Mammalian hibernation is a strategy employed by many species to survive fluctuations in resource availability and environmental conditions. Hibernating mammals endure conditions of dramatically depressed heart rate, body temperature, and oxygen consumption; yet do not show the typical pathological responses. Because of the high abundance and metabolic cost of skeletal muscle, not only must it adjust to the constraints of hibernation, but it is also positioned to play a more active role in the initiation and maintenance of the hibernation phenotype. My M.S. thesis research has primarily focused on the generation and analysis of two high-throughput ‘omics screens in thirteen-lined ground squirrel skeletal muscle. A transcriptomic analysis using Illumina HiSeq2000 technology identified 1,466 differentially expressed genes throughout their circannual cycle. This RNAseq data allowed for greater protein identifications in an iTRAQ based proteogenomic analysis of the same animals. Of the 1,563 proteins identified by this proteogenomic approach, 232 were differentially expressed. These data support previously reported physiological transitions, while also offering new insight into specific mechanisms of how hibernator muscles might be reducing nitrogenous waste, preserving mass and function, and signaling to other tissues. Sarcolipin is a specific gene of interest that shows a 10-fold difference in expression between hibernation and spring collection points. Because of sarcolipin’s role in muscle-based thermogenesis and calcium homeostasis bioenergetics, I have been developing methods to measure the consequences of this differential expression. Results suggest that this may be a major mechanism contributing to whole-body cooling and metabolic depression in hibernating mammals.