Indian Institute of Science
Centre for BioSystems Science and Engineering
BSSE Seminar

14 December 2020, 04:00 p.m., Virtual

Atypical Ubiquitination in Host-Pathogen Interaction

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About the speaker:

Dr. Chittaranjan Das graduated from MBU (Thesis advisor: Prof. P Balaram), Indian Institute of Science, in 2000 with a Ph.D. in the broad area of bioorganic chemistry, working on designed peptides and their conformational properties. For his postdoctoral fellowship he joined the lab of Michael Wolfe, Harvard Medical School, where he studied the mechanism of action of an intramembrane protease called gamma secretase (presenilin). After four years, he decided to join the lab of Prof. Greg Petsko and Dagmar Ringe (Brandeis University) to pursue the crystal structure of a neuronal deubiquitinating enzyme called UCHL1. In 2007, he joined the faculty of the Chemistry Department of Purdue University as an assistant professor. Currently he is an Associate Professor of Chemistry in the same department. His group studies structural mechanism of enzymes involved in ubiquitin signalling.

Abstract:

In addition to the wide array of functions regulated by ubiquitination, it serves as the first line of defense against invading pathogens by mediating a host of signalling events leading to innate immune response. Accordingly, the ubiquitin system is often targeted by prokaryotic pathogens which have evolved diverse means to block ubiquitination-mediated defence of the host. Beyond just blocking ubiquitination, some pathogens have even learned to hijack the ubiquitination machinery of the host to serve their own purpose. In two recently described examples, Legionella pneumophila, the causative agent of Legionnaires disease, was shown to use radically different means to ubiquitinate host targets by employing mechanisms that do not depend on the classical E1-E2-E3 three enzyme system of eukaryotes. The SidE effectors use NAD+ to ubiquitinate serine residues of host targets via a phospho-ribose (PR) linker between the hydroxyl group and Arg42 of Ub, whereas the MavC effector uses a transglutaminase mechanism to crosslink Gln40 of Ub with a critical lysine residue of a key host enzyme Ube2N, a mechanism that does not even require any nucleotide cofactor. In this talk I will describe applications of ubiquitin-based probes in characterizing these enzymes. I will also discuss mechanism of these effectors deduced from structural analysis and biochemical studies.