BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: DEEKSHA WAGHELA

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

POSITION TITLE: Postdoctoral Research Scholar

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Govt. Model Science College (Autonomous) Jabalpur, Madhya Pradesh, India	B.Sc.	08/2012	07/2015	Biotechnology
The Maharaja Sayajirao University of Baroda, Vadodara, Gujarat, India	M.Sc.	07/2015	06/2017	Biotechnology
Indian Institute of Technology Hyderabad, India	Ph.D.	07/2017	10/2023	Structural Biology
Memorial Sloan Kettering Cancer Center, New York, NY	Postdoctoral Research Scholar	10/2023	Present	Structural Biology

A. Personal Statement

I completed my PhD under supervision of Prof. Rajakumara Eerappa from the Indian Institute of Technology Hyderabad (IITH), India. In my doctoral studies, I focused on exploring the binding preferences of PARP1 for different nucleic acid polymers and how these polymers regulate the activity of PARP1, using multi-pronged biochemical and biophysical approaches. Besides my thesis project, I have also been involved in structure determination of protein complexes using X-ray crystallography. I also significantly contributed to the collaborative projects which were related to (i) developing dressing material for burn wounds, and (ii) drug designing for ALS and IVF, and understanding their mechanisms of action. I have co-authored a total of 14 publications. One of my research articles was selected as Editor's choice and was featured on cover page of The FEBS Journal. Besides research, I was actively involved in setting up Prof. Rajakumara's lab and mentoring students.

At present, I am a postdoctoral research scholar in Prof. Dinshaw Patel Lab at Memorial Sloan Kettering Cancer Center. Prof. Patel is a globally renowned scientist in field of Structural Biology. In Prof. Patel's lab, my research focuses on unraveling structural and molecular basis of (i) innate bacterial antiphage defense systems and (ii) transcription regulatory proteins in humans. I am using multi-pronged techniques including cryogenic electron microscopy (Cryo-EM), macromolecular X-ray crystallography, along with other biophysical and biochemical approaches. Furthermore, this postdoctoral training will strengthen my skills of grant writing and presentations which will help me to achieve my log-term goal to become an independent researcher to explore structural and functional aspects of various biological processes like epigenetic regulation, immunological response to infections and design targeted therapeutics.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2023 – Present Postdoctoral Research Scholar, Memorial Sloan Kettering Cancer Center, New York, NY

Honors

2023 'Excellence in Research' award, Indian Institute of Technology Hyderabad, India
2019 – 2022 Senior Research Fellowship, University Grants Commission, Govt. of India
2017 – 2019 Junior Research Fellowship, University Grants Commission, Govt. of India
2017 All India Rank 66 in General Aptitude Test in Engineering (GATE)
2016 All India Rank 43 in Joint CSIR-UGC National Eligibility Test

C. Contributions to Science

1. **Allosteric regulation:**
PARP1 is a modular protein which senses the DNA breaks, both double strand and single strand break and catalyzes the formation of Poly (ADP-ribose) (PAR), which is an important post translational modification for recruitment of repair machinery proteins at the site. Using biochemical and biophysical approaches we unraveled (i) a novel feedback allosteric regulation of PARP1 by its catalytic product PAR, (ii) regulation of PARP1 by single strand DNA and (iii) regulation of PARP1 during apoptosis. I have also co-authored a review article on the allosteric regulations of modular proteins.

    a. **Deeksha W** & Rajakumara E. (2024) Regulatory apoptotic fragment of PARP1 complements catalytic fragment for PAR and DNA-dependent activity but inhibits PARP2 activity. DNA Repair. 133, 103593.

    b. **Deeksha W**, Abhishek S & Rajakumara E. (2023) PAR recognition by PARP1 regulates DNA-dependent activities and independently stimulates catalytic activity of PARP1. FEBS J. 290 (21), 5098-5113.

    c. **Deeksha W**, Abhishek S & Rajakumara E. (2023) Regulation of PARP1 and its apoptotic variant activity by single-stranded DNA. FEBS J. 290(18), 4533-4542.

    d. Abhishek S*, **Deeksha W***, Nethravathi KR, Davari MD, & Rajakumara E. (2023) Allosteric crosstalk in modular proteins: Function fine-tuning and drug design. Comput Struct Biotechnol J. 21, 5003-5015.

2. **Epigenetic regulation:**
Epigenetic modifications i.e., alterations in chromatin, both DNA and histone proteins without changing the DNA sequence can control and regulate the expression of genes. Reader domains of regulator proteins recognize these epigenetic marks and subsequently elicit the signal for further processing. One such protein in plants is SUVH5, which contains SRA reader domain that recognize methylated cytosines. Using biophysical and computational approaches we revealed how SRA domain modulates the histone methylation by SET domain of SUVH5. In humans, UHRF1 protein also contain SRA domains which is bona fide reader of hemi-methylated cytosine in CpG DNA context. Our biophysical and structural studies unraveled it can also bind to fully methylated cytosine in both CpG DNA and CpHpG DNA context. Another set reader domains in UHRF1 are Tandem Tudor domain (TTD) and Plant Homeodomain (PHD) that recognize methylated lysine 9 on histone H3 (H3K9me1/2/3) and unmodified arginine 2 (H3R2), respectively. Our studies establishes that TTD domain has a higher preference for di-methylated H3K9. PHD finger similar to UHRF1-PHD is present in a plant protein called VIM1 but it does not recognize H3R2 mark. Through structural, biophysical and computational approaches we identified that the revealed the conformational changes in the peptide recognition motifs in the VIM1-PHD abrogates H3R2 binding.

    a. Abhishek S*, **Deeksha W*** & Rajakumara E. (2022) 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

    b. 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. Biochemistry, 60, 2652-2662.

    c. Abhishek S*, Nakarakanti NK*, **Deeksha W***, & Rajakumara E. (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.

d. Abhishek S, Nivya MA, Nakarakanti NK, **Deeksha W**, Khosla S, & Rajakumara E. (2018) Biochemical and dynamic basis for combinatorial recognition of H3R2K9me2 by dual domains of UHRF1. Biochimie, 149, 105–114.

3. Drug design and therapeutics:

In collaboration with Dr. Basant K Patel, IIT Hyderabad, we contributed to (i) analyze binding of a molecule (EGCG) in green tea that can modulation the aggregation of TDP-43, a pathogenic protein in neurodegenerative disease ALS, (ii) develop a small molecule inhibitor (AIM4) against TDP-43 and (iii) understand HSA dependent abrogation of TDP-43 aggregation. In collaboration with Dr. Jyotsnendu Giri, IIT Hyderabad, we contributed to assess the antibacterial properties of nanofiber-based burn wound healing dressing material. In collaboration with Dr. Guruprasad Kalthur, Manipal Academy of Higher Education, India, using in silico approach we designed an analogue (PTX-m1) of an existing drug pentoxiphylline (PTX). PTX-m1 was confirmed to be more potent drug for IVF through in vitro and in ex vivo experiments. We employed computational approaches and proposed the mechanism of action of a drug, Auranofin, which inhibits thioredoxin/glutathione reductases (TR/GRs) in bacteria and protozoa.

a. Meshram VD, Balaji R, Saravanan P, Subbamanda Y, **Deeksha W**, Bajpai A, Joshi H, Bhargava A, Patel BK. (2023) In silico and in vitro studies suggest epigallocatechin gallate (EGCG), a polyphenol in green tea, can bind and modulate the aggregation and cytotoxicity of the full-length TDP-43 protein implicated in TDP-43 proteinopathies. BioRxiv. 10.1101/2023.12.22.573011.

b. Nirwal S, Saravanan P, Bajpai A, Meshram VD, Raju G, **Deeksha W**, Prabusankar G, Patel BK. (2022) In Vitro Interaction of a C-Terminal Fragment of TDP-43 Protein with Human Serum Albumin Modulates Its Aggregation. J Phys Chem B. 126, 9137-9151.

c. Singh R, Roopmani P, Chauhan M, Basu SM, **Deeksha W**, Kazem MD, Hazra S, Rajakumara E, Giri J. (2022) Silver sulfadiazine loaded core-shell airbrushed nanofibers for burn wound healing application. Int J Pharm. 613, 121358.

d. Satish M, Kumari S, **Deeksha W**, Abhishek S, Adiga SK, Dasappa JP, Kalthur G & Rajakumara E. (2021) Structure based redesigning of pentoxifylline against selective phosphodiesterases to modulate sperm functional competence for assisted reproductive technologies. Sci Rep, 11, 12293.

e. Girdhar A, Bharathi V, Tiwari VR, Abhishek S, **Deeksha W**, Mahawar US, Raju G, Singh SK, Prabusankar G, Rajakumara E, & Patel BK. (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.

f. Abhishek S, Sivadas S, Satish M, **Deeksha W**, & Rajakumara E. (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.