Nicotine and Genistein as Novel Therapeutic Agents for Alzheimer's Disease

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Alzheimer’s Disease (AD) occurs when aggregated Beta-Amyloid (ABeta) protein causes massive neuronal death, resulting in atrophy of affected brain regions, memory loss, and eventually death. My goal is to understand how to prevent ABeta aggregation and how this may be applicable for AD, as there are no effective methods of treatment or prevention for AD currently available. For the past 3 years, I have pursued this objective: in the first two years, I identified a mechanism in kidney cells for degrading ABeta, dormant in brain cells, and by mass spectrometry, identified Heat Shock Proteins 56 and 70 (HSP56 & HSP70) as possible regulators of ABeta. Last year, I found both HSPs to be potent in degrading ABeta, and that HSP expression could be upregulated with chemicals Nicotine and Genistein. I now hypothesize that Nicotine and Genistein have potential as therapeutic agents for AD by decreasing levels of ABeta and improving neuronal function. To test my hypothesis, I incubated stably-ABeta-expressing and wild-type neuronal cells with Nicotine and Genistein and analyzed the effects on ABeta, Glutamate (Glu), and Acetylcholine (Ach) levels by western blotting and on cell viability by Fluorescence Microscopy. I found Nicotine and Genistein to regulate ABeta expression, prevent aggregation, and police Glu and Ach levels. Genistein significantly improved neuronal activity and growth, showing potential for long-term treatment and prevention. Nicotine was mildly toxic, but thoroughly degraded ABeta and eventually improved neuronal growth, indicating potential as a short-term treatment. Based upon this, I conclude that Nicotine and Genistein indeed have strong potential as effective therapeutic agents for AD and am interested in pursuing preclinical animal studies.

Awards Won:

Second Award of $2,000