

2nd International Conference on

Parkinson's Disease & Movement Disorders

December 05-07, 2016 Phoenix, USA

Activation of NLRP3-inflammasome in the MPTP mouse model of Parkinson's disease might be triggered by HMGB1-MAC-1 axis

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Mounting evidence suggests the involvement of the immune system in neurodegenerative disorders including Parkinson's disease (PD). We recently reported increased levels of HMGB1 in PD patients as well as in the MPTP animal model of PD. In the present study we explored whether the release of HMGB1 in our mouse model of PD caused the activation of the NLRP3 (NOD-like Receptor Protein 3) positive inflammasome. NLRP3-inflammasome is a multiprotein complex, and part of the innate immune system that is activated in aseptic conditions such as tissue damage or metabolic impairment. Its activation leads ultimately to both formation and release of the proinflammatory cytokine IL-1 β . C57BL6J mice were injected with the sub-acute regimen (30 mg/kg/day for five consecutive days i.p., control animals were injected with equivalent volume of saline solution) of the neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP). Brain tissue was harvested 1-2 days post-injection. Tissue was then prepared for double immunofluorescent staining of three different cell types: dopaminergic neurons, astrocytes and microglia, performed on midbrain sections inclusive of substantia nigra, or for western blotting experiments conducted on protein lysate from ventral midbrain. Our confocal microscopy analysis confirmed an increase in NLRP3 protein levels in the cytoplasm of microglia one day after MPTP injections. In parallel, heightened levels of the microglial MAC-1 protein were confirmed histologically at the level of the substantia nigra and by western blotting. This up-regulation of MAC-1, a surface receptor for HMGB1, may therefore constitute a critical link in the activation of cytoplasmic pathways leading to activation of the NLRP3-inflammasome in Parkinsonism.

Biography

Matteo Santoro successfully graduated in Chemistry and Pharmaceutical Technology at the University of Calabria, Italy in the year 2012. He is currently working on Parkinson's disease and investigating the role of a protein called HMGB1 in the pathophysiology of the disease. During his PhD Matteo Santoro has received four different prizes for best PhD student poster presentation and talks at different conferences within and outside the University of Aberdeen. He successfully co-authored two peer reviewed research articles on Parkinson's disease. The latest publication has seen him the main contributor of the study. He is presently a PhD student on the behavioral characterization of three different MPTP mouse models of Parkinson's disease and investigating the role of acquired and innate immune system in Parkinson's disease.

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