Undergraduate Research Symposium May 17, 2013 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Commons West, Easel 29

11:00 AM to 12:30 PM

Regulators of rDNA Copy Number

Xiaobin (Summer) Wang, Sophomore, Biology (Molecular, Cellular & Developmental)
Mentor: Bonita Brewer, Genome Sciences
Mentor: Elizabeth Kwan, Genome Sciences

Eukaryotic genomes contain many copies of ribosomal DNA (rDNA) encoding the RNA components of ribosomes, ranging from 150 tandem repeated copies in the budding yeast Saccharomyces cerevisiae to approximately 700 copies total in diploid human cells. It is not known what dictates rDNA copy number, but we hope to gain insight by identifying genetic regulators of rDNA copy number. Recent work in the Brewer/Raghuraman lab using S. cerevisiae reveals connections between rDNA copy number and cellular processes, such as genome replication and replicative aging. These studies suggest that too few rDNA copies cannot satisfy ribosome demand and too many copies can interfere with DNA replication. Thus, certain genetic pathways must function to maintain such balance. Our preliminary survey finds that some strains with specific single gene deletions have varying rDNA copy numbers, suggesting genetic control of the flexibility of rDNA copy number. Our goal is to identify genetic regulators of rDNA copy number in a systematic genome-wide screen. I have developed a high throughput screen to look for strains with variation in rDNA copy number by measuring the size of chromosome XII, the chromosome that carries the rDNA locus. I will use this method to screen a yeast library of approximately 5000 non-essential single gene deletions. After finding and analyzing mutant strains with chromosome XII size changes, we will have a more comprehensive understanding of the cellular mechanism that controls rDNA repeat number. As rDNA repeat number is linked to replicative lifespan, we hope to uncover the common genetic pathways that regulate rDNA copy number and longevity.

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Does Early Replication of Centromeres Prevent Genetic Instability?

Seungbeen (Steven) Lee, Junior, Biochemistry
Mentor: Bonita Brewer, Genome Sciences
Mentor: Thomas Pohl, Molecular and Cellular Biology Program

DNA replication is vital for cell division as it produces exact copies of all chromosomes for the two daughter cells. During S-phase of the cell cycle, DNA replication begins at specific, defined locations within a chromosome known as origins of replication. Interestingly, some origins activate in early S-phase while others activate late. The biological significance of this temporal control of replication is largely unknown. In multiple species, centromeric DNA, the site of recruitment for proteins required for separation of chromosomes during mitosis, has been found to be early replicating. The Brewer/Raghuraman lab has recently shown that centromeres in the budding yeast *Saccharomyces cerevisiae* promote their own early replication by advancing the activation time of their neighboring origins. The conservation of early centromere replication coupled with the Brewer/Raghuraman lab's recent finding suggests that early centromere replication may be important for chromosome maintenance. We set out to determine the consequences of a late replicating centromere by artificially delaying its replication time in *S. cerevisae*, through replacing its nearby origins with drug resistant markers. To enhance sensitivity of the experiment, I impaired the activity of the spindle checkpoint that monitors correct chromosome segregation. I also constructed a control chromosome with an early replicating centromere and the same markers. I will then compare the degree of chromosomal instability, as measured by survival on drug plates, of the control cells to those that contain a late replicating centromere. We expect the experimental group to show an increase in the number of cells that have lost the chromosome compared to the control cells. Even if the effect is small we will perform long-term growth experiments to analyze how the cells cope with reduced genetic stability. The results of this study will provide a better understanding of the biological importance of the temporal replication program.