**Manbir Sandhu, PhD**

St. Jude Children’s Research Hospital Postdoctoral Researcher

Department of Structural Biology Laboratory of Dr. M Madan Babu

262 Danny Thomas Place Center of Excellence in Data Driven Discovery

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**Education**

**08/2014 – 06/2019 Irell & Manella Graduate School of Biological Sciences**

**Beckman Research Institute at City of Hope National Medical Center**

***Ph.D. in Biological Sciences***

*Research focus: Computational Structural Biology*

**09/2006 – 06/2011 University of California, San Diego**

***Bachelor of Science***

Major: Human Biology

Minor: Political Science

**Research Summary**

**02/2020 – Present Postdoctoral Researcher**

M Madan Babu, Ph.D., Member/Professor, Dept. of Structural Biology

St. Jude Children’s Research Hospital

* Identify and use predictive models and statistical techniques to integrate multi-omics (RNA-seq, miRNA-seq, snRNA-seq, ATAC-seq, surface proteomics) data generated by international consortia colleagues to identify cellular signaling and metabolic gene network changes in adipocytes of lean and obese mice and adipocytes from human tissue donors
* Collaborate with cross-functional team of bioinformaticists and molecular and cellular biologists to identify novel therapeutic targets for mediating changes to adipocyte signaling and metabolic networks in high-fat diet feeding obesity model
* Report project findings, interpretations, and visualization of datasets, and recommend follow-up actions at quarterly meetings of consortia members. Update scientific advisory board and Novo Nordisk Foundation members at annual meetings through oral presentation and written reports
* Use natural language processing and machine learning methods to construct knowledge graphs and databases to interpret and integrate multiple largescale transcriptomic datasets to deconvolute regulation of GPCR signaling pathways across multiple cell types in physiologic and disease models.

**07/2015 – 01/2020 Thesis Laboratory**

Nagarajan Vaidehi Ph.D., Professor, Dept. of Immunology

Beckman Research Institute at the City of Hope

* Developing informatics based methods to predict amino acid residues critical for binding specificity of GPCRs to G proteins.
* Using multiscale molecular dynamics (MD) tools to analyze structural models of GPCR and G protein interaction, and evaluate predictions of residues critical to GPCR/ G protein binding selectivity.
* Generate MD simulations to analyze residue stress and allosteric communication pathways in protein activation.
* Use computational alanine-scanning method to predict thermal stabilizing mutations for improving expression and purification of transmembrane proteins.
* Generate receptor-based pharmacophore hypotheses for biased signaling at GPCRs from simulation and biophysical data

**07/2012 – 05/2014 Research Associate**

Mark Moasser M.D., Professor in Residence,

Dept. of Hematology/Oncology

University of California, San Francisco Mt. Zion Cancer Research Center

* Elucidated the mechanisms of acquiring “oncogene addiction” in HER2 amplified breast cancer cell lines using next-generation sequencing, gene expression micro-array, and molecular techniques to characterize systemic differences in addicted and non-addicted cells.
* Studied mechanisms of HER3 mediated drug resistance in HER2 amplified cell lines, resulting in publication cited below.

**05/2012 – 07/2012 Research Associate**

Coyote Pharmaceuticals

Molecular Medicine Research Institute, Sunnyvale, CA

* Assisted in pre-IND study on therapeutic efficacy of proprietary drug “CNS-102.”
* Responsibilities included: drug administration by oral gavage, stereotaxic injection to hippocampus for inducing brain injury, post-mortem brain tissue collection, and histological analysis of hippocampus damage.
* Designed protocol for preliminary analysis of proprietary compound “CNS-102” efficacy in mouse model of familial ALS.

**07/2011 – 02/2012 Research Associate**

Maike Sander M.D., Professor

Dept. of Pediatrics and Cellular & Molecular Medicine

Sanford Consortium for Regenerative Medicine, La Jolla, CA

* Research associate for a study focused on the role of Notch signaling in cell fate determination of pancreatic progenitors into ductal or endocrine cells. The study looked at the concentration dependent feedback mechanism of Notch signaling in mediating the expression of Sox9 and Hes1 to control pro-endocrine-Ngn3 expression in embryonic pancreas explant cultures, resulting in publication cited below.

**06/2009 – 06/2010 Independent Undergraduate Research Student**

Maike Sander M.D., Associate Professor,

University of California, San Diego School of Medicine

*The Role of Beta-1 Integrin in pancreas embryonic development*

* Developed and implemented study investigating the role of cellular adhesion molecules, Beta1-Integrin and E-cadherin, in the developmental function of pancreas branching morphogenesis in early mouse embryos.
* Responsibilities included: husbandry of various transgenic mouse lines, embryonic mouse dissections, tissue processing, ex-vivo culture techniques, and two-photon confocal microscopy.

**Awards and Positions**

**Feb 2019** Gordon Research Seminar Oral Presentation – Mol. Pharm. GRC, Ventura

**Feb 2019** Graduate School Travel Award – City of Hope

**Mar 2017** Gordon Research Conference Travel Award – Mol. Pharm. GRC, Tuscany

**Mar 2017** Graduate School Travel Award – City of Hope

**2016 – 2017** Helen and Morgan Chu Fellowship – City of Hope

**2015 – 2016** H.N. & Frances Berger Foundation Fellowship – City of Hope

**June 2015** Graduate School Travel Award – City of Hope

**2010 – 2011** Chancellors Undergraduate Research Scholarship – UC San Diego

**Peer-Reviewed Publications**

**Sandhu M.**, Swenson A., Dysthe M., Sadler F., Sivaramakrishnan S., Vaidehi N. *Conformational plasticity of the intracellular cavity of GPCR-G-protein complexes leads to G‑protein promiscuity and selectivity.* (2019) Proc Natl Acad Sci U S A. 116 (24), 11956-11965.

Okashah N, Wan Q, Ghosh S, **Sandhu M**, Inoue A, Vaidehi N, Lambert NA. *Variable G protein determinants of GPCR coupling selectivity.* (2019) Proc Natl Acad Sci U S A. 116 (24), 12054-12059.

Bhargava, R., **Sandhu, M.**, Muk, S., Lee, G., Vaidehi, N., and Stark, J.M. *C-NHEJ without indels is robust and requires synergistic function of distinct XLF domains.* (2018) Nature Communications 9, 2484.

Ning Ma, Lisa G. Lippert, Titu Devamani, Benjamin Levy, Sangbae Lee, **Manbir Sandhu**, Nagarajan Vaidehi, and Sivaraj Sivaramakrishnan. *Bitopic Inhibition of ATP and Substrate Binding in Ser/Thr Kinases through a Conserved Allosteric Mechanism* (2018) Biochemistry 57 (45), 6387-6390

Li H, **Sandhu M**, Malkas LH, Hickey RJ, Vaidehi N. *How Does the Proliferating Cell Nuclear Antigen Modulate Binding Specificity to Multiple Partner Proteins?* (2017) J Chem Inf Model. 57(12), 3011-3021.

Lee S, Devamani T, Song HD, **Sandhu M**, Larsen A, Sommese R, Jain A, Vaidehi N, Sivaramakrishnan S. *Distinct structural mechanisms determine substrate affinity and kinase activity of protein kinase Cα.* (2017) J Biol Chem. 292 (39), 16300-16309.

Semack A.\*, **Sandhu, M.**\*, Malik, R. U., Vaidehi, N. & Sivaramakrishnan, S. (2016) *Structural Elements in the Gαs and Gαq C-Termini That Mediate Selective G Protein-coupled Receptor*

*(GPCR) Signaling.* J. Biol. Chem. 291, 17929–17940 \*Authors contributed equally

Ruiz-Saenz A., **Sandhu M.**, Yazmin Carrasco, Rebecca Maglathlin, Jack Taunton, and Mark Moasser (2015) *Targeting HER3 by interfering with its Sec61-mediated cotranslational insertion into the endoplasmic reticulum.* Oncogene 2015 Jan 26. doi: 10.1038/onc.2014.455.

Hung Ping Shih, Janel L. Kopp, **Manbir Sandhu**, Claire L. Dubois, Philip A. Seymour, Anne Grapin-Botton, and Maike Sander (2012) *A Notch-dependent molecular circuitry initiates pancreatic endocrine and ductal cell differentiation.* Development, 139, 2488-2499.

**Selected Posters and Presentations**

**Manbir Sandhu,** Anja Swenson, Matthew Dysthe, Sivaraj Sivaramakrisnan, Nagarajan Vaidehi. Structural dynamics of GPCR-G protein complexes reveal hotspots for G protein selectivity. Poster Presentation, ASPET Experimental Biology 2018, April 21-25, 2018, San Diego Convention Center, San Diego, CA

**Manbir Sandhu,** Anja Swenson, Matthew Dysthe, Sivaraj Sivaramakrisnan, Nagarajan Vaidehi. Structural dynamics of GPCR-G protein complexes reveal hotspots for G protein selectivity. Poster Presentation, Keystone Symposium B8 GPCR Structure and Function: Taking GPCR Drug Development and Discovery to the Next Level, February 16-20, 2018, El Dorado Hotel & Spa, Santa Fe, NM

**Manbir Sandhu,** Ansley Semack, Tejas Gupte, Sivaraj Sivaramakrisnan, Nagarajan Vaidehi. Delineating the Structural Basis of G-protein selectivity in GPCRs using Multiscale Molecular Dynamics and FRET Sensors in Live Cells. Poster Presentation, Gordon Research Conference in Molecular Pharmacology, March 11-17, 2017; Renaissance Tuscany Il Ciocco Resort; Barga, Italy

**Manbir Sandhu,** Ansley Semack, Rabia Malik, Sivaraj Sivaramakrisnan, Nagarajan Vaidehi. Structural Determinants of GPCR-G protein selectivity. Oral Presentation, City of Hope Research Staff Organization Retreat 2017, May 1-3, 2016; UCLA Lake Arrowhead Conference Center; Lake Arrowhead, California