Background: Alpha-1-adrenoceptors (α₁-ARs) play a complex role in heart failure. Clinical trials with α₁-AR antagonists in heart failure patients have shown negative outcome, and in various transgenic mouse models of heart failure α₁-ARs have been shown to preserve cardiac function and to increase survival. Therefore, although these receptors induce hypertrophy in cardiomyocyte cultures, α₁-AR stimulation seems to be beneficial in heart failure. The mechanisms underlying these findings remain unknown. An interesting model to study the role of α₁-ARs in heart failure is the mouse with cardiomyocyte specific inducible deletion of the Serca2 gene. This deletion is associated with development of acute heart failure. Cardiac function is gradually reduced until day 6 after induction of gene excision, after which myocardial contractile function gradually improves in face of a progressive SERCA2 loss. Regulation of compensatory mechanisms is not known.

Hypothesis: α₁-AR signalling is important for the compensatory mechanisms operating during acute heart failure. Firstly, increased α₁-AR mediated positive inotropic response increases cardiac contractility. Secondly, increased α₁-AR activation induces upregulation of proteins important for improving myocardial contractility.

Methods: Left ventricular strips were harvested at different time points after excision of the Serca2 gene, and contraction-relaxation-cycles were recorded in the absence and presence of α₁-AR agonist.

Results: Preliminary results show no alterations in α₁-AR mediated positive inotropic response (PIR) 4 days after gene deletion. 6 days after deletion the PIRs were of the same magnitude, but the early negative component in the triphasic response was absent. After 12 days, α₁-AR mediated PIR is increased compared to control.

Conclusion: α₁-AR mediated PIR is altered both in development and amplitude after deletion of the Serca2 gene. The data suggest that alpha-1-AR has an important role in regulation of compensatory mechanisms of contractility in Serca2 KO mice, and in further experiments we will test the effect of alpha-1-AR blockers on in vivo contractile function.