ABSTRACT SUBMISSION FORM

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CHILD HEALTH RESEARCH DAYS

CHRD 2020: Abstract Submission Form

Submitter Name
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Title
Lost In Translation: Investigating the translation defect in Bowen-Conradi Syndrome

Background
Bowen-Conradi Syndrome (BCS) is an inherited ribosome assembly disorder (ribosomopathy) present in the Hutterite population at a rate of 1/355 births. BCS presents with severe developmental delay, a failure to thrive, and death in infancy. BCS is due to a D86G variant in the pseudouridine methyltransferase and SSU processome protein Emg1, responsible for both ribosome assembly and methylation of a pseudouridine in the decoding P site of the small subunit of the ribosome. This 18S rRNA pseudouridine is post-transcriptionally hypermodified and critical to the translational fidelity of the ribosome in mRNA decoding.

Objective
As with other ribosomopathies (such as Diamond-Blackfan anemia and Treacher-Collins syndrome), the consequences of ribosome mis-assembly on translational fidelity and alterations to the proteome has been under-investigated. Here, we investigate suspected translation defects in BCS.

Methods
Using a yeast model system of the disorder, the translation terminating antibiotic puromycin was used to probe the molecular effects of BCS on translation. The translation of new proteins is then monitored by western blot analysis using an anti-puromycin antibody.

Results
The puromycin translation assay reveals that BCS cells are translationally compromised in a number of differ ways. This includes a decrease in overall translational capacity, along with a likely change in translational preferences.

Conclusion
Our results reveal, for the first time, that BCS cells are translationally compromised. This is consistent with

recent results suggesting that the rRNA target site of Emg1 is hypomodified in all cancers. Ongoing investigations will further characterize the nature of the translational defect (mis-incorporation, frame-shifting, stop codon read-through) along with changes to the proteome.

Theme:
Basic Science

Do you have a table/figure to upload?
No

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

Presenter Status:
Non-Trainee

What was your role in the project?
All; design, experiments, analysis, writing

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