BIOGRAPHICAL SKETCH

NAME Jennifer W. Hill	POSITION TITLE Associate Professor
eRA COMMONS USER NAME (credential, e.g., agency login)	

EDUCATION/TRAINING: INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY (date of completion)	FIELD OF STUDY
Williams College, Williamstown MA	B.A.	06/97	Biology
Northwestern University, Evanston, IL	Ph.D.	06/03	Neuroscience
Beth Israel Deaconess Medical Center, Boston	Postdoc	12/05	Neuroendocrinology
University of Texas Southwestern, Dallas TX	Postdoc	06/07	Neuroendocrinology
University of Texas Southwestern, Dallas TX	Instructor	05/09	Neuroendocrinology

A. Personal Statement

I received my Ph.D. in 2003 from Northwestern University under the supervision of Dr. Jon E. Levine, a leader in the field of the neural control of reproduction. I was awarded an NIH F32 NRSA Individual Post-doctoral Fellowship to study the function of PI3 kinase (PI3K) in appetite suppressing neurons of the hypothalamus under the mentorship of Dr. Joel K. Elmquist at Beth Israel Deaconess Medical Center in Boston. In 2008, I obtained an NICHD K99/R00 Pathway to Independence Award to investigate the interaction between leptin and insulin signaling in POMC neurons at the University of Texas Southwestern at Dallas. My work there led to publications in leading scientific journals such as Cell Metabolism, Journal of Clinical Investigation, and Endocrinology. I became an Assistant Professor in the Department of Physiology and Pharmacology at the University of Toledo College of Medicine since July 2009, where I have been investigating my novel findings of a critical regulatory role for hypothalamic POMC neurons in fertility. For that research, I won the Endocrine Society Young Investigator Award in 2013. I received tenure and Associate Professor status in January of 2016. I am a guest associate editor for Frontiers in systems and Translational Endocrinology and recently joined the editorial board for American Journal of Physiology Endocrinology and Metabolism. I have also served as an external expert reviewer for the NICHD SCCPIR program, the NIH Molecular, Cellular, and Developmental Neuroscience Study Section, and the NSF Neural Systems Cluster (BIO/IOS). I serve as an ad hoc reviewer for numerous scientific journals including Frontiers in Neuroendocrinology, Cell Metabolism, Obesity, Endocrinology, and PLoS One. Since joining the University of Toledo, I have twice been awarded the NIH LRP Award for Fertility and Contraception Research. My laboratory has also received an R01 Research Award and an R21 Exploratory/Developmental Research Grant Award from the NICHD.

My mentoring experience includes both PhD and MD students. I am currently mentoring three PhD students and one MD/PhD student in my laboratory, including one who has received an NIH F31 NRSA award to pursue her research. A former PhD student in my lab who received his degree is now pursuing a postdoctoral fellowship at SUNY Stony Brook. In addition, a former postdoctoral fellow has recently joined the faculty of the University of North Carolina at Charlotte as a tenure track assistant professor. In addition to other undergraduate and Master's students doing short-term projects in my laboratory, I have supervised one medical student doing a research project during her clinical years, and 7 preclinical medical students doing research projects in my lab lasting between 3 and 18 months.

B. Positions and Honors

Positions

1993	Veterinary Assistant
1994-1995	Neuroscience Lab Assistant for Dr. Heather Williams, Dept of Biology, Williams College
1996-1997	Senior Thesis Researcher with Dr. Heather Williams, Dept. of Biology, Williams College
1997	Assistant Scientist, Dr. Muriel Ross supervisor, Space Biology Group, Lockheed
1998	Teaching Assistant, Dept of Neurobiology and Physiology, Northwestern University
1999-2003	Graduate Student, Dr. Jon E. Levine advisor, Dept. of Neurobiology and Physiology, Northwestern

1999	Teaching Asst. for Dr. Neena Schwartz, Dept of Neurobiology and Physiology, Northwestern
2003-2006	Postdoctoral Fellow, Dr. Joel K. Elmquist advisor, Department of Endocrinology and Metabolism, BIDMC/Harvard Medical School
2006-2007	Postdoctoral Fellow, Dr. Joel K. Elmquist advisor, Dept. of Internal Medicine, UT Southwestern Medical Center
2007-2009	Instructor, Department of Internal Medicine, UT Southwestern Medical Center
2009-2015	Assistant Professor, Department of Physiology and Pharmacology, College of Medicine, University of Toledo
2009-2015	Assistant Professor (joint appointment), Department of Obstetrics and Gynecology, College of Medicine, University of Toledo
2016-present	Associate Professor, Department of Physiology and Pharmacology, College of Medicine, University of Toledo
2016-present	Associate Professor (joint appointment), Department of Obstetrics and Gynecology, College of Medicine, University of Toledo

Honors

1993	The Cum Laude Society
1993	Bank of America Achievement Award for Math and Science
1997	Sigma Xi Honor Society
2002	Competitive Travel Grant, Office of Vice President for Research, Northwestern U.
2007-2012	NIH LRP Award for Fertility and Contraception Research
2012	Endocrine Society Travel Award for annual meeting
2013	Endocrine Society Young Investigator Award
2013	Eleni and Evangelos Theodosiou Young Investigator Award, Sigma Xi
2014	Dean's Award for Mentoring, University of Toledo College of Medicine and Life Sciences

Professional Memberships and Committees

2003-present	Society for Neuroscience, Member
2003-present	Endocrine Society, Associate Member
2010-present	American Diabetes Association, Professional Member
2011-present	Guest Associate Editor, Frontiers in Systems and Translational Endocrinology
2013	External Expert Reviewer for NICHD Fertility and Infertility Branch U54 Specialized Cooperative Centers Program in Reproduction and Infertility Research (SCCPIR) program March 2013
2014	Mail Reviewer, National Science Foundation (NSF) Neural Systems Cluster (BIO/IOS), October 2014
2015	Phone Reviewer, National Institutes of Health (NIH) Molecular, Cellular, and Developmental Neuroscience Study Section (MDCN-R 86) R15 AREA Applications Panel, March 2015
2015-present	Association for Women in Science, Member
2015-present	Editorial Board Member, American Journal of Physiology Endocrinology and Metabolism

C. Contribution to Science

My bibliography/NCBI:
http://www.ncbi.nlm.nih.gov/sites/myncbi/jennifer.hill.2/collections/49249553/public/

1. In early publications, my studies focused on the role of metabolically responsive neurons in the control of the hypothalamic-pituitary-gonadal axis. In the early 2000s, the circulating adipokine leptin was found to target specific hypothalamic neurons. Using genetic ablation, physiological approaches, and primary cell culture, we were the first to demonstrate that neuropeptide Y is required in mice for a normal luteinizing hormone (LH) surge and the suppression of LH due to fasting. Our studies stimulated interest in the interconnectedness of energy balance and neuroendocrine regulation.

1) Xu M, Urban JH, **Hill JW**, Levine JE. Regulation of hypothalamic neuropeptide Y Y1 receptor gene expression during the estrous cycle: role of progesterone receptors. Endocrinology. Sep;141(9): 3319-27, 2000
2) Xu M, **Hill JW**, Levine JE. Attenuation of luteinizing hormone surges in neuropeptide Y knockout mice. Neuroendocrinology. Nov; 72(5): 263-71, 2000
3) **Hill JW**, Levine JE. Abnormal response of the neuropeptide Y-deficient mouse reproductive axis to food deprivation but not lactation. Endocrinology. 144(5):1780-6, 2003
4) **Hill JW**, Urban JH, Xu M, Levine JE. Estrogen Induces Neuropeptide Y (NPY) Y1 Receptor Gene Expression and Responsiveness to NPY in Gonadotrope-Enriched Pituitary Cell Cultures. Endocrinology. May;145(5):2283-90, 2004

2. I then chose to pursue intensive study of the nature of leptin sensing by hypothalamic circuits controlling metabolism. At the time, the Jak-Stat3 pathway was believed to mediate the actions of leptin on feeding and energy expenditure. My research provided pivotal evidence that PI3K signaling drives many of the actions of both leptin and insulin in proopiomelanocortin (POMC) neurons and in the ventromedial nucleus of the hypothalamus. These studies also produced pioneering work on the critical control of hepatic glucose production exerted by POMC neurons.

1) **Hill JW**, Williams KW, Ye C, Luo J, Balthasar N, Coppari R, Cowley MA, Cantley LC, Lowell BB, Elmquist JK. Acute effects of leptin require PI3K signaling in hypothalamic proopiomelanocortin neurons in mice. J Clin Invest. May 1;118(5):1796-1805, 2008
2) Fukuda M, Jones JE, Olson D, **Hill J**, Lee CE, Gautron L, Choi M, Zigman JM, Lowell BB, Elmquist JK. Monitoring FoxO1 localization in chemically identified neurons. J Neurosci. Dec 10;28(50):13640-8. PMID: 19074037, 2008
3) **Hill JW**, Yong X, Preitner F, Fukuda M, Cho Y, Luo J, Balthasar N, Coppari R, Cantley LC, Kahn B, Zhao JJ, Elmquist JK. Phosphatidyl Inositol 3-Kinase Signaling in Hypothalamic Proopiomelanocortin Neurons Contributes to the Regulation of Glucose Homeostasis. Endocrinology. Nov;150(11):4874-82, 2009

4) **Hill JW**, Elias CF, Fukuda M, Williams KW, Berglund ED, Holland WL, Cho Y, Chuang J, Xu Y, Choi M, Lauzon D, Lee CE, Coppari R, Richardson JA, Zigman JM, Chua S, Scherer PE, Lowell BB, Bruning JC, Elmquist JK. Direct Insulin and Leptin Action in Pro-opiomelanocortin Neurons is Required for Normal Glucose Homeostasis and Fertility. Cell Metabolism. Apr 7;11(4):286-97, 2010 PMID: 20374961
5) Xu Y, **Hill JW** (joint first author), Fukuda M, Gautron L, Sohn J, Kim K, Lee CE, Choi MJ, Lauzon D, Dhillon H, Lowell BB, Zigman JM, Zhao JJ, Elmquist JK. PI3K signalling in the ventromedial hypothalamus is required for normal energy homeostasis. Cell Metabolism. July 4;12(1), 88-95, 2010 PMID: 20620998

3. As I began my independent career, my laboratory made a major breakthrough in the study of polycystic ovary syndrome (PCOS) by creating a novel mouse model of the disorder with chronic inflammation similar to what is seen in human patients. Unlike the most common rodent models of PCOS, the condition arises without pharmacological induction. Furthermore, it is not driven by an obese phenotype; our results strongly suggest that hypothalamic insensitivity to metabolic factors can directly lead to excess LH and T production.

1) **Hill JW**, Elias CF, Fukuda M, Williams KW, Berglund ED, Holland WL, Cho Y, Chuang J, Xu Y, Choi M, Lauzon D, Lee CE, Coppari R, Richardson JA, Zigman JM, Chua S, Scherer PE, Lowell BB, Bruning JC, Elmquist JK. Direct Insulin and Leptin Action in Pro-opiomelanocortin Neurons is Required for Normal Glucose Homeostasis and Fertility. Cell Metabolism. Apr 7;11(4):286-97, 2010 PMID: 20374961
2) Marino JS, Iler J, Dowling AR, Chua S, Bruning JC, Coppari R, **Hill JW**. Adipocyte Dysfunction in a Mouse Model of Polycystic Ovary Syndrome (PCOS): Evidence of Adipocyte Hypertrophy and Tissue-Specific Inflammation. PLoS One. 7(10):e48643, 2012 PMID: 23119079

3) Dowling AR, Nedorezov LB, Qiu X, Marino JS, **Hill JW**. Genetic factors modulate the impact of pubertal androgen excess on insulin sensitivity and fertility. PLoS One. Nov 20;8(11):e79849, 2013 PMID: 24278193

4. Whereas our previous work had identified hypothalamic sites linking insulin action and metabolism, I next chose to investigate the brain nuclei involved in insulin action in reproductive control. Given the central role of the Kiss1-Gpr54 system in the control of GnRH release, many speculated that these neurons must mediate the effects of insulin on fertility. Contrary to the expectations in the field, we demonstrated that direct action of insulin on Kiss1 neurons influences the timing of puberty, but otherwise is dispensable for fertility.

1) Qiu, X., Dowling, A., Marino J., Faulkner L., Brüning, J., Elias, CF, Bryant B., **Hill, JW.** Delayed Puberty but Normal Fertility in Mice with Selective Deletion of Insulin Receptor from Kiss1 Cells, Endocrinology. Mar;154(3):1337-48, 2013 PMID: 23392256
2) Qiu X, Dao H, Heston A, Garcia KM, Sangal A, Wang M, Dowling, AR, Faulkner L, Molitor SC, Elias CF, **Hill JW**. Insulin and leptin signaling interact in the Kiss1 neuron during the peripubertal period. Plos One May 6;10(5):e0121974, 2015 PMID: 25946091

5. Most recently, we have investigated the role of POMC neurons in sexual motivation rather than neuroendocrine control of fertility. While it is known that the POMC product α-MSH can affect sexual function in males, no studies had investigated whether low endogenous α-MSH production might impair libido. We used targeted genetic deletion of leptin and insulin signaling in POMC neurons to disrupt α-MSH production and demonstrated that reduced melanocortin signaling leads to reduced sexual motivation and performance. Given that impaired hypothalamic insulin and leptin signaling accompanies obesity and diabetes, our findings suggest that the erectile dysfunction in men with diabetes may in part have a central origin.

1) Faulkner LD, Dowling AR, Stuart RC, Nillni EA, **Hill JW**. Reduced melanocortin production causes sexual dysfunction in male mice with POMC neuronal insulin and leptin insensitivity. Endocrinology. Apr;156(4):1372-85, 2015 PMID: 25590244

D. Research Support

Ongoing

R01 HD081792 (PI: Hill) 04/01/2015-03/31/2020
NIH/NICHD
"Defective melanocortin signaling underlying T2D-associated erectile dysfunction"
The purpose of this grant is to determine whether low α-MSH levels associated with obesity lead to erectile dysfunction and to map the melanocortin pathways involved.

Michigan Pilot and Feasibility Study Grant (PI: Hill) 01/2016-12/2016
"Intergenerational obesity resulting from lactational impairment."
NIDDK funded program (P30DK092926) to support type 2 diabetes translational researchers who are members of the Michigan Diabetes Research and Training Center, to further stimulate new Investigators to enter the field, and to foster productive collaborations.

Completed

F31-HD-75608-02 (Sponsor: Hill) 01/01/2013 – 02/28/16
NIH/NICHD
"Simultaneous insulin and leptin signaling in POMC neurons promotes fertility"
The purpose of this grant is to support the training of graduate student Latrice Faulkner in the Hill laboratory.

Michigan Pilot and Feasibility Study Grant (PI: Hill) 01/2014-12/2014
"Inflammatory processes driving insulin resistance in polycystic ovary syndrome."

NIDDK funded program (P30DK092926) to support type 2 diabetes translational researchers who are members of the Michigan Diabetes Research and Training Center, to further stimulate new Investigators to enter the field, and to foster productive collaborations.

1R21HD071529-01A1 (PI: Hill) 4/2012-3/2014
NIH/NICHD
“Inflammatory triggers of polycystic ovarian syndrome.”
The purpose of this grant was to determine whether innate or acquired immune responses underlie insulin resistance in a genetic mouse model of PCOS.

deArce-Koch Memorial Fund Award (PI:Hill) 7/2012-6/2013
“Hypothalamic regulation of HDL cholesterol metabolism”
The purpose of this proposal was to determine which branch of the autonomic nervous system regulates the effects of melanocortin signaling on hepatic HDL metabolism.

R00HD056491 (PI: Hill) 04/2008 – 07/2012
NIH/NICHD
“Hypothalamic leptin and insulin signals aligning metabolic state and fertility.”
The purpose of this grant was to investigate whether insulin and leptin sensing by POMC neurons is required for normal glucose homeostasis and reproduction.