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Impact of inflammation on disease progression and extracellular matrix remodeling in failing hearts

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Background: Cardiovascular disease including heart failure (HF) are the most frequent cause of death in Europe. There are several pathophysiologic conditions which contribute to the pathogenesis of myocardial dysfunction such as ischemia, volume and/or pressure overload, aging Recently, immune cells and immune mediators have been reported to play important roles in these. Here, we aim to identify the role of cardiac antigen-specific T-cell activation and recruitment in the development of left ventricle (LV) hypertrophy, cardiac remodeling in non-ischemic HF.

We hypothesize that boosting protective immune responses by transferring antigen-specific T-cells into recipient mice subjected to pressure-overload induced heart failure enhances extracellular matrix remodeling.

Aim: Evaluate the effects of adoptive transfer of myosin heart-specific T-cells in an experimental murine model, to check whether these specific T-cells infiltrate the heart, modulate the inflammatory cardiac micromilieu and thereby healing outcomes.

Methods: Evaluate the effects of adoptive transfer of heart-specific T-cells in an experimental model of pressure-overload induced heart failure by transferring T-cells expressing transgenic TCRs specific for a cardiac myosin heavy chain alpha antigen (TCR-M cells). TCR-M cells will be purified from spleens and LN of donor mice using magnetic cell-sorting under sterile conditions and then transferred into syngeneic infarcted mice via the tail vein. As control group, we will adoptively transfer CD4+ T-cells specific for ovalbumin as this is an irrelevant antigen. Survival rate will be recorded. Cardiovascular outcome of recipient mice will be monitored by serial echocardiography (primary readout) on D7 and D28. Cardiac mass (hypertrophy) will be determined by LV weights, and lung congestion by wet lung weight. Interstitial fibrosis in the remote area will be quantified by histology (picrosirius red) and confirmed by collagen mRNA expression.