

Faculty Details

Name: Dr. Parul Mishra

Mail: pmsl@uohyd.ac.in

Contact: 91-40-23134595

Area Of Research: Ubiquitin mediated protein degradation, Protein Engineering, Chaperone networks in neurological diseases

and cancer

Faculty Details

Parul received her Master's degree in Biochemistry from the Lucknow University. She did her PhD at the Central Drug Research Institute (CDRI-JNU) where she was trained in biophysical and biochemical characterization of proteins. In her PhD work, she established the unique structure of a pathological phage protein, crystallized the protein to demonstrate its conformational specificity to the ligands and unveiled its structural transitions from soluble to fibrillar forms (Journal of Biological Chemistry, 2006; FEBS Journal, 2009; Journal of Biological Chemistry, 2009). She received the Best Thesis Award for her PhD work.

She did her postdoctoral training in directed evolution and analysing protein fitness landscapes with Daniel Bolon at the University of Massachusetts Chan Medical School, USA. She employed high throughput mutational approaches and protein engineering to delineate critical aspects of Hsp90 function and evolution (Eukaryotic Cell, 2012; Molecular Cell, 2014; PLOS Genetics, 2013, Cell Reports 2016; Proceedings of National Academy of Science, USA, 2018).

As an independent faculty at the University of Hyderabad, her research interests include rewiring the protein homeostasis network; particularly the chaperones and ubiquitin network to ameliorate the burden of misfolded or aggregated proteins in cells during neurodegeneration. She is also interested in developing synthetic yeast strains for enhanced production of industrially important metabolites.

Doctoral Research: Central Drug Research Institute, Lucknow (JNU)

Postdoctoral Research: University of Massachusetts Chan Medical School, Worcester, MA

Scholarships/Fellowships:

2015 : Ramalingaswami Re-entry Fellowship, DBT, GOI

2005: Senior research fellowship, CSIR, GOI.

2003: Junior research fellowship, CSIR, GOI

Awards/Recognitions:

2019: Smt. Kusum Sharma Young Women Scientist Award, IABS

2018: Har Govind Khorana- Innovative Young Biotechnologist Award, DBT, GOI

2008: Dr. M.M. Dhar memorial Best thesis award.

2006: Dr. D.L. Srivastava memorial young scientist award by the Society of Biological Chemists.

2005: Best poster presentation at the 74th annual general meeting of the SBC, CDRI, India.

2003: Chakravarty gold medal in M.Sc

2002: Rae Saheb Sheo Shanker memorial merit scholarship in M.Sc.

Notice Board

No Records Available

Students And Project Trainees

Students/Projects Trainees

Name	Joined As	Mail	Contact
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Ms. Subhashree Sahoo	Ph.D. Student	20laph02@uohyd.ac.in	---
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Ms. Amrita Arpita Padhy	PhD student (PMRF Fellow)	20laph01@uohyd.ac.in	---
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Ms. Kummari Shivani	PhD student	20laph14@uohyd.ac.in	---
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Mayukha Bommaraju	M.Sc. Project	21lams27@uohyd.ac.in	---
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Former Students/Projects Trainees

Name	Joined As	Working
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Mr. Siddharth Neog	M.Sc. Student	Ph.D. Student at IIT Guwahati
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Mr. Thaleswar Verma	M.Sc. Student	
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Ms. Varsha Kumari	JRF	
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Ms. Soniya Kangjam	M.Sc. Student	Mahatma Gandhi National Fellow, MSDE, GOI
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Mr. Mihir ranjan padhan	M.Sc. Student	PhD student IICT, Hyderabad
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K. Ishwarya Lakshmi	M.Sc. Project Student	BIONEST, University of Hyderabad
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Mayank Bajaj	M.Sc Project Student	
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Suman	M.Sc. Project	
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Publications

14 Sahoo S, Padhy AA, Kumari V, Mishra P (2022) , Role of Ubiquitin–Proteasome and Autophagy-Lysosome Pathways in α -Synuclein Aggregate Clearance , Molecular Neurobiology, ,,14,1-29 IF - 5.59.

13 Padhy AA*, Sahoo S*, Kumari S, Kumari V , Mishra P (* equal contribution) (2021) , Exploring Large-Scale Protein Function using Systematic Mutant Analysis , Advances in Protein Molecular and Structural Biology Methods, Elsevier, USA,,,

- 12 Sahoo S*, Padhy AA*, Kumari V, Kummari S, Mishra P (* equal contribution) (2021) , Therapeutic Potential of Leucine Rich Repeat Kinase 2 In Parkinson's Disease , Protein Kinase Inhibitors: From Discovery to Therapeutics, Elsevier,,,
- 11 Starr TN*, Flynn JM*, Mishra P*, Bolon DN, Thornton JW (2018) , Pervasive contingency and entrenchment in a billion years of Hsp90 evolution , Proceedings of the National Academy of Sciences of the United States of America, ,115 ,17,4453-4458 IF - 11.2.
- 10 Mishra P*, Flynn JM*, Starr TN, Bolon DN, (2016) , Systematic mutant analyses elucidate general and client-specific aspects of Hsp90 function , Cell reports, Cell Press,15,3,588-598 IF - 9.423.
- 9 Flynn JM*, Mishra P*, Bolon DN (2015) , Mechanistic asymmetry in Hsp90 dimers , Journal of Molecular Biology, Academic Press,427,18,2904-2911 IF - 4.76.
- 8 Mishra P, Bolon DN (2014) , Designed Hsp90 Heterodimers Reveal an Asymmetric ATPase-Driven Mechanism In Vivo , Molecular Cell, ,53,2,344-350 IF - 17.97.
- 7 Boucher J, Cote P, Flynn J, Jiang L, Laban A, Mishra P, Roscoe B, Bolon DN, (2014) , Viewing Protein Fitness Landscapes Through a Next-Gen Lens , Genetics, Genetics Society of America,198,,461–471.
- 6 Jiang L*, Mishra P*, Hietpas RT, Zeldovich KB, Bolon DN, (2013) , Latent effects of Hsp90 mutants revealed at reduced expression levels , PLoS Genetics, ,9,6,e1003600 IF - 5.175.
- 5 Pursell NW*, Mishra P*, Bolon DN, (2012) , Solubility-promoting function of Hsp90 contributes to client maturation and robust cell growth , Eukaryotic cell, American Society for Microbiology Journals,11,8,1033-1041 IF - 3.586.
- 4 Wayne N*, Mishra P*, Bolon DN (2011) , Hsp90 and client protein maturation , Molecular Chaperones, Humana Press,,,33-44.
- 3 Mishra P, Kumar PR, Ethayathulla AS, Singh N, Sharma S, Perbandt M, Betzel C, Kaur P, Srinivasan A, Bhakuni V (2009) , Polysaccharide binding sites in hyaluronate lyase—crystal structures of native phage—encoded hyaluronate lyase and its complexes with ascorbic acid and lactose , The FEBS journal, ,276,12,3392-3402 IF - 5.54.
- 2 Mishra P, Bhakuni V (2009) , Self-assembly of bacteriophage-associated hyaluronate lyase (HYLP2) into an enzymatically active fibrillar film , Journal of Biological Chemistry, ,284,8,5240-5249 IF - 5.15.
- 1 Mishra P, Akhtar MS, Bhakuni V, (2006) , Unusual structural features of the bacteriophage-associated hyaluronate lyase (hylp2) , Journal of Biological Chemistry, ,281,11,7143-7150 IF - 5.157.

Research

complete list of publications -Google scholar: <https://scholar.google.com/citations?user=stWgX-cAAAAJ&hl=en>

Functional proteins emerge as a consequence of a complex folding pathways. Mutations in the wild type gene sequence can result in a failure to acquire native conformation and is the underlying cause of protein misfolding and diseases like cancers and neurodegeneration. Interestingly, mutations can also revert pathological conditions and might confer advantage to the organism like prions or amyloid form of proteins serve as environmental shields forming biofilms, long-term memory acquisition, and drug resistance. Hence the functional space of proteins is much larger than anticipated by natively acquired conformations and unexplored for translational benefits. Our lab is deeply interested in exploring the sequence space of proteins to identify novel mutations with improved functions. We are currently focusing on exploring the escape mutants in aggregation of prion protein, synuclein and ataxin along with their regulatory protein, ubiquitin. The conformational changes in the mutant form of our target proteins can sculpt phenotypic landscapes as well as shape evolutionary processes. We employ high throughput mutagenesis, protein engineering and genetic manipulations in the unicellular eukaryote *Saccharomyces cerevisiae* (baker's yeast) as the host organism to investigate

(1) Dominant negative mutations to reveal critical protein-protein interactions

(2) Mutations with anti-aggregation phenotypes in amyloid proteins

(3) Mutations that inhibit enzymatic functions particularly of disease relevant deubiquitinases.

Yeast serve as a powerful unicellular eukaryote for unbiased high-throughput screening of mutations. The mutant proteins screened with desired phenotypes are further studied by a combination of biochemical and biophysical methods to uncover mechanistic details of their functions.

We are motivated to identify the cryptic/novel mutations in proteins which for multi-functional proteins can affect only desired interactions or can reverse the toxic oligomers of misfolded proteins to counteract the enigmatic disease conditions.

Joining the lab

For a trainee opportunity in our lab, please contact at pmsl@uohyd.ac.in

We encourage applications from highly motivated students and appreciate the applicant to write the aspects of our research that interests them to work with us. We welcome CSIR, UGC, ICMR or DBT fellowship holders as well as non-fellowship holders for PhD positions available through the University of Hyderabad PhD program. Application enclosing a CV, research interests and two references for evaluation should be sent by the prospective candidate.

Lab pics

pic attached