

**BIOGRAPHICAL SKETCH**

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NAME Alexander B. Niculescu III, MD, PhD		POSITION TITLE Associate Professor of Psychiatry and Medical Neuroscience	
eRA COMMONS USER NAME aniculescu			
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
University of Bucharest Carol Davila School of Medicine, Bucharest, Romania	M.D.	1991	Medicine
University of Geneva Medical School, Geneva, Switzerland	M.Sc.	1992	Medical Biology
The Scripps Research Institute Kellog School of Science and Technology, La Jolla, CA,	Ph.D.	1997	Molecular Biology
The Scripps Research Institute, La Jolla CA	Postdoctoral Residency	1997-1998	Neurobiology
University of California San Diego, La Jolla, CA		1998-2002	Psychiatry
University of California San Diego, La Jolla, CA	Fellowship	2001-2003	Biological Psychiatry and Neuroscience
American Board of Psychiatry and Neurology	Board Certification	2005	Psychiatry

**A. Personal Statement**

I have a broad background in psychiatry, neuroscience and molecular biology, with specific training and expertise in key research areas for our current work. The conception and first application of Convergent Functional Genomics in 1999, by myself and collaborators at UC San Diego, was an early breakthrough in terms of combining microarray gene expression data, a new field at that time, with human genetic linkage data, a mature field marred by difficulties in terms of zeroing in on good candidate genes. Moreover, the approach translationally integrated animal model data and human data. Since then, I have continued to expand this approach, integrating multiple lines of evidence in a Bayesian fashion, and publish its applications towards helping understand the genetic code of major neuropsychiatric disorders- bipolar (manic-depressive) illness, schizophrenia, and alcoholism. Our findings have been independently replicated by a number of groups, using different methodologies. Similar approaches to Convergent Functional Genomics, sometimes termed Integrative Genomics, have since become widely used in various fields- notably the work of Eric Landers's group at MIT and Eric Schadt's group at Rosseta /Merck. I was the first to publish blood evidence for a candidate gene for bipolar disorder being changed in lymphocytes, at a protein level, in relationship with severity of diagnosis. That very preliminary work was mostly ignored as a potential artifact until in 2004-2005 a number of groups, notably Vawter and Bunney at UC Irvine, and Ming Tsuang at UC San Diego (a collaborator and mentor of mine), have conducted larger studies in schizophrenia and bipolar disorder and provided some intriguing evidence for lymphocyte gene expression changes in relation to diagnosis. More recently, my group, together with collaborators at Scripps and UC San Diego, has used Convergent Functional Genomics as a powerful way for discovering objective blood biomarkers for mood state, as well as hallucinations and delusions. 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/animal studies lab). I was extensively trained as a researcher at Scripps, and as a clinician at UC San Diego. My PhD was in cancer molecular biology, a more mature and empirical field from which psychiatry can profitably learn. My track record reflects an ability to: 1. simplify things, 2. zero in on what I think are important questions and unmet needs, 3. borrow concepts and methodologies from one field and apply them to another (cancer to brain research, animal models to humans), 4. bring together large teams of collaborators who have complementary expertise, and 5. see complex projects to completion in the face of inherent setbacks, difficulties and initial rejection. Working at the interface of disciplines is scientifically very rewarding. However, it may not have been good classic grantsmanship. While I

have been fortunate to receive prestigious and competitive top awards for young investigators 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, a VA Merit Award), and the funding associated with them, I have had my share of discovery-based (non hypothesis-driven) grant applications not being funded initially by traditional study sections. Nevertheless, I am convinced the time has come to use broad, empirical, discovery-based approaches to map the genomic and phenomic landscape of major psychiatric disorders, as is happening in cancer, and we have continued to learn, refine and progress our work.

## **B. Positions and Honors**

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 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- 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, VA Medical Center Indianapolis  
2010 (July)- Associate Professor of Psychiatry with Tenure

## **Other Experience and Professional Memberships (selected):**

1999- Member, International Society for Psychiatric Genetics  
2005- Reviewer, NIMH Extramural Programs  
2005- Member, Institutional Review Board (IRB), Indiana University School of Medicine.  
2006- Assistant Editor, Psychiatric Genetics  
2007- Editorial Board, American Journal of Medical Genetics, Part B:Neuropsychiatric Genetics  
Editor, *Neurogenomics* textbook, Springer, projected publication 2011

## **Honors ( selected):**

2000 National Institute of Mental Health Outstanding Resident of the Year Award  
2000 Eli Lilly US Resident of the Year Award, US Psychiatric & Mental Health Congress, San Diego, CA.  
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

**C. Selected peer-reviewed publications (in chronological order) (\* corresponding author)**

**Niculescu AB**, Chen X, Smeets M, Hengst L, Prives C, Reed SI. Effects of p21 Cip1/Waf1 at both the G1/S and G2/M cell cycle transitions: pRb is a critical determinant in blocking DNA replication and preventing endoreduplication. *Molecular and Cellular Biology*. 1998; 18: 629-643.

\***Niculescu AB**. Prophylactic antidepressant treatment before patients are admitted *Lancet* 2000; 355: 406-7.

**Niculescu AB**. Will to live, suicide and euthanasia. *Archives of Internal Medicine* 2000; 160:1706.

\***Niculescu AB**, Segal D, Kuczynski 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.

\***Niculescu AB**, Kelsoe JR. Convergent functional genomics: application to bipolar disorder. *Annals of Medicine* 2001; 33:263-271.

\***Niculescu AB**, Akiskal HS. Proposed endophenotypes of dysthymia: evolutionary, clinical and pharmacogenomic considerations. *Molecular Psychiatry* 2001; 6: 363-366.

\***Niculescu AB**, Kelsoe JR. The Human Genome: Genetic Testing and Animal Models. *American Journal of Psychiatry* 2001; 158:1587

\***Niculescu AB**, Akiskal HS. Sex hormones, Darwinism and depression. *Archives of General Psychiatry* 2001; 58:1083-1084.

\***Niculescu AB**, Kelsoe JR. Finding Genes for Bipolar Disorder in the Functional Genomics Era: From Convergent Functional Genomics to Phenomics and Back. *CNS Spectrums* 2002; 7: 215-226.

Lohr JB, Kuczynski R, **Niculescu AB**. Oxidative Mechanisms and Tardive Dyskinesia. *CNS Drugs* 2003; 17:47-62.

Ogden CA, Rich ME, Schork NJ, Paulus MP, Geyer MA, Lohr JB, Kuczynski 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.

\***Niculescu AB**. Genomic studies of mood disorders: the brain as a muscle? *Genome Biology*. 2005. 6(4):215. Epub 2005 Mar 24.

Bertsch B, Ogden CA, Sidhu K, Le-Niculescu H, Kuczynski R, \***Niculescu AB**. Convergent functional genomics: a Bayesian candidate gene identification approach for complex disorders. *Methods* 2005; 37(3):274-279.

Caligiuri MP, Brown GG, Meloy MJ, Ebersson S, **Niculescu AB**, Lohr JB. Striatopallidal regulation of affect in bipolar disorder. *The Journal of Affective Disorders* 2006; 91(2-3):235-42.

\***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.

Rodd ZA, Bertsch B, Strother WN, Le-Niculescu H, Jerome RE, Lumeng L, Nurnberger JI Jr., Edenberg HJ, McBride WJ, and \***Niculescu AB**. Candidate genes, pathways and mechanisms for alcoholism and related

disorders: an expanded convergent functional genomics approach. *The Pharmacogenomics Journal* 2007;7(4):222-56.

\***Niculescu AB**. Polypharmacy in oligopopulations: what psychiatric genetics can teach biological psychiatry. *Psychiatric Genetics*. 2006. 16(6):241-244.

Le-Niculescu H, Balaraman Y, Patel S, Tan J, Sidhu K, Jerome RE, Kuczenski R, Geyer MA, Edenberg HJ, Nurnberger JI, Faraone SV, Tsuang MT and \***Niculescu AB**. Towards understanding the schizophrenia code: an expanded convergent functional genomics approach. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*. 2007; 144B (2):129-158.

Le-Niculescu H, McFarland MJ, Mamidipalli S, Ogden CA, Kuczenski R, Kurian SM, Salomon DR, Tsuang MT, Nurnberger Jr JI, \***Niculescu AB**. Convergent Functional Genomics of bipolar disorder: From animal model pharmacogenomics to human genetics and biomarkers. *Neurosci Biobehav Rev*. 2007 31(6):897-903.

Le-Niculescu H, McFarland MJ, Ogden CA, Balaraman Y, Tan J, Patel S, Rich ME, Paulus M, Edenberg HJ, Nurnberger JI, Rodd ZA, Geyer M, Glatt SJ, Faraone SV, Kuczenski R, Tsuang MT and \***Niculescu AB**. Phenomic, convergent functional genomic and biomarker studies in a stress-reactive genetic animal model of bipolar disorder and co-morbid alcoholism. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*. 2008 Mar 5;147(2):134-66.

Liu L, Foroud T, Xuei X, Berrettini W, Byerley W, Coryell W, El-Mallakh R, Gershon E, Kelsoe J, Lawson W, MacKinnon D, McInnis M, McMahon F, Murphy D, Rice J, Scheftner W, **Niculescu AB**, Meyer ET, Edenberg HJ, Nurnberger Jr. JI. Evidence of association between brain-derived neurotrophic factor (*BDNF*) gene and bipolar disorder. *Psychiatric Genetics*. 2008;18(6):267-74.

Le-Niculescu H, Kurian SM, Yehyaw 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.

Le-Niculescu H, Patel SD, Bhat M, Kuczenski R, Faraone SV, Tsuang MT, McMahon F, Schork NJ, Nurnberger Jr. JI, \***Niculescu AB**. Convergent Functional Genomics of Genome-Wide Association Data for Bipolar Disorder: Comprehensive Identification of Candidate Genes, Pathways and Mechanisms. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*. 2009 150B(2):155-181. Epub 2008 Nov21.

Caligiuri MP, Teulings HL, Dean CE, **Niculescu AB**, Lohr J. Handwriting movement analyses for monitoring drug-induced motor side effects in schizophrenia patients treated with risperidone. *Hum Mov Sci*. 2009 28(5):633-42. Epub 2009 Aug 18

\***Niculescu AB**, Schork NJ, Salomon DR. Mindscape: a convergent perspective on life, mind, consciousness and happiness. *Journal of Affective Disorders* 2009. July 10 Epub ahead of print.

Kurian SM, Le-Niculescu H, Patel S, Bertram D, Davis J, Dike C, Yehyaw 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* 2009. November 24 Epub ahead of print.

McGrath CL, Glatt SJ, Sklar P, Le-Niculescu H, Kuczenski R, Doyle EA, Biederman J, Mick E, Faraone SV, \***Niculescu AB**, Tsuang MT. Evidence for Genetic Association of RORB with Bipolar Disorder. *BMC Psychiatry* 2009. November 12 Epub ahead of print.

Caligiuri MP, Teulings HL, Dean CE, **Niculescu AB 3rd**, Lohr JB. Handwriting movement kinematics for quantifying extrapyramidal side effects in patients treated with atypical antipsychotics. *Psychiatry Res.* 2010 May 15;177(1-2):77-83.

\***Niculescu AB**, Le-Niculescu H. Convergent Functional Genomics: What we have learned and can learn about genes, pathways and mechanisms. *Neuropsychopharmacology* 2010. 35(1):355-6.

\***Niculescu AB**, Hulvershorn L. Toward Early, Personalized, Rational Polypharmacy In Psychiatry: A Tri-Dimensional Approach. *Psychopharm Review* 2010. 45(2): 9-16.

\***Niculescu AB**, Le-Niculescu H. The P-Value Illusion: How to Improve (Psychiatric) Genetic Studies. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*. 2010. Epub Mar 17.

Patel SD, Le-Niculescu H, Koller DL, Green SD, Lahiri DK, McMahon F, Nurnberger JI, \***Niculescu AB**. Coming to Grips With Complex Disorders: Genetic Risk Prediction in Bipolar Disorder Using Panels of Genes Identified Through Convergent Functional Genomics. *American Journal of Medical Genetics Part B (Neuropsychiatric Genetics)*. 2010. Epub April 9.

## **D. Research Support**

### **Active:**

2009-2012 "Mood State Blood Biomarkers: A Discovery Based Approach."

VA Merit Award (Niculescu, AB - PI)

Goals: To discover biomarkers through blood gene expression studies in bipolar disorder.

My role: P.I.

### **Completed (in the last 3 years):**

2004-2008 "Translational studies of cycling in bipolar disorders."

NIMH R01 MH071912-01 (Tsuang, MT- PI)

Goals: To integrate gene expression studies in animal models with candidate gene studies in bipolar families.

My role: Co- Investigator/site P.I.

2006-2008 "Handwriting Quantification for Screening in Schizophrenia"

NIMH SBIR grant

Goals: To assess and develop new motor endophenotypes.

My role: Co-Investigator (Teulings, HL-PI)

2006-2008 "INBRAIN- Indiana Center for Biomarker Research In Neuropsychiatry"

Eli Lilly

Goals: To identify candidate biomarkers for neuropsychiatric disorders.

My role: P.I

2005-2007 "Convergent functional genomics studies in mice lacking the clock gene DBP: a possible animal model of bipolar depression"

NARSAD Mogens Schou Young Investigator Award.

Goals: Convergent functional genomics studies of a mouse model of bipolar disorder.

My role: P.I.

2005-2006 "PhenoChipping of psychotic disorders: genotype to phenotype integration"

APA/Astra-Zeneca Young Minds in Psychiatry Award

Goals: To develop better phenotypic instruments for human genetic research

My role: P.I