

Role of the IL-13 system in dopaminergic cell death

<https://neurodegenerationresearch.eu/survey/role-of-the-il-13-system-in-dopaminergic-cell-death/>

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Country

USA

Title of project or programme

Role of the IL-13 system in dopaminergic cell death

Source of funding information

NIH (NINDS)

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€ 1,940,853.21

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01/09/2013

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2

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

IL-13, IL-13Ralpha1, Dopaminergic Cell, Interleukin-13, Interleukin-4, dopaminergic neuron

Research Abstract

DESCRIPTION (provided by applicant): We hypothesize that the anti-inflammatory cytokines IL-13 and IL-4 play an important role in the death of dopaminergic neurons in the Substantia nigra pars compacta (SNc), the same cells that are lost in human Parkinson's disease (PD). This

hypothesis is based on our preliminary studies in mice which showed that interleukin 13 receptor alpha 1 chain (IL-13Ralpha1), is highly expressed in DA neurons in the SNc and that mice that are deficient in this receptor are protected from the loss of dopaminergic (DA) neurons that occurs during chronic peripheral injection with low doses of LPS. Furthermore, in vitro studies using a dopaminergic cell line showed that while IL-13 alone does not have harmful effects on DA neurons, it strongly potentiates the toxicity of mild oxidative stress. Similar results were obtained with IL-4, another cytokine capable of activating IL-13Ralpha1-dependent signaling. Together these results suggest a novel mechanism whereby anti-inflammatory cytokines can contribute to neuronal loss under conditions of stress. We propose to investigate our hypothesis in three specific aims. In SA1, we will determine how the interaction between IL-13 (and IL-4) signaling and oxidative stress induces neuronal damage in vitro. In SA2, we will investigate the contribution of each of these cytokines to neuronal loss in vivo in a model of neuro-inflammation. In SA3, we will determine the cellular source of IL-13 and IL-4 during inflammation. These studies are highly relevant to understanding the role of inflammation in the pathogenesis of PD and may identify novel therapeutic targets for the treatment of this disease.

Lay Summary

PUBLIC HEALTH RELEVANCE: We propose to investigate the role of two cytokine signaling molecules, interleukins 13 and 4, in the survival of dopaminergic neurons in the brain during neuro-inflammation. The results are highly relevant to understanding the pathophysiology of Parkinson's Disease.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Parkinson's disease & PD-related disorders

Years:

2016

Database Categories:

N/A

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