

## BIOGRAPHICAL SKETCH

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NAME <b>Atwood, Craig Stephen</b>	POSITION TITLE <b>Associate Professor of Medicine          Research Director, Wisconsin Alzheimer's Institute</b>		
eRA COMMONS USER NAME (credential, e.g., agency login) <b>catwood</b>			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
The University of Western Australia, Australia	B.Sc. (Hons.)	04/1985	Biochemistry
The University of Western Australia, Australia	Ph.D.	04/1993	Biochemistry
Laboratory of Molecular & Cellular Endocrinology National Cancer Institute, NIH, Bethesda, MD	Fogarty Fellow	01/1994- 09/1995	Cellular and Molecular Endocrinology
Genetics and Aging Unit, Neuroscience Center, Massachusetts General Hospital, Charlestown, MA	Research Fellow	09/1995- 10/1997	Neuroscience and Protein Chemistry

### A. Personal Statement

The goal of the proposed research is to identify hormonal mechanisms leading to the development of Alzheimer's disease. Specifically, we plan to identify 1) genetic alterations in steroidogenic pathway family members (SPFMs) that predict AD, 2) genetic alterations in SPFMs that regulate circulating and brain sex steroid synthesis, and 3) the molecular mechanisms by which SPFMs modulate sex steroid synthesis. I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a strong background in neuroendocrinology and neurogenetics with specific training and expertise in key research areas for this application. As a post-doctoral fellow at the National Cancer Institute, I received training in the endocrinology of breast cancer. As a post-doctoral fellow at Massachusetts General Hospital, I gained experience in neuroscience as it relates to Alzheimer's disease. At Case Western Reserve University, I combined these areas of expertise to examine the neuroendocrinology of Alzheimer's disease, and this research continues today at the University of Wisconsin-Madison. As PI or Co-Investigator on several previous NIH-, VA-, university- and industry-funded grants, I was able to apply my knowledge to the neurobiology and neurogenetics of this disease and this has laid the groundwork for the proposed research. In related projects involving the Wisconsin Longitudinal Study, and the Wisconsin Registry for Alzheimer's Prevention, we have pursued the identification of gene-gene interactions that associate to phenotypic data such as disease state. I successfully administered these projects (e.g. staffing, research protections, budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. 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 I have chosen a collaborator (Dr. Vadakkadath Meethal) who provides additional and complimentary expertise in cellular and molecular biology of neuroendocrinological systems. In summary, I have a demonstrated record of successful and productive research projects in an area of high relevance for our aging VA population, and my expertise and experience have prepared me to lead the proposed project.

### 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-pres.	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 Director, Wisconsin Alzheimer's Institute, and Research Director, Wisconsin Comprehensive Memory Program, University of Wisconsin–Madison, WI  
 2003–pres. Research Scientist, Geriatric Research, Education and Clinical Center (GRECC), William S. Middleton Memorial Veterans Hospital, Madison, WI  
 2007–pres. Associate Professor (with tenure), Department of Medicine, University of Wisconsin–Madison

### **Editorial Positions**

Journal of Alzheimer's Disease, Senior Editor, 2002–pres.; Current Alzheimer's Research, Editor, 2003–pres.; Recent Patent Reviews on CNS Drug Discovery, Editor, 2005–pres.; Open Biochemistry Journal, Editor, 2007–pres.; The Open Aging Journal, Editor, 2007–pres.; Neural Regeneration Research, Editor, 2007–pres.; International Journal of Biomedical Nanoscience and Nanotechnology, Editor, 2007–pres.; International Journal of Clinical and Experimental Medicine, Executive Editorial Board, 2007–pres.; Recent Patents on Biotechnology, Editorial Board, 2008–pres.; Current Neuropharmacology, Editorial Advisory Board, 2008–pres.; International Journal of Alzheimer's Disease, Editorial Board, 2009–pres.; World Journal of Stem Cells, Editorial Board, 2009–pres., Journal of Aging Research, Editorial Board, 2009–pres, Diabetes and Nutrition, Senior Editor, 2010–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.

### **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.

### **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  
 2009- Biomarker Core Leader, Wisconsin ADRC  
 2009- Consultant, International Journal of Alzheimer's Disease

## **C. Selected Peer-reviewed Publications (Selected from 75 peer-reviewed publications)**

### **Most relevant to the current application**

1. 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.
2. 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, 1329-1339.
3. 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 Biophysica. Acta - Molecular Basis of Disease*, 1782, 401-407.

4. 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  $\epsilon$ 4 Allele, *BMC Medical Genetics*, 9, 37.
5. 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.

**Additional recent publications of importance to the field (in chronological order)**

1. Dong, J., Atwood, C.S., Anderson, V.E., Siedlak, S.L., Perry, G., Smith, M.A. and Carey, P.R. (2003). Metal binding and oxidation of amyloid- $\beta$  within isolated senile plaque cores: Raman microscopic evidence. *Biochemistry*, 42, 2768-2773.
2. 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- $\beta$  protein precursor and amyloid- $\beta$  deposition. *Journal of Biological Chemistry*, 279, 20539-20545.
3. Atwood, C.S., Perry, G., Zeng, H., Kato, Y., Jones, W.D., Ling, K.Q., Huang, X., Moir, R.D., Wang, D., Sayre, L.M., Smith M.A., Chen, S.G. and Bush, A.I. (2004). Copper mediated crosslinking reactions of Alzheimer's amyloid- $\beta$ . *Biochemistry*, 43, 560-568.
4. Liu, T., Perry, G., Chan, H.W., Verdile, G., Martins, R.N., Smith, M.A. and Atwood, C.S. (2004). Amyloid- $\beta$ -induced toxicity of primary neurons is dependent upon differentiation associated increases in tau and cyclin-dependent kinase 5. *Journal of Neurochemistry*, 88, 554-563.
5. Zhu, X., McShea, A., Harris, P.L.R., Raina, A.K., Castellani, R.J., Funk, J.O., Shah, S., Atwood, C.S., Bowen, R., Bowser, R., Morelli, L., Perry, G. and Smith, M.A. (2004). Elevated expression of a regulator of the G2/M phase of the cell cycle, neuronal CIP-1-associated regulator of cyclin B, in Alzheimer's disease. *Journal of Neuroscience Research*, 75, 698-703.
6. Wung, J.K., Perry, G., Kowalski, A., Harris, P.L.R., Bishop, G.M., Trivedi, M.A., Johnson, S.C., Smith, M.A., Denhardt, D.T. and Atwood, C.S. (2007). Increased expression of the remodeling- and tumorigenic-associated factor osteopontin in pyramidal neurons of the Alzheimer's disease brain. *Current Alzheimer Research*, 4, 67-72.
7. Porayette, P., Gallego, M.J., Kaltcheva, M.M., Vadakkadath Meethal, S. and Atwood, C.S. (2007). Amyloid- $\beta$  precursor protein expression and modulation in human embryonic stem cells: A novel role for human chorionic gonadotropin. *Biochemical and Biophysical Research Communications*, 364, 522-527.
8. Rodrigues, M.A., Verdile, G., Foster, J.K., Hogervorst, E., Joesbury, K., Dhaliwal, S., Corder, E.H., Laws, S.M., Hone, E., Prince, R., Devine, A., Mehta, P., Beilby, J., Atwood, C.S. and Martins, R.N. (2008). Gonadotropins and cognition in older women. *Journal of Alzheimer's Disease*, 13, 267-274.
9. 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, 737-740.
10. 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, 23806-23817.

**D. Research Support**

**Ongoing Research Support**

NIH/NIA P50 Asthana (PI) 05/01/09-04/30/14

"Wisconsin Alzheimer's Disease Research Center "

The Wisconsin ADRC plans to provide detailed characterization of the evolving Alzheimer disease brain across the disease continuum from presymptomatic disease to death.

Role: Leader, Biomarker Core

NIH/NIA R01 Sagar (PI) 04/01/07-03/31/12

"Wisconsin Registry for Alzheimer's Prevention"

To assess family history in the etiology of Alzheimer's disease using a cohort of at-risk younger family members.

Role: Co-investigator

Department of Medicine, UW-Madison      Atwood (PI)      07/01/10–06/30/11

*“Multi-Locus Interactions in the Steroidogenic Pathway Predict Alzheimer’s Disease”*

This grant will assess steroidogenic enzyme genotype and function in unaffected individuals and those with Alzheimer’s disease.

**Completed Research Support**

Department of Medicine, UW-Madison      Atwood (PI)      10/01/08–09/30/09

*“Progesterone Induction of Neurogenesis in Human Embryonic Stem Cells”*

This grant examined the role of progesterone in the differentiation of embryonic stem cells into neural precursor cells during neurulation.

Alzheimer’s Association, Zenith Award      Atwood (PI)      10/01/06–09/30/08

*“Leuprolide Acetate in the Treatment of Alzheimer’s Disease”*

This grant explored the role of GnRH analogues in modulating cell cycle signaling in neurons.

VA Merit Review      Atwood (PI)      10/01/04–09/30/07

*“Pituitary Hormone-Lowering Drugs Suppress Alzheimer’s Neurodegeneration”*

This grant examined the role of hormones in regulating APP processing, amyloid- $\beta$  generation, tau phosphorylation and cognition. Anti-gonadotropin drugs that modulate hypothalamic-pituitary-gonadal axis hormones were examined as potential interventions to limit biochemical and cognitive changes associated with Alzheimer’s disease.