Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, October 4th, 2024 @ 12:45 p.m.

presented by:

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(Advisor: Dr. Jim Uniacke)

"Evaluating the function of hypoxia-induced RPS24 alternative splicing isoforms in glioblastoma"

Glioblastoma is the most aggressive type of malignant primary brain tumour. With less than 5% of patients surviving 5 years after diagnosis, research into the oncogenic mechanisms of survival and progression is integral to improving treatment and patient prognosis. In a solid cancer like glioblastoma, the center of a tumour often exists in a hypoxic state due to insufficient vasculature and rapid growth. These cells do not receive enough oxygen to function normally and instead mount a stress response, wherein they worsen a variety of cancer progression characteristics, such as stemness, angiogenesis, metastasis, therapy resistance, and alternative splicing. One such hypoxia-induced alternative splicing event occurs in ribosomal protein S24 (RPS24), creating long and short variants. Under hypoxic conditions, the long variant is preferentially expressed. Inclusion of either of these RPS24 isoforms in the ribosome may differentially regulate the translation of key genes involved in the hypoxic response and worsen patient prognosis. Previous work from the Uniacke lab generated stably-transfected human glioblastoma cells overexpressing either the long or short RPS24 isoform. The short overexpressors showed a significant decrease in viability under hypoxic conditions, which was not seen in the long overexpressors. When grown in a 3D tumour model (spheroids), the short overexpressors displayed less growth but more invasion and migration than the long overexpressors. My project aims to explore the functions of these alternatively spliced RPS24 isoforms using a polysome profiling and RT-qPCR approach. I also aim to investigate the differences between the RPS24 short- and long-expressing spheroids using immunofluorescence.