INDRAPRASTHA INSTITUTE *of*
INFORMATION TECHNOLOGY **DELHI**

Invitation to MTech Thesis Defense of **Arvind krishnamurthy** July 20, 2018 (Monday): 03.00-04.30 IST

In Partial Fulfillment of the Requirements for the Degree of
M.Tech CB

Arvind Krishnamurthy (MT16122)

Will defend his thesis

Title: "Revealing dynamic architecture of lipidated proteins"

IIIT-D Faculty and Students are invited

Date: July 20th 2018 (Friday)
Time: 03.00-04.30 IST
Place: Meeting Room, 3rd Floor(NAB)

Examiner:	**Internal:**	**Debarka Sengupta**
	External/Internal:	**S. Ramachandran (CSIR)**
	Advisor:	**Lipi Thukral & Angshul Mazumdar**

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Abstract

Proteins post-translational modifications (PTMs) act as a multilayered regulation mechanism for selective and controlled expression of cellular proteins. Lipidated proteins are one of the major components of virtually all cells, whereby lipid chains are attached covalently to the target residue site. There are strong emerging links between non-functional lipid-modified proteins and a number of disorders but how these altered systems contribute to respective disease phenotypes is completely unknown. Here we performed the proteome-scale study by analyzing ~8000 proteins with diverse lipid modifications with integrated multi-omics, clinical datasets, and biomolecular simulations to unravel diversity of lipidation in compositional context. More than 20 types of lipid modifications (LMs) were found, with five types of LMs constituting >90% of protein dataset. We identified distinct single- and higher-order combinations (>1 LM per protein), with >90% of lipidated sites occurring at protein termini. We also developed an in-house algorithm to compute evolutionary significance of LM. Across protein orthologs, discrete residue composition was found at lipidated site albeit spatial arrangement of residues remained altered. Further, mapped of clinically-relevant mutations on human proteins revealed that 42% proteins harboured atleast one variation at lipidated region implicated to multiple cancers including skin, colon, pancreatic etc. By analyzing major protein machineries in humans, including GPCRs, Transporters, enzymes, secretory proteins we found that there is a specificity of LMs in these categories. Lastly we performed molecular dynamics simulations to understand the spatial-temporal and membrane interacting region of LMs. Together, our results reveal a robust typological model governing diversity of lipidated proteins and provide insights underlying molecular and variation data for targeted therapeutics.