BIOGRAPHICAL SKETCH

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NAME: William Bradley Ruzicka

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

POSITION TITLE: Assistant Professor of Psychiatry

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
University of Chicago	BS	06/99	Biological Chemistry
University of Illinois at Chicago	MD PhD	05/08	Molecular Genetics
Massachusetts Gen Hospital and McLean Hospital Adult Psychiatry Residency		07/08-06/12	Psychiatry
American Board of Psychiatry and Neurology		09/12	Psychiatry

A. Personal Statement

My research investigates the genomic and epigenomic mechanisms that drive the establishment and maintanance of the vastly complex cytoarchitecture of the human brain, and how these mechanisms partition psychiatric illness related pathologies to affected neuronal circuits and cell types. My laboratory applies emerging genomics and single-cell genomics technologies and advanced tissue-clearing based histological methods to postmortem human brain tissue in investigating the roles of these mechanisms in the pathophysiology of psychotic disorders. My goal is to understand these complex mechanisms at the resolution of single cell types and single neuronal circuits within the brain to ultimately advance the development of novel and more effective treatments for patients.

1. **Ruzicka WB**, Subburaju S, Coyle JT, Benes FM. Location Matters: Distinct DNA Methylation Patterns in GABAergic Interneuronal Populations from Separate Microcircuits within the Human Hippocampus. Human Molecular Genetics. 2018 January 15; 27(2):254-265. PMID 29106556.
2. **Ruzicka WB**, Subburaju S, Benes FM. Variability of DNA methylation within schizophrenia risk loci across subregions of human hippocampus. Genes. 2017 May 15;8(5). PMID 28505127.
3. **Ruzicka WB**, Subburaju S, Benes FM. Circuit and diagnosis specific DNA methylation changes at GABA related genes in postmortem human hippocampus in schizophrenia and bipolar disorder. JAMA Psychiatry. 2015 Jun 1; 72(6):541-51. PMID 25738424.
4. **Ruzicka WB**, Zhubi A, Veldic M, Grayson DR, Costa E, Guidotti A. Selective epigenetic alteration of layer I GABAergic neurons isolated from prefrontal cortex of schizophrenia patients using laser-assisted microdissection. Molecular Psychiatry. 2007; 12(4): 385-397. PMID 17264840.
5. Tremolizzo L, Carboni G, **Ruzicka WB**, Mitchell CP, Sugaya I, Tueting P, Sharma R, Grayson DR, Costa E, Guidotti A. An epigenetic mouse model for molecular and behavioral neuropathologies related to schizophrenia vulnerability. Proceedings of the National Academy of Sciences. 2002 99: 17095-17100. PMCID 139275.

B. Positions and Honors

Positions and Employment

2008-2012 Clinical Fellow in Psychiatry, Massachusetts General Hospital
2008-2012 Clinical Fellow in Psychiatry, McLean Hospital
2012-2018 Instructor in Psychiatry, Harvard Medical School
2012-2018 Staff Psychiatrist, McLean Hospital
2014-2016 Associate Medical Director, Appleton Residence, McLean Hospital
2014-2016 Assistant Director, Research Concentration Program, MGH/McLean Psychiatry Residency
2016-Present Associate Clinical Director, Harvard Brain Tissue Resource Center
2017-Present Clinical Fellow, Massachusetts Institute of Technology Computational Biology Laboratory
2017-Present Associated Scientist, The Broad Institute
2018-Present Assistant Professor of Psychiatry, Harvard Medical School
2018-Present Associate Psychiatrist, McLean Hospital
2018-Present Director, Laboratory for Epigenomics in Human Psychopathology, McLean Hospital

Other Experience and Professional Memberships
2002-2008 The Society for Neuroscience, Student Member
2005-2012 The American Physician Scientist Association, Member
2011-2012 The American Psychiatric Association, Member
2011 Research Colloquium for Junior Investigators, American Psychiatric Association
2013 Career Development Institute for Psychiatry, University of Pittsburgh and Stanford
2017-Present The Society of Biological Psychiatry, Member
2019-Present McLean Hospital Leadership Forum, Member
2019 High Throughput Biology: From Sequence to Networks, Cold Spring Harbor Laboratory

Honors
1995 Materials Science Merit Scholarship, University of Illinois
1999 Phi Beta Kappa, Beta of Illinois, University of Chicago
2004 Student Travel Award, HealthEmotions Symposium, University of Wisconsin
2005 Student Travel Award, HealthEmotions Symposium, University of Wisconsin
2006 Graduate Student Symposium - 1st Place, Society for Neuroscience Chicago Chapter
2006 Neuroscience Graduate Student Symposium - 1st Place, U of Illinois
2006 Graduate Student Travel Award Fellowship, Society for Neuroscience
2007 Student Travel Award, HealthEmotions Symposium, University of Wisconsin
2012 APA/Pfizer MD/PhD Psychiatric Research Fellowship, American Psychiatric Association
2012 Dupont-Warren Fellowship Award, Harvard Medical School Psychiatry
2012 Livingston Fellowship Award, Harvard Medical School Psychiatry
2012 Harry C. and Maida Solomon Award, Harvard Medical School Psychiatry
2012 NARSAD Young Investigator Grant, Brain and Behavior Research Foundation
2012 NIH Loan Repayment Program
2013 NCDEU New Investigator Award, American Society of Clinical Psychopharmacology
2013 Andrew P. Merrill Memorial Research Fellowship, McLean Hospital
2014 Maria Lorenz Pope Fellowship, McLean Hospital
2014 NIH Loan Repayment Program
2015 Maria Lorenz Pope Fellowship, McLean Hospital
2015 Epigenetics Initiative Travel Grant, Harvard Medical School
2016 Society of Biological Psychiatry Early Career Investigator Travel Fellowship
2016 The Alfred Pope Award for Young Investigators, McLean Hospital
2016 American College of Neuropsychopharmacology Travel Award

C. Contribution to Science

1. Circuit-location specificity of molecular pathophysiology of psychotic disorders
The human brain contains a large number of distinct neuronal subtypes orchestrated to form a complex cytoarchitecture and functional circuitry. Disease mechanisms and pathological findings are not homogenously distributed across this cytoarchitecture but are specific to cellular subpopulations and circuit locations. Most existing investigation of brain tissue depends on homogenization of whole structures, discarding a wealth of information and increasing the probability of succumbing to type II error. In my graduate and postdoctoral work

I have focused on application of laser-microdissection coupled with advanced assays of chromatin structure to demonstrate the specificity of pathology to classes of interneurons at specific locations within the circuitry of postmortem human brain in subjects with psychotic disorders.

a. **Ruzicka WB**, Subburaju S, Coyle JT, Benes FM. Location Matters: Distinct DNA Methylation Patterns in GABAergic Interneuronal Populations from Separate Microcircuits within the Human Hippocampus. Human Molecular Genetics. 2018 January 15; 27(2):254-265. PMID 29106556.
b. **Ruzicka WB**, Subburaju S, Benes FM. Variability of DNA methylation within schizophrenia risk loci across subregions of human hippocampus. Genes. 2017 May 15;8(5). PMID 28505127.
c. **Ruzicka WB**, Subburaju S, Benes FM. Circuit and diagnosis specific DNA methylation changes at GABA related genes in postmortem human hippocampus in schizophrenia and bipolar disorder. JAMA Psychiatry. 2015 Jun 1; 72(6):541-51. PMID 25738424.
d. **Ruzicka WB**. Epigenetic mechanisms in the pathophysiology and treatment of psychotic disorders. Harvard Review of Psychiatry. 2015 May-June; 23(3):212-22. PMID 25943315.
e. **Ruzicka WB**, Zhubi A, Veldic M, Grayson DR, Costa E, Guidotti A. Selective epigenetic alteration of layer I GABAergic neurons isolated from prefrontal cortex of schizophrenia patients using laser-assisted microdissection. Molecular Psychiatry. 2007; 12(4): 385-397. PMID 17264840.

2. Aberrant chromatin regulatory mechanisms and dysregulation of GABA in psychotic disorders

Among the most robust and widely replicated findings in molecular analyses of schizophrenia is the downregulation of the GAD1 gene, with resultant decreased expression of glutamic acid decarboxylase 67 (GAD_{67}), the rate-limiting enzyme in GABA synthesis, and abnormal GABAergic neurotransmission. Despite this robust finding GAD1 has not been identified as a risk gene by increasingly large GWAS studies, indicating that as mutation does not appear to be the driving factor, regulation of GAD1 expression through epigenetic mechanisms must be at work. In my graduate and postdoctoral work I have investigated alterations in chromatin regulation, its functional impact on the GABA system, and pharmacological intervention into these phenomena in postmortem human brain as well as animal models.

a. Tremolizzo L, Carboni G, **Ruzicka WB**, Mitchell CP, Sugaya I, Tueting P, Sharma R, Grayson DR, Costa E, Guidotti A. An epigenetic mouse model for molecular and behavioral neuropathologies related to schizophrenia vulnerability. Proceedings of the National Academy of Sciences. 2002 99: 17095-17100. PMCID139275.
b. Subburaju S, Coleman AJ, **Ruzicka WB**, Benes FM. Toward dissecting the etiology of schizophrenia: HDAC1 and DAXX regulate GAD67 expression in an in vitro hippocampal GABA neuron model. Translational Psychiatry. 2016 January 26; 6:e723. PMID 26812044.
c. Dong E, **Ruzicka WB**, Grayson DR, Guidotti A. DNMT1 binding to CpG rich GABAergic and BDNF promoters is increased in brain of psychotic patients. Schizophrenia Research. 2015 167(1-3): 35-41. PMID 25476119.
d. Guidotti A, **Ruzicka W**, Grayson DR, Veldic M, Davis JM, Costa E. S-adenosyl methionine and DNA methyltransferase 1 overexpression in psychosis. Neuroreport. 2007 18(1): 57-60.
e. Costa E, Chen Y, Dong E, Grayson DR, Kundakovic M, Maloku E, **Ruzicka W**, Satta R, Veldic M, Zhubi A, Guidotti A. GABAergic promoter hypermethylation as a model to study the neurochemistry of schizophrenia vulnerability. Expert Reviews in Neurotherapeutics. 2009 9(1): 87-98.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1BU3sJ9zKVgA-/bibliography/46430707/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support

NIMH - K08 MH 109759 12/1/2016-11/30/2020
Neuronal and Circuitry Specific Chromatin Dynamics in Psychotic Disorders
This project is investigating the role of genome-wide DNA methylation and histone modifications at specific locations within the circuitry of postmortem human hippocampus in FACS purified populations of neuronal and non-neuronal cells. The training component of this award is focused on statistics and bioinformatics.

Cell-type and circuitry specific transcriptional dysregulation in psychotic disorders 5/1/2017-4/30/2022
Wilf Family Foundations - Role PI
This project will expand the scope of my K08 funded research to investigate the impact of epigenetic changes in FACS sorted neurons and non-neurons microdissected from specific hippocampal subfields in postmortem tissue from individuals with schizophrenia, bipolar disorder, and controls on gene expression and production of mRNA splice variants.

Completed Research Support

Harvard Medical School - Dupont-Warren Fellowship Award 7/01/2012-6/30/2013
American Psychiatric Association – 7/01/2012-6/30/2014
APA/Pfizer MD/PhD Psychiatric Research Fellowship
Mclean Hospital - Andrew P. Merrill Memorial Research Fellowship 7/01/2013-6/30/2014
NARSAD Young Investigator Grant 7/01/2013-6/30/2015
Mclean Hospital – Maria Lorenz Pope Fellowship 7/01/2014-6/30/2016

DNA methylation in the pathologic changes observed in the GAD1 regulatory network in schizophrenia and bipolar disorder
This project investigated the role of DNA methylation in gene expression changes significant to regulation of the GABAergic phenotype in the hippocampus of schizophrenia and bipolar disorder patients using microarray analysis of DNA extracted from post mortem human brain.
Role: Principal Investigator

NIH - NIH Clinical Research Loan Repayment Program 7/01/2012-6/30/2017
This program is designed to retain highly qualified health professionals in research careers focused on clinical investigation.
Role: Awardee