

SPECIAL RESEARCH SEMINAR

Presented by the Center for Vascular and Heart Research at the Fralin Biomedical Research Institute at VTC



FRALIN BIOMEDICAL RESEARCH INSTITUTE AT VTC
CENTER FOR VASCULAR
AND HEART RESEARCH
VIRGINIA TECH.



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In Person Seminar: Cardiac Protein O-GlcNAcylation Induces Cardiac Hypertrophy and Increases Risk of Heart Failure

The severity and development of cardiovascular disease can be affected by lifestyle and metabolic diseases, which can impact various mechanisms, including post-translational modifications (PTM). A specific PTM, known as protein O-linked β -N acetylglucosamine modification (O-GlcNAc), has been linked to both physiological responses and pathological progression of heart failure. Dr. Wende's lab's work aims to test whether sustained O-GlcNAc of proteins in cardiomyocytes contributes to cardiac adaptations or is sufficient to progress toward pathophysiology. Using a novel transgenic mouse model to overexpress a naturally occurring dominant-negative O-GlcNAcase (dnOGA) in an inducible and cardiomyocyte-specific manner (dnOGAh), the lab induced dnOGA in male and female 8-10-weeks-old mice, and examined the effects of 2-weeks (2wk) and 24-weeks (24wk) dnOGA overexpression (which leads to a 1.8-fold increase in O-GlcNAc levels). A 2wk increase in protein O-GlcNAc levels did not impact heart weight or function; however, 24wk of elevated protein O-GlcNAc led to cardiac hypertrophy, mitochondrial dysfunction, fibrosis, and diastolic dysfunction compared to Control (Con; single transgenic mice). Others have shown in clinical studies that diabetes increases cardiac disease risk, even after patients return to tight glycemic control. Dr. Wende hypothesizes that an increase in O-GlcNAc (known to occur in diabetes) is sufficient to exacerbate adverse cardiac remodeling under subsequent pressure-overload. He proposes that this is due to epigenetic modifications causing persistent changes in gene expression. Using the model described above the lab subjected Con and dnOGAh mice to 2-wk induction and subsequent 2-wk washout, followed by transverse-aortic constriction (TAC) or Sham surgery. In both Con+TAC and dnOGA+TAC vs. Sham groups, systolic function decreased, and ventricular weight is increased. Interestingly, the lab sees further exacerbation of cardiac hypertrophy and pulmonary edema between dnOGA+TAC vs. Con+TAC groups. These results support the hypothesis that a transient increase in cardiac O-GlcNAc levels is sufficient to increase susceptibility to subsequent cardiac pathology.

MONDAY, MAY 15, 2023 at 11 a.m.

Room G101 A/B, 4 Riverside Circle.

Or watch via Zoom at <https://virginiatech.zoom.us/j/85661403607>



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