Abstract: P119

Cardiac remodeling in response to cold and deacclimation: role of autophagy

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Introduction: Chronic exposure to cold is known to cause cardiac hypertrophy independently of elevations in blood pressure. This phenomenon is reversible after returning to thermo-neutral conditions. The aim of this study was to investigate the role of autophagy in cold-induced cardiac hypertrophy development and its posterior reversion.

Methods: Studies in vivo were performed in two-month old mice, exposed to cold (4 ºC) for 24 hours or three weeks. After this period, the animals were put into thermo-neutral conditions (30ºC) for 24 hours or one week.

Results: Chronic cold exposure significantly increased the heart weight/tibia length (HW/TL) ratio as well as the mean area of cardiomyocytes. Moreover, the expression of hypertrophic marker genes (Anf, a-Actinin and α/β-Mhc ratio) was significantly up-regulated in our conditions whereas genes involved in fatty acid oxidation were down-regulated, suggesting a switch in the energy substrate used by the cardiac tissue under hypertrophic conditions. One week of thermo-neutral deacclimation led to a significant decrease in the hypertrophic markers compared to animals exposed to chronic cold. The analysis of the protein levels of the autophagy markers Lc3b II and p62 in heart indicated that autophagy was repressed in response to cold, and re-activated during the first 24 hours after returning to thermo-neutral conditions. The autophagic flux, determined by assessment of LC3b II after leupeptin treatment in vivo, was repressed during cold exposure and strongly reactivated after 24 hours of thermoneutrality. We further confirmed these results using electron microscopy and we found increased abundance of autophagosomes after acute deacclimation.

Conclusions: Our data indicates that mice exposed to three weeks of cold develop a marked cardiac hypertrophy, reversed after one week of deacclimation. We propose autophagy as one of the mechanisms leading to heart remodeling in response to cold exposure and its posterior reversion after deacclimation.