MODULATION OF CARDIAC REMODELING AFTER CHRONIC ISCHEMIA BY LECTIN-LIKE OXIDIZED LOW-DENSITY LIPOPROTEIN RECEPTOR-1 DELETION

ACC Poster Contributions
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Background: Activation of LOX-1, a lectin-like ox-LDL receptor-1, exerts a significant role in collagen formation. We hypothesized that LOX-1 deletion may inhibit inflammatory/oxidative stress signals and reduce collagen accumulation, and attenuate cardiac remodeling after chronic ischemia.

Methods: Wild-type and LOX-1 KO mice were subjected to occlusion of left coronary artery for 3 wks. Markers of cardiac hypertrophy (ANP), fibrosis (collagen IV and fibronectin), activity of matrix metalloproteinases and their tissue inhibitors (Masson's Trichrome staining, Western blotting, multiplex bead system or gelatin zymography) were analyzed.

Results: LOX-1 KO mice had 20% increase in survival over the 3-wk period (P<0.05). LOX-1 deletion reduced (P<0.01) inflammatory signals, interleukin -1β and interleukin-6, and phosphorylated MAPKs (P38, ERK and JNK) in the myocardium. Further, LOX-1 KO mice hearts exhibited reduced Adam 17, MMP2 activity and MT1-MMP, and increased TIMP2. These alterations in inflammatory signals and oxidant load were associated with markedly less (~75%, P<0.01) collagen accumulation. Reduced scar formation was associated with improved cardiac hemodynamics (as assessed by left ventricular ±dP/dt and cardiac ejection fraction).

Conclusion: We demonstrate for the first time that LOX-1 deletion reduces cardiac remodeling after chronic ischemia by interruption of pro-inflammatory and pro-oxidant signals.