Suppression of Inflammation-induced Abdominal Aortic Aneurysm Formation by Induction of Elastin Tolerance

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Abdominal aortic aneurysm (AAA) is a vascular disease process whereby the aorta expands to a point where rupture may occur. This serious condition is diagnosed in approximately 200,000 people in the United States per year and accounts for over 15,000 deaths annually. The only medical intervention proven to reduce the risk of AAA rupture is surgical repair; however, such repair is associated with high risk of death, reduced quality of life, and high expense. AAA is caused by the weakening of the artery wall due to inflammation-induced destruction of its structural components. Our clinical data shows increased levels of circulating elastin degradation products in patients with AAA, especially smokers, compared to risk factor matched controls. This observation led us to hypothesize that an immune reaction to elastin fragments initiates the inflammatory cascade in the aorta that leads to AAA formation.

To test this hypothesis, C57BL/6 mice were injected with poly(lactide-co-glycolide) nanoparticle-encapsulated IL-10 to induce immune tolerance or nanoparticle-encapsulated control ovalbumin. Injection of elastin fragments was performed 7 days later to induce an immune response. AAA of the infrarenal aorta was induced by topical application of elastase during laparotomy procedure 14 days after nanoparticle injection. Aorta diameter was measured 16 days post-operatively with Microfil. Immunologic changes were evaluated by cytokine analysis, Tr1/Th17 cell ratio in peripheral blood, and splenic Th17 and Tr1 response to elastin. Based on prior work, we expect that induction of elastin tolerance using poly(lactide-co-glycolide) nanoparticle-encapsulated IL-10 will suppress abdominal aortic aneurysm expansion and promote an anti-inflammatory environment characterized by increased Tr1/Th17 cell ratio, increased levels of anti-inflammatory cytokines, and decreased pro-inflammatory cytokine expression.