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External Seminar Speaker

Dr. Anja Karlstaedt
Department of Internal Medicine
University of Texas Medical School Houston

Place: **Analysezentrum 3, 2. OG, Room 02.332**
Date: **Wednesday, October 25th**
Time: **5.30 pm**

Cancer and the heart – Oncometabolic dysregulation of cardiac metabolism

Intermediary metabolism does not exist in isolation. Metabolic changes are the result of an integrated response from the nonlinear interactions between genes, proteins and metabolites. Metabolic reprogramming is a hallmark of cancer and cardiac metabolism, because certain metabolic features are observed in the heart during an altered physiologic or metabolic environment as well as across many types of tumors. Among cancer survivors, cardiovascular disease is the leading cause of death and disability. Improved treatments have increased patient survival, but despite these efforts survivors have a five-fold higher risk for developing heart failure irrespective of the chemotherapies. The challenge is now to develop new strategies that target the tumor while protecting the heart from failing. Precisely how metabolic alterations are enabling structural remodeling in the heart and how to exploit metabolism for therapeutic benefit are key questions. In isocitrate dehydrogenase (*IDH*) 1 and 2 mutant tumors, the increased production of the oncometabolite D-2-hydroxy-glutarate (D2-HG) is associated with systemic effects, including dilated cardiomyopathy. About 20% of acute myeloid leujemia (AML) cases harbor mutations of the IDH, which lead to significantly reduced patient survival and cause metabolic dysfunction through a neomorphic activity of reducing α-ketoglutarate to the oncometabolite D2-HG. We recently discovered that D2-HG mediates cardiac dysfunction by inhibiting α-ketoglutarate dehydrogenase (α-KGDH), which in turn leads to redirection of Krebs cycle intermediates, increased ATP citrate lyase activity (ACL), and increased histone 3 pan-acetylation. Our goal is to identify metabolic pathways and specific proteins that can be targeted to slow cancer growth and, at the same time, protect the heart. In short, understanding how oncometabolic stress drives development of heart failure will change the way cancer and heart failure patients are treated.

Host: **Prof. Dr. med. Johannes Backs**
Director of the Department Molecular Cardiology and Epigenetics
Department of Internal Medicine VIII
University of Heidelberg