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Title:

A Novel Role of the *st*eroidogenic *a*cute *r*egulatory (StAR) Protein in Non-steroidogenic Cardiac Cells: Induction of a Survival Factor Following Myocardial Infarction

המפגש יתקיים
ביום א', 14 יוני 2015, בשעה 9:00
מועדון סגל
(6/14/2015, 9:00, Faculty Club)

Abstract:

StAR was discovered a vital mitochondrial protein essential for high output steroid hormone synthesis in specialized cells of the gonads and the adrenal cortex. Nearly 20 years later, we have recently reported that StAR is also highly expressed in the non-steroidogenic cardiac tissue of the left ventricle in mouse heart recovering from experimental myocardial infarction (MI) (Anuka et al., Mol Endocrinol 27:1502, 2013). We show that StAR expression peaks at days 1-3 after MI, a period that constitutes a typical inflammatory phase known to occur in the damaged heart tissue suffering necrotic and apoptotic cell death. Immuno-histochemical studies suggest that StAR is not expressed in the cardiomyocytes. Instead, high content of mitochondrial StAR is expressed in resident cardiac fibroblasts, in endothelial cells ($CD31^+$) and blood-born progenitor cells ($CD34^+$) exclusively observed in blood vessels of the infarct area. Altogether, this pattern suggests that StAR is expressed in pre- or proto-myofibroblasts known to optionally differentiate *in vivo* from these progenitor cell types.

What then is the new role of StAR in the heart fibroblasts? I shall show that cardiac fibroblasts isolated from normal adult rat heart and put to culture, differentiate to myofibroblasts. Prior and following differentiation, such cells can be induced to express high StAR content when exposed to a strong pro-apoptotic inducer, staurosporine. While expressing StAR, the cells acquire anti-apoptotic robustness that solely depends on StAR presence and activity since StAR knockdown by siRNA, or expression of loss-of-function StAR mutants failed to protect the cells from apoptosis. Further studies suggest that StAR function also inhibits the association and activation of the pro-apoptotic BAX protein tethered to the mitochondrial outer membrane, cytochrome c release, mitochondrial fission and binding of annexin V to the cells. We therefore hypothesize that cardiac StAR protein functions in the capacity of anti-apoptotic survival factor protecting the fibroblast progenitor cells from cell death when recruited to the detrimental infarct environment. Hence, the spared cells can thus proliferate and differentiate to myofibroblasts responsible for the post-MI wound healing and tissue repair process.

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