TANMOY SARKAR, Ph.D.

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Hematology, Cancer Biology and Human Genetics
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RESEARCH PROFILE

Biomedical researcher with doctoral training in human genetics and more than six years of postdoctoral research at the National Cancer Institute (NCI Frederick) on normal and malignant hematopoiesis. My work defines how Inhibitor of DNA binding (ID) proteins control hematopoietic stem cell (HSC) quiescence, the endothelial niche and acute myeloid leukemia (AML) progression. I now aim to uncover the mechanisms of chemoresistance in AML and to develop therapeutics against chemoresistant disease.

SELECTED HIGHLIGHTS

- Author of seven peer-reviewed publications, including J Clin Invest (2022), Cell Reports (2020) and Frontiers in Immunology (2022).
- Contributed to the finding that *ID2* supports HSC quiescence in part through *HIF-1α*, and that *ID2* is associated with poor survival and chemoresistance in AML.
- Contributed to showing that *Id1* and *Id3* sustain steady-state hematopoiesis through sinusoidal endothelial cells in the niche.
- Characterized four novel pathogenic mutations (*PAX9*, *EDA1*) in the first study in India on the genetic basis of congenital tooth agenesis.
- Recipient of CSIR-UGC Junior and Senior Research Fellowships; mentor to undergraduate, post-baccalaureate and NCI WHK-SIP trainees.

EDUCATION AND TRAINING

Ph.D., Human Genetics (Zoology) | Banaras Hindu University, Uttar Pradesh

M.Sc., Zoology | University of North Bengal, West Bengal

B.Sc., Zoology | University of North Bengal, West Bengal

RESEARCH EXPERIENCE

Scientific Project Manager | University of Pennsylvania, Philadelphia, PA
2024 - 2026

- **Leukemia xenograft models.** Developed leukemia xenograft mouse models to support preclinical testing in AML.
- **Collaborative research coordination.** Coordinated collaborative research projects, aligning the work, timelines and deliverables of the investigators and teams involved.
- **Novel combinatorial therapy.** Developed a novel combinatorial therapy against chemoresistant AML.

Postdoctoral Fellow | National Cancer Institute (NCI) Frederick, Frederick, MD
2018 - 2024

Studied the role of ID proteins in normal and malignant hematopoiesis. Contributed to three connected projects:

- ***Id1* and *Id3* in the hematopoietic niche.** Determined how *Id1* and *Id3* maintain endothelial cells in the niche during steady-state hematopoiesis. *Id1* and *Id3* were found to promote sinusoidal endothelial cell survival and regeneration (Cell Rep, 2020).
- ***ID2* in HSC maintenance.** Showed that *ID2* promotes normal stem cell quiescence, in part by stabilizing *HIF-1α*, and collaborates with *HIF-1α* to protect quiescent HSCs from activation, differentiation and exhaustion (J Clin Invest, 2022).
- ***ID1* and *ID2* in AML.** Analyzed AML transcriptomes in the TCGA database, which showed *ID2* expression in patients with poor overall survival and in chemotherapy-resistant AML. Using AML cell lines and patient-derived xenografts, found that *ID2* knockdown reduces primitive leukemic stem cells and prevents in vivo leukemogenesis in NSG mice, whereas *ID2* overexpression enhances

leukemogenesis. Investigating *HIF-1α* stabilization and *ID2*-induced senescence as mechanisms that may protect leukemic cells from chemotherapy.

- **Scholarly synthesis.** Co-authored (equal contribution) a review of ID proteins as orchestrators of steady-state, stress and malignant hematopoiesis (Front Immunol, 2022).
- **Mentoring.** Mentored WHK-SIP student interns and post-baccalaureate trainees.

Doctoral Researcher, Human Genetics | Banaras Hindu University, Uttar Pradesh
CSIR-UGC Junior and Senior Research Fellow, 2010 - 2015

Identified and characterized novel genetic mutations behind congenital tooth agenesis, in the first study of its kind in India. Four novel pathogenic mutations were found in four families:

- ***PAX9* initiation-codon mutation (c.3G>A):** inhibits transcription of *PAX9* (Gene, 2017).
- ***PAX9* missense mutation (c.336C>G, p.Cys112Trp):** inhibits DNA binding, activity and protein-protein interaction with the partner transcription factor *MSX1* (Mol Genet Genomics, 2023).
- ***EDA1* nonsense mutation (c.180C>A, p.Cys60*) and missense mutation (c.956G>T, p.Ser319Ile):** identified using whole genome sequencing, including a novel non-synonymous EDA mutation in X-linked dominant tooth agenesis (PLoS One, 2014).
- Contact with patients with congenital anomalies, including chronic and acute myeloid leukemia, led to my focus on hematopoietic malignancies.
- **Mentoring.** Mentored undergraduate summer interns during Ph.D. training.

Collaborative Research, Nanomedicine | Gene delivery in cancer cells

- **Collaboration in nanomedicine.** Contributed to the development of layered double hydroxide nanoparticles for efficient gene delivery to cancer cells (Bioconjug Chem, 2019).

RESEARCH INTERESTS

- Mechanisms of chemoresistance in acute myeloid leukemia
- Therapeutics against chemoresistant AML
- ID proteins in normal and leukemic stem cell quiescence, senescence and the *HIF-1α* pathway
- Hematopoietic stem cell niche biology
- Human genetics and functional characterization of disease-associated mutations

TECHNICAL EXPERTISE

- **Leukemia and stem cell models:** AML cell lines, patient-derived xenografts, NSG mouse leukemogenesis assays, gene knockdown and overexpression.
- **Genomics and bioinformatics:** whole genome sequencing, mutation identification and characterization, computational validation, analysis of TCGA transcriptome data.
- **Functional molecular assays:** transcriptional activity, DNA binding and protein-protein interaction assays of mutant transcription factors.
- **Gene delivery:** nanoparticle-based gene delivery in cancer cells.

PUBLICATIONS

Listed by research theme, most recent first. Author name in bold.

ID proteins in hematopoiesis and leukemia

1. Singh S, **Sarkar T**, Jakubison B, Gadomski S, Spradlin A, Gudmundsson KO, Keller JR. Inhibitor of DNA binding proteins revealed as orchestrators of steady state, stress and malignant hematopoiesis. Front Immunol. 2022 Aug 5;13:934624. doi: 10.3389/fimmu.2022.934624. PMID: 35990659; PMCID: PMC9389078. (Equal contribution)
2. Jakubison BL, **Sarkar T**, Gudmundsson KO, Singh S, Sun L, Morris H, Klarmann K, Keller JR. *ID2* and *HIF-1α* Collaborate to Protect Quiescent Hematopoietic Stem Cells from Activation, Differentiation and Exhaustion. J Clin Invest. 2022 Jul 1;132(13):e152599. doi: 10.1172/JCI152599. PMID: 35775482; PMCID: PMC9246389.

3. Gadomski S, Singh SK, Singh S, **Sarkar T**, Klarmann KD, Berenschot M, Seaman S, Jakubison B, Gudmundsson KO, Lockett S, Keller JR. *Id1* and *Id3* Maintain Steady-State Hematopoiesis by Promoting Sinusoidal Endothelial Cell Survival and Regeneration. Cell Rep. 2020 Apr 28;31(4):107572. PMCID: PMC8459380.

Nanoparticle-based gene delivery in cancer

4. Senapati S, **Sarkar T**, Das P, Maiti P. Layered Double Hydroxide Nanoparticles for Efficient Gene Delivery for Cancer Treatment. Bioconjug Chem. 2019;30(10):2544-2554. PMID: 31498987.

Human genetics of congenital tooth agenesis

5. **Sarkar T**, Ranjan P, Kanathur S, Gupta A, Das P. An in vitro and computational validation of a novel loss-of-functional mutation in *PAX9* associated with non-syndromic tooth agenesis. Mol Genet Genomics. 2023 Jan;298(1):183-199. doi: 10.1007/s00438-022-01970-7. PMID: 36374296.
6. **Sarkar T**, Bansal R, Das P. A novel G to A transition at initiation codon and exon-intron boundary of *PAX9* identified in association with familial isolated oligodontia. Gene. 2017 Nov 30;635:69-76. PMID: 28847717.
7. **Sarkar T**, Bansal R, Das P. Whole genome sequencing reveals novel non-synonymous mutation in ectodysplasin A (EDA) associated with non-syndromic X-linked dominant congenital tooth agenesis. PLoS One. 2014;9(9):e106811. PMCID: PMC4159272.

HONORS AND FELLOWSHIPS

- **2012 - 2015:** Senior Research Fellow, CSIR-UGC, India
- **2010 - 2012:** Junior Research Fellow, CSIR-UGC, India

MENTORING AND TRAINING

- Mentor, Werner H. Kristen Student Intern Program (WHK-SIP) students, during postdoctoral training.
- Mentor, post-baccalaureate students, during postdoctoral training.
- Mentor, undergraduate students during summer internships, during Ph.D. training.

PROFESSIONAL MEMBERSHIPS

- American Society of Hematology
- American Association for Cancer Research
- Indian Society of Human Genetics