

Public Abstract

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Title: Role of Pro α 2(I) Collagen Chains and Collagen Crosslinking in Thoracic Aortic Biomechanical Integrity During Aging Using the *Oim* Mouse Model

The extracellular matrix (ECM) is an important constituent for a variety of tissues including vascular tissue in which the ECM maintains aortic wall integrity. An important component of vascular tissue ECM is type I collagen. Type I collagen is normally a molecule composed of three collagen chains of which two are the same chain [pro α 1(I)] and one is distinctly different [pro α 2(I)]. The focus of this dissertation is to examine the role of the pro α 2(I) chain in determining thoracic aorta integrity and how the thoracic aortic integrity changes with age. To assess the role of pro α 2(I) chains we used a mouse model, termed '*oim*', that produces only pro α 1(I) chains and evaluated thoracic aortas of our mouse model at 3, 8, and 18 months old of age. We evaluated thoracic aortic strength, stiffness, ECM content, ECM gene expression, and collagen crosslinking at each age point.

Oim mice exhibited reduced aortic strength and stiffness at each age group and exhibited increased aortic strength and stiffness at 18 months of age compared to 3 months of age. *Oim* mice also exhibited reduced aortic collagen content, while other aortic ECM components were unchanged. However, aortic collagen content was significantly increased at 8 and 18 months of age as compared to 3 months of age. Aortic ECM gene expression demonstrated reduced expression at 18 months of age as compared to 3 months of age. In addition, *oim* aortas demonstrated increased collagen crosslinks at each age group, while the ratio of collagen crosslinking remained the same at each age group.

Our results demonstrate that pro α 2(I) collagen is central for proper aortic strength and stiffness even in the presence of increased collagen crosslinking and increasing collagen content of homotrimeric type I collagen with age. This study suggests that fibrils composed of homotrimeric type I collagen are inherently weaker than fibrils composed of heterotrimeric type I collagen.