OMB No. 0925-0001 and 0925-0002 (Rev. 10/2021 Approved Through 01/31/2026)

BIOGRAPHICAL SKETCH

**Provide the following information for the Senior/key personnel and other significant contributors.**

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NAME: Sodhi, Komal

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

POSITION TITLE: Associate Professor (tenured)

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 |
| --- | --- | --- | --- |
| Mahatma Gandhi Memorial Medical College, Indore, India | MBBS (M.D.) | 01/2000 | Medicine |
| Jaipur Golden Hospital, New Delhi, India | D.N.B (Residency) | 01/2005 | Medicine |

# A. Personal Statement

My principal research focus is to investigate the contributions of chronic oxidative stress to cardiovascular diseases, chronic kidney disease (CKD), neurodegeneration, obesity, and metabolic syndrome as well as their associated long-term complications. My laboratory focuses on the regulation of the cellular antioxidant defense system in pathophysiological states associated with chronic redox imbalance, specifically caused by Na/K-ATPase-mediated Src signaling. Studies from our group have shown that oxidative stress is an important component in the activation of Na/K-ATPase-mediated Src signaling and subsequent feed-forward ROS amplification. Based on these studies, my laboratory used Na/K-ATPase mimetic peptide, pNaKtide, to restore cellular redox balance and suppress oxidative stress in various disease condition. My previously published studies have extensively shown the role of Na/K-ATPase/Src signaling in several clinical conditions like obesity, atherosclerosis and uremic cardiomyopathy. Subsequently, recently published study also demonstrated that lentiviral mediated delivery of NaKtide, targeted specifically to adipocytes, attenuated obesity and metabolic homeostasis and also improved uremic cardiomyopathy. I have also elucidated the role of Na/K-ATPase/Src signaling-mediated oxidative stress in the pathogenesis of obesity-associated cognitive decline and neurodegeneration.

I have built extensive collaborations across multiple departments at Marshall University School of Medicine, including Nephrology, Cardiology, Geriatrics, Internal Medicine, and Surgery, and secured research support through grants and departmental funds. I also hold leadership roles as Director of Clinical Research at Cardiology Department, and Mentor of Clinical Research in the Surgery Department for mentoring and guiding fellows, residents, and medical students in achieving research goals. My clinical research has established the molecular mechanism of various pathophysiological alterations associated with CKD and has received NIH grant for the study on CKD and renal failure-associated complications. Furthermore, I have successfully completed NIH Office of Research on Women’s Health Bench-to-Bedside study, which demonstrated the potential role of CKD in the progression of cognitive impairment. My ongoing NIH-R01 grant deals with the elucidation of the role of adipose tissue-derived exosomes in cellular stress signaling pathways associated with cardiovascular complications. As a clinical research scientist with proven expertise in elucidating the pathophysiological complications associated with various chronic diseases including Alzheimer’s disease (AD), my goal is to develop novel prognostic and therapeutic strategies that can combat these pathological conditions to improve the clinical outcome. Thus far, my research projects have been diverse and incorporated techniques, such as cell culture, animal models, molecular and cell biology. My laboratory has extensive experience with experimental model systems, including animal models of atherosclerosis, chronic kidney disease, and metabolic syndrome as well as various in vitro models of human and mouse cells. Further, we are well versed in tissue-specific lentiviral gene expression in vivo; therefore, we are uniquely equipped to carry out these studies.

Following is the list of four most relevant papers to this study:

1. Pillai SS, Pereira DG, Zhang J, Huang W, Beg MA, Knaack DA, de Souza Goncalves B, Sahoo D, Silverstein RL, Shapiro JI, **Sodhi K**, Chen Y. Contribution of adipocyte Na/K-ATPase α1/CD36 signaling induced exosome secretion in response to oxidized LDL. Front Cardiovasc Med. 2023 Apr 27;10:1046495. doi: 10.3389/fcvm.2023.1046495.
2. Goguet-Rubio P, Klug RL, Sharma DL, Srikanthan K, Puri N, Lakhani VH, Nichols A, O'Hanlon KM, Abraham NG, Shapiro JI, **Sodhi K**. [Existence of a Strong Correlation of Biomarkers and miRNA in Females with Metabolic Syndrome and Obesity in a Population of West Virginia.](https://www.ncbi.nlm.nih.gov/pubmed/28638270/)Int J Med Sci. 2017;14(6):543-553. doi: 10.7150/ijms.18988. eCollection 2017. PubMed PMID: 28638270; PubMed Central PMCID: PMC5479123.

**Ongoing projects that I would like to highlight include:**

NIH 1R01 HL164460-01A1 (R01)

Komal Sodhi (Co-PI; 50% effort)

04/01/2023 – 03/31/2028

NKA/CD36 signaling in adipocytes promotes oxidative stress and drives chronic inflammation in atherosclerosis

NIH 1R01DK129937-01 (R01)

Komal Sodhi (Co-Investigator, 7% effort)

08/24/2021 – 06/30/2025

ATP1A1-depeendent Regulation of Sodium Handling by the Renal Proximal Tubule: Mechanism and Implications in Salt-Sensitivity

NIH 1R15HL164682-01 (R15)

Komal Sodhi (Co-Investigator, 7% effort)

9/01/2022 – 8/31/2025

The Role of Oxidative Signaling through Na/K-ATPase in PNx-induced Anemia

**Recently finished**

NIH 1R15HL150721 (R15)

Komal Sodhi (Principal Investigator)

8/5/2020 – 7/31/2023

Role of adipocyte Na/K-ATPase signaling in the development and progression of uremic cardiomyopathy

NIH Office of Research on Women’s Health (ORWH) Bench-to-Bedside Award (Number: 736214)

Komal Sodhi (Extramural PI)

5/5/2021 – 5/31/2023

Fibrosis markers in kidney disease associated with dementia in women vs men.

# B. Positions, Scientific Appointments and Honors

## Positions and Employment

2016-present Associate Professor, Department of Biomedical Sciences/Surgery, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

2013- 2016 Assistant Professor, Department of Biomedical Sciences/Surgery, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

2010-2012 Research Associate, Department of Physiology & Pharmacology, The University of Toledo College of Medicine, Toledo, OH

2008-2010 Post-Doctoral Fellow, Department of Pharmacology, New York Medical College Valhalla, NY.

2005-2006 Attending Physician, Jaipur Golden Hospital, New Delhi, India.

## Other Experience and Professional Memberships

2010-present Lectures for advanced lecture series in CVMD graduate course.

2008-present Trained several fellows, graduate and undergraduate students and postdoctoral fellows in the laboratory and classroom setting.

2002-2006 Trained medical students, residents and the graduate students in the principals and practice of medicine, family medicine and surgery.

2020-present Member of American Heart Association

2021-present Member of American Physiological Society, USA

2019-present Member of American Society of Nephrology

2021-present. Guest Editor for the Journal Frontiers in Cardiovascular Medicine

2020-present. Editorial Board Member Journal of Pharmacogenomics & Pharmacoproteomics

2021-present. Editorial Board Member Integrative Pharmaceutical Research

2021-present. Editorial Board Member SRL Metabolic Syndromes

2017-present. Journal Peer review (Ad hoc): American Journal of Kidney Diseases, International Journal of Hypertension, Journal of Cardiovascular Pharmacology, Evidence-Based Complementary and Alternative Medicine, Journal of Prostaglandins and Other Lipid Mediators, Basic & Clinical Pharmacology & Toxicology, Journal of hypertension, PLOS One, **International Journal of Molecular Sciences,** Frontiers in Physiology

# C. Contribution to Science

1. **My lab conducts extensive highly translational clinical research in close collaborations with basic scientists and clinicians.** I have established extensive collaborations with various departments in Marshall University School of Medicine including, Geriatrics, Nephrology**,** Cardiology, Internal Medicine, and Surgery. Together, my research utilizes novel research methodologies and studies pathways to target diseases that are of public health concern, including CKD, obesity, non-alcoholic fatty liver disease, metabolic syndrome, aging, and drug-induced cardiotoxicity.
2. Pillai SS, Lakhani HV, Zehra M, Wang J, Dilip A, Puri N, O'Hanlon K, **Sodhi K**. Predicting Nonalcoholic Fatty Liver Disease through a Panel of Plasma Biomarkers and MicroRNAs in Female West Virginia Population. Int J Mol Sci. 2020 Sep 13;21(18):6698. doi: 10.3390/ijms21186698. PMID: 32933141; PMCID: PMC7554851.
3. Lakhani HV, Khanal T, Gabi A, Yousef G, Alam MB, Sharma D, Aljoudi H, Puri N, Thompson E, Shapiro JI, **Sodhi K**. Developing a panel of biomarkers and miRNA in patients with myocardial infarction for early intervention strategies of heart failure in West Virginian population. PLoS One. 2018 Oct 24;13(10):e0205329. doi: 10.1371/journal.pone.0205329. PMID: 30356307; PMCID: PMC6200226..
4. Goguet-Rubio P, Klug RL, Sharma DL, Srikanthan K, Puri N, Lakhani VH, Nichols A, O'Hanlon KM, Abraham NG, Shapiro JI, **Sodhi K**. Existence of a Strong Correlation of Biomarkers and miRNA in Females with Metabolic Syndrome and Obesity in a Population of West Virginia. Int J Med Sci. 2017 Apr 19;14(6):543-553. doi: 10.7150/ijms.18988. PMID: 28638270; PMCID: PMC5479123.
5. Oxidative stress is known to play a role in the generation and maintenance of an obesity phenotype in both isolated adipocytes and animal models. My research have shown that Na/K-ATPase signaling can amplify oxidative stress through mechanisms distinct from its well-understood ion pumping function. The α1 subunit of Na/K-ATPase serves a scaffolding function with Src and initiate a signaling cascade. In addition to the well-characterized cardiotonic steroid ligands for Na/K-ATPase, we have found that ROS are also activators of NKA signaling. This is achieved via carbonylation of the α1 subunit, which activates the SFK signaling cascade. Because Na/K-ATPase can amplify oxidant signaling, we studied a peptide, pNaKtide, designed to inhibit this pathway, as it might ameliorate various stress-signaling pathways associated with chronic diseases. Administration of pNaKtide in mice fed western diet, reduced body weight gain, restored systemic redox and inflammatory milieu and crucially, improved insulin sensitivity. Recently, we also demonstrated that pNaKtide improved dyslipidemia and atherosclerosis in ApoE deficient mice fed a western diet. We recently elucidated the central role of adipocyte Na/K-ATPase signaling in CKD and renal failure associated cardiomyopathy. We established animal model of 4/6th and 5/6th nephrectomy to induce CKD along with renal and cardiac fibrosis. We elucidated several mechanisms of Na/K-ATPase signaling in CKD and cardiac dysfunction associated with CKD. We have also elucidated the role of Na/K-ATPase/Src signaling-mediated oxidative stress in the pathogenesis of obesity-associated cognitive decline and neurodegeneration. Thus, the inhibition of Na/K-ATPase signalingmay be a novel way to combat metabolic syndrome, cardiovascular disease, CKD and neurodegenerative diseases.
6. **Sodhi K**, Wang X, Chaudhary MA, Lakhani HV, Zehra M, Nawab A, Cottrill CL, Bai F, Liu J, Sanabria JR, Xie Z, Shapiro JI. Adipocyte Na, K-ATPase Signaling Attenuates Experimental Uremic Cardiomyopathy. Cell Mol Biol (Noisy-le-grand). 2023 May 31;69(5):197-206. doi: 10.14715/cmb/2023.69.5.31. PMID: 37571879.
7. **Sodhi K**, Srikanthan K, Goguet-Rubio P, Nichols A, Nawab A, Shah P, Chaudhry M, El-Hamdani M, Xie Z, Shapiro J. Inhibition of Na/K-ATPase signaling Attenuates Steatohepatitis and Atherosclerosis in Mice Fed a Western Diet. Cell Mol Biol (Noisy-le-grand). 2023 Feb 28;69(2):162-171. doi: 10.14715/cmb/2023.69.2.27. PMID: 37224028.
8. **Sodhi K**, Pratt R, Wang X, Lakhani HV, Pillai SS, Zehra M, Wang J, Grover L, Henderson B, Denvir J,Liu J, Pierre S, Nelson T, Shapiro JI. Role of adipocyte Na,K-ATPase oxidant amplification loop in cognitive decline and neurodegeneration. iScience. 2021 Oct 12;24(11):103262. doi: 10.1016/j.isci.2021.103262.
9. **Sodhi K**, Maxwell K, Yan Y, Liu J, Chaudhry MA, Xie Z, Shapiro JI. pNaKtide Inhibits Na/K-ATPase Signaling and Attenuates Obesity. J Clin Med Sci. 2023;7(4):1000238. Epub 2023 Jul 28. PMID: 38283397; PMCID: PMC10812088.
10. During my post-doctoral fellowship with Dr. Nader G. Abraham, my extensive research elucidated that heme oxygenase (HO) plays a role in ameliorating obesity, hypertension, diabetes, and other features of metabolic syndrome. HO converts the pro-oxidant heme molecule into carbon monoxide and the antioxidant biliverdin. This research has focused on the oxidative stress-induced inflammatory processes that leads to adipocyte dysfunction, vascular dysfunction and altered metabolic profile, and the effect that HO-1 exerts on attenuating these processes. The research has also investigated novel treatment strategies involving HO upregulation, including lentiviral-mediated HO-1 gene therapy and CoPP-induced HO upregulation in various animal models treated with high fat/fructose diets and several in vitro models to attenuate metabolic imbalance. We believe, that HO represents a promising treatment pathway for the pro-oxidant and inflammatory processes that drive features of metabolic syndrome.
11. **Sodhi K**, Inoue K, Gotlinger KH, Canestraro M, Vanella L, Kim DH, Manthati VL, Koduru SR, Falck JR, Schwartzman ML, Abraham NG. Epoxyeicosatrienoic acid agonist rescues the metabolic syndrome phenotype of HO-2-null mice. J Pharmacol Exp Ther. 2009 Dec;331(3):906-16. doi: 10.1124/jpet.109.157545. Epub 2009 Aug 28.
12. **Sodhi K**, Wu CC, Cheng J, Gotlinger K, Inoue K, Goli M, Falck JR, Abraham NG, Schwartzman ML. CYP4A2-induced hypertension is 20-hydroxyeicosatetraenoic acid- and angiotensin II-dependent. Hypertension (Dallas, Tex.: 1979). 2010; 56(5):871-8. NIHMSID: NIHMS252932 PMID: 20837888
13. Cao J, **Sodhi K**, Inoue K, Quilley J, Rezzani R, Rodella L, Vanella L, Germinario L, Stec DE, Abraham NG, Kappas A. Lentiviral-human heme oxygenase targeting endothelium improved vascular function in angiotensin II animal model of hypertension. Hum Gene Ther. 2011 Mar;22(3):271-82. doi: 10.1089/hum.2010.059. Both Authors contributed equally.

4. An equally exciting focus of my previous research entailed examining HO-dependent regulation of eicosanoids and their physiological effects, particularly in the vasculature and perivascular adipocytes. I have studied the interaction between EET and HO-1 in regulation of vascular function.The central hypothesis focuses on heme oxygenase (the most potent anti-oxidant gene in human body)-adiponectin-EET plays an essential role in vascular function.

a. **Sodhi K**, Puri N, Inoue K, Falck JR, Schwartzman ML, Abraham NG. EET agonist prevents adiposity and vascular dysfunction in rats fed a high fat diet via a decrease in Bach 1 and an increase in HO-1 levels. Prostaglandinsn Other Lipid Mediat. 2012 Aug;98(3-4):133-42. doi: 10.1016/j.prostaglandins.2011.12.004. Epub 2011 Dec 24. PubMed PMID: 22209722; PubMed Central PMCID: PMC3449325.

b. **Sodhi K**, Wu CC, Cheng J, Gotlinger K, Inoue K, Goli M, Falck JR, Abraham NG, Schwartzman ML. CYP4A2-induced hypertension is 20-hydroxyeicosatetraenoic acid- and angiotensin II-dependent. Hypertension. 2010 Nov;56(5):871-8. doi: 10.1161/HYPERTENSIONAHA.110.154559. Epub 2010 Sep 13. PubMed PMID: 20837888; PubMed Central PMCID: PMC2995375.

c. Nader G. Abraham, **Sodhi K**, Silvis A, Vanella L, Favero G, Rezzani R, Zeldin D, Schwartzman ML. CYP2J2 Targeting to Endothelial Cells Attenuates Adiposity and Vascular Dysfunction in Mice Fed a High-Fat Diet by Reprogramming Adipocyte Phenotype. Hypertension 2014. MS ID: HYPE201403884D. Both Authors contributed equally.

## Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/komal.sodhi.1/bibliography/public/>