Guest Editorial

Jan-Christoph Simon* and Carsten Werner

12 years more than just skin and bones: the CRC Transregio 67

<https://doi.org/10.1515/hsz-2021-0353>

In 2009, the German Research Foundation (DFG) established the collaborative research center (CRC) TRR67 “Functional biomaterials for controlling healing processes in bone and skin tissue – from material science to clinical application” (<https://research.uni-leipzig.de/trr67/>) as a joint effort of Leipzig University and Technische Universität Dresden with partners from Jena and the Technische Universität Berlin.

The demographic trends in Germany and other industrialized nations result in a considerable increase in patients with bone defects and chronic wounds. This requires the development of novel functional biomaterials, which improve bone and skin regeneration in an aging, multimorbid population. New knowledge about the role of the extracellular matrix (ECM) for the regeneration of tissues opens up new opportunities for the design of innovative biomaterials. In particular, the structure and composition of ECM significantly influences cellular differentiation and function and the healing of tissues. Hence, the aim of the TRR 67 was to develop and investigate novel functional biomaterials based on naturally occurring and chemically modified, artificial ECM. Essential functional components of these materials are glycosaminoglycan (GAG) derivatives and proteoglycan analogs in combination with structural proteins or synthetic carrier components.

To address these questions, the CRC TRR67 relied on an innovative, highly interdisciplinary approach, bringing together experts from chemistry, material science, cell biology, engineering, mathematical modeling, medical physics, immunology, pharmaceutical technology and clinicians treating patients with skin and bone defects. The CRC built on four research areas:

Research Area A Matrix Engineering comprised the material science/chemistry oriented projects, including analytics and modeling: The subprojects A1 and A3 focused on the production of carrier substances and the design of GAG-based biomaterials. Of central importance was the targeted chemical functionalization of selected GAGs (A8, A10), the synthesis of three-dimensional artificial extracellular matrix (aECM) (A3, A10) and their coupling to carrier substances (immobilization, delivery systems, scaffolds, A1, A4, A10). The aim was to generate multifunctional materials by combining different mechanisms (e.g. sequestration and delivery) with good degradability. This was complemented by a detailed biochemical, biophysical and *in silico* characterization of the interactions of GAG derivatives with the bone and skin by A3, A4, A6, A7 and the rational design of GAG derivatives, so-called rationally engineered GAG (reGAG).

Research Area B Biological profiles in cellular systems and aECM-based tissue regeneration bundled projects with cell biological and preclinical orientation. One line of investigation was the systematic characterization of matrix/cell interactions in complex systems. A particular focus was on cell types that entered into intensive matrix contacts during bone and skin regeneration, such as mesenchymal stem cells, osteoblasts, osteoclasts, osteocytes (B1, B2, B11), immunocompetent cells, keratinocytes, melanocytes and fibroblasts (B3, B4, B10).

Project Area T – Transfer: Here we aimed to use our knowledge about the regenerative abilities of ECM components to significantly improve the osseointegration of orthopedic implants. Together with an industry partner, we established coating procedures for existing biomaterial products and optimized the process considering the material shelf life, reproducibility and sterilization process to meet the requirements for medical product approval. The bioactivity was tested both *in vitro* and finally validated in a relevant preclinical large animal model. This served the long-term goal to identify a novel coating that significantly enhanced implant integration and enabled the clinical application of these individualized biomaterials.

Project Area Z combined methodologically oriented projects that provided service to all subprojects such as all

*Corresponding author: Jan-Christoph Simon, Department of Dermatology, Venerology and Allergology, Leipzig University, Leipzig, Germany, E-mail: Jan-Christoph.Simon@medizin.uni-leipzig.de
Carsten Werner, Leibniz-Institut für Polymerforschung eV, Dresden, Germany, E-mail: carsten.werner@tu-dresden.de. <https://orcid.org/0000-0003-0189-3448>

routine syntheses and the analysis of GAG derivatives as well as the generation of aECM (Z3) and a proteomics platform for qualitative and quantitative analysis of proteins from cellular test systems and animal models (Z4).

The highlights of TRR67 research from the last four years are summarized in this Highlight Issue of *Biological Chemistry*, either in form of a review or with original research papers. The reviews provide a summary of the results obtained in the last funding period, whereas the original articles refer to very recent data – accordingly we consider it a good mixture to present the work of the TRR67 to the readership of the journal.

We cordially thank the DFG for sustained support that not only has allowed performing research, but also the

training of young scientists in the Integrated Research Training Group (IRTG) “Matrix Engineering”. We are grateful to the editorial staff of *Biological Chemistry*, in particular to the Managing Editor, Torsten Krüger, who supported the publication of this Highlight Issue.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: The CRC Transregio 67 was supported by the Deutsche Forschungsgemeinschaft, Projektnummer 59307082.

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.