

BIOCHEMISTRY SEMINAR SERIES

Midstream Presentation - Fall 2020



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“CryoEM structure of the LCD of hnRNPA2 and its conversion to pathogenic amyloid”

Human ribonucleoprotein heterogeneous nuclear ribonucleoprotein A2 (hnRNPA2) is involved in RNA metabolism. It forms amyloid-like fibrils both under cellular stress and in the mutated form in neurodegenerative diseases such as Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD). Previous work established that the C-terminal low-complexity domain (LCD) of hnRNPA2 fibrillizes under stress, and missense mutations in this domain are found in the disease multisystem proteinopathy (MSP). Here, we undertook biochemical and structural studies, using cryo-electron microscopy and crystallography, to demonstrate the atomic-level structure of hnRNPA2-LCD fibril core and its capability to form a reversible hydrogel in vitro containing amyloid-like fibrils, as well as how the reversible, functional hnRNPA2-LCD fibril can convert to pathogenic fibrils, leading to neurodegenerative diseases.

Tuesday, October 6, 2020

via Zoom

4:00 pm