BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
ATWOOD, Craig Stephen	Associate Professor, Department of Medicine, University of Wisconsin-Madison Research Scientist, Geriatric Research, Education and Clinical Center, VA Hospital, Madison, WI CEO/CSO, JangoBio, LLC
eRA COMMONS USER NAME (credential, e.g., agency login) catwood	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YY	FIELD OF STUDY
The University of Western Australia, Australia	B.Sc. (Hons.)	04/85	Biochemistry
The University of Western Australia, Australia	Ph.D.	04/93	Biochemistry
Laboratory of Molecular & Cellular Endocrinology National Cancer Institute, NIH, Bethesda, MD	Fogarty Fellow	01/94-09/95	Cellular and Molecular Endocrinology
Genetics and Aging Unit, Neuroscience Center, Massachusetts General Hospital, Charleston, MA	Research Fellow	09/95-10/97	Neuroscience and Protein Chemistry

A. Personal Statement

I have a broad background in the biomedical sciences, including training and expertise in the areas of gerontology, endocrinology, biochemistry, developmental endocrinology, neuroendocrinology, neurodegeneration, neuroregeneration and protein chemistry. As PI or co-Investigator on several NIH-, VA-, foundation-, university- and company-funded grants, I laid the groundwork for the proposed research by developing an integrative model of the endocrinological underpinnings of human growth and development, tissue maintenance, and tissue senescence known as the Reproductive-Cell Cycle Theory of Aging. This framework for understanding human life makes it possible to develop and test hypotheses related to each phase of life. My research career has involved stints at the National Cancer Institute, Harvard Medical School, Case Western Reserve University and currently UW-Madison. My productivity and recognition in these fields is evidenced by my *h*-index of 44 (ISI Web of Knowledge, August. 2015) and the more than 10,000 citations to my 200 plus publications and 8 patents. I have the training, expertise, leadership, and motivation necessary to carry out the proposed research project. I have successfully established 3 laboratories during my career, administered numerous projects at these institutions (e.g. staffing, research protections, budget, IRB/IACUC protocols), collaborated with numerous researchers, and produced significant numbers of peer-reviewed publications from each arm of research encompassed by the Reproductive Cell-Cycle Theory of Aging. As a result of these previous experiences, I am aware of the importance of frequent communication among project members and of constructing a realistic research plan, timeline, and budget. The current application builds logically on my prior work and aims to implement practical measures of rebalancing the reproductive hormone axis.

1. Bowen, R.L. and **Atwood, C.S.** (2004). Living and Dying for Sex: A theory of aging based on the modulation of cell cycle signaling by reproductive hormones. Gerontology, 50(5), 265-290.
2. **Atwood C.S.** and Bowen R.L. (2011). The reproductive-cell cycle theory of aging: An update. Experimental Gerontology, 46(2-3), 100-107.
3. **Atwood, C.S.,** Vadakkadath Meethal, S., Liu, T., Wilson, A.C., Gallego, M., Smith, M.A. and Bowen, R.L. (2005). Dysregulation of the Hypothalamic-Pituitary-Gonadal Axis with Menopause and Andropause Promotes Neurodegenerative Senescence. Journal of Neuropathology and Experimental Neurology, 64(2), 93-103.

B. Positions and Honors

Positions and Employment

1996–2000 Assistant Biochemist, Genetics and Aging Unit, Neuroscience Center, Massachusetts General Hospital, Charlestown, MA
1997–2001 Instructor of Neuroscience, Harvard Medical School, Department of Psychiatry, Boston, MA
2000–2003 Assistant Professor, Institute of Pathology, School of Medicine, CWRU, Cleveland, OH

2003–2010 Adjunct Associate Professor, Department of Pathology, Case Western Reserve University, Cleveland, OH
2003–2007 Assistant Professor, Department of Medicine, University of Wisconsin–Madison, WI
2003–pres. Research Scientist, Geriatric Research, Education and Clinical Center (GRECC), William S. Middleton Memorial Veterans Hospital, Madison, WI
2003–pres. Research Director, Wisconsin Alzheimer's Institute, and Research Director, Wisconsin Comprehensive Memory Program, University of Wisconsin–Madison, WI
2007–pres. Associate Professor (with tenure), Department of Medicine, University of Wisconsin–Madison

Editorial Positions (selected from 52)

Journal of Biological Chemistry, Editor, 2011-pres.; Frontiers in Dementia, Review Editor, 2010-pres.; Neuroscience and Medicine, Editorial Board, 2010-pres.; Nutrition and Diabetes, Senior Editor, 2010-pres.; Journal of Aging Research, Editorial Board, 2009-pres; International Journal of Alzheimer's Disease, Editorial Board, 2009-pres.; Current Neuropharmacology, Editorial Advisory Board, 2008-pres.; Recent Patents on Biotechnology, Editorial Board, 2008–pres.; International Journal of Clinical and Experimental Medicine, Executive Editorial Board, 2007–pres.; International Journal of Biomedical Nanoscience and Nanotechnology, Editor, 2007–pres.; Neural Regeneration Research, Editor, 2007-pres.; Recent Patent Reviews on CNS Drug Discovery, Editor, 2005–pres.; Current Alzheimer's Research, Editor, 2003–pres.; Journal of Alzheimer's Disease, Senior Editor, 2002–pres.

Review Boards

Alzheimer's Association, 1998–pres.; Neurological Foundation of New Zealand Project Grants, 1999; American Institute for Biological Sciences (Parkinson's Disease, Panel C member), 2000, 2002, 2004; National Health and Medical Research Council of Australia, 2001–2003; The Wellcome Trust, 2002; National Institutes of Health - Brain Disorders and Clinical Neuroscience–3 Study Section 2002–2005, 2008, 2009, Special Emphasis Panel, 2004-2005, Child Health and Human Development-C, 2007-2008, ad hoc viewer; Medical Research Council, UK, 2004; American Chemical Society (The Petroleum Research Fund), 2004; Catalan Agency for Health Technology Assessment and Research, Barcelona, Spain, 2006; American Federation for Aging Research, 2007–pres.; Research Into Aging, UK, 2007, 2010.

Other Experience and Professional Memberships

1995- Member, New York Academy of Sciences
1996- Member, Society for Neuroscience
2004- Member, Endocrine Society
2006- Member, UW/VA Brain Bank Committee (Wisconsin Brain Donor Program)
2009- Biomarker Core Leader, Wisconsin ADRC
2009- Consultant, International Journal of Alzheimer's Disease
2010- American Society for Biochemistry and Molecular Biology
2012- Member, Gerontological Society of America

Honors and Awards

Beckman Student Prize, 1991; Organon Young Investigators Award, 1992; Fogarty International Research Fellowship, 1994-1995; Gordon Conference Poster Prize, 1995; Highly-cited author, SPAR, 2005; MSA Partners Report, 2006; Zenith Fellows Award, Alzheimer's Association, 2006; Delegate to National Academies Keck Futures Initiative, 2007-2008; Undergraduate Mentoring Award for Biological Sciences, University of Wisconsin, Madison, WI, 2014; ***h*-index = 44 (ISI Web of Knowledge, Aug. 2015).**

C. Contribution to Science

1. **Aging:** Research in my laboratory involves understanding aging throughout life as described in the Reproductive-Cell Cycle Theory of Aging. This theory evolved from basic research into the endocrinological mechanisms driving neurodegeneration in Alzheimer's disease. The basic premise behind the theory and the research in my laboratory is that the hormones that regulate reproduction act in an antagonistic pleiotropic manner to control aging via cell cycle signaling; promoting growth and development early in life in order to achieve reproduction, but later in life, in a futile attempt to maintain reproduction, become dysregulated and drive senescence. The theory is able to explain why and how we age at the evolutionary, physiological and molecular levels. The power of the theory is evidenced by the fact that it is able to explain many phenomena

associated with aging:

1. the simultaneous regulation of the rate of aging and reproduction
2. how differing rates of reproduction between species are associated with differences in their lifespan;
3. the rate of growth and development and the ultimate size of an animal;
4. the apparent paradox that size is directly proportional to lifespan and inversely proportional to fertility between species but vice versa within a species;
5. how we grow and develop during early life, and maintain tissue homeostasis during adulthood;
6. why and how we develop age-related diseases; and
7. provides a credible reason for why and how aging occurs at the evolutionary, physiological and molecular levels.

In addition, the theory is able to explain the caveats that other aging theories can not explain, such as why organisms with predator evading attributes such as birds and turtles live so long and how caloric restriction extends longevity.

a. Bowen, R.L. and **Atwood, C.S.** (2004). Living and Dying for Sex: A theory of aging based on the modulation of cell cycle signaling by reproductive hormones. *Gerontology*, 50(5), 265-290.
b. Atwood C.S. and **Bowen R.L.** (2011). The reproductive-cell cycle theory of aging: An update. *Experimental Gerontology*, 46(2-3), 100-107.
c. Yonker, J.A., Chang, V., Roetker, N.S., Hauser, T.S., Hauser, R.M. and **Atwood, C.S.** (2013) Hypothalamic-pituitary-gonadal axis homeostasis predicts longevity. *Age (Dordr)*. 35(1), 129-138. doi: 10.1007/s11357-011-9342-1. Epub 2011 Dec 4.

2. **Growth and Development:** Our research has defined hormonal signals required for early embryogenesis. Our aim was to identify those hormones responsible for the division and differentiation of the human zygote into a morula, and then into a blastocyst. Utilizing human embryonic stem cells (hESC) as a model of early embryogenesis, our data indicates that the pregnancy hormone human chorionic gonadotropin (hCG), the fetal equivalent of luteinizing hormone (LH), drives stem cell proliferation during blastulation, while hCG upregulation of hESC progesterone synthesis drives neurulation. These studies indicate that hypothalamic-pituitary-gonadal (HPG) hormones are upregulated starting at conception.

a. Gallego, M.J., Porayette, P. Kaltcheva, M.M., Vadakkadath Meethal, S. and **Atwood, C.S.** (2009). Opioid and progesterone signaling is obligatory for early human embryogenesis. *Stem Cells and Development*, 18(5), 737-740.
b. Porayette, P., Gallego, M.J., Kaltcheva, M.M., Bowen, R.L., Vadakkadath Meethal, S. and **Atwood, C.S.** (2009). Differential processing of amyloid-beta precursor protein directs human embryonic stem cell proliferation and differentiation into neuronal precursor cells. *Journal of Biological Chemistry*, 284(35), 23806-23817.
c. Gallego, M.J., Porayette, P., Kaltcheva, M.M., Bowen, R.L., Vadakkadath Meethal, S. and **Atwood, C.S.** (2010). The pregnancy hormones human chorionic gonadotropin and progesterone induce human embryonic stem cell proliferation and differentiation into neuroectodermal rosettes. *Stem Cell Research & Therapy*, 1:28.
d. **Atwood, C.S.** and Vadakkadath Meethal, S. (2011). Human Embryonic Stem Cells as a Model System for Understanding Early Human Embryogenesis and Age-related Diseases. In: *Embryonic Stem Cells*. Ed. Craig S. Atwood. InTech, Rijeka, Croatia. Chapter 14, 251-270. ISBN: 978-953-307-196-1

3. **Tissue Maintenance:** Our data indicates that HPG hormones are responsible for maintaining tissues and for cell turnover during our reproductive adult years. In this respect, we have determined the presence of a 'Mini-HPG' axis within the brain that regulates neurohormone synthesis. Our results suggest the presence of such axes in all tissues of the body that coordinate with the endocrine HPG axis.

a. Wilson, A.C., Salamat, S., Haasl, R.J., Roche, K.M., Karande, A., Vadakkadath Meethal, S., Terasawa, E., Bowen, R.L. and **Atwood, C.S.** (2006). Human extra-pituitary neurons possess GnRH I receptors that respond to GnRH by expressing luteinizing hormone. *Journal of Endocrinology*, 191, 651-665.
b. Liu, T., Wimalasena, J., Bowen, R.L. and **Atwood, C.S.** (2007). Luteinizing hormone receptor mediates neuronal pregnenolone production via upregulation of steroidogenic acute regulatory protein expression. *Journal of Neurochemistry*, 100(5), 1329-1339.
c. Wilson, A.C., Clemente, L., Liu, T., Bowen, R.L., Vadakkadath Meethal, S. and **Atwood, C.S.** (2008). Reproductive hormones regulate the selective permeability of the blood-brain barrier. *Biochimica et Biophysica Acta - Molecular Basis of Disease*, 1782(6), 401-407.

d. Vadakkadath Meethal, S., Liu, T., Chan, H., Ginsburg, E., Wilson, A.C., Gray, D.N., Bowen, R.L., Vonderhaar, B.K. and **Atwood, C.S.** (2009). Identification of a regulatory loop for the synthesis of neurosteroids: A StAR-dependent mechanism involving HPG axis receptors. *Journal of Neurochemistry*, 110, 1014-1027.
e. **Atwood, C.S.** and Vadakkadath Meethal, S. (2011). Gonadotropins and Progestogens: Obligatory Developmental Functions during Early Embryogenesis and their Role in Adult Neurogenesis, Neuroregeneration, and Neurodegeneration. In: *Hormones in Neurodegeneration, Neuroprotection and Neurogenesis*, Eds. Achille Gravanis and Synthia Mellon, WILEY-VCH Verlag GmbH & Co. KgaA, Weinheim, Germany. Chapter 18, pp 305-319. ISBN: 978-3-527-31920-6

4. **Aging-related Diseases:** The dysregulation of the HPG axis (reproductive endocrine dyscrasia) at menopause in women and with andropause in men drives aberrant cell cycle signaling that promotes neurodegeneration. Rebalancing of the axis with Lupron has been demonstrated to preserve cognitive function in patients taking an acetylcholineesterase inhibitor with mild to moderate Alzheimer's disease over a 1 year period. We also have discovered that the disruption in activin signaling promotes cell detachment and is pivotal in the development of metastatic cancer.

a. Bowen, R.L., Verdile, G., Liu, T., Perry, G., Smith, M.A., Martins, R.N. and **Atwood, C.S.** (2004). Luteinizing hormone, a reproductive regulator that modulates the processing of amyloid-ß protein precursor and amyloid-ß deposition. *Journal of Biological Chemistry*, 279(19), 20539-45.
b. Casadesus, G., Webber, K.M., **Atwood, C.S.,** Pappolla, M.A., Perry, G., Bowen, R.L. and Smith, M.A. (2006). Luteinizing hormone modulates cognition and amyloid-ß deposition in Alzheimer APP transgenic mice. *Biochemica Biophyica. Acta* 1762(4), 447-452.
c. Haasl, R.J., Reza Ahmadi, M., Vadakkadath Meethal, S., Gleason, C.E., Johnson, S.C., Asthana, S., Bowen, R.L. and **Atwood, C.S.** (2008). A luteinizing hormone receptor intronic variant is significantly associated with decreased risk of Alzheimer's disease in males carrying an apolipoprotein E ε4 Allele. *BMC Medical Genetics*, 9(1):37.
d. Simon, D., Vadakkadath Meethal, S., Wilson, A.C., Gallego, M.J., Weinecke, S.L., Bruce, E., Lyons, P., Haasl, R.J., Bowen, R.L. and **Atwood, C.S.** (2009). Activin receptor signaling regulates prostatic epithelial cell adhesion and viability. *Neoplasia*, 11(4), 365-376.
e. Bowen, R.L., Perry, G., Xiong, C., Smith, M.A., **Atwood, C.S.** (2015). A clinical study of Lupron Depot in the treatment of women with Alzheimer's disease: Preservation of cognitive function in patients taking an acetylcholinesterase inhibitor and treated with high dose Lupron over 48 weeks. *Journal of Alzheimer's Disease*, 44(2), 549-560. doi: 10.3233/JAD-141626.

D. Research Support

Ongoing Research Support

1I21RX001371 VA Merit Review Atwood (PI) 04/01/14–03/31/16
Title: *hCG Therapy in the Treatment of Traumatic Brain Injury*
Aim: To test hCG as a treatment for traumatic brain injury using a rat model.

P50 AG033514 NIH/NIA Asthana (PI) 04/01/14–03/31/19
Title: *Wisconsin Alzheimer's Disease Research Center*
Aim: The Neuropathology and Biomarker Core collects biological samples and provides biomarker analyses in the ADRC cohorts and expertise to ADRC affiliated investigators.
Role: Leader, Biomarker Core

R01 AG21079 NIH/NIA Herd, Hauser and Freese (PIs) 07/01/13-06/30/18
Title: *A Longitudinal Resource for Genetic Research in Behavioral & Health Sciences*
Aim: Whole genome sequencing of the Wisconsin Longitudinal Study.
Role: Co-Investigator

Center for Demography of Health and Aging Atwood (PI) 01/01/15-03/31/16
Title: *Veteran Health in the WLS*
Aim: To examine health outcomes of veterans in the Wisconsin Longitudinal Study.

Completed Research Support

Graduate School, UW-Madison Atwood (PI) 07/01/14–06/30/15
Title: *Utilization of Fibroblasts as a Diagnostic Marker for Alzheimer's Disease*
Aim: To assess the potential of fibroblasts as a measure of neurosteroid synthesis for predicting cognitive decline.

5I21BX001623 VA Merit Review Atwood (PI) 10/01/12–09/30/14
Title: *Epistasis in Steroidogenic Genes in the Prediction of Alzheimer's Disease*
Aim: To generate pilot data on genetic variants in steroidogenic pathway genes that predict AD.

R56 AG041913 NIH Atwood, Druger, Ryff, Seeman (PIs) 09/15/13-08/31/14
Title: *What Genes Experience: Environmental Moderators of Genetic Risk in MIDUS*
Aim: To investigate the molecular genetics of the Midlife in the U.S. Study (MIDUS), a large cohort of American adults followed from early adulthood through later life.

Department of Medicine, UW-Madison Atwood (PI) 07/01/12–12/31/13
Title: *Identification of AβPP Cleavage Products that Promote Re-activation of the Cell Cycle in Post-mitotic Neurons*
Aim: To assess how AβPP and its cleavage products regulate stem cell proliferation and differentiation into neural precursor cells.

R01 AG027161 NIH/NIA Sager (PI) 04/01/07–03/31/12
Title: *Wisconsin Registry for Alzheimer's Prevention*
Aim: To assess family history in the etiology of Alzheimer's disease using a cohort of at-risk younger family members.
Role: Co-investigator