RANTES and Eotaxin: New players in PD progression

https://neurodegenerationresearch.eu/survey/rantes-and-eotaxin-new-players-in-pd-progression/ Principal Investigators

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Contact information of lead PI Country

USA

Title of project or programme

RANTES and Eotaxin: New players in PD progression

Source of funding information

NIH (NINDS)

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30/09/2013

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2

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Eotaxin, RANTES, Parkinson Disease, Disease Progression, glial activation

Research Abstract

DESCRIPTION (provided by applicant): Parkinson's disease (PD) is the second most common and debilitating age-associated human neurodegenerative disorder. Clinically, PD is characterized by tremor, slowness of movement, stiffness, and postural instability. Pathologically, it is indicated by activation of glial cells and progressive degeneration of the nigrostriatal dopaminergic neurons associated with the presence of intracytoplasmic inclusions (Lewy bodies). This application addresses an important aspect of PD. Although the rate of disease progression varies from patient to patient, PD is a progressive neurodegenerative disorder. However, the mechanism behind disease progression is poorly understood. We hypothesize that RANTES and eotaxin could hold the key for driving disease progression and that targeting these two chemokines may be an important strategy to control T cell infiltration and hence the disease progression in PD. Here this hypothesis will be tested from several experiments on mice, monkeys and humans. It is known that nigrostriatal pathology does not persist in acute MPTP mouse model. Under Specific aim I, we will investigate if supplementation of RANTES and eotaxin induces persistent and progressive disease in acute MPTP-intoxicated mice. Specific aim II has been planned to determine whether PD patients have higher levels of RANTES and eotaxin by monitoring the level of these two chemokines in serum of PD patients and age-matched controls. Finally, we have devoted the Specific aim III to delineate if blocking the functions of RANTES and eotaxin by maraviroc, an inhibitor of CCR5 and a FDA- approved drug, halt the disease progression in hemiparkinsonian monkeys. A positive outcome of this study will establish RANTES and eotaxin as targets for PD, translate CCR5-based treatment (maraviroc) to PD clinic, uncover the clue for the progression of PD, and find a drug to stop the progression of PD.

Lay Summary

PUBLIC HEALTH RELEVANCE: Parkinson's disease (PD) is a progressive neurodegenerative disorder. However, the mechanism behind disease progression is poorly understood. Here we will test the hypothesis that RANTES and eotaxin are key chemokines for driving disease progression and that targeting these two chemokines may be an important strategy to control the disease progression in PD. A positive outcome of this study will establish RANTES and eotaxin as targets for PD, translate CCR5-based treatment (maraviroc) to PD clinic, uncover the clue for the progression of PD, and find a drug to stop the progression of PD.

Further information available at:

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