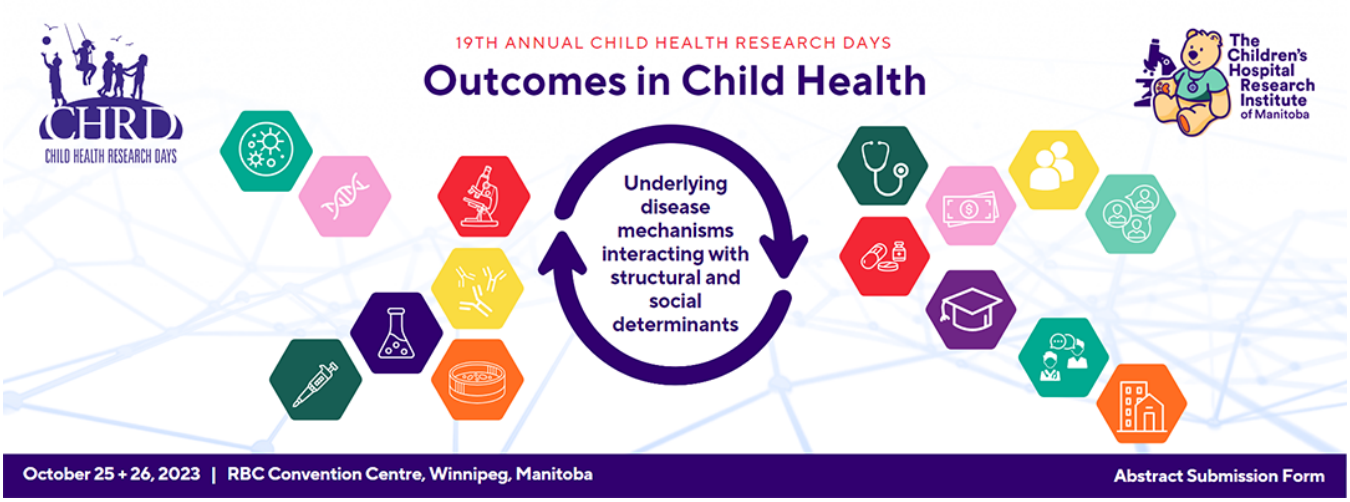

CHRD 2023: Abstract Submission Form

Submitter Name
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Presenter Name
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Presenter Status
Undergraduate Students

Research Category
Basic Science

Role in the project
Design
Perform Experiments
Analyze Data
Write Abstract

Title
The Bowen-Conradi Syndrome protein EMG1 is a Hypomorphic Allele

Background
Bowen-Conradi Syndrome (BCS) is a rare genetic disorder exclusively found in the Hutterite population of the Canadian Prairies. Children with BCS fail to thrive, display growth and developmental delays, craniofacial malformations, and death in early childhood. BCS is due to a D86G variant in the SSU processome methyltransferase protein EMG1 involved in ribosome assembly.

Objective
Published reports have indicated a significant decrease in the abundance of the BCS variant EMG1. We sough to quantify the levels of the WT and BCS variant EMG1 in order to better understand the contribution of decrease protein levels to the disorder.

Methods
To study the molecular pathogenesis of BCS, we created a yeast model of the disorder. We are able to monitor EMG1 protein levels by western blot. As many genetic diseases are due to a loss of interactions between proteins, we asked if BCS is due to a loss of protein-protein interactions. For this, we used the yeast two-hybrid system and additionally monitored the abundance of the WT and BCS variant EMG1 proteins by western blot.

Results
Our yeast BCS model displays reduced growth and temperature sensitivity. Western analysis shows a

decreased abundance of the EMG1 BCS variant relative to WT. Together, these suggest that the BCS variant partially destabilizes/unfolds the protein resulting in a hypomorphic allele. We also find that the BCS variant EMG1 causes a loss of protein-protein interaction. This loss of protein-protein interaction is likely due in part to the unfolding of the BCS variant EMG1 and to its decreased protein abundance.

Conclusion
Together, these suggest that BCS is due in part to reduced EMG1 protein abundance, thus uncovering one key element of the molecular pathogenesis of the disease. Our results suggest that stabilizing and increasing the abundance of the BCS variant EMG1 protein could be a therapeutic avenue.

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