BIOGRAPHICAL SKETCH

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NAME: Weeks, Janis C.

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

POSITION TITLE: Co-Founder and Chief Scientific Officer, NemaMetrix Inc.

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
Massachusetts Institute of Technology	B.S.	6/1975	Applied Life Sciences (course 7B)
University of California, San Diego	Ph.D.	6/1980	Biology/Neuroscience
University of Washington, Seattle	Postdoctoral	12/1984	Zoology (since renamed Biology)

A. Personal Statement

My career as a neuroscientist performing translational research has equipped me to oversee and ensure the scientific rigor of ScreenChip system. I work in cellular and systems neuroscience, focusing on pharmacology, ion channels, neurotransmitter receptors, and synaptic physiology, in the context of neural circuits underlying behavior. Much of this work was performed using insects (*Manduca sexta and Drosophila melanogaster*), utilizing the hormonally-mediated reorganization of the CNS during metamorphosis as a powerful model for steroid hormone effects on the human CNS in health and disease. Starting about 5 years ago, I pivoted my research toward innovative neurophysiological methods to accelerate drug discovery for human diseases. Notably, my University of Oregon (UO) colleague, Dr. Shawn Lockery, and I validated a combined microfluidic and electrophysiological screening platform using the nematode, *C. elegans*. With Dr. Lockery, I co-founded and serve as CSO of NemaMetrix Inc., a UO spin-off formed in 2011 to commercialize the EPG platform. My undergraduate degree at MIT was in Applied Biology, and electrophysiological instrumentation and analytic software applications are daily tools in my research. My research has been funded by NIH, NSF, Muscular Dystrophy Foundation, Oregon Partnership for Alzheimer's Research, The Bill and Melinda Gates Foundation and other organizations. I have 30 years' experience managing a successful research laboratory at R1 universities and mentoring younger scientists, especially from underrepresented minority groups. I thus bring extensive experience in research management and in leading diverse interdisciplinary teams in achieving milestones.

1. Lockery S.R., E. Hulme, W.M. Roberts, K.J. Robinson, A. Laromaine, T.H. Lindsay, G.M. Whitesides and J.C. Weeks (2012) A microfluidic device for whole-animal drug screening using electrophysiological measures in the nematode *C. elegans*. *Lab on a Chip*, 12:2211-20.

B. Positions and Honors

Positions and Employment

1985-88 Assistant Professor, Dept. of Entomology and Parasitology, UC Berkeley
1988 Associate Professor, Dept. of Entomology and Parasitology, UC Berkeley
1989-95 Associate Professor, Dept. of Biology, Univ. Oregon
1995- Professor of Biology, Univ. Oregon
1998-2001 Head, Department of Biology, UO

2011-	Co-Founder and Chief Scientific Officer, NemaMetrix Inc. (nemametrix.com)
2012	Visiting Scholar, University of Washington School of Medicine, Division of Allergy and Infectious Disease, and Visiting Scholar, Seattle Biomedical Research Institute.
2014-	Visiting Researcher, The George Washington University School of Medicine & Health Sciences, Dept. of Microbiology, Immunology and Tropical Disease, Center for Neglected Diseases of Poverty.

Other Experience and Professional Memberships

1985-2004	Instructor, "Neural Systems and Behavior" course, Marine Biological Laboratory, Woods Hole, MA (plus 3 years as a teaching assistant prior to this)
1989-1992	Coordinator/Director of NIH-funded Institute of Neuroscience summer research program for minority high school students (NIH S03 RR03138)
1990-98	Director, Systems Physiology Training Program (NIH T32 GM07257) at Institute of Neuroscience, University of Oregon
1992-95	Member, NSF Advisory Panel for Neuroendocrinology
1995-99	Co-Director (with Prof. H.H. Zakon, University of Texas) of "Neural Systems and Behavior" course, Marine Biological Laboratory, Woods Hole, MA
1996-	Instructor in and/or organizer of IBRO (International Brain Research Organization) neuroscience courses in Africa (including Democratic Republic of Congo, Egypt, Ghana, Kenya, Morocco, Nigeria, Senegal and South Africa).
2000-03	Elected member, Science Council, Marine Biological Laboratory, Woods Hole, MA
2001-05	Member, External Advisory Committee, NIH Specialized Neuroscience Research Program, Univ. Texas San Antonio
2005-09	Member, NIH International and Cooperative Projects Study Section 1 (reviews Fogarty International Research Collaboration Awards)
2006-11	President, The Grass Foundation (www.grassfoundation.org), which funds research and education in neuroscience.
2007-11	Member, Advisory Committee for the Office of International Science and Engineering, at the National Science Foundation
2008	Chair, NIH National Institute of Neurological Disorders and Stroke Special Emphasis Panel ZNS1 SRB-P (41)
2012	Visiting Scholar, Univ. Washington School of Medicine, Division of Allergy and Infectious Disease, and Seattle Biomedical Research Institute. Sabbatical research testing lead compounds (bumped kinase inhibitors) as malaria transmission blockers.
2012-	Member, Board on Life Sciences, National Academy of Sciences

Honors

1986-88	Alfred P. Sloan Research Fellow in Neuroscience
1988-1993	NSF Presidential Young Investigator Award
1989-1994	NIH Research Career Development Award (K04 NS017473)
1996-97	Fellow, John Simon Guggenheim Memorial Foundation (for sabbatical research at the German Cancer Research Center, Heidelberg)
2009	Recipient, UO Biology Dept. Teaching Achievement Award, for BI309 “Tropical Diseases in Africa.” Award based on student nominations.
2011	Recipient, University of Oregon Martin Luther King Jr. AwardC. Contribution to Science

C. Contribution to Science

1. In mammals, changes in circulating steroid hormone levels are correlated with striking changes in the dendritic complexity of specific groups of neurons. When I began this work, it was (logically) hypothesized that hormone-induced changes in dendritic architecture alter the electrophysiological strength of synaptic connections and, through the appropriate neural circuits, modify behavior. However, the complexity of the mammalian CNS precluded a direct test of this hypothesis. My colleagues and I were the first to perform such a test, thereby confirming this fundamental tenet of the field of hormones and behavior. We utilized the metamorphosis of the hawkmoth, *Manduca sexta*, which is regulated by a class of steroid hormones termed ecdysteroids. We identified the neural circuit underlying a larval-specific withdrawal reflex and showed by electrophysiological and anatomical means that ecdysteroid-induced dendritic regression in a

motoneuron (MN) physically disconnected its dendrites from the axonal terminals of sensory neurons (SNs), weakening the strength of monosynaptic EPSPs (excitatory postsynaptic potentials) produced at these synapses. We further showed that the steroid-induced weakening of the SN-MN synapses was both necessary and sufficient to developmentally dismantle the neural circuit for the withdrawal reflex and eliminate the behavior. We also characterized pharmacologically the role of nicotinic and muscarinic acetylcholine receptors (AChRs) at the SN-to-MN synapses. This work demonstrated for the first time that a steroid-induced change in neuronal structure causes synaptic changes responsible for the developmental loss of a specific behavior. This work was performed in my laboratory, under my guidance.

a. Weeks, J.C. and G.A. Jacobs (1987) A reflex behavior mediated by monosynaptic connections between hair afferents and motoneurons in the larval tobacco hornworm, *Manduca sexta*. *J. Comp. Physiol*. *A.* 160:315-329. PMID: 3572850
b. Trimmer, B.A. and J.C. Weeks (1989) Effects of nicotinic and muscarinic agents on an identified motoneurone and its direct afferent inputs in larval *Manduca sexta*. *J. exp. Biol*. 144:303-337.
c. Jacobs, G.A. and J.C. Weeks (1990) Postsynaptic changes at a sensory-to-motoneuron synapse contribute to the developmental loss of a reflex behavior during insect metamorphosis. *J. Neurosci*. 10:1341-1356. PMID: 2158532
d. Gray, J.R. and J.C. Weeks (2003) Steroid-induced dendritic regression reduces anatomical contacts between neurons during synaptic weakening and the developmental loss of a behavior. *J. Neurosci*. 23:1406-1415. PMID: 12598629

2. Another striking phenomenon during insect metamorphosis is the programmed cell death (PCD) of neurons and muscles not required for the next life stage. We discovered a segment-specific pattern of MN and muscle death in *Manduca*, in which segmentally-repeated proleg MNs and muscles die in specific segmental patterns in response to a rise in ecdysteroids at pupation, or a fall in ecdysteroids at the end of pupal life. Similarly, in mammals, circulating steroid levels can cause neurodegeneration or be neuroprotective, but controversy existed regarding the extent to which such effects are mediated directly vs. indirectly (e.g., transynaptically). We tested the hypothesis that the PCD of proleg MNs during metamorphosis occurs in direct response to circulating steroid hormones. To do so, we developed methods to fluorescently label proleg MNs from different body segments and place them in primary cell culture, and made two notable findings: (1) steroids act directly and cell-autonomously on the MNs to trigger death and (2) survival or death in response to a specific steroid cue is governed by the intrinsic segmental identity of individual MNs, which persists following removal of these neurons from the body. This was the first demonstration of either of these findings in any system. We further determined that MN death occurs by autophagy and identified key molecular players in the steroid-induced PCD cascade. This work was performed in my laboratory, under my guidance.
    a. Streichert, L.C., J.T. Pierce, J.A. Nelson and J.C. Weeks (1997) Segment-specific programmed cell death of identified motoneurons triggered directly by steroid hormones in vitro. *Devel. Biol*. 183:95-107. PMID: 7869112
    b. Zee, M.C. and J.C. Weeks (2001) Developmental change in the steroid hormone signal for cell-autonomous, segment-specific programmed cell death of a motoneuron. *Devel. Biol*. 235:45-61. PMID: 11412026
    c. Hoffman, K.L. and J.C. Weeks (2001) Role of caspases and mitochondria in the steroid-induced programmed cell death of a motoneuron during metamorphosis. *Devel. Biol*. 229:517-536. PMID: 11203705
    d. Kinch, G.L., K.L Hoffman, E.M. Rodrigues, M.C. Zee, and J.C. Weeks (2003) Steroid-triggered programmed cell death of a motoneuron is autophagic and involves structural changes in mitochondria. *J. Comp. Neurol*. 457:384-403. PMID: 12561078

3. Although the above experiments produced the breakthrough demonstration of direct steroid-hormone induction of neurodegeneration, we were stymied in making further progress with molecular mechanisms because *Manduca* offered few molecular-genetic tools. To surmount this barrier, we developed a parallel experimental system in *Drosophila*, using an unrelated set of larval MNs (RP2s). We generated the genetic constructs to drive GFP expression in larval RP2s and optimized methods to remove RP2s from the CNS and culture them in vitro. As in *Manduca*, we found that PCD of the *Drosophila* MNs at pupation was triggered directly by ecdysteroids and depended on the MNs' intrinsic segmental identity. To my knowledge, our work in *Manduca* and *Drosophila* represents the first demonstration of such effects on

steroid-sensitive neurons and paves the way for further elucidating the underlying genetic pathway(s) for cellular suicide. This work was performed in my laboratory, under my guidance, by a talented African-American Ph.D. student.

   a. Winbush, A.S. and J.C. Weeks (2011) Steroid-triggered, cell-autonomous death of a *Drosophila* motoneuron during metamorphosis. Neural Development 6:15. PMCID: PMC3098771

4. The patent-pending microfluidic EPG chip to be used in this project was first developed and validated at UO by Dr. Shawn Lockery and I. The inaugural paper on the technology, published in *Lab on a Chip*, was rated among the top 10% of papers published by the journal that year. In 2014, the EPG platform placed in the top 5 of over 900 entries in a competition held by the White House Office of Science and Technology Policy (OSTP), to identify new platforms that could revolutionize the life sciences. The EPG drug screening platform represents a potentially disruptive new tool for enhancing drug discovery in many areas of human health. In addition to the published paper below, four more from my laboratory are currently in preparation. This work was done in collaboration with the inventor of the EPG chip, Dr. Shawn Lockery, and other collaborators. My laboratory performed all of the electrophysiological experiments in the paper. Since this publication, we have made substantial technological progress at NemaMetrix, including developing the ScreenChip platform that forms the basis of this SBIR project. Furthermore, with Bill & Melinda Gates Foundation funding to my UO laboratory, I optimized the 8-channel EPG chip for use with intestinal parasites of humans (hookworm and roundworm), with several papers in preparation. This advance promises to accelerate the development of new, urgently-needed, anthelmintic drugs to treat human infections.

   a. Lockery S.R., E. Hulme, W.M. Roberts, K.J. Robinson, A. Laromaine, T.H. Lindsay, G.M. Whitesides and J.C. Weeks (2012) A microfluidic device for whole-animal drug screening using electrophysiological measures in the nematode *C. elegans*. Lab on a Chip**,** 12:2211-20. PMCID: PMC3372093

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/janis.weeks.1/bibliography/44365351/public/?sort=date&direction=ascending.

D. Research Support

Ongoing Research Support

(At Univ. Oregon) National Center for Veterinary Parasitology 11/01/14 - 12/31/15
A. Wolstenholme (Univ. of Georgia) and Weeks (Co-PIs)
Microfluidic electrophysiological recordings from *Haemonchus contortus* as a new tool for anthelmintic research
The goal of the project is to optimize biological protocols and microfluidic electropharyngeogram technology for use with blood-feeding *Haemonchus contortus*, a significant parasite of small ruminants, to advance animal health research
Role: Co-Investigator

(At Univ. Oregon) UO Office of the Vice President for Research & Innovation 04/01/15 -12/31/15
Weeks (PI)
Bridge funding to support research
This funding supports the completion of work funded by a Phase I Global Challenges Explorations from the Bill & Melinda Gates Foundation, and other projects.
Role: PI

(**At NemaMetrix**) Oregon Translational Research and Development Institute 08/01/13 - 12/31/15
Weeks (PI)
Development and optimization of a two-phase anthelmintic screening platform
This grant funds a partnership between NemaMetrix and OTRADI to: (1) optimize a high throughput, primary screening platform for anthelmintic activity using *C. elegans*, and screen an OTRADI library of ~2000 compounds; (2) perform secondary screening on a subset of the hits using NemaMetrix's microfluidic electropharyngeogram platform.

Role: PI

Completed Research Support

(At NemaMetrix) NIH/NIA R01 1R43 AG047020-01 02/01/14 - 5/31/15
McCormick (PI)
Microfluidic screening devices for health-span extending drugs
The goal of the proposed project is to develop a microfluidic device for long-term culture and electropharyngeogram recordings from *C. elegans*, to enhance the throughput and resolution of health span screening in *C. elegans* and thereby accelerate the discovery of compounds that extend health span in humans.
Role: Co-Investigator

(At Univ. Oregon) Bill and Melinda Gates Foundation, Grand Challenges Explorations Round 10 05/01/13 - 10/31/14
Weeks (PI)
Neurophysiology-based platform for STH (soil-transmitted helminth) drug discovery
The major goal of this project was to redesign a microfluidic device designed for recording electropharyngeograms from *C. elegans*, for use on parasitic nematodes (hookworm, whipworm) that cause human disease.
Role: PI

(At Univ. Oregon) ONAMI (Oregon Nanoscience and Microtechnology Institute) Gap Funding Program 02/01/12 - 05/31/15
Doe* (PI)
*For COI purposes, Prof. Christopher Doe (UO) is the named PI.
Microfluidic devices for drug discovery using electrophysiological measures in nematode worms.
The major goal of this project is to accelerate the development of new anthelmintic (anti-nematode) drugs for human and animal health by designing and validating novel, medium-throughout microfluidic devices capable of making electrophysiological recordings from the nematode worm, *C. elegans*. Includes subcontract to NemaMetrix.
Role: PI

(At Univ. Oregon) Gabon-Oregon Center (GOC) at the Univ. of Oregon 10/1/2013-10/31/2013
Weeks (PI)
Travel award to promote anthelmintic drug development collaboration in Gabon
This project supports a research collaboration between Gabonese scientists at IPHAMETRA (Institut de Pharmacopée et de Médecine Traditionnelle) in Libreville, Gabon, and the 'Laboratory of Anthelmintic Drug Discovery' (the Weeks lab at UO).
Role: PI