MISSISSIPPI STATE UNIVERSITY

Department of Chemistry

The Department of Chemistry Seminar Series Presents

Diverse Roles for Disorder in Protein Function; From the Nano- to Meso-Scale

by

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Please join us for a reception with the speaker at 3:00 PM on 4/17/2015 in Hand Lab 1135, followed by the seminar at 3:30 PM in room 1144.

Abstract:

The classic structure-function paradigm has been challenged by a recently identified class of proteins: intrinsically disordered proteins (IDPs). Despite their lack of stable secondary or tertiary structure, IDPs are prevalent in all forms of life and perform myriad cellular functions, including signaling and regulation. Importantly, disruption of IDP homeostasis is associated with numerous human diseases, including cancer and neurodegeneration. Despite wide recognition of IDPs, the molecular mechanisms underlying their functions are not fully understood. We will discuss several different types of IDPs to illustrate some of the mechanisms that underlie their biological functions. One topic will be the IDPs, p21 and p27, which regulate cyclin-dependent kinases (Cdk) that control cell division. Studies of p21 bound to Cdk2/cyclin A revealed that a helix stretching mechanism mediates binding promiscuity. Further, investigations of Tyr88-phosphorylated p27 identified a signaling conduit that controls cell division and is disrupted in certain cancers. We will discuss how these mechanisms rely upon a balance between nascent structure in the free state, induced folding upon binding, and persistent flexibility within functional complexes. A very exciting emerging area in IDP research involves disordered proteins that mediate the formation of membrane-less organelles, such as the nucleolus. We will discuss the phenomenon of phase separation by disordered proteins to form liquid-like structures, with focus on those involved in ribosome biogenesis within the nucleolus. Insights into the mechanisms of phase separation and possible links to the process of ribosome biogenesis will be presented. These two case studies will highlight the use of a wide variety of structural, biophysical, biochemical and cellular techniques in elucidation of the functional mechanisms of disordered proteins.