BIOGRAPHICAL SKETCH

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NAME: Malany, Siobhan

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

POSITION TITLE Associate Professor

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
Augustana College, Rock Island, IL	B.A.	05/1992	Chemistry
University of Iowa, Iowa City, IA	Ph.D.	12/1997	Bioorganic Chemistry
University of California, San Diego, CA	Postdoc	10/2000	Pharmacology
Max-Planck Institute for Brain Research	AvH Fellow	05/2002	Neuropharmacology

A. Personal Statement

My research as an associate professor in the pharmacodynamics department at UF is in large part focused on advancement of receptor target-based platforms using receptor-specific ligands and new pharmacology tools to elucidate drug mode of action. I have established a combined medicinal chemistry and cell-biology laboratory and recently received a four year R01 to advance small molecule CXCR4 agonists for diabetic would healing to pre-clinical stage. This and other related projects in my lab has emerged from my earlier work as a drug discovery and translational scientist in biotechnology focused on cell- based assay development, and particularly using human stem cells, to support high throughput screening and lead drug optimization of G-protein-coupled receptor targets to IND stage as shown by my publication record. My collaboration with Drs. Aldrich and have been highly synergistic. We have been awarded an internal PROSPER grant for “Assessing Allosteric Mechanisms of Opioid Signaling.” I have two provisional patents covering CXCR6 antagonists and Guanyal cyclase A receptor modulators submitted June 2020.

My laboratory is also part of the Tissue Chip Consortium, an initiative funded by the National Center for Advancing Translational Science (NCATS) to develop bioengineered devices that support the structure and function of human tissues as better models to predict human drug efficacy and toxicity. We have engineered a “Human muscle-on-Chip” that tests the feasibility of microfluidic devices embedded with 3D muscle-hydrogel bundles connected to electrodes to track muscle function in the presence and absence of clinical drug candidates. We will be sending our muscle chips to the International Space Station (ISS) on Spx-21 scheduled to launch late October 2020 to leverage the microgravity conditions on the ISS for the study of changes in muscle biology related to muscle degeneration, which appears to occur more rapidly in space then on earth. The long-term goal of the investigation, which incorporates patient-specific cells form muscle biopsies, is to provide treatment options for patients on earth suffering from sarcopenia, a major healthcare problem, as well as develop countermeasures for astronauts during long-term space flight.

2020 patent and publications include:

1. Parafati, M, and **Malany, S**. 2020. *Advances in Stem Cell Biology.* ‘IPSC Derived 3D Human Fatty Liver Models’ in “Induced Pluripotent Stem Cells-Novel Concepts”. Elsevier Publishing. Oxford UK. *Invited and accepted*
2. Peddibhotla S, Hershberger PM, Kirby RJ, Sugarman E, Maloney P, Sessions H, Divlianska D, Morfa, CJ, Terry D, Pinkerton AB, Smith LH, **Malany S**. Discovery of small molecule antagonists of chemokine receptor CXCR6 that arrest tumor growth in SK-HEP-1 mouse xenografts as a model of hepatocellular carcinoma. *Bioorg Med Chem Lett.* 2020; 30:126899.

B. Positions and Honors

Positions and Employment

1997-2000	TRDRP Postdoctoral Fellow, Pharmacology Department, UCSD, San Diego, CA
2000-2002	Humboldt Research Fellow, Max-Planck Institute for Brain Research, Frankfurt, Germany
2002-2003	Research Scientist II Structural Bioinformatics, San Diego, CA
2003-2007	Research Scientist II, Neurocrine Biosciences, San Diego, CA
2007-2010	Principal Scientist, Tanabe Research Laboratories, San Diego, CA
2010-2015	Chemical Biology Team Leader, Sanford-Burnham Medical Research Institute, Orlando FL
2015-2018	Director of Translational Biology, Sanford Burnham Prebys, Orlando, FL
2015-Present	President Micro-gRx, Inc. State of Florida
2018-2019	Research Associate Professor, University of Florida, College of Pharmacy, Gainesville, FL
2019-Present	Associate Professor, University of Florida, College of Pharmacy, Gainesville, FL

Other Experience and Professional Memberships

2003-2009	Association for Women in Science Member & Board Member, San Diego
2013-2015	Member Society of Laboratory Automation and Screening
7/2014	Ad Hoc Reviewer Biological Chemistry, Biophysics, and Drug Discovery SBRI grants
11/2014	Ad Hoc Reviewer Biological Chemistry, Biophysics, and Drug Discovery SBRI grants
2014-2015	Technical review board for Florida Translational Program
2015-2020	Reviewer for *J. Biomol. Screen*., *PLOS one*, *Toxicol. Appl. Pharm*., *Stem Cells and Development, IJMS, Biology Open*
2016	Ad Hoc Reviewer for NIDDK DiaComp Pilot and Feasibility Funding Program
2017-Present	Central Florida Foundation 100 Women Strong member
11/2019	Ad Hoc Reviewer Small Business: Biological Chemistry, Biophysics and Assay Development

Honors

1990-1991	PEW & Petroleum Research Fund undergraduate Award, Northwestern University
1994-1997	Center for Biocatalysis and Bioprocessing Ph.D. Fellowship
1997-2000	Tobacco-Related Disease Research Program Postdoctoral Fellowship (simultaneously awarded NIH and AHA fellowships)
2000-2002	Alexander von Humboldt Foundation Research Fellowship
2012-2014	Awarded Space Florida International Space Station Research Competition, KSC, FL
2014-2015	Awarded FTRP Grant to identify inhibitors of cell death in hiPSC-derived cardio cells
2014-2016	Winner of GSK Fast Track Challenge to identify inhibitors for resistant hypertension
2015-2017	Awarded Diversified Translational Laboratory (DTL) Initiative grant from SBP
2015-2017	Recipient of Space Florida-Israel Innovation Program 2nd call for Micro-gRx
2016-2018	CASIS Organ-on-Chip Grand Challenge for Micro-gRx
2016-2017	Awarded FTRP Collaboration grant to identify inhibitors of CXCR6 receptor for fibrosis
2017	Featured in Florida High Tech Magazine Faces of Technology
2017	Featured in Florida Trend Magazine
2017-2018	Recipient of Space Florida-Israel Innovation Program 4th call for Micro-gRx
2018	Mayoral Proclamation for STEM research, Springfield, IL
2020	Featured in *Orlando Business Journal, Authority Magazine and Thrive Global*

C. Contribution to Science

In the biotechnology Industry, I have a strong track record of drug discovery work, characterizing compounds targeting CNS GPCRs as therapeutics for insomnia, and Parkinson's Disease. I contributed to the Investigational New Drug application for Histamine H1 antagonist for sleep therapy. In addition, I developed and validated an *ex vivo* competition kinetics model. The method is a first description for the simultaneous measurement of receptor occupancy and dissociation rate for an unlabeled ligand and is a powerful tool to characterize drug candidates based on their kinetic properties. I also spearheaded pharmacology efforts for an A2A program for Parkinson's Disease.

3. **Malany S**, Hernandez LM, Smith WF, Crowe PD, Hoare SR. Analytical method for simultaneously measuring *ex vivo* drug receptor occupancy and dissociation rate: application to (R)-dimethindene occupancy of central histamine H1 receptors. *J Recept Signal Transduct Res.* 2009;29(2):84-93. PMID: 19308787.
4. Hoare SR, Brown BT, Santos MA, **Malany S**, Betz SF, Grigoriadis DE. Single amino acid residue

determinants of non-peptide antagonist binding to the corticotropin-releasing factor1 (CRF1) receptor. *Biochem Pharmacol*. 2006 Jul14;72(2):244-55. PMID: 16750175.

5. Lanier MC, Moorjani M, Luo Z, Chen Y, Lin E, Tellew JE, Zhang X, Williams JP, Gross RS, Lechner SM, Markison S, Joswig T, Kargo W, Piercey J, Santos M, **Malany S**, Zhao M, Petroski R, Crespo MI, Díaz JL, Saunders J, Wen J, O'Brien Z, Jalali K, Madan A, Slee DH. N -[6Amino2-(heteroaryl)pyrimidin-4-yl]acetamides as A 2A Receptor Antagonists with Improved Drug Like Properties and in Vivo Efficacy. *J Med* Chem. 2009; 52(3):709-717. PMID: 19140664.
6. Moree WJ, Li BF, Jovic F, Coon T, Yu J, Gross RS, Tucci F, Marinkovic D, Zamani-Kord S, **Malany S**, Bradbury MJ, Hernandez LM, O'Brien Z, Wen J, Wang H, Hoare SR, Petroski RE, Sacaan A, Madan A, Crowe PD, Beaton G. Characterization of novel selective H1-antihistamines for clinical evaluation in the treatment of insomnia. *J Med Chem.* 2009 Sep 10;52(17):5307-10. PMID: 19663387.

As Director of Translational Biology at Sanford Burnham Prebys (SBP) Medical Discovery Institute, I led a chemical biology team from high throughput screening and hit-to-lead studies to declaration of six probe candidates under the Molecular Libraries Probe Production Centers Network Roadmap Initiative and the Florida Translational Research Program which resulted in several published probe, a provisional patent filing and several collaborative publications. These studies have enabled the discovery small molecule modulators for specific targets and pathways and assays and the translation of laboratory concepts into drug discovery platforms.

7. Ahn B, Soundarapandian M, Sessions H, Peddibholta M, Roth G, Li J-L, Sugarman E, **Malany S**, Wang M, Yea K, Brooks J, Leone TC, Han X, Vega RB, Kelly DP. MondoA Links Skeletal Myocyte Lipid Homeostasis to Insulin Signaling. J. Clinical Investigation. *J. Clin Invest*. 2016; 126: 3567-79.
8. Sugarman E, Koo A, Suyama E, Ruidiaz ME, Heynen-Genel S, Nguyen KH, Vasile S, Soundarapandian MM, Vega RB, Kelly DP, Smith LH, **Malany, S**. Identification of Inhibitors of Triacylglyceride Accumulation in Muscle Cells: Comparing HTS Results from 1536-Well Plate-Based and High-Content Platforms. *J Biomol Screen.* 2014 Jan;19(1):77-87.
9. Moussaud S, **Malany S**, Mehta A, Vasile S, Smith LH, McLean PJ. Targeting α-synuclein oligomers by protein-fragment complementation for drug discovery in synucleinopathies. *Expert Opin Ther Targets*. 2015 Mar 18:1-15. PMID: 25785645.
10. Petrilli AM, Fuse MA, Donnan MS, Bott M, Sparrow NA, Tondera D, Huffziger J, Frenzel C, **Malany S**, Echeverri CJ, Smith LH, Fernández-Valle C. A chemical biology approach identified PI3K as a potential therapeutic target for neurofibromatosis type 2. *Am J Transl Res.* 2014;6(5):471-493. PMID: 25360213. PMCID: PMC4212923.

In 2015, I refocused my drug discovery efforts to incorporate stem cells as phenotypic screening platforms. I collaborated with the stem cell company, Cellular Dynamics, to develop drug discovery platforms in iPSC-derived cardiomyocytes and hepatocytes which led to multiple publications and a funded program with the USAF Cellular Sentinels of Toxicity Program and a collaboration with Astra Zeneca to utilize the companies annotated library set. My work established the use of iPSC as phenotypic HTS platforms, identified cardioprotectant molecules, and characterized molecular signaling pathways in iPSC cells treated with disease-inducing compounds.

11. Parafati M, Kirby RJ, Khorasanizadeh S, Rastinejad R, **Malany S**. A nonalcoholic fatty liver disease model in human induced pluripotent stem cell-derived hepatocytes, created by endoplasmic reticulum stress-induced steatosis. *Disease Models and Mechanisms* 2018; 11: 1-15.
12. Kirby RJ, Divlianska DB, Whig K, Bryan N, Morfa CJ, Koo A, Nguyen KH, Maloney P, Peddibhotla M, Sessions EH, Hershberger PM, Smith LH, **Malany S**. Discovery of Novel Small Molecule Inducers of Heme Oxygenase-1 that Protect Human iPSC-derived Cardiomyocytes from Oxidative Stress. *J Pharmacol Exp Ther* 2017; 364:1-10.
13. Kirby RJ, Qi F, Phatak S, Smith LH, **Malany S**. Assessment of drug-induced arrhythmic risk using limit cycle and autocorrelation analysis of human iPSC-cardiomyocyte contractility. *Toxicol and Appl Pharmacol* 2016; 305: 250-258.
14. Sugarman E, Koo A, Suyama E, Ruidiaz ME, Heynen-Genel S, Nguyen KH, Vasile S, Soundarapandian MM, Vega RB, Kelly DP, Smith LH, **Malany, S**. Identification of Inhibitors of Triacylglyceride Accumulation in Muscle Cells: Comparing HTS Results from 1536-Well Plate-Based and High-Content Platforms. *J Biomol Screen.* 2014 Jan;19(1):77-87.

Most recently, I have become part of the Tissue Chip Consortium with a UG3/UH3 grant funded through the NIH-NCATS Tissue Chip program to study cellular stress on primary muscle myotubes in a lab-on-chip for use

in microgravity as a microscale model of musculoskeletal disease. The project is a collaboration with the bioengineering group at UF, Advent Health and NASA sanctioned implementation partners. This is a very new field with several publications forthcoming. My work has been highlighted in the following publications and communications: Giulianotti MA, Low LA, McLamb WT, Selimovic S, Roberts MS, Tagle DA. **Tissue Chips in Space**. IAC-19 A2.7.5x53999 2019. https://www.issnationallab.org/research-on-the-iss/reports/tissue-chips-in-space/ and Low LA, Giulianotti MA. **Tissue Chips in Space: Modeling Human Diseases in Microgravity.** Pharm Res. 2019 Dec 17;37(1):8. doi: 10.1007/s11095-019-2742-0. PMID: 31848830. In addition, I was featured in the Orlando Business Journal 2020 https://www.bizjournals.com/orlando/news/2020/03/02/how-this-woman-transformed-a-logo-into-a-space.html and Authority magazine https://medium.com/authority-magazine/wisdom-from-the-women-leading-the-space-industry-with-dr-siobhan-malany-founder-and-president-of-5771d9626602

A complete list of my 46 publications may be found here: https://www.ncbi.nlm.nih.gov/myncbi/siobhan.malany.1/bibliography/public/

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D. Research Support

Current Research Support

R01 DK126371-01 (7 percentile) (MPI: Leitchy, Malany, Xu) 7/1/2020 – 6/30/2025
NIH/NIDDK
Small molecule CXCR4 agonists to improve diabetic wound healing
Goal: Advance small molecule CXCR4 agonist with efficacy in porcine model of diabetic wound healing to IND enabling studies.
Role: Co-Principal Investigator

1UH3TR002598-04 (Malany) 9/1/2020 – 8/30/2022
NIH/NCATS
Electrical Stimulation of Human Myocytes in Microgravity: An In Vitro Model to Evaluate Therapeutics to Counteract Muscle Wasting
Goal: studying the effects of microgravity on human muscle biology using an automated tissue chip system as a microphysiological model of age-related musculoskeletal disease.
Role: Principal Investigator 1UG3TR002598-01 (Malany) 9/30/2018 – 9/30/2020 NCE 8/30/2021

NIH/NCATS
Electrical Stimulation of Human Myocytes in Microgravity: An In Vitro Model to Evaluate Therapeutics to Counteract Muscle Wasting
Goal: studying the effects of microgravity on human muscle biology using an automated tissue chip system as a microphysiological model of age-related musculoskeletal disease.
Role: Principal Investigator

R01 AG056315 (MPI: Sangaralingham, Malany and Burnett) 07/01/2017 - 06/30/2021
NIH/NIA
Small Molecule Discovery for Particulate Guanylyl Cyclase Receptor B Enhancers
Goal: To discover novel small molecular pGC-B receptor enhancers which may represent a novel therapeutic strategy for the treatment and prevention of age-related fibrosis and organ failure such as heart failure.
Role: Co-Principal Investigator

CSRA 16-01FL (Malany) 01/1/2019 – 05/30/2020
micro-gRx, Inc.
Development of 'Lab on a Chip' to Evaluate Protein Expression Changes in Stem Cell Derived Cell Types
Goal: To implement cell-based assays using human skeletal muscle cells into a microfluidic device that will enable life science researchers an automated work-flow for performing cell-based assays in microgravity for human disease research and disease modeling related to muscle wasting.
Role: Principal Investigator

Selected Completed Research Support

R01 DK105010 (Liechty, Children's Hospital Colorado) 06/15/2016 – 11/30/2019
NIH/NIDDK
Identifying CXCR4 Receptor Agonists to Improve Diabetic Healing
Goal: The goal is to expand the testing funnel and test a small library as proof of concept studies for a larger high through put screen to identify CXCR4 agonists for diabetic wound healing.
Role: Principal Investigator of Subaward

R01 DK103850 (Burnett, Mayo Clinic) 07/01/2015 – 06/30/2018
NIH/NIDDK
Small molecule discovery for GC-A Activators
Goal: The goal is to complete a high-throughput screening campaign, together with confirmatory assays and mechanistic studies to identify potentiators of the GC-A receptor for heart failure and metabolic disease.
Role: Principal Investigator of Subaward

R01 DK101520 (Rastinejad) 04/01/2014 - 03/31/2017 NIH/NIDDK
Identification of Rev-Erb alpha/beta nuclear receptor modulators
Goal: The goal of this work is to begin identifying new classes of potentially therapeutic molecules that could be developed for treating obesity, type II diabetes, and hypercholesterolemia.
Role: Co-Investigator

R56 DK105010 (Liechty) 04/01/2015 – 03/31/2016
NIH/NIDDK
Identifying CXCR4 Receptor Agonists to Improve Diabetic Healing
Goal: The goal is to expand the testing funnel and test a small library as proof of concept studies for a larger high through put screen to identify CXCR4 agonists for diabetic wound healing.
Role: Co-Investigator

R01 DK097475 (Rastinejad) 12/05/2012-05/31/2016
NIH/NIDDK
Identification of Allosteric Ligands for Hepatic Nuclear Factor 4-alpha
Goal: The goal is to complete a high-throughput screening campaign, together with confirmatory assays and Mechanistic studies that exploit new sites in HNF4α.
Role: Co-Investigator