Due to their high prevalence, liver diseases are of great clinical and socio-economic importance. Liver diseases are frequently chronic and are systemically relevant because they can affect the function of other organ systems. Apart from prophylactic measures, therapeutic approaches are required which target at the molecular and cell biological level the pathogenetic events which lead to liver damage and accompanying extrahepatic manifestations, and simultaneously support liver regeneration. The events that lead to the restoration of liver tissue after injury at the molecular, cellular, organ and systemic level are complex and incompletely understood. They involve not only the proliferation of hepatocytes and, if necessary, the recruitment of stem/progenitor cell compartments, but also a multitude of other factors that control and influence the regenerative process in the liver. Such factors include cytokines, chemokines and growth factors, cell hydration, mechanical forces, organic osmolytes, extracellular matrix constituents, complement factors, bile salts and liver pathogens. Since many of these factors are also involved in the pathogenesis of liver damage, it becomes clear that liver damage and regeneration are closely interrelated.

An indispensible prerequisite for the understanding of liver damage and regeneration is an in-depth knowledge about liver function under physiological and pathological conditions. This was addressed in two consecutive Collaborative Research Centers (CRC), i.e. the CRCs 575 and 974 funded by the Deutsche Forschungsgemeinschaft (DFG). The CRC 575 „Experimental Hepatology“ was established in 2001 and ended in December 2011 after its maximal funding period, and already in January 2012 the CRC 974 „Communication and System Relevance in Liver Injury and Regeneration“ started its work, which ended in 2021. This allowed for an uninterrupted and highly successful interdisciplinary liver research at the Heinrich Heine University Düsseldorf over a period of more than 20 years. Major achievements and discoveries in the CRCs 575 and 974 were the identification of liver cell volume as a dynamic parameter, which controls various aspects of liver function by means of mechanosensing and -signaling pathways. Mechanosensing by sinusoidal endothelial cells and hepatic stellate cells was established as an important trigger for liver regeneration. Hepatic stellate cells were identified as mesenchymal stem cells and the space of Disse as a stem cell niche. A nowadays widely accepted model for the pathogenesis of hepatic encephalopathy has been developed. Further discoveries include enforced viral replication, novel aspects on hepatic ammonia handling and on hepatobiliary transport, the role of bile acid receptors in health and disease, and the role of cytokine signaling for liver damage and regeneration. In collaboration with other partners several human diseases were described for the first time, such as congenital glutamine synthetase deficiency, taurine transporter (TAUT) deficiency and antibody-induced BSEP deficiency. Essential for the success of the CRCs was the interdisciplinary approach, which brought together the expertise of clinical hepatology, neurology, immunology, cell and molecular biology, biochemistry, protein and structure chemistry and molecular dynamics simulations.

The present Highlight Issue of Biological Chemistry provides reviews on some topics of the CRCs, and we thank the DFG for continued support and the possibility to train young scientists in the integrated research training group and to bring them into contact with the international scientific community. Finally we are grateful to the support by the editorial staff of Biological Chemistry, in particular to the Managing Editor Torsten Krüger.

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