Technology Offer

Ref.-No. M0208

CREM-IbΔC-X transgenic mice as a tool to study atrial fibrillation

Introduction

The transcriptional activation mediated by cAMP-response element (CRE) and transcription factors of the CRE-binding protein (CREB)/CRE modulator (CREM) family represents an important mechanism of cAMP-dependent gene regulation possibly implicated in detrimental effects of chronic β-adrenergic stimulation in end-stage heart failure.
The detailed knowledge of CREM-mediated transcriptional control and of specific downstream targets of CREM in the human heart will therefore be of great interest for understanding the pathophysiology of heart failure.

There is a strong demand for an animal model to investigate heart failure, explicit atrial fibrillation in detail.

The Mouse Model

The transgenic mice have heart-directed expression of CREM-IbΔC-X, a human cardiac CREM isoform.
Ectopic heart-directed expression of human cardiac CREM isoform CREM-IbΔC-X in transgenic mice evoke a complex phenotype with changes in cardiac function that are contrary to alterations observed in CREM-deficient mice and fundamentally different from phenotypes of related mouse models with heart-directed expression of other suppressors of CRE-mediated transcriptional activation. CREM-IbΔC-X transgenic hearts showed complex changes in the expression or function of various regulatory proteins.
In transgenic ventricles, reduced phosphorylation of phospholamban and of the CREB was associated with increased activity of serine-threonine protein phosphatase 1. The density of ß1-adrenoreceptor was increased, and messenger RNAs encoding transcription factor dHAND and small G-protein RhoB were decreased in transgenic hearts as compared with wild-type controls. The results indicate that heart-directed expression of CREM-IbΔC-X leads to complex cardiac alterations, suggesting CREM as a central regulator of cardiac morphology, function, and gene expression.
CREM-IbΔC-X transgenic mice develop atrial fibrillation, probably as a consequence of dilatation and hypertrophy of atria, and might therefore represent a useful genetic mouse model to study the pathophysiology of this kind of arrhythmia.

Further Reading

Müller et al., Journal of Biological Chemistry, 2005, 280(8): 6906–6914

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