BIOGRAPHICAL SKETCH

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NAME: Sharma, Ravindra K

eRA COMMONS USER NAME (credential, e.g., agency login): rsharma1

POSITION TITLE: Assistant Scientist

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)	END DATE MM/YYYY	FIELD OF STUDY
Jiwaji University, Gwalior, Madhya Pradesh	BS	07/2004	Biology
Jiwaji University, Gwalior, Madhya Pradesh	MS	07/2006	Biotechnology
University of Delhi, New Delhi, New Delhi	PHD	03/2015	Medical Physiology
University of Florida, Gainesville, Florida	Postdoctoral Fellow	04/2020	Cardiovascular Physiology

A. Personal Statement

My current research interests are to understand the central mechanisms underlying cardio-vascular complications of chronic kidney disease (CKD). I am also interested in studying the role of circadian clock in the the regulation of cardiovascular disorders. My background in cardiovascular physiology and as a part of my work performed in previous projects, I have established my laboratory techniques to understand the brain, heart, kidney and vascular functions in animal models of cardiovascular diseases. I have more than 12 years of experience in recording of various cardiovascular parameters such as radio-telemetry blood pressure, right ventricular systolic pressure (RVSP), ventricular pressure with Millar catheter, echocardiographic imaging to analyze heart/vessels functions and renal sympathetic nerve recording in rodents. I routinely perform surgeries such as stereotaxic, 5/6 nephrectomy and nerve recording in rodents. My primary responsibility is to run a research program, designing experiments, obtain regulatory approval, perform and supervise animal experiments, analyze the data and prepare manuscripts. I have developed collaborative projects with a highly successful team of researchers in the University of Florida, dedicated to studying the cardiovascular complications of kidney diseases. During my postdoctoral training, my research focus was to understand the role of neuroinflammation and other cellular mechanisms of central nervous system in the pathophysiology of hypertension and pulmonary hypertension. I have discovered that microglial cells in the cardio-regulatory areas of the brain have direct communication with gut microbiota in the regulation of gut-brain-axis in hypertension. In addition to that, my work on pulmonary hypertension (PH) showed that PH is a systemic disease involving interplay among multiorgan systems rather a disease of pulmonary vasculature. I have successfully demonstrated for the first time the association of gut microbial dysbiosis in two different rodent models of PH and further showed that overexpression of angiotensin-converting enzyme 2 (ACE2) alleviate PH and associated right heart pathologies. These findings led us to propose a dysfunctional brain-gut-lung axis in PH. For this work, I received “New Investigator Award” and received travel support from the American Heart Association (AHA) in Council on Hypertension Meeting 2018. I have demonstrated excellent productivity in research evidenced by my publications record which includes more than 16 peer-reviewed publications in high-impact journals including Circulation Research, Hypertension and Clinical Science. My recent publications highlighting my experience and qualification are listed under the subheading of “Contribution of Science”. I have expertise, motivation, multidisciplinary training and our laboratory has all of the primary equipment to carry out the proposed work. I believe our excellent research environment at the University of Florida will aid us in successfully completing the proposed research. For this O'Brein Kidney Resources Alliance (OKRA) opportunity Pool Program, I will utilize my surgery and animal handling expertise as well as my experience with integrative physiology to help complete these important studies on the role of neuroinflammation and sympathetic activation in CKD.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2020 - Assistant Scientist, University of Florida, Gainesville, FL

Honors

2024 - 2027 Second Century Early Career Independence Award, American Heart Association
2018 New Investigator Award, American Heart Association (AHA)

C. Contribution to Science

1. As an early-stage investigator, I have made some significant contributions to advance science. The main findings are listed below.

   Aortic Stiffness in Chronic Kidney Disease: Patients with chronic kidney disease (CKD) are at increased risk for adverse cardiovascular events. CKD is associated with increases in arterial stiffness, whereas improvements in arterial stiffness correlate with better survival. Utilizing multidisciplinary approaches, my recent study have demonstrated that increased aortic stiffness (pulse wave velocity) is associated with CKD which is independent of hypertension and calcification. In addition to this, we recently reviewed how disrupted circadian clock involved in atherosclerosis and hypertension. These studies were published recently in AJP Renal Physiology and Canadian Journal of Cardiology.

   a. Costello HM, Sharma RK, McKee AR, Gumz ML. Circadian Disruption and the Molecular Clock in Atherosclerosis and Hypertension. Can J Cardiol. 2023 Dec;39(12):1757-1771. PubMed PMID: 37355229.
   b. Sharma RK, Kamble SH, Krishnan S, Gomes J, To B, Li S, Liu IC, Gumz ML, Mohandas R. Involvement of lysyl oxidase in the pathogenesis of arterial stiffness in chronic kidney disease. Am J Physiol Renal Physiol. 2023 Apr 1;324(4):F364-F373. PubMed Central PMCID: PMC10069822.

2. Gut-Brain Axis in Hypertension: Hypertension is associated with neuroinflammation and gut microbiota dysbiosis, but the mechanisms remain elusive. Utilizing multidisciplinary approaches, I have discovered that microglial cells in the cardio-regulatory areas of the brain have direct communication with gut microbiota in the regulation of gut-brain-axis in hypertension. We have demonstrated that chemically modified tetracycline 3 (CMT-3) inhibition of microglial cells in the autonomic regulatory areas of the brain, selectively impact the gut microbiota and protects against hypertension. These findings were published in Circulation Research and Frontiers in Physiology.

   a. Zubcevic J, Santisteban MM, Perez PD, Arocha R, Hiller H, Malphurs WL, Colon-Perez LM, Sharma RK, de Kloet A, Krause EG, Febo M, Raizada MK. A Single Angiotensin II Hypertensive Stimulus Is Associated with Prolonged Neuronal and Immune System Activation in Wistar-Kyoto Rats. Front Physiol. 2017;8:592. PubMed Central PMCID: PMC5583219.
   b. Donertas Ayaz B, Oliveira AC, Malphurs WL, Redler T, de Araujo AM, Sharma RK, Sirmagul B, Zubcevic J. Central Administration of Hydrogen Sulfide Donor NaHS Reduces Iba1-Positive Cells in the PVN and Attenuates Rodent Angiotensin II Hypertension. Front Neurosci. 2021;15:690919. PubMed Central PMCID: PMC8479468.
   c. Sharma RK, Yang T, Oliveira AC, Lobaton GO, Aquino V, Kim S, Richards EM, Pepine CJ, Sumners C, Raizada MK. Microglial Cells Impact Gut Microbiota and Gut Pathology in Angiotensin II-Induced Hypertension. Circ Res. 2019 Mar;124(5):727-736. PubMed Central PMCID: PMC6395495.

3. Neuro-inflammation in Pulmonary Hypertension: My work on pulmonary hypertension shows an association between the neuro-inflammation and pulmonary hypertension. I have demonstrated for

the first time that activated microglia and other neuro-inflammatory processes in the brain involved pulmonary hypertension and associated right heart pathologies. This data was published in Hypertension. In addition to that, I have successfully demonstrated that gut pathological and microbial changes were associated with pulmonary hypertension (demonstrated in two different models of pulmonary hypertension). This data is published in Hypertension, ERJ-Open Research and AJRCMB.

a. Oliveira AC, Sharma RK, Aquino V, Lobaton G, Bryant AJ, Harrison JK, Richards EM, Raizada MK. Involvement of Microglial Cells in Hypoxia-induced Pulmonary Hypertension. Am J Respir Cell Mol Biol. 2018 Aug;59(2):271-273. PubMed Central PMCID: PMC6096340.
b. Sharma RK, Oliveira AC, Kim S, Rigatto K, Zubcevic J, Rathinasabapathy A, Kumar A, Lebowitz JJ, Khoshbouei H, Lobaton G, Aquino V, Richards EM, Katovich MJ, Shenoy V, Raizada MK. Involvement of Neuroinflammation in the Pathogenesis of Monocrotaline-Induced Pulmonary Hypertension. Hypertension. 2018 Jun;71(6):1156-1163. PubMed Central PMCID: PMC5945302.
c. Sharma RK, Oliveira AC, Yang T, Kim S, Zubcevic J, Aquino V, Lobaton GO, Goel R, Richards EM, Raizada MK. Pulmonary arterial hypertension-associated changes in gut pathology and microbiota. ERJ Open Res. 2020 Jul;6(3) PubMed Central PMCID: PMC7383054.

4. a. Sharma RK, Stevens BR, Obukhov AG, Grant MB, Oudit GY, Li Q, Richards EM, Pepine CJ, Raizada MK. ACE2 (Angiotensin-Converting Enzyme 2) in Cardiopulmonary Diseases: Ramifications for the Control of SARS-CoV-2. Hypertension. 2020 Sep;76(3):651-661. PubMed Central PMCID: PMC7430041.
b. Sharma RK, Li J, Krishnan S, Richards EM, Raizada MK, Mohandas R. Angiotensin-converting enzyme 2 and COVID-19 in cardiorenal diseases. Clin Sci (Lond). 2021 Jan 15;135(1):1-17. PubMed Central PMCID: PMC7796300.
c. Oliveira AC, Yang T, Li J, Sharma RK, Karas MK, Bryant AJ, de Kloet AD, Krause EG, Joe B, Richards EM, Raizada MK. Fecal matter transplant from Ace2 overexpressing mice counteracts chronic hypoxia-induced pulmonary hypertension. Pulm Circ. 2022 Jan;12(1):e12015. PubMed Central PMCID: PMC9052990.
d. Sharma RK, Oliveira AC, Yang T, Karas MM, Li J, Lobaton GO, Aquino VP, Robles-Vera I, de Kloet AD, Krause EG, Bryant AJ, Verma A, Li Q, Richards EM, Raizada MK. Gut Pathology and Its Rescue by ACE2 (Angiotensin-Converting Enzyme 2) in Hypoxia-Induced Pulmonary Hypertension. Hypertension. 2020 Jul;76(1):206-216. PubMed Central PMCID: PMC7505091.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/myncbi/ravindra.sharma.1/bibliography/public/