Title: The Effect of Muscle Cell Differentiation on IRE1α Activation and the Unfolded Protein Response

Authors: **Marco Zamora**, Jenna Kastenschmidt, Jovani Cataland, Dr. Armando Villalta

The endoplasmic reticulum (ER), one of the base structures of a cell, is the site in which newly synthesized proteins are folded. This process is tightly regulated to ensure that the cell is working at optimal capacity and homeostasis, balance, is maintained. When the folding capacity of new proteins is surpassed, cells enter a state of stress called endoplasmic reticular stress (ER stress), which triggers the Unfolded Protein Response (UPR). The UPR is regulated by three main proteins inositol requiring enzyme 1 α (IRE1α), protein kinase RNA-like endoplasmic reticulum kinase (PERK), and activating transcription factor 6 (ATF 6), providing different pathways to assist the cell in its goal of homeostasis. The main function of the UPR is to help the ER catch up to cellular demand and restore homeostasis. However, irremediable ER stress and chronic activation of the UPR results in cell death (apoptosis). The C2C12 stem cell, a mouse myoblast cell line, can develop into myotubules, the basic structures of skeletal muscle, providing an in vitro system to test the effect of ER stress and the UPR on muscle differentiation. To test the hypothesis that IRE1α regulates muscle cell differentiation we differentiated C2C12 in the presence of thapsigargin, a chemical that induces IRE1α-mediated ER stress. We anticipate that in increasing the concentrations of thapsigargin thus inducing ER stress, will lead to increased splicing of X-Box Binding Protein 1 (sXBP1) and increases muscle cell differentiation.