Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, October 13, 2023 @12:00 p.m.

presented by:

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"Investigating the biological significance of the ribosomal protein S24 short and long isoforms in hypoxia"

Over the course of the past decade, the concept of ribosome heterogeneity has experienced a mild renaissance. Erstwhile portrayed as a static molecular machine that plays a passive and indiscriminate role in the synthesis of proteins, this view has since been discarded in favor of a model which depicts the ribosome as a dynamic macromolecular complex with specialized roles in the cell. The behavior of the ribosome is somewhat analogous to a factory whose modes of operation and lines of production are regulated by the needs of the cell. Several lines of evidence indicate that ribosomes translate different pools of mRNA in response to stress in order to produce an ensemble of proteins aimed at promoting cell survival, preventing DNA damage, and recovery. Conformably to the well-known observation that hypoxia-induced alternative splicing is a hallmark of cancer, a research study published by the Uniacke Lab found that hypoxia, induces alternative splicing patterns in five ribosomal proteins, most prominently in spheroids (3D hypoxic cell culture models). In particular, the inclusion of a 22 base pair cassette exon in the coding region of the ribosomal protein S24 is upregulated in hypoxia, and results in increased cell viability in low oxygen conditions. My research aims to investigate the effect of alternative splicing of RPS24 in conferring the ribosomes the ability to translate specific subsets of transcripts aimed at promoting survival in hypoxia. Furthermore, I am investigating post-translational modifications of the C-terminus of RPS24-short isoform through site-directed mutagenesis, in light of the observation that its hypoxic counterpart loses three residues, namely a lysine. Hypoxia in tumors is associated with metastasis, poor prognosis and resistance to treatment. It is therefore an important area of cancer research, where the discovery of hypoxic biomarkers could help in the early detection of tumors, and where critical hypoxic processes are promising targets for tumor-specific treatments.