
BIOGRAPHICAL SKETCH

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NAME Jyoti J. Watters	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME JJWATTERS			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Arizona, Tucson	B.S.	1986-1990	Microbiol/Immunology
University of Washington, Seattle	Ph.D.	1992-1997	Pharmacology
University of Wisconsin, Madison	Post-doc	1998-2002	Biochem./Biomol. Chem

A. Personal Statement

The overall goal of my research program is to investigate the cellular and molecular mechanisms whereby microglia contribute to CNS recovery from chronic neuroinflammatory disorders. Chronic intermittent hypoxia (IH), a hallmark of sleep disordered breathing, is associated with many neurological and peripheral disorders, and promotes neuroinflammation, neuronal apoptosis and cognitive impairment. However, with prolonged exposure, the CNS adapts in part to this chronic insult by a partial recovery in cognition, and the creation of new neurons (neurogenesis). The mechanisms underlying this adaptation and compensation for the chronic IH insult are poorly understood, but we hypothesize involve shifts in the microglial phenotype from inflammatory to neurotrophic. Our studies are focused on understanding the long-lasting, epigenetic changes induced by IH in microglia that contribute to their shift in phenotype and function. My research expertise involves studying signal transduction and gene transcriptional mechanisms in microglia *in vitro* and *in vivo*. I have a broad background in neuroimmunology and pharmacology with specific training and expertise in key research areas fundamental to our ongoing projects. The effects of IH on microglial activities and their contributions to neuroinflammation have not been previously addressed, nor have molecular pathways governing their phenotypic transitions from pro-inflammatory to neurotrophic in different phases of chronic IH. To our knowledge, we are the first to initiate studies evaluating the roles of microRNAs and other epigenetic modifications in microglia following exposure to IH, and we have developed new tools to enable cell-specific analyses of these aspects *in vivo*. I actively train graduate, post-doctoral and undergraduate students, and I teach both graduate and professional veterinary medicine courses.

B. Positions and Honors

Positions and Employment

1990-1992	Research Technologist, University of Washington, Veteran's Administration Hospital
1992-1997	Graduate Student, University of Washington, Seattle with Dr. Daniel M. Dorsa
1998-2001	Post-Doctoral Associate, Department of Biochemistry, University of Wisconsin, Madison with Dr. Jack Gorski
1999-2002	NIH Post-Doctoral Fellow (8/99-7/01), Department of Biomolecular Chemistry, University of Wisconsin, Madison with Dr. Paul J. Bertics
2002-2009	Assistant Professor, Department of Comparative Biosciences, School of Veterinary Medicine, University of Wisconsin
2009-present	Associate Professor, Department of Comparative Biosciences, School of Veterinary Medicine, University of Wisconsin

Professional Memberships

1993	American Association for the Advancement of Science
1994	Society for Neuroscience
1998	Endocrine Society
2001	Women in Endocrinology, Women in Neuroscience

2005 American Society for Neurochemistry
2009 American Physiological Society

Honors and Awards

Honors B.S. Cum Laude, University of Arizona, 1990
NIH Predoctoral Trainee, University of Washington, 1993-1996
Endocrine Society Travel Award 1999, 2002
Women in Endocrinology Travel Award 2002
NIH/NRSA Postdoctoral Fellow (National Cancer Institute) University of Wisconsin 8/99-7/01
New investigator award Society for Women's Health Research Conference 2000-2003
Inaugurated into the International Biography Center, Cambridge, England 2006
Inaugurated into Who's Who Among Executives and Professionals, Honors Edition 2008
Vilas Mid-Career Faculty Award 2014

C. Selected peer-reviewed publications (in chronological order) (Total publications=49; h-index=25)

Watters, J.J., Campbell, J.S., Cunningham, M.J., Krebs, E.G. and Dorsa, D.M. 1997 Rapid membrane effects of steroids in neuroblastoma cells: Effects of estrogen on mitogen activated protein kinase signaling cascade and c-fos immediate early gene transcription. Endocrinology 138(9): 4030-4033. (PMID: 9275096)

Watters, J.J. and Dorsa, D.M. 1998 Transcriptional effects of estrogen on neurotensin gene expression involve cAMP/protein kinase A-dependent signaling mechanisms. J. Neuroscience 18(17): 6672-6680. (PMID: 9712639)

Watters, J.J., Chun, T.Y., Kim, Y.N., Bertics, P.J. and Gorski, J. 2000 Estrogen modulation of prolactin gene expression requires an intact mitogen activated protein kinase signal transduction pathway in cultured rat pituitary cells. Molecular Endocrinology 14(11): 1872-1881. (PMID: 11075818)

Watters, J.J., Sommer, J.A., Pfeiffer, Z.A., Guerra, A.N., Prabhu, U. and Bertics, P.J. 2002 LPS potently induces nitric oxide and interleukin-1 β production but fails to activate ERK-1 and ERK-2 in murine microglial cells. J. Biological Chemistry 277:9077-9087. (PMID: 11786532)

Brautigam, V.M., Frasier, C., Nikodemova, M. and **Watters, J.J.** 2005 Purinergic Receptor Modulation of Microglial Cell Activity: Potential Involvement of p38 MAP Kinase and CREB. J. Neuroimmunol, (166)113-125. (PMID: 15979729)

Nikodemova, M., Duncan, I.D. and **Watters, J.J.** 2006 Minocycline exerts inhibitory effects on multiple members of the mitogen-activated protein kinases in a stimulus specific manner in microglia in vitro. J. Neurochemistry, 96:314-323. (PMID: 16336636)

Nikodemova, M., **Watters, J.J.**, Jackson, S.J., Young, S.K. and Duncan, I.D. 2007 Minocycline downregulates MHC II expression in microglia and macrophages through inhibition of IRF-1 and PKC α / β II. J. Biol. Chem., 282(20):15208-15216. (PMID: 17395590)

Crain, J.M., Nikodemova, M. and **Watters, J.J.** 2009 Purinergic receptor expression varies with age and sex in freshly isolated brain microglia. J. Neuroinflammation, 6:24. (PMCID: PMC2744668).

Friedle, S.A., Nikodemova, M., Wright, M.L. and **Watters, J.J.** 2011 The P2X7-Egr Pathway Regulates Nucleotide-Dependent Inflammatory Gene Expression in Microglia. Glia. 59(1):1-13. (PMCID: PMC2981661)

Nikodemova, M. and **Watters, J.J.** 2011 Outbred ICR/CD1 mice display more severe neuroinflammation mediated by microglial TLR4/CD14 activation than inbred C57Bl/6 mice. Neuroscience. 190:67-74 (PMCID: PMC3156380)

Nikodemova, M. and **Watters, J.J.** 2012 Efficient isolation of live microglia with preserved phenotypes from adult mouse brain. J. Neuroinflammation. 9:147. (PMC Journal: PMC3418565)

Crain, J.M.*, Nikodemova, M.* and **Watters, J.J.** 2013 Microglia express distinct M1 and M2 phenotypic

markers in the postnatal and adult CNS in male and female mice. J. Neurosci. Res. 91(4):1143-1151. (PMCID: PMC3715560) *Both authors contributed equally

Nikodemova, M., Small, A.L., Smith, S.M., Mitchell, G.S. and **Watters, J.J.** 2013 Spinal but not cortical microglia acquire an atypical phenotype with high VEGF, galectin-3 and osteopontin, and blunted inflammatory responses in ALS rats. Neurobiology of Disease, in press. (PMCID: PMC24269728).

Smith, S.M.C., Mitchell, G.S., Friedle, S.A. and **Watters, J.J.** 2013 Chronic intermittent hypoxia exerts CNS region-specific effects on rat microglial inflammatory and TLR4 gene expression. PLoS One, 8(12):e81584 (PMCID: PMC3852519).

Smith, S.M.C., Kimyon, R.S. and **Watters, J.J.** 2014 Cell-Type Specific Expression of Jumonji Histone Demethylases in the Healthy Rat CNS: Detection By A Novel Flow Cytometry Method. ASN Neuro, 6(3) pii: e00146 (PMCID: PMC4034710).

D. Research Support

Ongoing Research Support

Agency: R01 National Institutes of Health 01/15/12 - 12/31/16 (HL111598)
Title: Intermittent Hypoxia-Induced Inflammation Modulates Respiratory Plasticity (\$1,950,000)
Role: co-Principal Investigator, 15%
Subject: Investigate cellular mechanisms whereby inflammation interferes with respiratory plasticity

Agency: Department of Defense (Otto- PI) 11/01/10 - 10/31/15
Title: Normal and accelerated failure assessment of new quantitative *in vitro* and *in vivo* neural interfaces (\$3,900,000)
Role: Project Leader (co-I), 15%
Subject: Investigate the role of microglia in neural interface failure, and mechanisms of intervention

Agency: Becton Dickinson and Company 06/01/12 - 05/30/2015
Title: A Novel Method Using Multicolor Flow Cytometry and FACS to Enable Multiparametric Examination of the CNS Cellular Response to Intermittent Hypoxia (\$10,000)
Role: PI
Subject: Optimize flow cytometry method to sort cells using intracellular stains while retaining the ability to isolate nucleic acids

Agency: National Institutes of Health DiaComp Pilot Study (C. Vezina, PI) 10/01/13 - 09/30/14
Title: Intermittent Hypoxia and Urologic Complications of Diabetes (\$65,000)
Role: co-Investigator, 2.5%
Subject: The goal of this project is to investigate the cellular and molecular mechanisms whereby respiratory plasticity is enhanced and undermined during spinal cord injury

Agency: R01 National Institutes of Health, NHLBI (G. Mitchell, PI) - 02/01/14 - 01/31/18
Title: "Respiratory plasticity and spinal cord injury (\$1,625,000)
Role: co-Investigator, 5%
Subject: The goal of this project is to investigate the cellular and molecular mechanisms whereby respiratory plasticity is enhanced and undermined during spinal cord injury

Pending Research Support

Agency: R01 National Institutes of Health (NINDS) (\$250,000 DC/yr)
Title: Regulation of microglial plasticity by miRNAs
Role: Principal Investigator (20%)
Subject: Investigate the mechanisms whereby miRNAs regulate microglial phenotype in a chronic neuroinflammatory disorder (chronic intermittent hypoxia).

Agency: R01 National Institutes of Health (NHLBI) (\$250,000 DC/yr)
Title: GABA-A Epsilon Receptor Subunit Expression in Medullary Respiratory Neurons (R01)
Role: co-Principal Investigator, 15% (S. Johnson, PI)
Subject: Investigate the mechanisms whereby GABA-A epsilon subunits contribute to respiratory rhythm generation in the brainstem and how subunit expression is regulated by intermittent hypoxia

Completed Research Support

Agency: R01 National Institutes of Health (NINDS) 6/1/05 - 5/31/11
Title: Microglia, adenine nucleotides and hypoxia (NS049033)
Role: Principal Investigator
Subject: Investigate the mechanisms by which purinergic receptors decrease microglial inflammatory functions in response to hypoxia and combinatorial stimuli

Agency: R01 National Institutes of Health (Mitchell- PI) 1/1/10 - 12/31/14
Title: Mechanisms of respiratory long-term facilitation (\$1,000,000)
Role: Co-investigator, 10%.
Subject: Investigate the cellular and molecular mechanisms involved in respiratory motor neuron plasticity following exposure to intermittent hypoxia