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SPATIAL TRANSCRIPTOMIC PROFILING OF BICUSPID AORTIC VALVES

PRINCIPAL INVESTIGATOR: JOY LINCOLN, PHD
CO-INVESTIGATOR: JOHN LADISA, PHD

Bicuspid Aortic Valve (BAV) is the most common congenital heart defect affecting 1-2% of all live births. The most significant concern for BAV is not necessarily the defect itself, but that children often experience significant complications by young adulthood, including accelerated calcification and pulmonary valve stenosis. Despite this, most children with BAV only have periodic check-ins with their cardiologist to see if the complications are arising. That often results in reacting to problems after the fact, rather than proactively taking measures as part of the child's care plan.

To address this, Dr. Lincoln's work focuses on developing risk profiles for patients with BAV. Using available genetic patient data and trials of lab mice, Dr. Lincoln will develop a statistical analysis to determine which patients are most likely at risk for long-term complications, and thus who may benefit from proactive, preventive care.

The Abstract:
Bicuspid Aortic Valve (BAV) is the most common congenital heart defect affecting 1-2% of all live births. However, it is not the structural malformation that enforces the need for treatment, but the accelerated development of calcification and stenosis in up to 50% of young adult patients. Despite this, clinical management is limited to periodic surveillance of valve dysfunction, and only when the valve becomes stenotic is intervention recommended, which is often limited to sub-optimal outcomes. Therefore, children with BAV would benefit from a comprehensive assessment of their risk profile prior to calcification to develop more effective clinical management strategies.

To address this, we are performing long-term, integrate spatial studies correlating abnormal biomechanical indices with pro-calcification mRNA profiles in pediatric patients, and mice of BAV. However short-term, our objective is to utilize funds from this Project Bubaloo award to advance innovative transcriptomic studies to define the spatial pro-calcific molecular profiles in bicuspid valves utilizing a mouse model of BAV in our lab. Successful completion will for the first time allow for full statistical analysis of our spatial dataset identifying differentially expressed genes that correlate with the abnormal biomechanical indices induced by the bicuspid valve anatomy.

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DEVELOPMENT OF A NOVEL BIOMARKER TO MEASURE EXPOSURE TO MEDICAL RADIATION IN CHILDREN WITH CONGENITAL HEART DISEASE

PRINCIPAL INVESTIGATOR: JOHN BAKER, PHDCO-INVESTIGATOR: AOY TOMITA-MITCHELL, PHD

While cardiac catheterizations have been integral to minimizing the need for invasive, open-heart surgery, it's not without risks. Catheterization procedures deliver one of the highest radiation doses to patients, which can result in damage to DNA and/or inflation that can result in diseases later in life. As of today, we do not have great studies on how much radiation exposure is present during these procedures. Dr. Baker's research will focus on developing more measurements to quantify how much impact cath procedures can have on the body.

The Abstract: With an estimated 1.3 million people currently living with congenital heart disease in the US, understanding the magnitude of radiation exposure during childhood is critically important.

Pediatric cardiac catheterizations are an essential tool in the management of children with congenital heart disease, however, they also deliver one of the highest radiation doses to patients. Exposure to radiation results in damage to DNA and inflammation. This can predispose the cells in the body to diseases during post-natal development and into adulthood. Current biomarkers of exposure to radiation may underestimate radiation risks. The proposed study will contribute to improving the management of children with congenital heart disease by developing a biomarker of their exposure to ionizing radiation. Our objective is to develop a measurement for cell-free DNA (cfDNA) in urine and blood as a biomarker of DNA damage caused by radiation exposure that can be predictive of clinical outcomes and radiogenic disease.