Calcium signaling is integral to the life of a cell in innumerable ways, not the least of which include metabolism, autophagy, and apoptosis. The presence of calcium in the mitochondria is central to the function of several of the dehydrogenases in the tricarboxylic acid cycle, as well as for complexes I, III, and IV of the electron transport chain; basal autophagy is regulated by the constitutive release of calcium, and a complex calcium signaling pathway triggers an increase in crisis-response autophagy; and calcium controls the transition of the cell through the stages of its life cycle, most notably triggering apoptosis by interacting with the Bcl-2 family of proteins to release cytochrome c from the mitochondria to form the apoptosome, from which all other events of apoptosis are derived. These are just a few examples of the varying roles of calcium in the cell; calcium also influences secretion, cytoskeleton homeostasis, mitotic division, and the redistribution of the mitochondria. Because of the pervasive effects of calcium, regulation of calcium signaling allows the tight control of the cell's life cycle and response to both internal and external signals of danger. Of physical significance in calcium homeostasis and signaling is the flux of calcium from the endoplasmic reticulum (ER) to the mitochondria. Regulated, responsive calcium flux between the ER and mitochondria has been suggested to play a key role in the development of many cancers and neurodegenerative diseases because of its centrality in the control of the cell life cycle. While the importance of this topic is widely recognized, a gap in knowledge exists surrounding the mechanisms by which these calcium flux mechanisms can lead to disease. In this study, we seek to examine the impact of constitutive activation of KRAS via a G13D mutation on the ER-mitochondrial calcium flux in colorectal cancer cells. We use three isogenic colorectal cancer cell lines for this purpose, in order to eliminate complicating factors such as cell type and stage of oncogenic development. Our aim is to examine the specific impact of a KRAS mutation on the ER-mitochondrial calcium

flux, which will provide direction for further studies to identify the proteins and complexes involved in this process and how they are affected by a mutated KRAS. This information will contribute to a framework of information that will guide therapeutic approaches to treating colorectal cancer in affected patients.