CHEMISTRY & CHEMICAL BIOLOGY COLLOQUIUM:

Allosteric Tuning of Dynamics Can Drive Cold Adaptation in an Enzyme

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Date:
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Time:
1:30 PM-2:50 PM

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About The Speaker:

Vincent Hilser is Professor and Chair of Biology, and a Professor of Biophysics at Johns Hopkins University. His research focuses on the study of protein dynamics and local unfolding in proteins, and its effect on allostery and enzymatic activity. His recent work has addressed the role of intrinsic disorder on signaling using both in vitro and in vivo systems, and the role of disorder in mediating thermal adaptation of enzymes. He is also involved in thermodynamics-based protein homology and design. Dr. Hilser received a B.S. in Chemistry from St John's University in 1987, an M.S. in Biotechnology from Manhattan College in 1991, and a Ph.D. in Biochemistry from Johns Hopkins University in 1995. He was a post-doctoral fellow in the Biocalorimetry Center/Department of Biology from 1995-1997. From 1997-2010, he was an Assistant (1997-2002), Associate (2002-2006) and Full Professor (2006-2010) in the Department of Biochemistry and Molecular Biology at the University of Texas Medical Branch (UTMB) in Galveston Texas. From 2005-2010, he also served as the Director of the Sealy Center for Structural Biology and Molecular Biophysics at UTMB before relocating to Johns Hopkins University in 2010. He has served as Chair of Biology since 2014. He is a recipient of an NSF CAREER award, the Michael and Kate Bárány Young Investigator Award from the Biophysical Society, and was named the Charles Marc Pomerat Distinguished Professor in Biological Sciences in 2009. In 2010, he was elected Fellow of the American Association for the Advancement of Science (AAAS).

Abstract:

The ability of organisms to diverge and adapt to different environmental niches is a hallmark of evolution, and one of the most prevalent examples is that of thermal adaptation, where two similar organisms can evolve to survive at different extremes of temperature. Underlying the physiological differences between such organisms are changes in the enzymes that catalyze the various reactions, and these changes are often located at surface-exposed amino acids distant from the active site. How such changes mediate the observed differences is activity is not clear. Here we examine surface-exposed GLY mutations to LID and AMPbd domains of E. Coli. adenylate kinase (AK), two domains that are purported to be responsible for mediating enzyme turnover. We show using advanced NMR techniques as well a both isothermal titration (ITC) and differential scanning calorimetry (DSC) that Km (or substrate affinity for ligand), and kcat can be independently and rationally tuned, by making specific surface-exposed mutations in different regions of the molecule. These studies provide insight into how enzymes can evolve to utilize local fluctuations to control catalysis and how evolution can precisely and independently tune these parameters.

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