



Dr. Subhankar Paul

Present Position

Assistant Professor

National Institute of Technology Rourkela
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Education

Ph.D (Protein Biology) **Indian Institute of Technology, Delhi**, New Delhi, India,
July 2003 - February 2007.

M. Tech. (Chemical Engineering) **Indian Institute of Technology, Kanpur**, India, 2001.

B. E. (Chemical Engineering) **Jadavpur University**, Kolkata, India, 1999.

Courses Taught at National Institute of Technology Rourkela: *Biochemical Engineering, Advanced Bioseparations, Biophysics and structural Biology, Cell & Molecular Biology*

Current Research

The primary focus of my research is to understand how Hsp90, Bcl-2, apoptotic genes caspases are linked to breast cancer pathogenesis. Apoptosis, or programmed cell death, is a physiological process of selective cell elimination that is involved in embryogenesis, immune function, and tissue homeostasis. Dysregulation of apoptosis leads to various pathological diseases including cancer. Apoptosis/programmed cell death has been reported to have a crucial role in breast cancer development. Overexpression of *Bcl-2* gene has been observed in 70% of breast carcinomas and the expression levels of Bcl-2 proteins correlate with resistance to a wide spectrum of chemotherapeutic drugs and radiation therapy. One of the most important observations has been the implication of heat shock protein Hsp90

chaperones in breast cancer progression. Disruption of the Hsp90-client protein complexes leads to proteasome-mediated degradation of client proteins. Although Hsp90 expression is high in breast cancer cell lines, yet no large studies have been conducted on expression in human tumors and the association with clinical/pathologic variables. Hsp90-targeting agents are in clinical trials for breast cancer. Till now, it is not clear whether Hsp90 expression has any implication with the aberrant expression of different caspase family of proteins like caspase-2, -5, -6, -7 and -8 and bcl-2 family proteins or HER protein in breast cancer cells.

Hsp90 inhibitors such as 17-dimethylaminoethylamino-17-demethoxygeldanamycin (17-DMAG) are new therapies that were developed and have already been shown to treat various types of cancers, including breast cancer. Studies on Hsp90 inhibitors, such as the 17-AAG and 17-DMAG geldanamycin derivatives, have demonstrated these agents to be effective in inhibiting the proliferation of various types of cancers through the induction of apoptosis and arrest of the cell cycle. However, the detailed mechanism of how they act is still unclear.

I am primarily interested in the following topics:

1. To Define the role of Hsp90, caspases and antiapoptotic proteins Bcl-2 and Bcl-x(L) in human breast cancer.
2. To test the expression level of Hsp90, caspases and antiapoptotic proteins Bcl-2 and Bcl-x(L) in human breast cancer cell lines and in mouse xenograft models.
3. To modulate the expression of Hsp90 to observe the expression level of caspases and antiapoptotic proteins Bcl-2, Bcl-x(L) and HER in human breast cancer cell lines and in mouse xenograft models.
4. To observe the effect of proteasome inhibitors/activators on the expression level of Hsp90, caspases and Bcl class of proteins for developing a therapeutic approach.

Description of Ph.D Research

Chaperone Mediated protein folding in vivo and in vitro (At the level of my Ph.D. research at Indian Institute of Technology, Delhi, India)

I have worked with chaperone-mediated protein folding problem. The issues which I wanted to address is how newly synthesized proteins fold in the cell using bacterial chaperone GroEL and its co-chaperonin GroES in the presence of nucleotide ATP. The other aspect of my project was to find out the molecular mechanism of how molecular chaperones help in folding relatively larger substrate proteins. All of the studies I have carried out with a enzyme, *Escherichia coli* Maltodextrin glucosidase (MalZ), which degrades maltoheptaose and short maltodextrins (maltotriose to maltoheptaose) to shorter oligosaccharides, the final hydrolysis products being maltose and glucose. I have come to the following conclusions, MalZ requires the complete chaperonin system GroEL/ES and ATP for its correct folding, trans sided folding occurs to MalZ folding in oppose to cis-sided mechanism for smaller proteins, MalZ stays bound with GroEL, cannot fold in presence of SR1/ES and ATP during the refolding process of MalZ. This work has been published in The **FASEB Journal**.

Unfolding of maltodextrin glucosidase (At the level of my Ph.D. research at Indian Institute of Technology, Delhi, India)

I have worked on Purification, Detailed physico-chemical characterization, and unfolding/refolding studies of a medium molecular weight enzyme Maltodextrin glucosidase (MalZ) from *Escherichia coli*. Both the chemical and thermal unfolding studies was carried out on MalZ and monitored by the loss of enzyme activity, intrinsic and extrinsic fluorescence measurement and Circular Dichroism. It was found that the protein gets destabilized rapidly during unfolding process by guanidium hydrochloride and follows a three state kinetic pathway. The results have been communicated in **BMC Structural Biology Journal**.

Teaching Experience

- ❖ Lecturer (July, 2007- Present) continuing teaching B.Tech, M.Tech students in the Dept. of Biotechnology and Medical Engineering at National Institute of Technology Rourkela since July 2007.
- ❖ Visiting Faculty (Jan. 2007-July. 2007) in The dept. of Biotechnology, Motilal Nehru National Institute of Technology, Allahabad.
- ❖ Lecturer (Oct., 2006- Jan. 2007) in the Dept. of Biotechnology, Heritage Institute of Technology, Kolkata.
- ❖ Guiding M.Tech students in their major projects as part of the Indian Institute of Technology Fellowship program during Ph.D. Program.
- ❖ B.Tech, M.Tech and Ph.D. laboratory classes (Microbiology, Biochemistry, Molecular Biology and Biophysics) as part of the Indian Institute of Technology Fellowship program during Ph.D. Program.

On going sponsored research projects:

Title of project: *Hsp-90-based therapeutic approach for breast cancer*

Scheme: SERC Fast Track Proposals for Young Scientists

Funding Agency: Department of Science and Technology

Publications

(a) Published in International Journal

1. **Subhankar Paul*** and Apurba Dey. Wnt Signaling and cancer development: a therapeutic implication. *Neoplasma* (2008) 55: 165-176.

2. **Subhankar Paul*** and Tapan k Chaudhuri. Factors affect Solubilization of recombinant maltodextrin glucosidase in Escherichia coli. *Journal of Applied Microbiology* (2008) 104: 35–41. ([Impact Factor: 2.2](#))
3. **Subhankar Paul***, Shasikala Punam and Tapan K Chaudhuri. Chaperone-assisted refolding of *Escherichia coli* maltodextrin glucosidase. *FEBS Journal* (2007) 274: 6000-10. ([Impact Factor: 3.6](#))
4. **Subhankar Paul**, Chanpreet Singh, Saroj Mishra and Tapan K. Chaudhuri. The 69-kDa Escherichia coli Maltodextrin Glucosidase does not Get Encapsulated Underneath GroES and Folds through trans Mechanism During GroEL/GroES Assisted Folding. *The FASEB journal*, (2007) 21: 2874-2895. ([Impact Factor: 7.2](#))
5. RamGopal Nitharwal, **Subhankar Paul**, Rajesh K Soni, Sukrat Sinha, Dhaneeswar Prusthy, Tara Keshav, Nirupam RoyChoudhury, Gauranga Mukhopadhyay, Tapan K. Chaudhuri, Samudrala Gourinath, and Suman Kumar Dhar. The unique domain structure of Helicobacter pylori DnaB helicase: The N terminal region can be dispensable for helicase activity whereas the extreme C terminal region is essential for its function. *Nucleic Acid Research (NAR)*, (2007) 35: 2861-2874. ([Impact Factor: 7.6](#))
6. **Subhankar Paul***. (2007) Polyglutamine-mediated neurodegeneration: Use of Chaperones as prevention strategy. *Biochemistry (Moscow)* (2007) 72: 359-66.
7. Tapan K. Chaudhuri and **Subhankar Paul**. Protein-misfolding diseases and chaperone-based therapeutic approaches. *FEBS journal* (2006) 273: 1331-1349. ([Impact Factor: 3.6](#))
8. **Subhankar Paul***. Dysfunction of ubiquitin proteasome system and disease propagation: therapeutic approaches. *BioEssays journal* (2008) (In Press). ([Impact Factor: 6.8](#))
9. **Subhankar Paul*** and Tapan K. Chaudhuri. Fluorescence quenching study of *E.coli* Maltodextrin glucosidase. *Biochemistry (Moscow) Journal* (2008) (In Press).

* Corresponding author

(b) Conference

1. **Subhankar Paul** and Tapan K. Chaudhuri. “*Escherichia coli* protein Maltodextrin Glucosidase (MalZ) folds through *trans* sided mechanism in the GroEL-GroES assisted pathway”. Society of Biological Chemists (India), SBC 2006, New Delhi, India.
2. RamGopal Nitharwal, **Subhankar Paul**, Rajesh K Soni, Sukrat Sinha, Dhaneeswar Prusthy, Tara Keshav, Nirupam RoyChoudhury, Gauranga Mukhopadhyay, Tapan K. Chaudhuri, Samudrala Gourinath, and Suman Kumar Dhar. “The unique domain structure of Helicobacter pylori DnaB helicase: The N terminal region can be dispensable for helicase activity whereas the extreme C terminal region is essential for its function”. Society of Biological Chemists (India), SBC 2006, New Delhi, India.
3. **Subhankar Paul** and Tapan k. Chaudhuri. “GroEL-GroES assisted and unassisted in vivo and in vitro folding of a large recombinant Escherichia coli protein Maltodextrin Glucosidase” (2006), pp 93:

Molecules, Interactions and Design: A Biophysical Perspective, National symposium, IBS 2006, Kolkata, India.

4. Debjit Sanpui, **Subhankar Paul** and Ashok Khanna.” Validation of a non-equilibrium mass transfer model, for liquid-liquid extraction”. Recent trends in Heat and Mass Transfer, 2000.
5. Debjit Sanpui, **Subhankar Paul** and Ashok Khanna.” Validation of a non-equilibrium mass transfer model, for liquid-liquid extraction”. Recent trends in Heat and Mass Transfer, 2000.

Work Experiences

1. Assistant Professor (July, 2008- Present) continuing teaching B.Tech, M.Tech, Ph.D students in the Dept. of Biotechnology and Medical Engineering at National Institute of Technology Rourkela since July 2007.
2. Lecturer (July, 2007- Present) continuing teaching B.Tech, M.Tech, Ph.D students in the Dept. of Biotechnology and Medical Engineering at National Institute of Technology Rourkela since July 2007.
3. Visiting Faculty (Jan. 2007-July 2007) in the Dept. of Biotechnology, Motilal Nehru National Institute of Technology, Allahabad.
4. Lecturer (Oct., 2006- Jan. 2007) in the Dept. of Biotechnology, Heritage Institute of Technology, Kolkata.
5. Trainee Software Engineer (April, 2001-Oct. 2001) in Mahindra British Telecom Limited, Pune.

Awards/Honors

1. Editorial Review Board member of Scientific Journals International (SJI). (<http://www.scientificjournals.org/index.php>)
2. Research Fellowship, Indian Institute of Technology Delhi.
3. Qualified in Graduate Aptitude Test in Engineering (GATE), for Master’s fellowship.