

Neuron death in Parkinsons disease: The role of Trib3

<https://www.neurodegenerationresearch.eu/survey/neuron-death-in-parkinsons-disease-the-role-of-trib3/>

Principal Investigators

GREENE, LLOYD A

Institution

COLUMBIA UNIVERSITY HEALTH SCIENCES

Contact information of lead PI

Country

USA

Title of project or programme

Neuron death in Parkinsons disease: The role of Trib3

Source of funding information

NIH (NINDS)

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€ 1,591,055.96

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01/06/2012

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1

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

neuron loss, Parkinson Disease, Nerve Degeneration, reduce symptoms, synuclein

Research Abstract

DESCRIPTION (provided by applicant): The long-term goals of this project are to understand the molecular mechanisms that underlie the degeneration and death of neurons in Parkinson's Disease (PD) and to use this information in turn to devise treatments to suppress the

progression of this disorder in patients. The proposed studies will test the over-arching hypothesis that neuron degeneration and death in PD are due to inactivation of the key enzyme Akt which is required for nerve cell function and survival, and that this is mediated by induction of the stress-responsive protein Trib3, an inhibitor of Akt activation. The specific aims will assess four hypotheses: (1) that Trib3 expression is elevated in PD models and in PD; (2) that Trib3 mediates neuron degeneration and death in models of PD; (3) that Trib3 promotes neuron death by interfering with phosphorylation/activation of Akt; and (4) that induction of Trib3 in PD models and PD is mediated by the transcription factor ATF4. Multiple experimental approaches will be employed. These will include assessing Trib3 expression in toxin- and alpha- synuclein based cell culture models of PD, in animal models of the disease and in post-mortem brain tissues from PD patients and controls; determining whether loss of Trib3 expression, either via shRNAs or gene deletion, protects neurons from death in cell culture and animal models of PD; ascertaining (by over- expression or loss-of function studies) whether Trib3 is responsible for mediating the loss of Akt activity that occurs in cellular models of PD; and establishing whether manipulating expression of ATF4 in culture and animal models influences Trib3 induction in culture and animal models of PD. If successful, these studies will establish Trib3 as a required element in the mechanism that leads to neuron death and degeneration in PD and will provide insight as to how it does this, and how it is induced in this disorder. Such information will be exploited in the long term to formulate new approaches to suppress progression of PD in patients.

Lay Summary

Parkinson's disease (PD) is characterized by progressive degeneration and death of specific types of nerve cells. Current treatments are aimed at ameliorating the symptoms of this disease rather than its progression. The proposed studies seek to uncover the molecular mechanisms underlying nerve cell degeneration and death in PD so as to lead to generation of new strategies to suppress disease progression.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Parkinson's disease & PD-related disorders

Years:

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Database Categories:

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