CHRD 2024: Abstract Submission Form

Presenter Name
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Presenter Status
Undergraduate Students

Role in the project
Perform Experiments
Analyze Data
Write Abstract

Research Category
Basic Science

Title
The Bowen-Conradi Syndrome EMG1 Variant Protein is a Temperature-Dependent Hypomorphic Allele

Background
Bowen-Conradi Syndrome (BCS) presents clinically as failure to thrive with death in infancy. Within a cell, the variant BCS methyltransferase EMG1, required for ribosomal maturation, becomes destabilized by the substitution of negatively charged aspartic acid with an electrically neutral glycine.

Objective
In a yeast model system, if the BCS variant EMG1 is a hypomorphic allele presenting a partial loss of function, the deficiencies in growth and protein abundance may be quantified and expressed as a percentage <100%.

Methods
In yeast, chromosomal wild-type EMG1 is repressed while a plasmid-encoded protein is constitutively expressed. Plasmid contents vary from homologous human and yeast EMG1 of either wild-type, BCS variant or empty vector control. Cultures are grown at temperatures ranging from near metabolic relevance of human (35ºC) to yeast (30ºC).

Results
At 30ºC in yeast, the yeast BCS variant Emg1 (D90G) displays a significant growth decrease relative to wild-type Emg1. However, human BCS variant EMG1 (D86G), at 30ºC, grows as wild-type only displaying a growth defect at 35ºC. By western blot analysis, at 35ºC, human BCS variant EMG1 shows a 17.6% relative abundance to the human wild-type EMG1. Differences in human WT/BCS protein abundance at temperatures below physiological relevance are insignificant. Homologous yeast BCS variant EMG1 in yeast displays a significant decrease in abundance at 30ºC. Recognition of the hypomorphism of BCS variant EMG1 suggests a strong positive correlation in protein abundance and EMG1 functional capacities at physiological temperature.

Conclusion
Thus, the BCS variant EMG1 is a hypomorphic allele, with a protein abundance that is dependent on temperature. At 30ºC, the human BCS variant EMG1 is likely more stable and retains wild-type-like growth and protein levels. However, at 35C, close to physiological temperature, the BCS variant EMG1 becomes destabilized, with a growth defect and a decrease in protein levels.

Do you have a table/figure to upload?
No

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