THE 2019 MARY AND JOSEPH A. PIGNOLO, SR. AWARD AND LECTURESHIP IN AGING RESEARCH

TAU-COFACTOR COMPLEXES AS BUILDING BLOCKS OF TAU FIBRILS

"The aggregation of the human tau protein into neurofibrillary tangles is directly diagnostic of many neurodegenerative conditions termed tauopathies. The species, factors and events that are responsible for the initiation and propagation of tau aggregation are not clearly established, even in a simplified and artificial in vitro system. This motivates the mechanistic study of in vitro aggregation of recombinant tau from soluble to fibrillar forms, for which polyanionic cofactors are the most commonly used external inducer. We find that cofactors are often limiting factor to generate ThT-active tau fibrils and act as templating reactant to trigger tau conformational rearrangement. We show that tau and cofactors form intermediate complexes whose evolution toward ThT-active fibrils is tightly regulated by tau-cofactor interactions. Remarkably, it is possible to find mild cofactors that complex with tau without forming ThT-active species, except when an external catalyst, such as cell-derived seed is provided to overcome the energy barrier. In a cellular context, we propose that tau could associate with cofactors to form a metastable complex that remains "inert" and reversible, until encountering a relevant seed that can trigger an irreversible transition to -sheet. The formation and property of liquid-liquid phase separation of tau and its connection to tau fibrilization processes will also be discussed. My talk will highlight our current understanding (or lack thereof) of controlling tau fibrilization pathways."

- Dr. Han

Songi Han, PhD
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January 13, 2020 | 2:30 - 3:00 (Reception) | 3:00 - 4:00pm (Lecture)

Biomedical Research Building (BRB) | 421 Curie Blvd, Philadelphia, PA 19104

Perelman School of Medicine at the University of Pennsylvania

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