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Prof. Ulrich Kintscher, M.D.
Charité - Universitätsmedizin Berlin
Director, Institute of Pharmacology, Center for Cardiovascular Research, CCR, Berlin, Germany

Adipose Tissue Lipolysis and Chronic Heart Failure

Adipose tissue lipolysis often occurs during the development of chronic heart failure (CHF) because of chronic adrenergic stimulation and increased natriuretic peptide levels. However, the impact of enhanced lipolysis on cardiac function is mainly unknown. To investigate the role of ATL during CHF-development we generated mice with impaired lipolytic capacity. Mice deficient for adipose triglyceride lipase (ATGL) (atATGL-KO) were subjected to transverse aortic constriction (TAC). The cardiac mouse lipidome was analyzed by shotgun lipidomics using a Q-Exactive mass spectrometer. TAC-induced cardiac dysfunction was attenuated in atATGL-KO compared to control (wt) mice. In particular, TAC-induced increases in left ventricular mass (LVM) was significantly reduced in those mice. In addition, atATGL-KO mice were completely protected against TAC-induced systolic LV-failure. Perturbation of ATL in atATGL-KO mice resulted in the prevention of major cardiac lipidome changes observed after TAC in wt mice. Lipidomics data indicated that phosphatidylethanolamines were markedly induced solely in failing wt-hearts. TAC-induced cardiac PE-induction resulted in a lipid species-specific decrease of PC/ PE-ratios exclusively in failing wt-hearts, a process previously associated with apoptosis.

Perturbation of adipose tissue lipolysis leads to an improvement of CHF, accompanied with the prevention of deleterious cardiac lipidome changes. Therefore, modulation of the cardiac lipidome may play an important role in the pathogenesis of CHF.