

CABMM's **Professor Brigitte von Rechenberg** on the translational medicine and research undertaken by the competence centre

Not lost in translation

Translational medicine is the key issue where results from *in vitro* and *in vivo* experiments are taken to novel therapeutic approaches in clinics. The expertise of medical doctors and veterinarians as clinicians and basic scientists are combined for studying pathomechanisms and etiologies of diseases and translating them into novel therapies, often in combination with the expertise of members of the biotechnology and/or regenerative field.

Proof of principle testing is performed in preclinical studies with experimental animals under good laboratory practice (GLP) conditions including small rodents and large animals such as sheep, goats and pigs. The Vetsuisse Faculty provides an ideal environment for preclinical studies. Furthermore, clinical trials are conducted in animals and humans until (biotechnological) products can be brought to market safely and for the benefit of patients (good clinical practice (GCP) – accreditation at the University Hospital of Zurich).

The variety and tight collaboration between members in this application field at CABMM is impressive. In the group led by F Althaus, the roles of poly (ADP-ribose) polymerases (PAR) and poly (ADP-ribose) glycohydrolases (PARG) in cell death and autophagy are investigated. Mechanisms of the tight connection between the uterus and the placenta are the focus in the field of reproduction with A Boos and his team.

M Blauth studies osteoporosis as one of the prominent medical problems of the aged society in collaboration with the CABMM platform (P Richards). Together they showed that aminobisphosphonates enhance the osteogenic properties of bone mesenchymal stem cells in human patients. Furthermore, calcium metabolism plays an important role in this context (A Liesegang).



Clinical facilities at the Vetsuisse Faculty UZH with suitable infrastructure for preclinical studies and clinical expertise of personnel. Preclinical studies are conducted under GLP regulation

Osseointegration of medical devices, either in dental or orthopaedic surgery, are investigated by various groups clinically or experimentally (C Hämmerle, S Stübinger), while other members are interested in cartilage resurfacing (L Laurant-Applegate, B von Rechenberg) or bone substitutes (B von Rechenberg).

These preclinical and clinical studies are conducted by collaborating with basic researchers from the biotechnology or molecular medicine field who produce the novel cartilage matrices (W Stark, M Zenobi-Wong) or cell composites (P Cinelli).

Muscle degeneration

Muscle degeneration related to rotator cuff problems is the topic in other research groups (C Gerber, D Meyer, B von Rechenberg), where a valuable sheep model serves well to study the mechanisms of fatty degeneration and the influence of mechanical, pharmacological or cellular measures to enhance muscle regeneration together with members from the basic fields (J Snedeker). Clinical documentation, evaluation and validation of outcome instruments are the strength of clinical groups (L Audigé). Close to their work and tightly connected between groups is the research in tendon or ligament regeneration (T Fürst,

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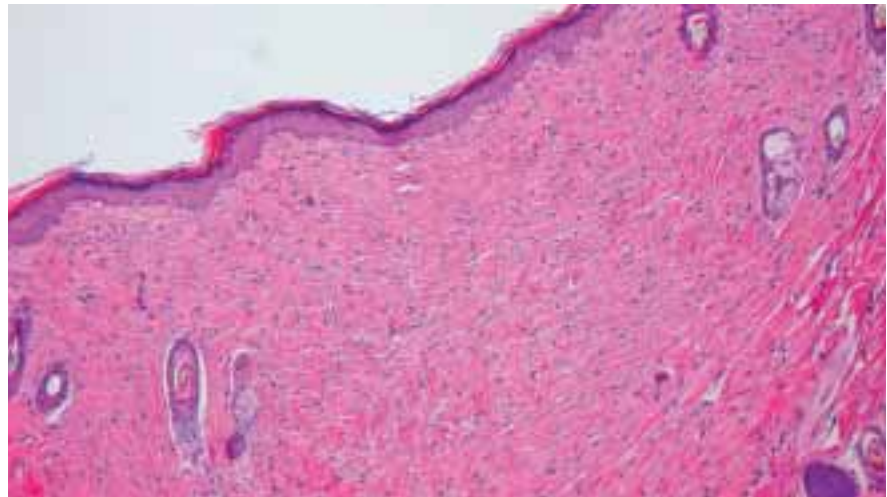
D Spreng), where dogs and horses are valuable disease models. Spine problems due to disc degeneration unite other members of the CABMM to search for novel surgical interventions (O Hausmann, F Steffen, B von Rechenberg) and/or regenerative therapies together with members from the regenerative field (S Ferguson, K Würtz, B Gantenbein).

Vascular abnormalities such as aneurisms are another focus field (D Rüfenacht, S Marbacher) and modern technologies for echocardiographs in large animals, as well as mice and rats, are available (C Schwarzwald).

Balanced anaesthesia and pain management are instrumental for patients and tissue regeneration, and are also important factors for ethical considerations using experimental animals and therefore research is also devoted to this area (P Kronen, C Spadavecchia). Diagnostic imaging plays a central part for diagnostics and measuring outcome parameters. The CABMM profits from its modern infrastructure and expertise at the Department of Diagnostic Imaging, and also by investigating improved technologies and contrast agents (P Kircher).

Translational research

Translational research is part of the new framework programme Horizon 2020 from the European Union. There are not many centres that, independently from grant projects, have a translational research network set up at their own universities, where basic scientists, clinicians, material scientists and industrial partners routinely work together to bring novel solutions and innovations in the field of biotechnology and molecular medicine to the medical market. The CABMM is such a network and an official competence centre at the University of Zurich (UZH), Switzerland.



Wound healing with biotechnological product after 28 days. Experiment in rats, note fully reconstituted epithelium and regular arrangement of collagen fibres in the dermis after such a short time period. Reduced scar tissue formation due to internal up-regulation of TGF-beta3

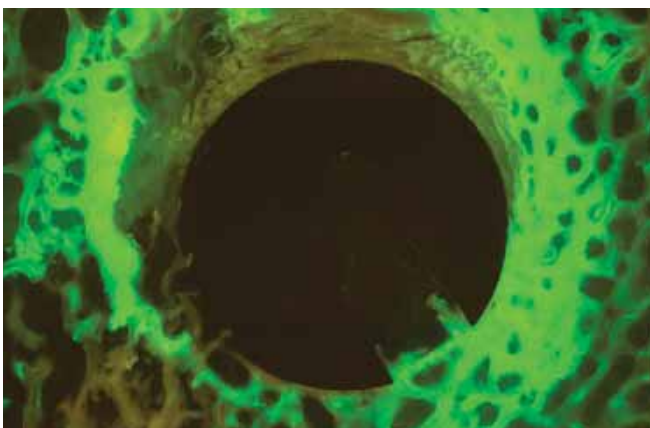
The location in Zurich is ideal for this network, where leading research institutions at the medical faculty and Vetsuisse Faculty of the UZH, as well as the Federal Institute of Technology (ETHZ), are within walking distance and where scientific exchange is facilitated by close and daily interactions on all levels. All three schools belong to the leading institutions in Europe and again being unique, there is no other location in Europe (where the expertise of the medical and veterinary school with facilities for preclinical studies and researchers from the technology side at the ETHZ) can encounter this daily exchange. An ultramodern and vast infrastructure at all institutions guarantees access to the most modern technologies in the field of biotechnology.

Unique approach

Normally, research networks centre on a research topic. However, the CABMM has a different approach, making it unique, since translation in applied biotechnology and molecular medicine is not centered on a research topic, but includes many different areas in the medical, veterinary and materials field that finally make translation possible. Four major fields are represented in the CABMM: experimental medicine and surgery; molecular medicine; regenerative medicine; and applied biotechnology.

Regulatory affairs are cornerstones in translational medicine for bringing novel solutions to the patient and to the market. The CABMM is the only network at a university in Europe that offers solutions for regulatory affairs under one roof. Accreditations for good manufacturing practice (GMP), good clinical practice (GCP) and good laboratory practice (GLP) that are required for the registration of novel medical products at the Food and Drug Administration (FDA) are available at the CABMM, and make it possible to keep translation from the very beginning of an innovation in focus, and get there effectively also for industrial partners.

Bone apposition close to a ligament reconstruction with pressfit technique at three months after surgery. Green fluorescence shows the newly formed bone around the implant. The ligament is visible too close to the anchor



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