BIOGRAPHICAL SKETCH

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NAME: Bowman, Aaron Blaine

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

POSITION TITLE: Professor and Head, School of Health Sciences, Purdue University, West Lafayette, IN

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
Brigham Young University, Provo, UT	BS	04/1995	Microbiology
University of San Diego, San Diego, CA	PhD	06/2000	BioMedical Sciences
Princeton University, Princeton, NJ	Postdoc	02/2003	Epigenetics
Baylor College of Medicine, Houston, TX	Postdoc	08/2006	Neurobiology

A. Personal Statement

My lab studies toxicological interactions between metals (e.g. manganese and methylmercury (MeHg)) and genetic factors that contribute to selective neuropathology via neurodevelopmental and neuronal lineage-specific vulnerabilities. A diverse range of model systems are employed including patient-derived induced pluripotent stem cells (iPSCs), neuronal cultures and mouse models as well as a multifaceted approach including -omics, molecular genetics, pharmacology, biochemistry, cell and developmental biology. Our work to date has focused on genetic risk factors associated with neurological diseases (e.g. Parkinson's Disease (PD) and other parkinsonisms, Huntington's Disease) and neurological cell signaling and vulnerabilities. We aim to define mechanisms of neuronal dysfunction and understand the basis of selective neuropathology, by characterizing the molecular function of disease genes and their interaction with environmental risk factors under both normal and pathological conditions. My lab has established protocols to generate iPSC lines and differentiate them down cortical, striatal and midbrain neural lineages. We have developed techniques to examine toxicological and neurodegenerative/neurological related phenotypes in this patient-specific model system. My long-term goal is to use a personalized medicine approach to investigate patient-specific toxicant vulnerabilities and develop neuroprotective strategies that mitigate neurological diseases with environmental etiologies.

Recent articles relevant to my expertise for this proposal are listed here:

a. Prince LM, Neely MD, Warren EB, Thomas MG, Henley MR, Smith K, Aschner M, Bowman AB. Environmentally relevant developmental methylmercury exposure disrupts neuronal differentiation in a human-induced pluripotent stem cell model. **Food Chem Toxicol.** 2021; *in press*

b. Ke T, Tsatsakis A, Santamaría A, Antunes Soare FA, Tinkov AA, Docea AO, Skalny A, Bowman AB, Aschner M. Chronic exposure to methylmercury induces puncta formation in cephalic dopaminergic neurons in Caenorhabditis elegans. **Neurotoxicology.** 2020 Mar;77:105-113. PubMed PMID: 31935438; PubMed Central PMCID: PMC7061079.

c. Joshi P, Bodnya C, Ilieva I, Neely MD, Aschner M, Bowman AB. Huntington's disease associated resistance to Mn neurotoxicity is neurodevelopmental stage and neuronal lineage dependent. **Neurotoxicology**. 2019 Dec; 75:148-157. PMCID: PMC6961782

d. Prince LM, Aschner M, Bowman AB. Human-induced pluripotent stems cells as a model to dissect the selective neurotoxicity of methylmercury. **Biochim Biophys Acta Gen Subj.** 2019 Feb 10. pii: S0304-4165(19)30028-5.

B. Positions and Honors

Positions

2000-2003 Postdoctoral Fellow, Dr. Shirley M. Tilghman, Princeton University
2003-2006 Postdoctoral Fellow, Dr. Huda Y. Zoghbi, Baylor College of Medicine
2006-2015 Assistant Professor, Dept Neurology, Div. Movement disorders, Vanderbilt Univ. Med Ctr
2006-2018 Investigator, Vanderbilt Kennedy Center for Research on Human Development
2006-2018 Investigator, Vanderbilt Brain Institute
2008-2016 Investigator, Vanderbilt Center in Molecular Toxicology
2009-2018 Member, Vanderbilt Center for Stem Cell Biology
2015-2016 Associate Professor, Dept. Neurology, Vanderbilt University Med. Ctr.
2015-2018 Associate Professor, Dept. of Pediatrics, Div. Pediatric Neurology, Vanderbilt Univ. Med. Ctr.
2015-2018 Associate Professor, Secondary Appt, Dept. Biochemistry, Vanderbilt University
2015-2018 Director, Vanderbilt Training Program in Environmental Toxicology
2016-2018 Associate Professor, Secondary Appt, Dept. Neurology, Vanderbilt Univ. Med. Ctr.
2018– Professor and Head, School of Health Sciences, Purdue University

Professional Experience, Committee Memberships, Scientific Session Chairs and Honors

1995-2000 Lucille P. Markey Fellow in Biomedical Sciences, UCSD
2001-2003 Life Sciences Research Foundation (LSRF) Postdoctoral Fellowship
2003-2006 Hereditary Disease Foundation (HDF) Postdoctoral Fellowship
2008 National Parkinson Foundation Scientific Advisory Board, Ad hoc member
2008-2013 Outstanding New Environmental Scientist (ONES) Award, NIEHS
2009-2013 Secretary/Treasurer and continued service Middle TN Chapter Society for Neuroscience
2011-2015 Editorial Board Member, NeuroToxicology, Elsevier
2011 The Michael J. Fox Foundation for Parkinson's Research, Ad hoc Reviewer
2011– Gulf War Illness Review Panel, Department of Defense/CDMRP (**3 study sections since 2011)**
2011 Invited Speaker, Gordon Research Conference, Cellular and Molecular Mech. of Toxicity.
2011 Keynote Speaker, 27th Neurotoxicology Conference
2012 NIH, NIDA, CEBRA grant *Ad hoc* peer review panels (Spring and Fall)
2012 TEVA Pharmaceuticals Inc., Rasagiline Pre-Clinical Advisory Board
2013 Peer Reviewer, New York Health Department and Empire State Stem Cell Board (NYSTEM)
2017 CE Course Co-organizer and Speaker, Society of Toxicology (SOT) Annual Meeting
2014– NIH, NIEHS/CSR, Special Emphasis Panel reviewer (**14 study sections completed**)
2014 Invited Speaker, NorCal SOT Fall Symposium, 'Beyond small molecules', San Francisco, CA.
2015-2016 Symposium Chair and session organizer (3 sessions), SOT 2015/2016 Annual Meetings.
2015-2018 Member, SOT Education Committee, Undergraduate and Graduate Education Subcommittees
2015 Nanosymposium Speaker, Huntington's Disease session, Society for Neuroscience Annual Mtg
2015– Veterans Affairs, Merit Review Panelist & Chair, Neurobiology-E (**2 study sections completed**)
2016– NIH, NINDS/CSR, Special Emphasis Panel reviewer (**1 study sections completed**)
2016-2017 Senior Councilor, Stem Cells Specialty Section of SOT
2018-2022 SOT, Appointed member, Scientific Program Committee
2018 Co-chair, The first **all** trainee (pre- and post-doctoral) Symposia Session, SOT Annual Meeting
2019-2020 SOT, Appointed member, Education and Career Development Committee
2019-2021 SOT, Elected member, SOT Awards Committee

Professional Leadership Appointments and Major Review/Editorial Appointments

2015 President, Neurotoxicology Specialty Section (NTSS) of SOT (presidential line 2012-2016)
2015-2017 Editorial Board & Handling Editor, Nature – Scientific Reports, Neuroscience Section
2015-2017 Co-Chair, Soc. of Toxicology, Undergraduate Education Subcommittee
2016- Associate Editor, NeuroToxicology
2016-2022 Standing Member, Neurotoxiology and Alcohol (NAL) Study Section, NIH/CSR
2016 Veterans Affairs, Merit Review Subcommittee Chair, Neurobiology-E, Spring 2016
2016-2017 Appointed Chair, Graduate Education Subcommittee, Society of Toxicology
2017- Associate Editor, Toxicological Sciences

2017- SOT Representative and Member, FASEB Training and Career Opportunities Subcommittee.
2018- Associate Editor, Toxicology and Applied Pharmacology
2021- President-elect, International Neurotoxicology Association (presidential line 2022-2024)

C. Contributions to Science

1. Early Career: Genetic and cellular mechanisms of Neurodegeneration in Spinocerebellar Ataxia and Axonal transport. As a PhD student my work discovered the first kinesin cargo adaptor for microtubule dependent axonal transport, as well as the last remaining light chain subunit of cytoplasmic dynein using *Drosophila* and cellular model systems. As a postdoctoral fellow, my work advanced understanding of the molecular and biochemical mechanisms of spinocerebellar ataxia types 1 and 7 using mouse models. My research discovered the dominant protein complex that Ataxin-1 is associated with, and that this interaction is necessary for disease.

a. Bowman AB, Lam YC, Jafar-Nejad P, Chen HK, Richman R, Samaco RC, Fryer JD, Kahle JJ, Orr HT, Zoghbi HY. Duplication of *Atxn1l* suppresses SCA1 neuropathology by decreasing incorporation of polyglutamine-expanded ataxin-1 into native complexes. 2007. **Nature Genetics**. 39(3): 373-379.
b. *****Lam YC, *****Bowman AB, Jafar-Nejad P, Lim J, Richman R, Fryer JD, Hyun E, Duvick LA, Orr HT, Botas J, Zoghbi HY. ATAXIN-1 interacts with the repressor Capicua in its native complex to cause SCA1 neuropathology. 2006. **Cell**. 127(7): 1335-1347. ** denotes co-first authorship.*
c. Bowman AB, Kamal A, Ritchings BW, Philp AV, Mcgrail M, Gindhart J, Goldstein LSB. Kinesin dependent axonal transport is mediated by the Sunday Driver (SYD) protein. 2000. **Cell**. 103(4): 583-594.
d. Bowman AB, Patel-King RS, Benashski SE, McCaffery JM, Goldstein LSB, King SM. Drosophila roadblock and Chlamydomonas LC7: A conserved family of dynein-associated proteins involved in axonal transport, flagellar motility and mitosis. 1999. **Journal of Cell Biology**. 146(1): 165-179.

2. Gene by environmental interactions in neurodevelopmental and neurological disease, the impact on neuronal vulnerability to metal toxicity. We have utilized patient-based induced pluripotent stem cell derived neuronal models to explore gene by environment interactions for genetic risk factors of neurological disease alter vulnerability to environmental risk factors for these same diseases. This work has shown that mutations in genes associated with vital neurological processes impact metal biology and vulnerabilities to metal neurotoxicity. This work supports an overarching hypothesis that environmental risk factors and genetic determinants/risk factors of neurodegenerative and neurolgoical disorders may impinge upon the same cellular pathways to cause disease.

a. Ke T, Prince LM, Bowman AB, Aschner M. Latent alterations in swimming behavior by developmental methylmercury exposure are modulated by the homolog of tyrosine hydroxylase in Caenorhabditis elegans. **Neurotoxicol Teratol**. 2021 Feb 21;85:106963. doi: 10.1016/j.ntt.2021.106963. Epub ahead of print. PMID: 33626374.
b. Warren EB, Bryan MR, Morcillo P, Hardeman KN, Aschner M, Bowman AB. Manganese-induced mitochondrial dysfunction is not detectable at exposures below the acute cytotoxic threshold in neuronal cell types. **Toxicol Sci.** 2020 Jun 3:kfaa079. doi: 10.1093/toxsci/kfaa079. Epub ahead of print. PMID: 32492146
c. Ke T, Santamaria A, Rocha JBT, Tinkov A, Bornhorst J, Bowman AB, Aschner M. Cephalic Neuronal Vesicle Formation is Developmentally Dependent and Modified by Methylmercury and sti-1 in Caenorhabditis elegans. **Neurochem Res.** 2020 Dec;45(12):2939-2948. doi: 10.1007/s11064-020-03142-8. Epub 2020 Oct 10. PMID: 33037975.
d. Neely MD, Davison CA, Aschner M, Bowman AB. From the cover: Manganese and rotenone-induced oxidative stress signatures differ in iPSC-derived human dopamine neurons. 2017. **Toxicological Sciences**. 159(2):366-379. PMC5837701

3. Chemical biology, -omics, pharmacological and engineered systems approaches to gene x environment interactions in neurological disease. My lab has utilized high throughput assays to identify mechanisms of toxicant transport and toxicological outcomes. We utilize -omics based approaches to define biological pathways underlying toxicant influence in genetic systems. Further, we have collaborated with biomedical engineers to develop and utilize physiological model systems for study of neurological diseases with environmental and genetic etiologies.

a. Pfalzer AC, Wilcox JM, Codreanu SG, Totten M, Bichell TJV, Halbesma T, Umashanker P, Yang KL, Parmalee NL, Sherrod SD, Erikson KM, Harrison FE, McLean JA, Aschner M, Bowman AB. Huntington's disease genotype suppresses global manganese-responsive processes in pre-manifest and manifest YAC128 mice. **Metallomics**. 2020 May 18. doi: 10.1039/d0mt00081g. Epub ahead of print. PMID: 32421118.
b. Horning KJ, Joshi P, Nitin R, Balachandran RC, Yanko FM, Kim K, Christov P, Aschner M, Sulikowski GA, Weaver CD, Bowman AB. Identification of a selective manganese ionophore that enables nonlethal quantification of cellular manganese. **J Biol Chem**. 2020 Mar 20;295(12):3875-3890. PubMed PMID: 32047113; PMCID: PMC7086026
c. Wages PA, Joshi P, Tallman KA, Kim HH, Bowman AB, Porter NA. Screening ToxCast™ for Chemicals That Affect Cholesterol Biosynthesis: Studies in Cell Culture and Human Induced Pluripotent Stem Cell-Derived Neuroprogenitors. **Environ Health Perspect.** 2020 Jan;128(1):17014. PMCID: PMC7015578.
d. Brown JA, Codreanu SG, Shi M, Sherrod SD, Markov DA, Neely MD, Britt CM, Hoilett OS, Reiserer RS, Samson PC, McCawley LJ, Webb DJ, Bowman AB, McLean JA, Wikswo JP. Metabolic consequences of inflammatory disruption of the blood-brain barrier in an organ-on-chip model of the human neurovascular unit. 2016. **Journal of Neuroinflammation.** 13(1):306. PMC5153753

4. **Gene by environmental interactions in Huntington's disease.** Discovery that the genetic mutation underlying Huntington's disease selectively inhibits manganese (Mn) neurotoxicity and impairs Mn-dependent biological responses and Mn transport. A disease-toxicant interaction screen was performed in a mouse striatal progenitor model of HD that revealed an unexpected resistance to Mn neurotoxicity by cells expressing the pathogenic form of *HTT*. We have discovered that the underlying cause of this resistance to Mn-induced toxicity is a defect in neuronal Mn handling, such that net Mn uptake is severely reduced. This effect occurs prior to onset of neurodegenerative phenotypes. Several prominent pathogenic pathways implicated in HD involve Mn-dependent enzymes and the pathogenic changes are consistent with a loss of activity. Our research supports a hypothesis that at least some, and perhaps many aspects of HD pathogenesis may be caused by a selective neuronal Mn deficiency. Further, this work revealed a gene x environment interaction between mutant HTT and neuronal Mn transport, metabolism and homeostasis.
    a. Bryan MR, Nordham KD, Rose DIR, O'Brien MT, Joshi P, Foshage AM, Gonçalves FM, Nitin R, Uhouse MA, Aschner M, Bowman AB. Manganese Acts upon Insulin/IGF Receptors to Phosphorylate AKT and Increase Glucose Uptake in Huntington's Disease Cells. 2019. **Mol Neurobiol**. Mar;57(3):1570-1593. PMCID: PMC7062569
    b. Joshi P, Bodnya C, Ilieva I, Neely MD, Aschner M, Bowman AB. Huntington's disease associated resistance to Mn neurotoxicity is neurodevelopmental stage and neuronal lineage dependent. 2019. **Neurotoxicology**. Dec;75:148-157. PMCID: PMC6961782
    c. Bryan MR, O'Brien MT, Nordham KD, Rose DIR, Foshage AM, Joshi P, Nitin R, Uhouse MA, Di Pardo A, Zhang Z, Maglione V, Aschner M, Bowman AB. Acute manganese treatment restores defective autophagic cargo loading in Huntington's disease cell lines. 2019. **Hum Mol Genet**. 2019 doi: 10.1093/hmg/ddz209. PubMed PMID: 31600787.
    d. Bichell TJ, Wegrzynowicz M, Grace Tipps K, Bradley EM, Uhouse MA, Bryan M, Horning K, Fisher N, Dudek K, Halbesma T, Umashanker P, Stubbs AD, Holt HK, Kwakye GF, Tidball AM, Colbran RJ, Aschner M, Diana Neely M, Di Pardo A, Maglione V, Osmand A, Bowman AB. Reduced bioavailable manganese causes striatal urea cycle pathology in Huntington's disease mouse model. 2017. **Biochim Biophys Acta (BBA) - Molecular Basis of Disease**. 1863(6):1596-1604. PMC551527

Complete List of Published Work:
https://www.ncbi.nlm.nih.gov/myncbi/aaron.bowman.1/bibliography/public/

D. Additional Information: Research Support

Current

R01 ES031401; Harrison (PI) and Bowman (MPI) 2/1/2020– 10/31/2024
NIH/NIEHS Role: MPI
Manganese exposure susceptibility as a modifier of excitotoxicity in Alzheimer's Disease
To test the central hypothesis is that chronic elevated manganese (Mn) exposure drives cognitive decline through impaired glutamate homeostasis. Our long-term objectives are to isolate the direct link(s) between Mn and cognitive decline by demonstrating how chronic Mn exposure affects altered glutamate clearance and other pathologies to a greater extent in mouse and human stem cell models of AD than in controls

R01 ES010563-17; Aschner (PI) and Bowman (MPI) 4/1/2018 – 3/31/2023
NIH/NIEHS Role: MPI
Mechanisms of Manganese Toxicity
In the third competitive renewal, this program is testing the hypothesis that threshold-level Mn neurotoxicity occurs via alteration of Mn-dependent/-activated biological functions such as insulin/insulin-like growth factor and related metabolic signaling pathways and dopamine neuronal function in worms and mammalian systems.

R01 ES07331-21, Aschner (PI) and Bowman (MPI) 6/1/2016 – 5/31/2021
NIH/NIEHS Role: MPI
Mechanisms of Methylmercury-Induced Neuronal Toxicity
This study aims to (1) identify genetic modifiers of MeHg-induced neurotoxicity in *C. elegans*, (2) compare and contrast MeHg neurotoxicological outcomes in human nigral versus cortical neural lineages, and (3) evaluate mechanisms by which genetic pathways modify MeHg neurotoxicity.

Past

UG3/UH3 TR002097-01 (MPI – Wikswo, Neely and Ess) 7/21/2017 – 6/30/2020
NIH/NCATS (UG3/UH3) Role: MPI (till 7/31/18), then coI
Drug development for tuberous sclerosis complex and other pediatric epileptogenic diseases using neurovascular and cardiac microphysiological models
This research will develop *in vitro* tissue chip models of the neurological disorder tuberous sclerosis complex and other pediatric epileptogenic diseases by creating neural and cardiac tissue models of drug responses.

R01 ES016931-6; Bowman (PI) 8/15/2008 – 2/28/2020 (NCE)
NIH/NIEHS (NIEHS ONES Award yrs 1-5) Role: PI
Gene-Neurotoxicant Interactions in Huntington Disease
Define the cellular processes underlying modulation of Huntington Disease (HD) by environmental factors. Test the hypothesis that mutant *HTT* dysregulates stress response pathways (e.g. p53 and AKT/mTOR signaling) that protect neurons from specific classes of environmental stressors (e.g. Mn, Fe and metabolic inhibitors).

RO1 ES016931-12S1; Bowman (PI) 8/29/2018 – 2/28/2020 (NCE)
NIH/NIA
Gene-Neurotoxicant Interactions in Huntington Disease
NOT-AG-18-008 administrative supplement to NIH/NIEHS RO1 ES016931 to examine potential mechanistic links between manganese neurotoxicity and Alzheimer's disease using rodent and primary culture models.

T32 ES007028-40; Bowman (PI) 7/1/2014 – 7/31/2018
NIH/NIEHS Role: PI
Training Program in Environmental Toxicology
This T32 supports 7 predoctoral (PhD candidates) and six postdoctoral trainees of the Vanderbilt University Training Program in Environmental Toxicology.

UH3 TR000491-05S1, Wikswo (MPI, corresponding) 8/1/2016 – 6/30/2018 (NCE)
NIH/NCATS Role: Co-I
Neurovascular Unit on a Chip: Regional Chemical Communication, Drug and Toxin Responses