Sanghamitra Mylavarapu, Ph.D.

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Profile

An accomplished biomedical scientist, with over 15 years' research experience in the fields of oncology, molecular biology and biotechnology.

US trained Cancer & Molecular Biologist with multiple peer-reviewed publications and patents

Through science-based innovation, and fruitful collaborations, developed novel clinic-ready immunotherapy, poised for Investigational New Drug (IND) submission to the US-FDA.

Thrives in cross-functional and multi-disciplinary environments, leading team towards bringing solutions to complex problems with cutting-edge science.

Skills & Abilities

- Conceptualized, initiated, designed, developed and supervised pre-clinical studies for oncology drug development through interdisciplinary and translational approaches, using cell biology, molecular biology and high-resolution imaging strategies.
- Expertise in translational R&D, biomarkers, project management, inventor on patents.

Education

Ph.D. | 2019 | DEPT. OF BIOTECHNOLOGY, DELHI TECHNOLOGICAL UNIVERSITY (FORMERLY, DELHI COLLEGE OF ENGINEERING)

- Thesis title: Identification and characterization of novel molecular markers in cancer prevalent among Indian patients

Identified underlying molecular mechanisms driving differential response to standard treatment regimens for colorectal cancer among Indian patients. A primary tumor-derived cell line from an Indian colorectal cancer patient was established and extensive molecular studies were carried out to gain insights into the fundamental mechanistic differences that led to the dampened response to drugs that are currently in clinical practice for treatment of colorectal cancer.

M.Sc. | 1997 | PONDICHERRY UNIVERSITY

- Medical Entomology

B.Sc. | 1995 | DELHI UNIVERSITY

- Zoology (Hons)

Experience

INDUSTRY

SENIOR SCIENTIST, PRE-CLINICAL BIOLOGY | AKAMARA BIOMEDICINE PVT. LTD. | 2019-PRESENT

Leading the *in vitro* biology team for developing a novel B-cell activating immunomodulator from the early discovery phase through pre-clinical studies and clinic-ready pre-IND phase. Designed and guided team for

conducting all *in vitro* studies to unravel the molecular mechanism of action of the novel drug for B-cell mediated immune response. Actively leading efforts to identify potential biomarkers that could either be used for monitoring disease progression in the clinic or patient stratification.

- *In vitro* team lead for conducting pre-IND studies for the lead drug candidate molecule.
- Team lead for elucidating the mechanism of action of the lead candidate molecule.
- Development of prognostic and exploratory biomarkers for phase-I clinical trials for the lead molecule
- Set up collaborations with other research establishments, including academic research institutions and CROs.
- Project management for meeting timelines for deliverables.
- Mentoring/training team members.

PROJECT LEAD | INVICTUS ONCOLOGY PVT. LTD. | 2015-2019

- Development of biological assays for screening libraries of compounds for drug development pipeline.
- Set up collaborations as the lead liaison with industrial and academic establishments for multiple projects.
- Mentoring/training team members.
- Develop and maintain SOPs.

FOUNDING SCIENTIST | INVICTUS ONCOLOGY PVT. LTD. | 2011-2015

- Setting up a fully functional R&D unit including instrument procurement, personnel recruitment and build capacity to facilitate the drug development program.
- Design and conduct proof-of-concept research for the New Chemical Entities (NCEs) under development.
- Train new lab personnel on various experimental techniques employed in conducting the research.

ACADEMIA

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, WORCESTER, MA, USA | 2008-2010

- Research Associate, Department of Neurobiology, University of Massachusetts Medical School, Worcester, Massachusetts, USA, 2008 – 2010.

BOSTON BIOMEDICAL RESEARCH INSTITUTE, WATERTOWN, MASSACHUSETTS, USA | 2007-2008

- Research Associate, Boston Biomedical Research Institute, Watertown, Massachusetts, USA, 2007 – 2008

UNIVERSITY OF MASSACHUSETTS MEDICAL SCHOOL, WORCESTER, MA, USA | 2002-2007

- Research Associate, Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, Massachusetts, USA. 2002 – 2007.

POST GRADUATE RESEARCH TRAINING | 1997-2002

- Research Assistant, Institute of Genomics and Integrative Biology, New Delhi, India, 1999 – 2002.
- Research trainee, School of Biotechnology, Jawaharlal Nehru University, New Delhi, India, 1998 – 1999.
- Research Assistant, Department of Microbiology, All India Institute of Medical Science, New Delhi, India, 1997 – 1998.

AREA OF RESEARCH

- **Cancer Biology**

  Identified underlying molecular mechanisms driving differential response to standard treatment regimens for colorectal cancer among Indian patients. A primary tumor-derived cell line from an Indian colorectal cancer patient was established and extensive molecular studies were carried out to gain insights into the fundamental mechanistic differences that led to the dampened response to drugs that are currently in clinical practice for treatment of colorectal cancer.

- **Cell Biology**

  At the **Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, Worcester, Massachusetts, USA**, I worked on understanding the mechanisms of translocation of newly synthesized polypeptide chain from the cytosol to the endoplasmic reticulum lumen for glycosylation and proper folding into the final functional conformation. Also studied the mechanism of N-linked glycosylation of proteins inside the ER lumen by oligosaccharyltransferase that promotes appropriate protein folding. *S. cerevisiae* was used as eukaryotic model system for these studies.

- **Neurobiology**

  At the **Institute of Genomics and Integrative Biology, New Delhi, India,** I worked on the genomic analyses of a group of neurodegenerative disorders known as the Spinocerebellar Ataxias and Huntington's disease, caused by expansion of CAA/CAG repeats, in patient samples. Genotyping and DNA sequencing methods were used for detecting these repeat expansions at specific loci. Further, at **Boston Biomedical Research Institute, Watertown, Massachusetts, USA,** worked on understanding the molecular mechanisms of Huntington's disease propagation using *S. cerevisiae* as a model system. At the **Department of Neurobiology, University of Massachusetts Medical School, Worcester, Massachusetts, USA,** I used *Drosophila* as a model to study Wallerian Degeneration post axonal injury and the role of glial cells in debris clearance post axonal ablation.

Research Interests

- Cellular signaling circuits that are active during embryogenesis are typically inactivated once embryonic development is complete. However, these signaling pathways are re-activated during cancer pathogenesis. Mis-regulation of one such pathway, the canonical Wnt/β-catenin signaling is a key contributor to colorectal cancer progression. The role of β-catenin as a signaling as well as a transcription co-activator during carcinogenesis has been deeply studied. However, recent findings have indicated that β-catenin function is also critical in cellular division, although mechanistic insights are few. One of the key focus areas of my research would be to unravel the function of the Wnt signaling components in mammalian cell division. I would use cell biology, 2D and 3D cell culture techniques, biochemical methods, high-resolution light microscopy and molecular biology techniques to unravel the role of β-catenin and other signaling molecules to gain insight into their functional significance in the basic mechanism of cellular division. Further, a collaborative initiative for designing and synthesis of small molecule inhibitors to block key molecular interactions would leverage efforts towards translational research.

Teaching Interests

- Would be interested in teaching theoretical and laboratory practical courses on cancer biology, cell biology and drug development at both under-graduation and post-graduation levels.

Technical Expertise

- **Biochemistry**

Expression and purification of recombinant proteins, western blot analysis, chromatographic techniques (HPLC, FPLC, SDS-PAGE, gel filtration, ion-exchange), cell fractionation (mammalian and yeast cells), immunoprecipitation, *in vitro* enzymatic activity assays.

- **Molecular Biology**

PCR, cloning, automated DNA sequencing and genotyping, hybridization techniques, gene expression analysis by qPCR.

- **High resolution light microscopy**

Immunofluorescence analysis of cultured mammalian cells, central nervous system of *Drosophila* embryo, larval and adult *Drosophila* using confocal and brightfield microscopy.

- **Microbiology**

Yeast: Transformations, growth assays, yeast sporulation and spore analysis (tetrad dissection and random spore analysis), genetic manipulation and maintaining yeast strains.
Bacteria: Transformations for cloning related genetic manipulations, large-scale (fermentor) growths for use in protein purifications. Maintaining isolates on plates and in suspension.

- **Mammalian cell culture**

Generation and maintenance of tumor cell lines from mice. *In vitro* assays for screening of NCEs. 3D-cultures of primary and established mammalian cell lines. Co-culturing murine B-cells and tumor cells for immunological assays.

- **Immunohistochemistry**

Preparation of serial sections from FFPE and cryo-preserved tissues. Immunohistological staining of these sections for cell surface immune markers. *In situ* detection of DNA fragmentation in tumor sections.

- ***Drosophila* techniques**

Designing and setting up fly crosses for generating recombinant fly lines, immunohistochemistry on fly embryos, microdissection of larval and adult central nervous system of flies, immunostaining of central nervous system of larval and adult flies.

Publications

PEER REVIEWED ARTICLES:

(Pubmed search terms: Mylavarapu S, Roy S)

1. **Mylavarapu S**, Kumar H, Kumari S, Sravanthi LS, Jain M, Basu A, Biswas M, Mylavarapu SVS, Das A, Roy M., Activation of Epithelial-Mesenchymal Transition and Altered β-Catenin Signaling in a Novel Indian Colorectal Carcinoma Cell Line, Front Oncol. 2019 Feb 15;9:54.

2. **Mylavarapu S**, Das A, Roy M., Role of BRCA Mutations in the Modulation of Response to Platinum Therapy, Front Oncol. 2018 Feb 5;8:16.

3. Mittal U, **Roy S**, Jain S, Srivastava AK, Mukerji M., Post-zygotic de novo trinucleotide repeat expansion at spinocerebellar ataxia type 7 locus: evidence from an Indian family, J Hum Genet. 2005;50(3):155-7.

4. Padiath QS, Srivastava AK, **Roy S**, Jain S, Brahmachari SK., Identification of a novel 45 repeat unstable allele associated with a disease phenotype at the MJD1/SCA3 locus, Am J Med Genet B Neuropsychiatr Genet. 2005 Feb 5;133B(1):124-6.

5. Saleem Q, **Roy S**, Murgood U, Saxena R, Verma IC, Anand A, Muthane U, Jain S, Brahmachari SK., Molecular analysis of Huntington's disease and linked polymorphisms in the Indian population, Acta Neurol Scand. 2003 Oct;108(4):281-6.

6. Srivastava AK, Choudhry S, Gopinath MS, **Roy S**, Tripathi M, Brahmachari SK, Jain S., Molecular and clinical correlation in five Indian families with spinocerebellar ataxia 12, Ann Neurol. 2001 Dec;50(6):796-800.

PUBLISHED CONFERENCE PROCEEDINGS:

1. **Sanghamitra Mylavarapu**, Shelly Kaushik, Yashpal Yadav, Monideepa Roy, Aniruddha Sengupta, Shiladitya Sengupta, IO125 is a potent inducer of tumor immunogenicity, Proceedings: AACR 107th Annual Meeting 2016; April 16-20, 2016; New Orleans, LA.

2. Sengupta A, Roy M, Sarkar A, **Mylavarapu S**, Modi S, Gupta N, B H, Hossain S, Ansari A, Pandey M, Yadav Y, Sengupta S. Designing a novel platinum chemotherapeutic (IO-125) for treatment of breast cancer. Proceedings of the Thirty-Eighth Annual CTRC-AACR San Antonio Breast Cancer Symposium: 2015 AACR; Cancer Res 2016;76(4 Suppl):Abstract nr P5-03-03.

3. Aniruddha Sengupta, **Sanghamitra Mylavarapu**, Smita Kumari, Samad Hossain, Nimish Gupta, Arindam Sarkar, Aasif Ansari, Thirumurthy Velpandian, Monideepa Roy, Shiladitya Sengupta, IO-125: A novel supramolecular platinum chemotherapy for triple negative breast cancer, Proceedings: American Society of Clinical Oncology, 2015, Journal of Clinical Oncology 33(28_suppl):153.

4. Monideepa Roy, Sk Samad Hossain, Arindam Sarkar, Aniruddha Sengupta, Nimish Gupta, Sajid Hussain, Aasif Ansari, **Sanghamitra Mylavarapu** and Shiladitya Sengupta, Abstract 4483: IO125, a novel Pt-based supramolecular therapeutic exhibits increased anti-cancer efficacy compared with oxaliplatin, Proceedings: AACR Annual Meeting 2014; April 5-9, 2014; San Diego, CA.

PATENTS:

1. US patent granted (US10,426,75): Supramolecular combinatorial therapeutics.
2. US patent filed (WO/2018/047090): Immune memory induction by platinum compounds.

Conferences and symposia attended

1. **Poster presented:** International Congress of Cell Biology, 2018. "Differentially regulated Wnt/β-catenin signaling in a novel primary colorectal cancer cell line of Indian origin". **Sanghamitra Mylavarapu**, Harsh Kumar, Sivaram VS Mylavarapu, Asmita Das, Monideepa Roy.
2. **Poster presented:** IOPL Symposium, 2017. "Wnt/β-catenin pathway in CRC02 cell line". **Sanghamitra Mylavarapu,** Monideepa Roy.
3. NextGen Genomics and Bioinformatics Technologies (NGBT) Conference, New Delhi, 2013.
4. AACR New Horizons in Cancer Research, December 13-16, 2011, Gurgaon, India.

Workshops attended

NGS Bioinformatics Workshop, November 14-16, 2013, Institute of Genomics and Integrative Biology, New Delhi, India.

References

Will be provided upon request.