Stanford

Rajat Rohatgi

Associate Professor of Biochemistry and of Medicine (Oncology)

Curriculum Vitae available Online

Bio

ACADEMIC APPOINTMENTS

- Associate Professor, Biochemistry
- Associate Professor, Medicine - Oncology
- Member, Bio-X
- Member, Cardiovascular Institute
- Member, Maternal & Child Health Research Institute (MCHRI)
- Member, Stanford Cancer Institute
- Member, Wu Tsai Neurosciences Institute

HONORS AND AWARDS

- Fellowship Award, Damon Runyon Cancer Research Fund (2006)
- Howard Temin Pathway to Independance Award (K99/R00), NCI/NIH (2007)
- Young Investigator Award, American Society for Clinical Oncology (2007)
- Josephine Q. Berry Faculty Scholar in Cancer Research, Stanford University (2009)
- Martin D. Abeloff Scholar, V Foundation for Cancer Research (2009-2011)
- Distinguished Scientist Award, Sontag Foundation (2010)
- Basil O' Connor Starter Scholar Award, March of Dimes Foundation (2010-2012)
- Stand Up To Cancer Innovation Research Grant, American Association for Cancer Research (2010-2013)
- NIH Director's New Innovator Award, NIH (2012)
- Maximizing Investigators' Research Award (MIRA), NIGMS/NIH (2016)

PROFESSIONAL EDUCATION

- Fellowship, Stanford Hospital , Medical Oncology (2008)
- Residency, Stanford Hospital , Internal Medicine (2004)
- Ph.D., Harvard Medical School , Cell Biology (2002)
- M.D., Harvard Medical School (2002)
- A.B., Harvard University , Biochemical Sciences (1994)

LINKS

- My Lab Website: http://rohatgilab.stanford.edu/

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

Areas of research in the Rohatgi Lab:

1. The Hedgehog and WNT pathways, two cell-cell communication systems that regulate the formation of most tissues during development. These same pathways play central roles in tissue stem-cell function and organ regeneration in adults. Defects in these systems are associated with degenerative conditions and cancer.

2. Signal transduction at the primary cilium and the mechanism of cilia-associated human diseases. Primary cilia are solitary hair-like projections found on most cells in our bodies that function as critical hubs for signal transduction pathways (such as Hedgehog). Over fifty human genetic diseases, called “ciliopathies,” are caused by defects in cilia. Patients with ciliopathies can show phenotypes in nearly all organ systems, suffering from abnormalities ranging from birth defects to obesity.

3. Regulation of signaling pathways by endogenous lipids. The landscape of endogenous small-molecules and their biological functions remains a terra incognita, one that provides many opportunities to discover new regulatory layers in signaling pathways.

4. Phase separation in signal transduction. The formation of reversible, membrane-less compartments in cells by the segregation of proteins into liquid phases, hydrogels or amyloid-like assemblies is an emerging principle of cellular organization, with broad implications for areas that include signaling at the cell surface, stress response pathways, and neuro-degeneration.

5. Cellular responses to osmolar stresses. Maintaining a stable concentration of intracellular macromolecules and ions in a fluctuating environment is a universal challenge to homeostasis faced by all cells. In our own bodies, cells of the kidney and cells in inflammatory environments face tissue osmolality levels that are 3-fold higher than blood!

Strategies:

1. CRISPR/Cas9-based genome-wide, loss-of-function screens targeting signaling pathways.
• Enhancer and suppressor screens to comprehensively identify pathway components.
• Synthetic screens to identify the genetic vulnerabilities of cells carrying mutations in human oncogenes and tumor suppressor genes.
• Screens based on complex, physiological read-outs of signaling, such as differentiation.

2. Protein biochemistry: proteomics, structure-guided analysis, activity-based purification and cell-free reconstitution of signaling reactions in extracts and using purified components.

3. Chemical Biology: new probes to assay the interactions between proteins and small molecules.

4. Imaging: Live-cell imaging with innovative optical probes and genetically-encoded reporters to monitor the temporal and spatial progression of signaling, the quantitative phase separation behavior of proteins, and the dynamic, signal-regulated trafficking of proteins.

5. Collaborations: With experts in structural biology (Christian Siebold, Oxford, Elife 2013, 2016 and Nature 2016), genome-wide screening (Jan Carette, Stanford, Elife and Cancer Research 2016), protein and genome evolution (L. Aravind, NIH, Dev Cell 2014 and 2018), and developmental biology (James Briscoe, Francis Crick Institute, Dev Cell 2018).

CLINICAL TRIALS

- Molecular Analysis of Thoracic Malignancies, Recruiting
- Erlotinib in Patients With Resected, Early Stage NSCLC With Confirmed Mutations in the EGFR, Not Recruiting
- Erlotinib Plus Tivantinib (ARQ 197) Versus Single Agent Chemotherapy in Locally Advanced or Metastatic Non-Small Cell Lung Cancer, Not Recruiting
- Erlotinib With or Without Hydroxychloroquine in Chemo-Naive Advanced NSCLC and (EGFR) Mutations, Not Recruiting
- Identification of Circulating Tumor Cells in the Peripheral Blood of Lung Cancer Patients, Not Recruiting

Teaching

COURSES

2019-20

- Advanced Cell Biology: BIO 214, BIOC 224, MCP 221 (Win)
- Development of Thesis Research: BIOC 350 (Aut)

2018-19

- Advanced Cell Biology: BIO 214, BIOC 224, MCP 221 (Win)
- Development of Thesis Research: BIOC 350 (Aut)

2017-18

- Advanced Cell Biology: BIO 214, BIOC 224, MCP 221 (Win)
- Development of Thesis Research: BIOC 350 (Aut)

2016-17

- Advanced Cell Biology: BIO 214, BIOC 224, MCP 221 (Win)
- Development of Thesis Research: BIOC 350 (Aut)

STANFORD ADVISEES

Doctoral Dissertation Reader (AC)

Brian Alford, Peter Chou, Sabrina Ergun, Julio Flores Servin, Lauren Lahey, Yong Tang

Postdoctoral Faculty Sponsor

Jennifer Kong, Mandi Ma

Doctoral Dissertation Advisor (AC)

Ellen Iverson, Maia Kinnebrew, Chandni Patel

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Biochemistry (Phd Program)
- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

- **Biochemical mechanisms of vertebrate hedgehog signaling.** *Development (Cambridge, England)*
  Kong, J. H., Siebold, C., Rohatgi, R.
  2019; 146 (10)

- **G protein-coupled receptors control the sensitivity of cells to the morphogen Sonic Hedgehog.** *Science signaling*
  Pusapati, G. V., Kong, J. H., Patel, B. B., Gouti, M., Sagner, A., Sircar, R., Luchetti, G., Ingham, P. W., Briscoe, J., Rohatgi, R.
  2018; 11 (516)

- **CRISPR Screens Uncover Genes that Regulate Target Cell Sensitivity to the Morphogen Sonic Hedgehog.** *Developmental cell*
  Pusapati, G. V., Kong, J. H., Patel, B. B., Krishnan, A., Sagner, A., Kinnebrew, M., Briscoe, J., Aravind, L., Rohatgi, R.
  2018; 44 (1): 113–29.e8

- **R-spondins can potentiate WNT signaling without LGRs.** *eLife*
  Lebensohn, A. M., Rohatgi, R.
  2018; 7

- **Comparative genetic screens in human cells reveal new regulatory mechanisms in WNT signaling** *ELIFE*
  Lebensohn, A. M., Dubey, R., Neitzel, L. R., Tacchelly-Benites, O., Yang, E., Marceau, C. D., Davis, E. M., Patel, B. B., Bahrami-Nejad, Z., Travaglini, K. J., Ahmed, Y., Lee, E., Carette, et al
  2016; 5

- **Cholesterol activates the G-protein coupled receptor Smoothened to promote morphogenetic signaling.** *eLife*
  Luchetti, G., Sircar, R., Kong, J. H., Nachtergaele, S., Sagner, A., Byrne, E. F., Covey, D. F., Siebold, C., Rohatgi, R.
  2016; 5

- **In Vivo Formation of Vacuolated Multi-phase Compartments Lacking Membranes.** *Cell reports*
  Schmidt, H. B., Rohatgi, R.
  2016; 16 (5): 1228-1236

- **Structural basis of Smoothened regulation by its extracellular domains.** *Nature*
  Byrne, E. F., Sircar, R., Miller, P. S., Hedger, G., Luchetti, G., Nachtergaele, S., Tully, M. D., Mydock-McGrane, L., Covey, D. F., Rambo, R. P., Sansom, M. S., Newstead, S., Rohatgi, et al
  2016; 535 (7613): 517-522

- **EFCAB7 and IQCE Regulate Hedgehog Signaling by Tethering the EVC-EVC2 Complex to the Base of Primary Cilia** *DEVELOPMENTAL CELL*
  Pusapati, G. V., Hughes, C. E., Dorn, K. V., Zhang, D., Sugianto, P., Aravind, L., Rohatgi, R.
  2014; 28 (5): 483-496

- **Gli protein activity is controlled by multisite phosphorylation in vertebrate hedgehog signaling.** *Cell reports*
  Niewiadomski, P., Kong, J. H., Ahrends, R., Ma, Y., Humke, E. W., Khan, S., Teruel, M. N., Novitch, B. G., Rohatgi, R.
  2014; 6 (1): 168-181

- **Structure and function of the Smoothened extracellular domain in vertebrate Hedgehog signaling.** *eLife*
  Nachtergaele, S., Whalen, D. M., Mydock, L. K., Zhao, Z., Malinauskas, T., Krishnan, K., Ingham, P. W., Covey, D. F., Siebold, C., Rohatgi, R.
  2013; 2

- **A Smoothened-Evc2 Complex Transduces the Hedgehog Signal at Primary Cilia** *DEVELOPMENTAL CELL*
  Dorn, K. V., Hughes, C. E., Rohatgi, R.
  2012; 23 (4): 823-835

- **Oxysterols are allosteric activators of the oncoprotein Smoothened** *NATURE CHEMICAL BIOLOGY*
  Nachtergaele, S., Mydock, L. K., Krishnan, K., Rammohan, J., Schlesinger, P. H., Covey, D. F., Rohatgi, R.
  2012; 8 (2): 211-220

- **The output of Hedgehog signaling is controlled by the dynamic association between Suppressor of Fused and the Gli proteins** *GENES & DEVELOPMENT*
  Humke, E. W., Dorn, K. V., Milenkovic, L., Scott, M. P., Rohatgi, R.

2010; 24 (7): 670-682

- **Discovery of gene regulatory elements through a new bioinformatics analysis of haploid genetic screens.** *PloS one*
  Patel, B. B., Lebensohn, A. M., Pusapati, G. V., Carette, J. E., Salzman, J., Rohatgi, R.
  2019; 14 (1): e0198463
- **Structures of vertebrate Patched and Smoothened reveal intimate links between cholesterol and Hedgehog signalling.** *Current opinion in structural biology*
  Kowatsch, C., Woolley, R. E., Kinnebrew, M., Rohatgi, R., Siebold, C.
  2019; 57: 204–14
- **Cholesterol Interaction Sites on the Transmembrane Domain of the Hedgehog Signal Transducer and Class F G Protein-Coupled Receptor Smoothened.** *Structure (London, England : 1993)*
  Hedger, G., Koldso, H., Chavent, M., Siebold, C., Rohatgi, R., Sansom, M. S.
  2018
- **A single N-terminal phosphomimic disrupts TDP-43 polymerization, phase separation, and RNA splicing.** *The EMBO journal*
  Wang, A., Conicella, A. E., Schmidt, H. B., Martin, E. W., Rhoads, S. N., Reeb, A. N., Nourse, A., Ramirez Montero, D., Ryan, V. H., Rohatgi, R., Shewmaker, F., Naik, M. T., Mittag, et al
  2018; 37 (5)
- **Spatiotemporal manipulation of ciliary glutamylation reveals its roles in intraciliary trafficking and Hedgehog signaling.** *Nature communications*
  Hong, S. R., Wang, C. L., Huang, Y. S., Chang, Y. C., Chang, Y. C., Pusapati, G. V., Lin, C. Y., Hsu, N., Cheng, H. C., Chiang, Y. C., Huang, W. E., Shaner, N. C., Rohatgi, et al
  2018; 9 (1): 1732
- **Dynamic Remodeling of Membrane Composition Drives Cell Cycle through Primary Cilia Excision.** *Cell*
  Phua, S. C., Chiba, S., Suzuki, M., Su, E., Roberson, E. C., Pusapati, G. V., Setou, M., Rohatgi, R., Reiter, J. F., Ikegami, K., Inoue, T.
  2017; 168 (1-2): 264-279 e15
- **Multiple ligand binding sites regulate the Hedgehog signal transducer Smoothened in vertebrates.** *Current opinion in cell biology*
  Byrne, E. F., Luchetti, G., Rohatgi, R., Siebold, C.
  2017; 51: 81–88
- **Chromatin-Remodeling Complex SWI/SNF Controls Multidrug Resistance by Transcriptionally Regulating the Drug Efflux Pump ABCB1** *CANCER RESEARCH*
  Dubey, R., Lebensohn, A. M., Bahrami-Nejad, Z., Marceau, C., Champion, M., Gevaert, O., Sikic, B. I., Carette, J. E., Rohatgi, R.
  2016; 76 (19): 5810-5821
- **An essential role for Grk2 in Hedgehog signalling downstream of Smoothened** *EMBO REPORTS*
  Zhao, Z., Lee, R. T., Pusapati, G. V., Iyu, A., Rohatgi, R., Ingham, P. W.
  2016; 17 (5): 739-752
- **Functional Divergence in the Role of N-Linked Glycosylation in Smoothened Signaling.** *PLoS genetics*
  Marada, S., Navarro, G., Truong, A., Stewart, D. P., Arensdorf, A. M., Nachtergaele, S., Angelats, E., Opferman, J. T., Rohatgi, R., McCormick, P. J., Ogden, S. K.
  2015; 11 (8)
- **Notch Activity Modulates the Responsiveness of Neural Progenitors to Sonic Hedgehog Signaling** *DEVELOPMENTAL CELL*
  Kong, J. H., Yang, L., Dessaud, E., Chuang, K., Moore, D. M., Rohatgi, R., Briscoe, J., Novitch, B. G.
  2015; 33 (4): 373-387
- **Location, location, and location: compartmentalization of Hedgehog signaling at primary cilia.** *EMBO journal*
  Pusapati, G. V., Rohatgi, R.
  2014; 33 (17): 1852-1854
- **G-protein-coupled receptors, Hedgehog signaling and primary cilia.** *Seminars in cell & developmental biology*
  Mukhopadhyay, S., Rohatgi, R.
  2014; 33: 63-72
- **G-protein-coupled receptors, Hedgehog signaling and primary cilia** *SEMINARS IN CELL & DEVELOPMENTAL BIOLOGY*
  Mukhopadhyay, S., Rohatgi, R.
  2014; 33: 63-72

- **A Novel Osteogenic Oxysterol Compound for Therapeutic Development to Promote Bone Growth: Activation of Hedgehog Signaling and Osteogenesis Through Smoothened Binding** *JOURNAL OF BONE AND MINERAL RESEARCH*
  Montgomery, S. R., Nargizyan, T., Meliton, V., Nachtergaele, S., Rohatgi, R., Stappenbeck, F., Jung, M. E., Johnson, J. S., Aghdasi, B., Tian, H., Weintraub, G., Inoue, H., Atti, et al
  2014; 29 (8): 1872-1885

- **Tracking the Subcellular Fate of 20(S)-Hydroxycholesterol with Click Chemistry Reveals a Transport Pathway to the Golgi** *JOURNAL OF BIOLOGICAL CHEMISTRY*
  Peyrot, S. M., Nachtergaele, S., Luchetti, G., Mydock-McGrane, L. K., Fujiwara, H., Scherrer, D., Jallouk, A., Schlesinger, P. H., Ory, D. S., Covey, D. F., Rohatgi, R.
  2014; 289 (16): 11095-11110

- **Isolation and mutational analysis of circulating tumor cells from lung cancer patients with magnetic sifters and biochips** *LAB ON A CHIP*
  Earhart, C. M., Hughes, C. E., Gaster, R. S., Ooi, C. C., Wilson, R. J., Zhou, L. Y., Humke, E. W., Xu, L., Wong, D. J., Willingham, S. B., Schwartz, E. J., Weissman, I. L., Jeffrey, et al
  2014; 14 (1): 78-88

- **Isolation and mutational analysis of circulating tumor cells from lung cancer patients with magnetic sifters and biochips.** *Lab on a chip*
  Earhart, C. M., Hughes, C. E., Gaster, R. S., Ooi, C. C., Wilson, R. J., Zhou, L. Y., Humke, E. W., Xu, L., Wong, D. J., Willingham, S. B., Schwartz, E. J., Weissman, I. L., Jeffrey, et al
  2013; 14 (1): 78-88

- **Cancer risk after use of recombinant bone morphogenetic protein-2 for spinal arthrodesis.** *journal of bone and joint surgery. American volume*
  Carragee, E. J., Chu, G., Rohatgi, R., Hurwitz, E. L., Weiner, B. K., Yoon, S. T., Comer, G., Kopjar, B.
  2013; 95 (17): 1537-1545

- **Cancer Risk After Use of Recombinant Bone Morphogenetic Protein-2 for Spinal Arthrodesis** *JOURNAL OF BONE AND JOINT SURGERY-AMERICAN VOLUME*
  Carragee, E. J., Chu, G., Rohatgi, R., Hurwitz, E. L., Weiner, B. K., Yoon, S. T., Comer, G., Kopjar, B.
  2013; 95A (17): 1537-1545

- **Chemically inducible diffusion trap at cilia reveals molecular sieve-like barrier.** *Nature chemical biology*
  Lin, Y., Niewiadomski, P., Lin, B., Nakamura, H., Phua, S. C., Jiao, J., Levchenko, A., Inoue, T., Rohatgi, R., Inoue, T.
  2013; 9 (7): 437-443

- **Singapore signalling: the 2012 hedgehog pathway cocktail** *EMBO REPORTS*
  Briscoe, J., Rohatgi, R.
  2012; 13 (7): 580-583

- **Cilia 2010: The Surprise Organelle of the Decade** *SCIENCE SIGNALING*
  Smith, E. F., Rohatgi, R.
  2011; 4 (155)

- **The ciliary membrane** *CURRENT OPINION IN CELL BIOLOGY*
  Rohatgi, R., Snell, W. J.
  2010; 22 (4): 541-546

- **Role of Lipid Metabolism in Smoothened Derepression in Hedgehog Signaling** *DEVELOPMENTAL CELL*
  Yavan, A., Nagaraj, R., Owusu-Ansah, E., Folick, A., Ngo, K., Hillman, T., Call, G., Rohatgi, R., Scott, M. P., Banerjee, U.
  2010; 19 (1): 54-65

- **Lateral transport of Smoothened from the plasma membrane to the membrane of the cilium** *JOURNAL OF CELL BIOLOGY*
  Milenkovic, L., Scott, M. P., Rohatgi, R.
  2009; 187 (3): 365-374

- **Hedgehog signal transduction by smoothened: pharmacological evidence for a two-step activation process.** *Proceedings of the National Academy of Sciences USA*
  Rohatgi R, M., Corcoran RB, Scott MP
  2009; 106: 3196-3201

- **Arrestin? Movement in Cilia.** *Science*

Rohatgi R, Scott MP
2008; 320 (5884): 1777-1781

- **Patching the gaps in Hedgehog signaling.** *Nat Cell Bio*
  Rohatgi R, Scott MP
  2007; 9 (9): 1005-1009
- **Patched1 regulates Hedgehog signaling at the primary cilium.** *Science*
  Rohatgi R, M., Scott MP
  2007; 317 (5836): 372-376
- **In vitro reconstitution of cdc42-mediated actin assembly using purified components.** *Methods in Enzymology*
  Ho HY, Rohatgi R, Lebensohn A, Kirschner MW
  2006; 406: 174-190
- **Loss-of-function Analysis of EphA Receptors in Retinotectal mapping.** *Journal of Neuroscience*
  Feldheim DA, Nakamoto M, Osterfield M, Gale NW, DeChiara TM, Rohatgi R, Yancopoulos GD, Flanagan JG
  2004; 24 (10): 2542-2550
- **Toca-1 Mediates Cdc42- Dependent Actin Nucleation by Activating the N-WASP-WIP Complex.** *Cell*
  Ho HY, R., Lebensohn A, Ma L, Li L, Gygi SP, Kirschner MW
  2004; 118 (2): 203-216
- **The Mechanism of Regulation of WAVE1-induced Actin Nucleation by Rac1 and Nck.** *Nature*
  Eden S, Rohatgi R, Podtelejnikov AV, Mann M, Kirschner MW
  2002; 418 (6899): 790-793
- **Nck and Phosphatidylinositol 4,5 Bisphosphate Synergistically Activate Actin Polymerization Through the N-WASP-Arp2/3 Pathway.** *Journal of Biological Chemistry*
  Rohatgi R, Nollau P, Ho HY, Kirschner MW, Mayer BJ
  2001; 276 (28): 26448-26452
- **CR16 Forms a Complex with N-WASP in Brain and is a Novel Member of a Conserved Proline-Rich Actin-Binding Protein Family.** *Proceedings of the National Academy of Sciences USA*
  Ho HY, R., Ma L, Kirschner MW
  2001; 98 (20): 11306-11311
- **WIP Regulates N-WASP-Mediated Actin Polymerization and Filopodium Formation.** *Nature Cell Biology*
  Martinez-Quiles N, Rohatgi R, Anton IM, Medina M, Saville SP, Miki H, Yamaguchi H, Takenawa T, Hartwig JH, Geha RS, Ramesh N
  2001; 3 (5): 484-491
- **Mechanism of N-WASP Activation by CDC42 and Phosphatidylinositol 4, 5-Bisphosphate.** *Journal of Cell Biology*
  Rohatgi R, H., Kirschner MW
  2000; 150 (6): 1299-1310
- **The Interaction Between N-WASP and the Arp2/3 Complex Links Cdc42-Dependent Signals to Actin Assembly.** *Cell*
  Rohatgi R, M., Miki H, Lopez M, Kirchhausen T, Takenawa T, Kirschner MW
  1999; 97 (2): 221-231
- **The Arp2/3 Complex Mediates Actin Polymerization Induced by the Small GTP-Binding Protein Cdc42.** *Proceedings of the National Academy of Sciences USA*
  Ma L, Rohatgi R, Kirschner MW
  1998; 95 (26): 15362-15367
- **Non-Enzymatic, Template-Directed Ligation of Oligoribonucleotides is Highly Regioselective for the Formation of 3'-5'-Phosphodiester Bonds** *Journal of the American Chemical Society*
  Rohatgi R, Bartel DP, Szostak JW
  1996; 118 (14): 3340-3344
- **Kinetic and Mechanistic Analysis of Non-Enzymatic, Template-Directed Oligoribonucleotide Ligation.** *Journal of the American Chemical Society*
  Rohatgi R, Bartel DP, Szostak JW

1996; 118 (14): 3332-3339