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ATHEROPROTECTIVE EFFECTS OF TUMOR NECROSIS FACTOR-STIMULATED GENE-6

Poster Contributions
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Background: Tumor necrosis factor-stimulated gene-6 (TSG-6), an anti-inflammatory protein, was shown to be localized in the neointima of injury-induced rat arteries. However, the modulatory effect of TSG-6 on atherogenesis has not yet been reported.

Methods: We aimed to evaluate the atheroprotective effects of TSG-6 on human endothelial cells (HECs), human monocyte-derived macrophages (HMDMs), human aortic smooth muscle cells (HASMCs) *in vitro*, and aortic lesions in apolipoprotein E-deficient ($ApoE^{-/-}$) mice, along with its expression levels in coronary lesions and plasma from patients with coronary artery disease (CAD).

Results: TSG-6 was abundantly expressed in HECs, HMDMs, and HASMCs *in vitro*. TSG-6 significantly suppressed cell proliferation and lipopolysaccharide-induced up-regulation of monocyte chemotactic protein-1, intercellular adhesion molecule-1, and vascular adhesion molecule-1 in HECs. TSG-6 significantly suppressed inflammatory M1 phenotype, and suppressed oxidized low-density lipoprotein-induced foam cell formation associated with down-regulation of CD36 and acyl-CoA:cholesterol acyltransferase-1 in HMDMs. In HASMCs, TSG-6 significantly suppressed migration and proliferation, but increased collagen-1 and collagen-3 expressions. Four-week-infusion of TSG-6 into $ApoE^{-/-}$ mice significantly retarded the development of aortic atherosclerotic lesions with decreased vascular inflammation, monocyte/macrophage, and SMC contents and increased collagen fibers. In addition, it decreased peritoneal M1 macrophages with down-regulation of inflammatory molecules, and lowered plasma total cholesterol levels. In CAD patients, plasma TSG-6 levels were significantly increased and TSG-6 was highly expressed in the fibrous cap within coronary atherosclerotic plaques.

Conclusions: These results suggest that TSG-6 contributes to the prevention and stability of atherosclerotic plaques. Thus, TSG-6 may serve as a novel therapeutic target for CAD.