Collagen Fibril Abnormalities in Human and Mice Abdominal Aortic Aneurysm

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Introduction: Vascular diseases like abdominal aortic aneurysms (AAA) are characterized by a drastic remodeling of the vessel wall, accompanied with changes in the elastin and collagen content. At the macromolecular level, the elastin fibers in AAA have been reported to undergo significant structural alterations. While the undulations (waviness) of the collagen fibers is also reduced in AAA, very little is understood about changes in the collagen fibril at the sub-fiber level in AAA as well as in other vascular pathologies.

Materials and Methods: In this study we investigated structural changes in collagen fibrils in human AAA tissue extracted at the time of vascular surgery and in aorta extracted from angiotensin II (AngII) infused *ApoE*$^{-/-}$ mouse model of AAA. Collagen fibril structure was examined using transmission electron microscopy and atomic force microscopy. Images were analyzed to ascertain length and depth of D-periodicity, fibril diameter and fibril curvature. Tissues were also stained using collagen hybridizing peptide (CHP) and analyzed using fluorescent microscopy and second harmonic generation (SHG) microscopy to locate regions of healthy and degraded collagen.

Results: Abnormal collagen fibrils with compromised D-periodic banding were observed in the excised human tissue and in remodeled regions of AAA in AngII infused mice (**Figure 1**). These abnormal fibrils were characterized by statistically significant reduction in depths of D-periods and an increased curvature of collagen fibrils. These features were more pronounced in human AAA as compared to murine samples. Additionally, regions of abnormal collagen were located within the remodeled areas of AAA tissue and were distinct from healthy collagen regions as ascertained using CHP staining and SHG (**Figure 1**). Thoracic aorta from Ang II-infused mice, abdominal aorta from saline-infused mice, and abdominal aorta from non-AAA human controls did not contain abnormal collagen fibrils.

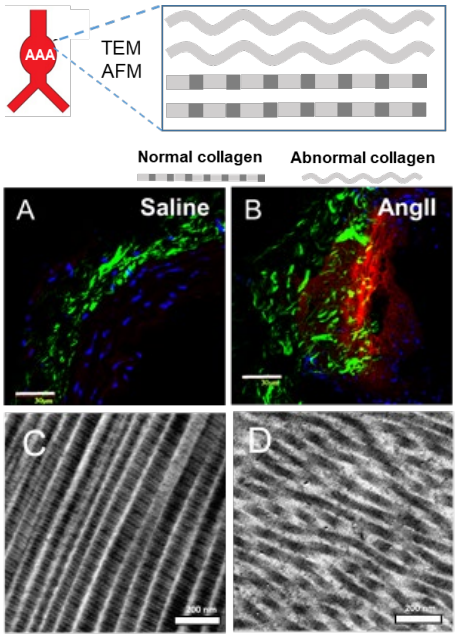

Figure 1: Schematic of normal and abnormal collagen in AAA. Multiphoton microscopy images of control (A) and AAA (B) mice aorta. Blue is cell nuclei (DAPI), green is native collagen (SHG), and red is degraded collagen (CHP). TEM images of control (C) and AAA (D) mice aorta. Control tissues contained collagen fibrils 'normal' in appearance, while AAA tissues contained regions of disrupted or 'abnormal' collagen fibrils exhibiting disrupted or diminished periodic structure.

Conclusions: The structural alterations in abnormal collagen fibrils appear similar to those reported for collagen fibrils subjected to mechanical overload or chronic inflammation in other tissues. Detection of abnormal collagen could be utilized to better understand the functional properties of the underlying extracellular matrix in vascular as well as other pathologies.

References: Jones B, Tonniges JR, Debski A, Albert B, Yeung DA, Gadde N, Mahajan A, Sharma N, Calomeni EP, Go MR, Hans CP and Agarwal G. (in press). Collagen fibril abnormalities in human and mice abdominal aortic aneurysm. *Acta Biomater*.