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: **Jonathan S. Williams, M.D., M.MSc.**

eRA COMMONS USER NAME: JSW123

POSITION TITLE: Associate Professor of Medicine, Harvard Medical School
Associate Physician, Brigham & Women's Hospital

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Brigham Young University, Provo, UT	B.S.	12/1991	Microbiology
Hahnemann University, Philadelphia, PA	M.D.	06/1998	Medicine
Harvard Medical School, Boston, MA	M.MSc.	06/2004	Clinical Research

A. Personal Statement:

I will serve as a Faculty Member in the outlined Training Program in Hypertension. My specific expertise is related to the conduct of diet-controlled clinical trials, e.g. diet composition (R01 HL77234, K23 HL084236 DASH Diet and Cardiovascular Mechanisms), dietary salt intake (R01HL141406 "Central mechanisms and novel biomarkers of the salt-sensitivity of blood pressure", R01HL144779 "Salt sensitive hypertension and striatin", R01 HL67098 "Macronutrients and Cardiovascular Risk Trial" caloric restriction (funded R01 HL102780 "Obesity, salt sensitivity and the natriuretic peptides"). My research interest is deciphering the genetic underpinnings of cardiometabolic risk in humans. Specifically, I perform human physiological investigations of environmental factors that affect renin-angiotensin-aldosterone system activity. This includes understanding the inherent/genetic susceptibility in Blacks (1R01 HL127146 "Lysine-specific demethylase-1 and salt sensitivity in hypertension"). My research program is uniquely qualified to mentor all levels of research trainees. Over the past 15 years I have mentored 16 post-doctoral fellows, of which 15 remain in research intensive careers, and 14 undergraduate research students, with whom I have co-authored over 50 original research publications. I have served as Co-Director of the Harvard CTSA Clinical and Translational Research Academy and its predecessor programs for the past 12 years. This is a 2-year former K30 program that trains clinical research physician scientists. In this capacity, I have served on over 30 individual research advisory committees. I founded 3 research training efforts at our institution (The Northeastern University Cooperative Program in Endocrine Research, The Brigham Young University-Harvard Summer Internship, and the Clinical Investigations Pathway for the Brigham and Women's Hospital Researc in Residency Program). I also serve as a member of the NIDDK-DDK-B study section which reviews training grants and career mentoring awards. Thus, I feel that I am well qualified to serve as a faculty member on this T32 program.

1. Hornik ES, Altman-Merino AE, Koefoed AW, Meyer KM, Stone IB, Green JA, Williams GH, Adler GK, **Williams JS.** A clinical trial to evaluate the effect of statin use on lowering aldosterone levels. BMC Endocrine Disorders. 2020 (in press).
2. Maris SA, **Williams JS**, Sun B, Brown S, Mitchell GF, Conlin PR. Interactions of the DASH Diet with the Renin-Angiotensin-Aldosterone System. Curr Dev Nutr. 2019 Jul 31;3(9):nzz091. doi: 10.1093/cdn/nzz091. PMID: 31528838; PMCID: PMC6735835.
3. Baudrand R, Goodarzi MO, Vaidya A, Underwood PC, **Williams JS**, Jeunemaitre X, Hopkins PN, Brown N, Raby BA, Lasky-Su J, Adler GK, Cui J, Guo X, Taylor KD, Chen YD, Xiang A, Raffel LJ, Buchanan TA, Rotter JI, Williams GH, Pojoga LH. A prevalent caveolin-1 gene variant is associated with the metabolic syndrome in Caucasians and Hispanics. *Metabolism*. 2015 Dec;64(12):1674-81 PMCID:PMC4641791.

4. **Williams JS**, Chamarthi B, Goodarzi MO, Pojoga LH, Sun B, Garza AE, Raby BA, Adler GK, Hopkins PN, Brown NJ, Jeunemaitre X, Ferri C, Fang R, Leonor T, Cui J, Guo X, Taylor KD, Ida Chen YD, Xiang A, Raffel LJ, Buchanan TA, Rotter JI, Williams GH, Shi Y. Lysine-specific demethylase 1: an epigenetic regulator of salt-sensitive hypertension. *Am J Hypertens*. 2012 Jul;25(7):812-7. PMCID: PMC3721725.
5. Sun B, **Williams JS**, Svetkey LP, Kolatkar NS, Conlin PR. Beta2-adrenergic receptor genotype affects the renin-angiotensin-aldosterone system response to the Dietary Approaches to Stop Hypertension (DASH) dietary pattern. Am J Clin Nutr. 2010 Aug;92(2):444-9. doi: 10.3945/ajcn.2009.28924. Epub 2010 Jun 2. PMID: 20519561; PMCID: PMC2904038.

B. Positions and Honors

1998-2001	Resident Physician, Internal Medicine, Brigham and Women's Hospital, Boston, MA
2001-2004	Fellow in Endocrinology, Brigham and Women's Hospital, Boston, MA
2003-	Staff Physician, VA Boston Healthcare System, Boston, MA
2004-2008	Instructor in Medicine, Harvard Medical School, Boston, MA
2004-	Associate Physician, Division of Endocrinology, Diabetes and Hypertension, Brigham and Women's Hospital, Boston, MA
2005-	Co-director, Cardiovascular Endocrinology Genetics Research Program, Division of Endocrinology, Diabetes, Hypertension, Brigham and Women's Hospital, Boston, MA
2008-	Assistant Professor of Medicine, Harvard Medical School, Boston, MA
2013-2015	Co-director, Masters' Program in Clinical and Translational Investigations, Harvard Medical School, Boston, MA
2015-	Co-director, Program in Clinical and Translational Sciences, Harvard Medical School, Boston, MA
2016-	Director, Non-invasive Research Imaging Core, Brigham and Women's Hospital, Boston
2017-	Director, Clinical Investigations Pathway, Department of Medicine, Brigham and Women's Hospital, Boston, MA
2018-	Lead Medical Research Officer, Harvard Catalyst/Brigham and Women's Hospital
2018-	Associate Director, Center for Clinical Investigations, Brigham and Women's Hospital, Boston, MA
2021-	Chair, Institutional Review Board, Brigham and Women's Hospital, Boston, MA
2021	Member, Executive Committee on Research, Mass General Brigham, Boston, MA

Other Experience and Professional Memberships

1994-	American Medical Association, Member
1996-	Alpha Omega Alpha National Medical Honor Society, Member
2001-	Endocrine Society, Member
2001-	Massachusetts Medical Society, Member
2003-	American Association of Clinical Endocrinologists, Member
2006-	Member, Institutional Review Board, Partners Healthcare Systems/Brigham and Women's Hospital
2009-	Member, American Heart Association
2011-2013	Board of Directors, Association of Patient-oriented Research
2011-2015	Associate Editor, *Metabolism: Clinical and Experimental*
2012-	Standing Committee Member, Association for Clinical and Translational Science, Membership and Nominations Committee
2012-	Standing Committee Member, Association for Clinical and Translational Science, Patient-Oriented Research Committee
2014-2019	Ad hoc reviewer, NIDDK/NHLBI Study Sections, Special Emphasis Grant Reviews
2020-	Member, NIH/NIDDK-DDKB Study Section

Honors

1996	Alpha Omega Alpha National Medical Honor Society, Zeta Chapter, Hahnemann University School of Medicine, Philadelphia, PA
2006-2013	Nomination, Excellence in Mentoring Award, Harvard Medical School, Boston, MA
2012	Early Career Mentoring Award, Brigham and Women's Hospital, Boston, MA

2016 Chair's Research Award, Brigham and Women's Hospital, Boston, MA
2016 Employee of the Year Award, Boston VA Healthcare System, Boston, MA

C. Contribution to Science

1. **Influence of Dietary Salt Intake on Cardiometabolic Health**. Dietary salt intake has long been associated with cardiometabolic diseases, including cardiovascular conditions, insulin resistance, and obesity. It has been described as an important modifiable environmental risk factor in broad epidemiologic and large-scale research efforts for decades. Sodium homeostasis is critical in volume-pressure regulation, and under the influence of several complex neurohormonal systems. Susceptibility to disease onset, progression, and severity is most often viewed as a manifestation of underlying genetic predisposition coupled with environmental interaction. As the medical treatment paradigm transitions from population- to individual-based treatment programs it has necessitated the refinement of investigative techniques and strategies. One approach is the rational pathway-based approach which provides clarity by "sub-setting" a disease category, such as diabetes, according to common pathophysiologic phenotypes. We have used this approach successfully and have utilized a genetic overlay that provides the potential to identify individuals "at risk" for developing conditions as well as design more specific or "tailored" therapeutic options that target the individual defect. Over the past 15 years, I, along with my trainees and collaborators, have identified several genetic variants among at risk populations that explains a large portion of salt-sensitivity. We have corroborated findings with human and animal mechanistic studies to provide evidence beyond mere association and build a foundation for causality. As we continue our discovery process, we are more recently transitioning to a targeted treatment effort, in which individuals with specific genetic and corresponding pathologic hormonal susceptibility are randomized to more specific treatment programs in a clinical trial setting. The culmination of these efforts would be the ability to identify individuals at risk for developing cardiometabolic disease by simply genotyping, which would in turn guide monitoring and treatment programs.

    a. Sun B*, **Williams JS*,** Svetky L, Conlin PR. Beta adrenergic receptor genotype affects the renin-angiotensin-aldosterone system response to the Dietary Approaches to Stop Hypertension (DASH) dietary pattern. *Amer J Clin Nutr* 2010 92:444-9. PMC2904038
    b. **Williams JS**, Sun B, Garg R. Effect of low salt diet on insulin resistance in salt sensitive versus salt resistant hypertension. *Hypertension* 2014 64:1384-7. PMC4230999
    c. Hamnvik OP, Choueiri T, Turchin A, McKay R, Goyal L, Davis M, Kaymakalan M, **Williams JS**. Clinical risk factors for the development of hypertension in patients treated with small-molecule inhibitors of the VEGF signaling pathway. *Cancer* 2015 121:311-9. PMC4293233
    d. Maris SA*, **Williams JS***, Sun B, Brown S, Mitchell GF, Conlin PR. Interactions of the DASH Diet with the Renin-Angiotensin-Aldosterone System. *Curr Dev Nutr.* 2019 Jul 31;3(9): PMCID:PMC6735835.

2. **Vitamin D and interaction with the renin-angiotensin-aldosterone system.** Vitamin D has been touted as a hormone with widely described pleiotropic effects in human disease and well-being. Much of the described work in the medical literature is associative in nature with very few physiology or clinical trials to validate these associations or shed light on underling mechanisms. Over the past 10 years we have detailed how Vitamin D interacts with renin to impact blood pressure, hormone regulation, and renovascular function in normal physiology, hypertension, and diabetes.

    a. Forman JP, **Williams JS**, Fisher NDK. Plasma 25-hydroxyvitamin D levels and the renin-angiotensin system in humans. Hypertension 2010 May;55:1283-8. PMC3023301
    b. Vaidya A, Forman JP, **Williams JS**. Vitamin D deficiency blunts vascular reactivity to angiotensin II in obesity. J Hum Hypertens 2011 Nov;25:672-8. PMC3146961
    c. Vaidya A, Sun B, Larson C, Forman JP, **Williams JS**. Vitamin D3 therapy corrects the tissue sensitivity to angiotensin II akin to the action of converting enzyme inhibitor in obese hypertensives: A prospective study. J Clin Endocrin and Metab 2012 July:97:2456-65. PMC3387405
    d. Zaheer S, Taquechel K, Brown JM, Adler GK, **Williams JS**, Vaidya A. A randomized intervention study to evaluate the effect of calcitriol therapy on the renin-angiotensin system in diabetes. J Renin Angiotensin Aldosterone Syst. 2018 Jan-Mar;19(1):1470320317754178 PMC5896865

3. **Obesity and mechanisms of salt sensitivity.** Obesity is a complex syndromic condition that often displays salt sensitivity. Salt sensitivity and obesity together increase cardiovascular risk. This research program seeks to identify the mechanisms that underlie the relationship between obesity and salt sensitivity, focusing on the neurohormonal activity.
    a. Arora P, Reingold J, Baggish A, Guanaga DP, Wu C, Ghorbani A, Song Y, Chen-Tournaux A, Khan AM, Tainsh LT, Buys ES, **Williams JS**, Heublein DM, Burnett JC, Semigran MJ, Bloch KD, Scherrer-Crosbie M, Newton-Cheh C, Kaplan LM, Wang TJ. Weight loss, saline loading, and the natriuretic peptide system. J Am Heart Assoc. 2015 Jan 16;4(1):e001265. doi: 10.1161/JAHA.114.001265. PMID: 25595796; PMCID: PMC4330054.
    b. Vaidya A, Forman JP, **Williams JS**. Vitamin D deficiency blunts vascular reactivity to angiotensin II in obesity. J Hum Hypertens. 2011;25:672-8
    c. Vaidya A, Formin JP, Underwood PC, Jeunemaitre X, Hopkins PN, Brown NJ, Williams GH, Pojoga L, **Williams JS.** The influence of body mass index and renin-angiotensin system activity on the relationship between 25-hydroxyvitamin D and adiponectin in Caucasian men. Eur J Endocrin. 2011; 164:995-1002.
    d. Vaidya A, **Williams JS**, Forman JP. The independent association between 25-hydroxyvitamin D and adiponectin and its relationship with BMI in two large cohorts: the NHS and HPFS. Obesity (Silver Spring). 2012;20:185-91.

4. **Genetic mechanisms of cardiometabolic risk**. The focus of this ongoing program is to decipher the genetic underpinnings of cardiovascular risk. I have been the Director of the Cardiovascular Endocrine Genetics Research Group for the past several years which houses the HyperPATH cohort. This specialized cohort consists of over 2,500 finally phenotyped research volunteers from a network of research collaborators around the globe. It has over 35 years continuous NIH funding with 100's of original research publications.
    a. Haas A, Baudrand R, Easly RM, Murray GR, Touyz RH, Pojoga LH, Jeumemaitre X, Hopkins PN, Rosner B, **Williams JS**, Adler GK, Williams GH. The interplay between statins, caveolin-1, and aldosterone. Hypertension. 2020 (in press).
    b. Stone IB, Green JAEM, Koefoed AW, Hornik ES; **Williams JS,** Adler GK, Williams GH. Genotype-Based, Mineralocorticoid Receptor Antagonist-Driven Clinical Trial (StiMRAD): Study Rationale and Design. Pharmacogenetics and Genomics. 2020 (in press).
    c. Treesaranuwattana T, Wong KYH, Brooks DL, Tay CS, Williams GH, **Williams JS**, Pojoga LH. Lysine-specific demethylase-1 deficiency increases agonist signaling via the mineralocorticoid receptor. Hypertension. 2020;75(4):1045-53.
    d. Zhang X, Frame AA, **Williams JS,** Wainford RD. GNAI1 polymorphic variance associates with salt sensitivity of blood pressure in the Genetic Epidemiology Network of Salt Sensitivity study. Physiol Genomics. 2018;50(9):724-5.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/jonathan.williams.1/bibliography/40547519/public/?sort=date&direction=descending