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Toxic effect of pathogenic tau on the nucleus

SEMINAR & VISITING SPEAKER SERIES

WORLD WIDE NEURO PLATFORM

DATE

Monday, April 26, 2021
12:00 PM (noon) CST

WORLD WIDE NEURO LINK

https://www.crowdcast.io/e/mnn-seminar-26April21

MEETING ID & PASSCODE

None required

SPEAKER

Bess Frost, PhD

Bartell Zachry Distinguished Professor for Research in Neurodegenerative Disorders
University of Texas Health San Antonio Barshop Institute for Longevity and Aging Studies
Glenn Biggs Institute for Neurodegenerative Disorders

BIO

Dr. Frost obtained her B.S. degree in biochemistry and molecular biology from the University of Texas, Austin in 2004. She went on to earn her Ph.D. from the University of California San Francisco in the laboratory of Dr. Marc Diamond. As a graduate student, Dr. Frost pioneered work that ignited a now prominent area of research, which is that tau adopts prion-like characteristics that help explain its pathological spread through the brain and the diverse disease phenotypes of the human tauopathies. Dr. Frost performed her postdoctoral training at Harvard Medical School in the laboratory of Dr. Mel Feany, where she developed a multi-system approach to studying tauopathy, interweaving studies in Drosophila, mice and postmortem human brain tissue. Dr. Frost began her independent laboratory as an Assistant Professor at the Barshop Institute for Longevity and Aging Studies, the Glenn Biggs Institute for Alzheimer's and Neurodegenerative Disorders, and the Department of Cell Systems and Anatomy at the University of Texas Health San Antonio in 2015.

The research focus of Dr. Frost's laboratory revolves around the basic neurobiology connecting toxic forms of tau to neuronal death and dysfunction. Specifically, her group has found that the detrimental effects of pathogenic tau on nuclear and genomic architecture activate "jumping genes" and disrupt RNA trafficking. Through this work, Dr. Frost and her team have identified novel targets for therapeutic treatment of tauopathies, as well as compounds that interfere with these processes and suppress tau-induced neurotoxicity.

RESEARCH

The nuclear envelope is a lipid bilayer that encases the genome and provides a physical boundary between the cytoplasm and the nucleoplasm. While the nucleus is typically depicted as a sphere encircled by a smooth surface of nuclear envelope, the smooth exterior can be interrupted by tubular invaginations of the nuclear envelope into the deep nuclear interior. Such structures are termed the "nucleoplasmic reticulum." Increased frequency of nuclear envelope invagination occurs in disease states including various cancers, viral infections, and laminopathies, a group of heterogeneous disorders that arise due to mutations in the gene encoding lamin A. A significant increase in the frequency of nuclear envelope invaginations in the human Alzheimer's disease brain has recently been reported. Nuclear envelope invaginations are caused by pathogenic tau, one of the two major pathological hallmarks of Alzheimer's disease. Pathogenic tau-induced dysfunction of the lamin nucleoskeleton drives nuclear envelope invagination and consequent accumulation of polyadenylated RNA within invaginations, both of which drive neuronal death. Our ongoing studies suggest that maintaining proper cytoskeletal, nucleoskeletal, and genomic architecture are critical for survival and function of adult neurons.

OBJECTIVES

1. Introduce the tau protein and its role in neurodegenerative disorders

2. Provide an overview of cytoskeletal/nucleoskeletal coupling

3. Describe the effects of pathogenic tau on nuclear and genomic architecture, and how this drives neurodegeneration

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