‘Regulators of protein half-life in the cell : A structural perspective’

Speaker: **Prof. Sudip Kundu** (*University of Calcutta, Kolkata*)

Date: 12th June, 2018 (Tuesday)
Time: 10.30 AM
Venue: Charaka

Talk Abstract:

Proteins in the cell are regularly degraded and replaced with newly synthesized copies. This regular turnover minimizes the accumulation of toxic damage and ensures a functional proteome throughout the cell's lifetime. An elegant balance between translation and degradation rates maintains protein concentration within a cell and assigns each protein a specific half-life.

Whether and how do the intrinsic structural features affect the lifetime of a protein? Our work extends the realm of this question by distinguishing topology of eukaryotic proteins and their potential to oligomerize into multicomponent complexes as two master regulators of protein half-life in the cell, apart from previously known ubiquitinoylation sites and the presence of intrinsically disordered regions amenable to proteasomal engagement. We exploit the experimental genome-scale half-life data of yeast and mouse proteins and relative degradation rate data of human proteins, along with wide-ranging information about their 3D geometry and extensive biochemical characterization of the complexes they assemble into, to develop a theory demonstrating how a wide spectrum of structural constraints regulates protein half-life in the cell. Native topology acts as a molecular marker of monomeric protein’s mechanical resistance and regulates their half-life on a genomic scale. Sequestration into multimeric complexes elongates oligomeric protein halflife in the cell, probably by burying ubiquitinoylation sites and disordered segments required for proteasomal engagement. Diversification of topology and sequestration into non-identical sets of complexes are further exploited to alter protein half-life during evolution. This work not only evaluates the independent and combined influence of different structural constraints on protein half-life, and places them into genomic context, but further deepens our understanding of the designing principles of biological macromolecules.

Reference:

Mallik and Kundu, Topology and Oligomerization of Mono- and Oligomeric Proteins Regulate Their Half-Lives in the Cell, Structure (2018), https://doi.org/10.1016/j.str.2018.04.015