Reha Rabbani

Dr. Ravichandran Ramasamy

Dr. Henry Ruiz

Abstract

RAGE is a multi-ligand receptor that binds to AGE (advanced glycation end product) and leads to a series of cellular immune responses. These immune responses are exacerbated in an obese condition and can in turn lead to replicative cellular senescence. Replicative senescence occurs when telomeres become shortened and DNA damage occurs, therefore arresting the cell cycle. It has been shown through previous research that RAGE expression increases with obesity. It is hypothesized that obesity leads to cellular senescence, and that RAGE may accelerate this process in oxidative tissue like heart. To investigate our hypothesis, hearts were isolated from mice that were categorized into 4 groups based off of their diet: Standard Chow, High Fat Diet Wild Type, Standard Chow High Sucrose, and High Fat Diet High Sucrose. The mice with high fat diets consumed 60% calories from fat. RNA extraction was performed, and RT PCR (reverse transcriptase polymerase chain reaction) was performed to probe for senescence markers cyclin-dependent kinase inhibitor 2a (Cdkn2a) and cyclin-dependent kinase inhibitor 2b (Cdkn2b). Initial studies demonstrated feasibility for the proposed hypothesis.

After analysis of the data graphically, there was seen to be a doubling of the presence of Cdkn2b in mice that were fed a high fat, standard chow high sucrose, and high fat high sucrose diet compared to the control standard chow group. There was no clear increase in Cdkn2a. However, when standard paired t-tests and Mann Whitney tests were performed comparing all the subgroups amongst each other, there was seen to be no significant difference between the presence of Cdkn2a or Cdkn2b in the mice with different diets. Some factors contributing to these results could be the small sample size or pipetting errors in the final RT PCR process. There is further research needed in order to display a definitive link between aging and the accumulation of Cdkn2a and Cdkn2b senescence markers, along with the interaction of RAGE. With future research, we will investigate this same hypothesis with a larger sample size, and with RKO and Wild Type mice.