

BIOGRAPHICAL SKETCH

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NAME Aschner, Michael	POSITION TITLE Professor of Pediatrics, Pharmacology and Senior Investigator at the Kennedy Center for Research on Human Development
eRA COMMONS USER NAME maschner	

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 Rochester, Rochester, NY	BS	1980	Natural Sciences
University of Rochester, School of Medicine	MS	1983	Anatomy
University of Rochester, School of Medicine	PhD	1985	Neurobiology/Anatomy
University of Rochester, School of Medicine	Postdoc	1987	Toxicology

A. Positions and Honors.**Positions and Employment**

- 1988-1994 Assistant Professor (1988-1992); Associate Professor (1992-1994), Dept. of Pharmacology & Toxicology, Albany Medical College, Albany, NY
- 1994-2004 Associate Professor (1994-1999); Professor (1999-2004), Dept. of Physiology & Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC
- 2004- Gray E. B. Stahlman Chair in Neuroscience, Professor of Pediatrics and Pharmacology, and Senior Scientist at the Kennedy Center for Research on Human Health, Vanderbilt University Medical Center, Nashville, TN
- 2005- Director, Division of Pediatric Toxicology, Department of Pediatrics, Vanderbilt University Medical Center

Selected Other Experience and Professional Memberships

- 1995-Pres. Associate Editor, Neurotoxicology
- 1995-Pres. Editorial Board, Fundamental & Applied Toxicology (FAAT), presently Toxicological Sciences
- 1997-Pres. Member, Academy of Toxicological Sciences
- 2002-Pres. Editorial Board (2002-2005) and Associated Editor (2005-Pres.), the Scientific World Journal.
- 1997-2003 Member, Technical Advisory Panel on the Health Effects of Methylcyclopentadienyl Manganese Tricarbonyl (MMT), Chemical Industry Institute of Toxicology, Research Triangle Park, NC
- 1997 Ad hoc reviewer, International Human Frontier Science Program (HFSP), France
- 1997-Pres. Reviewer, Agency for Toxic Substances and Disease Registry (ATSDR)
- 1997-1998 President (elected), Neurotoxicology Specialty Section of the Society of Toxicology
- 1998 Ad hoc reviewer, National Science Foundation (NSF)
- 1998-Pres. Member, Scientific Advisory Group (SAG) of the International Manganese Institute, Paris, France
- 1998-Pres. International referee, Neurological Foundation of New Zealand
- 1998-2002 Member, Alcohol and Toxicology 3 Study Section, NIH
- 1998-2000 Member, Committee on Health Effects Associated With Exposures Experienced During The Gulf War, Institute of Medicine, Division of Health Promotion and Disease Prevention, National Academy of Sciences
- 1999-2001 President (elected) International Neurotoxicology Association
- 1999-2000 Member, Committee to Review EPA's Maximum Contaminant Level Goal for Copper in Drinking Water, National Research Council, National Academy of Sciences
- 2001 External Reviewer, National Academy of Science, Committee on Thimerosal and Neurodevelopmental Outcomes, Institute of Medicine Immunization Safety Review Committee, National Academy Press, Washington, DC
- 1995-Pres. Reviewer, multiple Special Emphasis Panels NIH, EPA, ATSDR, FDA
- 2002-2003 Chair, Alcohol and Toxicology (ALTX) 3 Study Section, NIH

- 2005 Chair, External Advisory Committee, Collaborative Centers for Parkinson's Environmental Research (CCPDER) Program, NIEHS, Asilomar, Pacific Grove, CA
- 2005 Reviewer, Research Management Group, Linthicum Heights, MD
- 2006-Pres. Member, External Advisory Board, The Wake Forest and Brigham and Women's Center for Botanical Lipids, Wake Forest University Health Sciences, Department of Physiology and Pharmacology, Winston-Salem, NC.
- 2006-Pres. Consultant, the National Vaccine Injury Compensation Program, US Department of Justice
- 2007-Pres. Member, Scientific Committee on the Toxicology of Metals under the International Commission on Occupational Health (ICOH).
- 2007-2008 Member, Committee on Health Effects Associated With Exposures Experienced During the Gulf War, Institute of Medicine, Division of Health Promotion and Disease Prevention, National Academy of Sciences.

Selected Publications (from >250 peer reviewed publications and book chapters; since 1995)

- Rising L, Vitarella D, Kimelberg HK, Aschner M. Metallothionein induction in neonatal rat primary astrocyte cultures protects against methylmercury cytotoxicity. *J Neurochem* 1995; 65:1562-1568.
- Aschner M. The functional significance of brain metallothioneins, *FASEB J*. 1996; 10:1129-1136.
- Rutledge EM, Aschner M, Kimelberg HK. Pharmacological characterization of swelling induced [³H]-D-aspartate release from primary astrocyte cultures. *Am J Physiol* 1998; 274:C1511-C1520.
- Hutson SM, Berkich D, Drown P, Xu B, Aschner M, LaNoue KF. Role of branched chain aminotransferase isoenzymes and gabapentin in neurotransmitter metabolism. *J Neurochem* 1998; 71:863-874.
- Verity MA, Aschner M. Mechanisms of the toxic action of manganese: animal models. *Neurotoxicology* 1998; 19:483-485.
- Conklin DR, Tan KH, Aschner M. Dimethyl sulfoxide, but not acidosis-induced metallothionein mRNA expression in neonatal rat primary astrocyte cultures is inhibited by the bioflavonoid, quercetin. *Brain Res* 1998; 794:304-308.
- Zheng W, Zhao Q, Slavkovich V, Aschner M, Graziano JH. Alteration in iron homeostasis following chronic exposure to manganese in rats. *Brain Res* 1999; 833:125-132.
- Aschner M, Vrana KE, Zheng W. Manganese uptake and distribution in the central nervous system (CNS). *Neurotoxicology* 1999; 20:173-180.
- Aschner M, Allen JW, Kimelberg HK, LoPachin RM, Streit JW. Glial Cells in Neurotoxicity Development. *Annual Rev Pharmacol Toxicol* 1999; 39:151-173.
- Aschner M. Manganese: Brain transport and emerging research needs. *Environ Health Persp* 2000; 108:429-432.
- Aschner M. Neuron-astrocyte interactions: implications for cellular energetics and antioxidant levels. *Neurotoxicology* 2001; 21:1101-1108.
- Allen JW, Shanker G, Aschner M. Methylmercury inhibits the in vitro uptake of the glutathione precursor, cystine, in astrocytes but not in neurons. *Brain Res* 2001; 891:148-157.
- Allen JW, Shanker G, Aschner M. Mercuric chloride, but not methylmercury inhibit glutamine synthetase activity in primary cultures of cortical astrocytes. *Brain Res* 2001; 894:131-140.
- Aschner M, Allen JW, Mutkus LA, Cao C-C. Ethanol-induced swelling in neonatal rat primary astrocyte cultures. *Brain Res* 2001; 900:219-226.
- Worley CG, Bombick D, Allen JW, Suber RL, Aschner M. Effects of manganese on oxidative-stress in CATH.a cells. *Neurotoxicology* 2002; 23:159-164.
- Shanker G, Mutkus LA, Walker S, Aschner M. Methylmercury enhances arachidonic acid release and cytosolic phospholipase A2 expression in primary cultures of neonatal astrocytes. *Mol Brain Res* 2002; 106:1-11.
- Gunter KK, Miller LM, Aschner M, Eliseev R, Depuis D, Gavin CE, Gunter TE. XANES spectroscopy: A promising tool for toxicology: A tutorial. *Neurotoxicology* 2002; 23:127-146.
- Erikson KM, Aschner M. Manganese Neurotoxicity and Glutamate Metabolism. *Neurochem Int* 2003; 43:475-80.
- Aschner M, Aschner Y, Sonnewald U. The Neuron-Glia Unit in Neuropathology: Is it a Double-Edged Sword? *Jap J Cereb Blood Flow Metab* 2003; 15:95-100.

- Zheng W, Aschner M, Ghersi-Egea J-F. Brain barrier systems contributions to metal-induced neurotoxicities. *Toxicol Appl Pharmacol* 2003; 192:1-11.
- Erikson KM, Syversen T, Steinnes E, Aschner M. Globus pallidus: a target brain region for divalent metal accumulation associated with dietary iron deficiency. *J Nutr Biochem* 2004; 15:335-341.
- Mutkus LA, Aschner JL, Fitsanakis VA, Aschner M. The *in vitro* uptake of glutamate in GLAST and GLT-1 transfected mutant CHO-K1 cells is inhibited by manganese. *Biol Trace Element Res* 2005; 107:221-230.
- Erikson KM, John CE, Jones SR, Aschner, M. Manganese accumulation in striatum of mice exposed to toxic doses is dependent upon a functional dopamine transporter. *Environ Toxicol Pharmacol* 2005; 20:390-394.
- Gunter KK, Aschner M, Miller LM, Eliseev R, Salter J, Anderson K, Hammond S, Gunter TE. Determination of the oxidation states of manganese in PC12 and NGF-induced PC12 cells. *Free Radical Biol Med* 39:164-81, 2005.
- Aschner M, Aschner JL. Nutritional aspects of manganese neurotoxicity. *Trace Elements, Oxidant Stress, and Human Health. Mol Asp Med* 2005; 26:353-362.
- Fitsanakis VA, Piccola G, Aschner JL, Aschner M. Manganese (Mn) transport in rat brain endothelial cell (RBE4) monolayers cultured in the presence of astrocyte conditioned media (ACM) is an active process. *J Neurosci Res* 81:235-243, 2005.
- Fitsanakis VA, Piccola G, Aschner JL, Aschner M. Characteristics of Mn transport in rat brain endothelial (RBE4) cells, a model of the blood-brain barrier. *Neurotoxicology* 2006; 27:60-70.
- Erikson KM, Aschner M. Increased manganese uptake by primary astrocyte cultures with altered iron status is mediated primarily by divalent metal transporter. *Neurotoxicology* 2006; 27:125-130.
- Aschner M, Dorman DC. Manganese: Pharmacokinetics and molecular mechanisms of brain uptake. *Toxicol Rev* 2007; 25:147-154.
- Garcia JC, Gellein K, Syversen T, Aschner M. Iron deficient and manganese supplemented diets alter metals and transporters in the developing rat brain. *Toxicol Sci* 2007; 95:205-214.
- Zhang Y, Milatovic D, Aschner M, Feustel PJ, Kimelberg HK. Neuroprotection by tamoxifen in focal cerebral ischemia is not dependent on the action at estrogen receptors but is associated with antioxidant activity. *Exp Neurol* 2007; 204:819-27.

C. Research Support

Active

- 1) W81XWH-0510239 (Aschner, M) 02/01/05-01/31/08 1.2 calendar months
Department of Defense \$1,844,262

Manganese Health Research Project

This Program is composed of 7 Research Projects, and an administrative core. Dr. Aschner oversees the administrative core and is the PI on a project aimed at assessing the potential of iron overload to reduce Mn deposition in the rodent brain. Measurements are carried out by MRI. Overall, the MHRP identifies factors, such as age, nutritional deficiencies, pre-existing disease, and genetics that make individuals more susceptible to the effects of manganese, develops common exposure assessment protocols and exposure reconstruction methodologies and assesses the physiological mechanisms that govern manganese accumulation within the brain, including the role of olfactory transport of the metal.

- 2) W81XWH-0510239 (Aschner, M) 03/01/06-02/28/08 0.96 calendar months
Department of Defense/Subcontract (Nass, R) \$213,750 (total project)
Role of Toxins and Genetics in Mn-Induced DA Neuron Degeneration \$14,577 (subcontract)

This study will conduct genome-wide screen to identify mediators and suppressors of MN₂₊-induced toxicity that will facilitate the identification of novel genes and molecular pathways involved in highly relevant health and environmental concern.

- 3) W81XWH-0510239 (Aschner, M) 03/01/06-02/28/08 0.6 calendar months
Department of Defense/Subcontract (McLaughlin, B) \$120,327 (total project)
Molecular Mechanisms Underlying Mn Neurotoxicity \$9,110 (subcontract)

This project seeks to use cutting edge microarray and proteomic technologies to identify early changes in gene expression and protein products following Mn exposure.

- 4) W81XWH-0510239 (Aschner, M) 03/01/06-02/28/08 0.24 calendar months
 Department of Defense – Subcontract (Zheng, Wei)
Biomarkers of Early Onset of Manganese Neurotoxicities among Occupationally Exposed Chinese Workers
 This study will establish the dose-response relationship of airborne Mn levels and Mn concentrations in biological matrices, will define reliable biomarkers in serum, urine, saliva, or hair, and will determine the no adverse effect level (NOAEL) for regulatory purposes.
- 5) Afton Chemical Corp. (Aschner, M) 10/01/05 – 10/31/07 0.12 calendar months
 Tier II Supplement to: \$75,778
The Effects of Manganese on Brain
 This proposal examines oxidative endpoints (metallothionein, glutathione) along with the activity of enzymes (tyrosine hydroxylase, glutamine synthetase) upon inhalation exposure of rodents to manganese salts (sulfate, phosphate).
- 6) 5R01 ES07331-12 (Aschner, M) 08/01/04 - 04/30/09 2.40 calendar months
 NIH/NIEHS (total project period 05/01/04-04/30/09)
Mechanisms of Methylmercury-Induced Neuronal Toxicity \$231,919
 We will examine the hypothesis that activation of the astrocyte-specific enzyme, cytosolic phospholipase A₂ (cPLA₂) and the ensuing hydrolysis and release of arachidonic acid (AA) are mediators for glutamate release upon exposure to MeHg. Additional studies are directed at the role of heat shock protein 90 (Hsp90) in mediating the neurotoxicity of MeHg.
- 7) 1 R01 ES014459-01 (Nass, R) 01/01/06-12/31/10 .60 calendar months
 NIH/NIEHS \$213,750
Molecular Genetics of Manganese Induced Dopamine Neuron Toxicity
 The present proposal tests the hypotheses that in *C. elegans* Mn²⁺-induced neurodegeneration is dependent on DA and that Mn transport is mediated via the DMT-1 homologues *smf-2/3*.
- 8) 1R21 ES013730-01 (Aschner, Judy) 06/08/06—5/31/08 0.60 calendar months
 NIH/NIEHS \$150,000
Brain Manganese Deposition in High Risk Neonates
 The major goals of this R21 clinical pilot project are to determine whether infants requiring prolonged parenteral nutrition have increased brain manganese deposition as assessed by magnetic resonance imaging.
- 9) Gerber Foundation (Aschner, Judy) 07/01/06-06/30/09 0.60 calendar months
Neurodevelopment and Neuroimaging in Parenterally-Fed Infants and Young Children \$235,538
 The objectives are to identify neonatal and young pediatric populations at increased risk of excessive brain Mn deposition and altered cognitive and motor development and to make sound and evidence-based recommendations of appropriate Mn supplementation and monitoring of infants and young children receiving parenteral nutrition.
- 10) ES R01 (Gunter, TE; University of Rochester, NY) 09/01/06-08/31/11 1.20 calendar months
 Mitochondrial Role in Manganese Toxicity \$226,982
 The objective of this study is to determine the effects of manganese on mitochondrial respiration and enzymes associated with oxidative phosphorylation.