The SERCA2 Ca\textsuperscript{2+}-ATPase is of central importance for refilling of the sarcoplasmic reticulum (SR) Ca\textsuperscript{2+} store and cardiac contractility. Reduced SERCA2 function is associated with heart failure in animal models of heart failure and in human patients. We hypothesized that loss of SERCA2 would result in immediate severe myocardial contractile dysfunction and death. In a new transgenic mouse model, the *Serca2* (*Atp2a2*) gene is excised in the cardiomyocytes by tamoxifen administration in adult animals. We have previously shown that SERCA2 expression is reduced to a background level (<5%) in the myocardium within 3 week and is not detectable in isolated cardiomyocytes at 4 weeks. At the 4 weeks time point, cardiac function was remarkably well preserved. We found that the left atrial diameter, lung mass and left-ventricular end-diastolic pressure (LVEDP) were slightly increased in SERCA2KO mice compared with controls, and the maximal rates of pressure development and decline in the left ventricle were affected with a prolongation of the ventricular relaxation time. Furthermore, calcium cycling over the plasma membrane was enhanced and the relationship between calcium transients and contractions suggested an enhancement of myofilament Ca\textsuperscript{2+} responsiveness.

Seven to eight weeks after deletion of the *Serca2* gene, SERCA2KO mice developed severe terminal congestive heart failure with poor contractile function, elevated LVEDP and pronounced increases in lung and atrial mass. SERCA2KO hearts developed dilated atria and right ventricle, but only a modest increase in right ventricular mass. In contrast, the left ventricle did not dilate and the left ventricular mass was unaltered in SERCA2KO mice compared with controls. Even so, mRNA transcripts regarded as hypertrophy markers, such as b-myosin heavy chain, ANP and BNP, were strongly induced in the left ventricle at 7 weeks. With the exception of b-myosin heavy chain, contractile protein transcripts were unchanged or modestly altered. Thus, SERCA2KO mice at the 7 week time point did not reflect the typical hypertrophic response seen in post-infarction or pressure overload heart failure mice. Throughout the time course (1-7 weeks), there was no major visible myocardial disarray, with a scattered modest deposition of collagen surrounding individual fibers.

In conclusion, loss of SERCA2 function in the cardiomyocytes and poor cardiac function per se does not induce a left ventricular hypertrophic response. Furthermore, the mechanisms that compensate for the loss of SERCA2 at earlier time points (<4 weeks) are not sufficient for long-term support (>7 weeks) of heart function in adult SERCA2KO mice.