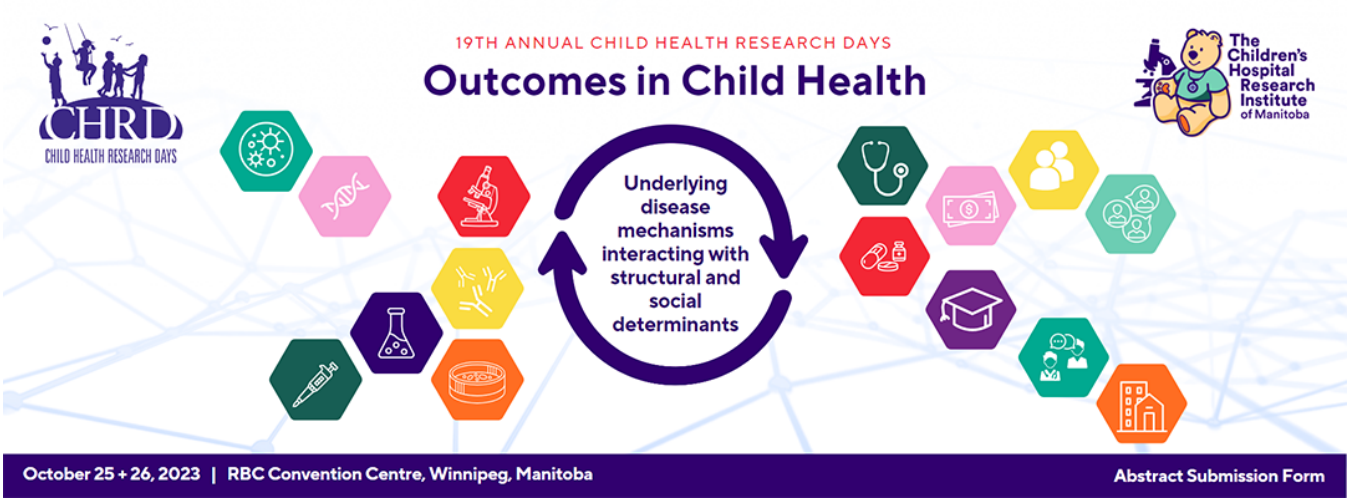

CHRD 2023: Abstract Submission Form

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
Using the Proteasome Inhibitor MG132 to Increase the Abundance of EMG1 in a Yeast Model of Bowen-Conradi Syndrome

Background
Bowen-Conradi Syndrome (BCS) tragically affects 1 in 355 births in the Hutterite population. The autosomal recessive disease is caused by a D86G sequence variant in the EMG1 gene responsible for SSU ribosome assembly. Individuals with BCS present with various clinical symptoms such as foot and digit deformities, as well as growth and development delays. The D86G sequence variant causes a decrease in EMG1 protein stability which we suspect causes it to be targeted for degradation via ubiquitination. While previous research has been done to characterize the molecular basis of the disease, treatments and therapeutic options have not been adequately examined.

Objective
One of our current focuses is on gaining insight to whether there is a viable treatment to BCS. To do so, we have chosen MG132, a proteasome inhibitor that reduces the degradation of ubiquitinated proteins in animal and yeast cells. We hypothesize that by reducing the degradation of the BCS variant EMG1, protein levels can be restored and growth defects can be partially rescued.

Methods
To test our hypothesis, we treated a yeast model of BCS as well as WT cells with and without MG132, and monitored protein abundance via western blots.

Results
Our results have shown a significant qualitative increase of EMG1 abundance in both WT and BCS variant cells treated with MG132.

Conclusion
Future densitometry assays will allow for more precise and quantitative insight into the efficacy of the proteasome inhibitor as a therapeutic option. The next steps in researching the effects of MG132 on the BCS variant EMG1 protein is to examine if the known growth defects can be partially rescued, and if ribosome assembly levels could be restored. Should our hypothesis be correct, it would be promising for future experiments where human BCS patient cells could be examined.

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