9th Annual Sarkar Lecture

Regulated Unfolding in Signaling by Proteins

Dr. Richard Kriwacki

Department of Structural Biology
St. Jude Children's Research Hospital

Monday, May 13, 2013
Lecture: Daniels Hollywood Theatre Room 1246, The Hospital for Sick Children
1:00 p.m.
Pizza lunch will be provided at 12:30 p.m. in Room 1248

Q & A with Dr. Kriwacki 2:30 p.m., Room 3426
Coffee and refreshments will be provided

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Proteins serve as switches in signaling networks and their switch-like behavior is often controlled by inputs such as ligand binding, post-translational modification, and light irradiation. Disordered proteins and domains, which are prevalent in eukaryotic proteomes, often serve as hubs within signaling networks. Motifs within disordered protein regions mediate their multifarious interactions, and these interactions are often regulated by post-translational modifications. However, folded proteins also participate in signaling networks and exhibit switch-like behavior. Interestingly, we have observed that some folded proteins function as signaling switches through transitions to disordered states due to ligand binding or post-translational modification—a phenomenon we term "regulated unfolding". It is well appreciated that many proteins that are disordered in isolation fold upon binding their biological targets. We have observed that these proteins, in their functional, bound states, also exhibit regulated unfolding as a mechanism of signaling. We will discuss several examples of regulated unfolding from the realms of both folded and disordered proteins. Observations from us and others suggest that the biological palette of protein disorder is more diverse than currently understood and that the opportunity for regulated order-to-disorder transitions within folded proteins is a means to increase their functional complexity.