BCHM421/422

Project #1 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 a good general review 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.

Here, we are interested in studying mitochondrial fission and fusion, particularly in cancer cells (Senft and Ronai 2016). 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 (Spinelli and Haigis 2018)). The mechanisms linking mitochondrial dynamics (fission and fusion) to cell metabolism remain poorly understood, and this is particularly the case in cancer cells. A number of studies have suggested that the mitochondrial fission protein Drp1 is required for metabolic reprogramming to promote high levels of cancer cell growth (as one good example, see (Serasinghe et al. 2015)). On the other hand, more 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 further study roles for key regulatory fusion proteins (Opa1, Mitofusin1 and 2). These key regulators will be genetically targeted in cancer cell models. 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.

Supervisor: Edmond Chan

Project title: Investigating mitochondrial fusion in cancer cell metabolism and downstream stress responses

Keywords:	Mitochondria	Cell metabolism
	Cancer biology	Cell growth

Project goals: To define the signalling events linking mitochondrial dynamics and cell growth.

Experimental approaches: You will learn how to culture mammalian cells. 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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