Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, April 7, 2017 in SSC 1511 @ 12 noon

presented by:

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Investigating the role of DDX28 as a negative regulator of translation initiation in low oxygen conditions

The most common form of translation initiation in eukaryotes occurs in a cap-dependent manner, which requires the recruitment of the eukaryotic translation initiation factor 4F (eIF4F) to the m^7GTP cap located at the 5' end of all cellular mRNAs. eIF4F is a heterotrimeric protein complex composed of the cap binding factor eIF4E, the RNA helicase eIF4A, and the scaffolding protein eIF4G, which together function to initiate cap-dependent translation. However, in response to hypoxia, a common feature of the tumour microenvironment, intricate signaling pathways are activated that culminate in the inhibition of eIF4E. Recently, it was discovered that hypoxic cells are able to utilize an alternate 5' cap binding mechanism, whereby cells switch to the use of the eIF4E homologue, eIF4E2, in order to maintain selective cap-dependent translation of critical hypoxic mRNAs. While there is some understanding of how this hypoxic translation initiation complex, $eIF4F^H$, is functioning, there is still little known about how it is regulated. Preliminary research has identified DDX28, a member of the DEAD-box family of RNA helicases, as a potential negative regulator of eIF4E2. The proposed research will aim to characterize the regulatory role of DDX28 in $eIF4F^H$-mediated translation through the generation of stable DDX28 knockdown cell lines, co-immunoprecipitation, cap-affinity assays, and polysome profiling. Given the novelty of this hypoxic cap-dependent translation mechanism, identification and characterization of $eIF4F^H$ regulators will not only aid in our understanding of translational versatility, but could also ultimately lead to the development of cancer-therapeutics that selectively target the hypoxic protein synthesis machinery.