Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, March 1, 2024 @ 12:30 p.m.

presented by:

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(Advisor: Dr. Jim Uniacke)

" Investigating the mTOR-dependent and -independent signaling cascades that lead to a shift in ribosomal protein S24 isoforms during hypoxia in U87MG glioblastoma"

Hypoxia, or low oxygen levels, is a hallmark of tumor microenvironments. Previous research conducted by the Uniacke lab has found that one cellular adaptation that is driven by hypoxia involves the alterations in ribosomal protein isoforms, particularly ribosomal protein S24 (RPS24), which undergoes alternative splicing, yielding short (RPS24S) and long (RPS24L) mRNA transcript variants. Later studies have confirmed that the RPS24L/RPS24S ratio increases with prolonged hypoxic exposure and RPS24L induction is autophagy dependent. In this research, we aim to investigate the mTOR-dependent and -independent autophagy signaling cascades that lead to the induction of RPS24L in U87MG glioblastoma cells during hypoxia through utilizing inhibitors and activators targeting key components involved in autophagy signaling, including ULK1, AMPK, calcium channels, and dopamine receptors. Experimental approaches include western blot analysis to confirm drug activities, assess autophagic flux and mTOR activity, as well as qRT-PCR to quantify RPS24L expression levels. Additionally, cell viability assays under hypoxia and serum starvation conditions will be used to evaluate the functional significance of RPS24L overexpression. Overall, this study could contribute to understanding the molecular mechanisms underlying hypoxia-induced alterations in ribosomal protein isoforms and hold implications for targeting autophagy pathways as a potential therapeutic strategy for hypoxia-driven cancers.

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