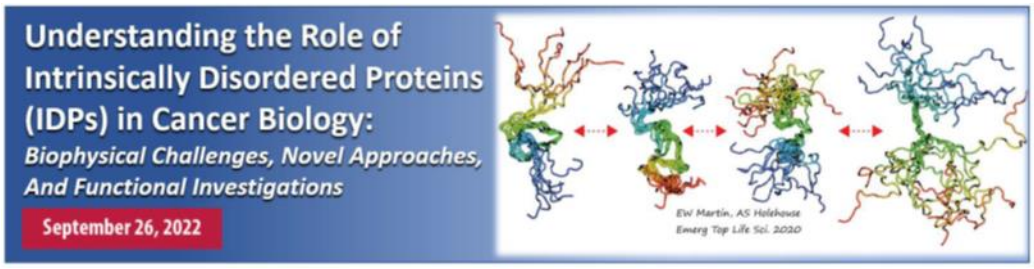
NIH NATIONAL CANCER INSTITUTE



UNDERSTANDING THE ROLE OF INTRINSICALLY DISORDERED PROTEINS (IDPS) IN CANCER BIOLOGY: BIOPHYSICAL CHALLENGES, NOVEL APPROACHES, AND FUNCTIONAL INVESTIGATIONS

SEPTEMBER 26, 2022

Organized by the Division of Cancer Biology at NCI

WORKSHOP CONCEPT AND GOALS

Intrinsically disordered proteins (IDPs), which lack a conventional ordered structure, are involved in many fundamental cellular processes such as splicing, signaling, and transcriptional regulation. The dysregulation of IDPs has been connected to many human diseases, including cancer. The oncogenic transcription factor c-Myc is a prominent example of an IDP that affects cell growth, apoptosis, and metabolic processes. IDPs interact through high-specificity/low-affinity binding sites with other proteins in protein networks. IDPs' structural information to understand the functions of the proteins and their protein interaction networks is instrumental for progress in cancer biology, especially for therapeutics development. Despite advancements, structural information of disordered proteins still presents a significant obstacle due to remarkable conformational flexibility and plasticity. Therefore, developing new technologies and methods that investigate IDPs' structural dynamics and interaction with binding partners is valuable. Recent progress in CryoEM, nuclear magnetic resonance (NMR) spectroscopy, electron paramagnetic resonance (EPR) spectroscopy, single-molecule FRET, and microscopy-based technologies can offer alternatives to unravel the structure and dynamics of IDPs. Besides, accurate prediction of IDP structures through computational approaches, e.g., the recently developed AI program AlphaFold, can also be valuable. These technological advancements in understanding IDPs will help generate new research opportunities and cross-disciplinary collaborations that pave the way for characterizing their links to disease phenotypes, especially cancer. This workshop aims to illustrate how technological advancements enlighten cell biological investigations of IDPs.

AGENDA: MONDAY, SEPTEMBER 26, 2022

8:30 am – 8:35 am	**Anowarul Amin, Ph.D.,** Division of Cancer Biology (DCB), NCI	Welcome
8:35 am – 8:40 am	**Dan Gallahan, Ph.D., Director** Division of Cancer Biology (DCB), NCI	Opening Remarks
8:40 am – 8:45 am	**Stefan Maas, Ph.D.,** Division of Cancer Biology (DCB), NCI	Logistics and Introduction of Keynote Speaker

8:45 am – 9:25 am **Keynote + Q&A**	***Richard Kriwacki, Ph.D.*** St. Jude Children's Research Hospital	Defining the Condensate Landscape of Fusion Oncoproteins
9:25 am – 12:30 pm	**SESSION 1: Biophysics of IDPs** *each 15 min + 5 min Q&A*	Moderated by Anowarul Amin
9:25 am – 9:45 am	***Elizabeth Rhoades, Ph.D.*** University of Pennsylvania	Characterizing conformational ensembles of IDPs with smFRET
9:45 am – 10:05 am	***Robert Tycko, Ph.D.*** NIDDK, NIH	Time-resolved and static studies of structure formation by IDPs, using solid-state NMR and cryoEM
10:05 am – 10:25 am	***Alexander Sobolevsky, Ph.D.*** Columbia University	Order versus disorder in physiologically important regions of TRP channels studied by cryo-EM
10:25 am – 10:45 am	**BREAK**	
10:45 am – 11:05 am	***Jin Zhang, Ph.D.*** University of California San Diego	Illuminating the Biochemical Activity Architecture of the Cell
11:05 am – 11:25 am	***Alex Holehouse, Ph.D.*** Washington University St. Louis	A computational ecosystem for understanding sequence-to-function relationships in IDRs
11:25 am – 11:45 am	***Sarah Bondos, Ph.D.*** Texas A&M University	The Critical Role of Intrinsic Disorder in Creating Bioactive Materials
11:45 am – 12:30 pm	**Panel Discussion** All session speakers, chaired by R. Kriwacki	**Biophysics of IDPs**

12:30 – 1:30 pm	**LUNCH BREAK**

1:30 pm – 5:45 pm	**SESSION 2: Biological properties of IDPs** *each 15 min + 5 min Q&A*	Moderated by Stefan Maas
1:30 pm – 1:50 pm	***Priya Banerjee, Ph.D.*** SUNY at Buffalo	Role of Prion-like Domains in FET Fusion Oncoprotein Phase Separation and Recruitment of SWI/SNF Complex
1:50 pm – 2:10 pm	***Jennifer Hurley, Ph.D.*** Rensselaer Polytechnic Institute	Intrinsic Disorder in the Highly Ordered Circadian Clock

2:10 pm – 2:30 pm	***Joshua Mendell, M.D., Ph.D.*** UT Southwestern Medical Center	Regulation of Pumilio RNA binding proteins by *NORAD*-induced phase separation
2:30 pm – 2:50 pm	***Wenbo Li, Ph.D.*** UT Health Science Center Houston	Epitranscriptome-epigenome crosstalk: roles of enhancer RNA m6A methylation, its reader YTHDC1, and transcriptional condensate
2:50 pm – 3:10 pm	***Yixian Zheng, Ph.D.*** Carnegie Institution for Science	Protein phase separation in the assembly of microtubule and spindle apparatus
3:10 pm – 3:30 pm	**BREAK**	
3:30 pm – 3:50 pm	***Hao Jiang, Ph.D.*** University of Virginia	Regulation of gene expression and tumorigenesis by intrinsically disordered proteins
3:50 pm – 4:10 pm	***May Khanna, Ph.D.*** New York University	Disordered loops define flexibility in TDP-43's N-terminal domain and drive a gatekeeping role against non-specific binding
4:10 pm – 4:30 pm	***Paul Robustelli, Ph.D.*** Dartmouth College	Targeting Intrinsically Disordered Proteins and Biomolecular Condensates with Small Molecule Drugs
4:30 pm – 5:30 pm	**Panel Discussion** All session speakers, chaired by J. Mendell	**Biology of IDPs**

5:30 pm – 5:45 pm	**ADJOURN**