Yasmine C. Ferrell
High School
Thomas Jefferson Academy for Advanced Studies, Gretna, LA

Mentor: Jorgelina Calandria, PhD.
LSUHSC School of Medicine: Department of Neurology, Neuroscience Center of Excellence

"Maresin-1 protects Dopaminergic neurons in the Sustantia Nigra in a rat model using misfolded alpha-synuclein seeding."

Parkinson's Disease (PD) is a neurodegenerative disease affecting approximately one million people yearly, with it being ranked as the forty seventh leading cause of death. PD is characterized by the loss of neurons in the Sustantia Nigra pars compacta (SNpc) in the brain. Furthermore, the dopaminergic neurons lost are primarily involved in the control of movement and are usually diagnosed when 60-80% of the neurons in the SNpc are dead, affecting motor skills in late stages. A prevalent early symptom found in the disease is the loss of smell, indicating that the olfactory system is impaired. Due to this occurrence, olfactory dysfunction could be used as a starting point to find a general timeline for PD, which can then be used in early detection and treatment of the disease to rescue the dopaminergic neurons from dying. Recently, it was shown that Maresin-1 (MaR-1), an omega-3 derivative found to reduce the inflammatory effect of cells, can prevent the death of the dopaminergic neurons. In these cells, an excess of pro-inflammatory cytokines expression can cause inflammation in the neurons and recruit microglia and other inflammatory cells. We hypothesize that an early event in the formation of alpha-synuclein (α-Syn) aggregates found in Lewy Bodies (LB) occurs in the olfactory system and their spread to the SNpc and other regions is facilitated by inflammation affecting astrocytes and microglia phenotypes, thus Mar-1 halts the pathological process.

By administering preformed fibrils (PFFs) consisting of α-Syn- misfolded proteins intranasally in rat models, we can follow the early events leading to the formation of aggregates and damage in the SNpc. We treated the rats intranasally with two weekly doses of Mar-1 (5 µg each), starting one day after the PFF administration. The objective was to compare the control group (treated only with saline) with the groups that received PFF alone and with MaR-1. For this purpose, we used a weekly Food buried behavioral test that consisted of placing each group in a clean cage with a piece of cereal (Fruit Loops) in a random corner and the time spent by the animals until they found the food was recorded. This study was used to determine if there were impairments in smell, motor skills, and memory. We then use the brain tissue to determine if aggregation occurred, using Congo Red staining.

After around twenty-four weeks from the administration of PFF, it was prevalent that the group with only PFF started showing higher times during the tests, suggesting that olfactory impairment was taking place. The Congo Red staining showed initial formation of protein aggregates, which were less prominent in the Mar-1 treated rats. In conclusion, the loss of olfaction correlated with the formation of protein aggregates in the SNpc preceding the massive loss of dopaminergic neurons, and the protective effects of Mar-1. In the future experiments, we will determine the astrocyte implications in the mechanisms leading to the death of the dopaminergic neurons in SNpc and we will investigate the effects of MaR-1 on neurons and astrocytes during the early stages of PD.