COMPUTER SCIENCE

SEMINAR SERIES

Title: Intrinsically Disordered Proteins, Alternative Splicing, and Post-translational Modification (IDP-AS-PTM): A Toolkit for Developmental Biology

Friday, 02/22/19 | 12n-1pm | West Hall, W105

Speaker: Keith Dunker

Abstract: Intrinsically disordered proteins and regions (IDPs and IDRs) lack well-defined tertiary structures, yet carry out various important cellular functions. Studies that critically depend on IDPs have received high recognition, including gene regulation (1965 Nobel Prize, Physiology and Medicine), autophagy (2016 Nobel prize, Physiology and Medicine), circadian rhythms (2017 Nobel Prize, Physiology and Medicine), and phage display (2018 Nobel Prize, Chemistry), yet research community and even the Nobel Laurates are/were not aware of the pivotal roles played by IDPs in these phenomena. In eukaryotes, IDPs and IDRs contain the preferred loci for both protein segments encoded by alternatively spliced pre-mRNA (AS) and many post-translational modifications (PTMs). Furthermore, AS and/or PTMs alter the signaling outcomes associated with these IDPs or IDRs. However, the signal-altering mechanisms by which AS and PTMs modulate function and the extent to which they collaborate remain unknown. Here we focus on three important signaling and regulatory IDR-containing protein families in humans, namely G-protein coupled receptors (GPCRs), which are transmembrane signaling proteins, the nuclear factors of activated T-cells (NFATs), which are transcription factors (TFs), and the Src family kinases (SFKs), which are signaling enzymes. The goal is to determine how AS and PTMs individually alter the outcomes of the signaling carried out by the various IDRs and to determine whether AS and PTMs work together to bring about differential cellular responses. We also present data indicating that a wide range of other signaling IDPs or signaling proteins containing IDRs also undergo both AS- and PTM-based modifications, suggesting that these many proteins likely take advantage of signal outcome modulations that result from collaboration among these three features. We propose that the widespread cooperation of IDPs, AS and/or PTMs substantially contributes to, or even provides the basis for, the vast complexity of eukaryotic cell signaling.

Bio: Dr. Dunker received B.S. in Chemistry from UC Berkeley in 1965, and M.S. in Physics and Ph.D. in Biophysics from the University of Wisconsin at Madison in 1967 and 1969, respectively. Dr. Dunker started research in computational biology and bioinformatics in the mid-1980s and began using bioinformatics to study IDPs in the mid-1990s, where he and his collaborators were the first to consider these proteins as a distinct class with important biological functions. From late 1995 he and co-workers have published 300+ papers on these topics, see https://scholar.google.com/citations?user=4agt6FcAAAAJ.

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