**ADIPOCYTES PROMOTE IL18 BINDING TO ITS RECEPTORS DURING ABDOMINAL AORTIC ANEURYSM FORMATION IN MICE**

**G.-P. Shi**

Brigham and Women's Hospital, Boston, MA, USA

IL18 receptor (IL18r) and Na-Cl co-transporter (NCC) both mediate IL18 actions. We reported that IL18 use both IL18r and NCC as its receptors and participate directly in atherogenesis. Here we demonstrate increased expression of these IL18 receptors in human and mouse abdominal aortic aneurysm (AAA) lesions. In angiotensin II perfusion-induced AAA in mice, deficiency of either receptor reduces AAA growth. Compound deficiency of IL18r and NCC shows synergistic effect in aortic dilation, AAA lesion inflammation, and aortic wall remodeling. Immunofluorescent staining localizes IL18 to NCC and IL18r on cells at regions enriched in adipocytes or adjacent to perivascular adipose tissue. Differentiated 3T3-L1 adipocytes enhance IL18 binding to macrophages, aortic SMCs, and endothelial cells by inducing the expression of both receptors on these cells. Adipocytes also enhance IL18r and IL18 expression on T-cells, modulate AAA-pertinent protease expression from macrophages, and induce SMC apoptosis. Perivascular implantation of fat tissue from obese mice exacerbates AAA development and lesion inflammatory cell accumulation in mice. Further experiments establish an essential role of adipocyte leptin and fatty acid binding protein 4 (FABP4) in promoting IL18 binding to macrophages by inducing the expression of IL18, IL18r, and NCC. Fat tissues from wild-type mice, but not those from leptin-deficient *ob/ob* mice increase IL18 binding to macrophages and expression of IL18, IL18r, and NCC. Recombinant leptin and FABP4 show the similar activities to those of fat tissues. Together, this study establishes a role of adipocyte leptin and possibly FABP4 in promoting IL18 activity in AAA by enhancing IL18 binding to its receptors.