**SLC3A2 IS A NOVEL ER STRESS-RELATED SIGNALING PROTEIN THAT REGULATES BOTH UPR AND APOPTOSISIN CARDIOMYOCYTES**

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Cardiomyocytes are terminal differentiation cells. The key to governing heart disease is to reduce apoptosis. Imbalances in unfolded/misfolded proteins in the endoplasmic reticulum (ER), resulting in ER stress, have been related to a wide variety of heart diseases including heart failure. To better understand the mechanisms involved in the cellular response to ER stress in cardiomyocytes, we previously screened genes on a genome-wide scale in an ER stress model. Amino acid transporter heavy chain, member 2 (SLC3A2) was highlighted as an important factor in ER stress. In the present study, we characterized the role of SLC3A2 during the unfolded protein response (UPR), which is one of the primary pathways activated during ER stress. To do so, we first confirmed the activation of SLC3A2 mRNA following treatment with various ER stress inducers in H9C2 and PC12 cells. Using siRNA to inhibit SLC3A2, this factor was then shown to function upstream of ATF4, ATF6, and XBP1, three important UPR proteins. To gain a more thorough understanding of SLC3A2 function, RNA-seq was used and successfully identified a list of 23 highly differentially regulated genes. These data further validated the influence of SLC3A2 in UPR as well as amino acid transport. Notably, SLC3A2 inhibition was also observed to enhance apoptosis in flow cytometry experiments. Taken together, SLC3A2 is a complex, multifunctional signaling protein that acts upstream of well-known UPR proteins and has anti-apoptotic properties.SLC3A2 may be a potential drug target in heart disease.