

Marbella R. Maristany
The Willow High School
LSU Health Sciences Center, New Orleans, LA

Jorgelina M. Calandria PhD
LSUHSC, School of Medicine - Department of Neurology, Neuroscience Center of Excellence

“ α -syn PFF Triggers Stress Responses in Human Astrocytes That Induce senescence”

The substantia nigra pars compacta (SNpc) is a structure of the midbrain that is crucial for modulating the initiation of motor movement, among other specific cognitive and emotion-processing functions and is composed of a group of neurons that fire rhythmically at a rate of 2–10 Hz. This characteristic makes SNpc vulnerable to metabolic stress, characteristic that is altered in Parkinson’s Disease (PD) patients. In normal conditions, astrocytes sustain neuronal function. Recently, it came to our attention that there is a wide spectrum of phenotypes that astrocytes may acquire depending on the signaling they encounter, but the most striking observation is that astrocytes become progressively impaired under protein-misfolded pathological conditions. We hypothesize that astrocytes exposed to neurons undergoing degeneration related to α -syn aggregates become reactive and Maresin-1 revert this status. To determine the changes in phenotype, we exposed rat and human astrocytes in culture to α -synuclein preformed fibrils (α -syn PFF) in the presence or absence of Maresin-1 and recorded the nuclear translocation of NFkB/p65, a pro-inflammatory transcription factor; the expression of markers of senescence stress and inflammation and the activity of ALOX12, an enzyme in the synthetic pathway of Mar-1. α -syn PFF induced the upregulation of the senescence marker CDKN2B/p15INKB along with the activation of p65 and the increase transcription of HMGB1 and IL1B. Mar-1 addition decreased all four parameters. In addition, the activity of ALOX12 was decreased by α -syn PFF, suggesting that the aberrant form of α -syn may induce not only senescence but also an impairment of the astrocytes to secrete the pro-survival bioactive lipid Mar-1. Altogether, the results point to an induction in the impairment of the astrocytes by the α -syn PFF instead of promoting an inflammatory phenotype. In future directions we will focus on the mechanisms by which α -syn PFF induces senescence and the link between this cellular process and the decrease in the synthesis of Mar-1.