BIOGRAPHICAL SKETCH

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NAME: SHREYA GUPTA

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Postdoctoral Fellow

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Gujarat Technological University, Ahmedabad, India	BPharm	09/2013	05/2017	Pharmacy
National Institute of Pharmaceutical Education and Research (NIPER), Mohali, India	MS (Pharm)	07/2017	06/2019	Biotechnology
Kent State University, Kent, OH	PhD	08/2019	02/2025	Pharmacology
Stanford University, Stanford, CA	Postdoctoral	04/2025	Present	Pharmacology/ Epigenetics/ Bioinformatics

A. Personal Statement

My long-term career goal is to become an independent vascular biologist, investigating how chronic metabolic diseases such as diabetes reprogram the vascular genome and epigenome, and translating these insights into targeted therapies to prevent or reverse vascular complications. I envision myself in a faculty position leading my own lab where I can integrate discovery-based research with mentorship, scientific advocacy, and the training of diverse future cardiovascular scientists.

This vision has been shaped by both my personal and academic experiences. Growing up in India, I witnessed firsthand the toll of diabetes on families and communities. As a pharmacy student, I was initially drawn to drug development, but my curiosity about disease mechanisms led me to pursue a master's degree in biotechnology at the National Institute of Pharmaceutical Education and Research (NIPER). There, I received rigorous training in recombinant protein purification and co-authored a publication on engineering protein therapeutics with improved pharmacokinetics (Iyengar et al., 2019). Conversations with friends living with diabetes deepened my resolve to study the biology driving disease progression, not just its treatment.

At Northeast Ohio Medical University (NEOMED), I pursued my PhD under Dr. Priya Raman, focusing on Thrombospondin-1 (TSP-1) as a regulator of smooth muscle cell phenotypes in metabolic syndrome. We used transgenic mouse models and transcriptomics to show that TSP-1 promotes inflammation, dedifferentiation, and lesion formation, and identified sex-specific vascular responses in metabolic disease (Gupta et al., 2022). I also led a study linking cognitive dysfunction to metabolic syndrome, uncovering sex-specific associations between tau pathology and impaired O-GlcNAc signaling in aging mice (Gupta et al., 2023). These experiences solidified my interest in transcriptional and epigenetic regulation in vascular disease.

To build on this work, I joined Stanford University as a postdoctoral researcher under the mentorship of Dr. Paul Cheng and Dr. Thomas Quertermous. I am currently investigating how NOTCH3 signaling modulates gene networks in vascular cells under diabetic stress, using bulk RNA sequencing, gene perturbation assays, and pathway analysis. This proposal outlines training in single-cell RNA-seq, ATAC-seq, and integrative multi-omics, which are critical tools for dissecting gene regulatory programs underlying vascular dysfunction.

Beyond research, I am committed to mentorship and inclusion in science. As an international woman in STEM, I've served as a peer mentor and student senator and aim to foster a lab culture that values both scientific excellence and equity. This AHA fellowship will provide essential training in genomic technologies and professional development in grant writing, teaching, and lab leadership. It is a crucial step toward my goal of becoming an independent investigator and advancing precision therapies for vascular complications in diabetes.

Citations:
1. **Gupta S,** Mathias A, Lallo J, Bhavnani N, Raman, P. Abstract P3033: Thrombospondin-1 Promotes Vascular Smooth Muscle Cell De-differentiation In Diabetes. *Circulation Research*, 2023 Aug 4;133(Suppl_1):AP3033-AP3033.
2. **Gupta S**, Jinka SK, Khanal S, Bhavnani N, Almashhori F, Lallo J, Mathias A, Al-Rhayyel Y, Herman D, Holden JG, Fleming SM, Raman P. Cognitive dysfunction and increased phosphorylated tau are associated with reduced O-GlcNAc signaling in an aging mouse model of metabolic syndrome. *Journal of Neuroscience Research*, 2023 Aug;101(8):1324-1344. DOI: 10.1002/jnr.25196. PMID: 37031439.
3. **Gupta S,** Khanal S, Bhavnani N, Mathias A, Lallo J, Kiriakou A, Ferrell J, Raman P. Sex-specific differences in atherosclerosis, thrombospondin-1, and smooth muscle cell differentiation in metabolic syndrome versus non-metabolic syndrome mice. *Frontiers in Cardiovascular Medicine* 2022 Nov 23:9:1020006. DOI: 10.3389/fcvm.2022.1020006. PMCID: PMC9727198.
4. Ganguly R, Khanal S, Mathias A, **Gupta S,** Lallo J, Sahu S, Ohanyan V, Patel A, Storm K, Datta S, Raman P. (2021). TSP-1 (thrombospondin-1) deficiency protects ApoE−/− mice against leptin-induced atherosclerosis. *Arteriosclerosis, thrombosis, and vascular biology* 2021 Feb;41(2):e112-e127. DOI: 10.1161/ATVBAHA.120.314962. PMCID: PMC8105272.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2025-Present	Postdoctoral Researcher, Stanford University, Stanford, CA
2019-2025	Graduate Research Assistant, Northeast Ohio Medical University (NEOMED) Rootstown,OH
2024-2025	Member, North American Vascular Biology Organization (NAVBO)
2023-2024	Member, South Asian Heart Research (SAHR)
2019-2024	Member, Cardiovascular Research Group, NEOMED
2022-2023	Member, Basic Cardiovascular Science (BCVS), AHA
2020-2022	Member, Atherosclerosis Thrombosis and Vascular Biology (ATVB), AHA

Honors

2024	Domestic Travel Award, Kent State Graduate Student Senate
2024	Student Success Award, Kent State Biomedical Science Department
2023	1st place, Data Blitz Competition, Asian Cardiovascular Symposium, AHA-BCVS
2023	Research Award, Kent State Graduate Student Senate
2023	People's Choice Award- Kent State Annual Flash Pitch Competition
2022	Top 10% Best Abstracts of AHA Specialty Conferences
2022	Emerging Scientist Finalist Award- ATVB, AHA
2021	Outstanding Oral Presentation, ASIOA 9th National Annual Meeting
2017	Gold Medalist, BPharm

C. Contributions to Science

1. Master's Research: **Early Scientific Contributions in Protein Engineering and Therapeutics (India)**
During my master's training in biotechnology at NIPER, I focused on engineering recombinant protein therapeutics. I contributed to the development of protein chimerization strategies to improve pharmacokinetics and therapeutic efficacy. I also developed a novel protocol for yeast protein purification, enhancing process efficiency. This early work helped shape my molecular and biochemical foundation.

a) Iyengar AS, **Gupta S**, Jawalekar S, Pande AH. Protein chimerization: a new frontier for engineering protein therapeutics with improved pharmacokinetics. *J Pharmacol Exp Ther.* 2019; 370(3):703-714. DOI:10.1124/jpet.119.257063. PMID: 31010843.

2. PhD Research: Vascular Smooth Muscle Cell Plasticity and Diabetes

During my PhD career, my research has uncovered sex-specific differences in the development of atherosclerosis in metabolic syndrome and defined a novel role for Thrombospondin-1 (TSP-1) in regulating vascular smooth muscle cell phenotype. Using diabetic mouse models, we demonstrated that TSP-1 expression is significantly elevated under hyperglycemic conditions and contributes to vascular inflammation, SMC dedifferentiation, and lesion formation. I developed and optimized a protocol for isolating and culturing primary murine smooth muscle cells tagged with a Yellow Fluorescent Protein (YFP) reporter, which enabled mechanistic dissection of TSP-1 function at the cellular level. My work identified key transcriptional regulators downstream of hyperglycemia that modulate TSP-1 signaling, and I generated a novel smooth muscle cell–specific TSP-1 knockdown mouse on the KKAy ApoE-/- background to further investigate its *in vivo* role. In parallel, I collaborated on a project that showed deletion of smooth muscle–specific O-GlcNAc transferase protects against atherosclerosis in hyperglycemic ApoE-/- mice, linking nutrient-sensing pathways to vascular inflammation. Collectively, these studies expanded our understanding of SMC plasticity and matrix remodeling in the diabetic vasculature.

a) **Gupta S,** Khanal S, Bhavnani N, Mathias A, Lallo J, Kiriakou A, Ferrell J, Raman P. Sex-specific differences in atherosclerosis, thrombospondin-1, and smooth muscle cell differentiation in metabolic syndrome versus non-metabolic syndrome mice. *Frontiers in Cardiovascular Medicine* 2022 Nov 23;9:1020006. DOI: 10.3389/fcvm.2022.1020006. PMCID: PMC9727198.
b) Gupta S, Khanal S, Mathias A, Lallo J, Raman P. Sex-specific Differences In The Role Of TSP1 On Metabolic Syndrome-induced Atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology. 2022 May;42(Suppl_1):A135-A135.
c) Khanal S, Bhavnani N, Mathias A, Lallo J, **Gupta S**, Ohanyan V, Ferrell JM, Raman P. (2023). Deletion of smooth muscle O-GlcNAc transferase prevents development of atherosclerosis in western diet-fed hyperglycemic ApoE-/-mice in vivo. *International Journal of Molecular Sciences*, 2023 Apr 26;24(9):7899. DOI: 10.3390/ijms24097899. PMCID: PMC10178779.
d) Ganguly R, Khanal S, Mathias A, **Gupta S,** Lallo J, Sahu S, Ohanyan V, Patel A, Storm K, Datta S, Raman P. (2021). TSP-1 (thrombospondin-1) deficiency protects ApoE−/− mice against leptin-induced atherosclerosis. *Arteriosclerosis, thrombosis, and vascular biology* 2021 Feb;41(2):e112-e127. DOI: 10.1161/ATVBAHA.120.314962. PMCID: PMC8105272.

3. PhD Research: Linking cognitive dysfunction to metabolic disorder

I led studies linking metabolic syndrome (MetS) to cognitive dysfunction and neurodegenerative markers. In this work, I conducted behavioral assessments in aging mice with metabolic syndrome and performed molecular analyses on the frontal cortex and hippocampus. This study provides compelling evidence for a synergistic interaction between aging and MetS in promoting tau pathology. Notably, we observed a sex-specific association: female MetS mice exhibited increased tau phosphorylation, impaired cognition, and reduced signaling, indicating a molecular mechanism of vulnerability in the aging female brain under metabolic stress. These findings bridge cardiometabolic and neurodegenerative disease pathways, and may have implications for sex-specific therapeutic strategies.

a) **Gupta S**, Jinka SK, Khanal S, Bhavnani N, Almashhori F, Lallo J, Mathias A, Al-Rhayyel Y, Herman D, Holden JG, Fleming SM, Raman P. Cognitive dysfunction and increased phosphorylated tau are associated with reduced O-GlcNAc signaling in an aging mouse model of metabolic syndrome. *Journal of Neuroscience Research* 2023 Aug;101(8):1324-1344. DOI: 10.1002/jnr.25196. PMID: 37031439.
b) Jinka S, Lallo J, **Gupta S**, Mathias A, Khanal S, Al-Rhayyel Y, Herman D, Fleming S, Raman P. Alzheimer's Disease-Related Pathology and Impaired Cognitive Function Associate with Reduced O-GlcNAc Transferase in Aged Metabolic Syndrome KKAy+/− Mice. *The FASEB Journal* 2020 Apr;34(S1):1-1.

4. Postdoctoral Career: Role of SMC-specific NOTCH3 in fibrous cap cell plasticity

As a postdoctoral fellow at Stanford University, my research focuses on defining the role of NOTCH3 in regulating fibrous cap smooth muscle cell (SMC) plasticity in atherosclerosis. Using murine lineage tracing combined with single-cell transcriptomics, we demonstrated that fibrous cap cells originate from a rare SMC subpopulation that is present even in healthy vessels. These NOTCH3+ cells comprise only ~2% of all medial SMCs, yet exhibit distinct transcriptional and functional signatures relevant to plaque stability. I am studying that NOTCH3

expression in human coronary artery smooth muscle cells (HCASMCs) correlates with, and regulates, fibrous cap–associated genes, suggesting a conserved role in human coronary artery disease. These findings will challenge the existing paradigm of SMC phenotypic modulation in atherosclerosis and uncover a previously unrecognized, targetable SMC subpopulation. Building on this work, I am leveraging a novel murine model to selectively manipulate NOTCH3^{+} fibrous cap cells, with the goal of elucidating their regulatory networks and unique biology to inform strategies for plaque stabilization.

Complete list of published work in my Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/12kU8zxXrvmQmu/bibliography/public/