BIOGRAPHICAL SKETCH

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NAME: Scheuer, Deborah

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

POSITION TITLE: Associate Professor of Physiology & Functional Genomics

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
University of Hawaii, Honolulu, HI	BS Honors	1981	Biology
Univ. of California, San Francisco	Ph.D.	1988	Physiology
Univ. of TX Health Science Center, San Antonio, TX	Post-doc	1988-91	Neural Control of the Circulation

A. Personal Statement

I have been investigating the interactions between the endocrine system and nervous system in the control of blood pressure since I was in graduate school at the University of California, San Francisco, with the exception of two years that I spent in the pharmaceutical industry. I have had continuous NIH funding for this work since 1997. My research currently focuses on two interrelated areas: effects of Angiotensin II on the central nervous system control of blood pressure and the role of corticosteroids and stress in central nervous system control of blood pressure. The research effort planned in the current application is directly related to one of my emphasis areas, the effects of Angiotensin II on the central nervous system control of blood pressure. I have extensive experience with major survival surgery, measurement of cardiovascular and endocrine parameters (including baroreflex function) under unstressed and stressed conditions, Real Time rtPCR and immunohistochemistry. I also have previous experience with electrophysiological methods that will allow for additional mechanistic experiments beyond the ones proposed in the present application. Furthermore, I have breadth and depth of expertise in the Nucleus of the Solitary tract (NTS), the region of the brain that is the focus of the application. I am aware of the complex nature of the role that GABAergic neurotransmission contributes to the processing of visceral afferent and descending inputs within the NTS. Additionally, pertinent to this application that focuses on the angiotensin type 2 receptor (AT2R), I was among the first to report that AT2R could mediate a reduction in blood pressure in the presence of angiotensin type 1 receptor (AT1R) blockade. The central hypothesis of this application arose from the unique synergistic expertise of Dr. Krause, Dr. Sumners and myself, and we have an established collaboration. Therefore, I feel that I provide important expertise to the group and I am excited to be a member of this research team.

Scheuer D.A. and Perrone M.H. Angiotensin type 2 receptors mediate depressor phase of biphasic pressure response to angiotensin. *Am. J. Physiol. Regul. Integr. Comp. Physiol.* 264: R917-R923, 1993. PMID: 8498601

B. Positions and Employment

1982-84 Laboratory Instructor, Physiology, Schools of Medicine, Dentistry and Pharmacy, University of California, San Francisco, CA (Dr. R. Kellog). Instructor, National Dental Board Examination Review, School of Dentistry, University of California, San Francisco CA

1990 Co-coordinator and Instructor, Graduate Physiology, Department of Kinesiology, The University of Texas, Austin TX

1988-91 Postdoctoral Fellow, Department of Pharmacology, University of Texas Health Science Center, San Antonio TX (DR. V. S. Bishop)

1991-93 Research Scientist, Cardiovascular Biology, Rhone-Poulenc Rorer, Inc.
1993 Sr. Research Scientist, Cardiovascular Biology, Rhone-Poulenc Rorer, Inc.
1994 Consultant, Cardiovascular Biology, Rhone-Poulenc Rorer, Inc.
1993-98 Instructor, Department of Pharmacology, The University of Texas Health Science Center, San Antonio
1998-99 Research Assistant Professor, Department of Pharmacology, The University of Texas Health Science Center, San Antonio
1999-05 Assistant Professor, Division of Pharmacology, University of Missouri-Kansas City
2005-06 Associate Professor, Division of Pharmacology, University of Missouri-Kansas City
2006- Associate Professor, Dept. Of Physiology & Functional Genomics, University of Florida

Other Experience and Professional Memberships

1987-present American Physiological Society
1998-present American Heart Association (FAHA since 2001)
2002- 2005 Member, American Physiological Society Careers in Physiology Committee
2006-present Endocrine Society
2001-2013 Ad Hoc reviewer for NIH
2005-2008 Member, Programming Committee, Neural Control of Autonomic Function section of the American Physiological Society
2006-2007 National American Heart Association study section member
2008-2011 American Heart Association Affiliate study section
2009-2012 Member, NCAR Steering Committee, American Physiological Society
2009-2012 Member, Committee on Committees, American Physiological Society
2010-2015 Ad hoc Chair, NIH PO1 Study Section
2010-present Member *Hypertension* Editorial Board
2013- Member, NIH Study Section (Hypertension and Microcirculation)
2014- Member, *American Journal of Physiology Heart and Circulatory Physiology* Editorial Board

Honors

1983-84 Regents Scholarship, University of California, San Francisco, CA
1984-85 Chancellors Fellowship, University of California, San Francisco, CA
2004 Member of NIH Working Group on Cardiovascular Consequences of Chronic Stress
2009 Organizer and Chair, Experimental Biology cross-sectional symposium
2011, 2013 University of Florida College of Medicine Exemplary Teacher Award

C. Contribution to Science

1. **Neural and hormonal control of renin secretion**. My early work, while I was in graduate school, focused on the roles of the renal sympathetic nerves and atrial natriuretic peptide (ANP) in the control of renin secretion. ANP was discovered while I was in graduate school and we were the first to show that release of ANP caused by elevated right atrial pressure could inhibit the renin response to systemic hypotension. The work also demonstrated that ANP was a potent inhibitor of renal baroreceptor-induced renin secretion. All these experiments were performed in chronically instrumented conscious dogs. This work added significantly to the understanding of how atrial natriuretic peptide could counteract the renin-angiotensin-aldosterone system.

   a) Scheuer DA, Thrasher TN, Keil LC and Ramsay DJ. Mechanism of inhibition of renin response to hypotension by atrial natriuretic factor. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 257: R194-203, 1989. PMID: 2546456
   b) Scheuer DA, Thrasher TN and Ramsay DJ. Role of renal sympathetic nerves in renin inhibition by elevated left atrial pressure. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 256: R413-R420, 1989. PMID: 2644850
   c) Scheuer, DA, Thrasher TN, Quillen EW Jr, Metzler CH and Ramsay DJ. Atrial natriuretic peptide blocks renin response to renal hypotension. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 251: R423-R427, 1987. PMID: 2949634

2. **Novel mechanisms of baroreflex regulation.** One of my areas of expertise is in the reflex control of blood pressure, especially with regard to NTS mechanisms controlling arterial baroreflex function. While working with Dr. Vernon Bishop I performed experiments that investigated how arginine vasopressin (AVP) acts at the area postrema to alter nucleus of the solitary tract (NTS) processing of the baroreceptor reflex. This work contributed to the understanding that AVP, while being a potent vasoconstrictor, can also enhance arterial baroreflex function to modulate the vasoconstriction-induced increases in blood pressure. I subsequently worked with Dr. Steve Mifflin and performed experiments that advanced our understanding of the processing of baroreceptor afferent information at the first synapse in the NTS. We demonstrated that neurons receiving monosynaptic input from baroreceptor afferents are resistant to time-dependent inhibition, and thus can relay afferent information regarding prevailing blood pressure with high fidelity. These experiments, in addition to data in the literature, led me to conduct experiments showing for the first time that glucocorticoids (a primary stress hormone) can act in the NTS to produce a long-term attenuation of baroreflex function that could promote the development and maintenance of hypertension, in part by modulating AMPA-receptor mediated effects. This work reversed the previous dogma that glucocorticoids acted within the CNS to reduce blood pressure.

   a) Bechtold AG and Scheuer DA. Glucocorticoids act in the dorsal hindbrain to modulate baroreflex control of heart rate. *Am. J. Physiol. Regul Integr Comp Physiol.*, 290: R1003-R1011, 2006. PMID: 16269575
   b) Shank S and Scheuer DA. Glucocorticoids reduce responses to AMPA receptor activation and blockade in nucleus tractus solitarius. *Am. J. Physiol. Heart Circ. Physiol.,* 284: H1751-H1761, 2003. PMID: 12531728
   c) Scheuer DA, Zhang J, Toney GM and Mifflin SW. Temporal processing of aortic nerve evoked activity in the nucleus of the solitary tract. *J. Neurophysiol*, 76: 3750-3757, 1996. PMID: 8985873
   d) Scheuer DA and Bishop VS. Effect of arginine vasopressin on baroreflex control of hindquarter vascular resistance and lumbar sympathetic nerve activity. *Am. J. Physiol. Heart Circ. Physiol.*, 270: H1963-H1971, 1996. PMID: 8764245

3. **Glucocorticoids and neural control of blood pressure and cardiovascular function in stress-beyond the baroreflex.** The mechanisms linking chronic stress to hypertension remain poorly understood. The experiments described above demonstrating that glucocorticoids can act in the NTS to modulate baroreflex function and promote hypertension led to the hypothesis that elevated glucocorticoids contribute to the adverse effects of stress on cardiovascular function. This body of work has demonstrated that glucocorticoids can mimic and mediate some of these adverse cardiovascular effects including elevated baseline blood pressure and sympathetic nerve activity, exaggerated blood pressure responses to acute novel stress and exacerbated cardiac injury during myocardial ischemia.
   a) Daubert D, Looney B, Clifton R, Cho J. and Scheuer DA. Elevated corticosterone in the dorsal hindbrain increases plasma norepinephrine and neuropeptide Y, and recruits a vasopressin response to stress. Am J Physiol Regul Integr Comp Physiol. 307: 212-224, 2014. PMID: 24829502
   b) Bechtold AG, Patel G, Hochhaus G and Scheuer DA. Chronic blockade of hindbrain glucocorticoid receptors reduces blood pressure responses to novel stress and attenuates adaptation to repeated stress. *Am. J. Physiol. Regul Integr Comp Physiol.*, 296: R1445-R1454, 2009. PMID: 19279295
   c) Bechtold AG, Vernon K, Hines T and Scheuer DA. Genetic predisposition to hypertension sensitizes borderline hypertensive rats to the hypertensive effects of prenatal glucocorticoid exposure. *J. Physiol.*, 586: 673-684, 2008. PMID: 18006585
   d) Scheuer DA. and Mifflin SW. Chronic corticosterone treatment increases myocardial infarct size in rats with ischemia reperfusion injury. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 272: R2017-R2024, 1997. PMID: 9227623

4. **Novel mechanisms in the paraventricular nucleus of the hypothalamus (PVN) that influence stress-induced elevations in blood pressure.** More recently I have been collaborating with Dr. Sumners and Dr. Krause to investigate PVN mechanisms of blood pressure regulation during stress. Others have shown that osmotic and psychological stress-induced increases in blood pressure and HPA axis function are mediated in part by elevated angiotensin II in the PVN. We have determined that macrophage migration inhibitory factor is a negative regulator, while brain derived neurotrophic factor is a positive regulator, of these angiotensin-mediated effects. In a separate line of investigation we have demonstrated

that osmotic stress coupled with psychological stress can induce plasticity of neurotransmitter expression in PVN neurons. These findings are new, and lay the groundwork for the discovery of mechanisms of neuroplasticity that underlie stress-induced hypertension.

a) Smith JA, Scheuer DA, Hiller H, Wang L, de Kloet AD, Krause E. Chronic salt loading increases corticotrophin releasing hormone expression within pre-autonomic neurons in the paraventricular nucleus of male *Mus musculus*. J. Comp. Neurol., in revision.
b) Erdos B, Clifton RR, Liu M, McCowan ML, Sumners C and Scheuer DA. Novel mechanism within the paraventricular nucleus reduces both blood pressure and hypothalamic pituitary-adrenal axis responses to acute stress. Am. J. Physiol. Heart Circ. Physiol. 309: H634-645, 2015. PMID: 26071542
c) Erdos B., Backes I., McCowan ML, Hayward LF and Scheuer DA. Brain-derived neurotrophic factor modulates angiotensin signaling in the hypothalamus to increase blood pressure in rats. Am. J. Physiol. Heart Circ. Physiol, 308:H612-622, 2015. PMID: 25576628

Complete list of Published work in PubMed: http://www.ncbi.nlm.nih.gov/pubmed/?term=Scheuer+da

D. Research Support

ACTIVE

D. Research Support.
Ongoing Research Support

2 R01 HL076807-07A2 Scheuer (PI) 07/18/11 - 06/308/16
NIH/NHLBI with dual assignment to NIDDK
"Glucocorticoids, Stress and Blood Pressure Regulation"
The major goal of this project is to determine the role of dorsal hindbrain glucocorticoid receptors on glucocorticoid-mediated modulation of blood pressure regulation
Role: PI

Recently Completed Support

1 R01 HL093186-01A1 (Scheuer and Sumners, Multiple PI) 08/01/2009-07/31/2015
NIH/NHLBI
"Paraventricular nucleus regulatory mechanisms in stress and hypertension"
The major goal of this project is to investigate the interactive roles of angiotensin II and macrophage migration inhibitory factor within the paraventricular nucleus of the hypothalamus in the regulation of cardiovascular and neuroendocrine responses to stress.
Role: Co-PI

10GRNT4460047 Scheuer 07/01/10-06/30/2013
American Heart Association, Southeast Affiliate Grant-in-Aid
"Nucleus Tractus Solitarius catecholaminergic neurons and glucocorticoid-mediated blood pressure regulation"
The major goal of this project is to determine the Nucleus of the Solitary Tract catecholaminergic neurons on mediating the cardiovascular effects of glucocorticoids and stress.
Role: PI

R01 HD056288-01 Keller-Wood (PI) 06/01/06 – 05/31/2013
NIH/NICHD
"The baroreflex in pregnancy: effects of adrenal and placental steroids"
The major goal of this project is to determine if the effects of cortisol on the baroreflex responsiveness in pregnant and nonpregnant ewes are mediated by MR or GR and to test for interactions of estradiol and progesterone on the effect of cortisol.
Role: Co-Investigator

OVERLAP

There is no scientific or budgetary overlap.