

Veena Prahlad

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- Education:**
- Northwestern University, Evanston*** Evanston, IL
 Postdoctoral Fellow in Dr. Richard I. Morimoto's laboratory
 Department of Biochemistry, Cell and Molecular Biology
 (June 2004-present)
- University of Madison, Wisconsin*** Madison, WI
 Postdoctoral Fellow in Dr. Elizabeth B. Goodwin's laboratory
 Department of Genetics
 (February 2000-June 2004)
- University of Alberta, Edmonton, Canada*** Edmonton, Canada
 Visiting postdoctoral fellow in Dr. Dave Pilgrim's laboratory
 Department of Biological Sciences
 (June 2000-November 2000)
- Northwestern University, Chicago*** Chicago, IL
 Ph.D Integrated Program in Life Sciences
 Thesis: The assembly of Intermediate Filaments
 Mentor: Dr. R.D. Goldman
 (August 1992–December 1999)
 This included work at the Marine Biological
 Laboratories, Woods Hole, during the summers of
 1998 and 1999.
- Jawaharlal Nehru University, New Delhi*** New Delhi, India
 Masters of Science (M.Sc.), Life Sciences
 (1990-1992)
- St. Joseph's College, Bangalore*** Bangalore, India
 Bachelor of Science (B.Sc.), Chemistry Botany, Zoology
 (1987-1990)
 Honors in Microbiology. Thesis: Identification and characterization of
 carriers of nosocomial diseases in Bangalore.
 (June 1992)

Talks at Meetings: **“Cell non-autonomous regulation of heat-shock response in *Caenorhabditis elegans* by the thermosensory neuronal network.”**
2008 Midwest Stress Response and Molecular Chaperones,
Northwestern University, Evanston, Illinois. January, 2008

“Identification of a bacterial component that induces postembryonic sexual transformation and genomic instability in *C. elegans*.”
15th International *C. elegans* Conference
Los Angeles, USA. June 2005

“Developmental plasticity in the sex determination mechanism of *C. elegans* requires mating.”
14th International *C. elegans* Conference
Los Angeles, USA, June-July 2003

“Regulating the Polymers of the Cytoskeleton”.
American Society for Cell Biology, Minisymposium
Washington D.C, USA. December, 1997

Invited Talks: **“How food makes males: the case of *C. elegans*.”:** Keynote speaker
“Graduate Student Research Days”,
Department of Biological Sciences,
University of Alberta, Edmonton, Canada. February, 2006

“Biological Strategies: What Biology Can Teach Engineers”. Keynote speaker
Department of Smart Materials and Material Sciences,
National Aeronautics Laboratories, Bangalore, India: June, 2000:

“The formation of IF networks.” Invited speaker
Department of Cell and Molecular Biology,
University of Cincinnati, USA. April, 2000:

Publications:

1. Prahlad, V. and Morimoto, R.I. (invited review; in press). Integrating the stress response: lessons for neurodegenerative diseases from *C. elegans*. *Trends Cell Biol.*

2. Prahlad, V., Cornelius, T., Morimoto, R.I. (2008). Regulation of the cellular heat shock response in *Caenorhabditis elegans* by thermosensory neurons. *Science* 320:811-814.

Commentary on this article:

Faculty of 1000 evaluation: Must Read

Podrabsky, J.E. (2008). "Neuronal control of cellular heat shock response in nematodes". *J. Exp. Biol.* 211.

Highlighted in:

Ray, B.L. (2008) "Wholesale Heat Shock". Editor's Choice, *Sci Signal* 1, ec180.

<http://stke.sciencemag.org/cgi/content/abstract/1/19/ec180>

Flight, M.H. (2008). "Sensory Systems: Beating the Heat". *Nat. Rev. Neurosci.* 9, 500.

3. Prahlad, V., Pilgrim, D., Goodwin, E.B. (2003). Roles for mating and environment in *C.elegans* Sex Determination. *Science* 302:1046-1049.

Commentary on this article:

- Faculty of 1000 evaluation: Must Read
- "Sex in the Soil". ScienceDaily (Nov 7, 2003).

Highlighted in:

Editor's Choice (2003) "Flexible Sex and Suspended Animation in Nematodes" *Sci STKE* (2003) tw438.

4. Prahlad, V., Helfand B., Langford, G.M., Vale, R.D. and R.D. Goldman (2000). Fast transport of neurofilament protein along axonal microtubules. *J. Cell Sci.* 113: 3939-3946.

5. Goldman, R.D., Chou, Y.-H., **Prahlad, V.** and M. Yoon (1999). Intermediate filaments: dynamic processes regulating their assembly, motility, and interactions with other cytoskeletal systems. Supplement 2 to the *FASEB Journal*. 13: S261-S265.

6. Steinert, P.M., Chou, Y.-H., **Prahlad, V.**, Parry, D.A.D., Marekov, L., Wu, K., Jang, S.-I., and R.D. Goldman (1999). A high molecular weight intermediate filament-associated protein in BHK-21 cells is nestin, a Type VI intermediate filament protein. *J. Biol. Chem.* 274: 9881-9890.

7. Prahlad, V., Yoon, M., Moir, R.D., Vale, R.D. and R.D. Goldman (1998). Rapid movements of vimentin on microtubule tracks: kinesin-dependent assembly of intermediate filament networks. *J. Cell Biol.* 143-159-170.

Highlighted in:

Clarke, E.J. and Allan, V. (2002) "Intermediate Filaments: Vimentin moves in." *Curr. Biol.* 12 R596-R598.

8. Yoon, M., Moir, R.D., **Prahlad, V.** and R.D. Goldman (1998). Motile properties of vimentin intermediate filament networks in living cells. *J. Cell Biol.* 143: 147-157.

Research Experience:

**Northwestern University, Evanston,
Department of Biochemistry, Molecular Biology, and Cell Biology**

Mentor: Richard I. Morimoto

Evanston, IL

My current work focuses on the systemic response of organisms to environmental stress. Specifically, I am interested in understanding how the response of individual cells to proteotoxic stress is coordinated and integrated within metazoans to deliver an adaptive response at the organismal level. The stress response of isolated mammalian cells and unicellular organisms is well- studied. This response is thought to be regulated in a cell autonomous manner, triggered by the increase in misfolded or damaged cellular proteins caused by the environmental stressors. It consists of a multi-step, auto-regulatory process orchestrated by the transcription factor HSF1, whose activity results in the upregulation of the cytoprotective heat shock proteins (HSPs). HSP expression subsequently allows cells to readjust their protein biogenesis and protein folding homeostasis to suit the altered environmental and physiological conditions.

My studies showed that within the metazoan *C. elegans* a prototypic stress response, the heat shock response, is no longer cell-autonomous, but instead regulated by the animals neurosensory system. Mutations affecting two thermosensory neurons (AFDs) amongst the animals 959 cells disrupted HSF1- dependent *hsp* transcription throughout the organism, following heat shock. This included many somatic, non-neuronal cells. The regulation by the thermosensory AFD neurons was specific to temperature- stress; the stress response that is induced upon exposure to another class of stressors such as cadmium was not affected. In addition, the regulation of *hsp* transcription by the AFD neurons was modulated by growth and metabolic signals, suggesting that the stress response of somatic cells within *C. elegans* was an integrated response to the numerous facets of its environment. These data suggest a model for the cell non-autonomous regulation of the heat shock response by the neurosensory system of *C. elegans* whereby the cellular stress response machinery is negatively regulated by two mutually inhibitory signals, one from the AFD neurons, and the other that depends on the organism's growth and metabolic status.

These studies provide the first direct evidence that the heat shock response is regulated in a cell non-autonomous manner within an organism, and suggest novel levels of regulation of the stress response and protein folding homeostasis machinery. The use of *C. elegans* for this study offers an exciting opportunity to dissect the hierarchical levels of regulation of HSF1-dependent HSP transcription within an organism, and map the neuronal correlates of stress induced gene expression. In addition, they allow us to address how fundamental cellular functions regulated cell autonomously in isolated cells and unicellular organisms, may have been come under neuroendocrine control within metazoans. The characterization of the genes and pathways involved in the neuronal regulation of stress in *C. elegans*, and identification of their mammalian orthologs may also ultimately prove relevant to our understanding of fever, human protein conformational diseases and chaperone over-expression diseases including cancer.

University of Madison, Wisconsin
Department of Genetics and
University of Alberta, Edmonton, Canada
Mentor: Elizabeth B. Goodwin

Madison, WI

Edmonton, Canada

As a postdoctoral fellow in Dr. Goodwin's laboratory, I discovered the existence of a surprising plasticity in the sex determination mechanism of *C. elegans* in response to specific environmental conditions. The two sexes in *C. elegans*, hermaphrodites and males were thought to be determined irreversibly at fertilization by the ratio of X chromosomes to sets of autosomes (X:A ratio) of the embryo: XX embryos become hermaphrodites and XO, males. My studies showed that both the sexual phenotype and the genotype of *C. elegans* could also be altered post-embryonically by specific bacterial metabolites, in a manner that requires

sexual reproduction. When grown in metabolites from log phase bacteria XX larvae generated by mating switched sexual fate and developed as males instead of hermaphrodites. This was accompanied by the loss of their paternal X chromosome. XX larvae produced by hermaphrodite self-fertilization, on the other hand, neither changed sexual phenotype nor showed evidence of chromosomal instability under similar conditions.

My studies were the first to demonstrate this sexual plasticity, and X chromosome instability in *C. elegans* in response to environmental factors. Phenotypic plasticity, the development of different morphological, biochemical or behavioral phenotypes depending upon environmental conditions, is thought to be key to generating diversity and directing evolutionary trajectories amongst organisms. The plasticity of the sexual phenotype and the concomitant loss of the paternal X chromosome in this process may offer some clues into this mechanism. My studies also indicated that even in a highly inbred species there exist inherent differences between genotypically identical progeny derived by self-fertilization (self-progeny) and by cross-fertilization (cross-progeny): while the development of cross-progeny was more amenable to environmental signals, self-progeny appeared more set in their developmental course. These studies thus suggest that sexual reproduction may confer an advantage to progeny by producing greater developmental plasticity and allowing them to better adapt to changing environments. Thus they offer answers to the question why sexual reproduction exists despite the prediction that populations of asexually reproducing individuals should double twice as fast as sexually reproducing ones and rapidly replace them. I have subsequently characterized some of the features of the bacterial metabolites, that induce the observed genomic instability and sexual transformation in order to understand what advantages are conferred by this sexual plasticity.

Northwestern University, Chicago
Department of Cell and Molecular Biology
Mentor: Robert D. Goldman

Chicago, IL

My graduate work focused on the mechanism by which cells organize their cytoskeletal networks of intermediate filament proteins. At the time the intermediate filament network was generally regarded as a rigid cytoskeletal network whose main function was to confer mechanical support to cells. However, my work showed that these complex networks are in constant flux, and more plastic than was previously thought. Specifically, I discovered that the intermediate filament (IF) proteins were transported as particulate complexes by the microtubule and kinesin-dependent fast transport ($0.55 \pm 0.24 \mu\text{m}/\text{sec}$) to the peripheral regions of the cell. Once delivered to these regions, the particles assembled initially into short disconnected filaments and subsequently polymerized into longer cytoskeletal networks (Prahlad et al., 1998, Prahlad et al., 2000). The initial observations were made in cultured mammalian cells, but subsequently, during two summers at the Marine Biological laboratories at Woods Hole I extended it to show that this was a more general aspect of IF transport. For this, I developed a method to directly visualize the movements of endogenous neurofilament protein particles in preparations of extruded squid axoplasm. The method combined Video Enhanced Differential Interference microscopy (AVEC-DIC) with immunolocalization (Prahlad et al, 2000). In preliminary studies I isolated the transported particles and found that they contain numerous other proteins that were co-transported as complexes for local cellular assembly. I purified and biochemically characterized one of them, the cytoskeletal IF protein nestin (Steinert et al., 1998), and showed that it is a component of the transported particles, inhibited vimentin polymerization, and associated with tubulin, suggesting that it might play a

key role in regulating the regional polymerization of IF particles.

This work was one of the first reported instances of intracellular trafficking of non-membranous cytoskeletal proteins along microtubules using kinesin (Prahlad et al., 1998; Goldman et al., 1999). These studies also showed that, contrary to previous models, the axonal transport of non-membranous cytoskeletal proteins could occur at fast rates (Prahlad et al., 2000), and may have implications regarding the pathogenicity of disease like ALS and Alzheimers where intermediate filament networks are markedly affected.

Teaching

Experience:

Mentored Northwestern University undergraduate students in “Independent Study” for credit. This involved teaching laboratory techniques and experimental design, overseeing experiments and reports required for obtaining credit, and even resulted in one of the students becoming a co-author on a publication.

Mentored high school students as part of their senior internship program at IMSA (Illinois Math Science Academy).

Mentored a Masters of Science (M.Sc) student from Ecole Normale Superieuer, Paris. This involved guiding the student through the design of a M.Sc. project, design, implementation and interpretation of experiments, and writing of the Masters thesis.

Mentored Masters of Science (M.Sc) student in the Biotechnology Program, Northwestern University, Evanston.

Services:

Aided in the review of papers for PLoS Biology, Science, Nature, Proceedings of the National Academy of Sciences, Genes and Development.

Volunteered to mentor students for Illinois Academy of Science, Minority Program, 2002.

Meetings:

Gordon Research Conference, Oxford, UK., 2007
 Midwest Stress Response and Molecular Chaperones, 2006,2007,2008.
C.elegans International Conference, 2001, 2003,2005
 Developmental Biology, Madison, USA. 2002.
 Gordon Research Conference, Holderness, NH, 1996, 1998.
 “Cytoskeleton”, Cold Spring Harbor, New York, 1994
 American Society for Cell Biology, 1993, 1994, 1996, 1997, 1998, 1999.