CHRD 2021: Abstract & Poster Submission Form

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Research Category:

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

What was your role in the project?

- ☑ Design
- ☑ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Presenter Status:

- ◉ Undergraduate Students
- ○ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ○ Non-Trainee

Title

The Bowen-Conradi Syndrome Protein EMG1 Contains an N-Terminal Intrinsically Disordered Region

Background

Bowen-Conradi Syndrome (BCS) is a rare genetic disorder in the Hutterite population of the prairies. This ribosome assembly disorder or ribosomopathy presents with severe developmental delay with death in infancy. BCS is due to a genetic variant in the EMG1 protein, an essential ribosome assembly protein and SSU processome component. We have identified an unstructured/intrinsically disordered region (IDR) in the N-terminal region of EMG1. This region is also heavily post-translationally modified, a common feature of IDRs.

Objective

Our aim is to validate the presence of this novel IDR and to determine its function in the role of EMG1 in ribosome assembly.

Methods

We used IDR predictors to identify the novel IDR in EMG1 which we validated by amino acid compositional bias and protein structural analysis. We then cloned EMG1 into a yeast over-expression plasmid and created a series of IDR truncations. The function of the EMG1 IDR was assessed by yeast cell growth and ribosomal RNA analysis. The stability of IDR truncations was determined by western analysis. The IDR's contribution to protein-protein interactions with Utp2/Nop14 was assessed by yeast two-hybrid analysis (Y2H).

Results

Growth analysis using IDR truncations find that the IDR is necessary for cell growth and contributes to the stability of the protein as seen by western blot analysis. Analysis of the IDR's contribution to ribosome assembly is ongoing. Analysis of a cryoEM structure of the SSU processome identifies the EMG1 IDR as mediating protein-protein interactions with an IDR region in Utp2/Nop14, one of the few IDR-IDR mediated protein-protein interactions described. Experimental validation of the function of the IDR by Y2H is ongoing.

Conclusion

Our results identify an N-terminal IDR in EMG1 that is essential for protein stability and function. This will help determine the function of EMG1 in ribosome assembly which is required to better understand the disease mechanism of BCS.

Authors

- For each author, please click "**[+] Add Item**" and provide the author's information

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