**THE MOLECULAR MECHANISM OF GALECTIN-3-STIMULATED CARDIAC FIBROBLAST PROLIFERATION**

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Background: Cardiac fibroblasts can proliferate and increase the deposition of the extracellular matrix proteins leading to cardiac fibrosis and subsequent diastolic dysfunction. In the failing heart, aside from dynamic overload, immunologic and inflammatory processes also play an important role. Previous data revealed that cardiac macrophages are activated at an early stage in failure-prone, hypertrophied hearts and that these macrophages express galectin-3, a 26 KDa-galactoside-binding protein. In this study, we aim to investigate the proliferative effects of exogenously added galectin-3 on cultured cardiac fibroblasts, identify cell surface glycoproteins attached by galectin-3 and determine intracellular signaling pathways triggered by galectin-3.

Material and Method: Culture of cardiac fibroblasts, MTT assay, BrdUrd incorporation, Western blot analysis, Immunoprecipitation assay, and Immunocytochemistry.

Result: MTT assay revealed that the growth of cardiac fibroblasts treated with galectin-3 for 24hr significantly increased in a dose-dependent manner and BrdUrd incorporation assay showed the 1.24-fold increase of cell proliferation compared with control (p<0.05). Western blot analysis showed galectin-3 treatment increased tyrosine phosphorylation of epidermal growth factor receptor (EGFR) and phosphorylation of downstream mitogenic signal molecular ERK1/2. Immunoprecipitation assay revealed that galectin-3 interact with EGFR on cell membrane. In addition, we demonstrated colocalization of EGFR and galectin-3 by immunocytochemistry.

Conclusion: This study showed that exogenous galectin-3 cross-link with receptor tyrosine kinase, EGFR and induced autophosphorylation of EGFR and subsequent phosphorylation and activation of downstream mitogenic ERK pathway, ultimately leading to cardiac fibroblast proliferation. Our data may provide molecular basis for galectin-3 as a potential therapeutic target in the treatment of heart failure.