Investigating the role of COQ8B in aortic smooth muscle cells.

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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 (H₂O₂) 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 H₂O₂ 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 H₂O₂ 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.