BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Jussara Marcia do Carmo

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

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
State University of Paraiba, Brazil	BS	12/1993	Physical Therapy
Federal University of Pernambuco, Brazil	M.S.	05/1999	Physiology
University of Sao Paulo	Ph.D.	10/2006	Physiology
Univ. Mississippi Medical Center, Jackson, MS	Postdoctoral Fellow	06/2008	Physiology

A. Personal Statement

The focus of my research has been to understand the mechanisms of renal injury and hypertension that develop in offspring from obese parents. Specifically, we are investigating renal mechanisms by which developmental programming caused by parental obesity and its metabolic abnormalities lead to activation of P2X purinoceptor 7 (P2X7R) and amplification of kidney injury in the offspring, and how therapeutic interventions may improve the long-term health of the offspring from obese parents. In the execution of these studies, we noticed that not only the kidneys are affected by parental obesity, but found that offspring from obese parents develop diastolic dysfunction even when the offspring remain lean, and this cardiac dysfunction worsens with aging and consumption of obesogenic diets. Therefore, a new focus of our team has been to unravel the mechanisms of parental obesity-induced developmental programming of cardiac dysfunction. Our laboratory has also focused on unravelling the central nervous system (CNS) signaling mechanisms and brain regions involved in the regulation of metabolic and cardiovascular function by the leptin-melanocortin axis. Additionally, we are investigating the powerful beneficial effects of the leptin-melanocortin axis on cardiac function in models of myocardial infarction and ischemia/reperfusion injury. We have generated novel genetic mouse models that allow us to unravel the role of the leptin-melanocortin pathway in specific brain nuclei which accompanied by our expertise in conducting acute and chronic sophisticated and integrative physiological studies in mice provide unique and powerful approach to determine the complex circuits and signaling pathways of the CNS control of appetite, BP regulation, cardiac and metabolic functions with broad implication for clinical treatment of cardiovascular and metabolic diseases.

Ongoing and recently completed projects that I would like to highlight include:

RO1 DK121411 (JM do Carmo, PI
NIH/NIDDK “Long-term consequences of parental obesity on developmental programming of cardiorenal diseases in offspring”
Role: PI

P20 GM 104357 (JE Hall, PI)
National Institutes of Health, National Institute of General Medical Science

Cardiorenal and Metabolic Diseases Research Center
Role: Sub-Core Director, Basic Science

P20GM121334 (J Reckelhoff, PI)
National Institutes of Health, National Institute of General Medical Science
Role of microRNA-21 in the androgen-induced metabolic effects in Polycystic Ovary Syndrome – Mississippi Center of Excellence in Perinatal Research – Damian Romero (PI) - Project V.
Role: Co-investigator

Completed Research Support

PO1 HL519717 (JE Hall, PI)
NIH/NHLBI "Cardiovascular dynamics and their control"
The major long-term goal of this project is to investigate the central nervous system signaling pathways that mediate the antidiabetic actions of leptin.
Role: Co-Investigator of Project I

P20 RR024217 do Carmo (PI of Project II)
NIH/NHLBI
"Hypertension and Cardiorenal Diseases Research Center"
The major long-term goal of this project is to investigate the effects of ambient temperature in modulating the actions of leptin on appetite, metabolic and cardiovascular function.
Role: PI of Project II

Citations:

1. Gava FN, da Silva AA, Dai X, Harmancey R, Ashraf S, Omoto ACM, Salgado MC, Moak SP, Li X, Hall JE, **do Carmo JM**. Restoration of cardiac function after myocardial infarction by long-term activation of the CNS leptin-melanocortin system. JACC: Basic Transl Sci. 2021; 6: 55-70
2. da Silva AA, Pinkerton MA, Spradley FT, Palei AC, Hall JE, **do Carmo JM**. Chronic CNS-mediated cardiometabolic actions of leptin: potential role of sex differences. Am J Regul Integr Comp Physiol. 2021; 320: R173-R181.
3. **do Carmo JM**, da Silva AA, Gava, FN, Moak SP, Dai X, Hall, JE. Impact of leptin deficiency compared with neuronal-specific leptin receptor deletion on cardiometabolic regulation. Am J Regul Integr Comp Physiol. 2019; 317: R552-R562.
4. **do Carmo JM**, da Silva AA, Romero DG, Hall JE. Changes in ambient temperature elicit divergent control of metabolic and cardiovascular actions by leptin. FASEB J. 2017; 31: 2418:2428.
5. Rezq Samar, Huffman AM, Syed M, Basnet J, **do Carmo JM**, Moak SP, Cardozo LLY, Romero DG. MicroRNA21- modulates white adipose tissue browning and altered thermogenensis in a mouse model of polycystic ovary syndrome. J Endocr Soc. 2021; 5: A775-A776.
6. Hall JE, Mouton A, da Silva AA, Omoto ACM, Wang Z, Li X, **do Carmo JM**. Obesity, kidney dysfunction and inflammation: interactions in hypertension. Cardiovasc Res. 2020; 1:cvaa336.

B. Positions and Honors

PROFESSIONAL EXPERIENCE/POST GRADUATE TRAINING

1993-1996 Assistant Professor, State University of Paraiba, Campina Grande, State of Paraiba, Brazil.
1996-2002 Assistant Professor, University of Tiradentes, Aracaju, State of Sergipe, Brazil.
1996-1999 Graduate Student, Master in Physiology, Federal University of Pernambuco, State of Pernambuco, Brazil.
2002-2006 Graduate Student – Doctorate in Physiology, University of Sao Paulo, State of Sao Paulo, Brazil.
2006-2008 Postdoctoral Fellowship, University of Mississippi Medical Center, Dept. Physiology, Jackson, Mississippi, USA
2009-2010 Instructor, University of Mississippi Medical Center, Dept. Physiology, Jackson, Mississippi, USA.

2011-218 Assistant Professor, University of Mississippi Medical Center, Dept. Physiology, Jackson, Mississippi.
2018-present Associate Professor, University of Mississippi Medical Center, Dept. Physiology, Jackson, Mississippi.
2012-present Fellow, American Heart Association.

Other Experience and Professional Memberships

1995-present – Brazilian Physiology and Therapeutics Society
2006-present – American Physiological Society
2006-present – American Heart Association
2012-present – Fellow, American Heart Association

FELLOWSHIPS, AWARDS, HONORS

1993-1996	Scholarship recipient, Pre-Doc, Coordination of the Improvement of Higher Education Personnel (CAPES), Research Foundation, Brazil
2002-2006	Doctoral fellowship grant from Coordination of the Improvement of Higher Education Personnel (CAPES), Research Foundation, Brazil
2003	Travel Award from Foundation of Support to Teaching and Research (FAEPA), University of Sao Paulo, Brazil
2004	Travel Award from Office of Dean for Doctoral Program (Pro-Reitoria), University of Sao Paulo
2007	Young Investigator Travel Award, Council for High Blood Pressure Research, Tucson, AZ
2011	Physiological Society (APS)/NIDDK Minority Travel Fellowship Award, Experimental Biology 2011, Washington, DC.
2011-2014	Scientist Development Grant – American Heart Association (AHA)
2011	Finalist, Harry Goldblatt Award for New Investigators, American Heart Association, Council for High Blood Pressure Research
2012	Recipient, Harry Goldblatt Award for New Investigators American Heart Association, Council for High Blood Pressure Research
2013	Young Investigator Award, American Heart Association - Council for High Blood Pressure Research in Australia. Melbourne, Australia
2013	Excellence in Research Award – University of Mississippi Medical Center – Silver Medallion
2014	NISBRE Highlighted Poster, Mississippi IDeA Network of Biomedical Research Excellence (INBRE) Conference, Biloxi, MS – Cardiovascular Section
2016	Excellence in Research Award – University of Mississippi Medical Center – Gold Medallion
2017	Distinction in Scholarship; Selection for APS Select, *The American Journal of Physiology – Endocrinology and Metabolism,* article title: "Role of autonomic nervous system in chronic CNS-mediated antidiabetic action of leptin" APS Select.

C. Contributions to Science

(Selected from over 65 publications which can be found at My NCBI Bibliography)
My NCBI Bibliography: https://www.ncbi.nlm.nih.gov/myncbi/1x7imfM1imy5D/bibliography/public/

1. The leptin-melanocortin system plays a crucial role in regulating appetite, energy expenditure and sympathetic nervous system (SNS) activity. This is evident by the fact that mutation of ob (leptin) gene or melanocortin-4 receptors (MC4R) result in severe obese phenotype in mice and human due to increased food intake and reduced energy expenditure but they have normal or slightly reduced blood pressure. Besides its effect on body weight regulation and SNS activity, leptin-melanocortin system also regulates peripheral glucose uptake. The past few decades have witnessed an unprecedented increase in the

incidence of cardiovascular, renal and metabolic diseases such as diabetes. Of the people diagnosed with diabetes, about 80 to 90 percent are diagnosed as obese suggesting the close link between diabetes and obesity. My early paper examined the role of leptin on glucose regulation and baroreflex sensitivity in streptozotocin (STZ) - induced diabetes. We showed that central nervous system actions of leptin abolished the hyperglycemia and altered baroreflex sensitivity and intrinsic heart rate in this model of diabetes. We also showed that leptin receptor in proopiomelanocortin neurons is necessary for the chronic effects of leptin to raise blood pressure and reduce glucose levels. Recently we demonstrated that the brain leptin-melacortin axis also exert remarkable effects that protect the heart against progressive cardiac dysfunction and heart failure after myocardial infarction (MI). However, many questions still unanswered, for instance, the central nervous system mechanisms triggered by chronic leptin infusion that mediates increased peripheral glucose uptake and improve cardiac function after MI is still unknown and it is one of the focus of our research effort.

a. Gava FN, da Silva AA, Dai X, Harmancey R, Ashraf S, Omoto ACM, Salgado MC, Moak SP, Li X, Hall JE, **do Carmo JM**. Restoration of cardiac function after myocardial infarction by long-term activation of the CNS leptin-melanocortin system. JACC: Basic Transl Sci. 2021; 6: 55-70

b. da Silva AA, Spradley FT, Granger JP, Hall JE, **do Carmo JM**. Brain-mediated antidiabetic, anorexic, and cardiovascular actions of leptin require melanocortin-4 receptor signaling. *J Neurophysiol* 113: 2786-91, 2015. PMID: 25717164.

c. **do Carmo JM**, da Silva AA, Cai Z, Lin S, Dubinion JH, Hall JE. Control of blood pressure, appetite, and glucose by leptin in mice lacking leptin receptors in proopiomelanocortin neurons. *Hypertension*. 57: 918-926. 2011. PMID: 21422382

d. da Silva AA, **do Carmo JM**, Freeman JN, Tallam LS, Hall JE. A functional melanocortin system is required for CNS-mediated antidiabetic and cardiovascular actions of leptin. *Diabetes*. 58: 1749-1756, 2009. PMID: 19491210

e. **do Carmo** JM, Hall JE, da Silva AA. Chronic central leptin infusion restores cardiac sympathetic-vagal balance and baroreflex activity in diabetic rats. Am J Physiol Heart Circ Physiol. 295: H1974-81, 2008. PMID: 18790839

f. da Silva AA, **do Carmo JM**, Wang Z, Hall JE. The brain melanocortin system, sympathetic control and obesity hypertension. *Physiology (Bethesda)* 29:196-202, 2014.

g. da Silva AA, **do Carmo JM**, Hall JE. CNS Regulation of Glucose Homeostasis: Role of the Leptin-Melanocortin System. *Curr Diab Rep* 20(7):29, 2020. PMID: 32451760.

2. In addition to the studies described above, we have also examined the role of the brain leptin-melanocortin system in linking obesity with increased sympathetic activity and hypertension. These studies emphasized which specific brain regions are most important in mediating the effects of leptin-melanocortin-4 receptor activation on food intake, energy expenditure and blood pressure regulation. This body of work is providing us fundamental insights into metabolic and cardiovascular regulation that may lead to therapeutic approaches to improve body weight control and metabolic functions independent of increased blood pressure.

a. **do Carmo JM**, da Silva AA, Hall JE. Role of hindbrain melanocortin-4 receptor activity in controlling cardiovascular and metabolic functions in spontaneously hypertensive rats. *J Physiol Hypertens* 33: 1201-6, 2015. PMID: 25668357

b. **do Carmo JM**, da Silva AA, Dubinion J, Sessums PO, Ebaady SH, Wang Z, Hall JE. Control of metabolic and cardiovascular function by the leptin-brain melanocortin pathway. *IUBMB Life* 65(8):692-8, 2013.

c. do Carmo JM, da Silva AA, Rushing JS, Pace B, Hall JE. Differential control of appetite and cardiovascular function in mice with selective rescue of melanocortin-4 receptor in proopiomelanocortin neurons. *Am J Physiol Regul Integr Comp Physiol* 305(4):R359-68, 2013.

d. **do Carmo JM**, Bassi M, da Silva AA, Hall JE. Systemic but not central nervous system nitric oxide synthase inhibition exacerbates the hypertensive effects of chronic melanocortin-3/4 receptor activation. *Hypertension*. 57: 428-34, 2011. PMID: 21263126

e. **do Carmo JM**, da Silva AA, Rushing JS, Hall JE. Activation of the central melanocortin system contributes to the increased arterial pressure in obese Zucker rats. *Am J Physiol Regul Integr Comp Physiol* 302(5):R561-R567, 2012. PMID: 22204957

f. **do Carmo JM**, Tallam SM, Roberts JV, Brandon EL, Biglane J, Silva AA Hall JE. Impact of obesity on renal structure and function in the presence and absence of hypertension: evidence from melanocortin 4 receptor deficient mice. *Am J Physiol Regul Integr Comp Physiol.* 297: R803:R812, 2009. PMID: 19605765

3. The complex central nervous system (CNS) circuits and cell signaling mechanisms for the differential control of leptin's metabolic and cardiovascular effects remain poorly understood. We are using novel genetically engineered mouse models and sophisticated state-of-the-art molecular and integrative physiological phenotyping to study the role of leptin receptor signaling via downstrain signaling in specific areas of the CNS in mediating its chronic metabolic and cardiovascular effects. The outcome from our experiments will provide important and novel information that could lead to new therapeutic approaches for the treatment of hypertension and metabolic disorders, including obesity and diabetes, which are major causes of cardiovascular and renal disease worldwide.
   a. **do Carmo JM**, da Silva AA, Freeman JN, Wang Z, Moak SP, Hankins MW, Drummond HA, Hall JE. Neuronal Suppressor of Cytokine Signaling 3: Role in Modulating Chronic Metabolic and Cardiovascular Effects of Leptin. Hypertension *Hypertension*. 71: 1248-1257, 2018. PMID: 29686012.
   b. da Silva AA, Freeman JN, Hall JE, **do Carmo JM**. Control of Appetite, Blood Glucose ad Blood Pressure During Melanocortin-4 Activation in Normoglycemic and Diabetic NPY Deficient Mice. *Am J Physiol Integr Comp Physiol*. 314: R533-R539, 2017PMID: 29351428
   c. **do Carmo JM**, da Silva AA, Ebaady SE, Sessums PO, Abraham RS, Elmquist JK, Lowell BB, Hall JE. Shp2 signaling in Pomc neurons is important for leptin's actions on blood pressure, energy balance and glucose regulation. *Am J Physiol Regul Integr Com Physiol* 307: R1438-47, 2014. PMID: 25339680
   d. da Silva AA, **do Carmo JM**, Wang Z, Hall JE. The brain melanocortin system, sympathetic control and obesity hypertension. *Physiology (Bethesda)* 29:196-202, 2014.
   e. do Carmo JM, **da Silva AA**, Gava FN, Moak SP, Dai X, Hall JE. Impact of leptin deficiency compared with neuronal-specific leptin receptor deletion on cardiometabolic regulation. *Am J Physiol Regul Integr Comp Physiol* 317(4):R552-62, 2019. PMID: 31411897
   f. Wang Z, **do Carmo JM**, Aberdein N, Zhou X, Williams JM, da Silva AA, Hall JE. Synergistic interaction of hypertension and diabetes in promoting kidney injury and the role of endoplasmic reticulum stress. *Hypertension*. 2017; 69: 879-891. PMID: 28348018