BCHM 421/422 – 2022-23

Targeting Mitochondrial fusion in cancer cell metabolism and cell death regulation

Outline: Mitochondria are mainly considered as the central energy source for the cell, using acetyl-CoA to produce ATP. While mitochondria are typically drawn as oval-shaped tubes with internal cristae, these organelles are much more fluid and dynamic (for an excellent review to start see: (Youle and van der Bliek 2012)). In fact, mitochondria are constantly undergoing cycles of fission (to split into smaller units), or fusion (to form a large network). In normal cells, there is a coordinated balance of fission and fusion to help maintain a healthy pool in the cell.

We are studying roles, particularly for mitochondrial fusion, as a potential target in cancer cells. Importantly, mitochondria have wider roles coordinating cell metabolism and this overall function is intimately interrelated to the control of cell growth and death (reviewed with more detail in (Vyas et al. 2016)). Recent studies have suggested that mitochondrial fusion may be important for driving metabcolic reprogramming (Zhou et al. 2019), progression towards more metastatic state (epithelial-mesenchymal transition, EMT) (Wu et al. 2019) or resistance to chemotherapeutic treatments (Chen et al. 2019).

This project aims to determine roles for the mitochondrial fusion protein Opa1 as compared to Mitofusin1 and 2. These key regulators will be genetically targeted in cell models of breast cancer. We will study downstream effects in the coordination of cell metabolism and related stress response pathways. In addition, we will test effects of mitochondrial fusion alterations in responses to chemotherapeutic drugs in cell death assays. Findings could suggest potential targets to modulate mitochondrial function and reduce growth in cancer.

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Keywords: Mitochondria, Cell metabolism, Breast Cancer, Cell growth

Experimental approaches: You will learn how to culture breast cancer cell model. These cell models will be treated with gene targeting constructs to target mitochondrial dynamics pathways. Effects on cell metabolism will be measured by western-blot analysis of cell signalling and compared with parallel microscopy based analysis of mitochondrial dynamics. Cell growth and cell death pathways will be monitored following drug treatments.

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