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Basic Science

Abstract Title

Understanding the Biological Basis of Bowen-Conradi Syndrome

Background

In 1976, the ribosome assembly disorder Bowen-Conradi Syndrome (BCS) was first described. Its presentations include severe developmental delays and overall failure to thrive. These presentations are now attributed to a disease variant in the EMG1 ribosome assembly protein. To tease apart the mechanisms underlying the clinical presentation of BCS, we aim to first expand our knowledge of ribosomal biogenesis (assembly), the role of small nucleolar RNAs (snoRNAs) and the essential functions of EMG1 both inside and outside the context of Bowen-Conradi Syndrome.

Objective

The objective of our study is to first identify the functional roles of snoRNAs guiding processing and maturation of the 18S rRNA small subunit of the ribosome (snR35 [and its overlapping partner snR36]; snR57 and snR87) by single gene deletion within a context of otherwise naive yeast model cells. Secondly, we aim to identify and validate interactions between these snoRNAs and the BCS variant Emg1 utilizing engineered compound yeast models: single snoRNA gene deletion and enforced expression of BCS variant Emg1.

Methods

Using single snoRNA gene deletions in naive yeast and snoRNA gene deletions in our yeast BCS model, genetic interactions between select snoRNAs and the BCS protein Emg1 can be observed as growth delays and quantified.

Results

The single deletions of snR35, snR57 and snR87 result in equivalent growth delays relative to the naive parental yeast strain. In contrast, deletion of snR36 – a snoRNA containing overlapping binding sites to that of snR35 (and snR85) and Emg1– presents the greatest growth delay demonstrating possible binding and release mechanisms within snoRNA processing.

Conclusion

We emphasize that understanding the functional dynamics of ribosomal processing factors (Emg1 and snoRNA's) is fundamental to our understanding of molecular biology and ribosomal biogenesis. This will increase our understanding of Bowen-Conradi Syndrome along with the mechanisms of childhood cancers associated with the dysregulation of ribosome assembly.

Authors

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