

Presenting Author Name

Court Geer

Phonetic spelling of your (full) name

KORT

Presenting Author Category

Masters Student

Supervisor Name

Michael Charette

Research Category

Basic Science

Abstract Title

Overexpression of Sam2 synthetase partially rescues a yeast model of the Bowen-Conradi Syndrome ribosome assembly disorder

Authors

Name	Role	Profession
Court L. Geer	Presenting Author	Graduate
J. Michael Charette	Co Author	Assistant Professor

Background

Bowen-Conradi Syndrome (BCS) is a lethal ribosomopathy caused by an inherited D86G variant in the pseudouridine methyltransferase protein, EMG1. BCS presents with severe developmental delays, a failure to thrive, and death in childhood. The EMG1 protein participates in creating a “hypermodified” uridine residue; a process requiring methyl (EMG1) and aminocarboxypropyl group donation from S-adenosylmethionine (SAM). SAM is also the methyl donor for 2'-O-methylation (Nm), a common rRNA modification essential for stability and function.

Objective

We postulate that Sam2 synthetase (responsible for SAM synthesis) overexpression will improve the BCS model's growth defect due to the importance of SAM in base methylation by EMG1 and in Nm.

Methods

We investigated the effects of Sam2 synthetase overexpression using a yeast model recapitulating BCS. Spot plates and growth curves were performed to investigate the growth of Sam2 synthetase-overexpressing BCS yeast cells (BCS-Sam2). Colony size differences were investigated via dot plate and growth assay, followed by mixed factorial ANOVA. The strains also underwent ribosome methylation sequencing (RiboMethSeq), followed by principal component analysis, to assess Nm profiles.

Results

A significant 2.6-fold increase in the growth of BCS-Sam2 cells relative to normal BCS cells (BCS-EV) is revealed by growth curve analysis ($P = 0.017$). Additionally, BCS-Sam2 cells formed significantly larger colonies ($P < 0.001$) during the first few days of growth compared to BCS-EV cells. Principal component analysis of Nm profiles shows clustering of BCS-Sam2 cells with normal (WT-EV) and Sam2-

overexpressing WT cells (WT-Sam2). Three Nm sites in the 25S rRNA (663, 2197, and 2347) are differentially methylated in BCS-Sam2 cells.

Conclusion

BCS-Sam2 cells demonstrate a significant growth recovery and an increase in early colony size compared to BCS-EV cells, as well as changes in ribosomal Nm profile, supporting our hypothesis. Ongoing metabolomic studies will further characterize the effects of Sam2 synthetase overexpression in BCS cells.