Kshitiz, PhD
Institute of Systems Biology
Yale University

Brief Curriculum Vitae

Name Kshitiz

Position Associate Research Scientist
Institute of Systems Biology, Yale University

Email *kshitiz.gupta@yale.edu* Website: *www.kshitiz.info*

Education & Training

2014-Current	Ass Res Scientist, Biomedical Engineering, Yale University
2012-2014	CSO, Cardiac Mimetics Inc., Seattle
2012-2014	Post Doc, Bioengineering, University of Washington, Seattle ***Advisors:*** *Dr. Charles Murry, Dr. Deok-Ho Kim*
2011-2012	Post Doc, Biomedical Engineering, Johns Hopkins Medicine ***Advisor:*** *Dr. Gregg L. Semenza, Dr. Andre Levchenko*
2005-2011	Ph.D., Biomedical Engineering, Johns Hopkins Medicine ***Advisor:*** *Dr. Andre Levchenko*
	B.Tech., Computer Science & Engineering, IIT Bombay, India ***Advisor:*** *Dr. K.V.Venkatesh*

Research Interests **Cell-cell communication, cancer-stroma interaction, mechanobiology, regenerative cardiovascular biology, cancer heterogeneity**

Research Statement

I bring a diverse background of computer science, bioengineering, systems biology, and mechanobiology to the mechanistic understanding of cancer invasion, and cardiovascular regeneration. My future research plan is to investigate the molecular nature of cellular interaction with other cells, and the microenvironment, and understand the genetic and metabolic underpinnings of cancer invasion, cancer-immune interaction, as well as stem cell mediated cardiovascular repair. In the long term, I envision leading a research program at the conflux of cancer and stem cell biology, bioengineering, and computation to answer fundamental biomedical questions about cellular communication with their surroundings in cancer, aging, in response to infarct or injury, and to develop bio-inspired therapeutic modalities to treat diseases.

Selected Publications

No. of peer reviewed publications: 25 No. of patents: 3 Citations: 1050

1. **Kshitiz** & Hubbi ME et al. (2012). Matrix rigidity coordinates the proliferation, differentiation, and morphogenesis of endothelial cells derived from cardiac progenitors, *Science Signaling*, 5(227):ra41. (cover article, also featured in *Science*).
2. **Kshitiz** et al. (2014). Mechanotransduction via p190RhoGAP regulates a switch between cardiomyogenic and endothelial lineages in adult cardiac progenitors, *Stem Cells,* 32(8): 1999 2007.
3. Hubbi ME & **Kshitiz** et al. (2013). A non-transcriptional role for HIF-1a as a direct inhibitor of DNA replication, *Science Signaling*, 6(262), ra10. (**cover article**, with a running commentary in *Science***).**
4. **Kshitiz**, et al. (2015). Control of the interface between heterotypic cell populations reveals mechanism of intercellular transfer of signaling proteins, *Integrative Biology*, 7, 364-372.
5. **Kshitiz***, Kim DH*, Smith R, Kim P, Marban E, Suh KY, Levchenko A, Nanopatterned Cardiac Cell Patches Promote Stem Cell Niche Formation and Myocardial Regeneration, *Integrative Biology*, 4(9):1019-33. (**cover article**)
6. **Kshitiz,** Ahn EH, Kim Y et al. (2014). Spatial control of adult stem cell fate using nanotopographic cues, *Biomaterials*, 35(8):2401-10.
7. **Kshitiz** et al. (2011). Micro- and nanoengineering for stem cell biology: the promise with a caution, *Trends in Biotech*, 29(8):399-408.
8. Rey S, Lee K, Wang CJ, **Gupta K**, Chen S, McMillan A, Bhise N, Levchenko A, Semenza GL. (2009). Synergistic effect of HIF-1alpha gene therapy and HIF-1-activated bone marrow-derived angiogenic cells in a mouse model of limb ischemia, *Proc Natl Acad Sci USA*. 106(48):20399-404.

Current Research Support

1. **Principal Investigator**, American Heart Association Innovator Research Grant (16IRG27260356) 01/01-2016 to 12/30/2017 Funding: $150K
2. **Investigator**, National Institutes of Health for Systems Biology in Cancer (CA209992-01) 08/01/2016-07/30/2016 Funding: $200K

Awards

1. American Heart Association Pre-Doctoral Fellowship -2010
2. Collegiate Inventor's Award Finalist (organized by Inventors Hall of Fame, U.S. Patent & Trademark Office, Abbot Funds, and Kauffman Foundation) -2011
3. Technical Citation by the President, IIT Bombay (highest student award in the Institute) -2004
4. Best Office Bearer, IIT Bombay (as part of the founder of Science Club, making it into the largest student led science across many universities interest group in Mumbai)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Kshitiz

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

POSITION TITLE: Associate Research Scientist

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Indian Institute of Technology, Bombay	B. Tech.	08/04	Computer Science
Indian Institute of Technology, Bombay	Research Analyst	05/05	Biosciences
Johns Hopkins University School of Medicine	Ph.D.	07/11	Biomedical Engineering
Johns Hopkins University School of Medicine	Post Doc	06/12	Biomedical Engineering
University of Washington	Post Doc		Bioengineering
Cardiac Mimetics, Inc. (startup)	Chief Scientific Officer	05/14	Drug Screening
Yale University	Ass Res Scientist	05/14 Current	Biomedical Engineering

A. Personal Statement

I am currently an Associate Research Scientist (Research Assistant Professor) in the Yale University, in the Department of Biomedical Engineering with broad interest in stem cell systems biology, cardiac tissue engineering, mechanobiology, and the systems biology of cancer. I bring a diverse background of computer science, bioengineering, cardiac tissue engineering, as well as commercial ventures to my academic pursuit of finding innovative solutions to long standing scientific problems. Previous to Yale, I served as an interim acting Chief Scientific Officer of Cardiac Mimetics, Inc. a startup company in the Center for Commercialization at University of Washington. During my PhD, I investigated the role of matrix rigidity as a regulator of cellular phenotypes, and implicated its role as a fundamental cue that controls various cellular phenomena including proliferation, differentiation, and morphogenesis via a single molecule. In addition, in collaboration with Dr. Gregg Semenza, I also worked extensively on HIF signaling, and understanding cellular response to hypoxia.

Currently, I am creating methods to fundamentally understand how cells communicate with each other. With Dr. Chi Dang, I am investigating a novel phenomenon of quorum sensing in cancer populations. I am investigating the evolutionary basis of cancer invasion with Dr. Gunter Wagner, and the mechanistics of cancer-stroma interaction. With my training in systems biology, as well as in cell signaling, microfabrication, and computer science, I bring the important ingredients to mechanistically understand how and how cancer cells interact with immune cells, its role in regulation of cancer invasion into stroma and metastasis.

B. Positions and Honors

Positions and Employment

2003-2004 Undergraduate Research Assistant, Department of Computer Science & Engineering, IIT Bombay, Mumbai, India

2004-2005 Research Analyst, Department of Chemical Engineering, School of Biosciences &

	Bioengineering, IIT Bombay, Mumbai, India
2005-2011	Graduate Research Assistant, Department of Biomedical Engineering, Johns Hopkins University
2011-2012	Post Graduate Research Fellow, Institute of Cell Engineering, Johns Hopkins Medical Institutions
2012-2014	Post Graduate Research Fellow, Department of Bioengineering, University of Washington
2015-	Associate Research Scientist, Department of Biomedical Engineering, Yale University

Honors

2002	Dean's Distinguished Certification
2003-2004	Best Office Bearer, Science Group, IIT Bombay
2000-2004	Technical Citation, IIT Bombay (highest student award for organization and excellence in Technical activities)
2003-2004	Technical Nominee to the Dean, IIT Bombay
2004	First, Original Idea Presentation Contest
2010	American Heart Association Pre-Doctoral Fellowship
2011	Collegiate Inventor's Award Finalist (organized by Inventors Hall of Fame, U.S. Patent and Trademark Office, Abbot funds, and Kauffman foundation)

Intellectual Property

1. United States patent application No. 14/390,490 filed March 15, 2013, entitled "Systems and method for engineering muscle tissue". Inventors: Deok-Ho Kim, Michael Laflamme, Charles Murry, **Kshitiz Gupta**, Hyok Yoo, Alex Jiao
2. United States patent application No. 14/028,530 published Sep 18, 2014, entitled "Device and methods comprising microelectrode arrays for electroconductive cells". Inventors: Deok-Ho Kim, Machael Laflamme, Junseok Chae, **Kshitiz Gupta**
3. United States patent, Submitted Nov 17, 2015, entitled "Novel Methods and Devices for High-Throughput Quantification, Detection and Temporal Profiling of Cellular Secretions, and Compositions Identified Using Same". Inventors: David Ellison, **Kshitiz Gupta**, Yasir Suhail, Junaid Afzal, Andre Levchenko.

C. Contribution to Science

Complete List of Published Work in MyBibliography
http://www.ncbi.nlm.nih.gov/sites/myncbi/1pczCvbI4FFkF/bibliography/42745915/public/?sort=date&direction=descending *no. of published manuscripts: 25* *citations: 1050* *h-index: 15*

* Below, Authors contributed equally to the manuscript

C.1. Signaling mechanisms in mechanotransduction by stem cells: How cells respond to their mechanical microenvironment has a significant bearing on their structure and function. My major contributions highlighted p190RhoGAP, a master regulator that could sense extracellular matrix rigidity and act as a central signal conduit regulating transcription. p190RhoGAP choreographs a variety of cellular processes temporally regulating the selective proliferation of c-kit+ stem cells from a heterogeneous cardiac stem-cell like population, their subsequent differentiation into endothelial cells, followed by their morphogenesis into luminal structures resembling blood vessels.

1. **Kshitiz***, Hubbi ME*, Ahn EH, Downey J, Kim DH, Rey S, Kundu A, Semenza GL, Abraham RM, Levchenko, A. (2012). Matrix rigidity coordinates the proliferation, differentiation, and morphogenesis of endothelial cells derived from cardiac progenitors, *Science Signaling*, 5(227):ra41. (cover article, also featured in *Science*)
2. **Kshitiz**, Afzal J, Kim DH, Levchenko A (2014). Mechanotransduction via p190RhoGAP regulates a switch between cardiomyogenic and endothelial lineages in adult cardiac progenitors, *Stem Cells,* 32(8): 1999 2007.
3. **Kshitiz**, Park JS, Kim P, Helen W, Engler AJ, Levchenko A, Kim DH. (2012). Control of stem cell fate and function by engineering physical microenvironment, *Integrative Biology*, 4:1008-18.
4. **Kshitiz**, Afzal J, Chang H, Goyal R, Levchenko A (2015). Mechanics of Microenvironment as Instructive Cues Guiding Stem Cell Behavior, *Current Stem Cell Biology*, (In Press).

C.2. Role of hypoxia in regulating cellular response: Hypoxia is one of the most important signal available to cancer cells. It is also one of the most important and connected proteins in nature. Hypoxia is known to influence nearly every single biological processes, including cell division, cell shape, migration of cancer cells, metabolism, etc. In a series of articles, I have contributed to our understanding of how HIF-1α regulates cell cycle in a non-transcriptional manner, as well as towards finding non-canonical mechanisms of HIF-1α degradation. My scientific and technical contributions further extend to developing platforms to study the role of hypoxia signaling in bone marrow repair, intercommunication between breast cancer and mesenchymal cells, as well as in metabolism.

1. **Kshitiz***, Hubbi ME*, Gilkes DM, Rey S, Wong CC, Luo W, Kim DH, Dang CV, Levchenko A, Semenza GL (2013). A non-transcriptional role for HIF-1a as a direct inhibitor of DNA replication, *Science Signaling*, 6(262), ra10. (**cover article**, also with a running commentary in *Science*)**.**
2. Hubbi ME, Hu H, **Kshitiz**, Gilkes DM, Semenza GL (2013). Sirtuin-7 inhibits the activity of hypoxia-inducible factors, *J. Biol. Chem.*, 288(29):20768-75.
3. Hubbi ME, Hu Hongxia, Kshitiz, Ahmed I, Levchenko A, Semenza GL (2013). Chaperone-mediated autophagy targets HIF1a for lysosomal degradation, *J. Biol. Chem.*, 288(15):10703-14.
4. Rey S, Lee K, Wang CJ, **Gupta K**, Chen S, McMillan A, Bhise N, Levchenko A, Semenza GL. (2009). Synergistic effect of HIF-1alpha gene therapy and HIF-1-activated bone marrow-derived angiogenic cells in a mouse model of limb ischemia, *Proc Natl Acad Sci USA*. 106(48):20399-404.

C.3. Intercellular communication between cells: Cell-cell communication plays important roles in various physiological or pathological contexts. A recently described phenomenon of direct protein transfer is a very different form of transfer of biological materials between cells. Our paper was among the first reports detailing this phenomenon. In recent works, I have developed computational modeling explaining the relatively uncontrolled intercellular transfer of membrane as well as cytosolic proteins, as well as experimentally demonstrated that even cytosolic proteins can be transferred between cancer and endothelial cells.

1. **Kshitiz**, Afzal J, Suhail Y, Ahn EH, Goyal R, Hubbi ME, Hussaini Q, Ellison DD, Goyal J, Nacev B, Kim DH, Lee JH, Frankel S, Gray K, Bankoti R, Chien AJ, Levchenko A (2015). Control of the interface between heterotypic cell populations reveals the mechanism of intercellular transfer of signaling proteins, *Integrative Biology*, 7, 364-372.
2. Suhail Y*, **Kshitiz***, Lee J, Walker M, Kim DH, Brennan MD, Bader JS, Levchenko A (2013). Modeling intercellular transfer of biomolecules through tunneling nanotubes, *Bulletin of Mathematical Biology*, 75(8):1400-16.
3. Niu X, **Gupta K**, Yang JT, Shamblott MJ, Levchenko A. (2009). Physical transfer of membrane and cytoplasmic components as a general mechanism of cell-cell communication, *J Cell Sci.*, 122(Pt 5):600-610.

C.4. Cellular response to matrix nanotopography: Living cells can sense the local geometry of complex and well-defined structures of extracellular matrix (ECM) to control their shape, motility, and fate. However, the extent and the importance of micro- and nanotopography of ECM in defining cell phenotypes are poorly understood, in part due to an almost complete neglect of this factor in most in vitro experimentation. My contribution in this area have helped in a) adding to the experimental toolbox for scientists to study nanotopography, b) finding a few key players regulating topography sensing, and topography induced cellular migration: topotaxis. I have contributed to many articles, and invited reviews in unraveling the mechanistic underpinnings of topography sensing. With ours, as well as many other seminal contributions, nanotopography is now considered as an important physiological stimuli, regulating a variety of cellular processes, including shape, anisotropy, migration, and fate.

1. **Kshitiz***, Kim DH*, Smith R, Kim P, Marban E, Suh KY, Levchenko A, Nanopatterned Cardiac Cell Patches Promote Stem Cell Niche Formation and Myocardial Regeneration, *Integrative Biology*, 4(9):1019-33. (**cover article**)

2. **Kshitiz**, Kim DH, Beebe D, Levchenko A. (2011). Micro- and nanoengineering for stem cell biology: the promise with a caution, *Trends in Biotech*, 29(8):399-408.
3. **Gupta K**, Kim DH, Ellison D, Smith C, Kundu A, Tuan J, Suh KY, Levchenko A. (2011). Lab-on- a-chip devices as an emerging platform for stem cell biology, *Lab on a Chip*, 10(16):2019-31.
4. **Kshitiz*,** Ahn EH*, Kim Y*, An SS, Afzal J, Lee S, Kwak M, Suh KY, Kim DH, Levchenko A (2014). Spatial control of adult stem cell fate using nanotopographic cues, *Biomaterials*, 35(8):2401-10.

C.5. Bioinformatics prediction of protein structure: With my background in computer science, I had developed novel algorithms to compare the structures of proteins by comparing the amino acid sequence as a queue of their known physical characteristics (e.g. hydrophobicity, electric charge) in the fourier space. We also used machine learning algorithms to classify protein sequences by cross training of known protein taxonomies.

1. **Gupta K***, Sehgal V*, Levchenko A. (2008). A method for probabilistic mapping between protein structure and function taxonomies through cross training, *BMC Structural Biology*, 8:40.
2. **Gupta K**, Thomas D, Vidya SV, Venkatesh KV, Ramakumar S. (2005).Detailed protein sequence alignment based on Spectral Similarity Score (SSS), *BMC Bioinformatics*, 6:105.

D. Research Support

Completed Research Support

0815104E Kshitiz (PI) 07/01/2010–07/08/2011
American Heart Association Predoctoral Fellowship
The goal of this work was to develop a comprehensive cytoprotective strategy for adult cardiac stem cell therapy post myocardial infarction
Role: PI

Current Research Support

16IRG27260356 Kshitiz (PI) 01/01/2016-12/31/2017
Funding: $75000/year
American Heart Association NCRP Innovator Research Grant
The goal of this work is to understand the stem cell secretion to create an informed cell-free method to treat myocardial infarction

CA209992-01 Kshitiz (co-I) 08/01/2016-07/31/2021
Funding: $65000/year
National Institutes of Health U54 Grant
Systems analysis of phenotypic switch in control of cancer invasion

Applied Research Support (funding decision not yet taken)

Pardee Foundation
Title: Investigating the role of hypoxic fluctuations in specifying cancer stem cells in a tumor
Applied: June 2016

National Institutes of Health R21
Title: Systematic understanding of the molecular language between macrophages and melanoma
Applied: September 2016