Potential Role of Cigarette Smoke Exposure on Elastin Sensitization and Aortic Pathophysiology in a Mouse Model of Abdominal Aortic Aneurysm

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In the US, 200,000 people annually are diagnosed with abdominal aortic aneurysm (AAA) and it accounts for over 15,000 deaths per year. The current paradigm for AAA progression includes cytotoxic T cell activation inducing inflammatory monocyte and macrophage recruitment. These cells secrete collagen and elastin degrading enzymes, leading to loss of structural integrity, aortic dilatation, and eventual rupture. Studies in AAA patients show an increase in cytotoxic T lymphocyte number and activity, a significant decrease in the number and immuno-suppressive activity of the T-regulatory (Treg) cells responsible for governing autoimmune responses, and decreased levels of circulating IL-10. Data from our group suggest that the immune system is sensitized to elastin in patients with early AAA. Cigarette smoking is one of the strongest risk factors for development of AAA in humans and smoke exposure has been shown to exacerbate aneurysm formation in mice. Our working hypothesis is that cigarette smoke causes lung damage via activation of tissue proteases which in turn generates antigenic elastin fragments that trigger an inflammatory reaction in the abdominal aorta resulting in an aneurysm.

The current study will evaluate the effect of cigarette smoke exposure in mice on the relative ratios of populations of pro-inflammatory and anti-inflammatory T-cell subtypes, serum levels of IL-10, miRNA related to IL-10, aortic pathology, and an assessment of potential self-sensitization to elastin. The results of this study will be used to develop a delayed type hypersensitivity assay for elastin that could be used to easily assess the presence of AAA in human patients.