BIOGRAPHICAL SKETCH

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NAME: Elise Peery Gomez-Sanchez

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

POSITION TITLE: Professor of Pharmacology & Physiology

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
Case Western Reserve University, Cleveland, OH	BS	1971	Biology
Texas A & M University , College Station, Texas	DVM	1977	Veterinary Medicine
Southwestern Medical School, Dallas, Texas	Post-doc	1977-8	Pharmacology
Texas A & M University , College Station, Texas	PhD	1982	Physiology & Pharmacology

NOTE: The Biographical Sketch may not exceed five pages. Follow the formats and instructions below.

A. Personal Statement

My primary recent research focus has been the regulation of the synthesis and action of adrenal steroids, especially aldosterone (1,2) (3-7), and the biology of the mineralocorticoid receptor (MR) and its ligands, reviewed in (8,9) , with particular focus on its role in pathological cardiac, renal and vascular remodeling and its actions in the central nervous system (10-12). I recently broadened my focus to include neuro and muscular degenerative diseases (13-18). Among techniques used have been pharmacological and physiological studies in animals and cultured cells, including those genetically engineered by us, biochemistry and molecular biology, and histopathology and immunohistochemistry. My change from full-time investigator at the VA for 30 years with 1/8th affiliation in the Department of medicine, to a full time professor position in the Department of Pharmacology & Toxicology allowed me much greater opportunity to teach Medical, Dental, and Graduate students, which I enjoyed immensely, while allowing me to continue research collaborations. The University and VA are across the street from each other, thus the distance posed no problem for communication. I was asked to retire in May of 2020, ostensibly as a cost saving measure for the university during the Sar-Cov2 pandemic. I retained enough University hours to honor commitments to ongoing funded research and continue collaborations while based primarily at the VA except for animal work, as the VA contracts space in the research animal facilities at UMMC. My recent publications are listed at
https://www.ncbi.nlm.nih.gov/myncbi/1z5ENUr_k7QkU/bibliography/public/

1. Vohra T, Kemter E, Sun N, Dobenecker B, Hinrichs A, Burrello J, Gomez-Sanchez EP, Gomez-Sanchez CE, Wang J, Kinker IS, Teupser D, Fischer K, Schnieke A, Peitzsch M, Eisenhofer G, Walch A, Reincke M, Wolf E, Williams TA. Effect of Dietary Sodium Modulation on Pig Adrenal Steroidogenesis and Transcriptome Profiles. *Hypertension*. 2020;76(6):1769-1777.
2. Gomez-Sanchez CE, Gomez-Sanchez EP. Immunohistochemistry of the adrenal in primary aldosteronism. *Current opinion in endocrinology, diabetes, and obesity*. 2016;23(3):242-248.
3. Gomez-Sanchez CE, Kuppusamy M, Gomez-Sanchez EP. Somatic mutations of the ATP1A1 gene and aldosterone-producing adenomas. *Molecular and cellular endocrinology*. 2015;408:213-219.

4. Gioco F, Seccia TM, Gomez-Sanchez EP, Rossi GP, Gomez-Sanchez CE. Adrenal histopathology in primary aldosteronism: is it time for a change? *Hypertension*. 2015;66(4):724-730.
5. Gomez-Sanchez CE, Qi X, Gomez-Sanchez EP, Sasano H, Bohlen MO, Wisgerhof M. Disordered zonal and cellular CYP11B2 enzyme expression in familial hyperaldosteronism type 3. *Molecular and cellular endocrinology*. 2017;439:74-80.
6. Oki K, Plonczynski MW, Gomez-Sanchez EP, Gomez-Sanchez CE. YPEL4 modulates HAC15 adrenal cell proliferation and is associated with tumor diameter. *Molecular and cellular endocrinology*. 2016;434:93-98.
7. Nishimoto K, Koga M, Seki T, Oki K, Gomez-Sanchez EP, Gomez-Sanchez CE, Naruse M, Sakaguchi T, Morita S, Kosaka T, Oya M, Ogishima T, Yasuda M, Suematsu M, Kabe Y, Omura M, Nishikawa T, Mukai K. Immunohistochemistry of aldosterone synthase leads the way to the pathogenesis of primary aldosteronism. *Molecular and cellular endocrinology*. 2017;441:124-133.
8. Gomez-Sanchez EP, Gomez-Sanchez CE. 11beta-hydroxysteroid dehydrogenases: A growing multi-tasking family. *Molecular and cellular endocrinology*. 2021;526:111210.
9. Gomez-Sanchez E, Gomez-Sanchez CE. The multifaceted mineralocorticoid receptor. *Compr Physiol*. 2014;4(3):965-994.
10. Gomez-Sanchez CE, Gomez-Sanchez EP. The Mineralocorticoid Receptor and the Heart. *Endocrinology*. 2021.
11. Gomez-Sanchez EP. Brain mineralocorticoid receptors in cognition and cardiovascular homeostasis. *Steroids*. 2014;91:20-31.
12. Chen J, Gomez-Sanchez CE, Penman A, May PJ, Gomez-Sanchez E. Expression of mineralocorticoid and glucocorticoid receptors in preautonomic neurons of the rat paraventricular nucleus. *American journal of physiology Regulatory, integrative and comparative physiology*. 2014;306(5):R328-340.
13. Chadwick JA, Hauck JS, Gomez-Sanchez CE, Gomez-Sanchez EP, Rafael-Fortney JA. Gene expression effects of glucocorticoid and mineralocorticoid receptor agonists and antagonists on normal human skeletal muscle. *Physiological genomics*. 2017;49(6):277-286.
14. Chadwick JA, Hauck JS, Lowe J, Shaw JJ, Guttridge DC, Gomez-Sanchez CE, Gomez-Sanchez EP, Rafael-Fortney JA. Mineralocorticoid receptors are present in skeletal muscle and represent a potential therapeutic target. *FASEB journal : official publication of the Federation of American Societies for Experimental Biology*. 2015;29(11):4544-4554.
15. Chadwick JA, Swager SA, Lowe J, Welc SS, Tidball JG, Gomez-Sanchez CE, Gomez-Sanchez EP, Rafael-Fortney JA. Myeloid cells are capable of synthesizing aldosterone to exacerbate damage in muscular dystrophy. *Human molecular genetics*. 2016;25(23):5167-5177.
16. Hauck JS, Howard ZM, Lowe J, Rastogi N, Pico MG, Swager SA, Petrosino JM, Gomez-Sanchez CE, Gomez-Sanchez EP, Accornero F, Rafael-Fortney JA. Mineralocorticoid Receptor Signaling Contributes to Normal Muscle Repair After Acute Injury. *Frontiers in physiology*. 2019;10:1324.
17. Lowe J, Floyd KT, Rastogi N, Schultz EJ, Chadwick JA, Swager SA, Zins JG, Kadakia FK, Smart S, Gomez-Sanchez EP, Gomez-Sanchez CE, Raman SV, Janssen PM, Rafael-Fortney JA. Similar efficacy from specific and non-specific mineralocorticoid receptor antagonist treatment of muscular dystrophy mice. *Journal of neuromuscular diseases*. 2016;3(3):395-404.
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B. Positions & Honors

1980-1983: Instructor- Department of Internal Medicine, University of South Florida College of Medicine
1983-1993: Associate Professor, Departments of Internal Medicine & Pharmacology (adjunct), University of South Florida College of Medicine
1984-1993: Research Physiologist, James A Haley Veterans Administration Hospital, Tampa, FL
1993-1997: Associate Professor: Depts. of Internal Medicine, College of Medicine, & adjunct in Biomedical Sciences, College of Veterinary Medicine, University of Missouri-Columbia
1997-1999: Professor: Depts. of Internal Medicine, College of Medicine, & adjunct in Biomedical Sciences College of Veterinary Medicine, University of Missouri-Columbia
1993-1999: Research Scientist: Harry Truman VAMC, Columbia, MO.

1999- 2014: Professor: Department of Medicine
Adjunct professor Departments of Pharmacology & Toxicology and Neurobiology Anatomical Sciences, University of Mississippi Medical Center, Jackson MS.
1999-2014: Research Scientist: GV Montgomery VAMC, Jackson MS.
2012-2013: Acting ACOS for Research, G.V. Montgomery VA Medical
2014-2020: Professor: Department of Pharmacology & Toxicology
Course director: Mechanisms of Drug Action; Methods & Experimental Design
2014-2020: WOC (Worker with Out Compensation), G.V. Montgomery VAMC
Adjunct professor Departments of Medicine and Neurobiology & Anatomical Sciences, University of Mississippi Medical Center, Jackson MS.
2020- Professor: Department of Pharmacology & Toxicology part-time 0.1 FTE

Honors
Member, advisory board for *Comprehensive Physiology*; 2015-2020
Member, Editorial Board, Frontiers in Cardiovascular Medicine, 2014-present
Biosafety Officer, G.V. Montgomery VAMC, April 2010-present
Chairman, Radiation Safety Committee, G.V. Montgomery VAMC Center 2001-present
Associate Editor: *Cardiorenal Medicine:* 2013-2018
Member, Program in Neuroscience Executive Committee: 2014-2018
Chairman, Research Safety Committee, 2000-2010
NIH Study Sections: SBIR, Cardiovascular & Renal (reorganized to Hypertension & Microcirculation) 2003-2007; ZRG 2009-2010; CMRC: 2008-2012.
American Heart Association study sections: 1989-1994; 2008; 2013-present.
Veterans Affairs study sections: various: 1990-2013
Editorial Board: *Hypertension* 12/1997-2012; *Endocrinology* 2006-2010
Fellow, Council for High Blood Pressure Research, American Heart Association, 1995-present
Board of Professional Regulation for Veterinary Medicine in Florida 1987-1991; 1992-1993

C. Contribution to Science

1. We were the first to directly confirm the role of brain mineralocorticoid receptors (MR) in hypertension by demonstrating that the intracerebroventricular (icv) infusion of aldosterone at a dose that does not increase circulating aldosterone induces hypertension (19) and that the icv infusion of an MR antagonist at a dose that is ineffective systemically, blocks the hypertension induced by systemic aldosterone excess in normotensive rats and in salt-induced hypertension in Dahl Salt-Sensitive Rats(20,21). We also were first to report that well known mechanisms of MR action in the kidney, including epithelial sodium channel activation, are also involved in CNS regulation of the blood pressure(22,23). We demonstrated for the first time the cellular and subcellular localization of the MR, in the presympathetic neurons of the paraventricular nucleus (12) confirming direct modulation of the sympathetic nervous system by adrenocorticoid steroids.
2. We also demonstrated that MR-induced pathological cardiovascular remodeling occurred independently of hypertension(24), supporting the concept tested clinically in the RALES trial that showed that an MR antagonist significantly ameliorates heart failure at doses that do not lower blood pressure (25). MR antagonists are now standard therapy for heart failure and are increasingly used routinely to slow renal and cardiac fibrosis.
3. Studies of mechanisms for MR ligand specificity led to studies of splice variants and post translational modifications of the MR and enzymes of pre-receptor ligand modulation(26,27). To do this we produced the first truly specific antibodies to detect the MR(28,29), rat 11β-hydroxysteroid dehydrogenase 2, and H6PDH. Using these tools we demonstrated how aldosterone activates MR in pre-sympathetic neurons of the PVN despite the stoichiometric advantage of CNS glucocorticoid concentrations (12).
4. Our lab was the first to demonstrate that all of the steroidogenic enzymes required for aldosterone, cortisol and corticosterone synthesis from cholesterol were expressed and active in the human and rat brain(30-33) and that this extra-adrenal synthesis contributed to hypertension in the Dahl SS rat(34). More recently we collaborated with others to demonstrate extra-adrenal aldosterone synthesis by adipocytes (35) and myeloid cells associated with skeletal muscle (15).

5. To these ends we have had to develop very selective antibodies and sensitive assays to measure adrenal steroids and metabolites, but in particular, minute quantities of aldosterone and corticosterone in tissues. Our aldosterone antibody is used in the most widely sold human clinical assays in the USA (Millipore). Among the more recent antibodies that we have produced are those detecting human CYP11B1 & 2 enzymes required for the last step in synthesis of cortisol and aldosterone (36). These antibodies have revolutionized the diagnosis and study of mechanisms for human primary aldosteronism (37). All of the reagents developed for our studies, including poly- and monoclonal antibodies (clones have been donated to ATCC and NIH Developmental Studies Hybridoma Bank), cell models, plasmids, and viral vectors are provided at no cost to other investigators upon request.
6. More recently we have turned our attention to MR in other tissues, including skeletal muscle, and are collaborating with others at Ohio State University who have demonstrated an MR antagonist slows the progression of Duchenne muscular dystrophy mouse modes (13-18).

19. Gomez-Sanchez EP. Intracerebroventricular infusion of aldosterone induces hypertension in rats. *Endocrinology*. 1986;118(2):819-823.
20. Gomez-Sanchez EP, Fort CM, Gomez-Sanchez CE. Intracerebroventricular infusions of RU28318 blocks aldosterone-salt hypertension. *The American journal of physiology*. 1990;258:E482-E484.
21. Gomez-Sanchez EP, Fort C, Thwaites D. Central mineralocorticoid receptor antagonism blocks hypertension in Dahl S/JR rats. *The American journal of physiology*. 1992;262:E96-E99.
22. Gomez-Sanchez EP, Gomez-Sanchez CE. Effect of central amiloride infusion on mineralocorticoid hypertension. *The American journal of physiology*. 1994;267:E754-E758.
23. Gomez-Sanchez EP, Gomez-Sanchez CE. The effect of the central infusion of benzamil on Dahl S rat hypertension. *The American journal of physiology*. 1995;269:H1044-H1047.
24. Gomez-Sanchez CE, Gomez-Sanchez EP, Cozza EN. Endothelin stimulation of aldosterone secretion in bovine adrenal cells. In: Baldi E, Maggi M, Cameron IT, Dunn MJ, eds. Endothelins in Endocrinology: New advances. Rome: Ares Serono Symposia; 1995:227-233.
25. Pitt B, Zannad F, Remme WJ, Cody R, Castaigne A, Perez A, Palensky J, Wittes J. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med*. 1999;341(10):709-717.
26. Gomez-Sanchez EP, Gomez-Sanchez CE. Central Hypertensinogenic effects of glycyrrhizic acid and carbenoxolone. *The American journal of physiology*. 1992;263:E1125-E1130.
27. Gomez-Sanchez EP, Ganjam V, Chen YJ, Liu Y, Clark SA, Gomez-Sanchez CE. The 11beta hydroxysteroid dehydrogenase 2 exists as an inactive dimer. *Steroids*. 2001;66(11):845-848.
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29. Gomez-Sanchez CE, Warden M, Gomez-Sanchez MT, Hou X, Gomez-Sanchez EP. Diverse immunostaining patterns of mineralocorticoid receptor monoclonal antibodies. *Steroids*. 2011;76(14):1541-1545.
30. Gomez-Sanchez CE, Zhou MY, Cozza EN, Morita H, Eddleman FC, Gomez-Sanchez EP. Corticosteroid synthesis in the central nervous system. *Endocrine research*. 1996;22:463-470.
31. Gomez-Sanchez CE, Zhou MY, Cozza EN, Morita H, Foecking MF, Gomez-Sanchez EP. Aldosterone biosynthesis in the rat brain. *Endocrinology*. 1997;138:3369-3373.
32. Yu L, Romero DG, Gomez-Sanchez CE, Gomez-Sanchez EP. Steroidogenic enzyme gene expression in the human brain. *Molecular and cellular endocrinology*. 2002;190(1-2):9-17.
33. Gomez-Sanchez EP, Ahmad N, Romero DG, Gomez-Sanchez CE. Is aldosterone synthesized within the rat brain? *American journal of physiology Endocrinology and metabolism*. 2005;288(2):E342-346.
34. Gomez-Sanchez EP, Gomez-Sanchez CM, Plonczynski M, Gomez-Sanchez CE. Aldosterone synthesis in the brain contributes to Dahl salt-sensitive rat hypertension. *Experimental physiology*. 2010;95(1):120-130.
35. Briones AM, Cat AN, Callera GE, Yogi A, Burger D, He Y, Correa JW, Gagnon AM, Gomez-Sanchez CE, Gomez-Sanchez EP, Sorisky A, Ooi TC, Ruzicka M, Burns KD, Touyz RM. Adipocytes produce aldosterone through calcineurin-dependent signaling pathways: implications in diabetes mellitus-associated obesity and vascular dysfunction. *Hypertension*. 2012;59(5):1069-1078.

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37. Nakamura Y, Maekawa T, Felizola SJ, Satoh F, Qi X, Velarde-Miranda C, Plonczynski MW, Ise K, Kikuchi K, Rainey WE, Gomez-Sanchez EP, Gomez-Sanchez CE, Sasano H. Adrenal CYP11B1/2 expression in primary aldosteronism: Immunohistochemical analysis using novel monoclonal antibodies. *Molecular and cellular endocrinology*. 2014;392(1-2):73-79.

Bibliography at NCBI: https://www.ncbi.nlm.nih.gov/myncbi/1z5ENUr_k7QkU/bibliography/public/

D. Current Research Support

NHLBI R01 HL144847-2 **Adrenal cell ATP1A1 mutations and mechanisms of aldosterone biosynthesis** CE Gomez-Sanchez PI; EP Gomez-Sanchez co-PI 7/1/2019-6/30/2023 $250,000/year

The aim of this proposal is to study the mechanisms of the stimulation of aldosterone secretion mediated by mutations of the sodium potassium ATPase 1A1 (ATP1A1). Elise P. Gomez-Sanchez: role: joint design of experiments, data interpretation, and report and manuscript preparations. All animal work and tissue preparation

VA I01BX004681 CE Gomez-Sanchez; EP Gomez-Sanchez collaborator 10/01/2019-03/31/2023
Regulation of Mineralocorticoid Receptor Action $165,000/yr (+50,000 equipment for first year)
This proposal is to address mechanisms of aldosterone action, specifically the role of the carbonyl reductase in the protection of the mineralocorticoid receptor and the role of phosphorylation of the mineralocorticoid receptor in regulating its activity. Elise P. Gomez-Sanchez: role: joint design of experiments, data interpretation, and report and manuscript preparations. All animal work and tissue preparation.

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