Molecular Analysis of Genetic Pathways Coping with Genotoxic Stress Caused by DNA Over-Replication

Project Leader
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1. Objective

This project is aimed at understanding how eukaryotic cells cope with genotoxic stress, which is caused by the failure of tight replication control. Chromosomal DNA replication is tightly regulated in the eukaryotic cell cycle, however, escape from the tight regulation may happen. Such an escape is genotoxic and also might cause genome instability, a hallmark of cancer. By using a model eukaryote, the budding yeast *Saccharomyces cerevisiae*, we would like to understand how cells cope with the escape from replication control at the molecular levels.

2. Project Outline

To that end, the project will consist of the following phases:
(a) Construction of mutants lacking various genes functioning in genome maintenance pathways
(b) Identification of pathways involved in the maintenance of viability after inducing genotoxic DNA over-replication
(c) Understand how eukaryotic cells cope with the genotoxic stress caused by failure of tight replication control

3. Expected Performance

In this project, the successful candidate would be expected to:
(a) Play a significant role in the research project
(b) Work actively and collaboratively with other members of the research group

4. Required Skills and Knowledge

The successful candidate for this project will have the following knowledge and skills:
(a) A solid understanding on molecular biology, cell biology, and molecular genetics
(b) Basic knowledge of the eukaryotic cell cycle (preferred)
(c) General molecular biology skills

References

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(2) Tanaka, S., & Araki, H. (2013). Helicase activation and establishment of replication forks at chromosomal origins of replication. *Cold Spring Harbor perspectives in biology*, *5*(12), a010371.
(3) Tanaka, S., & Araki, H. (2011). Multiple regulatory mechanisms to inhibit untimely initiation of DNA replication are important for stable genome maintenance. *PLoS genetics*, *7*(6), e1002136.
(4) Tanaka, S., Umemori, T., Hirai, K., Muramatsu, S., Kamimura, Y., & Araki, H. (2007). CDK-dependent phosphorylation of Sld2 and Sld3 initiates DNA replication in budding yeast. *Nature*, *445*(7125), 328-332.

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