

New Collaborative Research Centers

Atherosclerosis and general homeostasis

LMU researchers will coordinate the work of two new Collaborative Research Centers, for which funding has now been approved by the *Deutsche Forschungsgemeinschaft* (DFG).

Atherosclerosis and the ability of the body to autonomously regulate its basic physiological processes in response to environmental changes are the central themes of two new DFG-funded Collaborative Research Centers (CRCs), which will both be coordinated by LMU researchers. The CRC on “Atherosclerosis – Mechanisms and New Networks of Therapeutic Target Structures”, whose Coordinator Professor Christian Weber is Director of the Institute for Cardiovascular Prevention (IPEK) at LMU, will investigate the molecular mechanisms that give rise to, and govern the development of, atherosclerosis. Professor Thomas Gudermann, Director of the Walther Straub Institute for Pharmacology and Toxicology at LMU, will serve as Coordinator for the CRC/Transregio on “Regulation of Whole-Body Homeostasis via TRP Channel Modules”. This CRC will explore the multiple roles of so-called TRP channels, which are involved in the regulation of a wide range of vital bodily functions.

Atherosclerosis – Mechanisms and New Networks of Therapeutic Target Structures

Despite considerable progress in its management and therapy, cardiovascular disease remains the major cause of death in the Western world. The underlying factor common to most of these conditions is atherosclerosis. Atherosclerosis is characterized by localized pathological changes in the inner lining of the arteries, which lead to chronic inflammation and obstruction of blood flow. Eventually, the vessel may become completely blocked – causing a heart attack or a stroke.

In order to develop more effective strategies for the prevention and treatment of arterial disease, a better understanding of the pathogenesis and progression of atherosclerosis is crucial. This is where the new Collaborative Research Center (CRC) aims to make a difference. “We plan to characterize the molecular mechanisms that underlie atherosclerosis in detail to enable more efficient and reliable identification and validation of potential drug targets for therapeutic interventions”, explains Professor Christian Weber, Director of LMU’s Institute for Cardiovascular Prevention (IPEK) and Coordinator of the new CRC.

The inflammation associated with atherosclerosis develops over the course of many years, and is a dysfunctional immune reaction. At sites in the vasculature that are subject to abnormal stress, specialized immune cells circulating in the blood can attach to the cells lining the arterial wall and subsequently infiltrate between and underneath them. They continue to produce signal molecules that attract still more immune cells. As a consequence of the continuing influx of these cells and their biochemical activities, atherosclerotic plaques form. Further synthesis and secretion of signal molecules causes the immune response to go out of control, leading to complications such as plaque ruptures and clot formation. The new CRC will explore several therapeutic options, focusing on potential targets such as chemokines, the signal molecules that drive the immune response, as well as on genetic and epigenetic factors that promote arterial pathogenesis. For the validation of newly identified therapeutic targets, novel high-resolution imaging technologies and a number of so-called conditional knockout models – transgenic mouse strains in which specific genes can be deleted by pharmacological intervention.

“The most important feature of the CRC ‘Atherosclerosis’ is its interdisciplinary nature. We will concentrate on integrated analyses and will study the causal links between metabolic processes, molecular signaling pathways and genetic factors,” says Christian Weber. In addition to several institutes affiliated with the Faculty of Medicine (IPEK, the Institutes for Stroke and Dementia Research, and for Laboratory Medicine, and the Clinics for Cardiology and Endocrinology), the Institute for Informatics at LMU will also contribute its expertise to the CRC.

The new Munich-based CRC begins on 1. October 2014, and has received funding amounting to around 11 million euros for the period up to 2018. In addition to LMU as coordinator, the Technical University Munich, the Helmholtz Center Munich and the Max Planck Institute for Biochemistry are partners in the project.

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