be an effective alternative to antimicrobial drugs for treating early to moderate infectious keratitis, especially in settings with limited access to antimicrobials or where resistance is a concern.

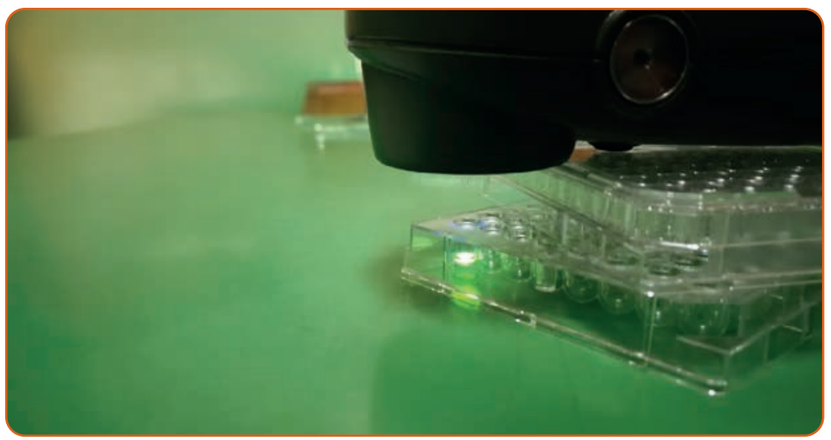


Figure 6: Experimental set-up: cross-linking the bacterial solutions.

Combining spectral-domain OCT and air-puff tonometry analysis to diagnose keratoconus
(publication 18, page 113)

Diagnosing the very early stages of keratoconus is a challenge. This study evaluated the use of spectral-domain optical coherence tomography (SD-OCT) combined with air-puff tonometry and artificial intelligence (AI) in distinguishing normal eyes from those with various stages of keratoconus, including forme fruste (FFKC), early (EKC), and advanced (AKC).

The cohort comprised patients with stable vision after laser vision correction surgery, and patients with a diagnosis of keratoconus. Data from SD-OCT and air-puff tonometry were used to train AI models to differentiate FFKC from normal eyes. The study included 223 normal, 69 FFKC, 72 EKC, and 258 AKC eyes. The best diagnostic performance was observed in AI models like the Pentacam Random Forest Index, Tomographic and Biomechanical Index, and Belin-Ambrósio Enhanced Ectasia Total Deviation Index. The random forest AI model, combining SD-OCT and air-puff tonometry, showed an AUC (area under the curve, i.e., accuracy) of 99 % for FFKC with 75 % sensitivity and 94.74 % specificity.

The study concluded that while AI is already effective in diagnosing advanced and early keratoconus, its capability in detecting FFKC is limited, but this could be improved with the integration of SD-OCT and air-puff tonometry data, enhancing diagnostic and treatment strategies for keratoconus.

Combinations of Scheimpflug tomography, OCT, and air-puff tonometry improve the detection of keratoconus
(publication 55, page 118)

Our group investigated enhancing keratoconus diagnosis, including forme fruste keratoconus (FFKC), by integrating various ocular diagnostic devices with AI. Methods involved Scheimpflug tomography, spectral-domain ocular coherence tomography (SD-OCT), and air-puff tonometry. Relevant diagnostic parameters were identified and used to train and validate AI models, including random forest (RF) and neural networks, to distinguish FFKC from normal eyes. The effectiveness of these models was evaluated using ROC curves, AUC (area under the curve, i.e., accuracy), sensitivity, and specificity. Air-puff tonometry alone showed the highest AUC for FFKC detection among single-device models, while the combination of SD-OCT and air-puff tonometry using RF achieved the highest AUC in two-device models. A three-device combination also yielded promising results.

The study concludes that integrating AI with diagnostic devices, particularly air-puff tonometry and either Scheimpflug tomography or SD-OCT, enhances FFKC diagnosis, though the benefit of using all three devices together is limited.

Optimized AI for enhanced ectasia detection (59)
(publication 59, page 118)

AI is increasingly gaining importance in ophthalmology. The capacity for detection of very early forms of corneal diseases such as ectasias like keratoconus might be improved using AI.

AI algorithmic enhancement of ectasia detection that integrates Scheimpflug-based corneal tomography and biomechanical data was investigated. This research aimed to improve early-stage corneal ectasia diagnosis and management. The study involved 3886 unoperated eyes from 3412 patients, including normal eyes, eyes with bilateral keratoconus, very asymmetric ectasia with normal topography (VAE-NT), and unoperated ectatic eyes from VAE (VAE-E). The study assessed the current Tomographic-Biomechanical Index (TBIv1) and developed a novel AI algorithm (TBIv2) using an RF algorithm with 18 features across 156 trees to enhance diagnostic accuracy. TBIv1 showed high sensitivity and specificity with an AUC (area under the curve, i.e., accuracy) of 0.999 for clinical ectasia but only 0.899 for VAE-NT. TBIv2 demonstrated an improved AUC of 0.945 for VAE-NT while maintaining high accuracy for clinical ectasia.

The study concludes that AI optimization in integrating Scheimpflug-based tomography and biomechanical assessments significantly improves ectasia detection accuracy, especially in identifying ectasia susceptibility in VAE-NT cases. It suggests the potential for unilateral ectasia in some VAE cases and highlights the future scope of incorporating additional data like epithelial thickness for further diagnostic refinement.

3. Skin Engineering Group
Group leader: Prof. Dr. med. Maurizio Calcagni
Platform user: Dr. Laura Frese (PhD)

Keratinocytes for the treatment of severe burns and other difficult healing wounds

The skin is the largest organ in the body and protects it from the environment. Healthy skin maintains the fluid balance, regulates body temperature, and is a sensory organ. Every burn represents a serious damage to the organism, skin integrity, and associated repair mechanisms. The absence of the skin as a protective layer promotes infiltration of pathogens and fluid loss and can lead to death. Various methods of skin transplantation are used in therapy. With burns of more than about 30 % of the body surface, a transplant has to be manufactured from the patient's keratinocytes.

So far, the manufacturing of these transplants rely on the use of animal components, e.g., activated murine cells, animal-derived enzymes, and media components like fetal bovine serum. The knowledge about the risks of disease transmission due to animal components has increased, causing the requirements of the regulatory authorities to become stricter. Replacing as many components of animal origin as possible with xenofree ones is preferable for clinical applications, thus guaranteeing safer and more standardized therapies. Moreover, the use of animal components poses not only a regulatory but also an ethical problem.

Collagen residues

In the previous years, we have succeeded in optimizing the production of keratinocyte sheets in such a way that no risky animal components are used. However, the most effective production in terms of time and quality was achieved when using bovine collagen as substrate for keratinocyte culture. In the treatment of burn patients, the factor time plays a very crucial role since failure to treat patients fast enough may result in sepsis, multiple organ failure, and, in the end, the death of the patient. Thus, due to its clear advantages in reducing the time of keratinocyte expansion and sheet formation as well as the size of donor biopsy area, collagen of bovine origin was used as substrate in this study. The potential risk associated with its use can be mitigated by procuring certified clinical-grade products being manufactured following the safety guidelines and current knowledge regarding the risk associated with Transmissible Spongiform Encephalopathy (TSE) and Bovine Spongiform Encephalopathy (BSE). Its risk profile is also be much lower compared to feeder layer systems (murine cells).

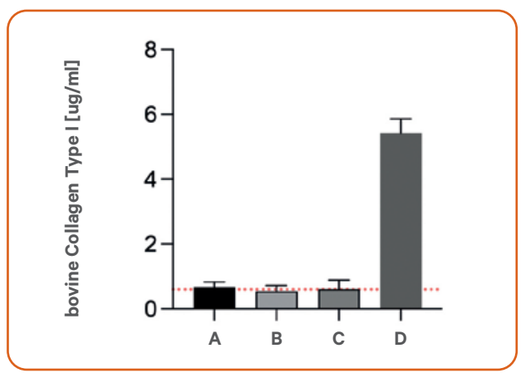


Figure 1: Analysis for bovine collagen residues in the keratinocyte transplants (keratinocyte sheet with collagen (B), keratinocyte sheet w/o collagen (C)). Freshly isoltaed cells act as negative control (A), the collagen coating solution as positive control (D).

For patient safety, we examined our keratinocyte sheets for bovine collagen residues. Isolated cells served as negative control, as they had never been in contact with bovine collagen, and collagen coating solution as positive control. Bovine collagen could not be detected in isolated cells or any of the keratinocyte sheets (Fig.1), demonstrating that bovine collagen is not recovered from the cell culture plate during the harvesting procedure and confirming that the final product does not contain any bovine collagen. The analyzed amount of about 0.5 - 0.8 µg/ml represents the background noise of the test (Fig. 1, red line).

Tumorigenicity study: Melanoma xenograft mouse model

In addition to preclinical studies aiming to optimize the production of keratinocyte sheets, preclinical evidence in the area of safety is being conducted. A tumorigenicity study is currently underway.

In vitro cell culture studies performed in the laboratory are only suitable to a very limited extent for determining the risk of tumor formation after keratinocyte implantation, as they cannot mimick the complex interactions of different cell and tissue types present in a living organism. That is why animal models, especially in rodents, are used to analyze side effects such as tumor formation after implantation of cell-based products.

Accordingly, we are currently performing an *in vivo* tumorigenicity study in which expanded human keratinocytes are injected subcutaneously into immunodeficient rodents and analyzed for induction of tumor growth over a 6-month period. Human keratinocytes from three different donors were isolated and expanded in the laboratory according to the established protocols (Frese *et al.,* 2022). As reference item, human patient-derived melanoma cell lines provided by the Melanoma Biobank, University Hospital Zurich were used, which were established from surplus material from primary cutaneous and metastatic melanoma removed by surgery. Written informed consent was obtained from patients, and the study was approved by the local IRB (EK647 and EK800; BASEC-Nr.2017-00494; BASEC-Nr.2014-0425). Melanoma cells were isolated from the tissue biopsies and grown as previously described (Raaijmakers *et al.,* 2015).

All animal experiments were performed according to the protocols approved by the Swiss Federal Food Safety and Veterinary Office (license Nr. ZH060/2023). Human keratinocytes (test item) as well as melanoma cells (reference item, positive control) were subcutaneously injected into female Crl:NIH-Foxn1rnu rats. After injection, the animals will survive for 26 weeks. At the end of the observation period (or when the termination criteria are met) the animals will be sacrificed. If tumor growth is observed, the sacrifice will be done earlier.

With this *in vivo* study, the safety of the human keratinocytes can be demonstrated. The study is being conducted in collaboration with the Musculoskeletal Research Unit (MSRU) of the Vetsuisse Faculty of the University of Zurich, following successful approval by the ethics committee.

Good Manufacturing Practice (GMP)

Beside the active cell culture experiments, we continue to work on translating the project into a clinical trial phase 1. This requires the implementation of our production protocol into Good Manufacturing Practice (GMP) standards.

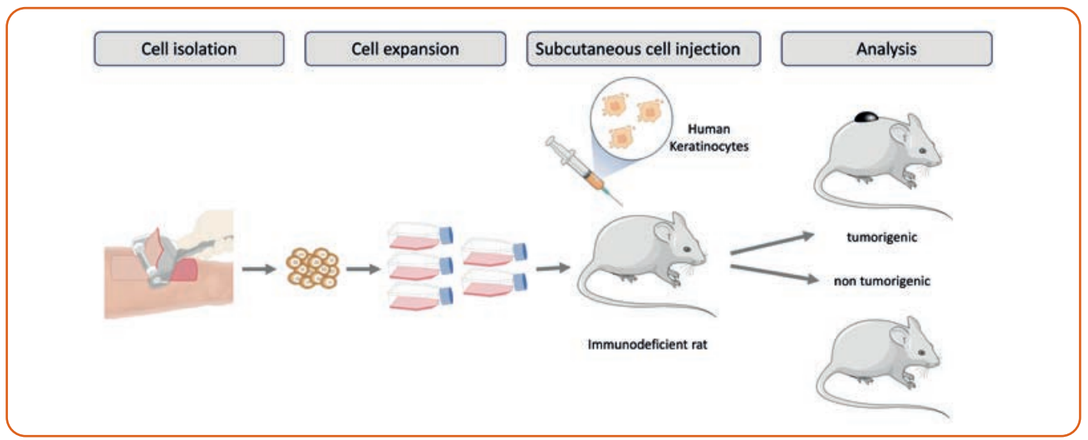


Figure 2: Schematic overview of the *in vivo* tumorigenicity safety study, to show that the cells to be transplanted have no transformation potential and thus no tumorigenicity.

In addition to our main research project, our group is also working on other technologies and is involved in other research projects to better understand and improve skin wound healing, one of which is described in more detail:

Safety of UV-based disinfection on human skin

This project is a collaboration between the Swiss Medtech startup Aseptuva AG and two research partners: the Center for Applied Biotechnology and Molecular Medicine (CABMM), University of Zurich, and the ZHAW School of Life Sciences and Facility Management, Wädenswil (Centre of Molecular Biology and Microbiology).

Aseptuva AG is developing a medical device to combat hospital acquired infections (HAI) through guided delivery of Far-UVC radiation at infection-prone regions around catheters and tubes, which are inserted into patients. Conventional UV disinfection lamps use a wavelength of 254 nm, which is known to be carcinogenic due to DNA damage on skin cells. Aseptuva has now developed a technology based on the use of a narrow window of Far-UVC wavelengths (~ 220 nm) that are strongly absorbed by the stratum corneum and the larger cytoplasm of human skin cells, thus shielding the cell nuclei from potential DNA damage.

In a first project, the three partners have collaborated on a proof-of-concept study, to test the safety and efficacy of 220 nm UVC using abdominal human skin biopsies from adult patients (n = 5 donors) and bacterial colonies of *Staphylococcus aureus, Escherichia coli, Bacillus subtilis,* etc., respectively.

For safety determination, quantitative assessment of DNA damage was done by measuring the formation of cyclobutane pyrimidine dimers (CPD) via enzyme-linked immunosorbent assay (ELISA). The ELISA protocol revealed that illumination of the skin tissue samples with 220 nm UVC radiation at a limiting energy exposure value of 25 mJ/cm² did not result in significant CPD formation (< 0.1 ng/ml), whereas a positive control sample illuminated by the conventional 254 nm UVC lamps resulted in severe DNA damage, as evident in the CPD levels > 30 ng/ml.

For efficacy, germicidal efficacy studies were performed using similar exposure levels. It was shown that 25 mJ/cm² can result in over 3 to 4 log reduction in commonly occurring bacteria such as *E. coli, B. subtilis* and *S. aureus.*

Through these independent safety and efficacy studies, Technology Readiness Level (TRL) 4 was attained for 220 nm Far-UVC wavelength in 2022.

A follow-up project was started in 2023, with the goal to achieve TRL 5. In this study, a functional prototype of an *in situ* disinfection adaptor for catheters inserted into the human body was used that was developed by Aseptuva. Far-UVC dosages were applied to an infection-mimicking *in vitro* full thickness 3D skin model (Fig. 3). Subsequently, the samples were evaluated for DNA damage and germicidal effect. Importantly, efficacy was quantified against current antiseptics such as chlorhexidine, to demonstrate the potential of Aseptuva's adaptors to effectively combat HAI developed by nearly 20 % of the patients in Intensive Care Units.

To determine germicidal efficacy, an original bacteria population was placed on the *in vitro* skin model. After Far-UVC ellumination at different dosages, the bacteria were once washed away using phosphate buffered saline solution or cell culture medium. Subsequently, the number of surviving microorganisms was determined by classical colony counting at regular intervals of a few hours for up to 24 hours. For safety, DNA damage was analyzed by ELISA using an anti-CPD antibody.

The analysis showed that Far-UVC dosages beyond the present threshold of 25 mJ/cm² were safe up to a total dosage of 100 mJ/cm². This new finding ensures a high safety margin for the usage of the Far-UVC adaptor. For efficacy measurements, *S. aureus* colonies have been successfully deposited on top of the skin layer, and two wash-out protocols were tested. The efficacy data obtained for up to 45 mJ/cm² showed a reduction of the bacterial population by 1-2 log.

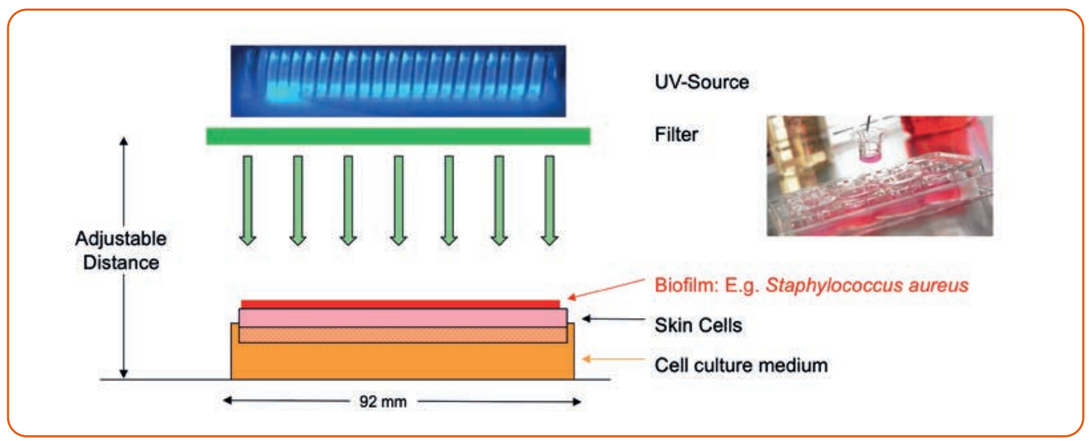


Figure 3: Scheme of the infected 3D skin model. The *in vitro* cell culture is coated with *S. aureus* before Far-UVC ellumination.

After having proven safety and efficacy using the cultured *in vitro* skin model in combination with bacterial cultures, we have now progressed into a stable *in situ* system using native porcine skin. In this pig skin model, we are currently performing safety and efficacy studies, which will be used as a translational step towards future *in vivo* animal studies.

cabmm start-up grant

The CABMM Start-up Grant is a peer-reviewed funding program designed to support collaborative research projects between CABMM members and was made possible through the generous financial support of the Mäxi foundation.

Over a period of one decade, the major support of the Mäxi foundation enabled the CABMM to finance several activities and to set up the CABMM Start-up Grant as its own funding program. The CABMM Start-up Grant aims to support young academics and to strengthen the CABMM network by promoting new collaborations between its members. Originally, it offered funding only for novel projects in the musculoskeletal field, later also for projects in the cardiovascular field. From the beginning, emphasis has been placed on proof of principle, high-risk studies, which would most likely not be supported by other more competitive funding agencies, expecting that the findings generated in these initial studies should be sufficient to enable further applications to be submitted to larger funding agencies.

The funds donated by the Mäxi foundation have been mainly spent now, and we are currently actively seeking follow-up funding for our successful program. So far, more than CHF 1.7 Mio was allocated to our funding program. In total, 52 projects were approved, resulting in 47 associated publications, thereof almost 15 % in this reporting period. The articles have been published, among others, in high-ranking journals such as Nature Communications, Molecular Cell, or the Nature Partner Journal Regenerative Medicine. Some projects even resulted in two or even more publications, illustrating the importance of our funding program as well as the scientific excellence of the supported projects. Additionally, the results obtained in those preliminary studies have allowed in approximately 70 % of the cases for the support of continuative studies by larger funding agencies, proving our strategy successful.

Short summaries of selected, successfully completed projects can be found on the following pages. If the project has been published in a scientific journal, the corresponding citation is indicated.

1. Development of an antimicrobial hydrogel for the prevention and treatment of multi-drug resistant prosthetic joint infections

Principal investigator: Dr. Philippe Abdel-Sayed
(Prof. Lee Ann Laurent-Applegate)
Collaborators: Dr. Shawna McCallin
(Prof. Lee Ann Laurent-Applegate)
Prof. Marcy Zenobi-Wong
Amount funded: CHF 37'461,14.–

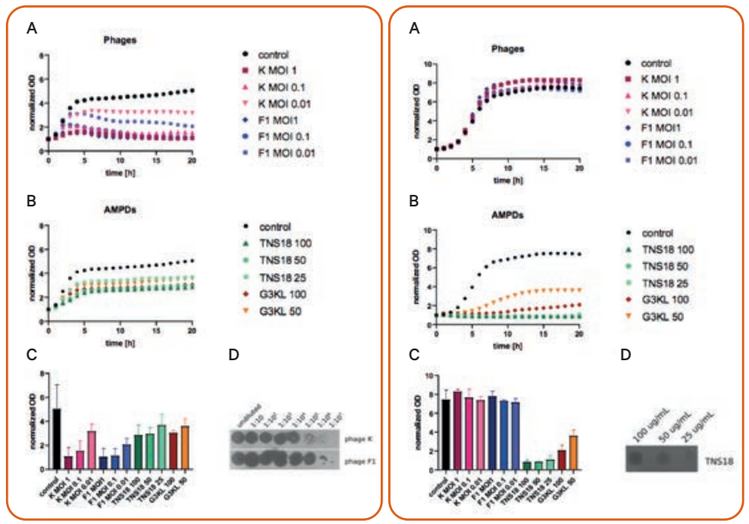
Background: Post-surgical infections of prosthetic joints are a serious cause of poor clinical outcomes for joint replacement surgeries. Infections first proceed by the formation of biofilms via bacterial adherence to the prosthetic surface; persistent infections are provoked by intracellular bacteria within host cells, thus conferring resistance to current antibiotic treatment regimens. With both prosthetic joint infections (PJIs) and antibiotic resistance on the rise, it is imperative that novel anti-microbial strategies are developed both to prevent and treat infections.

Aim: This project aims to evaluate novel antimicrobial strategies for PJIs caused by clinically relevant pathogens resistant to conventional antibiotics at Swiss hospitals. We address this clinical need by incorporating novel antimicrobial peptide dendrimers (AMPDs) and alternative therapies (bacteriophages) that can be incorporated into a sulphated alginate-derived hydrogel formulation developed by our collaborator, Prof. Marcy Zenobi-Wong (ETHZ). Antimicrobials will be tested for their biocompatibility with human cells and for their ability to prevent bacterial adherence to prosthetic joints in an *in vitro* biofilm assay, as well as to clear intracellular bacteria in a cell culture model of persistent infection.

Results: We showed that *S. aureus* as well as *S. epidermidis*, two bacterial pathogens often implicated in PJI, can be targeted by phage or AMPDs. While *S. aureus* clinical isolates tested during our studies were efficiently lysed by phage, but resistant to AMPDs, *S. epidermidis* isolates were highly susceptible to AMPDs, but insensitive to phage (Fig. 1). This led us to conclude that a combination of phage and AMPD might be necessary to concomitantly eradicate *S. aureus* as well as *S. epidermidis* strains, but this needs to be further confirmed with a biofilm model.

Conclusion / Significance: Given that staphylococci colonize prosthetic material by means of biofilm formation, the antibacterial effect of phage-AMPD combinations seems promising as alternative treatments for PJIs and in the face of growing antibiotic resistance worldwide.

Figure 1: Susceptibility of *S. aureus* strain (left panels) and of *S. epidermidis* strain (right panels) to phage K and F1 and the AMPDs, TNS18 and G3KL. Bacteria were incubated alone (control), with phage K or F1 at MOIs 1, 0.1 or 0.01 (panels A) or with AMPDs, TNS18 or G3KL, at concentrations of 100 µg/mL, 50 µg/mL and 25 µg/mL (only TNS18) (panels B) in liquid culture for 20 hours. For each sample, OD_{600} at each timepoint was normalized to OD_{600} at timepoint zero. Data depicts the mean of three biological replicates. C panels: Different representation of the data at timepoint 20h shown in A and B. D panels: Drop test of different dilutions of phage K and phage F1 and AMPDs, TNS18 and G3KL, at concentrations of 100 µg/mL, 50 µg/mL and 25 µg/mL (only TNS18).



2. Neuronal growth and angiogenesis in Modic type 1 changes

Principal investigator: Dr. Stefan Dudli
Collaborator: Dr. Ulrich Blache
(Prof. Jess Snedeker)
Amount funded: CHF 35'460.–

Background: Modic type 1 changes (MC) are chronic inflammatory changes of the vertebral bone marrow seen on MRI adjacent to degenerated discs. MC1 are specific for chronic low back pain (CLBP). Pain in MC1 is linked to neoinnervation of the endplates with vertebral sensory nerve fibers. Vertebral nerve fibers grow along blood vessels, which are surrounded by bone marrow stromal cells (BMSC). BMSCs can produce neurotrophic factors. We have previously shown that BMSC are pathologically relevant cells in MC1.

Aim: The aim of this study was to test if BMSCs in MC1 promote neurite growth.

Results: From six patients undergoing lumbar spinal fusion, aspirates from MC1 lesion and from a control bone marrow region from an adjacent vertebra were collected (Fig. 1A). BMSCs were isolated by plastic adherence and expanded to passage 2. By comparing the transcriptome of MC1 BMSCs vs. control BMSC, pathways related to brain-derived neurotrophic factor (BDNF) signaling and its receptor tropomyosin receptor kinase B (TrkB) were found upregulated (Fig. 1B). MC1 BMSCs co-cultured with the neuroblastoma cell line SH-SY5Y caused enhanced neurite outgrowth from the SH-SY5Y compared to intra-patient control BMSC (Fig. 1C, D). Analysis of the conditioned media from the co-culture revealed up-regulated BDNF and other neurotrophic cytokines in the MC1 vs. control BMSC co-culture (Fig. 1E). Yet, inhibition of BDNF signaling with the selective TrkB antagonist ANA 12 did not reduce neurite outgrowth from SH-SY5Y in the co-culture system, while ANA 12 inhibited outgrowth in the absence of BMSC.

Conclusion / Significance: These findings show that MC1 BMSCs provide strong pro-neurotrophic cues to nearby neurons. BDNF signaling plays a role, but the neurotrophic mechanisms are multifactorial. Therefore, therapeutics targeting neurotrophism in MC1 might be more effective by targeting the BMSC population than blocking individual neurotrophic factors.

Publications:

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"Role of C-reactive protein in the bone marrow of Modic type 1 changes"
J Orthop Res. 2023 May;41(5):1115-1122

Mengis T, Herger N, Heggli I, Devan J, Spirig JM, Laux CJ, Brunner F, Farshad M, Distler O, Dudli S
"Bone marrow stromal cells in Modic type 1 changes promote neurite outgrowth"
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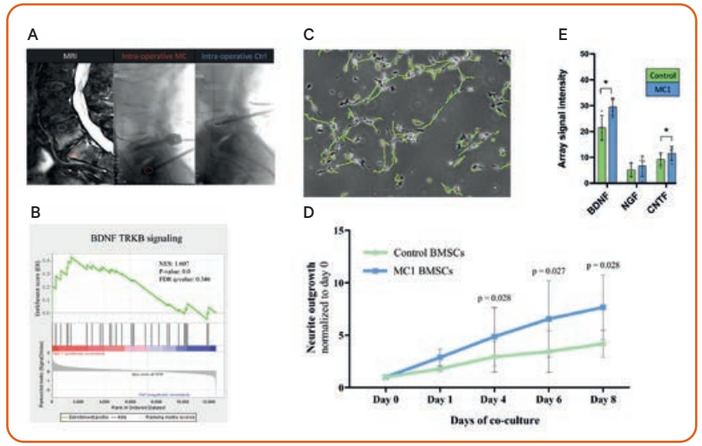


Figure 1: (A) Pre-operative MRI showing MC1 at L5/S1; intra-operative Xray with bone marrow aspiration needle in MC1 lesion (red circle) and control region (blue circle). (B) Gene set for BDNF/TrkB signaling is significantly enhanced in MC1 vs. intra-patient control BMSC. (C) Microscopic image of SH-SY5Y cell with neurite outgrowths, quantified with ImageJ Ridge detection. (D) Increased neurite outgrowth in MC1 vs. control BMSC over 8 days of co-culture. (E) Significant increased concentration of BDNF and CNTF in co-culture supernatant.

3. Aging hallmarks in human mesenchymal stromal cells

Principal investigators: Dr. Melanie Generali
(Prof. Simon Hoerstrup)
Dr. Debora Kehl
(Prof. Simon Hoerstrup)
Collaborator: PD Dr. Paolo Cinelli
Amount funded: CHF 36'397,60.–

Background: The use of mesenchymal stromal cells (MSCs) for therapeutic applications has gained major importance over the past decade. However, so far the efficacy of the first conducted clinical trials remains debated, mainly due to a lack of standardization and characterization of the applied cells. In particular, the regenerative potential of administered MSCs is considered to strongly decline with aging donors. Since the discovery of MSCs, adult bone marrow represents the standard tissue source for their isolation (BM-MSCs), but the process itself is very invasive and the amount of isolated cells is normally relatively low. In the past decade, many efforts have been spent to identify alternative tissue sources for the isolation of highly proliferative MSCs. Human fat tissue has been demonstrated to be a good source of MSCs (AD-MSCs) also due its relatively simple isolation procedure and the higher number of MSCs contained. More recently, umbilical cord Wharton's jelly (WJ-MSCs) was identified as an additional "younger" tissue source.

Aim: In our study, we aimed at characterizing human BM-MSCs, AD-MSCs and WJ-MSCs by transcriptome, proteome, and secretome analysis with particular focus in the identification of age-related differences.

Results: Our data indicated a high heterogeneity at all levels: at proteome but especially at secretome level MSCs strongly differed depending on their tissue of origin (Fig. 1A). In parallel to the omics-analysis (Fig. 1B) also proliferation capacity, cell cycle activity, and stage of senescence (Fig. 1C) were tested to assess aging hallmarks. No analyses leaded to significant differences between young and old MSC lines.

Conclusion / Significance: Our data suggest that MSCs isolated from different tissues are not the same cells, even if they share similar differentiation potentials. Additionally, our observations indicate that MSCs selection for therapeutic applications should be based on their specific differentiation potential and independent from the age of the donor. We could further identify a number of proteins commonly expressed by all cell types and tissue independent, which could represent new biomarkers for the characterization and isolation of MSCs.

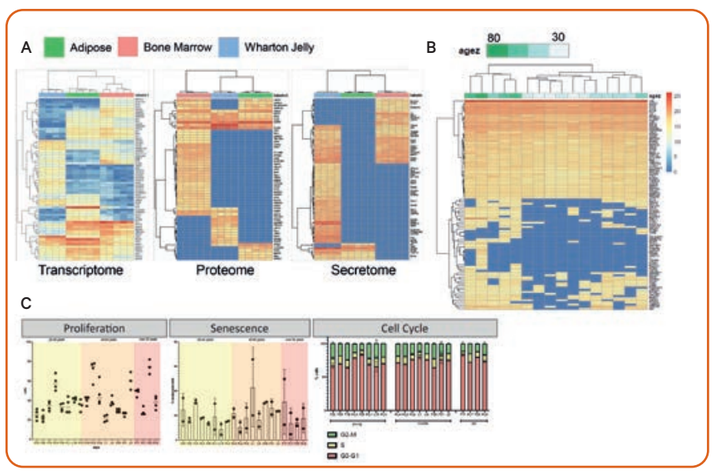


Figure 1: (A) Clustering of transcriptome, proteome, and secretome of AD-MSCs, BM-MSCs and WJ-MSCs; (B) Clustering of top 100 age correlated proteins; (C) For all MSC lines proliferation, senescence, and cell cycle were measured and compared.

Publication:
Generali M, Kehl D, Wanner D, Okoniewski MJ, Hoerstrup SP, Cinelli P
"Heterogenous expression of ACE2 and TMPRRS2 in mesenchymal stromal cells"
J Cell Mol Med. 2022 Jan;26(1):228-234

4. Assess the potency of a peptide-based probe to identify progressive stages of vascular atherosclerotic plaques: a first histological analysis

Principal investigator: Dr. Vahid Hosseini
(Prof. Viola Vogel)
Collaborator: Prof. Viola Vogel
Amount funded: CHF 40'000.–

Background: Cardiovascular disease (CVD) is the major cause of death worldwide, accounting for 31% of all global deaths and 45% of all deaths in Europe. In most cases, acute CVD is caused by arterial thrombosis, a complication of ruptured atherosclerotic plaques, so-called "vulnerable plaques", or eroded atherosclerotic plaques. Vulnerable plaques, in contrast to stable plaques, are often clinically silent before rupture. So far, the identification and precise localization of vulnerable plaques and their consequent treatment remain elusive and novel approaches are demanding.

Aim: We explored whether fibronectin-binding peptides that specifically recognize the tensional state of fibronectin fibers could serve as potent compounds to target diseased extracellular matrix (ECM) within atherosclerotic plaques.

Results: This study provides first evidence that relaxed fibronectin fibrils are abundant in ECM of human plaques compared to the healthy arterial wall and can be effectively targeted using the bacterial-derived FnBPA5. An enhanced binding of FnBPA5 to advanced plaques compared to calcified carotid with thickened intima, or healthy arteries was observed (Fig. 1). Our findings show that the tensional state of fibronectin in atherosclerosis plaque can be specifically targeted with our peptide sensor, which are significantly smaller than antibodies, and that their binding locations allow differentiating between advanced plaques versus the rest of the diseased wall in histological specimens. *Ex vivo* experiments using an intact extracted and intact human carotid plaque artery indicate the ability of the peptide to diffuse from the lumen into the plaque.

Conclusion / Significance: We present the first mechanosensitive peptide that is a potent candidate to target atherosclerotic plaques and has the ability to differentiate between advanced and early-stage plaques in histological and *ex vivo* experiments on human carotid arteries. Thereby, the peptide may find applications for diagnosing and grading arterial plaques or targeted drug delivery.

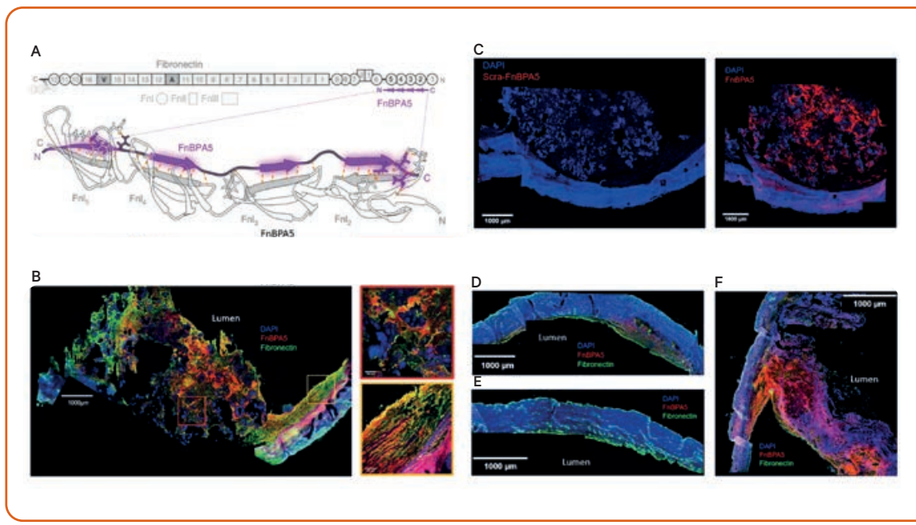


Figure 1: FnPBA5 binds to atherosclerotic plaques and thickened intima of human carotid arteries. (A) Schematic representation of the peptide. (B) A cryo-section of advanced human carotid plaque was stained with peptide (red), as well as immunostained with an antibody against fibronectin (green). (C) A scrambled Cy5-FnBPA5 derivative was used as negative control showing no specific binding. (D) A cryo-section of calcified carotid with thickened intima shows higher binding of Cy5-FnBPA5 to the intima layer, and (E) from the same artery a healthy wall shows minimal peptide-binding. (F) Cryosection of an advanced human carotid plaque.

5. Bio-printed 3D artery analogues for modeling atherosclerosis

Principal investigator: Dr. Anna Mallone
(Prof. Simon Hoerstrup)
Collaborator: Prof. Simon Hoerstrup
Amount funded: CHF 40'000.–

Background: Atherosclerosis is an arterial disease characterized by intravascular plaques. Disease hallmarks are vessel stenosis and hyperplasia, which eventually escalate into acute clinical presentations. Innate immunity and local variations in hemodynamics are core players in the pathology, but their effects have never been investigated before due to the lack of modeling systems with adequate degree of complexity.

Aim: The aim of the project was to combine computational fluid dynamics (CFD) and tissue engineering know-how to achieve, for the first time *in vitro*, a refined model of atherosclerotic plaque assembly. This advanced model aimed at incorporating induced pluripotent stem cell-derived populations into tissue-engineered arteries that are then cultured in atheroprone conditions. Moreover, our project aimed at adopting cutting edge machine learning-aided immunophenotyping approaches and molecular and nanoprobe-based tensile analyses.

Results: We were able to generate *in vitro* iPSC-derived (induced pluripotent stem cells-derived) 3D human vessels displaying immune cell populations, extracellular matrix components, and tensional state that were comparable to *ex vivo* human lesions. Notably, we were able to computationally predict atheroprone, hyperplasic, low-density lipoprotein-laden inflammatory niches within the tissue-engineered small caliber vessels and to later verify the veracity of such predictions by culturing the iPSC-derived 3D human vessels in dynamic and atheroprone conditions. Our results provide further insights into the relation between hemodynamics and inflammation, introducing a versatile, scalable modeling tool to study atherosclerosis onset and progression.

Conclusion / Significance: This project introduces a human plaque-on-a-chip *in vitro* model entirely developed with tissue-engineered vessels from syngeneic iPSC-derived cells. To serve our modeling purpose, we established a novel vascular tissue engineering (VTE) approach which included tailored iPSCs differentiation strategies and the alternation between static and dynamic culturing conditions in a customized fluidic device. The interdisciplinary approaches developed in this project are based on CFD prediction coupled with tissue engineering know-how and have the potential to contribute to the development of more accurate models, offering a new toolbox to gather insights into the physiologic and pathophysiologic remodeling phenomena observed in atherosclerosis but not limited to this field.

Publication:
Mallone A, Gericke C, Hosseini V, Chahbi K, Haenseler W, Emmert MY, von Eckardstein A, Walther JH, Vogel V, Weber B, Hoerstrup SP
"Human induced pluripotent stem cell-derived vessels as dynamic atherosclerosis model on a chip"
bioRxiv. 2020.11.27.401034

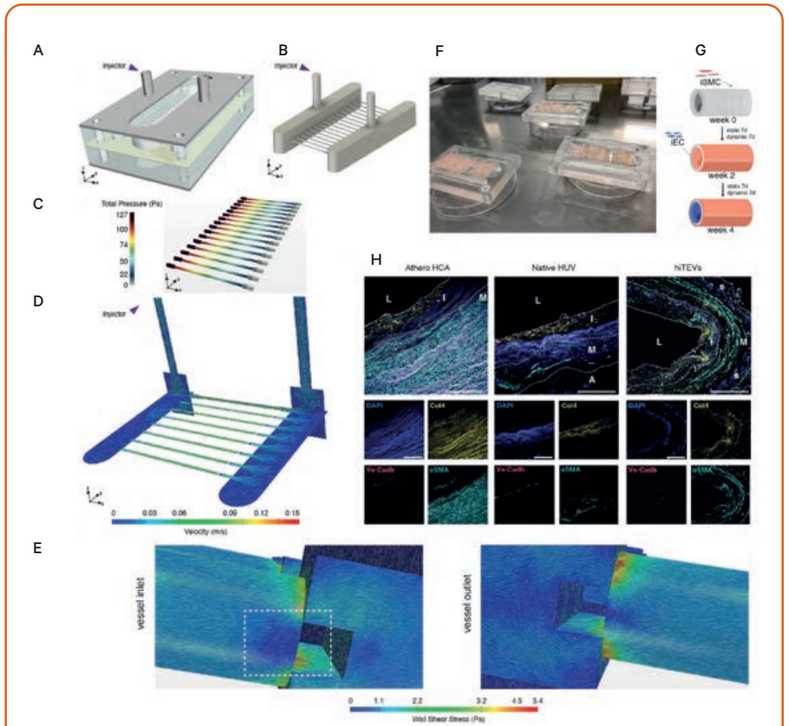


Figure 1: Small caliber human iPSC-derived tissue-engineered vessels. (A) CAD model of the assembled fluidic chamber. (B) Flow domain. Inner volume of the chamber occupied by the culturing medium. (C) Depiction of the pressure gradient within the tissue-engineered vessels (hiTEVs). (D) Cross-sectional and longitudinal view of the flow velocity in the chamber and in the hiTEVs. (E) Wall shear stress at the hiTEV-inlets and hiTEV-outlets. The velocity field is superimposed to the flow domain and depicted using line-integral convolution. Whirlpools are highlighted in the rectangle. (F) Multiple, sterile fluidic chambers loaded with hiTEVs after intraluminal seeding of iECs. (G) Schematics of the tissue engineering strategy adopted in the study. (H) IF comparison of carotid arteries from patients' samples (Athero HCA), Native human umbilical vessels (Native HUV), and tissue-engineered arteries from iPSCs (hiTEVs). L = lumen, I = intima layer, M = media layer, S = PGA/P4HB scaffold remains. Scale bars 100µm.

facts & figures

member profiles, joint research projects and publications

Performance, coordination and promotion of interdisciplinary and translational research – these are the main objectives of the CABMM. Therefore, we aim to create and continuously strengthen a network of active member groups from different fields. The number and quality of those members as well as their collaborative research projects and scientific publications reflect not only the activity within the CABMM network, but also show the success and quality of the CABMM.

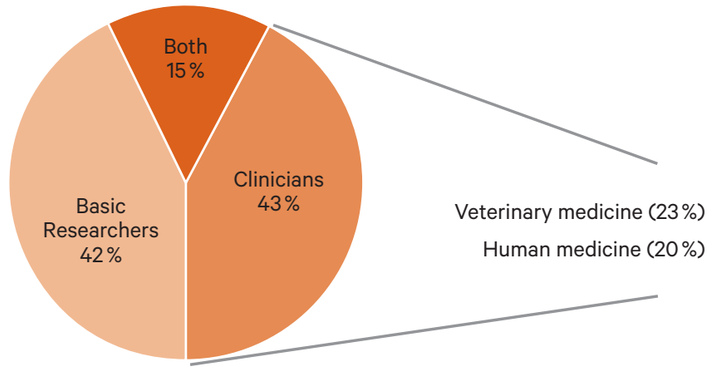
Since its foundation in 2008, the CABMM has gained acceptance and reputation in the field of interdisciplinary and translational research. Amongst others, this was made possible by the continuous commitment of the CABMM members. At the end of 2023, our network consisted of 80 members. Considering the number of team members behind every person, this makes for an impressive network! Although the majority of associated scientists belongs to institutions in Zurich, we also have strong affiliations with other institutions located elsewhere in Switzerland as well as in other countries. In this respect, it is nice to see that our members who leave Switzerland for professional purposes or get retired usually want to stay connected with the CABMM and often retain a close working relationship.

Special emphasis has to be placed on the networking within the CABMM. Basic researchers and clinicians from both human and veterinary medicine are working on numerous joint research projects, thus reflecting the multifaceted work within the CABMM. In the reporting period, 79 collaborative projects were recorded (see pages 104 - 111). Thereby, the collaborative work across disciplines is facilitated by the composition of the CABMM network. It comprises an almost equal number of basic researchers and clinicians, whereof again an almost equal number belongs to the veterinary and human medical field, providing the perfect basis for translational research.

Another testament to the scientific strengths and networking capabilities of our CABMM members is the fact that more than 400 peer-reviewed research articles with affiliation to the CABMM have been published in scientific journals since its creation, thereof almost 20 % in the reporting period (see pages 112 - 120).

To summarize and illustrate the diversity and multifaceted work within the CABMM, all our members are introduced with the assistance of short profiles on the following pages. Additionally, we provide tables detailing research projects performed within the CABMM as well as CABMM-affiliated articles published in scientific journals. We conclude this chapter by providing a short list of public relation articles connected to the CABMM, such as an article showcasing our contribution to the OLMA 2023, the Swiss trade fair for agriculture and food in St. Gallen.

Composition CABMM network 2022/2023



member profiles (in alphabetical order)

for further information on cabmm joint research projects and publications please refer to the respective numbers in the tabular summaries on pages 104 - 111 and 112 - 120

Name: **Achermann, Yvonne**
PD Dr. med.
Institution: Department of Dermatology, University Hospital Zurich; Internal Medicine and Infectious Diseases, Spital Zollikerberg
Grants: Gottfried und Julia Bangerter-Rhyner-Stiftung, Monique Dornonville de la Cour-Stiftung, Stiftung für wissenschaftliche Forschung an der Universität Zürich, USZ Innovation Pool, Wolfermann-Nägeli-Stiftung
CABMM collaborators: Nicole Borel, Stefan Dudli, Niels Kuster, Brigitte von Rechenberg
CABMM joint projects: 43, 73, 79

General research interest:
PD Dr. Yvonne Achermann is a medical doctor specialized in internal medicine and infectious diseases. Since 2008, her scientific focus is on implant-associated infections, mainly prosthetic joint infections. She combines basic research in the field of "prevention, diagnostic, and treatment of implant-associated infections" and clinical research in collaboration with the University Hospital Zurich, University Hospital Balgrist, and Schulthess Clinic. Her current experimental research focus is on prevention and treatment of periprosthetic joint infections using photodynamic therapy.

Name: **Ahmad, Sufian S.**
PD Dr. med.
Institution: Department of Orthopaedic Surgery, Medical School of Hannover MHH, Annastift Hospital, Hannover, Germany
Grants: Erwin-Röver Stiftung, Insel-Grant, Smith & Nephew Grant, Swiss Orthopaedics
CABMM collaborators: Benjamin Gantenbein
CABMM joint projects: 67
CABMM-affiliated publications: 23

General research interest:
Sufian S. Ahmad's research focus is on mechanobiology of cruciate ligaments, cellular biology for treatment of ligament ruptures as well as clinical studies. As a clinician, he emphasizes the need for providing clinically relevant research questions to the basic research laboratory, which would subsequently allow for smooth translation back into clinical practice.

Name: **Albers, Christoph E.**
Prof. Dr. med.
Institution: Department of Orthopaedic Surgery and Traumatology, University Hospital Bern
Grants: Gottfried und Julia Bangerter-Rhyner-Stiftung, Icotec, Lindenhof-Stiftung, Nexon Medical, ORTHO-TEAM, SUVA, Swiss Orthopaedics
CABMM collaborators: Stefan Dudli, Benjamin Gantenbein, Oliver Hausmann, Markus Loibl, Thomas Steffen
CABMM joint projects: 8
CABMM-affiliated publications: 11

General research interest:
Christoph Albers is a spine surgeon at the Department of Orthopaedic Surgery and Traumatology, University Hospital Bern. His scientific background includes bone metabolism, osteogenesis, and bone healing. Current research projects aim at improving and augmenting spinal fusion and intervertebral disc regeneration. As a clinician, he is interested in translating knowledge from basic science directly to clinical application.

Name: **Altmeyer, Matthias**
Prof. Dr. sc. nat.
Institution: Department of Molecular Mechanisms of Disease, University of Zurich
Grants: Comprehensive Cancer Center Zurich, ERC, EU MSCA RepliFate, Pfizer CTI, SNF, Rubicon NWO
CABMM collaborators: Cornel Fraefel, Michael O. Hottiger, Enni Markkanen

General research interest:
Research in our laboratory is aimed at elucidating cellular mechanisms of genome integrity maintenance and their deregulation in human diseases such as cancer. Currently, our work is focused on cell cycle regulation of DNA repair events and on the role of chromatin in modulating repair reactions, including those required for genome editing and gene therapy.

Name: **Audigé, Laurent**
Prof. Dr. (DVM), PhD
Institution: Research and Development Department, Shoulder and Elbow Surgery, Schulthess Clinic, Zurich (until 08/2023); Surgical Outcome Research Center, Department of Clinical Research, University Hospital Basel
Grants: SNF
CABMM collaborators: Christian Gerber
CABMM joint projects: 64

General research interest:
We are interested in a clinic-wide patient registry to monitor safety and assess cost effectiveness of orthopedic interventions. This implies the application of standardized instruments, including for documenting and reporting surgical complications. The development of a clinical decision support system based on register data is a long-term objective.
Furthermore, we contribute to the development and evaluation of new diagnostic tools (e.g., motion analysis), as well as implants and surgical techniques (e.g., biomechanics) to improve patient care.

Name: **Barbero, Andrea**
Prof. Dr. (PhD)
Institution: Cartilage Engineering Group, Department of Biomedicine, University of Basel and University Hospital Basel
Grants: Horizon Europe, SNF
CABMM collaborators:
Lee Ann Laurent-Applegate, Katja Nuss, Antonio Pozzi, Brigitte von Rechenberg, Gian Salzmann, Jivko Stoyanov, Marcy Zenobi-Wong
CABMM joint projects: 39, 46, 47, 49, 75
CABMM-affiliated publications: 7

General research interest:
Prof. Barbero's research is related to the establishment of 3D culture systems, combining cell biology, engineered technologies, and materials science. These systems are used to investigate fundamental aspects of cartilage development, and as grafts to induce tissue regeneration. A special focus lies in the use of nasal cartilage grafts for the treatment of nasal and articular cartilage and their potential use for intervertebral disc repair.

Name: **Bode, Jeffrey**
Prof. Dr. sc. nat.
Institution: Laboratory of Organic Chemistry, ETH Zurich
Grants: ERC Synergy Grant, industry, Innosuisse, NCCR Catalysis, NIBR Global Scholars Program, SNF, SNF Sinergia
CABMM collaborators: Marcy Zenobi-Wong
CABMM joint projects: 1

General research interest:
The Bode Group develops novel chemical reactions for the synthesis of organic molecules under physiological conditions, e.g., in water and in the presence of proteins, living cells, and tissues. Their application includes wound healing, drug delivery, cellular encapsulation, and artificial tissues.

Name: **Borel, Nicole**
Prof. Dr. med. vet., Dipl. ECVP, FVH pathology
Institution: Institute of Veterinary Pathology, Vetsuisse Faculty, University of Zurich
Grants: AgroVet-Strickhof, BAG, BLV, CSF ETHZ, Dr. med. h. c. Erwin Braun Stiftung, Sefunda AG, SNF, WOAH
CABMM collaborators: Yvonne Achermann, Anton Fürst, Colin Schwarzwald
CABMM joint projects: 56, 63, 79
CABMM-affiliated publications: 25

General research interest:
Application of water-filtered infrared A irradiation (wIRA) strongly inhibits chlamydial infection *in vitro* and reduces ocular pathology and chlamydial load in a guinea pig conjunctivitis model. We also applied wIRA in the context of skin fungal infections in humans.
A second research collaboration with the Equine Hospital at the Vetsuisse Faculty investigated the vascularization of the superficial digital flexor tendons in limb preparations from warmblood horses to shed light on the pathogenesis of tendons injuries. A current master thesis project investigates sudden death cases in horses with a special focus on cardiovascular failure.

Name: **Calcagni, Maurizio**
Prof. Dr. med.
Institution: Department of Plastic Surgery and Hand Surgery, University Hospital Zurich
Grants: Evi Diethelm-Winteler-Stiftung, Georg und Bertha Schwyzer-Winiker-Stiftung, Karitative Stiftung Dr. Gerber-ten Bosch, LaColline, Medartis, Stiftung für Naturwissenschaftliche und Technische Forschung, Stiftung Propter Homines
CABMM collaborators: Simon Hoerstrup, Peter Kronen, Lee Ann Laurent-Applegate, Katja Nuss, Caroline Ospelt, Brigitte von Rechenberg, Jess Snedeker, Viola Vogel
CABMM joint projects: 22, 32, 38, 54, 74
CABMM-affiliated publications: 4

General research interest:
The team led by Maurizio Calcagni works on the following projects:
- Tendon healing and adhesion
- 3D motion analysis of the hand and wrist, biomechanics of the wrist and hand
- Tissue engineering of skin and production of cultivated keratinocytes
- Patient reported outcome measurements in hand and wrist surgery

Name: **Cinelli, Paolo**
PD Dr. sc. nat.
Institution: Clinic for Trauma Surgery, University Hospital Zurich; Center for Surgical Research, University Hospital Zurich and University of Zurich
Grants: CABMM, Innovationspool USZ, Novartis Foundation for Medical-Biological Research, SNF
CABMM collaborators: Simon Hoerstrup, Michael O. Hottiger, Katja Nuss, Brigitte von Rechenberg, Raffaella Santoro, Wendelin Stark, Franz Weber, Marcy Zenobi-Wong
CABMM joint projects: 7, 23
CABMM-affiliated publications: 2, 49

General research interest:
Our laboratory is mainly interested in the analysis of the molecular mechanisms involved in the regulation of pluri/multipotency and differentiation of embryonic stem cells (ESCs), induced pluripotent stem cells (iPSCs) and mesenchymal stem cells (MSCs). We are especially interested in the use of these stem cells in bone regeneration.

Name: **Dudli, Stefan**
PD Dr. (PhD)
Institution: Center of Experimental Rheumatology, University Hospital Zurich and Balgrist University Hospital Zurich
Grants: Balgrist-Stiftung, EULAR, FOREUM, Gebauer Stiftung, ISSLS, NIH Back Pain Consortium (BACPAC), SNF, USZ Health Innovation Hub, Velux Stiftung
CABMM collaborators: Yvonne Achermann, Christoph Albers, Stephen Ferguson, Benjamin Gantenbein, Oliver Hausmann, Katja Nuss, Caroline Ospelt, Jess Snedeker, Annelies Zinkernagel
CABMM joint projects: 6, 8, 28, 34, 48
CABMM-affiliated publications: 11, 21, 53, 76

General research interest:
Modic changes (MC) are vertebral bone marrow lesions adjacent to rapidly degenerating intervertebral discs. About 40 % of all patients with chronic low back pain (cLBP) have MC, but there is no specific treatment for MC. Our particular interest is to understand the pathobiology of MC and disc degeneration and the development of targeted treatments for these patients.

Name: **Ferguson, Stephen**
Prof. Dr. (PhD)
Institution: Laboratory for Orthopaedic Technology, Institute for Biomechanics, ETH Zurich
Grants: ETH Zürich Foundation, EU, industry, SNF
CABMM collaborators: Stefan Dudli, Benjamin Gantenbein, Markus Loibl, Ralph Müller, Katja Nuss, Antonio Pozzi, Brigitte von Rechenberg, Markus Rottmar, Jess Snedeker, André Studart, Karin Würtz-Kozak, Marcy Zenobi-Wong
CABMM joint projects: 25, 34, 55, 68, 77
CABMM-affiliated publications: 58

General research interest:
The focus of our group's research is the study of the mechanical and biological mechanisms of musculoskeletal disorders and injuries and the use of innovative technologies for their treatment. Primary challenges we address include (i) extending the life of joint prostheses, (ii) preventing or improving the treatment of fractures and (iii) eliminating disc-related back pain. Our group studies new biomaterials, molecular therapies and implant concepts and develops the technical means for their application in the clinic.

Name: **Forterre, Franck**
Prof. Dr. med. vet.
Institution: Department of Clinical Veterinary Medicine, Small Animal Surgery, Vetsuisse Faculty, University of Bern
Grants: Formas, SNF
CABMM collaborators: Benjamin Gantenbein

General research interest:
The main focus of the research group of Prof. Forterre is directed towards canine intervertebral disc disease, atlantoaxial instability and spinal fusion with regard to biomechanics, inflammation, intramedullary blood flow and pressure changes. Because the dog is a recognized naturally occurring clinical model for human disc degeneration and spinal cord trauma, a translational aspect is present.

Name: **Fraefel, Cornel**
Prof. Dr. sc. nat.
Institution: Institute of Virology, Vetsuisse Faculty, University of Zurich
Grants: SNF
CABMM collaborators: Matthias Altmeyer, Michael O. Hottiger, Enni Markkanen, Raffaella Santoro

General research interest:
Viruses are potent tools to address specific questions in cell biology, immunology, and molecular biology. They are effective vehicles for applications in molecular medicine, such as vaccination and gene therapy. The focus of Prof. Fraefel's research group is the analysis of the molecular mechanisms of virus replication and the use of this information for applying viruses in biomedical research.

Name: **Franco-Obregón, Alfredo**
Prof. Dr. (PhD)
Institution: Institute for Health Innovation & Technology (iHealthTech) and Department of Surgery, National University Hospital Singapore, Singapore
Grants: National Health Innovation Centre Innovation to Develop, Singapore Food Story Seed Grant, Singapore-MIT Alliance for Research and Technology (SMART) Innovation Award, Singapore Therapeutics Development Review (STDR) Pre-Pilot Stream 2
CABMM collaborators: Benjamin Gantenbein, Marie-Noëlle Giraud, Lee Ann Laurent-Applegate, Ralph Müller, Gian Salzmann, Jess Snedeker, Viola Vogel, Karin Würtz-Kozak, Marcy Zenobi-Wong
CABMM-affiliated publications: 6, 31, 57

General research interest:
Skeletal muscle evolved to regulate whole body regeneration and metabolism. Muscle loss because of inactivity or old age is associated with metabolic and cardiovascular dysfunctions, compromised immunity and recovery from injury and increased risks of cancer. These healthful attributes of muscle are initiated by mitochondrial activation, upstream of myokine release, rendering systemic adaptations. The BICEPS (Biolonic Currents Electromagnetic Pulsing Systems) lab's main focus is to develop new therapeutic strategies to maintain muscle health in the elderly and clinically immobilized via a novel process of Magnetic Mitohormesis.

Name: **Fürst, Anton**
Prof. Dr. med. vet., Dipl. ECVS
Institution: Equine Hospital, Vetsuisse Faculty, University of Zurich
CABMM collaborators: Jörg Auer, Nicole Borel, Annette Liesegang, Brigitte von Rechenberg, Colin Schwarzwald, Jess Snedeker
CABMM joint projects: 56, 63

General research interest:
Our technical expertise and interests cover all fields of equine surgery. Currently, our research focuses mainly on equine orthopedics, e.g., the treatment of arthritis, subchondral cystic lesions (SCLs) and tendon injuries in the horse. After successful development of new treatment options *in vitro*, the clinical caseload offers direct future opportunities for their clinical application.

Name: **Gantenbein, Benjamin**
Prof. Dr. phil. nat.
Institution: Department for BioMedical Research (DBMR), University of Bern; Department of Orthopaedic Surgery and Traumatology, Inselspital, University of Bern
Grants: BRIDGE Discovery, CABMM, H2020 iPSpine, Marie Skłodowska Curie International Training Network (ITN) "Disc4All"
CABMM collaborators: Sufian Ahmad, Christoph Albers, Stefan Dudli, Stephen Ferguson, Franck Forterre, Alfredo Franco-Obregón, Marie-Noëlle Giraud, Oliver Hausmann, Simon Hoerstrup, Brigitte von Rechenberg, David Spreng, Jivko Stoyanov, Benedikt Weber, Franz Weber, Karin Würtz-Kozak, Marcy Zenobi-Wong
CABMM joint projects: 8, 42, 67
CABMM-affiliated publications: 11, 23

General research interest:
The Tissue Engineering for Orthopaedics & Mechanobiology (TOM) group, Bone & Joint Program, of the Department for BioMedical Research (DBMR) is performing basic research in the area of tissue engineering using a cross-disciplinary approach of biology and mechanics in collaboration with the Department of Orthopaedic Surgery and Traumatology, Inselspital, University of Bern. Our primary aim is to understand the cellular response to biomechanical stimuli and how cellular communities are affected *in situ* using 3D tissue and organ culture models. Our focus is on the regeneration or repair of the intervertebral disc and on the anterior cruciate ligament.

Name: **Giraud, Marie-Noëlle**
PD Dr. phil. nat.
Institution: Faculty of Science and Medicine, University of Fribourg
Grants: SNF, University of Fribourg
CABMM collaborators: MMartin Flück *, Alfredo Franco-Obregón, Benjamin Gantenbein, Daniel Rüfenacht
CABMM joint projects: 72

General research interest:
Acute coronary syndromes are associated with high morbidity and mortality rates. Associated myocardial infarction results in maladaptive remodeling as the hallmark of chronic heart failure. My laboratory focuses on the development of cell-matrix combinations as new therapeutic tools for cardiovascular diseases. In particular, we investigate the regenerative capacity of the vessels and the myocardium.

* CABMM member until 2022

Name: **Hafezi, Farhad**
Prof. Dr. med., MD, PhD, FARVO
Institution: ELZA Institute AG, Dietikon; CABMM, University of Zurich; Department of Ophthalmology, NYU Grossman School of Medicine, New York, USA; Department of Ophthalmology, University of Southern California, Los Angeles, USA; Department of Ophthalmology, Wenzhou Medical University, Wenzhou, China
Grants: Fondation Botnar, Light for Sight Foundation, SCHWIND eye-tech solutions, Velux Stiftung
CABMM collaborators: Simon Pot, Brigitte von Rechenberg
CABMM joint projects: 52
CABMM-affiliated publications: 1, 3, 5, 8, 17, 18, 19, 20, 22, 24, 26, 27, 28, 29, 30, 33, 34, 38, 43, 44, 48, 52, 55, 59, 60, 61, 63, 64, 65, 71, 74

General research interest:
Farhad Hafezi's main research interests are corneal wound healing, corneal infection treatment, ocular biomechanics, and therapeutic refractive laser surgery. The common link across these interests is a treatment approach called corneal cross-linking (CXL). CXL combines UV light and riboflavin (Vitamin B_2) to modify collagen structure and biomechanics. CXL can be used to treat corneal weakening diseases (ectasias) like keratoconus, and PACK-CXL is the use of CXL to treat bacterial and fungal corneal infections. In some cases, CXL, in combination with elements of refractive laser surgery can dramatically rehabilitate vision.

Name: **Hausmann, Oliver**
Prof. Dr. med.
Institution: Neuro- and Spine Center, Hirslanden Klinik St. Anna, Lucerne
Grants: CABMM
CABMM collaborators: Christoph Albers, Norbert Boos, Stefan Dudli, Benjamin Gantenbein, Karin Würtz-Kozak
CABMM joint projects: 8, 36

General research interest:
As chair of the Neuro- and Spine Center at the Hirslanden Klinik St. Anna in Lucerne, I focus my clinical work on degenerative changes of the adult spine.
Over the last years, a successful collaboration with the Tissue Regeneration and Mechanobiology Lab of Prof. Dr. Karin Würtz-Kozak could be established. With a translational bench-to-bedside approach inflammatory reactions within the degenerated human disc were analyzed and correlated to the clinical presentation.

Name: **Hirsch, Sven**
Prof. Dr. (PhD)
Institution: Institute of Computational Life Sciences and Digital Health Lab, ZHAW Zurich University of Applied Sciences
Grants: DIZH, Innosuisse
CABMM collaborators: Emanuela Keller, Zsolt Kulcsár, Niels Kuster, Serge Marbacher, Katja Nuss, Daniel Rüfenacht, Jess Snedeker, Stefan Stübinger, Isabel Wanke
CABMM joint projects: 61

General research interest:
Sven applies computational techniques to model selected aspects in complex physiological systems, which are subsequently validated using image data of real biological experiments. A strong focus is on vessel wall pathologies and their lifecycle, e.g., cerebral aneurysms.
He also directs the ZHAW Digital Health Lab, connecting expertise from specialized research groups. The lab coordinates application-oriented, interdisciplinary research and development while ensuring the transfer of knowledge and methods into education and practical application.

Name: **Hoerstrup, Simon P.**
Prof. Dr. med., PhD
Institution: Institute for Regenerative Medicine, University of Zurich; Wyss Zurich, ETH Zurich and University of Zurich
Grants: Jubiläumsstiftung von Swiss Life, Mäxi-Stiftung, Stiftung für wissenschaftliche Forschung an der Universität Zürich, Theodor und Ida Herzog-Egli-Stiftung
CABMM collaborators: Maurizio Calcagni, Paolo Cinelli, Benjamin Gantenbein, Michael O. Hottiger, Peter Kronen, Katja Nuss, Brigitte von Rechenberg, Viola Vogel, Isabel Wanke
CABMM joint projects: 7, 14, 18, 22, 31, 60, 70, 71
CABMM-affiliated publications: 2, 4

General research interest:
The research expertise of Prof. Simon P. Hoerstrup lies in the fields (1) tissue engineering including engineered blood vessels, heart valves and microscale strategies for myocardial regeneration, (2) regenerative medicine, e.g., development of cell-based implants out of *in vitro*-generated microtissues to improve myocardial functionality of the diseased heart as well as (3) disease modeling, e.g., studying inflammatory processes that occur in the early development of arteriosclerosis.

Name: **Hofbauer, Günther**
Prof. Dr. med.
Institution: Department of Dermatology, University Hospital Zurich
Grants: SNF
CABMM collaborators: Daniel Rüfenacht, Andreas Serra, Isabel Wanke, Benedikt Weber

General research interest:
The focus of Prof. Hofbauer's research group is on squamous cell carcinoma of the skin and their potential prevention and treatment. He is the head of the working group for dermatology and organ transplantation within the SGDV (Swiss Society for Dermatology and Venereology) and represents this group within the scientific committee of the Swiss Transplant Cohort Study.

Name: **Hofmann-Lehmann, Regina**
Prof. Dr. med. vet.
Institution: Clinical Laboratory, Department of Clinical Diagnostics and Services and Center for Clinical Studies, Vetsuisse Faculty, University of Zurich
Grants: BAFU, BAG, BLV, industry, Stiftung für wissenschaftliche Forschung an der Universität Zürich, SVK, UZH Global Strategy and Partnerships Funding Scheme
CABMM collaborators: Michael O. Hottiger, Anja Kipar, Annette Liesegang, Katja Nuss, Simon Pot
CABMM joint projects: 40, 66

General research interest:
Our primary research endeavors revolve around clinical infectiology and clinical pathology, with a particular emphasis on advancing our understanding of host-pathogen interactions through the utilization of animal models. Our dedicated team has successfully pioneered diagnostic assays for infectious and immunological parameters. Currently, our focal point is on coronaviruses, where we are actively engaged in a prospective interdisciplinary multi-center therapy study investigating fatal feline coronavirus infection (FIP), as well as a comprehensive examination of SARS-CoV-2 infections within a one-health framework. Our accomplished clinical pathologists, holding diplomas in ECVCP, bring their expertise to bear on various facets of laboratory animal hematology, chemistry, cytology, and beyond. Furthermore, within the Center for Clinical Studies, we actively facilitate and support laboratory-based clinical research, contributing to the advancement of our understanding in these critical fields.

Name: **Hottiger, Michael O.**
Prof. Dr. med. vet., Dr. phil. II
Institution: Department of Molecular Mechanisms of Disease, University of Zurich
Grants: Forschungskredit UZH, Marlis Geiser-Lemken Stiftung, SNF, URPP Translational Cancer Research
CABMM collaborators: Matthias Altmeyer, Paolo Cinelli, Cornel Fraefel, Simon Hoerstrup, Regina Hofmann-Lehmann, Anja Kipar, Katja Nuss, Antonio Pozzi, Brigitte von Rechenberg, Janine Reichenbach, Henning Richter, Daniel Rüfenacht, Raffaella Santoro, Jess Snedeker, Isabel Wanke
CABMM joint projects: 41

General research interest:
The innate immune response is the biological response of tissues to harmful stimuli such as pathogens, damaged cells, or irritants. It is a protective attempt by the organism to remove the harmful stimuli and initiate the healing process. Similar types of signaling are also observed in cancer cells (e.g., aberrant cytoplasmic nucleic acids).
My laboratory is interested in the molecular regulation of the innate immune response by ADP-ribosylation, a post-translational modification of proteins. Our current work focuses on the activation and function of the enzymes that catalyze ADP-ribosylation, the identification of their target proteins and their biological roles in the innate immune response.

Name: **Hugelshofer, Michael**
PD Dr. med., MSc
Institution: Department of Neurosurgery, University Hospital Zurich; Neurosurgical Clinic, Universitätsmedizin Mannheim, Germany
Grants: CSL Behring, Innosuisse, SNF, Uniscientia
CABMM collaborators: Emanuela Keller, Patrick Kircher, Peter Kronen, Serge Marbacher, Katja Nuss, Henning Richter
CABMM joint projects: 17, 59
CABMM publications: 47

General research interest:
PD Dr. Hugelshofer is an academic neurosurgeon currently working as an attending physician at the University Hospital in Mannheim, Germany. In addition, he leads a research group with a focus on neurovascular pathologies at the University of Zurich. In his role as PI at the Neuroscience Center Zurich (ZNZ) and in the Clinical Science PhD program of the Faculty of Medicine, he supervises ongoing translational research projects with the aim to improve diagnostic and therapeutic approaches to prevent secondary brain injury after intracranial hemorrhage.

Name: **Kipar, Anja**
Prof. Dr. med. vet.
Institution: Institute of Veterinary Pathology, Vetsuisse Faculty, University of Zurich
Grants: Jane and Aatos Erkko Foundation, Finland, Medical Research Council UK, SERI, SNF, Wellcome Trust, UK
CABMM collaborators: Regina Hofmann-Lehmann, Michael O. Hottiger, Annette Liesegang, Enni Markkanen, Katja Nuss, Simon Pot, Antonio Pozzi, Henning Richter, Marcy Zenobi-Wong
CABMM joint projects: 40, 41, 51, 58, 66
CABMM publications: 13

General research interest:
Main areas of research are a) the pathogenesis of viral infectious diseases, like Boid Inclusion Body Disease of snakes, Feline Infectious Peritonitis, Malignant Catarrhal Fever of bovids, and COVID-19; b) the pathogenesis of cardiomyopathies with specific emphasis on remodeling processes. Our animal work stretches from viral and bacterial diseases to toxicopathology. With the Laboratory for Animal Model Pathology (LAMP) we maintain a research platform that offers technical service and expert pathologist input to animal studies with a morphological component. Such collaborative, interdisciplinary approaches maximize the outcome.

Name: **Kircher, Patrick R.**
Prof. Dr. med. vet., PhD, EMBA UZH
Institution: Clinic for Diagnostic Imaging, Vetsuisse Faculty, University of Zurich
Grants: Innosuisse, SNF
CABMM collaborators: Michael Hugelshofer, Peter Kronen, Katja Nuss, Simon Pot, Antonio Pozzi, Henning Richter, Carla Rohrer Bley, Frank Steffen
CABMM joint projects: 59

General research interest:
We are interested in the development of Functional Magnetic Resonance Imaging (fMRI), and MR Spectroscopy, as well as cardiac MRI (cMRI) in animal patients and animal models. In general, the cross-sectional angiographic techniques are being optimized and utilized in the group. The Clinic for Diagnostic Imaging shall serve as center of expertise in animal imaging for all affiliates of the CABMM.

Name: **Kronen, Peter**
Dr. med. vet., DVM, Dipl. ECVAA
Institution: Department of Molecular Mechanisms of Disease, Musculoskeletal Research Unit, Vetsuisse Faculty, University of Zurich; Veterinary Anaesthesia Services International, Winterthur
Grants: EU, industry, Innosuisse, SNF Sinergia
CABMM collaborators: Maurizio Calcagni, Christian Gerber, Simon Hoerstrup, Michael Hugelshofer, Emanuela Keller, Patrick Kircher, Zsolt Kulcsár, Serge Marbacher, Katja Nuss, Brigitte von Rechenberg, Henning Richter, Stefan Stübinger, Franz Weber
CABMM joint projects: 17, 37, 59
CABMM-affiliated publications: 35, 47, 56, 58

General research interest:
- Improvement of anesthetic techniques and methods in large experimental animals (rabbits, sheep, pigs, goats)
- Pain diagnosis in behavioral schemes (pain scales), their comparison with neurophysiological parameters and clinical relevance
- Alternative administration techniques of anesthetic and analgesic drugs

Name: **Kulcsár, Zsolt**
PD Dr. med., Dr. sc. nat.
Institution: Department of Neuroradiology, University Hospital Zurich
CABMM collaborators: Sven Hirsch, Peter Kronen, Serge Marbacher
CABMM joint projects: 61
CABMM-affiliated publications: 47

General research interest:
Zsolt Kulcsár works at the University Hospital of Zurich, Zurich, Switzerland and he is the Head and Director of the Department of Neuroradiology. He has trained in Neuroradiology at the National Institute of Neurosurgery, Budapest, Hungary, with Prof. Istvan Szikora and later in Geneva, at the University Hospital of Geneva, Switzerland with Prof. Rüfenacht.
He has a PhD degree in Clinical Neurosciences and a habilitation degree in Radiology. He has major scientific interest in neurovascular diseases, specifically aneurysms, ischemic stroke, and vascular malformations of the brain. He is involved in clinical and experimental research related cerebrovascular diseases. His clinical interest relates to the imaging and therapy of complex neurovascular diseases.

Name: **Kuster, Niels**
Prof. em. Dr. sc. ETH Zurich
Institution: Foundation for Research on Information Technologies in Society (IT'IS), Zurich
Grants: ANSES, BAFU, BAG, ETH Domain – PHRT, EUREKA, EUROSTARS, Horizon Europe, Imperial College London, industry (several), Innosuisse, INERIS, NIH, SBFI, SNF
CABMM collaborators: Yvonne Achermann, Sven Hirsch, Daniel Rüfenacht
CABMM joint projects: 73

General research interest:
Core research areas: development of 1) experimental and computational electromagnetics from subHz to 300 GHz in complex environments, 2) computational life sciences, 3) virtual human and animal anatomical models functionalized with dynamic tissue models and 4) wireless and medical applications such as minimization/optimization of body-mounted transmitters/electrode configurations, neurostimulation, implant safety, *in silico* clinical trials, etc.

Name: **Laurent-Applegate, Lee Ann**
Prof. Dr. (PhD)
Institution: Department of Musculoskeletal Medicine, Service of Plastic and Reconstructive Surgery, Unit of Regenerative Therapy, Lausanne University Hospital; Oxford Suzhou Centre for Advanced Research, Suzhou, China
Grants: Flavie – Association suisse romande pour les victimes de brûlures, FRNS, Lausanne Hospital Priority Project Funding, Lausanne Orthopedic Research Foundation, Marie Skłodowska-Curie Fellowship
CABMM collaborators: Felix Althaus, Andrea Barbero, Maurizio Calcagni, Alfredo Franco-Obregón, Katja Nuss, Brigitte von Rechenberg, Gian Salzmann, Jess Snedeker, Marcy Zenobi-Wong
CABMM joint projects: 10, 11, 15, 20, 27, 35, 50, 69
CABMM-affiliated publications: 15, 39, 40, 41, 45, 51, 54, 62, 66, 67, 73

General research interest:
We are interested in addressing clinical problems of tissue repair based on the concept that unlike adult tissue, fetal tissue undergoes rapid healing with little inflammation and no scar tissue. As such, our laboratory has established cell banks of progenitor cells harvested from human bone, cartilage, disc, muscle, tendon, and skin, and some of these cell sources are being used to successfully develop cellular therapies for severely burned patients, acute and chronic wounds and for all other musculoskeletal tissues. We work closely with the CABMM to develop GLP large animal models for pre-clinical investigations for innovative API's (active pharmaceutical ingredients) and cellular therapeutics. In addition to the routine clinical use of cellular therapies for severe burn patients, we have clinical studies on-going for Progenitor Biological Bandages (PBB) in a Priority Burn Project and autologous chondrocyte cell therapy in the CHUV within the Swissmedic accredited GMP Cell Production Center.

Name: **Liesegang, Annette**
Prof. Dr. med. vet., Dipl. ECVCN, IVAS
Institution: Institute of Animal Nutrition and Dietetics, Vetsuisse Faculty, University of Zurich
Grants: Innosuisse, Royal Canin (Schweiz) AG, Stiftung für Kleintiere der Vetsuisse-Fakultät, SVWZH
CABMM collaborators: Alois Boos, Anton Fürst, Regina Hofmann-Lehmann, Anja Kipar, Antonio Pozzi, Brigitte von Rechenberg, Henning Richter, Stefan Stübinger
CABMM joint projects: 5, 13, 33, 66, 78

General research interest:
Focus on cartilage, bone and mineral research, energy metabolism and sustainability of different feed (from feed to food)
- Physiological and nutritional influences on bone metabolism and cartilage metabolism
- Bone and cartilage markers and bone mineral density (pQCT) during growth, gestation, and lactation
- Calcium resorption mechanisms in the intestines
- Mechanisms of longitudinal growth regulation within growth plates
- Hormones of calcium metabolism
- Osteoporosis
- Vitamin D metabolism in skin
- Bone metabolism in cats
- Energy and protein metabolism in cats
- Trace element metabolism and the influences on absorption

Name: **Loibl, Markus**
Prof. Dr. med.
Institution: Schulthess Clinic, Zurich
CABMM collaborators: Christoph Albers, Stephen Ferguson
CABMM joint projects: 25

General research interest:
Preclinical trials led to a better understanding of the demands of the native environment in the degenerating disc. I am interested in the regenerative effect of cell-based applications and locally applicable drugs in the intervertebral disc niche to prevent disc degeneration and promote disc regeneration. As a clinician, I am interested in translating basic science knowledge to develop appropriateness criteria for regenerative treatments in a clinical setting.

Name: **Marbacher, Serge**
Prof. Dr. med., PhD
Institution: Cerebrovascular Research Group, Department of Neurosurgery, Kantonsspital Aarau
Grants: Research Council Kantonsspital Aarau, SNF
CABMM collaborators: Sven Hirsch, Michael Hugelshofer, Peter Kronen, Zsolt Kulcsár, Brigitte von Rechenberg, Daniel Rüfenacht, Isabel Wanke

General research interest:
The Cerebrovascular Research Group focuses on cerebral aneurysms, e.g., endovascular treatment options to prevent aneurysm rupture and sequels of subarachnoid hemorrhage after their rupture. We currently work with a sidewall rat and rabbit bifurcation aneurysm model using degenerated arterial grafts to investigate treatment options and inflammatory processes eventually leading to aneurysm growth and rupture. It is our ultimate goal to find novel endovascular modalities that completely exclude the aneurysm from the circulation and reconstruct the diseased arterial segment. Furthermore, we explore non-occlusive endovascular bypass options.

Name: **Markkanen, Enni**
Prof. Dr. med. vet., Dr. sc. nat.
Institution: Institute of Veterinary Pharmacology and Toxicology, Vetsuisse Faculty, University of Zurich
Grants: American Kennel Club Canine Health Foundation, EveryCat Health Foundation, Kurt und Senta Herrmann-Stiftung, Morris Animal Foundation, SNF, Wolfermann-Nägeli-Stiftung
CABMM collaborators: Matthias Altmeyer, Cornel Fraefel, Anja Kipar, Simon Pot, Antonio Pozzi, Henning Richter, Carla Rohrer Bley, Viola Vogel
CABMM joint projects: 30, 58, 76

General research interest:
Our vision is to leverage the power of comparative oncology between humans, cats, and dogs to improve the diagnosis and therapy of cancer in all three species – from patient to the bench and back. To this end, we are applying spatially resolved proteomic and transcriptomic approaches to identify molecular correlates between human and animal tumor subtypes and be able to harness tumors in pets as naturally occurring models for the human disease. Currently, our research is focused on understanding the mechanisms by which stroma influences growth and malignancy of tumors, and the identification of novel targets for improved imaging and therapy of soft tissue sarcomas in human, canine, and feline patients.

Name: **Müller, Ralph**
Prof. Dr. sc.
Institution: Laboratory for Bone Biomechanics, Institute for Biomechanics, ETH Zurich
Grants: Australian Research Council, COST, ERC, EU, SFA-AM, SFA – Personalized Health and Related Technologies, SNF
CABMM collaborators: Stephen Ferguson, Alfredo Franco-Obregón, Jess Snedeker, André Studart, Marcy Zenobi-Wong

General research interest:
The research the Müller group has completed and is currently pursuing employs state-of-the-art biomechanical testing and simulation techniques as well as novel bioimaging and visualization strategies for musculoskeletal tissues. Today, these techniques are successfully employed for the quantitative assessment and monitoring of structure function relationships in tissue regeneration, growth, and adaptation. The approaches are now often used for precise phenotypic characterization of tissue response in mammalian genetics, mechanobiology as well as tissue engineering and regenerative medicine.

Name: **Nuss, Katja**
Dr. med. vet.
Institution: Department of Molecular Mechanisms of Disease, Musculoskeletal Research Unit, Vetsuisse Faculty, University of Zurich
Grants: Industry, Innosuisse, SNF, SNF Sinergia
CABMM collaborators: Andrea Barbero, Maurizio Calcagni, Paolo Cinelli, Stefan Dudli, Stephen Ferguson, Sven Hirsch, Simon Hoerstrup, Regina Hofmann-Lehmann, Michael O. Hottiger, Michael Hugelshofer, Anja Kipar, Patrick Kircher, Peter Kronen, Lee Ann Laurent-Applegate, Antonio Pozzi, Brigitte von Rechenberg, Janine Reichenbach, Henning Richter, Markus Rottmar, Daniel Rüfenacht, Jess Snedeker, Frank Steffen, Stefan Stübinger, Isabel Wanke, Marcy Zenobi-Wong
CABMM joint projects: 2, 6, 10, 11, 12, 14, 15, 19, 22, 24, 26, 38, 39, 44, 47, 49, 51, 53, 54, 55, 57, 59, 62, 68, 70, 71, 74, 75, 77
CABMM-affiliated publications: 36, 37, 56

General research interest:
Dr. Katja Nuss is one of three leaders of the Musculoskeletal Research Unit (MSRU). She is a specialist in veterinary surgery and in veterinary anesthesiology with a huge experience in clinical and experimental surgery. Special scientific interest includes intracranial aneurysms and its animal models; wound healing; bone, muscle, tendon, ligament biomaterials, and cartilage degeneration. The MSRU is a GLP accredited facility for preclinical studies.

Name: **Ospelt, Caroline**
Prof. Dr. med., PhD
Institution: Center of Experimental Rheumatology, University Hospital Zurich
Grants: SNF
CABMM collaborators: Maurizio Calcagni, Stefan Dudli, Steffen Gay, Jess Snedeker, Marcy Zenobi-Wong
CABMM joint projects: 45

General research interest:
In one of the leading centers worldwide for the analysis of synovial fibroblasts in rheumatoid arthritis, Prof. Ospelt's track record is the analysis of genetic and epigenetic changes within this complex field. Furthermore, the group uses single cell and spatial transcriptomics to analyze the role of specific fibroblasts subtypes in arthritis development.

Name: **Pot, Simon**
Prof. Dr., PhD, Dipl. ACVO/ECVO
Institution: Ophthalmology Section, Equine Department, Vetsuisse Faculty, University of Zurich
Grants: ACVO Vision for Animals Foundation Founders Clinical Research Grant, American Kennel Club Canine Health Foundation, ECVO Research Grant, Stiftung für wissenschaftliche Forschung an der Universität Zürich, Velux Stiftung
CABMM collaborators: Farhad Hafezi, Regina Hofmann-Lehmann, Anja Kipar, Patrick Kircher, Enni Markkanen, Henning Richter, Carla Rohrer Bley, Markus Rottmar, Viola Vogel
CABMM joint projects: 3, 4, 30, 40, 52, 76

General research interest:
Simon Pot's main research interests are on the following topics:
- Mechanobiology of corneal wound healing: Understanding the basic mechanisms governing the reciprocal force balance between fibroblasts and their extracellular matrix, an important regulator of wound healing and fibrosis.
- Infectious corneal disease: Evaluating the elimination of corneal infections and stabilization of the corneal stroma through pharmacological (antibacterial and antifungal agents) and physical (UV-A/Riboflavin corneal crosslinking - CXL) means.
- Ocular imaging: Evaluating the use of high-resolution advanced imaging technologies (ultrasound biomicroscopy, microcoil assisted MRT and Optical Coherence Tomography) for ocular imaging.

Name: **Pozzi, Antonio**
Prof. Dr. med. vet., Dipl. ECVS/ACVS, Dipl. ACVSMR
Institution: Clinic for Small Animal Surgery, Vetsuisse Faculty, University of Zurich
Grants: Arthrex, Geistlich, Legat Bachofner, Forschungskredit UZH, SNF
CABMM collaborators: Andrea Barbero, Stephen Ferguson, Michael O. Hottiger, Anja Kipar, Patrick Kircher, Annette Liesegang, Enni Markkanen, Katja Nuss, Brigitte von Rechenberg, Henning Richter, Carla Rohrer Bley, Frank Steffen, Stefan Stübinger
CABMM joint projects: 39, 44, 57, 58, 62

General research interest:
My main interest is musculoskeletal research with focus on joint physiology and pathophysiology, including knee, meniscus and cartilage injuries using animal models to understand diseases and develop novel treatments. We recently founded the digitalization motion group, focused on computer-assisted research on movement. As chair of the Clinic for Small Animal Surgery, I lead the clinic research program. The major goal of the research teams of the Clinic for Small Animal Surgery is to study clinical problems in companion animals that provide naturally occurring models for human diseases, including areas such as joint, spine, trauma, and oncologic surgery.

Name: **von Rechenberg, Brigitte**
Prof. em. Dr. med. vet., Dipl. ECVS
Institution: Brigitte von Rechenberg Consulting GmbH
Grants: Hans Jegen Stiftung, Vontobel-Stiftung
CABMM collaborators: Yvonne Achermann, Andrea Barbero, Maurizio Calcagni, Paolo Cinelli, Stephen Ferguson, Anton Fürst, Benjamin Gantenbein, Christian Gerber, Farhad Hafezi, Simon Hoerstrup, Michael O. Hottiger, Peter Kronen, Lee Ann Laurent-Applegate, Annette Liesegang, Serge Marbacher, Katja Nuss, Antonio Pozzi, Janine Reichenbach, Henning Richter, Jess Snedeker, Wendelin Stark, Frank Steffen, Viola Vogel, Marcy Zenobi-Wong
CABMM joint projects: 2, 10, 12, 13, 15, 19, 22, 24, 26, 31, 32, 35, 37, 43, 50, 53, 55, 57, 60, 65, 68, 77, 78
CABMM-affiliated publications: 4, 10, 14, 16, 35, 36, 37, 42, 56, 58, 68, 69

General research interest:
My main interest in musculoskeletal research is still focused on bone and cartilage, including fracture and defect healing, the influence of inflammation in bone, cartilage, and muscle healing as well as physiological remodeling of subchondral bone and cartilage. With my collaborators, expansion in wound healing and pain management was added. As a research consultant I am still related to the MSRU, a facility that is GLP-accredited by the Swissmedic. As a consultant I am still involved in other fields of experimental medicine and support other CABMM members with their animal experiments.

Name: **Reichenbach, Janine**
Prof. Dr. med.
Institution: Institute for Regenerative Medicine, University of Zurich; Division of Somatic Gene Therapy, University Children's Hospital Zurich
Grants: CRPP ImmuGene, UFSP ITINERARE, SNF, Wyss Zurich
CABMM collaborators: Simon Hoerstrup, Michael O. Hottiger, Katja Nuss, Brigitte von Rechenberg
CABMM joint projects: 18, 53
CABMM-affiliated publications: 75

General research interest:
The research group of Prof. Reichenbach is focused on the development of new therapeutic concepts and therapeutic correction by first-in-man clinical gene therapy for inborn errors of the immune and nervous system.

Name: **Richter, Henning**
Dr. sc. med. vet., PhD, Dipl. SVLAS
Institution: Diagnostic Imaging Research Unit (DIRU), Clinic for Diagnostic Imaging, Vetsuisse Faculty, University of Zurich
Grants: Innosuisse, SNF
CABMM collaborators: Michael O. Hottiger, Michael Hugelshofer, Emanuela Keller, Anja Kipar, Patrick Kircher, Peter Kronen, Annette Liesegang, Enni Markkanen, Katja Nuss, Simon Pot, Antonio Pozzi, Brigitte von Rechenberg, Carla Rohrer Bley, Daniel Rüfenacht, Frank Steffen, Isabel Wanke
CABMM joint projects: 17, 33, 59
CABMM-affiliated publications: 47

General research interest:
Dr. Richter leads the Diagnostic Imaging Research Unit (DIRU), which serves as a platform for internal and external research groups interested in veterinary and translational clinical studies. DIRU offers a wide range of imaging modalities, a high level of expertise in imaging, as well as in study organization and laboratory animal science. Scientific interest mainly centers on MRI and interventional imaging. Additionally, Dr. Richter leads a dog research facility at the Vetsuisse Faculty Zurich that supports various types of research, including the use of dog models.

Name: **Rohrer Bley, Carla**
Prof. Dr. med. vet.
Institution: Clinic for Radiation Oncology & Medical Oncology, Vetsuisse Faculty, University of Zurich
Grants: Albert-Heim-Stiftung, SNF, Swiss Cancer Foundation, Swiss Cancer League
CABMM collaborators: Patrick Kircher, Enni Markkanen, Simon Pot, Antonio Pozzi, Henning Richter, Frank Steffen
CABMM joint projects: 3, 16

General research interest:
My group's research is focused on radiation therapy in all aspects (basic and clinical radiobiology, radiotherapy). Our clinic is well equipped, counting to one of the most state-of-the-art veterinary cancer treatment facilities in Europe. While treating animal patients with spontaneously occurring tumors we believe that with research focusing on diseases or conditions similar to those occurring in human patients, we can make our contribution to increasing the complex knowledge about cancer.

Name: **Rottmar, Markus**
Dr. sc.
Institution: Cell-/Tissue Material Interactions, Lab for Biointerfaces, Swiss Federal Laboratories for Materials Science and Technology (Empa), St. Gallen
Grants: Heinz A. Oertli-Fonds, Innosuisse, ITI Foundation, OPO-Stiftung, Uniscientia Stiftung, Velux Stiftung
CABMM collaborators: Stephen Ferguson, Katja Nuss, Simon Pot, Gian Salzmann, Viola Vogel, Karin Würtz-Kozak, Marcy Zenobi-Wong
CABMM joint projects: 4

General research interest:
The team of Dr. Rottmar is interested in gaining a better understanding of how cells and tissues interact with biomaterials. The research focus is to elucidate the role of blood-material interaction and immune cell responses on downstream cell fate decisions and how this knowledge can be exploited to steer a desired tissue response (i.e., facilitating or preventing hard/soft tissue integration, enhance wound healing) by materials design.

Name: **Rüfenacht, Daniel A.**
Prof. Dr. med.
Institution: Neuroradiology, Klinik Hirslanden & SNRI/SCNSI, Zurich; InterventionalWorkResearch (IWR), SwissNeuroFoundation
Grants: Industry, SwissNeuroFoundation, University of Essen
CABMM collaborators: Marie-Noëlle Giraud, Sven Hirsch, Günther Hofbauer, Michael O. Hottiger, Niels Kuster, Serge Marbacher, Katja Nuss, Henning Richter, Andreas Serra, Isabel Wanke

General research interest:
The IWR group is interested in understanding, imaging, and visualization of neurovascular diseases and minimally invasive treatment options. Research focuses on vessel wall pathologies (esp. intracranial aneurysms), AVM, and vascular dementia. The biological pathways of interest include angiogenesis (mTOR) and degeneration (NF-κB). Translational research efforts include supporting exploratory workshops (iNEW), multiscale modeling, and methods connecting biomechanics with biological effects at cellular and organ system level. We support development of methodologies to investigate disease understanding and therapeutic effects and the development of a sustainable databank for neurovascular diseases (SwissNeuroFoundation).

Name: **Salzmann, Gian**
Prof. Dr. med.
Institution: Orthopaedics, Lower extremities, Schulthess Klinik, Zurich
Grants: Alwin Jäger Stiftung, GOTS, SNF, Stiftung Lindenhof Bern
CABMM collaborators: Andrea Barbero, Alfredo Franco-Obregón, Lee Ann Laurent-Applegate, Markus Rottmar, Marcy Zenobi-Wong

General research interest:
As a clinician-scientist, Prof. Salzmann is optimally positioned to observe first-hand the limitations of current cartilage repair procedures and will help towards translation from bench-to-bedside. Experimental research includes the application of gene therapy and mechanical loading on articular chondrocytes in small animal models and the use of chondrocytes and stem cells in clinical applications.

Name: **Santoro, Raffaella**
Prof. Dr. rer. nat.
Institution: Department of Molecular Mechanisms of Disease, University of Zurich
Grants: ERC Advanced Grant, Krebsliga Schweiz, SNF Sinergia, SNSF Excellence
CABMM collaborators: Paolo Cinelli, Cornel Fraefel, Michael O. Hottiger
CABMM joint projects: 23

General research interest:
Every cell contains the same genetic information, yet they differentiate into distinct tissues and organs. This property is mainly interpreted at the level of epigenetics and chromatin structure via non-coding RNAs and modifications at histones and DNA. We aim to elucidate how epigenetic mechanisms establish and maintain cell identity. Our mission is to identify chromatin and epigenetic regulators and to define the pathways contributing to pluripotency, neoplastic transformation, and metastasis.

Name: **Schwarzwald, Colin C.**
Prof. Dr. med. vet., PhD, Dipl. ACVIM, Dipl. ECEIM, FASE
Institution: Clinic for Equine Internal Medicine, Equine Department, Vetsuisse Faculty, University of Zurich
Grants: Danish Cardiovascular Academy
CABMM collaborators: Nicole Borel, Anton Fürst
CABMM joint projects: 63

General research interest:
Large animal and comparative cardiology, with emphasis on echocardiography, cardiac electrophysiology, hemodynamic monitoring, cardiovascular pharmacology, and cardiac biomarkers.

Name: **Serra, Andreas**
Prof. Dr. med., MPH
Institution: Department of Internal Medicine and Nephrology, Klinik Hirslanden, Zurich; Epidemiology, Biostatistics and Prevention Institute (EBPI), University of Zurich
Grants: Gebert Rüf Stiftung, industry
CABMM collaborators: Jörg Goldhahn, Günther Hofbauer, Daniel Rüfenacht, Isabel Wanke

General research interest:
Prof. Serra's research focus lies on mammalian target of rapamycin (mTOR) signaling pathway, therapies for autosomal dominant polycystic kidney disease (ADPKD) and treatment for tuberous sclerosis (TSC). As a result of his scientific background, he is head of the Suisse ADPKD cohort (www.adpkd.ch) and co-director of the Swiss TSC network (www.swissTSCnetwork.ch).

Name: **Snedeker, Jess G.**
Prof. Dr. (PhD)
Institution: Department of Orthopaedic Biomechanics, University of Zurich; Institute for Biomechanics, ETH Zurich
Grants: Balgrist Foundation, Chan Zuckerberg Initiative, ETH Zurich Research Grant, Innosuisse, Novartis Foundation, SNF, Vontobel-Stiftung
CABMM collaborators: Maurizio Calcagni, Stefan Dudli, Stephen Ferguson, Alfredo Franco-Obregón, Anton Fürst, Christian Gerber, Jörg Goldhahn, Sven Hirsch, Michael O. Hottiger, Lee Ann Laurent-Applegate, Ralph Müller, Katja Nuss, Caroline Ospelt, Brigitte von Rechenberg, Franz Weber, Marcy Zenobi-Wong, Annelies Zinkernagel
CABMM joint projects: 2, 21, 26, 28, 48
CABMM-affiliated publications: 69

General research interest:
The Snedeker Lab is a leading research group focused on tendon mechanobiology and regenerative orthopedic surgery. Beyond basic research, the group actively develops and clinically translates next-generation orthopedic devices for improved patient outcomes and better quality of life.

Name: **Spadavecchia, Claudia**
Prof. Dr. med. vet., PhD, Dipl. ECVAA
Institution: Institute of Veterinary Anaesthesiology and Pain Therapy, Department of Clinical Veterinary Medicine, Vetsuisse Faculty, University of Bern
Grants: SNF Spark, UniBern Forschungsstiftung

General research interest:
Our main research interest is pain in animals. We aim at developing objective, valid, and reliable tools to evaluate species-specific nociceptive physio-pathological processes and pain behaviour and at refining procedures and techniques to improve pain treatment in domestic and laboratory animals. Our major areas of interest are 1) neurophysiological characterization of acute and persistent pain to provide evidence in the context of animal welfare, 2) development of perioperative pain treatment strategies in clinical and experimental settings and 3) optimization of methods to recognize and treat acute perioperative and chronic pain.

Name: **Stark, Wendelin J.**
Prof. Dr. (PhD)
Institution: Functional Materials Laboratory, Institute for Chemical and Bioengineering, ETH Zurich
Grants: Botnar Research Centre for Child Health, ETH Foundation
CABMM collaborators: Paolo Cinelli, Brigitte von Rechenberg
CABMM-affiliated publications: 49

General research interest:
We develop biodegradable additives to make inert materials bioactive. This makes soft tissue implants adhere better to the implanted material and reduces friction, tear off and may potentially reduce risks for infections.
Since 2013, we have worked on soft implants, particularly with 3D printed heart like pumps, as part of the Zurich Heart Project.

Name: **Steffen, Frank**
Prof. Dr. med. vet., Dipl. ECVN
Institution: Section of Neurology, Department of Small Animals, Vetsuisse Faculty, University of Zurich
Grants: Albert-Heim-Stiftung, Legat Bachofner
CABMM collaborators: Patrick Kircher, Katja Nuss, Antonio Pozzi, Brigitte von Rechenberg, Henning Richter, Carla Rohrer Bley, Jivko Stoyanov, Karin Würtz-Kozak
CABMM joint projects: 16, 24, 29

General research interest:
There is a broad interest focused on clinical and surgical aspects of intervertebral disc degeneration including regeneration strategies, clinical assessment of outcome, diagnostic imaging follow-up and translational studies. We are exploring new methodologies for treating regeneration of intervertebral discs *in vitro* and *in vivo* and investigate pathomechanisms associated with disc degeneration.

Name: **Steffen, Thomas**
Prof. Dr. med., PhD, MBA
Institution: Orthopaedic Research Laboratory, Division of Orthopaedic Surgery, McGill University, Montréal General Hospital, Montréal, Canada
CABMM collaborators: Christoph Albers
CABMM-affiliated publications: 35, 68

General research interest:
Thomas Steffen received basic training in orthopedic surgery in Bern, Switzerland, then worked several decades in basic and applied spinal research at McGill University in Montréal, Canada. His expertise is in biomechanics of the musculoskeletal system, bone and bone substitutes, intervertebral disc degeneration and organ culture models, orthopedic implant development, animal models and translational research at large.

Name: **Stoyanov, Jivko**
Prof. Dr. (PhD)
Institution: SCI Population Biobanking & Translational Research, Swiss Paraplegic Research, Nottwil; Institute of Social and Preventive Medicine, University of Bern
Grants: SSPH, Swiss Paraplegic Foundation
CABMM collaborators: Andrea Barbero, Benjamin Gantenbein, Frank Steffen
CABMM joint projects: 46

General research interest:
Jivko Stoyanov leads the group of SCI Population Biobanking and Translational Research at Swiss Paraplegic Research and is head of the Swiss Spinal Cord Injury (SwiSCI) Cohort Study Biobank. The group is interested in optimizing cell interaction with tissue engineering matrices for the purpose of regeneration of pressure injuries following spinal cord injury and modulation of inflammation in intervertebral discs (IVD). They isolate and culture human and canine IVD cells and mesenchymal stem cells (MSCs) and have knowledge in hypoxic cell culture, molecular and biochemical methods, and live cell imaging. Furthermore, they have a substantial collection of matched (from same donor) cell sets – IVD cells, MSCs and PBMCs (peripheral blood mononuclear cells). Other focus areas are lifestyle modifications and their influence on the urinary, skin, and fecal microbiome as well as immunosenescence in persons with SCI.

Name: **Studart, André R.**
Prof. Dr. (PhD)
Institution: Complex Materials, Department of Materials, ETH Zurich
Grants: Industry, SNF, Strategic Focus Area Advanced Manufacturing
CABMM collaborators: Stephen Ferguson, Ralph Müller, Marcy Zenobi-Wong

General research interest:
Our research is focused on the design and assembly of new porous materials and functional capsules of potential use as scaffolds and drug release agents in regenerative medicine. In the area of porous materials, we are interested in studying hierarchical porous architectures that can provide physical and chemical cues to accelerate regeneration in soft and hard tissues. In the area of functional capsules, we use microfluidic devices to develop smart, responsive capsules that could potentially be used for the controlled release of drugs and growth factors in the body upon different types of external stimuli.

Name: **Stübinger, Stefan**
PD Dr. med. dent.
Institution: Medical Innovation and Smart Technologies, University Hospital Basel
Grants: Fondation Botnar, industry, Innosuisse, Swiss Nanoscience Institute
CABMM collaborators: Sven Hirsch, Peter Kronen, Annette Liesegang, Katja Nuss, Antonio Pozzi, Franz Weber

General research interest:
The group "Medical Innovation and Smart Technologies (MIOSTE)" was founded by Stefan Stübinger and Miodrag Savic. The primary aim is to foster advances in clinically oriented research, emerging technologies and innovative product development. Principal fields of interest are translational medicine including prototyping, experimental surgical techniques, regenerative medicine, applied biotechnology and molecular medicine with a focus on body fluids. Embedded within the University Hospital Basel, MIOSTE offers an open and interdisciplinary research unit for various disciplines and creates strategical collaborations developing novel and pragmatic approaches for solving complex health problems.

Name: **Vogel, Viola**
Prof. Dr. (PhD), Dr. h. c.
Institution: Laboratory of Applied Mechanobiology, Department for Health Sciences and Technology, ETH Zurich
Grants: Industry, NCCR, SNF
CABMM collaborators: Maurizio Calcagni, Alfredo Franco-Obregón, Jörg Goldhahn, Simon Hoerstrup, Enni Markkanen, Simon Pot, Brigitte von Rechenberg, Markus Rottmar, Benedikt Weber, Marcy Zenobi-Wong
CABMM joint projects: 9

General research interest:
The focus of Prof. Vogel's laboratory is to learn how mechanical forces are sensed by bacteria, cells, and tissues, how forces stretch proteins and thereby switch their structure-function relationships and how this in turn regulates cell signaling. By combining physical, engineering, and biological tools, we are asking how the mechanobiology of extracellular matrix and of macrophages directs homeostasis versus pathologies in human tissues and in *de novo* grown microtissues, and how such insights can be exploited for applications in bioengineering and regenerative medicine.

Name: **Wanke, Isabel**
Prof. Dr. med.
Institution: Neuroradiology, Klinik Hirslanden & SNRI/SCNSI, Zurich; InterventionalWorkResearch (IWR), SwissNeuroFoundation; Institute of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen, Germany
Grants: Industry, SwissNeuroFoundation, University of Essen
CABMM collaborators: Sven Hirsch, Günther Hofbauer, Michael O. Hottiger, Emanuela Keller, Serge Marbacher, Katja Nuss, Henning Richter, Daniel Rüfenacht, Andreas Serra

General research interest:
The IWR group is interested in understanding, imaging and visualization of neurovascular diseases and minimally invasive treatment options. Research focuses on vessel wall pathologies (esp. intracranial aneurysms), AVM and vascular dementia. The biological pathways of interest include angiogenesis (mTOR) and degeneration (NF-κB). Translational research efforts include supporting exploratory workshops (iNEW), multiscale modeling and methods connecting biomechanics with biological effects at cellular and organ system level. We support development of methodologies to investigate disease understanding and therapeutic effects and the development of a sustainable databank for neurovascular diseases (SwissNeuroFoundation).

Name: **Weber, Benedikt**
Prof. Dr. med., Dr. sc. nat.
Institution: Skin and Endothelium Research Division, Medical University of Vienna, Austria
Grants: FWF, Medizinisch-Wissenschaftlicher Fonds der Bundeshauptstadt Wien, WWTF
CABMM collaborators: Benjamin Gantenbein, Günther Hofbauer, Viola Vogel

General research interest:
The research focus of Prof. Weber is to investigate the use of different cell and stem cell sources for vascular bioengineering and for *in vitro* modeling of (cardio)vascular diseases. The group has demonstrated the successful *in vitro* manufacture and *in vivo* implantation of different vascular bioengineered structures, including heart valves, venous valves, and blood vessels. A major focus lies on the underlying remodeling mechanisms *in vivo* with regards to guiding *in situ* cellularization, scaffold (bio)degradation and neotissue formation.

Name: **Weber, Franz E.**
Prof. Dr. rer. nat.
Institution: Oral Biotechnology & Bioengineering, Center of Dentistry / MKG, University of Zurich
Grants: SNF
CABMM collaborators: Paolo Cinelli, Benjamin Gantenbein, Peter Kronen, Jess Snedeker, Stefan Stübinger, Marcy Zenobi-Wong
CABMM-affiliated publications: 9, 32, 49, 50, 70, 72

General research interest:
The main interest of our research laboratory is the healing of large bone defects of the mandible and the cranium by personalized bone substitutes. At present, we mainly focus on the micro- and nanostructure of 3D-printed bone substitutes to optimize osteoconduction and realize this topic by additive manufacturing of calcium phosphates and bioglass. Moreover, we started to evaluate micro- and nanoarchitectures optimal for bone augmentations, mainly needed for the placement of dental implants. Epigenetics, pulp regeneration and bone regeneration by osteoinduction are other subjects of research.

Name: **Würtz-Kozak, Karin**
Prof. Dr. hum. biol., MBA
Institution: Department of Biomedical Engineering, Rochester Institute of Technology, Rochester, New York, USA
Grants: DoD CDMRP, EUROSPINE, Horizon 2020, NIH, NSF, SNF
CABMM collaborators: Stephen Ferguson, Alfredo Franco-Obregón, Benjamin Gantenbein, Oliver Hausmann, Markus Rottmar, Frank Steffen
CABMM joint projects: 29, 36, 42

General research interest:
My research aims to improve the understanding of the cellular mechanisms underlying specific pathologies (predominantly musculoskeletal and skin disorders), with a focus on inflammation and inflammaging. This information is then utilized for the development of novel treatment options that allow for tissue regeneration and pain reduction, applying engineering principles (e.g., genome engineering, engineering of functional biomaterials) as well as principles from molecular medicine (e.g., pathway modulation).

Name: **Zenobi-Wong, Marcy**
Prof. Dr. (PhD)
Institution: Tissue Engineering and Biofabrication, Institute for Biomechanics, ETH Zurich
Grants: CABMM, ETH Zürich Foundation, SNF
CABMM collaborators: Andrea Barbero, Jeffrey Bode, Paolo Cinelli, Stephen Ferguson, Alfredo Franco-Obregón, Benjamin Gantenbein, Anja Kipar, Lee Ann Laurent-Applegate, Ralph Müller, Katja Nuss, Caroline Ospelt, Brigitte von Rechenberg, Markus Rottmar, Gian Salzmann, Jess Snedeker, Viola Vogel, Franz Weber
CABMM joint projects: 1, 12, 19, 20, 27, 35, 45, 51, 69

General research interest:
We use biomaterials and biofabrication techniques to create 3D cellular systems, primarily for cartilage regeneration. Biomimetic hydrogels are designed to control stem cell and chondrocyte fate, having engineered adhesion and growth factor binding properties. We use bioprinting to create complex functional mimics of cartilage tissue.

Name: **Zinkernagel, Annelies**
Prof. Dr. med., PhD
Institution: Department of Infectious Diseases and Hospital Epidemiology, University Hospital Zurich
Grants: KFSP BacVivo, NCCR AntiResist, SNF
CABMM collaborators: Stefan Dudli, Jess Snedeker
CABMM-affiliated publications: 21

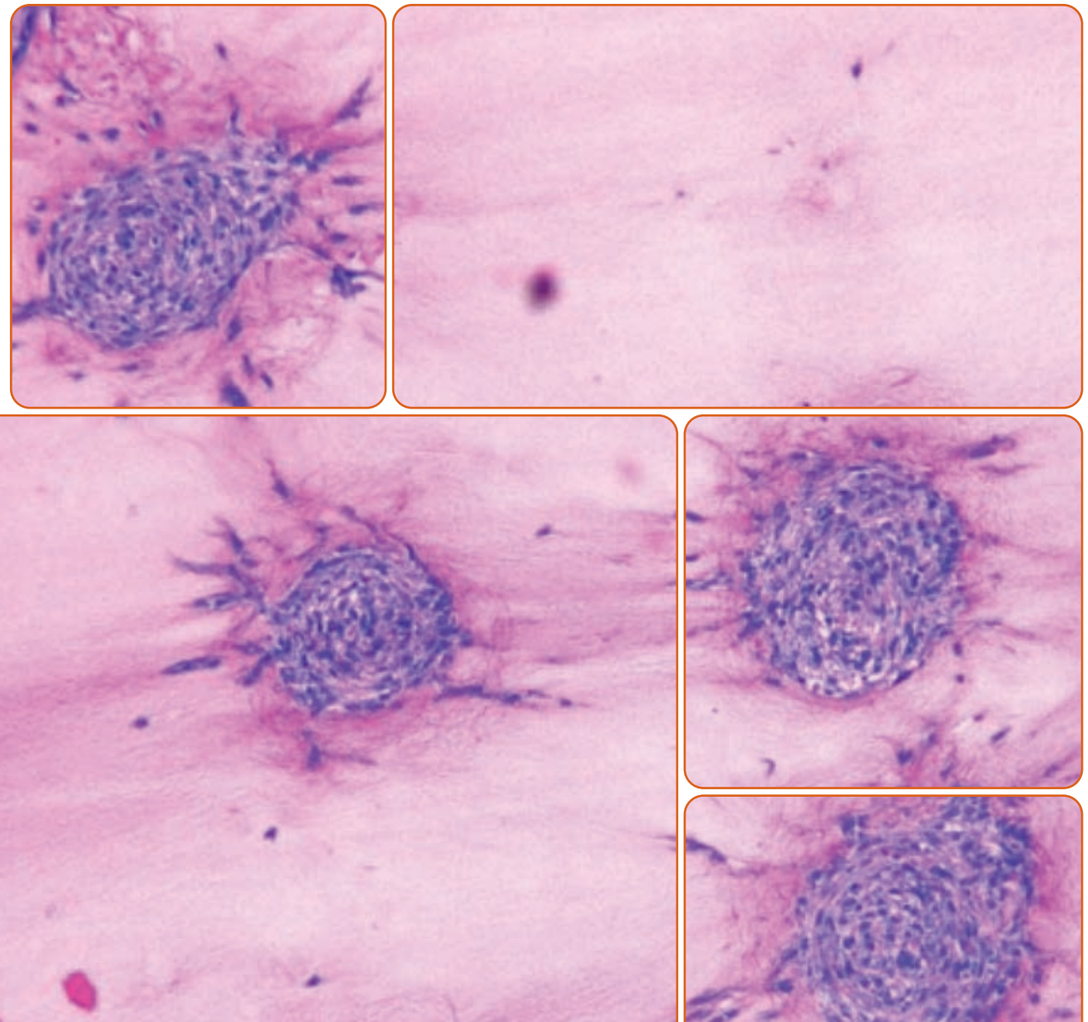
General research interest:
The scientific interest of Prof. Zinkernagel's group are bacterial pathogenesis, increasing antibiotic resistance and therefore possible new treatment strategies. Special focus lies on the role of virulence factors during pathogenesis, persistence of *Staphylococcus aureus* that goes along with antibiotic tolerance and high relapse rates and the characterization of bacteria within biofilms.

honorary members

Name: **Auer, Jörg A.**
Prof. em. Dr. med. vet., Dr. h. c., Dipl. ECVS/ACVS
Institution: Equine Hospital, Vetsuisse Faculty, University of Zurich

Name: **Hübscher, Ulrich**
Prof. em. Dr. med. vet.
Institution: Institute of Veterinary Biochemistry and Molecular Biology, University of Zurich

Name: **von Rechenberg, Brigitte**
Prof. em. Dr. med. vet., Dipl. ECVS
Institution: Musculoskeletal Research Unit, Vetsuisse Faculty, University of Zurich



alumni members

Name: **Althaus, Felix R.**
Prof. em. Dr. med. vet.
Institution: Institute of Veterinary Pharmacology and Toxicology, Vetsuisse Faculty, University of Zurich

Name: **Blauth, Michael**
Prof. Dr. med.
Institution: Department for Trauma Surgery, Medical University of Innsbruck, Austria

Name: **Boos, Alois**
Prof. em. Dr. med. vet.
Institution: Institute of Veterinary Anatomy, Vetsuisse Faculty, University of Zurich

Name: **Boos, Norbert**
Prof. Dr. med.
Institution: Prodorso, Centre for Spinal Medicine, Zurich

Name: **Bürki, Kurt**
Prof. em. Dr. sc. nat.
Institution: Institute of Laboratory Animal Science, Vetsuisse Faculty, University of Zurich

Name: **Dip, Ramiro**
PD Dr. med. vet., PhD
Institution: Institute of Veterinary Pharmacology and Toxicology, Vetsuisse Faculty, University of Zurich; Swiss Reinsurance Company Ltd.

Name: **Gay, Steffen**
Prof. em. Dr. med.
Institution: Center of Experimental Rheumatology, University Hospital Zurich

Name: **Gerber, Christian**
Prof. em. Dr. med.
Institution: Department of Orthopaedics, University Hospital Balgrist, Zurich

Name: **Goldhahn, Jörg**
Prof. Dr. med.
Institution: Department of Health Sciences and Technology, ETH Zurich

Name: **Keller, Emanuela**
Prof. Dr. med.
Institution: Department of Neurosurgery, University Hospital Zurich

Name: **Spreng, David**
Prof. Dr. med. vet.
Institution: Department of Veterinary Medicine, Vetsuisse Faculty, University of Bern

Name: **Wavreille, Vincent**
Dr. med. vet.
Institution: VetSpecialistes, Grand-Sacconex

joint research projects 2022 / 2023 (in alphabetical order)

Number	Title	Collaborators (CABMM members)
1	**3D Patterning of Proteins on Hydrogels**	Jeffrey Bode Marcy Zenobi-Wong *
2	**A novel patch to repair a partial tear of the infraspinatus muscle in sheep**	Katja Nuss / Salim Darwiche * Brigitte von Rechenberg Jess Snedeker
3	**A prospective pilot study on late toxicity from the use of image-guided intensity-modulated radiation therapy for canine sinonasal tumors**	Simon Pot Carla Rohrer Bley *
4	**A regenerative bioadhesive for the treatment of infected corneal ulcers**	Simon Pot Markus Rottmar *
5	**Absorption mechanisms in the intestines of goat and sheep**	Alois Boos **** Annette Liesegang *
6	**Activated neutrophils at the vertebral bone-disc junction promote cartilage endplate damage in Modic changes**	Stefan Dudli * Katja Nuss
7	**Aging hallmarks in human mesenchymal stromal cells: rejuvenation strategies for next generation therapies #**	Paolo Cinelli Melanie Generali * (Simon Hoerstrup **) Debora Kehl * (Simon Hoerstrup **)
8	**Analysing the Transcriptome of Cells in Intervertebral Discs with Modic Changes and its Relevance for Spinal Fusion #**	Christoph Albers Stefan Dudli Benjamin Gantenbein * Oliver Hausmann
9	**Assess the potency of a peptide-based probe to identify progressive stages of vascular atherosclerotic plaques: a first histological analysis #**	Vahid Hosseini * (Viola Vogel **) Viola Vogel
10	**Biocompatibility and efficacy testing of bone substitutes in the Drill Hole Model**	Lee Ann Laurent-Applegate Katja Nuss / Salim Darwiche * Brigitte von Rechenberg
11	**Biological Biodegradable Burn Wound Treatments – A proof of concept study in pigs**	Lee Ann Laurent-Applegate Katja Nuss / Salim Darwiche *
12	**Biphasic implants for osteochondral tissue repair and regeneration**	Katja Nuss / Salim Darwiche * Brigitte von Rechenberg Marcy Zenobi-Wong
13	**Bone metabolism of cats**	Annette Liesegang * Brigitte von Rechenberg
14	**Cardiovascular Tissue Engineering**	Simon Hoerstrup * Katja Nuss / Karina Klein
15	**Cartilage and IVD replacement using constructs with integrated fixation**	Lee Ann Laurent-Applegate Katja Nuss / Salim Darwiche * Brigitte von Rechenberg
16	**Challenging the standard therapy for meningoencephalomyelitis of unknown origin (MUO): can we make treatment easier for our patients?**	Carla Rohrer Bley * Frank Steffen *
17	**Clinical observational studies and translational models for hemoglobin toxicity after aneurysmal subarachnoid hemorrhage**	Michael Hugelshofer * Emanuela Keller **** Peter Kronen Henning Richter
18	**Clinical phase I/II study for p47phox Chronic Granulomatous Disease (CGD)**	Simon Hoerstrup Janine Reichenbach *
19	**Combination of a Collagen Scaffold and an Adhesive Hyaluronan-Based Hydrogel for Cartilage Regeneration**	Katja Nuss / Salim Darwiche / Karina Klein Brigitte von Rechenberg Marcy Zenobi-Wong *
20	**Development of an antimicrobial hydrogel for the prevention and treatment of multi-drug resistant prosthetic joint infections #**	Philippe Abdel-Sayed * (Lee Ann Laurent-Applegate **) Shawna McCallin (Lee Ann Laurent-Applegate **) Marcy Zenobi-Wong
21	**Diagnosis and minimally invasive treatment of rotator cuff tendon tear**	Christian Gerber */**** Jess Snedeker
22	**Effect of hypothermal conditioning on the quality and growth potential of *in vitro* cultured keratinocytes for skin grafts**	Maurizio Calcagni * Simon Hoerstrup Katja Nuss / Salim Darwiche Brigitte von Rechenberg

* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

Number	Title	Collaborators (CABMM members)
23	**Elucidation of mechanisms regulating ground state pluripotency**	Paolo Cinelli Raffaella Santoro *
24	**Engineered biological implant for canine disc replacement**	Katja Nuss / Salim Darwiche * / Karina Klein Brigitte von Rechenberg Frank Steffen
25	**Evaluating the influence of global sagittal alignment on proximal segment loading using musculoskeletal modeling**	Stephen Ferguson Markus Loibl *
26	**Evaluating the safety and efficacy of the Fiberlocker System – a sheep study using a partial tenotomy of the infraspinatus muscle**	Katja Nuss / Salim Darwiche * / Karina Klein Brigitte von Rechenberg Jess Snedeker
27	**Evaluation of the chondrogenic potential of human epiphyseal chondroprogenitor cells in alginate sulfate hydrogels #**	Lee Ann Laurent-Applegate Marcy Zenobi-Wong *
28	**Functionalized annulus fibrosous repair patch to prevent post-surgical disc infection**	Stefan Dudli * Jess Snedeker
29	**Identification of inflammatory and pain markers in degenerative spinal disease #**	Luc Smolders * (Frank Steffen **) Frank Steffen Karin Würtz-Kozak *
30	**Identification of profibrotic pathways and potential treatment targets in corneal fibrosis**	Enni Markkanen * Simon Pot *
31	**ImaValve**	Simon Hoerstrup * Brigitte von Rechenberg
32	**Influence of electrotherapy on the stratification of keratinocytes and epidermal regeneration**	Maurizio Calcagni * Brigitte von Rechenberg
33	**Influence of phosphorus source on kidney health in cats**	Annette Liesegang * Henning Richter
34	**Injectability of carriers for cell delivery in porous bone**	Stefan Dudli * Stephen Ferguson

* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

Number	Title	Collaborators (CABMM members)
35	**Injectable hyaluronan based adhesive technology for cartilage regeneration using epiphyseal chondroprogenitor cells**	Lee Ann Laurent-Applegate Brigitte von Rechenberg Marcy Zenobi-Wong *
36	**Intervertebral disc inflammaging**	Oliver Hausmann * Karin Würtz-Kozak *
37	**Intracranial tissue perfusion, pressure, and temperature**	Peter Kronen * Brigitte von Rechenberg
38	**Investigating hypercortisolemia-induced wound healing disturbances and the therapeutic potential of heme in skin models *in vitro***	Felicitas Boretti */*** Maurizio Calcagni Katja Nuss Nadja Sieber-Ruckstuhl ***
39	**Laser Assisted Robot Guided Cartilage Regeneration**	Andrea Barbero Katja Nuss / Salim Darwiche Antonio Pozzi Georg Rauter */***
40	**Long-term study of the effect and potential side effects of oral therapy with GS-441524 in cats with feline infectious peritonitis**	Regina Hofmann-Lehmann * Anja Kipar Simon Pot
41	**MacroD1 sustains mitochondrial integrity and oxidative metabolism**	Michael O. Hottiger * Anja Kipar
42	**Marie Skłodowska Curie International Training Network (ITN) Disc4All**	Benjamin Gantenbein Jérôme Noailly */*** Karin Würtz-Kozak
43	**Marvel: electromagnetic pulsed stimulation to prevent osteomyelitis**	Yvonne Achermann Beat Lechmann *** Brigitte von Rechenberg *
44	**Meniscal Strain in Normal and Degenerated Canine Menisci**	Katja Nuss / Salim Darwiche Antonio Pozzi *
45	**Microbiota and metabolic endotoxemia: the missing culprit of Osteoarthritis #**	Gonçalo Barreto * (Marcy Zenobi-Wong **) Caroline Ospelt Marcy Zenobi-Wong
46	**Nanoghosts as drug delivery platform in intervertebral disc repair**	Andrea Barbero * Jivko Stoyanov *

* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

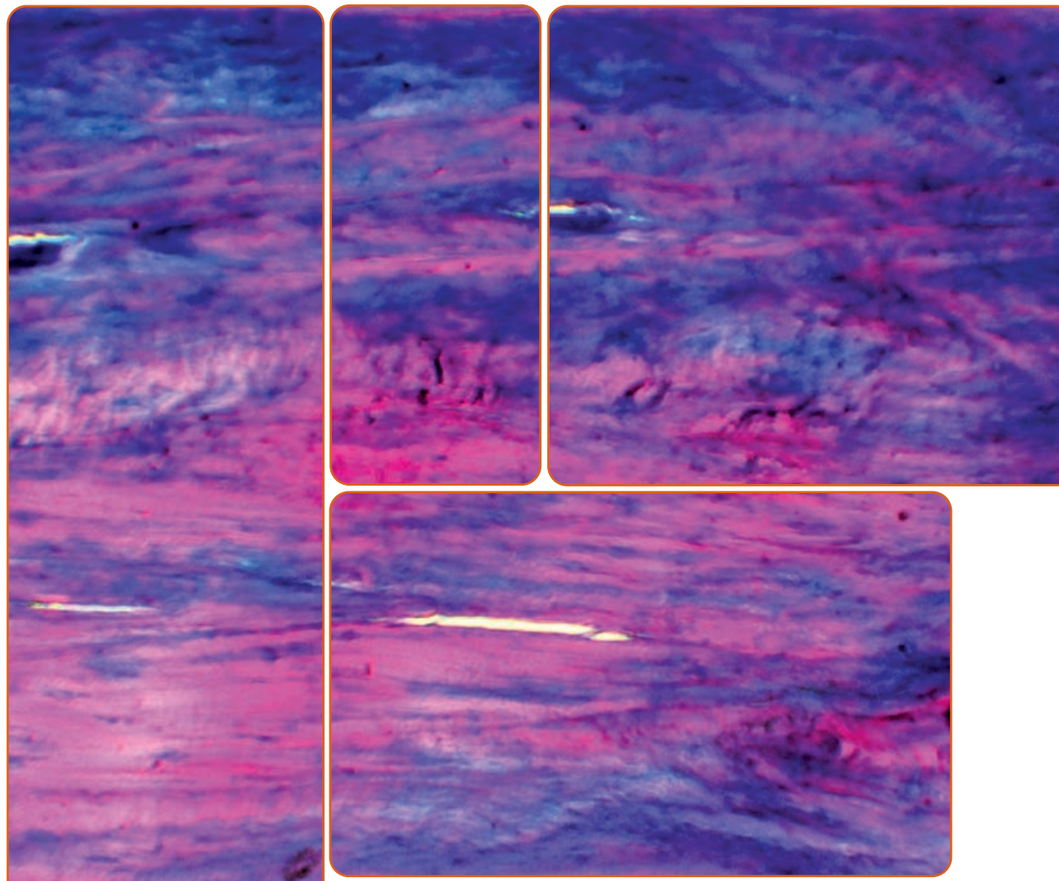
Number	Title	Collaborators (CABMM members)
47	**Nasal chondrocytes for the treatment of cartilage and disc pathologies**	Andrea Barbero * Katja Nuss / Salim Darwiche
48	**Neuronal growth and angiogenesis in Modic type 1 changes #**	Ulrich Blache (Jess Snedeker **) Stefan Dudli *
49	**Nucleus pulposus-on-a-chip as a model for mechanobiology research and therapeutic testing #**	Salim Darwiche (Katja Nuss **) Olga Krupkova * (Andrea Barbero **)
50	**Osteochondral bone stimulation with fetal progenitor cells**	Lee Ann Laurent-Applegate * Brigitte von Rechenberg
51	**Osteochondral Repair and Regeneration – Tackling the subchondral bone-cartilage junction**	Anja Kipar Katja Nuss / Salim Darwiche * Marcy Zenobi-Wong
52	**PACK-CXL for infectious keratitis**	Farhad Hafezi * Simon Pot *
53	**Preclinical GLP animal study on p47phox CGD mice to prepare IMPD for above clinical trial**	Katja Nuss Brigitte von Rechenberg Janine Reichenbach *
54	**Preliminary study to assess the impact of Far-UVC on human skin tissue**	Maurizio Calcagni * Katja Nuss / Salim Darwiche
55	**Pulsed electromagnetic field therapy enhances bone repair and regeneration in two tibia osteotomy models in sheep**	Stephen Ferguson Katja Nuss / Salim Darwiche * / Karina Klein Brigitte von Rechenberg
56	**Quantitative assessment of blood vessels in the superficial digital flexor tendons of horses**	Nicole Borel Anton Fürst *
57	**Regeneration of meniscus using injectable biomaterial**	Katja Nuss / Salim Darwiche * / Karina Klein Antonio Pozzi Brigitte von Rechenberg

* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

Number	Title	Collaborators (CABMM members)
58	**REVEAL-FS: Characterization of novel targets for near infrared fluorescence-guided surgery of fibrosarcomas #**	Franco Guscetti (Anja Kipar **) Enni Markkanen * Mirja Nolff (Antonio Pozzi **)
59	**Scavenging of cell-free hemoglobin in the subarachnoid space: Proof of therapeutic concept in chronic hemoglobin exposure**	Michael Hugelshofer * Patrick Kircher Peter Kronen Katja Nuss / Karina Klein Henning Richter
60	**Skin regeneration using MSC**	Simon Hoerstrup Brigitte von Rechenberg *
61	**Stroke DynamiX – Graphical and Causal Networks for Personalized Stroke Management**	Reinhard Furrer *** Sven Hirsch Zsolt Kulcsár Georg Spinner */***
62	**Studying Meniscus Degeneration *in vivo* simulating a horizontal complex meniscus tear in sheep**	Katja Nuss / Salim Darwiche * / Karina Klein Antonio Pozzi
63	**Sudden death in horses**	Nicole Borel * Anton Fürst Colin Schwarzwald
64	**Surgical safety and effectiveness in orthopedics: Swiss-wide multicenter evaluation and prediction of core outcomes in arthroscopic rotator cuff reconstruction**	Laurent Audigé * Christian Gerber ****
65	**The effect of pharmacological and mechanical stimulation on the chronically retracted torn rotator cuff muscle – An experimental study in sheep**	Christian Gerber */**** Brigitte von Rechenberg Karl Wieser ***
66	**The effect of reptarenavirus infection and Boid Inclusion Body Disease on hematology and blood biochemistry in captive Boa constrictor**	Regina Hofmann-Lehmann Anja Kipar * Annette Liesegang
67	**The importance of plasmin in synovial fluid for the healing of ACL ruptures #**	Sufian Ahmad Benjamin Gantenbein *

* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

Number	Title	Collaborators (CABMM members)
68	**Torsion Constants and Virtual Mechanical Tests are Valid Image-Based Surrogate Measures of Ovine Fracture Healing**	Hannah Dailey */*** Stephen Ferguson Katja Nuss / Salim Darwiche / Karina Klein Brigitte von Rechenberg
69	**Toward the combination of epigenetics and tissue engineering to generate cartilage *in vitro* #**	Killian Flégeau * (Marcy Zenobi-Wong **) Lee Ann Laurent-Applegate Marcy Zenobi-Wong
70	**Transcatheter aortic valve implantation of cell-free tissue engineered heart valves in sheep**	Simon Hoerstrup * Katja Nuss / Karina Klein
71	**Transcatheter pulmonary valve replacement of cell-free tissue engineered heart valves in sheep**	Simon Hoerstrup * Katja Nuss / Karina Klein
72	**Transplantation of autologous mesenchymal stem cells halts fatty atrophy of detached rotator cuff muscle after tendon repair: results from an ovine model**	Martin Flück */**** Marie-Noëlle Giraud
73	**Treatment of periprosthetic joint infections using photodynamic therapy**	Yvonne Achermann * Markus Grob *** Niels Kuster Peter Wahl *** Patrick Zingg ***
74	**Tumorgenicity after subcutaneous injection of a keratinocyte cell suspension – a safety study in nude rats**	Maurizio Calcagni Katja Nuss *
75	**Tumorigenicity of tissue engineered cartilage products – a safety study in mice**	Andrea Barbero Katja Nuss *
76	**Understanding myofibroblast activation in health and disease through spatially defined transcriptomic analysis of *de novo* grown microtissues**	Mario Benn */*** Enni Markkanen * Simon Pot *
77	**Virtual mechanical tests out-perform morphometric measures for assessment of mechanical stability of fracture healing *in vivo***	Hannah Dailey */*** Stephen Ferguson Katja Nuss / Salim Darwiche / Karina Klein Brigitte von Rechenberg
78	**Vitamin D metabolism in goat and sheep**	Annette Liesegang * Brigitte von Rechenberg
79	**Water-filtered infrared A (wIRA): new therapeutic strategies for treatment of chlamydial, other bacterial, and fungal infections in humans and animals**	Yvonne Achermann * Nicole Borel *



* principal investigator(s), ** corresponding CABMM member, *** no CABMM member, **** former CABMM member
# CABMM Start-up Grant project

summary publications 2022 (order date of publication)

Number	
1	Hafezi F, Hillen M, Kollros L, Hafezi NL, Torres-Netto EA **Corneal Cross-linking in Thin Corneas: From Origins to State of the Art** *touchREVIEWS in Ophthalmology, 2022;16(1):13-6*
2	Generali M, Kehl D, Wanner D, Okoniewski MJ, Hoerstrup SP, Cinelli P **Heterogenous expression of ACE2 and TMPRRS2 in mesenchymal stromal cells** *J Cell Mol Med, 2022 Jan;26(1):228-234*
3	Hafezi F, Kling S, Gilardoni F, Hafezi N, Hillen M, Abrishamchi R, Gomes JAP, Mazzotta C, Randleman JB, Torres-Netto EA **Reply to comment on: Indvidualized Corneal Cross-linking With Riboflavin and UV-A in Ultrathin Corneas: The Sub400 Protocol** *Am J Ophthalmol, 2022 Jan;233:243-245*
4	Frese L, Darwiche SE, Gunning ME, Hoerstrup SP, von Rechenberg B, Giovanoli P, Calcagni M **Optimizing large-scale autologous human keratinocyte sheets for major burns – Toward an animal-free production and a more accessible clinical application** *Health Sci Rep, 2022 Jan 7;5(1):e449*
5	Hafezi F, Hosny M, Shetty R, Knyazer B, Chen S, Wang Q, Hashemi H, Torres-Netto EA; PACK-CXL Working Group **PACK-CXL vs. antimicrobial therapy for bacterial, fungal, and mixed infectious keratitis: a prospective randomized phase 3 trial** *Eye Vis (Lond), 2022 Jan 7;9(1):2*
6	Tai YK, Chan KKW, Fong CHH, Ramanan S, Yap JLY, Yin JN, Yip YS, Tan WR, Koh APF, Tan NS, Chan CW, Huang RYJ, Li JZ, Fröhlich J, Franco-Obregón A **Modulated TRPC1 Expression Predicts Sensitivity of Breast Cancer to Doxorubicin and Magnetic Field Therapy: Segue Towards a Precision Medicine Approach** *Front Oncol, 2022 Jan 24;11:783803*
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UZH News

Thomas Gull, translation by Mark Rabinowitz
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The Ophthalmologist

Farhad Hafezi
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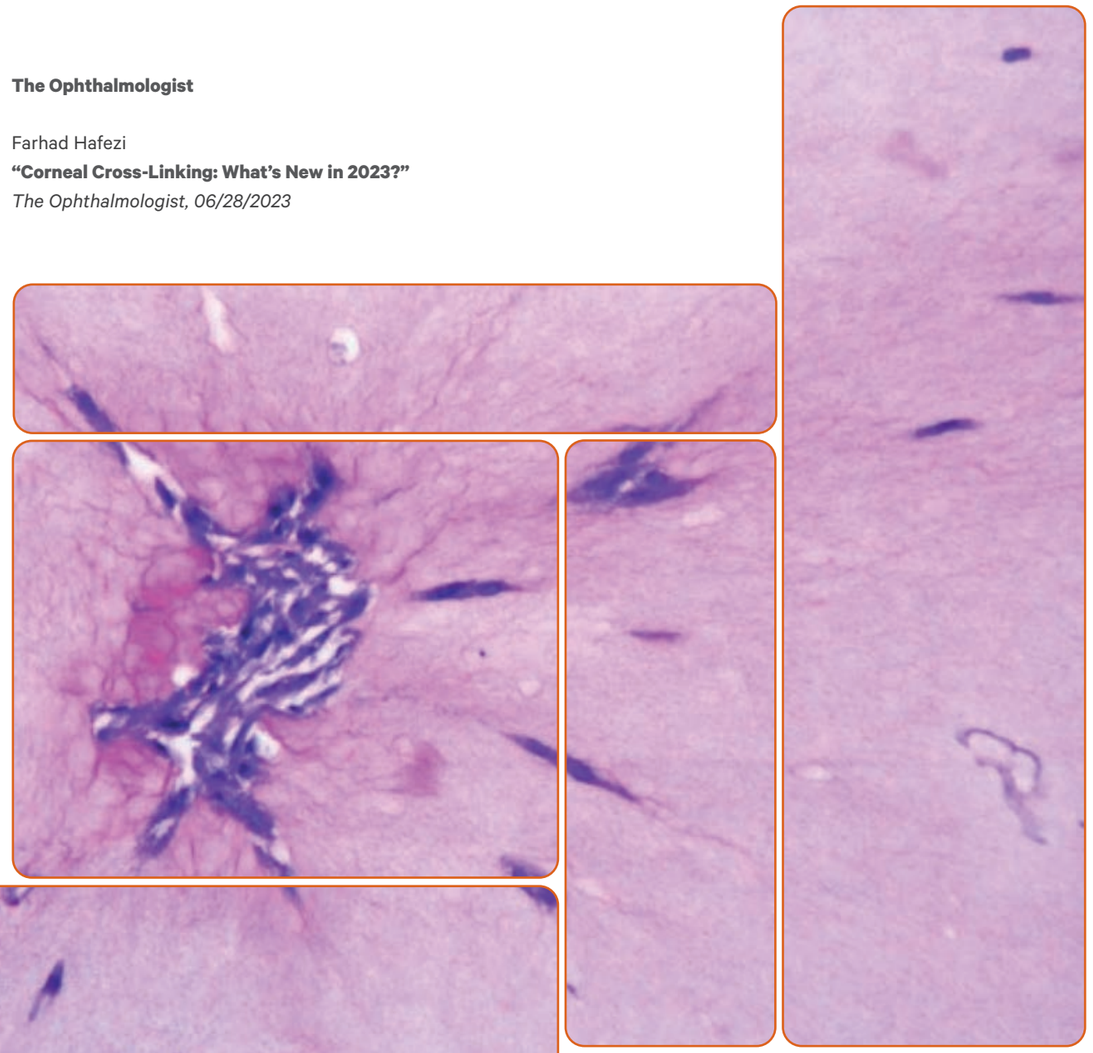
The Ophthalmologist, 06/28/2023



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