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"Analysis of the Role of ES1 Protein on Methylglyoxal (MGO) and Advanced Glycation End Products (AGEs)"

Methylglyoxal (MGO) is a dicarbonyl metabolite primarily derived from the spontaneous degradation of glycolysis intermediates such as triosephosphates and dihydroxyacetone phosphate. MGO is a major contributor to glycation, a nonenzymatic glycosylation process, which leads to the formation of advanced glycation end products (AGEs). In aging hearts and in various pathologies such as hypertrophy, the heart relies more on glycolysis for energy production. This increase in glycolysis increases MGO formation which induces dicarbonyl stress, leading to elevated AGE levels. Elevated AGEs are demonstrated to cause irreversible damage to proteins, disrupting their structure and function, which leads to further disease.

MGO should be removed by the dicarbonyl metabolic system, yet the mitochondrial mechanisms involved remain poorly understood. Previous studies suggest that the mitochondrial protein ES1 might exhibit either glyoxylase or deglycase activity, aiding in MGO degradation or AGE degradation. This study aims to investigate the role of ES1 in MGO degradation and AGE degradation. We hypothesize that cells overexpressing ES1 will exhibit increased survival and reduced AGE levels when treated with MGO compared to control cells.

To test this hypothesis, AC16 human cardiomyocyte cells were transduced with either control (green fluorescent protein, GFP) adenovirus or ES1 overexpression adenovirus on Day 0 for 48 hours. On Day 2, The GFP and ES1 transduced cells were treated with either 4 μM of MGO or control treatment for 24 hours. On Day 3, cells were lysed, and proteins were harvested using RIPA buffer. Western blotting was performed to confirm ES1 overexpression. MTT assay was performed to measure cell viability in the presence of 4 μM of MGO. Next, an ELISA was performed to measure AGE concentrations. The MTT assay results suggest that cells overexpressing ES1 had significantly higher survival in the presence of MGO compared to control cells. The ELISA results indicate that cells overexpressing ES1 had significantly less AGE concentrations than control cells.

The current results demonstrate that ES1 may increase cell survival and reduce AGE concentrations when exposed to high levels of MGO. Future experiments will help gain further insight into the role ES1 plays in the degradation of MGO and AGEs. If the mitochondrial dicarbonyl metabolic system and the role of ES1 in MGO and AGE degradation is fully understood, it can be used to help develop strategies for preventing AGE formation, thereby promoting heart health in aging and various pathologies.