BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Alexander B. Niculescu III, MD, PhD

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

POSITION TITLE: Professor of Psychiatry and Medical Neuroscience; Staff Psychiatrist and Investigator, VA

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)	Completio n Date MM/YYYY	FIELD OF STUDY
INSTITUTION AND LOCATION University of Bucharest Carol Davila School of Medicine, Bucharest, Romania	M.D.	7/1991	Medicine
University of Geneva Medical School, Geneva, Switzerland	M.Sc.	7/1992	Medical Biology
The Scripps Research Institute Kellog School of Science and Technology, La Jolla, CA,	Ph.D.	7/1997	Molecular Biology
The Scripps Research Institute, La Jolla CA	Postdoctoral	6/1998	Neurobiology
University of California San Diego, La Jolla, CA	Residency	7/2002	Psychiatry
University of California San Diego, La Jolla, CA	Fellowship	7/2003	Biological Psychiatry
American Board of Psychiatry and Neurology	Board Certification	7/2005	Psychiatry

A. Personal Statement

I have a broad background in clinical medicine as well as basic research. I was extensively trained as a researcher at Scripps, and as a clinician at UC San Diego. I am a physician/scientist, who continues to see patients, and run a research operation consisting of two labs (a human research lab, and a basic science/genomics lab). Our work is highly translational, and focused on developing precision medicine approaches in psychiatry. I have been fortunate to have early on great mentors, and subsequently great collaborators, as well as to receive over the years prestigious and competitive top awards in this field (NIMH Outstanding Resident of the Year, Pfizer Scholar, NARSAD Young Investigator Award (twice), APA/AstraZeneca Young Minds in Psychiatry International Award, Theodore Reich Award from the International Society for Psychiatric Genetics, VA Merit Award, NIH Directors' New Innovator Award), and the funding associated with them, which supported our pioneering work in convergent functional genomics and biomarkers. The time has come to use broad, empirical, discovery-based approaches to understand at a network level psychiatric disorders, as is happening in cancer, the field where I did my PhD.

B. Positions and Honors

Positions and Employment

1991-1992 Research Fellow, Department of Pathology, University of Geneva Medical School, Geneva, Switzerland

- 1992-1997 Graduate Student, Program in Macromolecular and Cellular Structure and Chemistry, The Scripps Research Institute Kellog School of Science and Technology, La Jolla, CA, Laboratory of Dr. Steven I. Reed.
- 1997-1998 Postdoctoral Fellow, Department Of Neurobiology, The Scripps Research Institute, La Jolla, CA, Laboratory of Nobel laureate Dr. Gerald M. Edelman.
- 1998-1999 Internship, UCSD School of Medicine, La Jolla, CA
- 1999- 2001 Resident, Department of Psychiatry, UCSD School of Medicine, La Jolla, CA
- 2001-2002 Chief Resident, Department of Psychiatry, UCSD School of Medicine, La Jolla, CA
- 2001- 2003 Fellow in Biological Psychiatry and Neuroscience, Department of Psychiatry, UCSD School of Medicine, La Jolla, CA
- 2003-2004 Assistant Clinical Professor, Department of Psychiatry, UCSD School of Medicine, La Jolla, CA
- 2002–2004 Staff Psychiatrist, VA San Diego Healthcare System; Chief, Cognitive Disorders Clinic; Associate Medical Director, Alcohol and Drug Treatment Program; Director, Laboratory of Neurophenomics, Department of Psychiatry, UCSD School of Medicine, La Jolla, CA.
- 2004-2010 Assistant Professor of Psychiatry and Medical Neuroscience, Indiana University School of Medicine, Indianapolis, IN; Director, INBRAIN and Laboratory of Neurophenomics, Institute of Psychiatric Research; Staff Psychiatrist and Investigator, VA Medical Center Indianapolis
- 2010- 2015 Associate Professor of Psychiatry and Medical Neuroscience with Tenure; Staff Psychiatrist and Investigator, VA Medical Center Indianapolis
- June 2015- Professor of Psychiatry and Medical Neuroscience; Staff Psychiatrist and Investigator, VA Medical Center Indianapolis

Other Experience and Professional Memberships (selected):

1999- Member, International Society for Psychiatric Genetics

2005- Reviewer, NIH and VA Extramural Programs. Most recently: NIH-Chair, ZRG1 BBBP S(03) 2010; VA-Member, Mental Health and Behavioral Sciences – B (MHBB) 2010; NIH ZMH1 ERB-S (04) 2012; NIH ZAT1 SRC (99) 2013; NIH ZAT1 PK 29 P 2014

2005- 2011 Member, Institutional Review Board (IRB), Indiana University School of Medicine.

2007- Editorial Board, American Journal of Medical Genetics, Part B:Neuropsychiatric Genetics

2011- Founding Editorial Board member, Translational Psychiatry, Nature Publishing Group

2014- Founding Associate Editor, Molecular Neuropsychiatry, Karger SA

Reviewer for other leading international journals: Molecular Psychiatry, JAMA Psychiatry, American Journal of Psychiatry, Biological Psychiatry, Neuropsychopharmacology, Lancet, NEJM, and others.

Honors (selected):

2000 National Institute of Mental Health Outstanding Resident of the Year Award

2002 Lewis L. Judd Chairman's Research Award, Department of Psychiatry, UC San Diego

2002-2005 Pfizer Fellow in Biological Psychiatry

2002-2004 National Alliance for Research in Schizophrenia and Depression (NARSAD) Young Investigator 2004 Department of Veterans Affairs Superior Performance Award, July 2004.

2005 American Psychiatric Association/ AstraZeneca Young Minds in Psychiatry International Award 2005-2007 National Alliance for Research in Schizophrenia and Depression (NARSAD) Mogens Schou Young Investigator

2007 Theodore Reich Award from the International Society for Psychiatric Genetics

- 2010 America's Top Psychiatrists, Consumers' Research Council of America
- 2010 NIH Directors' New Innovator Award

2012 Indiana University Trailblazer Award

C. Contribution to Science

Convergent Functional Genomics of psychiatric disorders

Combining gene expression and genetic data, from brain and blood, in humans and animal models, has proven to be very useful in terms of prioritizing true, reproducible, signal and minimizing noise inherent in each of the individual approaches. Such a convergent approach is in essence a de facto field-wide collaboration across silos, relying on our data and all the other published data in the field. I first invented the approach while a resident at UCSD in 1998, and described it in a first author/corresponding author publication in 1999. Since then my lab has developed, amplified, and successfully applied the approach to mapping the genetic landscape of psychiatric disorders (bipolar disorder, schizophrenia, alcoholism).

***Niculescu AB**, Segal D, Kuczenski R, Barrett T, Hauger R, Kelsoe JR. Identifying a series of candidate genes for mania and psychosis: a convergent functional genomics approach. *Physiological Genomics* 2000; 4: 83-91.

Ogden CA, Rich ME, Schork NJ, Paulus MP, Geyer MA, Lohr JB, Kuczenski R, ***Niculescu AB**. Candidate genes, pathways and mechanisms for bipolar (manic-depressive) and related disorders: an expanded convergent functional genomics approach. *Molecular Psychiatry* 2004; 9(11):1007-1029.

Ayalew M, Le-Niculescu H, Levey D, Jain N, Changala B, Patel SD, Winiger E, Breier A, Shekhar A, Amdur R, Koller D, Nurnberger JI, Corvin A, Geyer M, Tsuang MT, Salomon DR, Schork NJ, Fanous A, O'Donovan M, ***Niculescu AB.** Convergent Functional Genomics of Schizophrenia: From Comprehensive Understanding to Genetic Risk Prediction. *Molecular Psychiatry* 2012 Sep; 17(9):887-905. Epub 2012 May 15

D.F. Levey, H. Le-Niculescu, J. Frank, M. Ayalew, N. Jain, B. Kirlin, R. Learman, E. Winiger, Z.A. Rodd, A. Shekhar, N. J. Schork, F, Kiefe, N. Wodarz, B. Muller-Myhsok, N. Dahmer, GESGA Consortium, M. Nothen, R. Sherva, L. Farrer, A. H. Smith, H. Kranzler, M. Rietschel, J. Gelernter, **A. B. Niculescu***. Genetic Risk Prediction and Neurobiological Understanding of Alcoholism. *Translational Psychiatry*. 2014 May 20;4:e391. doi: 10.1038/tp.2014.29.

PhenoChipping of psychiatric disorders and mental landscape model (Mindscape)

Studying quantitative phenotypes (phenes) using tools from genomics may be productive in terms of understanding the true structure of psychiatric disorders, as opposed to the ad hoc description in DSM. I invented such an approach in 2004, terming it PhenoChipping, by analogy to GeneChipping, and described it in a first author/corresponding author publication in 2006. Since then, we have used such analyses as part of animal model and human studies. In addition, prior to the current emphasis on dimensional approaches in RDoC, I described a multidimensional mental landscape approach in a first author/corresponding author publication in 2009.

*Niculescu AB, Lulow L, Ogden CA, Le-Niculescu H, Salomon DR, Schork NJ, Caligiuri MP, Lohr JB. PhenoChipping of psychotic disorders: a novel approach for deconstructing and quantitating psychiatric phenotypes. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*. 2006. 141(6):653-662.

*Niculescu AB, Schork NJ, Salomon DR. Mindscape: a convergent perspective on life, mind, consciousness and happiness. *Journal of Affective Disorders* 2010 123(1-3):1-8. Epub 2009 July10.

Blood biomarkers for psychiatric disorders

In our original CFG work in 1999, we conducted a pilot blood gene expression study on one of our candidate genes for bipolar disorder, GRK3 (now called, ADARKB2), which suggested the possibility of a peripheral readout. As the target organ in psychiatry cannot be readily biopsied in live individuals, it is imperative to develop peripheral markers (liquid biopsies, as they are called in cancer). We have pursued this approach years later, using case-case and within subject designs in high risk psychiatric subjects, with validation in independent cohorts. We have thus demonstrated the identification of biomarkers for mood state, psychosis, and suicide.

Le-Niculescu H, Kurian SM, Yehyawi N, Dike C, Patel SD, Edenberg HJ, Tsuang MT, Salomon DR, Nurnberger Jr JI, ***Niculescu AB**. Identifying Blood Biomarkers For Mood Disorders Using Convergent Functional Genomics. *Molecular Psychiatry* 2009; 14(2):156-74. Epub 2008 Feb 26.

Kurian SM, Le-Niculescu H, Patel S, Bertram D, Davis J, Dike C, Yehyawi N, Lysaker P, Dustin J, Caligiuri M, Lohr J, Lahiri DK, Nurnberger JI, Faraone SV, Geyer MA, Tsuang MT, Schork NJ, Salomon DR, ***Niculescu AB.** Identification of Blood Biomarkers For Psychosis Using Convergent Functional Genomics. *Molecular Psychiatry* 2011 Jan;16(1):37-58. Epub 2009 November 24.

H. Le-Niculescu, D. F. Levey, M. Ayalew, L. Palmer, L. M. Gavrin, N. Jain, S. Bhosrekar, G. Shankar, E. Belanger, K. Olesek, H. Duckworth, J. Vergo, R. Schweitzer, M. Radel, M. Yard, A. Ballew, A. Shekhar, G. Sandusky, N. J. Schork, S. M. Kurian, D. R. Salomon, **A. B. Niculescu*.** Discovery and Validation of Blood Biomarkers for Suicidality. *Molecular Psychiatry* 2013 Dec;18(12):1249-64. doi: 10.1038/mp.2013.95. Epub 2013 Aug 20.

***Niculescu AB**, Levey DF, Le-Niculescu H, Niculescu E, Kurian SM, Salomon, D. Psychiatric blood biomarkers: avoiding jumping to premature negative or positive conclusions. *Molecular Psychiatry* 2015 Mar;20(3):286-8. doi: 10.1038/mp.2014.180. Epub 2015 Jan 13.

*Niculescu AB, Levey DF, Phalen PL, Le-Niculescu H, Dainton HD, Jain N, Belanger E, James A, George S, Weber H, Graham DL, Schweitzer R, Ladd TB, Learman R, Niculescu EM, Vanipenta NP, Khan FN, Mullen J, Shankar G, Cook S, Humbert C, Ballew A, Yard M, Gelbart T, Shekhar A, Schork NJ, Kurian SM, Sandusky GE, Salomon DR. Understanding and predicting suicidality using a combined genomic and clinical risk assessment approach. *Molecular Psychiatry* 2015 Aug 18. doi: 10.1038/mp.2015.112. [Epub ahead of print]

Complete List of Published Work:

http://www.ncbi.nlm.nih.gov/pubmed/?term=Niculescu+AB

Laboratory Website:

www.neurophenomics.info

Patent applications (in the last 3 years):

US Patent Application No. 61/770,696 "Blood Biomarkers For Suicidality" U.S. Patent Application Serial No. 62/174,880 "Predicting suicidality using a combined genomic and clinical risk assessment approach"

D. Research Support

<u>Active</u>

2013-2017 "Blood Biomarkers for Psychosis: Specificity vs Overlap with Mood Disorders" VA 2I01CX000139 VA Merit Award (Niculescu – P.I.) Goals: To discover biomarkers for psychosis and study the overlap between schizophrenia and mood disorders.

2010-2015 " Developing Blood Tests for Mood Disorders" NIH 1DP2OD007363 R01 NIH Director New Innovator Award (Niculescu - P.I.) Goals: To develop blood tests for mood and related disorders.

<u>Completed (in the last 3 years):</u> 2009-2012 "Mood State Blood Biomarkers: A Discovery Based Approach." VA 1I01CX000139 VA Merit Award (Niculescu – P.I.) Goals: To discover biomarkers through blood gene expression studies in bipolar disorder.