SESSION 1C

MOLECULAR CONTROL OF THE CELL

Session Moderator: Hannele Ruohola-Baker, Biochemistry
MGH 171
12:30 PM to 2:15 PM

* Note: Titles in order of presentation.

The Role of the Replication Fork Barrier in rDNA Instability
Sam Lynn Paskvan, Senior, Biochemistry
Mary Gates Scholar, UW Honors Program
Mentor: Bonita Brewer, Genome Sciences
Mentor: M.K. Raghuraman, Genome Sciences

Genes encoding the RNA portion of the ribosome (rDNA) are present in essentially all eukaryotic genomes as tandem repeated arrays. In humans, rDNA copy number is highly variable and an undervalued potential source of genetic disease. Changes in rDNA copy number can occur through DNA breakage and repair as well as through errors in DNA replication. High transcriptional activity at the rDNA locus poses challenges for replication; all tested eukaryotes have evolved replication fork barriers (RFBs), ensuring that replication machinery does not collide with transcribing RNA polymerases. In yeast, the RFB is a specific sequence to which the protein Fob1 binds, blocking replication forks that converge with transcription. Mutants lacking Fob1 have greatly reduced variation in rDNA copy number. There are currently two models to explain how Fob1 binding to the RFB produces rDNA copy number instability. One model suggests that binding of Fob1 actively recruits DNA break and repair machinery which induces recombination between rDNA repeats. Another model proposes that the stalled replication fork at the RFB is inherently fragile, increasing the likelihood of breakage. To distinguish between these two models, I am generating yeast strains where Fob1 binds to the RFB but does not arrest forks. Using CRISPR/Cas9 gene editing technology, I am reversing the direction of the RFB in each of the 150 rDNA repeats in yeast to prevent replication fork stalling. By confirming the absence of replication fork stalling and determining whether rDNA instability has also been reduced, I can distinguish whether Fob1 binding to the RFB in the absence of fork blocking contributes to rDNA copy number changes. Clarifying involvement of the RFB in rDNA copy number changes will additionally provide insights into the connections between transcriptional activity, replication fork stalling and genome instability.

POSTER SESSION 2

Commons West, Easel 20
1:00 PM to 2:30 PM

Examining Gender Differences in Student Perceptions of Strategies to Establish, Maintain, and Restore Student-Teacher Relationships
Nuradin J Abdalla, Senior, Psychology
Mentor: Jessica Coifman, SMART Center - Psychiatry & Behavioral Sciences
Mentor: Stephanie Brewer, Psychiatry and Behavioral Sciences
Mentor: Larissa Gaias, Psychiatry & Behavioral Sciences, UW Medicine

Establish-Maintain-Restore (EMR) is a professional development training for teachers to strengthen their relationships with their students. Previous studies have shown that the strategies presented in the training have significantly improved academically engaged time and reduced disruptive behavior among elementary and middle school students. The proposed study will examine 9th grade high school student perceptions of the appropriateness and effectiveness of the EMR strategies to improve student-teacher relationships within the school context. Additionally, this study will analyze whether there is a significant difference in these perceptions between the genders of students. It is predicted that male students will tend to perceive the EMR strategies as less effective and appropriate in improving student-teacher relationships compared to their female peers. A focus group was held to present the EMR strategies to 9th grade students at a racially/ethnically diverse high school in the Pacific Northwest. After the strategies were presented, students were asked to provide ratings and comments regarding the appropriateness and effectiveness of each individual strategy. The students were asked about the following items for each of the EMR strategies: appropriateness for school context, appropriateness for both students and teachers, and effectiveness at improving relationships with high school students. Findings from this study will offer insight for improving student-teacher relationships with consideration for the students' gen-

ders. Research has shown that strong student-teacher relationships can serve as a protective factor against high school dropout, and this study may help provide information about culturally responsive strategies to reduce the dropout rates among students of color and male students.

POSTER SESSION 4

MGH 241, Easel 131

4:00 PM to 6:00 PM

Modeling the Human Disease Meier-Gorlin Syndrome in Yeast

Anthony Cessna, Junior, Biology (Molecular, Cellular & Developmental)
Mentor: Bonita Brewer, Genome Sciences

Meier-Gorlin Syndrome (MGS), a form of human proportionate dwarfism, arises from mutations in proteins needed for chromosome replication, including the origin recognition complex protein Orc4. Yeast cells (*S. cerevisiae*) with the mutant allele (orc4MGS) have altered origin activity across the genome, but most dramatically, origin activity in the rDNA is abolished. The orc4MGS cells also display secondary phenotypes such as slow growth, temperature sensitivity, and sensitivity to the drugs hydroxyurea and cycloheximide. To deal with the lack of rDNA origin activity yeast with fewer rDNA repeats (about 10) overtake the culture. My research focuses on understanding whether the secondary yeast phenotypes are due to fewer rDNA repeats, or other consequences of mutant Orc4. To explore the distinction, I am using CRISPR/-Cas9, a system for precise gene editing, to replace the origins of replication in the rDNA region with more efficient origins (ARS1 and ARS1^{m}ax). CHEF gel electrophoresis provides a reliable way to quantify the copy number of rDNA repeats in my new strains. The copy number of rDNA increased in my mutant strains to about equal, or even above that of the parent strain. With the rDNA copy number of these new strains restored, I am retesting the previously secondary phenotypes of the orc4MGS strain. Testing is ongoing, but the data suggest that the strains I created now display intermediate phenotypes of growth rate, temperature sensitivity, and drug sensitivity. I conclude from the data that fewer rDNA repeats, as well as the mutant Orc4 protein contribute to the phenotypes observed in the original Meier-Gorlin yeast cells. I am currently determining the efficiency of the new origins in the rDNA, and asking how genome wide origin use has changed. With these experiments I hope to gain insights into some of the cellular mechanisms of Meier-Gorlin Syndrome.