### **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: Roussos, Panagiotis (Panos)

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

POSITION TITLE: Assistant Professor at the Department of Genetics and Genomics Sciences and the Department of Psychiatry

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

INSTITUTION AND LOCATION	DEGREE	START	END	FIELD OF
	(if applicable)	DATE	DATE	STUDY
		MM/YYYY	MM/YYYY	
University of Crete, Heraklion, Crete	MD	10/1998	07/2004	
University of Crete, Heraklion, Crete	MS	09/2004	07/2006	Neuroscience
University of Crete, Heraklion, Crete	PHD	09/2006	04/2010	Genetics
Icahn School of Medicine at Mount Sinai, New York, NY	Resident	07/2008	06/2012	Psychiatry
Icahn School of Medicine at Mount Sinai, New York, NY	Postdoctoral Fellow	07/2012	12/2013	Schizophrenia

#### A. Personal Statement

My extensive clinical and research training in psychiatry, neuroscience and genetics empowers me to study the genetic mechanisms through which risk genetic variants increase vulnerability for neuropsychiatric diseases, including schizophrenia, bipolar disorder and Alzheimer's disease. My early research focused on the genetic exploration of intermediate cognitive phenotypes, including the prepulse inhibition of the startle reflex in human subjects and restoration of deficits using a pharmacogenomic approach. I was the recipient of multiple Awards, including the Best Paper Award of Lilly Fellowship - BAP 2006. I then completed my residency in psychiatry (Physician-Scientist Research Track) at Icahn School of Medicine at Mount Sinai. As a resident, I worked on human postmortem studies by integrating genomics with gene expression and gene network approaches. As a resident, I received multiple Awards, including the Outstanding Resident Award by National Institute of Mental Health. Over the last 5 years, my research has focused on the integration of high-dimensional data, such as genomic, epigenomic and transcriptomic, using advanced biostatistical methods in order to identify some of the mechanisms through which risk genetic variants increase the risk for neuropsychiatric diseases. My team is part of large consortia, including CommonMind Consortium, psychENCODE and Accelerating Alzheimer's Research and Drug Development project that generate large scale molecular data in human brain tissue of control and disease (schizophrenia, bipolar and Alzheimer's disease) specimens. My Lab has optimized approaches to map the open chromatin regions in specific cell types collected from human brain tissue and study the somatic mosaicism in neuropsychiatric diseases. My overall work and contribution to schizophrenia research was recently recognized and awarded the Presidential Early Career Awards for Scientists and Engineers by President Obama. As a prolific researcher, I have published several high profile papers in Nature, Nature Genetics, Nature Neuroscience, Neuron, Molecular Psychiatry and JAMA Psychiatry. As of May 2017, my publications have been cited 5,062 times, according to Google Scholar. As PI of two grants funded by NIA (R01 AG050986) and NIMH (R01 MH109677), I am leading the effort of epigenetic profiling and integration of high-dimensional data in schizophrenia, bipolar disorder and Alzheimer's disease.

- 1. Hauberg ME, Zhang W, Giambartolomei C, Franzén O, Morris DL, Vyse TJ, Ruusalepp A, Sklar P, Schadt EE, Björkegren JLM, Roussos P. Large-Scale Identification of Common Trait and Disease Variants Affecting Gene Expression. Am J Hum Genet. 2017 Jun 1;100(6):885-894. PubMed PMID: 28552197.
- 2. Fullard JF, Giambartolomei C, Hauberg ME, Xu K, Voloudakis G, Shao Z, Bare C, Dudley JT, Mattheisen M, Robakis NK, Haroutunian V, Roussos P. Open chromatin profiling of human postmortem

- brain infers functional roles for non-coding schizophrenia loci. Hum Mol Genet. 2017 May 15;26(10):1942-1951. PubMed PMID: 28335009.
- 3. Fromer M, Roussos P, Sieberts SK, Johnson JS, Kavanagh DH, Perumal TM, Ruderfer DM, Oh EC, Topol A. Shah HR, Klei LL, Kramer R, Pinto D, Gümüs ZH, Cicek AE, Dang KK, Browne A, Lu C, Xie L. Readhead B, Stahl EA, Xiao J, Parvizi M, Hamamsy T, Fullard JF, Wang YC, Mahajan MC, Derry JM, Dudley JT, Hemby SE, Logsdon BA, Talbot K, Raj T, Bennett DA, De Jager PL, Zhu J, Zhang B, Sullivan PF, Chess A, Purcell SM, Shinobu LA, Mangravite LM, Toyoshiba H, Gur RE, Hahn CG, Lewis DA, Haroutunian V, Peters MA, Lipska BK, Buxbaum JD, Schadt EE, Hirai K, Roeder K, Brennand KJ, Katsanis N, Domenici E, Devlin B, Sklar P. Gene expression elucidates functional impact of polygenic risk for schizophrenia. Nat Neurosci. 2016 Nov;19(11):1442-1453. PubMed PMID: 27668389; PubMed Central PMCID: PMC5083142.
- 4. Franzén O, Ermel R, Cohain A, Akers NK, Di Narzo A, Talukdar HA, Foroughi-Asl H, Giambartolomei C, Fullard JF, Sukhavasi K, Köks S, Gan LM, Giannarelli C, Kovacic JC, Betsholtz C, Losic B, Michoel T, Hao K, Roussos P, Skogsberg J, Ruusalepp A, Schadt EE, Björkegren JL. Cardiometabolic risk loci share downstream cis- and trans-gene regulation across tissues and diseases. Science, 2016 Aug. 19;353(6301):827-30. PubMed PMID: 27540175.

### **B.** Positions and Honors

## **Positions and Employment**

- House Staff at the Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New 2008 - 2012 York, NY
- 2012 2013 Research Associate at the Department of Genetics and Genomics Sciences and the Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY
- 2014 -Assistant Professor at the Department of Genetics and Genomics Sciences and the Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY

# Other Experience and Professional Memberships

- Member, American Medical Association 2008 -
- 2008 -Member, American Psychiatric Association
- 2012 -Certification number: 004074, NYS Medical License
- Certification number: 65532, Board Certified in Psychiatry by the American Board of Psychiatry 2012 -& Neurology
- 2013 -Member, International Society of Psychiatric Genetics
- Associate Member, American College of Neuropsychopharmacology 2013 -
- Member, American College of Neuropsychopharmacology 2016 -

## Honors

2006	Lilly Fellowship and oral presentation for the best poster, BAP Summer Meeting, Oxford, UK
2010	Outstanding Resident Award, National Institute of Mental Health
2010	Travel Award, International Society of Psychiatric Genetics
2011	Best Research Paper, New York State Psychiatric Association Scientific Paper Contest
2012	Domestic Travel Fellowship Award, Society of Biological Psychiatry
2012	Research Colloquium for Junior Investigators - Travel Award , American Psychiatric Association
2012	Best Research Paper, New York State Psychiatric Association Scientific Paper Contest
2012	Travel Award, American College of Neuropsychopharmacology
2012	Early Academic Career Award, APA/Merck
2013	Best Research Paper, New York State Psychiatric Association Scientific Paper Contest
2013	Travel Award, International Congress on Schizophrenia Research

- 2013 Associate Member, American College of Neuropsychopharmacology
- 2015 Elected to attend and Awarded Funds, Charleston Conference on Alzheimer's Disease

### C. Contribution to Science

- 1. The majority of susceptible common risk loci are non-coding and it has been hypothesized that these variants affect gene expression through allele specific effect on cis regulatory elements. We have explored this hypothesis by: (1) generating large-scale genomics and transcriptomics data; (2) performing analysis to identify expression quantitative trait loci; and (3) applying integrative approaches to characterize the genetic architecture of multiple diseases by incorporating eQTL and epigenome data. My Lab is part of large consortia generating eQTL datasets in human brain tissue (CommonMind consortium) or peripheral tissues (STARNET).
  - a. Hauberg ME, Zhang W, Giambartolomei C, Franzén O, Morris DL, Vyse TJ, Ruusalepp A, Sklar P, Schadt EE, Björkegren JLM, Roussos P. Large-Scale Identification of Common Trait and Disease Variants Affecting Gene Expression. Am J Hum Genet. 2017 Jun 1;100(6):885-894. PubMed PMID: 28552197.
  - b. Fromer M, Roussos P, Sieberts SK, Johnson JS, Kavanagh DH, Perumal TM, Ruderfer DM, Oh EC, Topol A, Shah HR, Klei LL, Kramer R, Pinto D, Gümüş ZH, Cicek AE, Dang KK, Browne A, Lu C, Xie L, Readhead B, Stahl EA, Xiao J, Parvizi M, Hamamsy T, Fullard JF, Wang YC, Mahajan MC, Derry JM, Dudley JT, Hemby SE, Logsdon BA, Talbot K, Raj T, Bennett DA, De Jager PL, Zhu J, Zhang B, Sullivan PF, Chess A, Purcell SM, Shinobu LA, Mangravite LM, Toyoshiba H, Gur RE, Hahn CG, Lewis DA, Haroutunian V, Peters MA, Lipska BK, Buxbaum JD, Schadt EE, Hirai K, Roeder K, Brennand KJ, Katsanis N, Domenici E, Devlin B, Sklar P. Gene expression elucidates functional impact of polygenic risk for schizophrenia. Nat Neurosci. 2016 Nov;19(11):1442-1453. PubMed PMID: 27668389; PubMed Central PMCID: PMC5083142.
  - c. Franzén O, Ermel R, Cohain A, Akers NK, Di Narzo A, Talukdar HA, Foroughi-Asl H, Giambartolomei C, Fullard JF, Sukhavasi K, Köks S, Gan LM, Giannarelli C, Kovacic JC, Betsholtz C, Losic B, Michoel T, Hao K, Roussos P, Skogsberg J, Ruusalepp A, Schadt EE, Björkegren JL. Cardiometabolic risk loci share downstream cis- and trans-gene regulation across tissues and diseases. Science. 2016 Aug 19;353(6301):827-30. PubMed PMID: 27540175.
  - d. Roussos P, Mitchell AC, Voloudakis G, Fullard JF, Pothula VM, Tsang J, Stahl EA, Georgakopoulos A, Ruderfer DM, Charney A, Okada Y, Siminovitch KA, Worthington J, Padyukov L, Klareskog L, Gregersen PK, Plenge RM, Raychaudhuri S, Fromer M, Purcell SM, Brennand KJ, Robakis NK, Schadt EE, Akbarian S, Sklar P. A role for noncoding variation in schizophrenia. Cell Rep. 2014 Nov 20;9(4):1417-29. PubMed PMID: 25453756; PubMed Central PMCID: PMC4255904.
- 2. Risk genetic variants affect gene expression through alterations of cis regulatory elements. These mechanisms remain unexplored in the context of neuropsychiatric disorders. We have developed and optimized neuroepigenomic approaches to perform cell type-specific characterization of the epigenome in human brain. My Lab is part of psychENCODE.
  - a. Fullard JF, Giambartolomei C, Hauberg ME, Xu K, Voloudakis G, Shao Z, Bare C, Dudley JT, Mattheisen M, Robakis NK, Haroutunian V, Roussos P. Open chromatin profiling of human postmortem brain infers functional roles for non-coding schizophrenia loci. Hum Mol Genet. 2017 May 15;26(10):1942-1951. PubMed PMID: 28335009.
  - b. Kozlenkov A, Wang M, Roussos P, Rudchenko S, Barbu M, Bibikova M, Klotzle B, Dwork AJ, Zhang B, Hurd YL, Koonin EV, Wegner M, Dracheva S. Substantial DNA methylation differences between two major neuronal subtypes in human brain. Nucleic Acids Res. 2016 Apr 7;44(6):2593-612. PubMed PMID: 26612861; PubMed Central PMCID: PMC4824074.
  - c. Bharadwaj R, Peter CJ, Jiang Y, Roussos P, Vogel-Ciernia A, Shen EY, Mitchell AC, Mao W, Whittle C, Dincer A, Jakovcevski M, Pothula V, Rasmussen TP, Giakoumaki SG, Bitsios P, Sherif A, Gardner PD, Ernst P, Ghose S, Sklar P, Haroutunian V, Tamminga C, Myers RH, Futai K, Wood MA, Akbarian S. Conserved higher-order chromatin regulates NMDA receptor gene expression and cognition.

- Neuron. 2014 Dec 3;84(5):997-1008. PubMed PMID: <u>25467983</u>; PubMed Central PMCID: <u>PMC4258154</u>.
- d. Kozlenkov A, Roussos P, Timashpolsky A, Barbu M, Rudchenko S, Bibikova M, Klotzle B, Byne W, Lyddon R, Di Narzo AF, Hurd YL, Koonin EV, Dracheva S. Differences in DNA methylation between human neuronal and glial cells are concentrated in enhancers and non-CpG sites. Nucleic Acids Res. 2014 Jan;42(1):109-27. PubMed PMID: <a href="https://example.com/rubs/24057217">24057217</a>; PubMed Central PMCID: <a href="https://example.com/rubs/24057217">PMC3874157</a>.
- 3. Schizophrenia is a polygenic disorder affecting multiple genes. To better understand the genetic architecture of the disease, we have conducted systems biology analysis that aims to identify sets of genes that are more likely to be affected in schizophrenia.
  - a. Roussos P, Guennewig B, Kaczorowski DC, Barry G, Brennand KJ. Activity-Dependent Changes in Gene Expression in Schizophrenia Human-Induced Pluripotent Stem Cell Neurons. JAMA Psychiatry. 2016 Nov 1;73(11):1180-1188. PubMed PMID: 27732689; PubMed Central PMCID: PMC5437975.
  - b. Hauberg ME, Roussos P, Grove J, Børglum AD, Mattheisen M. Analyzing the Role of MicroRNAs in Schizophrenia in the Context of Common Genetic Risk Variants. JAMA Psychiatry. 2016 Apr;73(4):369-77. PubMed PMID: <u>26963595</u>.
  - c. Xu K, Schadt EE, Pollard KS, Roussos P, Dudley JT. Genomic and network patterns of schizophrenia genetic variation in human evolutionary accelerated regions. Mol Biol Evol. 2015 May;32(5):1148-60. PubMed PMID: 25681384; PubMed Central PMCID: PMC4408416.
  - d. Roussos P, Katsel P, Davis KL, Siever LJ, Haroutunian V. A system-level transcriptomic analysis of schizophrenia using postmortem brain tissue samples. Arch Gen Psychiatry. 2012 Dec;69(12):1205-13. PubMed PMID: 22868662.
- 4. Schizophrenia and Alzheimer's disease are heritable diseases. We have conducted or participated in large scale genetic association studies that have identified common, rare or de novo variants for neuropsychiatric disorders.
  - a. Contribution of copy number variants to schizophrenia from a genome-wide study of 41,321 subjects. Nat Genet. 2017 Jan;49(1):27-35. PubMed PMID: 27869829.
  - b. Biological insights from 108 schizophrenia-associated genetic loci. Nature. 2014 Jul 24;511(7510):421-7. PubMed PMID: <u>25056061</u>; PubMed Central PMCID: <u>PMC4112379</u>.
  - c. Purcell SM, Moran JL, Fromer M, Ruderfer D, Solovieff N, Roussos P, O'Dushlaine C, Chambert K, Bergen SE, Kähler A, Duncan L, Stahl E, Genovese G, Fernández E, Collins MO, Komiyama NH, Choudhary JS, Magnusson PK, Banks E, Shakir K, Garimella K, Fennell T, DePristo M, Grant SG, Haggarty SJ, Gabriel S, Scolnick EM, Lander ES, Hultman CM, Sullivan PF, McCarroll SA, Sklar P. A polygenic burden of rare disruptive mutations in schizophrenia. Nature. 2014 Feb 13;506(7487):185-90. PubMed PMID: 24463508; PubMed Central PMCID: PMC4136494.
  - d. Fromer M, Pocklington AJ, Kavanagh DH, Williams HJ, Dwyer S, Gormley P, Georgieva L, Rees E, Palta P, Ruderfer DM, Carrera N, Humphreys I, Johnson JS, Roussos P, Barker DD, Banks E, Milanova V, Grant SG, Hannon E, Rose SA, Chambert K, Mahajan M, Scolnick EM, Moran JL, Kirov G, Palotie A, McCarroll SA, Holmans P, Sklar P, Owen MJ, Purcell SM, O'Donovan MC. De novo mutations in schizophrenia implicate synaptic networks. Nature. 2014 Feb 13;506(7487):179-84. PubMed PMID: 24463507; PubMed Central PMCID: PMC4237002.
- 5. We were the first to evaluate the association of genetic variants on prepulse inhibition, including the first genome wide association study on prepulse inhibition. In addition, we applied a pharmacogenomic approach to restore cognitive deficits by tolcapone administration, an inhibitor of COMT enzyme that increases dopamine availability in cortical regions.
  - a. Roussos P, Giakoumaki SG, Zouraraki C, Fullard JF, Karagiorga VE, Tsapakis EM, Petraki Z, Siever LJ, Lencz T, Malhotra A, Spanaki C, Bitsios P. The Relationship of Common Risk Variants and Polygenic Risk for Schizophrenia to Sensorimotor Gating. Biol Psychiatry. 2016 Jun 15;79(12):988-96. PubMed PMID: 26212897.

- b. Roussos P, Giakoumaki SG, Adamaki E, Bitsios P. The influence of schizophrenia-related neuregulin-1 polymorphisms on sensorimotor gating in healthy males. Biol Psychiatry. 2011 Mar 1;69(5):479-86. PubMed PMID: 21035784.
- c. Roussos P, Giakoumaki SG, Bitsios P. Tolcapone effects on gating, working memory, and mood interact with the synonymous catechol-O-methyltransferase rs4818c/g polymorphism. Biol Psychiatry. 2009 Dec 1;66(11):997-1004. PubMed PMID: 19699472.
- d. Giakoumaki SG, Roussos P, Bitsios P. Improvement of prepulse inhibition and executive function by the COMT inhibitor tolcapone depends on COMT Val158Met polymorphism. Neuropsychopharmacology. 2008 Dec;33(13):3058-68. PubMed PMID: 18536698.

Complete List of Published Work in My Bibliography:

https://www.ncbi.nlm.nih.gov/sites/myncbi/12meUQ8S\_uxQL/bibliography/46871393/public/?sort=date&directi on=descending

# D. Additional Information: Research Support and/or Scholastic Performance

<b>Ongoing Research Sup</b>	port
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1R01MH109677-01, NIMH Roussos, Panagiotis (Panos) (PI) 08/01/16-05/31/21 Risk genetic variants and cis regulation of gene expression in Bipolar Disorder Role: PI R01AG050986, NIA Roussos, Panagiotis (Panos) (PI) 09/01/15-08/31/20 Higher Order Chromatin and Genetic Risk for Alzheimer's Disease Role: PI R01DA15446, Semmelweis-NIH SC Hurd, Yasmin (PI) 04/01/15-03/31/20 Molecular Neurobiology of Human Drug Abuse Role: PI

R01MH110921, NIH/NIMH Sklar, Pamela (PI) 09/01/16-06/30/20

Molecular Profiling of Schizophrenia

Role: Co-Investigator

R01MH109897, NIH/NIMH Sklar, Pamela (PI) 05/01/16-02/28/21

Integrated Multiscale Networks in Schizophrenia

Role: Co-Investigator

U01AG046170, NIH/NIA Schadt, Eric (PI) 12/01/13-11/30/18

Integrative Biology Approach to Complexity of Alzheimer's Disease

Role: Co-Investigator

R01MH106056, NIH/NIMH Akbarian, Schahram (PI) 09/01/14-08/31/17

Higher Order Chromatin and Genetic Risk for Schizophrenia

Role: Co-Investigator

**Completed Research Support** 

NIRG-340998, Alzheimer's Association Roussos, Panagiotis (Panos) (PI) 02/01/15-01/31/17

Dissecting the Cis Regulation of Gene Expression in Alzheimer's Disease

Role: PI

BX002395, Veterans Administration Roussos, Panagiotis (Panos) (PI) 10/01/13-03/31/17

Dissecting Cis Regulation of Gene Expression in Schizophrenia

Role: PI