1. Abstract

Targeting neuroinflammation induced by senescent cells in Parkinson's Disease to improve outcomes

Parkinson's disease (PD) is a debilitating neurodegenerative disorder affecting millions of people worldwide. PI Riessland has shown that, in PD, dopamine neurons become senescent cells, cells that have stopped functioning and are pro-inflammatory. Further, his work demonstrates that these senescent cells upregulate COX-2 and secrete pro-inflammatory cytokines and other molecules that contribute to the development of chronic inflammation. This inflammation exacerbates neuronal loss and PD symptomatology. The aim of this study is to investigate the role of targeting senescent cell-induced inflammation in PD for the first time in parallel preclinical and clinical models. We will compare the level of inflammation in the brains of mice and humans with PD, as well as in response to treatment using a brain penetrant anti-inflammatory (Cox-2 inhibitor). High resolution studies in mice will inform the molecular underpinning of neuroinflammation, quantified by positron emission tomography (PET) in mice and humans. Further, treatment with an anti-inflammatory in both models will reveal whether pathology induced by senescent cells can be reduced or reversed. This will allow an improved understanding of the relationship between senescent cells and inflammation. The ultimate goal is to acquire preliminary data for a multi-PI R01. Our team has a unique combination of expertise in molecular/cellular techniques, brain imaging and clinical management of PD. By understanding the effects of inflammation reduction in PD, we may ultimately be able to develop new treatments that disrupt the pathological mechanisms of senescent cells, leading to improved motor and non-motor symptoms in patients. Overall, this study has the potential to provide new insights into the pathogenesis of PD and identify novel therapeutic strategies for the treatment of this debilitating disease.