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Exploring the role of sex and gender on health research

CHRD
CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

Submitter Name
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Title
Studying the Gene Dosage and Genetic Interactions of the Bowen-Conradi Syndrome Protein Emg1

Background
Bowen-Conradi Syndrome (BCS) is a ribosome assembly disorder or ribosomopathy exclusively found in the Hutterite population of the Canadian Prairies. It presents with severe growth retardation and developmental delay, with death in early childhood. BCS is due to a D86G variant in the ribosome assembly and SSU processome protein Emg1. The mutation causes a hypomorphic allele, with localized or global unfolding of Emg1, leading to the loss of protein-protein interactions, cellular mislocalization, and decreased protein stability and abundance.

Objective
We are exploring the gene dosage and genetic interactions of Emg1 in a yeast model system of BCS using a variety of strategies. This includes the creation of a pseudo-diploid system mimicking the heterozygous/carrier situation, allowing us to identify possible interactions between WT and BCS alleles along with gene dosage effects. We are also examining gene dosage effects using low and high copy-number plasmids with different promoter strengths. Of Emg1's known genetic interactions, we are determining the molecular basis of the positive epistatic interaction between Emg1 and snR35, where deletion of the snoRNA rescues the lethal phenotype of the Emg1 depletion. Lastly, we will determine if over-expression of Emg1's only known protein-protein interacting partner, Utp2, can partially restore nucleolar levels of the Emg1-BCS variant.

Methods
Using a yeast model of BCS, ribosome assembly will be monitored using growth-curves and cold-sensitivity assays along with pre-rRNA processing northerns.

Results
Results suggest that increased expression of the Emg1-BCS variant rescues the growth defects. Similarly, over-expression of Emg1's binding partner Utp2 also rescues the growth defects. Interestingly, deletion of

the snoRNA snR35 reverses the growth defects of Emg1-BCS.

Conclusion
Here, we show that BCS is due in part to a reduction in gene dosage and that increased expression of the variant, or of its protein-protein interacting partner Utp2, restores growth. This will contribute to furthering our understanding of the molecular function of Emg1 in ribosome assembly, how it is perturbed in BCS, and may identify potential therapeutic strategies in the management and treatment of BCS.

Theme:
Basic Science

Do you have a table/figure to upload?
No

Are you willing to participate in Goodbear's Den?
Yes

Presenter Status:
Undergraduate Students

What was your role in the project?
perform experiments, analyze data, and write abstract

Authors

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