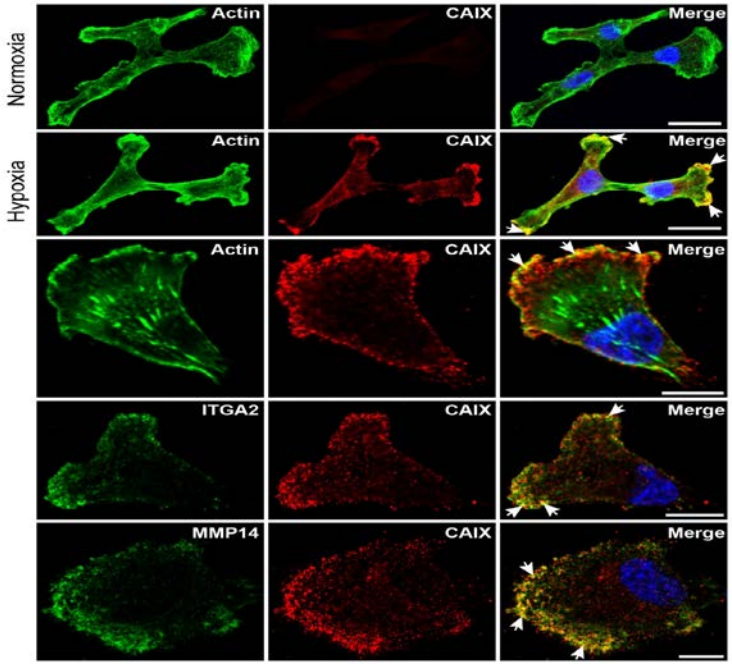
GUEST SPEAKER SEMINAR

Molecular Genetics
UNIVERSITY OF TORONTO

Coordinated Regulation of Metabolic Transporters and Tumour Cell Migration/Invasion by Hypoxia-Induced Carbonic Anhydrase IX



Hypoxia is a prominent feature of the tumor microenvironment (TME) and cancer cells must dynamically adapt their metabolism to survive in these conditions. A major consequence of metabolic rewiring by cancer cells in hypoxia is the accumulation of acidic metabolites, leading to perturbation of intracellular pH (pHi) homeostasis and increased acidosis in the TME. To mitigate the potentially detrimental consequences of an increasingly hypoxic and acidic TME, cancer cells employ a network of enzymes and transporters to regulate pH, particularly the extracellular facing carbonic anhydrase IX (CAIX) and CAXII. In addition to the role that these CAs play in the regulation of pH, recent Bio-ID, proteome-wide analyses have revealed the presence of a complex CAIX interactome in cancer cells with roles in metabolite transport, tumor cell migration and invasion. I will discuss the contributions of these interactions to the metabolic landscape of tumor cells in hypoxia and discuss the role of CAIX as a hub for the coordinated regulation of metabolic, migratory and invasive processes by cancer cells. I will also discuss recent work targeting CAIX activity in breast, pancreatic and brain (GBM) cancers with a highly selective small molecule inhibitors and briefly discuss ongoing clinical trials involving SLC-0111, a lead candidate small molecule inhibitor of CAIX/CAXII.

Dr. Shoukat Dedhar
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Host: Dr. Jason Moffat

Date: Thursday, March 22nd, 2018
Time: 4:00PM
Place: CCBR Red Seminar Room;
160 College St