Late Breaking Science: Linking Genes to Function in the Heart and Vasculature

BASIC ABSTRACTS

Exogenous Hematopoietic Stem Cells Can Regenerate Infarcted Myocardium

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Studies from our laboratory and others have shown that transgenic (Tg) mice expressing low levels of active protein kinase C ε (PKCε) exhibit resistance to ischemic injury, a cardiopro-
tected phenotype analogous to that observed during preconditioning. Although PKCε has been shown to activate multiple downstream targets in preconditioning, the molecular components that mediate PKCε signaling remain unclear. In this study, we explored the role of PKCa (a downstream effector of PKCε) in the heart in the context of preconditioning. We generated transgenic mice expressing PKCa under the control of the cardiac troponin C (TnC) promot.

Results: Transgenic mice expressing PKCa (TgPKCa) exhibited lower infarct size compared to control mice following ischemia-reperfusion injury. PKCa overexpression protected the heart against injury, with a significant reduction of cardiac troponin I (cTnI) and cTnT levels in the heart. Immunohistochemistry demonstrated that PKCa was localized to the cardiomyocytes and the extracellular matrix, indicating a role for PKCa in cardiac remodeling. The protective effect of PKCa overexpression was mediated by the PDZ-protein interacting with C kinase II (PI3K) pathway, which is a well-known signaling cascade in preconditioning. These findings suggest that PKCa could be a potential therapeutic target for the treatment of ischemic heart disease, providing a novel perspective for the development of novel treatments.

Transgenic mice expressing PKCa under the control of the cardiac troponin C (TnC) promoter were generated. Mice were subjected to ischemia-reperfusion injury followed by analysis of infarct size and cardiac function. Immunohistochemistry and Western blotting were performed to determine the localization and expression of PKCa. Cardiac function was assessed by echocardiography, and myocardial infarction was quantified by measuring cardiac troponin I (cTnI) and cTnT levels.

Conclusions: PKCa overexpression offers promise as a novel therapeutic target for the treatment of ischemic heart disease, highlighting the potential of PKCa as a regulator of cardiac remodeling.

Dual Modulation of Cell Survival and Cell Death by β2-Adrenergic Gi and Gs Signaling in Adult Mouse Cardiac Myocytes

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Cardiac β2-AR activates both Gs and Gi proteins whereas β1-AR couples only to Gs. The goal of this study is to determine whether β1-AR and β2-AR differ in regulating cardiomyocyte survival and apoptosis, if so, to explore underlying mechanisms. To avoid complicated crosstalks between β-AR subtypes, we express β1-AR or β2-AR individually in the null background (β2−/− or β1−/−, respectively). Using adult mouse myocyte culture and adenoviral gene transfer techniques, we observed the following results:

1. β1-AR, but not β2-AR, mediates cell survival effect.
2. β2-AR, but not β1-AR, mediates cell death effect.
3. The protective effect of β2-AR is mediated by the Gs-protein, whereas the pro-apoptotic effect is mediated by the Gi-protein.

Conclusion: β2-AR, but not β1-AR, couples to both Gi and Gs signaling pathways, regulating cardiac cell survival and death in different ways. This study provides important insights into the role of β-AR subtypes in cardiac function and disease.
Mutations in the R1α Regulatory Subunit of Protein Kinase A Cause Familial Cardiac Myxomas

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