The Biology of Neuroserpin

https://neurodegenerationresearch.eu/survey/the-biology-of-neuroserpin/

Principal Investigators

LAWRENCE, DANIEL A

Institution

UNIVERSITY OF MICHIGAN

Contact information of lead PI
Country

USA

Title of project or programme

The Biology of Neuroserpin

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,459,028.44

Start date of award

01/08/1995

Total duration of award in years

3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders|Alzheimer's disease & other dementias

Keywords

neuroserpin, Plasminogen Activator, platelet-derived growth factor C, neurovascular, Platelet-Derived Growth Factor alpha Receptor

Research Abstract
? DESCRIPTION (provided by applicant): Neurodegenerative disorders such as Alzheimer’s and Parkinson’s disease are devastating conditions affecting more than 6 million Americans in 2012, and according to the Alzheimer’s Association and the Parkinson’s Disease Foundation the incidences of both disorders are expected to more than double by 2050. Neurodegeneration

is the progressive loss of neuronal structure and function, and currently there are no effective treatments that halt or slow neurodegenerative diseases. The causes of most neurodegenerative diseases are not known; however, research has suggested that there may be common or overlapping pathways that promote their development. The identification of common pathways that affect the development and progression of neurodegenerative diseases would provide essential insight into these devastating disorders, and importantly offer novel opportunities for therapeutic intervention. One potential common pathway that may impact diverse central nervous system (CNS) disorders is dysregulation of neurovascular responses. Neurovascular responses are primarily controlled by the neurovascular unit (NVU) and recent work suggests that the serine protease tissue-type plasminogen activator (tPA) acting on the NVU may play a critical role in the regulation of neurovascular responses. The primary inhibitor of tPA in the CNS is the serine protease inhibitor (serpin) neuroserpin (Nsp), and data from the previous funding period of this application suggests that like tPA, Nsp can also regulate neurovascular responses. By using a combination of molecular and genetic approaches in vivo, studies will characterize the activities of Nsp and tPA in the CNS, and examine their role(s) in normal and pathologic CNS physiology. Based on our previous studies and the work of others, we will test the hypothesis that tPA in the NVU activates latent PDGF-CC which mediates neurovascular responses that can increase both cerebral blood flow and blood brain barrier (BBB) permeability, and that Nsp, expressed in vasoregulatory interneurons, can be released to moderate the activity of tPA and facilitate the return of the cerebral vessels to baseline levels o blood flow and permeability. Finally, we will test the highly innovative hypothesis that tPA/Nsp-mediated dysregulation of neurovascular responses may be a common feature in the development of neurodegenerative disorders.

Lay Summary

PUBLIC HEALTH RELEVANCE: Neurological disorders affect nearly one billion people worldwide; including 50 million who suffer from epilepsy and 10 million with Parkinson’s disease. This application examines how the regulation of blood vessels in the brain affect normal brain function, and the development of disorders of the brain such seizures and Parkinson’s disease. By understanding how incorrectly regulated blood vessel responses contribute to neurological disease, it is expected that new treatments for neurological diseases can be identified.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias, Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A