CHEMISTRY & BIOCHEMISTRY COLLOQUIUM: Study of PTM-Mediated Reversible Amyloids, Condensates, Autoinhibition, and Membrane Interactions of Human ALIX

Lalit Deshmukh
Assistant Professor, Department of Chemistry & Biochemistry
University of California, San Diego

Date:
11/5/2021

Time:
10:30 AM-11:50 AM

Link:
Please email snsgradstaff@ucmerced.edu for the Zoom information.

About the Speaker:

To learn about the speaker, visit https://deshmukhgroup.ucsd.edu/?people=dr-lalit-deshmukh .

Abstract:

Human ALIX, also known as PDCD6IP, is involved in diverse cellular and membrane processes, including apoptosis, cytokinesis, sorting of endo-lysosomal proteins, exosome biogenesis, tumorigenesis, and enveloped virus budding. The functional versatility of ALIX stems from its domain architecture where each of its three domains binds selectively to numerous partners, and is regulated by posttranslational modifications (PTMs), specifically tyrosine phosphorylation, which also facilitates its relocation from a membrane-bound active conformation to the cytosolic inactive state. In this presentation, I will show our latest results on ALIX. We discovered that ALIX, through its proline-rich domain (PRD), forms dynamic liquid-like condensates and β-sheet rich amyloid fibrils that surprisingly dissolve on Src-kinase mediated phosphorylation and reform on PTP1B-mediated dephosphorylation of conserved tyrosine residues of PRD. We also uncovered time-dependent hardening of ALIX condensates into fibrils. We discovered that Bro1 domain of ALIX binds to late endosomal membranes and hyperphosphorylated PRD via its same basic surface. These results reveal PRD-mediated autoinhibition of ALIX – endosomal membrane interactions, how tyrosine phosphorylation causes redistribution of ALIX away from late endosomal membranes into the cytosol, and the impact of tyrosine phosphorylation on intra- and intermolecular associations that dictate the broad functional repertoire of ALIX in cell signaling.

For more information, contact : Andy LiWang
aliwang@ucmerced.edu