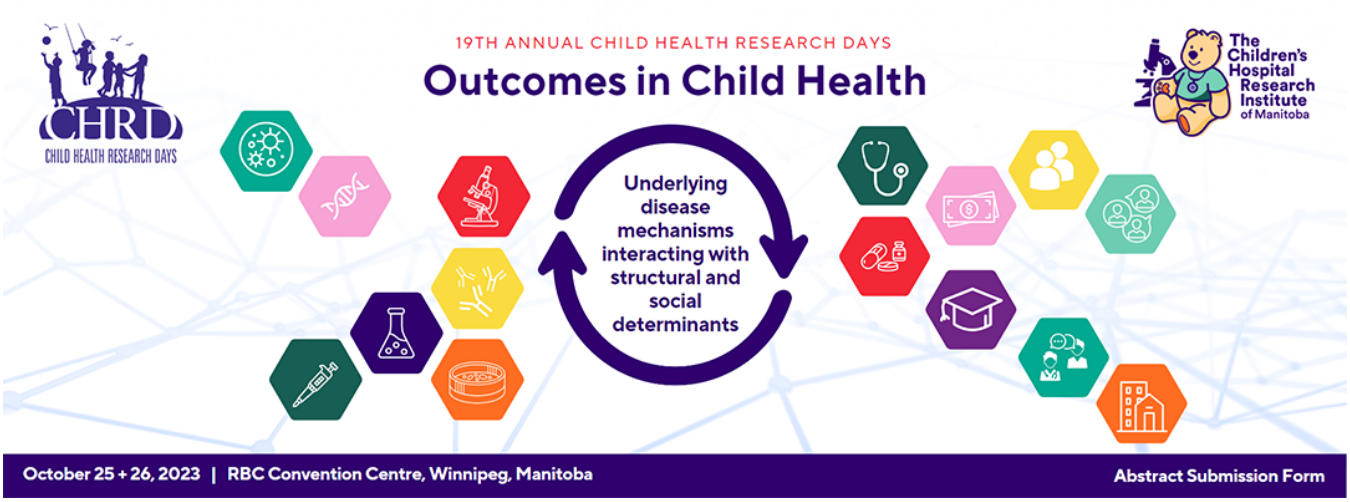

CHRD 2023: Abstract Submission Form

Submitter Name
Rabia Shuaib

Presenter Name
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Presenter Status
Undergraduate Students

Research Category
Basic Science

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Title
Mapping the Distribution of Adenylyl Cyclase Isoforms in Hypoxic Neonatal Pulmonary Arteries

Background
Persistent pulmonary hypertension of the newborn (PPHN) is characterized by hypoxia and pulmonary vasoconstriction. Adenylyl cyclase (AC) has 9 membrane-bound AC isoforms which impact many biological functions, including vasodilation. Previously, we found AC6 to be the main isoform expressed in cultured pulmonary arterial smooth muscle. Additionally, we've found that hypoxia reduces AC activity in a porcine hypoxia-induced PPHN model.

Objective
Our objective is to determine the expression patterns of each AC isoform throughout the pulmonary circuit, and if that expression profile changes in PPHN. We hypothesize that distal arteries would mainly express AC6.

Methods
PPHN was induced in newborn pigs by hypoxia exposure (10% O2) for 72 hours; controls were raised in normoxic conditions (N=3). Pulmonary arteries (PA) were microdissected and separated into proximal (conduit; 1st – 2nd interlobar branch), intermediate (3rd – 4th branch), and distal (resistance; 5th – 6th branch) samples. RNA was isolated and mRNA expression of each AC isoform was determined by qPCR.

Results
In control proximal PA, AC6 was the most expressed isoform. AC2, AC5, and AC9 expression increased in PPHN proximal PA, and AC2 to the greatest extent by 1.8 times. Conversely, AC4, AC6, AC7, and AC8

expression decreased in proximal PPHN arteries. In intermediate vessels, AC4 was most expressed; PPHN increased most AC isoform expression, however, AC6 expression decreased. In distal PA, AC6 and AC7 were highly expressed in normoxic controls, while AC9 increased in hypoxic tissues. Expression of all AC isoforms increased in distal PA from PPHN animals compared to controls; no isoform reported decreased expression after hypoxic exposure.

Conclusion
All AC isoforms are expressed in the pulmonary circuit; however, expression levels change from conduit to resistance arteries. AC6, AC7, and AC9 are the primary isoforms in the distal vessel. Hypoxia increases AC mRNA expression distally, yet relaxation remains impaired, thus enzyme activity may be regulated independently of expression.

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