BIOGRAPHICAL SKETCH

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NAME: Nader H. Moniri

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

POSITION TITLE: Professor and Associate Dean for Research

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Georgia State University, Atlanta, GA	B.S.	03/1997	Biological Sciences/ Chemistry
University of North Carolina at Chapel Hill, Chapel Hill, NC	Ph.D.	03/2004	Medicinal Chemistry
Duke University Medical Center	Post-Doc.	10/2005	Cell and Molecular Biology/Pharmacology

A. Personal Statement

My laboratory focuses on studying the molecular pharmacology, cell biology, and biochemistry of G protein-coupled receptors (GPCRs). I have extensive training in biochemical pharmacology of GPCRs, including training in medicinal chemistry and development of novel pharmaceutical agents that target this family of receptors. My training has included studies on the histamine H1, β2-adrenergic, α1-adrenergic, as well as free-fatty acid family of receptors. A central area of study in my lab centers on mechanisms of regulation of the free-fatty acid receptor-4 (FFA4, aka GPR120), and recently FFA1 (aka GPR40). The other major line of study in my lab relates to the role of reactive oxygen species (ROS) on regulation of the β2-adreneric receptor (β2AR). This project seeks to shed light on the relatively recently recognized paradigm of GPCR signaling to, and regulation by, ROS. As the publications below demonstrate, I have extensive experience in biochemical, pharmacological, and molecular biological approaches toward investigating GPCR signaling and cellular function.

B. Positions and Honors

1999-2004	Research Assistant, Division of Medicinal Chemistry, School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, NC.
2004-2005	Post-Doctoral Fellow, Departments of Surgery, Pharmacology and Cancer Biology, Duke University Medical Center, Durham, NC.
2005-2006	Senior Scientist, Department of Biochemistry and Molecular Pharmacology, Neurogen Corporation, Branford, CT.
7/2006-6/2012	Assistant Professor (tenure-track), Department of Pharmaceutical Sciences, College of Pharmacy and Health Sciences, Mercer University, Atlanta, GA.
7/2012-6/2018	Associate Professor with tenure, Department of Pharmaceutical Sciences, College of Pharmacy, Mercer University, Atlanta, GA.
7/2018-Present	Professor with tenure, Department of Pharmaceutical Sciences, College of Pharmacy, Mercer University, Atlanta, GA.
1/2014-Present	Associate Dean for Research, College of Pharmacy, Mercer University, Atlanta, GA.

Honors

2007	New Professor Recognition Award, 2006-2007, Rho Chi Honor Society, Mercer University
2008	Teacher of the Year Award, 2007-2008, Rho Chi Honor Society, Mercer University
2011	Teacher of the Year Award, 2009-2010, Rho Chi Honor Society, Mercer University
2010-2014	Research Grant Reviewer, American Association of Colleges of Pharmacy

2011-2012 Fellow, American Association of Colleges of Pharmacy, Academic Leadership Fellowship Program
2012 Teacher of the Year Award, 2011-2012, Rho Chi Honor Society, Mercer University
2012 National Institutes of Health, Molecular and Integrative Signal Transduction (MIST) Study Section Reviewer, Ad hoc. (June, 2012)
2014 Inductee, Rho Chi Pharmacy Honor Society
2014 Award for Excellence in Research, Mercer University College of Pharmacy
2014 National Institutes of Health, Molecular and Integrative Signal Transduction (MIST) Study Section Reviewer, Ad hoc. (June, 2014)
2014 Diabetes U.K., Invited Grant Reviewer
2016 Award for Excellence in Service, Mercer University College of Pharmacy
2016 Distinguished Educator Award, Mercer University College of Pharmacy
2016 National Institutes of Health, Center for Scientific Review, Cell Biology Special Emphasis Panel Study Section Reviewer (ZRG1 CB-T(81)A) (June 2016)
2017 U.K. Biotechnology and Biological Sciences Research Council (BBSRC), Invited Grant Reviewer
2017 Inductee, Phi Kappa Phi Honor Society
2009-2020 Elected Graduation Hooder, Classes of 2009, 2010, 2011, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, Mercer University College of Pharmacy
2020 U.K. Biotechnology and Biological Sciences Research Council (BBSRC), Invited Grant Reviewer
2020 Award for Excellence in Research, Mercer University College of Pharmacy

C. Contributions to Science

1. Functional Selectivity of GPCR Signaling: Studies early in my career focused on functional selectivity of the histamine H1 GPCR (H1R) and coincided with pharmacological characterization of H1 ligands that were able to selectively activate H1R-linked pathways coupling to both $G\alpha_{q/11}$ and $G\alpha_s$. Furthermore, these studies correlated with the role of H1R functional selectivity in promoting dopamine synthesis in the brain and in bovine adrenal chromaffin cells. These studies were at the core of the larger body of pioneering evidence in the early 2000's that demonstrated a physiological role for the phenomenon of ligand-directed functional selectivity in native tissues, and suggested that functionally selective H1R agonists could be therapeutically relevant for treatment of neurological disorders such as Parkinson's disease.

a. Booth RG, Moniri NH, Bakker RA, Choksi NY, Nix WB, Timmerman H, Leurs R. A novel phenylaminotetralin radioligand reveals a sub-population of histamine H1 receptors. *J Pharmacol Exp Ther*, 302:328-336, 2002. PMID: 12065734
b. Moniri NH, Covington-Strachan DW, Booth RG. Ligand-directed functional heterogeneity of histamine H_1 receptors: Novel agonists selectively activate and block H_1 mediated phospholipase C and adenylyl cyclase signaling in CHO cells. *J Pharmacol Exp Ther*, 311:274-281, 2004. PMID: 15169829
c. Moniri NH and Booth RG. Role of PKA and PKC in Histamine H1 Receptor-Mediated Activation of Catecholamine Neurotransmitter Synthesis. *Neurosci Lett*, 407:249-253, 2006. PMID: 16978782
d. Moniri NH and Booth RG. Functional heterogeneity of histamine H_1 receptors. *Inflamm Res,* 53:S71-72, 2004. PMID: 15054625

2. The role of GPCRs in cancer: As a post-doctoral fellow, I was involved in numerous studies that sought to investigate the role of GPCRs, particular the LPA receptors and the then-putative androgen GPCR in prostate cancers. These studies entailed work that elucidated cell proliferation, migration, invasion, and tumor xenografts, as related to this proposal.

a. Guo R, Kasbohm EA, Arora P, Sample CJ, Baban B, Sud N, Sivashanmugam P, Moniri NH, Daaka Y. Expression and function of lysophosphatidic acid LPA1 receptor in prostate cancer cells. *Endocrinology.*147:4883-4892, 2006. PMID: 16809448
b. Bagchi G, Wu J, French J, Kim J, Moniri NH, Daaka Y. Androgens transduce the Gαs-mediated activation of protein kinase A in prostate cells. *Cancer Research*. 68: 3225-3231, 2008. PMID: 18451148

3. The regulation of the β2-adrenergic receptor by ROS: As a post-doctoral fellow and into my independent research career, my laboratories work has provided critical insight into a novel dimension of regulation of the β2-

adrenergic receptor (β2AR). Specifically, we have shown that the agonism of the β2AR generates reactive oxygen species (ROS) and that ROS generation is required for the ability of the β2AR to signal through Gαs and β-arrestin, as well as for receptor phosphorylation and internalization. My lab has also shown that the mechanism of ROS-mediated regulation of β2AR occurs via oxidant-induced S-sulfenation of the β2AR on cysteine residues, an effect that occurs in an agonist-dependent manner. Together, these studies have shed light on the linkage between β2AR and ROS and deduced a novel mechanism of β2AR regulation via ROS. I serve as principal investigator on all of these studies with the exception of (a), which was performed as a post-doctoral fellow.

a. Wang G, Moniri NH, Ozawa K, Stamler JS, Daaka Y. Nitric oxide regulates endocytosis by S-nitrosylation of dynamin. *Proc Natl Acad Sci USA*, 103(5):1295-1300, 2006. PMID: 16432212
b. Moniri NH and Daaka Y. Agonist-stimulated reactive oxygen species formation regulates β2-adrenergic receptor signal transduction. *Biochem Pharmacol*, 74: 64-73, 2007. PMID: 17451656
c. Burns RN and Moniri NH. Agonist- and H_2O_2- mediated oxidation of the β2-adrenergic receptor: evidence of receptor S-sulfenation as detected by a modified biotin switch assay. *J Pharmacol Exp Ther*, 339(3):914-921, 2011. PMID: 21917560
d. Singh ML and Moniri NH. Reactive oxygen species are required for β2-adrenergic receptor-β-arrestin interactions and signaling to ERK1/2. *Biochem Pharmacol,* 84:661-669, 2012. PMID: 22728070
e. Singh M and Moniri NH. Reactive oxygen species as β2-adrenergic receptor signal transducers. *J. Pharmaceu Pharmacol.* 2(1): 8-15, 2014.
f. Rambacher KM and Moniri NH. The β2-adrenergic receptor-ROS signaling axis: An overlooked component of β2AR function? *Biochem Pharmacol*, 171:113690, 2020. PMID: 31697929
g. Rambacher KM and Moniri NH. Cysteine redox state regulates human β2-adrenergic receptor binding and function. *Sci Rep* 10, 2934, 1-15, 2020. PMID: 32076070

4. Characterization of FFA receptor FFA4 and the role of FFA receptors in health and disease: Free-fatty acid receptor-4 has gained considerable attention due to its ability to promote profound anti-inflammatory and anti-diabetic affects, including insulin resensitization, which is an effect that is dependent on β-arrestin signaling. My laboratory has contributed to the understanding of regulation of FFA4 signaling through phosphorylation, which itself drives β-arrestin signaling. We were the first to report on the phosphorylation of both isoforms of the receptor, and have revealed that FFA-4 short is phosphorylated heterologously by PKC and homologously by GRK6. We have also recently reported on regulation and differential signaling of the long isoform of FFA4. We have also shown that diets rich in omega-3 fatty acids, the endogenous agonists of FFA4, facilitate alterations in FFA4 and TNF-α expression in the rat colon. A recently funded NIH-grant has allowed us to study the role of FFA4 in the brain, including its role in neuroprotection in Parkinson's Disease, where we have recently reported that the endogenous agonist DHA is neuroprotective. Together, our work with FFA4 has contributed important knowledge in regard to the molecular pharmacology of the receptor that should be accounted for in drug development efforts which target FFA4. Recently, we have begun to study the role of FFA4 and the related FFA1 in cancers, which is the topic of the current proposal. I serve as principal investigator and corresponding author on all of these studies.

a. Burns RN and Moniri NH. Agonism with the omega-3 fatty acids alpha-linolenic acid and docosahexaenoic acid mediates phosphorylation of both the short and long isoforms of the human GPR120 receptor. *Biochem Biophys Res Commun,* 396: 1030-1035, 2010. PMID: 20471368
b. Burns RN, Singh M, Senatorov IS, Moniri NH. Mechanisms of homologous and heterologous phosphorylation of FFA receptor 4 (GPR120): GRK6 and PKC mediate phosphorylation of Thr347, Ser350, and Ser357 in the C-terminal tail. *Biochem Pharmacol*, 87:650-659, 2014. PMID: 24412271
c. Cheshmehkani A, Senatorov IS , Kandi P, Singh M, Britt A, Hayslett R, Moniri NH. Fish oil and flax seed oil supplemented diets increase FFAR4 expression in the rat colon. *Inflamm Res,* 64:809-15, 2015. PMID: 26275932
d. Moniri NH. Free-fatty acid receptor-4 (GPR120): cellular and molecular function and its role in metabolic disorders. *Biochem Pharmacol*, 110-111:1-15, 2016. PMID: 26827942
e. Cheshmehkani A, Senatorov IS, Dhuguru J, Ghoneim O, Moniri NH. Free-fatty acid receptor-4 (FFA4) modulates ROS generation and COX-2 expression via the C-terminal β-arrestin phosphosensor in Raw 264.7 macrophages. *Biochem Pharmacol*. 146:139-150, 2017. PMID: 28943238
f. Senatorov IS and Moniri NH. The role of free-fatty acid receptor-4 (FFA4) in human cancers and cancer cell lines. *Biochem Pharmacol*. 150:170-180, 2018. PMID: 29452095

g. Chitre NM, Wood B, Ray A, Moniri NH, Murnane KS. Docosahexaenoic acid protects motor function and increases dopamine synthesis in a rat model of Parkinson's disease via mechanisms associated with increased protein kinase activity in the striatum. *Neuropharmacology*, 167:107976, 2020. PMID: 32001239
h. Senatorov IS, Cheshmehkani A, Burns RN, Singh K, Moniri NH. Carboxy-terminal phosphoregulation of the long splice isoform of Free-Fatty Acid Receptor-4 mediates β-arrestin recruitment and signaling to ERK1/2. *Mol Pharmacol*. 97:304-313, 2020. PMID: 32132133

Complete List of Published Work:

https://www.ncbi.nlm.nih.gov/myncbi/nader.moniri.1/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Competitive Research Support:

NIH/NHLBI (1R15HL138603), 07/01/2017-06/30/2021 (NCE)
The role of ROS on β2-adrenergic receptor function in human airway
The major goal of this project is to fully elucidate the linkage between ROS generation and β2AR function in normal and asthma-diseased human airway.
Role: Principal Investigator
Priority score = 20

Completed Competitive Research Support:

United Soybean Board
Soy Health Research Program
The major goal of this project is to assess the roles of a variety of dietary oils in neuroprotection from Parkinson's Disease.
Role: Principal Investigator

NIH/NINDS (1R03NS095239), 03/01/2016 – 02/28/2019
FFAR4 and nigrostriatal function: A novel target for treatment of PD?
The major goal of this project is to characterize the neuroprotective role of FFAR4 on nigrostriatal neuron function in models of Parkinson's Disease.
Role: Principal Investigator
Priority Score = 25; Percentile = 7

NIH/NIDDK (1R15DK098730), 03/01/2013-02/28/2017
The role of phosphorylation in regulating the antidiabetic effects of O3FAR1 (FFAR4).
The major goal of this project is to fully elucidate the involvement of receptor phosphorylation on regulation of the antidiabetic effects of O3FAR1 (FFAR4).
Role: Principal Investigator
Priority score = 10

Mercer University Seed Grant, 07/01/2012 – 06/30/2013
Omega-3 fatty acid receptor-1 expression and function in the lung.
The major goal of this proposal is to characterize O3FAR1 expression and function in human lung cells.
Role: Principal Investigator

Mercer University Seed Grant, 07/01/2011 – 06/30/2012
The role of ROS on β2-adrenergic receptor mediated ERK1/2 activation.
The major goal of this proposal is to elucidate the role of ROS on β2-adrenergic receptor-mediated ERK1/2 signaling.
Role: Principal Investigator

Diabetes Action Research and Education Foundation, 01/01/2011 – 12/31/2011
Uncovering the molecular mechanisms involved in GPR120-mediated GLP-1 secretion.
The major goal of this study is to elucidate the signal transduction cascades involved in GPR120-mediated GLP-1 secretion.
Role: Principal Investigator

American Foundation for Pharmaceutical Education, 08/01/2010 – 07/31/2011
GPR120 intracellular signaling.
The major goal of this project is to assess intracellular signaling of GPR120.
Role: Principal Investigator, (Pre-doctoral fellowship awarded to Rebecca L. Burns, PharmD/PhD student)

Mercer University Seed Grant, 07/01/2010 – 06/30/2011
β2-Adrenergic receptor oxidation
The major goal of this proposal is to characterize agonist-induced □2-adrenergic receptor oxidation.
Role: Principal Investigator

Diabetes Action Research and Education Foundation, 01/01/2010 – 12/31/2010
In vivo analysis of the role of omega-3 fatty acids in regulation of GPR120 expression.
The major goal of this study is to examine the role of various omega-3 fatty acids in expression of GPR120 protein in rats.
Role: Principal Investigator

American Foundation for Pharmaceutical Education, 08/01/2009 – 07/31/2010
GPR120 intracellular signaling.
The major goal of this project is to assess intracellular signaling of GPR120.
Role: Principal Investigator, (Pre-doctoral fellowship awarded to Rebecca L. Burns, PharmD/PhD student)

Mercer University Seed Grant, 07/01/2009 – 06/30/2010
GPR120-mediated ERK1/2 phosphorylation.
The major goal of this proposal is to elucidate free fatty acid efficacy and potency with respect to GPR120-mediated ERK1/2 activation.
Role: Principal Investigator

American Association of Colleges of Pharmacy, New Investigators Award, 01/01/2009 – 12/31/2009
β2-receptor mediated ROS generation.
The major goal of this is to identify the NADPH oxidase isoforms expressed in HEK293 cells and to begin to assess their role in β2-receptor mediated ROS generation.
Role: Principal Investigator

Diabetes Action Research and Education Foundation, 01/01/2009 – 12/31/2009
The role of omega-3 fatty acids in regulation of GPR120 expression.
The major goal of this study is to examine the role of various omega-3 fatty acids in expression of GPR120 mRNA and protein.
Role: Principal Investigator

American Foundation for Pharmaceutical Education, 08/01/2008 – 07/31/2009
GPR120 intracellular signaling.
The major goal of this project is to assess intracellular signaling of GPR120.
Role: Principal Investigator, (Pre-doctoral fellowship awarded to Rebecca L. Burns, PharmD/PhD student)

Mercer University Seed Grant, 07/01/2008 – 06/30/2009
GPR120 desensitization.
The major goal of this proposal is to characterize free fatty acid mediated desensitization of GPR120.
Role: Principal Investigator