Parul Mishra, Ph.D. (JNU, New Delhi) – Protein Aggregation, Quality control and Degradation.

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Research interests:
All cellular functions require a finely orchestrated balance between protein synthesis, folding and degradation. Highly specialized components in the protein quality control network modulate protein folding and degradation pathways in order to avoid accumulation of misfolded proteins. This protein homeostasis or proteostasis network consists of several chaperones and co-chaperones, E3 ubiquitin ligases and deubiquitinases among other quality-control factors. Mutations in one or more components of this proteostasis network have been identified as the root cause of a number of diseases including cancer and neurodegenerative diseases.
My laboratory is interested in the mechanisms that mediate protein degradation particularly the ubiquitin-proteasome system (UPS). UPS is responsible for carrying out degradation of a large number of proteins inside cells. Proteins destined for degradation by UPS are tagged with the protein ubiquitin by a cascade of enzymes referred to as the ubiquitin-conjugating (E2) and ubiquitin ligase (E3) enzymes. The ubiquitin tag on these proteins is subsequently recognized by the proteasome, a large multi-protein complex that binds ubiquitin tags and degrades the protein to which the tag is attached.

Research in my laboratory aims at deciphering the following questions:

1. How is protein homeostasis maintained inside normal cells?
2. What changes in the protein homeostasis network lead to disease?
3. Can the protein homeostasis machinery be modulated to treat diseases?

To answer these questions we employ a multidisciplinary approach combining a variety of biochemical, genetic and next-generation sequencing tools.

Awards and Honors

- 2015: Ramalingaswami Re-entry Fellowship, Department of Biotechnology, Govt. of India.
- 2015: Assistant Professor-Biological Sciences, UGC-Faculty Recharge Program.
- 2008: Dr. M.M. Dhar Memorial Best Thesis Award.
- 2006: Dr. D.L. Srivastava Memorial Young Scientist Award by Society of Biological Chemists.
- 2005: Best poster award at the 74th Annual General Meeting of Society of Biological Chemists.
- 2005: Senior Research Fellowship, CSIR, Govt. of India
- 2003: Junior Research Fellowship, CSIR, Govt. of India
- 2003: Chakravarty Gold Medal in M.Sc.
- 2002: Rae Saheb Sheo Shanker Memorial Merit Scholarship in M.Sc.

Recent Publications:

- **Mishra P*,** Flynn J*, Starr TN, Bolon DN. Systematic mutant analyses elucidate general and client-specific aspects of Hsp90 function. ***Cell reports,*** 2016 Apr;15(3): 588-98***. (* equal contribution)***
  Spotlight article by- Zuehlke AD, Neckers L. Clients place unique functional constraints on Hsp90. ***Trends in Biochemical Sciences*****,** 2016 Jul;41(7):562-4.
- Flynn J*, **Mishra P*,** Bolon DN. Mechanistic asymmetry in Hsp90 dimers. ***Journal of Molecular Biology****,* 2015 Sep; 427(18): 2904-11.***(* equal contribution)***
- Boucher JI, Cote P, Flynn J, Jiang L, Laban A, **Mishra P**, Roscoe BP, Bolon DN. Viewing protein fitness landscapes through a next-gen lens. ***Genetics****,* 2014 Oct;198 (2):461-471.
- **Mishra P**, Bolon DN. Designed Hsp90 heterodimers reveal asymmetric ATPase-driven mechanism *in vivo*. ***Molecular Cell,*** 2014;Vol 53;Issue 2,344-350.
- Jiang L*, **Mishra P***, Hietpas R, Bolon DN. Latent effects of Hsp90 mutants revealed at reduced expression-levels. ***PLOS Genetics****,* 2013 Jun;9 (6): e1003600. ***(* equal contribution)***