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Basic Science

Abstract Title
Changes in the Structure and Function of the Ribosome as a Result of a Loss of a Crucial Hypermodified Uridine in Bowen-Conradi Syndrome

Background
Bowen-Conradi Syndrome (BCS) is a genetic disorder in children characterized by reduced growth and development, resulting in death during infancy. BCS is a ribosomopathy, a disorder associated with altered ribosome assembly which in turn likely affects the translation of the genetic code into proteins.

Objective
Our objectives were to investigate (1) the changes in ribosome structure and (2) translational fidelity in BCS.

Methods
BCS is in part due to a failure to chemically modify an important site within the rRNA of the ribosome, which undergoes a three-step modification process that likely affects ribosome structure and/or function. We created yeast strains that express different variations of the modifications of this site. We grew these strains on plates with media containing various ribosome-targeting antibiotics and compared growth to see whether certain antibiotics disrupt or improve cell growth at different temperatures, implying changes to the ribosome structure. To determine functional fidelity these strains were then used for a series of DLR assays, where they must overcome a ‘translational challenge’.

Results
The three step modification process of the site within the ribosome involves a snoRNA, a methyltransferase (EMG1), and then an aminocarboxypropyl transferase. We observed that the snoRNA deletion strain had a reduction in growth, the strain with the BCS variant of the EMG1 methyltransferase had a severe reduction in growth, and the deletion strain of the aminocarboxypropyl transferase had a minimal reduction in growth. We anticipate we will see a similar trend in translational fidelity in the DLR assays of our strains.

Conclusion
Our results show that differential growth is occurring between our strains, indicating that deletions of these ribosome-building factors and their corresponding modification does have an effect on the structure of the ribosome. We are currently uncovering translational changes through DLR assays. This research will give us insight into BCS and expand our knowledge of the ribosome.

Authors

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