Another project also received a TRP Starter Grant in 2022:

**Development of a novel platelet inhibitor for the prevention and treatment of atherothrombosis**

Platelet aggregation inhibitors have been shown to protect against heart attacks and are, therefore, a cornerstone of cardiovascular medicine. They prevent coronary arteries from closing when atherosclerosis breaks down and activates platelets. However, the use of conventional platelet aggregation inhibitors does not provide complete protection and is associated with bleeding complications. The project team has developed a new platelet inhibitor that prevents plaque-induced platelet aggregation in vitro and arterial thrombosis in a mouse model without interfering with hemostasis.
The group plans to investigate whether their findings can be translated to the human system. To do so, they plan to reproduce their previous results and generate additional data using alternative measurements of thrombus formation in stromal chamber models. In addition, the scientists will investigate the pharmacodynamics and pharmacokinetics of the new inhibitor.


Collaboration with Product Development Unit of DZIF

In 2021, the DZHK and the German Center for Infection Research (DZIF) have agreed on closer collaboration in the development of novel drugs and medical devices. The DZHK’s project leaders now can call on the DZIF’s Product Development Unit (PDU) for expert advice. In the year under review, two ongoing translational research projects used the PDU’s advisory services. The PDU supports the projects in project management and regulatory approval issues.

Cardiomyocyte–specific restoration of endogenous transcription of KLF15 as a novel therapeutic concept in heart failure

Many factors, including coronary artery disease and hypertension, contribute to a high prevalence of cardiovascular disease. These are characterized by weakening of the myocardium due to a loss of functional cardiomyocytes. The cause may be a dysregulation of healthy gene transcription. Researchers hypothesize that precise restoration of this healthy transcription may prevent the deterioration of cardiomyocyte function or rescue it from failure. Among these factors, the team of scientists has identified a repressor of disease pathways, Krüppel-like factor 15 (KLF15), which is lost during hypertrophic remodeling of the heart. When a genetic system is used to normalize transcription of KLF15 in cardiac muscle cells, attenuation of the pathological response and preservation of cardiac function is observed in mice. The scientists were also able to replicate the loss of KLF15 and repair the loss in a human heart muscle model. In this project, they will test the safety and efficacy of this novel therapeutic principle in a pig model.

Project lead: Laura C. Zelarayán-Behrend (Göttingen) | Participating scientists: Eric Schoger, Rabea Hinkel (both Göttingen partner site), Lorenz Lehmann (Heidelberg/Mannheim) | Duration: 2023–2024 | Budget: €149,976