Fibroblast-specific SOCS3 deficient mice exhibits decreased myocardial fibrosis and increased cardiomyocyte survival after acute myocardial infarction

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Background: Left ventricular (LV) remodeling after acute myocardial infarction (AMI) results in poor cardiac performance leading to heart failure. LV remodeling after AMI is characterized by infarct expansion, LV dilation, and fibrosis of viable myocardium. Suppressor of cytokine signaling-3 (SOCS3) is an endogenous negative-feedback regulator of the STAT3 signaling pathway. We previously reported that myocardial SOCS3 plays a detrimental role in LV remodeling after AMI; however, the role of STAT3 and SOCS3 within fibroblast in LV remodeling after AMI remains elusive.

Objective: The aim of this study is to clarify the role of STAT3 and SOCS3 within fibroblasts in LV remodeling during AMI in mice.

Methods: To investigate the role of STAT3 signaling and SOCS3 within fibroblast, we generated tamoxifen-induced fibroblast-specific SOCS3-deficient (fib-SOCS3 KO) mice. AMI was induced by permanent ligation of the left anterior descending artery in mice. After 2 weeks of induction with tamoxifen, histological evaluation by Hematoxylin Eosin staining and Picro-Sirius Red staining, cardiac function evaluation by echocardiography using a Vevo 3100 Echo Imaging System (Visual Sonics), and protein expression using Western blot analysis were performed.

Results: There was no significant difference in 2-week survival rate between fib-SOCS3 KO group and wild type (WT). Two weeks after AMI, ventricular weight was less in fib-SOCS3 KO mice compared to WT mice (p<0.05). In terms of cardiac function, LV ejection fraction was predominantly increased in fib-SOCS3 KO mice compared with WT mice, as measured by the Area method (p<0.05). There was no difference in LV end-diastolic area, but LV end-systolic area was significantly less in fib-SOCS3 KO mice than in WT mice. Histologically, residual viable myocardium in the infarcted area was greater in fib-SOCS3 KO mice compared with WT mice. The percentage of fibrotic area in the LV short-axis plane was significantly less in fib-SOCS3 KO mice than in WT mice. Western blot analysis revealed that phosphorylated-STAT3 tended to be elevated in fib-SOCS3 KO mice than in WT mice.

Conclusions: Our data suggest that STAT3 and SOCS3 within fibroblast may play an important role in the prevention of LV remodeling after AMI.