Mitochondria play an important role in maintaining cellular energy homeostasis and mitochondrial function is highly responsive (i.e., adaptable) to environmental cues. For example, expansion of the mitochondrial network is typically observed in response to exercise training and decrements in mitochondrial respiration are commonly detected in models of cellular disease and/or injury. During this seminar presentation, we will discuss the impact of high-fat diet on skeletal muscle and hippocampal mitochondrial function.