Investigating the role of COQ8B in aortic smooth muscle cells.

Henry Stadler[1], Stephanie Ware[2], Benjamin Landis[2]

[1]Indiana University School of Medicine, [2]Indiana University School of Medicine, Departments of Pediatrics and Medical and Molecular Genetics

Background and Hypothesis:

Thoracic aortic aneurysm (TAA) is an aortopathy characterized by aortic enlargement and life-threatening complications such as aortic dissection and sudden cardiac death. Previous studies identified *COQ8B* as a candidate genetic modifier of TAA severity. *COQ8B* is important for mitochondrial biosynthesis of coenzyme Q, but its precise functions are not defined. We hypothesize that alteration of *COQ8B* influences TAA pathogenesis via energy and oxidant metabolism pathways.

Experimental Design:

Smooth muscle cells (SMCs) were cultured directly from leftover healthy aortic tissues acquired during cardiac transplant operations. At confluence of 50-70%, cells were transfected with siRNA targeting *COQ8B* or a non-targeting negative control siRNA. Gene expression was measured using real-time quantitative polymerase chain reaction (RT-qPCR). Production of the reactive oxygen species hydrogen peroxide (H_2O_2) was measured using the fluorescence-based Amplex Red Hydrogen Peroxide Assay (Invitrogen) in basal growth medium.

Results:

Expression of *COQ8B* decreased by approximately 75% to 85% at 48 hours following siRNA transfection compared with negative control. This was associated with approximately 1.5 fold upregulation of the SMC contractile gene *CNN1* ($p<0.05$). Knockdown of *COQ8B* did not appear to alter H_2O_2 production measured at timepoints of 48 or 72 hours.

Conclusion and Impact:

Based on these preliminary data, decreased *COQ8B* expression appears to alter the contractile phenotype of SMCs but may not significantly influence extracellular levels of H_2O_2 under basal conditions. Exogenous activation of pathways important for TAA pathogenesis may be required to elucidate the role of *COQ8B*. Ultimately, this work may lead to improved clinical approaches.