BIOGRAPHICAL SKETCH

NAME: Kumar Srivastava, Dushyant

eRA COMMONS USER NAME (credential, e.g., agency login): SRIVASTAVAD

POSITION TITLE: Postdoctoral Scholar

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Calcutta, India	BSc. (Hons.)	07/2011	Zoology
University of Calcutta, India	MSc.	08/2013	Zoology
University of Calcutta, India (CSIR – Indian Institute of Chemical Biology)	Ph.D.	05/2022	Biochemistry
Oregon Health & Science University, Portland, OR	Postdoctoral	N/A	Structural Biology/Neuroscience

A. Personal Statement

My long-term interests lie in exploring the deeper questions underlying the mechanism of functioning of various life forms using structural biology. This led me to pursue my graduate research career in the field of structural biology. As part of my Ph.D. research work, I obtained training in the field of X-ray crystallography and biophysics with emphasis on obtaining a detailed molecular insight into the functioning of chromatin interacting proteins with special focus on histone chaperones from protozoan parasites and human chromatin reader proteins involved in readout of posttranslational modifications on histones and their interaction with chromatin remodeling complex.

For the next stage of my career, I joined as a postdoctoral scholar in Gouaux lab at OHSU and my work is focused on studying the structure of neurotransmitter transporters, particularly monoamine transporters (MAT), to gain a more holistic understanding of the underlying mechanism of the transport and inhibition. As part of this project, I was exposed to newer training opportunities which in many aspects was different than what I learned as part of my Ph.D. research. I learned the expression and purification of membrane proteins utilizing the mammalian expression system, cryo-electron microscopy (cryo-EM) sample preparation and image processing for structure determination using single particle cryo-EM. I successfully solved the first structure of the human dopamine transporter (hDAT) and mapped the binding site for its orthosteric ligands and discovered a novel allosteric site. We complemented and validated our structural data by mutational, ligand binding and functional experiments during which I learned

to perform biochemical and functional assays related to assessing the activity of membrane transport proteins. All the structural data and coordinates with the details of molecular insights have been deposited and are available in public repositories, namely, RCSB-Protein Data Bank (PDB) as well as in Electron Microscopy Data Bank (EMDB). Based on the initial results and findings, I am continuing my efforts in further characterizing the pharmacological potential of the newly identified allosteric site in hDAT to identify and pinpoint determinants for specificity of small molecules binding to this site in hDAT. To that end, I will develop binding assays to establish the kinetics of binding of small molecules to the hDAT allosteric site. A larger goal of my planned studies is identification of selective and high affinity allosteric inhibitors for hDAT with potential for future therapeutics of dopamine related disorders.

I will continue to acquaint myself with advancement in the field which will help in building up my independent career in membrane protein structural biology/structural neurobiology. As part of my long-term career goals, I will also learn and develop tools in the form of specific antibodies/fiducials with a larger goal to undertake structural and mechanistic studies in the *in-situ* context. A major learning part of this will be in the field of cryo-electron tomography (cryo-ET). The expertise gained will help me formulate strategies and develop framework for projects of diverse physiological context as I encounter new questions in my independent academic path.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2024-Present	Member, American Heart Association
2011-Present	Member, National Academy of Vector Borne Diseases, India
2010 & 2011	Summer Research Fellow, Joint SRFP Programme of the Indian National Science Academy, National Academy of Sciences of India and Indian Academy of Sciences. Host lab: National Institute of Malaria Research (Indian Council of Medical Research), Guwahati, India.

Selected Awards/Honors

2024	Discussion leader, Session on “Translational Insights in Transporter Research”, Gordon Research Seminar on Membrane Transport Proteins, 2024, Maine, USA.
2021	Travel Scholarship Awardee for Annual BioXFEL Conference, BioXFEL
2013	Awarded Junior Research Fellowship from the Indian Council of Medical Research to pursue Ph.D. programme

C. Contributions to Science

As part of my graduate research I have worked on the structural elucidation of proteins involved in chromatin structure maintenance and its dynamics. In the first part of my thesis, I have worked on the identification and determination of X-Ray crystal structure of a histone chaperone protein, Asf1 from *Plasmodium falciparum*.

a. Srivastava DK, Gunjan S, Das C, Seshadri V, Roy S. Structural insights into histone chaperone Asf1 and its characterization from Plasmodium falciparum. *Biochem J.* 2021 Mar 12;478(5):1117-1136. doi: 10.1042/BCJ20200891.

As part of the structural investigation of chromatin interacting protein, I have worked on the structural and functional characterization of mode of interaction of ZMYND8 with chromatin. I have also participated in a collaborative study which involved delineating the role of UBR7 in breast cancer Metastasis.

a. Adhikary S, Sanyal S, Basu M, Sengupta I, Sen S, Srivastava DK, Roy S, Das C. Selective Recognition of H3.1K36 Dimethylation/H4K16 Acetylation Facilitates the Regulation of All-trans-retinoic Acid (ATRA)-responsive Genes by Putative Chromatin Reader ZMYND8. *J Biol Chem.* 2016 Feb 5;291(6):2664-81.

b. Adhikary S, Chakravarti D, Terranova C, Sengupta I, Maitituoheti M, Dasgupta A, Srivastava DK, Ma J, Raman AT, Tarco E, Sahin AA, Bassett R, Yang F, Tapia C, Roy S, Rai K, Das C. Atypical plant homeodomain of UBR7 functions as an H2BK120Ub ligase and breast tumor suppressor. Nat Commun. 2019 Mar 28;10(1):1398.

As part of my postdoctoral work in the field of structural biology of monoamine neurotransmitter transporters, I have solved the first structure of human dopamine transporter and mapped the binding site for β-CFT, which is a cocaine analogue, to the central or orthosteric site, for MRS7292, which is an allosteric inhibitor to a structurally uncharacterized site and for divalent zinc ion.

a. Srivastava DK, Navratna V, Tosh DK, Chinn A, Sk MF, Tajkhorshid E, Jacobson KA, Gouaux E. Structure of the human dopamine transporter and mechanisms of inhibition. *Nature*. 2024 Aug;632(8025):672-677.

The PubMed link to my bibliography:
https://pubmed.ncbi.nlm.nih.gov/?term=Dushyant+Kumar+Srivastava