ER\(\beta\) prevents up-regulation of miRNAs under pressure overload in LV of female mice

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Sex differences have been observed in patients with aortic stenosis, women develop a more concentric form of myocardial hypertrophy than men and men have a stronger activation of profibrotic genes. Transverse aortic constriction induces more ventricular dilatation and fibrosis in male than in female mice which is partially mediated by oestrogen receptor beta (ER\(\beta\)). Cardiac microRNAs contribute to the regulation of gene expression in hypertrophy but their control by sex or ER\(\beta\) is yet unknown. We therefore analysed whether cardiac microRNA are regulated by sex or ER\(\beta\), whether this occurs under pressure overload and affects hypertrophy associated pathways.

Study objective: elucidate the involvement of microRNAs in the sex differences observed in heart diseases and identify the putative role of ER\(\beta\).

Methods: qRT-PCR quantification of 60 cardiac microRNAs isolated from the left ventricle of mice 9 week after TAC or sham surgery in control and ER\(\beta\) deleted animals.

Results: 33 microRNAs were regulated sex-specifically after pressure overload, 32 were more pronounced in males than in females. In mice lacking ER\(\beta\) the sex-specific up-regulation in males was abolished. A pathways enrichment analysis of targets of the sex-specifically regulated microRNAs identified MAPK signalling, extracellular matrix organization and mitochondrial metabolism genes.

Conclusion: Sex specific regulation of microRNA may contribute to sex differences in myocardial remodelling under pressure overload. ER\(\beta\) inhibits the sex-specific up-regulation of fibrosis- and metabolism-associated microRNAs in the female hearts under pressure overload and may thereby contribute to a more favourable remodelling in females.