

BCHM421/422: 2019

Project Outline: Mitochondria are commonly understood as the energy source for the cell, using acetyl-CoA to produce ATP. While mitochondria are typically drawn as oval-shaped tubes containing cristae, these organelles are much more dynamic, splitting, fusing and moving through the cell as a large network. As cells become energetically stressed, mitochondria re-model and part of this may be to interact properly with the cell autophagy pathway.

During autophagy, cells degrade a portion of their cytoplasm as a last resort to meet nutritional requirements. Autophagy also plays a critical role in degrading damaged mitochondria, a process termed mitophagy. Mitophagy is crucial for cell homeostasis since accumulation of damaged leaky mitochondria will very quickly poison the cell. In the current model, cancer cells hijack this system to elevate levels of mitochondrial fission to produce smaller fragments that may be better targets for maintenance via mitophagy. Cancer cells thus become reliant on mitophagy to support mitochondrial biosynthetic function required for growth. We have been investigating the mechanisms that coordinate mitochondrial dynamics and autophagy during stress. This project aims to study the mitochondrial fission and fusion pathways important in cancer cells.

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Project title: Regulation of mitochondria dynamics in cancer cells

Keywords: Mitochondria Cell metabolism
Signal transduction Protein kinase

Project goals: To define and target signalling events linking autophagy kinases to mitochondrial membrane dynamics

Experimental approaches: You will learn how to culture mammalian cells. Regulatory factors for mitochondrial dynamics will be targeted by RNAi and CRISPR-Cas9 based vectors. These cell models will be treated to different nutrient stress conditions or control stimulants. Signalling events will be measured using immuno-blotting protein biochemistry. Mitochondrial fusion will be measured using microscopy and computer-based analysis of mitochondria patterns.

References:

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