BIOGRAPHICAL SKETCH

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NAME: ABHISHEK SUMAN

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POSITION TITLE: Postdoctoral Research Scholar

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Lovely Professional University, Punjab, India	BTech	08/2009	05/2013	Biotechnology
ICMR-Rajendra Memorial Research Institute of Medical Sciences, Bihar, India	Research Intern	05/2013	07/2014	Microbiology
Lovely Professional University, Punjab, India	MTech	08/2014	05/2016	Biotechnology
Indian Institute of Technology Hyderabad, India	Ph.D.	07/2016	07/2022	Structural Biology
Memorial Sloan Kettering Cancer Center, New York, NY	Postdoctoral Research Scholar	02/2023	Present	Structural Biology

A. Personal Statement

I received my PhD in Structural Biology from the Indian Institute of Technology Hyderabad (IITH), India, where I worked with Prof. Eerappa Rajakumara to explore the mechanistic insights into the functioning of DNA binding proteins involved in epigenetic gene regulation. In my doctoral studies, I focused on exploring the binding preferences of epigenetic regulator proteins for different epigenetic marks on DNA and histone variants, using biochemical, biophysical, and computational approaches. I employed X-ray crystallography and computational biology approaches to explore the structural insights into epigenetic regulation. I also substantially contributed to the collaborative projects related to drug design and understanding their mechanisms of action, where we developed potential drug candidates for amyotrophic lateral sclerosis (ALS), which was featured as a 'Research highlight' in Nature India (Nature publishing group), and in vitro fertilization (IVF) which got national media coverage. I also started and established the computational biology facility in Prof. Rajakumara's lab. With substantial contribution, I co-authored 18 articles (15 published, 3 under review). One of my research publications was featured as the cover page article in Biochemistry (American Chemical Society publication). I also serve as a reviewer for scientific journals, including PLoS One, Biophysical Chemistry and Journal of Biomolecular Structure and Dynamics. Apart from research, I had also been involved in mentoring students, classroom teaching and live demonstrations, organizing workshops/seminars and was invited for a guest lecture.

Currently, I am a postdoctoral trainee in Prof. Dinshaw Patel group at Memorial Sloan Kettering Cancer Center. Prof. Patel is an internationally recognized leader in Structural Biology, with a h-index (Google Scholar) of 144 and has an extensive record of training postdoctoral fellows. In the group, my research focuses on exploring structural and mechanistic insights into the bacterial antiphage defense systems for which I am employing multi-pronged approaches including cryogenic electron microscopy (Cryo-EM), macromolecular X-ray crystallography, and other biophysical and biochemical approaches. In addition, the postdoctoral training outlines a set of career development activities including grant writing, public speaking, and lab management to enhance my ability to become an independent investigator. This postdoctoral training will be helpful in building a strong foundation for achieving my long-term research goal of exploring structural and mechanistic insights into diverse biological phenomena, including epigenetic regulation, antiviral surveillance, and drug designing for disease treatment.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 – Present Postdoctoral Research Scholar, Memorial Sloan Kettering Cancer Center, New York, NY
2013 – 2014 Research Intern, Indian Council of Medical Research (ICMR) – Rajendra Memorial Research Institute of Medical Sciences, Patna, Bihar, India

Honors

2022 'Excellence in Research' award, Indian Institute of Technology Hyderabad, India
2018 – 2022 Senior Research Fellowship, Ministry of Education, Govt. of India
2016 – 2018 Junior Research Fellowship, Ministry of Education, Govt. of India
2016 All India Rank 9 in General Aptitude Test in Engineering (GATE)
2016 M. Tech awarded with distinction, Lovely Professional University, India

C. Contributions to Science

1. **Epigenetic regulation:**
DNA and histone modifications, also known as 'epigenetic marks', play an important role in regulating gene expression. These modifications are recognized by specialized domains in regulator proteins that further relays a signal for downstream processing. The dual domain cassette containing Tandem Tudor domain (TTD) and Plant Homeodomain (PHD) of UHRF1, a eukaryotic protein, is one such 'reader' domain that has been known to recognize tri-methylated lysine 9 on histone H3 (K3K9me3) and unmodified arginine 2 (H3R2) through TTD and PHD domains, respectively. Our studies showed that TTD domain has a higher preference for di-methylated H3K9. PHD finger of another protein VIM1, which has similar sequence feature as PHD finger of UHRF1, doesn't recognize H3R2 mark. Our biophysical, structural, and computational studies revealed that though the sequence features are conserved, there is the conformational changes in the peptide recognition motifs lead to abrogation of H3R2 readout. Similarly, SRA domain recognizes methylated cytosine in DNA. SRA domain of UHRF1 (SRA_{UHRF1}) is. Known to be a bona fide reader of hemi-methylated cytosine in CpG DNA context (hemi-mCpG). Our biophysical and structural studies revealed that SRA_{UHRF1} also recognizes fully-methylated cytosine not only in CpG DNA (fully-mCpG) context, but also in CpHpG DNA (fully-mCpHpG), however the stoichiometry of protein:DNA is 1:1 in prior and 2:1 in the later contexts. Another SRA domain containing protein, SUVH5 from plant origin, recognizes methyl cytosine is all the DNA contexts (CpG, CpHpG and CpHpH) through SRA domain. In addition, SUVH5 also performs H3K9 methylation through SET domain. Our studies revealed that there is an allosteric crosstalk between the two domains. We also employed quantum-mechanical (QM) calculations to determine why the catalytic activity of the SET domain of SUVH5 is limited to di-methylation of H3K9 and not extended to tri-methylation.

    a. **Abhishek S**, et al. (2018). Biochemical and dynamic basis for combinatorial recognition of H3R2K9me2 by dual domains of UHRF1. *Biochimie*, 149, 105–114.

    b. **Abhishek S**, et al. (2021). Mechanistic insights into recognition of symmetric methylated cytosines in CpG and non-CpG DNA by UHRF1 SRA. *Int J Biol Macromol*, 170, 514-522.

    c. **Abhishek S**, Deeksha W & Rajakumara E. (2021) Helical and β-turn conformations in the peptide recognition regions of the VIM1 PHD finger abrogate H3K4 peptide recognition. *Biochem*, 60, 2652-62.

    d. **Abhishek S**, Deeksha W & Rajakumara E (2023) Mechanistic insights into allosteric regulation of methylated DNA and histone H3 recognition by SRA and SET domains of SUVH5 and the basis for di-methylation of lysine residue. *FEBS J*, 290 (4), 1060-1077.

    e. Satish M, Nivya MA, **Abhishek S**, et al. (2018). Computational characterization of substrate and product specificities, and functionality of S-adenosylmethionine binding pocket in histone lysine methyltransferases from Arabidopsis, rice and maize. *Proteins*, 86(1), 21–34.

2. **DNA repair:**
ADP-ribosylation is an important epigenetic mark which is catalyzed by PARP1, the genome guardian protein. PARP1 has been known to sense DNA breaks – double strand break (DSB) and single strand

break (SSB). We used biochemical and biophysical approaches to unravel the novel feedback allosteric regulation of PARP1 by its catalytic product poly(ADP-ribose) (PAR). We also showed that PARP1 not only senses DNA breaks, but also single stranded DNA (ssDNA), which further suggests the yet unexplored role of PARP1 in ssDNA regulation. We also unraveled the regulation and mechanism of PARP1 in apoptosis.

a. Deeksha W, **Abhishek S** & Rajakumara E. (2022) PAR recognition by PARP1 regulates DNA-dependent activities and independently stimulates catalytic activity of PARP1. BioRxiv, 2021.12.21.473685. *(Under review)*

b. Deeksha W, **Abhishek S**, Giri J & Rajakumara E. (2023) Regulation of PARP1 and its apoptotic variant activity by single-stranded DNA. *FEBS J*. 2023 May 28.

3. Drug/vaccine design:

In a collaboration with Dr. Guruprasad Kalthur, Manipal Academy of Higher Education, India, we design and optimize an inhibitor of sperm phosphodiesterase variants (PDEs) to enhance sperm functions for effective the treatment of infertility in males, using computational approaches. We further confirmed it by in vitro and in ex vivo experiments. In collaboration with Dr. Basant K Patel, IIT Hyderabad, we developed and tested a small molecule inhibitor, named as AIM4, against TDP-43, a key protein responsible for ALS. We also employed computational approaches to propose the mechanism of action of Auranofin, a known inhibitor of thioredoxin/glutathione reductases (TR/GRs) in different pathogens, including bacteria and protozoa. We showed that Auranofin has different target sites in bacterial and protozoal TRs/GRs. Using computational approaches, we also designed a multi-epitope fused ferritin nano-cage based vaccine candidate against SARS-CoV-2.

a. Satish M, Kumari S, Deeksha W, **Abhishek S**, et al. (2021) Structure based redesigning of pentoxifylline against selective phosphodiesterases to modulate sperm functional competence for assisted reproductive technologies. *Sci Rep*, 11, 12293.

b. Raj G, **Abhishek S**, Nitin K, Sreenath D, Rajakumara E. Computational, in vitro binding and competition binding studies of theophylline against phosphodiesterases functioning in sperm. *(Under review)*

c. Girdhar A, Bharathi V, Tiwari VR, **Abhishek S**, et al. (2020). Computational insights into mechanism of AIM4-mediated inhibition of aggregation of TDP-43 protein implicated in ALS and evidence for in vitro inhibition of liquid-liquid phase separation (LLPS) of TDP-432C-A315T by AIM4. *Int J Biol Macromol*, 147, 117–130.

d. **Abhishek S**, et al. (2019). Dynamic Basis for Auranofin Drug Recognition by Thiol-Reductases of Human Pathogens and Intermediate Coordinated Adduct Formation with Catalytic Cysteine Residues. *ACS Omega*, 4(5), 9593–9602.

e. Pratibha M, **Abhishek S** & Rajakumara E. (2022) Designing ferritin nanocage based vaccine candidates for SARS-CoV-2 by in silico engineering of its MHC I and MHC II epitope peptides. *J Biomol Struct Dyn*, Jul 22.

4. Other articles (published / under review)

Apart from above mentioned areas, I have a key contribution in other projects related to mechanistic studies on DNA bending by high mobility group (HMG) proteins, elucidating structure-function relationship of enzyme, mechanistic studies on toxin-induced stress in zebrafish, formulation of culture medium for *Leishmania* species. I have also co-authored review articles related to enzyme engineering, minichromosome maintenance, and allosteric regulation of proteins.

a. Rajakumara E, Satish M, & **Abhishek S**. (2020). In vitro studies on non-canonical DNA binding specificities of KAP6 and HMO1 and mechanistic insights into DNA bound and unbinding dynamics of KAP6. *Int J Biol Macromol*, 160, 925–933.

b. Uma Mahesh MVN, **Abhishek S**, Faidh MA, Rajakumara E & Chadha A. Structure and mechanism of an Ornithine cyclodeaminase/μ-crystallin homolog from the yeast Candida parapsilosis ATCC 7330. *(Under review)*

c. Pullaguri N, Grover P, **Abhishek S**, et al. (2021). Triclosan affects motor function in zebrafish larva by inhibiting ache and syn2a genes. *Chemosphere*, 266, 128930.

d. **Abhishek S**, et al. (2021) A simple monophasic LGPY medium for routine maintenance of Leishmania donovani promastigotes. *Parasitol Res*, 120, 1269-71.

e. Rajakumara E, **Abhishek S**, et al. (2022) Structure and Cooperativity in Substrate-Enzyme Interactions: Perspectives on Enzyme Engineering and Inhibitor Design. *ACS Chem Biol*, 17, 266-280.

f. Mehta G, Sanyal K, **Abhishek S**, et al. (2022) Minichromosome maintenance proteins in eukaryotic chromosome segregation. *Bioessays*, 44, e2100218.