

Molecular Insights into Cellular Quiescence: The Role of Uridylation and RNA Metabolism

My project aims to uncover the hidden mechanisms that allow cells to persist and recover from quiescence. Quiescence — a state where cells stop dividing but remain viable — remains one of biology's long-standing puzzles. It is a resting, non-dividing phase during which cells temporarily exit the cell cycle. Importantly, this state is reversible, and cells can repeatedly enter dormancy while awaiting favorable environmental conditions. Quiescence often arises in response to stresses such as nutrient deprivation or other environmental challenges. Understanding this process can provide valuable insights into life, disease, and the resilience of living systems.

I particularly focus my research on RNA modifications, especially a process called uridylation. **Uridylation** is a specific modification of RNA that involves adding uridine molecules (one of the building blocks of RNA) to its specific end. RNA, or ribonucleic acid, is one of the key molecules in living organisms. It acts as a 'messenger,' carrying genetic information from DNA to ribosomes, the protein factories in cells. This process enables cells to produce the proteins necessary for proper functioning. RNA is incredibly versatile—not only does it transmit information, but it also regulates genes and supports biochemical processes within cells.

Although uridylation might seem minor, it plays a critical role in cellular life. It is crucial for regulating RNA, as it tags RNA molecules destined for degradation, helping cells eliminate unnecessary or damaged RNA.

Studying uridylation can shed light on how cells manage their RNA resources, particularly under the challenging conditions of quiescence. Understanding these processes has implications not only for basic biology but also for medicine, as disruptions in cell division can lead to diseases such as cancer and neurodegenerative disorders.

My preliminary research suggests that uridylation is vital for protecting RNA from degradation and stabilizing transcripts. Understanding how this modification functions could reveal how cells survive extended periods of inactivity. To investigate these mechanisms, I will use fission yeast (*Schizosaccharomyces pombe*), a unicellular but powerful model organism. This yeast was also used by Prof. Paul Nurse in his Nobel Prize-winning studies on the cell cycle. Remarkably, about 80% of fission yeast genes have counterparts in the human genome, making it an invaluable model for understanding cellular processes relevant to human health.

Quiescence in fission yeast can be controllably induced by removing nitrogen from the growth medium, pushing cells into a non-dividing state. These yeast cells can survive for weeks under such conditions and resume division when nutrients are restored. Using advanced genetic engineering and sequencing techniques, I will study yeast strains with targeted disruptions in RNA uridylation and degradation pathways. By analyzing how these changes affect survival in the resting state, I aim to identify key factors that govern this remarkable phase.

The anticipated results of my project could have far-reaching impacts across diverse fields of life sciences. For instance, in agriculture, they could enhance our understanding of plant seeds, which also remain in a non-dividing (dormant) state until favorable conditions trigger germination. In medicine, my research could provide insights into human diseases linked to non-dividing cells, such as neurological disorders involving neurons. Additionally, understanding what signals drive oocytes to exit the resting state and re-enter the cell cycle could help uncover the causes of infertility. Finally, this work may pave the way for using fission yeast as a model system to study human disorders associated with cellular dormancy.