

## Physician-Scientist Track: Residents

Below please find several models of how trainees have progressed through our Physician-Scientist Research Track. Note that unless otherwise specified, narrative descriptions (and publication lists) refer primarily to residents' experiences during residency rather than featuring activities since graduation.

### Career Development in Residency



#### Mercedes Perez-Rodriguez, MD, PhD

Graduated 2012

##### **Current Position**

Assistant Training Director for Research, Department of Psychiatry

Assistant Professor of Psychiatry

Medical Director, PRISM (Psychosis Research Integrating Science and  
Medicine)

Icahn School of Medicine at Mount Sinai

I joined Mount Sinai in 2008 for residency training in Psychiatry in the Physician-Scientist Research Track. I served as the first Chief Resident for Research and helped to bolster the translational science curriculum for psychiatry residents. During residency, I was able to use protected research time to become involved in and develop numerous projects, focused on dissecting the neurobiology of mood and personality disorders using fMRI, PET, and integrating brain imaging and genetics. I completed the project "Tryptophan Hydroxylase 2 haplotype association with borderline personality disorder (BPD) and aggression," which resulted in a first-authored paper, an award-nominated poster at the annual meeting of the Society for Biological Psychiatry, and the APA New York County District Branch Resident Research Award. I also presented this project at the APA 2011 Research Colloquium for Young Investigators. I also first-authored the paper "Striatal Activity in Borderline Personality Disorder: Sex Differences," which received the APA New York State Scientific Paper Award. I was a Co- Investigator in the project "High Risk Suicidal Behavior in veterans: Assessment of Social Cognition" (Department of Veteran Affairs Mental Illness Research, Education, & Clinical Center pilot grant funding), which

resulted in a paper currently in preparation. I was also an investigator in the projects "Clinical Testing of a D1 Agonist for the Cognitive Enhancement of Schizotypal Personality Disorder," and "Pharmacology of Cognition in Schizotypal Personality Disorder (SPD)."

After graduating in 2012, I accepted a position as a MIRECC research fellow. My current NIH-funded research focuses on uncovering biomarkers of risk and resilience in bipolar disorder using an endophenotype approach and integrating multi-modal measures including neurocognition, brain imaging, and psychophysiology. My work is also focused on characterizing the neurobiology of social cognitive impairments across disorders and testing the effect and mechanism of intranasal oxytocin as a promising treatment.

### **Publications during residency:**

- Rianza Bermudo-Soriano C, **Perez-Rodriguez MM**, Vaquero-Lorenzo C, Baca-Garcia E. New perspectives in glutamate and anxiety. *Pharmacol Biochem Behav*. 2012 Feb;100(4):752-74. PubMed PMID: 21569789
- Hilario Blasco-Fontecilla, David Delgado-Gomez, Teresa Legido-Gil, Jose de Leon, **M. Mercedes Perez-Rodriguez** & Enrique Baca-Garcia (2012): Can the Holmes-Rahe Social Readjustment Rating Scale (SRRS) Be Used as a Suicide Risk Scale? An Exploratory Study, *Archives of Suicide Research*, 2012 16:1, 13-28
- **Perez-Rodriguez MM**, Hazlett EA, Rich EL, Ripoll LH, Weiner DM, Spence N, Goodman M, Koenigsberg HW, Siever LJ, New AS. Striatal activity in borderline personality disorder with comorbid intermittent explosive disorder: Sex differences. *J Psychiatr Res*. 2012 Jun;46(6):797-804. PubMed PMID: 22464337.
- Blasco-Fontecilla H, **Perez-Rodriguez MM**, Garcia-Nieto R, Fernandez-Navarro P, Galfalvy H, de Leon J, Baca-Garcia E. Worldwide impact of economic cycles on suicide trends over 3 decades: differences according to level of development. A mixed effect model study. *BMJ Open*. 2012 May 14;2(3). PubMed PMID: 22586285.
- Zisook S, Anzia J, Atri A, Baroni A, Clayton P, Haller E, Lomax JW, Mann JJ, Oquendo MA, Pato M, **Perez-Rodriguez MM**, Prabhakar D, Sen S, Thrall G, Yaseen ZS. Teaching Evidence-Based Approaches to Suicide Risk Assessment and Prevention that Enhance Psychiatric Training. *Compr Psychiatry*. 2012 Sep 17. doi:pii: S0010-440X(12)00142-3. PubMed PMID: 22995449.
- New AS, aan het Rot M, Ripoll LH, **Perez-Rodriguez MM**, Lazarus S, Zipursky E, Weinstein SR, Koenigsberg HW, Hazlett EA, Goodman M, Siever LJ. Empathy and alexithymia in borderline personality disorder: clinical and laboratory measures. *J Pers Disord*. 2012 Oct;26(5):660-75. PubMed PMID: 23013336.
- Baca-Garcia E, **Perez-Rodriguez MM**, Keyes KM, Oquendo MA, Hasin DS, Grant BF, Blanco C. Suicidal ideation and suicide attempts among Hispanic subgroups in the United States: 1991-1992 and 2001-2002. *J Psychiatr Res*. 2011 Apr;45(4):512-8. PubMed PMID: 20937507.
- de Leon J, Mallory P, Maw L, Susce MT, **Perez-Rodriguez MM**, Baca-Garcia E. Lack of replication of the association of low serum cholesterol and attempted suicide in another country raises more questions. *Ann Clin Psychiatry*. 2011 Aug;23(3):163-70. PubMed PMID: 21808747.
- Baca-Garcia E, **Perez-Rodriguez MM**, Oquendo MA, Keyes KM, Hasin DS, Grant BF, Blanco C. Estimating risk for suicide attempt: Are we asking the right questions? Passive suicidal ideation as a marker for suicidal behavior. *J Affect Disord*. 2011 Nov;134(1-3):327-32. PubMed PMID: 21784532.
- **Perez-Rodriguez MM**, Lopez-Castroman J, Martinez-Vigo M, Diaz-Sastre C, Ceverino A, Núñez-Beltrán A, Saiz-Ruiz J, de Leon J, Baca-Garcia E. Lack of association between testosterone and suicide attempts. *Neuropsychobiology*. 2011;63(2):125-30. PubMed PMID: 21196783.
- Baca-Garcia E, Vaquero-Lorenzo C, **Perez-Rodriguez MM**, Gratacòs M, Bayés M, Santiago-Mozos R, Leiva-Murillo JM, de Prado-Cumplido M, Artes-Rodriguez A, Ceverino A, Diaz-Sastre C, Fernandez-Navarro P,

Costas J, Fernandez-Piqueras J, Diaz-Hernandez M, de Leon J, Baca-Baldomero E, Saiz-Ruiz J, Mann JJ, Parsey RV, Carracedo A, Estivill X, Oquendo MA. Nucleotide variation in central nervous system genes among male suicide attempters. *Am J Med Genet B Neuropsychiatr Genet*. 2010 Jan 5;153B(1):208-13. PubMed PMID: 19455598.

- Baca-Garcia E, **Perez-Rodriguez MM**, Keyes KM, Oquendo MA, Hasin DS, Grant BF, Blanco C. Suicidal ideation and suicide attempts in the United States: 1991-1992 and 2001-2002. *Mol Psychiatry*. 2010 Mar;15(3):250-9. PubMed PMID: 18779820.
- Baca-Garcia E, Diaz-Sastre C, Ceverino A, **Perez-Rodriguez MM**, Navarro-Jimenez R, Lopez-Castroman J, Saiz-Ruiz J, de Leon J, Oquendo MA. Suicide attempts among women during low estradiol/low progesterone states. *J Psychiatr Res*. 2010 Mar;44(4):209-14. PubMed PMID: 19782376.
- Lopez-Castroman J, Gómez DD, Belloso JJ, Fernandez-Navarro P, **Perez-Rodriguez MM**, Villamor IB, Navarrete FF, Ginestar CM, Currier D, Torres MR, Navio-Acosta M, Saiz-Ruiz J, Jimenez-Arriero MA, Baca-Garcia E. Differences in maternal and paternal age between schizophrenia and other psychiatric disorders. *Schizophr Res*. 2010 Feb;116(2-3):184-90. PubMed PMID: 19945257.
- Carballo JJ, Baca-Garcia E, Blanco C, **Perez-Rodriguez MM**, Jimenez Arriero MA, Artes-Rodriguez A; Group for the Study of Evolution of Diagnosis (SED), Rynn M, Shaffer D, Oquendo MA. Stability of childhood anxiety disorder diagnoses: a follow-up naturalistic study in psychiatric care. *Eur Child Adolesc Psychiatry*. 2009 Oct 15. PubMed PMID: 19826859.
- **Perez-Rodriguez MM**, Weinstein S, New AS, Bevilacqua L, Yuan Q, Zhou Z, Hodgkinson C, Goodman M, Koenigsberg HW, Goldman D, Siever LJ. Tryptophan-hydroxylase 2 haplotype association with borderline personality disorder and aggression in a sample of patients with personality disorders and healthy controls. *J Psychiatr Res*. 2010 Nov;44(15):1075-81. PubMed PMID: 20451217.
- Blasco-Fontecilla H, Baca-Garcia E, Duberstein P, **Perez-Rodriguez MM**, Dervic K, Saiz-Ruiz J, Courtet P, de Leon J, Oquendo MA. An exploratory study of the relationship between diverse life events and specific personality disorders in a sample of suicide attempters. *J Pers Disord*. 2010 Dec;24(6):773-84. PubMed PMID: 21158599.
- Blasco-Fontecilla H, Baca-Garcia E, Dervic K, **Perez-Rodriguez MM**, Lopez-Castroman J, Saiz-Ruiz J, Oquendo MA. Specific features of suicidal behavior in patients with narcissistic personality disorder. *J Clin Psychiatry*. 2009 Nov;70(11):1583-7.
- Vaquero-Lorenzo C, Riza Bermudo-Soriano C, **Perez-Rodriguez MM**, Diaz-Hernandez M, López-Castromán J, Fernandez-Piqueras J, Saiz-Ruiz J, Baca-Garcia E. Positive association between SAT-1 -1415T/C polymorphism and anxiety. *Am J Med Genet B Neuropsychiatr Genet*. 2009 Jun 5;150B(4):515-9.
- López-Castromán J, Vaquero-Lorenzo C, **Perez-Rodriguez MM**, Diaz-Hernandez M, Fernandez-Piqueras J, Saiz-Ruiz J, Baca-Garcia E. Gender effect on association between DRD2 polymorphism and substance dependence in a Spanish sample. *Drug Alcohol Depend*. 2009 May 1;101(3):210-2.
- Baca-Garcia E, Sher L, **Perez-Rodriguez MM**, Burke AK, Sullivan GM, Grunebaum MF, Stanley BH, Mann JJ, Oquendo MA. Treatment of depressed bipolar patients with alcohol use disorders: plenty of room for improvement. *J Affect Disord*. 2009 May;115(1-2):262-8.
- Bermudo-Soriano CR, Vaquero-Lorenzo C, Diaz-Hernandez M, **Perez-Rodriguez MM**, Fernandez-Piqueras J, Saiz-Ruiz J, Baca-Garcia E. SAT-1 -1415T/C polymorphism and susceptibility to schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*. 2009 Mar 17;33(2):345-8.
- Blasco-Fontecilla H, Baca-Garcia E, Dervic K, **Perez-Rodriguez MM**, Saiz-Gonzalez MD, Saiz-Ruiz J, Oquendo MA, de Leon J. Severity of personality disorders and suicide attempt. *Acta Psychiatr Scand*. 2009 Feb;119(2):149-55.
- Alonso P, Gratacòs M, Menchón JM, Saiz-Ruiz J, Segalàs C, Baca-García E, Labad J, Fernández-Piqueras J,

Real E, Vaquero C, **Perez M**, Dolengevich H, González JR, Bayés M, Cid RD, Vallejo J, Estivill X. Extensive Genotyping of the BDNF and NTRK2 Genes Define Protective Haplotypes Against Obsessive-Compulsive Disorder. *Biol Psychiatry*. 2008 Mar 15;63(6):619-28.

- Baca-Garcia E, **Perez-Rodriguez MM**, Basurte-Villamor I, Quintero-Gutierrez FJ, Sevilla-Vicente J, Martinez-Vigo M, Artes-Rodriguez A, Fernandez del Moral AL, Jimenez-Arriero MA, Gonzalez de Rivera JL. Patterns of mental health service utilization in a general hospital and outpatient mental health facilities: analysis of 365,262 psychiatric consultations. *European archives of psychiatry and clinical neuroscience*. 2008 Mar;258(2):117-23.
- Vaquero-Lorenzo C, Baca-Garcia E, Diaz-Hernandez M, **Perez-Rodriguez MM**, Fernandez-Navarro P, Giner L, Carballo JJ, Saiz-Ruiz J, Fernandez-Piqueras J, Balamero EB, de Leon J, Oquendo MA. Association study of two polymorphisms of the serotonin-2A receptor gene and suicide attempts. *Am J Med Genet B Neuropsychiatr Genet*. 2008 Jul 5;147B(5):645-9.
- **Perez-Rodriguez MM**, Baca-Garcia E, Diaz-Sastre C, Garcia-Resa E, Ceverino A, Saiz-Ruiz J, Oquendo M, de Leon J. Low serum cholesterol may be associated with suicide attempt history. *J Clin Psychiatry*. 2008 Dec;69(12):1920-7.



## Panagiotis (Panos) Roussos, MD, PhD

Graduated 2012

### **Current Position**

Assistant Professor of Psychiatry  
Assistant Professor of Genetics and Genomic Sciences  
Icahn School of Medicine at Mount Sinai

### **My Background**

I was born and raised in Athens, Greece, where I spent my first 18 years. After finishing high school, I moved to Crete to study medicine. Early on I decided that I wanted to become a psychiatrist and be involved with research on the neurobiology and genetics of neuropsychiatric illnesses. Upon obtaining my medical degree, I continued with graduate studies in biological psychiatry, and I obtained my MSc in Neuroscience and PhD in behavioral genetics. Upon finishing my PhD, I made the decision to continue my career in the U.S. and pursue a career in academic psychiatry.

### **Why I Chose Mount Sinai**

During my interviews, I visited many large academic programs on the East Coast. I was interested in a program that

could provide me with (1) opportunities for being involved in innovative and important research, (2) support and mentorship to develop my skills, so I could acquire a tenure-track faculty position after residency, and (3) protected time for research during residency. At the time I was interviewing, Mount Sinai had created a dedicated research track with its own match and separate NRMP number; the offerings by Mount Sinai met all of my criteria and more, making it the perfect fit! My initial impression was correct: at Mount Sinai, not only do you get protected time (and even more time for research), but the administration is very supportive and committed to the success and development of young physician-scientists. Another determining factor was that Mount Sinai is located in the greatest city in the world! Everything is here: parks, restaurants, museums, and concerts. NYC is an exciting place to live and explore!

### ***My Professional Schedule and Life during My Time as a Research Track Resident***

My main interest has been exploring the genetic factors that increase the risk for neuropsychiatric illnesses. During my tenure as a resident, the protected research time was structured as 2 months during PGY1 and PGY2, 30% of time as PGY3, and 80% as PGY4. Upon starting residency, I was interested in 2 different approaches/disciplines: neuroimaging and human postmortem studies. The first 2 years is a good time period to rotate through different labs and work with different mentors. As a PGY1, I decided to explore neuroimaging research in schizophrenia by joining Monte Buchsbaum's Lab, where I got experience working with neuroimaging data, learning about the different modalities and normalization approaches, and applying statistical models to analyze data. As a PGY2, I moved to human postmortem brain tissue studies by joining Harry Haroutunian's Lab at the VA. During that year, I performed gene expression studies using human postmortem brain tissue and got experience analyzing gene expression microarray data. As a PGY3 and PGY4, I worked on 2 projects that involved the study of abnormalities in gene expression in schizophrenia. Realizing the need to acquire additional skills to analyze big data, I sought additional mentorship by joining Pamela Sklar's group. My main focus was to integrate big data, such as genetic, epigenetic, and gene expression, and identify genetic risk factors that drive the clinical manifestations of schizophrenia. That idea was later developed into a career development award proposal. After graduation I did a post-doctoral MIRECC fellowship in schizophrenia and subsequently became a faculty member at Mount Sinai.

During residency, I was involved in the following projects:

1. Examine the role of the NF-kappa B pathway in schizophrenia. Preliminary results from this project were successfully used to obtain funding (\$20K) from the federal Mental Illness Research Education and Clinical Center (MIRECC) to expand the analysis from human postmortem brain to living patients with schizophrenia and their unaffected first-degree relatives. The manuscript describing the postmortem findings was published in *Neuropsychopharmacology*.
2. Examine abnormalities of the Node of Ranvier in schizophrenia. In this study, we used a combined analysis of transcriptomic, proteomic, genetic, cognitive, and neuroimaging data to show that abnormalities of the Node of Ranvier exist in schizophrenia. The results of this study were presented in multiple conferences, as part of invited speaker engagements, and were published in the *Archives of General Psychiatry*. In addition, these results provided the preliminary findings in two recently submitted grants (Dr. Haroutunian – PI) for examining the role of two different genes using animal models. In both grants I participate as co-investigator. Finally, these results supported a successfully funded grant (Dr. Domna Karagogeos – PI; European Union/Hellenic Republic - Juxtaparanodal proteins in the molecular organization of myelinated axons; 600,000 euros for a total period of 4 years) in which I participated as a co-investigator.
3. Examine alteration in the transcriptome of patients with schizophrenia using systems biology approaches. The results of this study were presented in multiple conferences, as part of invited speaker engagements,

and are published in the *Archives of General Psychiatry*. In addition, these results were including as preliminary in submitted grants to examine the genetic basis of gene expression in schizophrenia.

4. The research protected time provided me the opportunity to continue working on multiple different projects and submitting manuscripts in collaboration with my previous institute, where I obtained my MD and PhD, as well as to finish 2 book chapters.
5. Finally, I participated as a co-investigator in multiple other projects with Dr. Larry Siever, which resulted in preliminary results that supported a successfully funded grant (Dr. Larry Siever-PI; VA Merit - White Matter Abnormalities in the Schizophrenia Spectrum; \$600,000 for a total period of 4 years).

**Partial list of publications during residency:**

- **Roussos P**, Giakoumaki SG, Georgakopoulos A, Chrisoulakis A, Somaraki K, Robakis NK, Bitsios P. Allelic variations in ANK3 and CACNA1C impact on spatial working memory, startle reactivity and personality traits in healthy males. *Bipolar Disorders*. 2011 13(3):250-9.
- **Roussos P**, Giakoumaki SG, Georgakopoulos A, Chrisoulakis A, Somaraki K, Robakis NK, Bitsios P. A D-amino acid oxidase Diplotype is Associated with Deficient PPI and Attenuated Anxiety in Healthy Males. *Neuropsychopharmacology*. 2011 36(8):1677-88.
- **Roussos P**, Katsel K, Davis KL, Bitsios P, Giakoumaki SG, Jogia J, Rozsnyai K, Collier D, Frangou S, Siever LJ, Haroutunian V. Molecular and Genetic Evidence for Abnormalities in the Nodes of Ranvier in Schizophrenia. *Archives of General Psychiatry*. 2012 69(1):7-15.
- **Roussos P**, Katsel P, Davis KL, Siever LJ, Haroutunian V. A System Level Transcriptomic Analysis in Schizophrenia Postmortem Brain. *Archives of General Psychiatry*. 2012 Dec;69(12):1205-13.
- **Roussos P**. Transcription factor 4 as an important determinant of gating function in schizophrenia. *PNAS*. 2012 Apr 17;109(16):5915-6

Dr. Roussos' overall work and contribution to schizophrenia research was recently recognized and awarded the Presidential Early Career Awards for Scientists and Engineers by President Obama. A prolific researcher who has published high profile papers in *Nature*, *Science*, *Nature Genetics*, *Nature Neuroscience*, *Neuron*, *Molecular Psychiatry*, and *JAMA Psychiatry*, Dr. Roussos currently has 2 RO1 grants, and he is leading the effort of epigenetic profiling and integration of high-dimensional data in schizophrenia, bipolar disorder, and Alzheimer's Disease.

**[For a current list of Dr. Roussos' PubMed-indexed work, use this link.](#)**



## Marc Lener, MD

Graduated 2015

### **Current Position**

Research Fellowship, NIMH

During my PGY-1 year, I completed work on projects I had begun prior to residency training, including a manuscript of a study that was recently published in *Schizophrenia Research* and a review article that compares the common neurobiological characteristics of temporal lobe epilepsy and schizophrenia.

During my PGY-2 year, in addition to completing chapters in clinical manuals in Adolescent Psychiatry and Interventional Pain, I began working in Dr. Erin Hazlett's lab studying white matter abnormalities via diffusion tensor imaging (DTI) analysis in brains of schizophrenic patients compared to brains of schizotypal personality disorder patients. The manuscript of this study was recently submitted for publication.

During my PGY-3 year, I have spent the majority of my outpatient clinical and research time in the Mood and Anxiety Disorders Program with Drs. Daniel Iosifescu and James Murrough, studying patients who have treatment resistant depression (TRD). During my PGY-3 and PGY-4 years, I performed two separate structural imaging analyses; one was a DTI analysis comparing a TRD population with a non-treatment resistant population (nTRD) to determine whether patients with TRD have a greater degree of illness as defined by white matter tract coherence within the spectrum of depressive illness, and the other was a volumetric analysis of patients with major depressive disorder compared to non-depressed patients who exhibited symptoms of depression. I was able to submit one of these projects as a research plan to the NIH and am currently under review by The NIH Clinical Research Loan Repayment Award for Individuals from Disadvantaged Backgrounds. My goal is to continue developing my research skills to help identify biological markers of depression and treatment response prediction.

### **Partial list of publications during residency:**

- **Lener MS**, Charney DS, Feder A. Anxiety Disorders. In Mount Sinai Expert Guides Series. Simon AB, New AS, Goodman WK. Wiley, London. In press.
- Aligene K, **Lener MS**, Spinner D, Khelemsky Y. Facial Pain. In Sackheim, Kimberly. (2015). Pain Management and Palliative Care: A Comprehensive Guide. Springer-Verlag, New York. p. 113-123.
- **Lener MS**, Kundu P, Wong E, Dewilde KE, Tang CY, Balchandani P, Murrough JW. Cortical abnormalities and association with symptom dimensions across the depressive spectrum. *J Affect Disord*. 2016 Jan 15;190:529-36.
- **Lener MS**, Iosifescu DV. In pursuit of neuroimaging biomarkers to guide treatment selection in major depressive disorder: a review of the literature. *Ann N Y Acad Sci*. 2015 May;1344:50-65.
- **Lener MS**, Wong E, Tang CY, Byne W, Goldstein KE, Blair NJ, Haznedar MM, New AS, Chemerinski E, Chu KW, Rinsky LS, Siever LJ, Koenigsberg HW, Hazlett EA. White matter abnormalities in schizophrenia and schizotypal personality disorder. *Schizophr Bull*. 2015 Jan;41(1):300-10.

- **Lener MS**, Wong E, Tang CY, Byne W, Goldstein KE, Blair NJ, Haznedar MM, New AS, Chemerinski E, Chu KW, Rimsky LS, Siever LJ, Koenigsberg HW, Hazlett EA. White Matter Abnormalities in Schizophrenia and Schizotypal Personality Disorder. *Schizophr Bull.* 2014 Jun 23.
- **Lener MS**, Goodnow SJ, Wood JA, Chowdari KV, Keshavan MS, Nimgaonkar V, Prasad KM. RGS4 and COMT risk variants are associated with brain structural alterations. *Schizophr Res.* 2013 Oct;150(1):321-2.
- **Lener MS**, Anderson SA, Ivanov I. Illicit Stimulant Abuse in Adolescents. In Substance Abuse in Adolescence and Young Adults: A Manual for Pediatric and Primary Care Physicians. Eds. Donald E. Greydanus MD, Gabriel Kaplan MD, Dilip Patel MD, Joav Merrick MD. De Gruyter, Berlin, 2013.



## Tobias Halene, MD, PhD

Graduated 2015

### **Current Position**

MIRECC Research Fellowship, James J Peters VAMC  
Icahn School of Medicine at Mount Sinai

I am a psychiatrist and scientist intrigued by psychosis. My research started with NMDA receptor pharmacology while in medical school, examined sensory processing in a mouse model of psychosis during graduate school, and studied the effect of antipsychotic medication on brain cell composition in a non-human primate model during psychiatric residency training.

I am currently a 2<sup>nd</sup> year research fellow interested in oligodendrocyte function and myelination as a dynamic process attuned to neuronal activity. I am currently preparing a mentored career award application, proposing that oligodendrocytes provide myelination in a context-dependent manner determined by the local microstructure of the brain. My goal is to integrate neuroimaging with cellular phenotype and the molecular biology that is driving it.

I was born and raised in Germany. There is a lot to be said for growing up on a farm in Germany's rural Northwest, but it was time to leave after high school and military service. My brother was the better farmer, and I thought medicine could be a good starting point to take my curiosity into the world. The European Erasmus program allowed me to venture out to Spain and Italy, where I spent two out of six years of medical school. After that I knew that this would not be the last time I had studied and worked abroad. For my doctoral thesis at the University of Münster/Germany, I studied the neural basis of opioid analgesia by expressing human NMDA receptors in *Xenopus* oocytes and used electro-physiological methods to determine their response to a variety of substances. As a result, I pointed out a mechanism that could explain the increased hyperalgesia after use of the opioid remifentanyl.

I started my psychiatry residency education in Aachen/Germany. After my first year of training, I joined a joint training program between the University in Aachen and the University of Pennsylvania and expanded my research training in Steve Siegel's lab at Penn, where I learned a wide array of skills, approaches, and strategies to study the neurobiology and treatment of schizophrenia using mouse models of behavioral and electrophysiological deficits. Furthermore, I thought about the potential use of PDE inhibitors in psychiatry and added to the idea that a specific class of PDE inhibitor could have antipsychotic effects.

I decided to stay for psychiatric residency training in the US, completed my ECFMG certification and matched into Mount Sinai's Physician-Scientist Track. Residency training was intense; starting my 1<sup>st</sup> year was like being a 3<sup>rd</sup> and 4<sup>th</sup> year med student and intern all at the same time, since I had never worked in the US healthcare system. I was happy to be part of a cohesive and supportive group of peers. With several non-psychiatric inpatient rotations, the 1<sup>st</sup> (and the 2<sup>nd</sup>) years were highly clinically-focused. At the same time, I used the 1<sup>st</sup> year to meet with several potential mentors, and I did a rotation in Schahram Akbarian's lab in my 2<sup>nd</sup> year. The 3<sup>rd</sup> and especially the 4<sup>th</sup> years allowed me to focus on research. I worked on the effect of chronic antipsychotic treatment on brain cell composition in the frontal cortex. Using post-mortem brain tissue gave me the flexibility to schedule my lab work around my clinical duties. I enjoyed using numerous techniques—from flow cytometry (FACS) and MRI image analysis to 3C and RT-PCR—to unravel the molecular fingerprint of isolated neuronal and glial nuclei.

I am grateful for both the clinical and research training I received at Mount Sinai, and I would do it again in a heartbeat. Clinically, I am comfortable treating a variety of psychiatric conditions with both psychotherapy and pharmacological interventions in inpatient and outpatient settings and with diverse patient populations. At the same time, I have excellent mentors, my career award application is taking shape, and I am excited to combine imaging with molecular biology.

#### **Partial list of publications during residency:**

- Maze I, Wenderski W, Noh KM, Bagot RC, Tzavaras N, Purushothaman I, Elsässer SJ, Guo Y, Ionete C, Hurd YL, Tamminga CA, **Halene T**, Farrelly L, Soshnev AA, Wen D, Rafii S, Birtwistle MR, Akbarian S, Buchholz BA, Blitzer RD, Nestler EJ, Yuan ZF, Garcia BA, Shen L, Molina H, Allis CD. Critical Role of Histone Turnover in Neuronal Transcription and Plasticity. *Neuron*. 2015 Jul 1;87(1):77-94.
- **Halene TB**, Peter CJ, Akbarian S. Epigenetic Dysregulation in the Schizophrenic Brain. *Curr Behav Neurosci Rep*. Epub: 2014 Mar 23.
- Akbarian S, **Halene T**. The neuroepigenetics of suicide. *Am J Psychiatry*. 2013 May 1;170(5):462-5.
- Hasan A, Mitchell A, Schneider A, **Halene T**, Akbarian S. Epigenetic dysregulation in schizophrenia: molecular and clinical aspects of histone deacetylase inhibitors. *Eur Arch Psychiatry Clin Neurosci*. 2013 Jun;263(4):273-84.
- Featherstone RE, Phillips JM, Thieu T, Ehrlichman RS, **Halene TB**, Leiser SC, Christian E, Johnson E, Lerman C, Siegel SJ. Nicotine receptor subtype-specific effects on auditory evoked oscillations and potentials. *PLoS One*. 2012;7(7):e39775.
- Carlson GC, Talbot K, **Halene TB**, Gandal MJ, Kazi HA, Schlosser L, Phung QH, Gur RE, Arnold SE, Siegel SJ. Dysbindin-1 mutant mice implicate reduced fast-phasic inhibition as a final common disease mechanism in schizophrenia. *Proc Natl Acad Sci USA*. 2011 Oct 25;108(43).

## Currently on Track



### Drew Kiraly, MD, PhD

Current PGY-4

#### ***My Background***

I was born and raised in a small town in Connecticut, and despite having lived within two hours of NYC my entire life, this is my first time living in the city. In college I majored in neurobiology and applied to medical school with the certainty that I would be pursuing a career in neurosurgery. While I was working on applications and going on interviews for medical school, I began work in a lab examining the molecular bases of addiction and depression. During this time, I made two important discoveries: 1) The thing that fascinates me about the brain is its ability to produce complex behaviors, and 2) I love research.

After deferring medical school for a year to get more time in lab, I applied to and was accepted in the MD-PhD program at the University of Connecticut two weeks before the fall semester started! Prior to medical school and throughout my MD-PhD training, my work has been focused on examining neuronal mechanisms of drug addiction, such as NMDA receptor signaling, changes in dendritic spine morphology, and changes in post-synaptic signaling complexes. I have also worked on the neuronal changes associated with chronic corticosterone exposure in various behavioral paradigms.

After eight wonderful and productive years in the greater Hartford area, my wife and I packed up and moved to the Upper East Side. Just to make the whole process a little simpler, my first child was born on the very first day of residency! After getting over the initial shock of moving to a new city, starting residency, and becoming a new father (all within one week's time), I have really settled into and come to love the City. Now, in my spare time I generally chase my three-year-old daughter around one of the many Central Park playgrounds or The Metropolitan Museum of Art (much to the dismay of the guards). When we have childcare, my wife and I often go out to local restaurants or head downtown to hear some jazz or go to a comedy club. While I had some initial apprehension about moving here, I have found it to be an interesting and welcoming place to live, explore, and raise a child.

#### ***Why I Chose Mount Sinai***

When I was searching for the right residency I interviewed at most of the large academic programs up and down the East Coast. My goal was to find a program that would provide me with the support and flexibility I needed to transition into a tenure-track faculty position after residency. While all the programs I visited had impressive things to offer, there were several things that ultimately made Mount Sinai my first choice. One of these was the flexibility that was offered in terms of setting my own schedule. Sinai had one of the largest amounts of protected research time of any program that I visited – and the amount of protected time has only increased since I came to the program. Importantly, I got the feeling that the administration worked to ensure that this protected time truly was protected and not just “protected” (I can tell you that this feeling was correct). While I was visiting, I also got the

sense that the administration placed great value on the development of young physician-scientists, and that they would work to ensure our developments. This is clearly evidenced by how many of our graduates have stayed on as faculty, as well as by the recent additions of the research-track salary supplement and technician support in lab. For me, the final piece of the puzzle was that my top choice for a research mentor, Eric Nestler, was at Mount Sinai and was very encouraging of me joining the program. While not all applicants would work in his lab, I continue to be amazed by how many amazing world class scientists are here (and the number seems to be growing all the time). Taking all of these things together, I decided that Mount Sinai would be the optimal environment for my growth as both a physician and a scientist.

### ***My Professional Schedule and Life***

During my PGY-1&2 years, in addition to learning to be a new physician and new father, I spent time finishing projects with my thesis lab examining the effects of the post-synaptic protein Kalirin-7 on cocaine self-administration, and another using mass spectrometry to look at quantitative changes in phosphorylation of post-synaptic proteins following acute or chronic cocaine exposure. During my time at the VA, I was able to work with attendings from the inpatient psychiatry unit and was first author on publishing two case reports and three book chapters. During those years I also worked on a project looking at cognitive effects of buprenorphine in patients recovering from opiate abuse; this study is currently being written up for publication.

In PGY-3, I used my protected research time to throw myself into multiple research projects with Eric Nestler as my primary research mentor. I was tasked with developing my own translational project that did not overlap with any of the ongoing lines of research in the lab – with the hope that this would become my own independent project after residency. After extensive review of the literature, I began projects examining the role of the immune system and the gut microbiome in the development of psychostimulant addiction. I chose this niche because the brain-immune system interaction is much more complex and important than previously understood, and I believe there is a tremendous therapeutic potential in immunomodulatory agents. At the same time, I began clinical research in the Mood and Anxiety Disorders Research Program (MAP) under the tutelage of Drs. James Murrough and Dan Iosifescu. Here, I started developing projects that feed into my own interests in the role of inflammation in mental illness, while also working as a study physician on multiple ongoing investigations to learn the details of how clinical trials are carried out. I also started work on setting up a collaboration with Dr. Alex Kolevzon of the Seaver Autism Center to develop a mouse model of autism to examine the pathogenic role of the gut microbiome in autism spectrum disorders. While starting all of these projects (in addition to taking on child and adult caseloads in the outpatient clinics) made for a busy start to PGY-3, it was also very exciting to be involved in so many collaborative projects and start being able to see ideas come to fruition.

At this point in time, I can honestly say that I am both busier and happier than I have been at any other time in residency. As a fourth-year research-track resident, the majority of my time is spent on various research endeavors. Based on my work in the Nestler lab, I have been named as a Leon Levy Fellow in Neuroscience, have a first author paper under review, and am applying for a K-award this coming fall. Given my interest in the gut microbiome, I also recently applied for, and was awarded, a fellowship through the Seaver Autism Center to examine how changes in the gut microbiome affect autism-like behaviors in a genetic mouse model of autism. While this may sound like a lot of work, my training within the Physician-Scientist Research Track has facilitated my being able to hire a full-time technician to join my growing research efforts for at least the next two years and keep things moving along when I am not in lab.

The bulk of my PGY-4 clinical work takes place in the Mood and Anxiety Disorders Research Program, with Dr. James Murrough. Here, I am a co-investigator on 7 different clinical trials working to find novel therapeutics for

depression and anxiety disorders. I perform detailed assessments of patients at intake and follow them through the clinical trial process to monitor their progress. From this work I currently have a first-author paper under review examining serum cytokines as potential biomarkers for ketamine treatment response. I am also a co-author on several other manuscripts currently under preparation. One of the most interesting parts of this work is that I also provide treatment for patients after they exit studies. Since most of our subjects have treatment-resistant depression, this is an interesting exercise in the art of psychopharmacology and psychotherapy and has shown me that many patients with refractory illnesses can get real relief with thoughtful application of treatments.

In addition to my clinical and research activities, I have also taken on an administrative role as the Chief Resident for Research for the past and current academic years. In this role I work with program leadership to guide current residents through the research tracks and have instituted a monthly works-in-progress series for our residents. Last year, I also created a semester-long course for our interns teaching Evidence-Based Psychiatry and Clinical Neuroscience, and I continue to serve as course director this year as well. Finally, during interview season I have the good fortune of meeting with and trying to recruit many of the fantastic candidates we interview each year.

After graduation, my hope is to join the faculty here in psychiatry and neuroscience to continue some of my translational work and translate my laboratory findings into early-stage clinical trials for addiction and depression. I hope I presented the full scope of what I have done and demonstrated that this is truly a program where a smart and motivated physician-scientist is given the freedom and flexibility to accomplish whatever they set their mind to. I have been tremendously happy with my choice of Mount Sinai, and I think you will be too.

#### **Publications during residency to-date:**

##### *Peer-Reviewed Papers*

- **Kiraly DD**, Horn SR, Van Dam NT, Costi S, Schwartz J, Kim-Schulze, Patel M, Hodes GE, Russo SJ, Merad M, Iosifescu DV, Charney DS, Murrough JW. Altered cytokine profiles in treatment-resistant depression – response to ketamine and prediction of treatment outcome. Under review at *Translational Psychiatry*.
- **Kiraly DD**, Walker DM, Calipari ES, Labonte B, Issler O, Pena CJ, Ribeiro E, Russo SJ, Nestler EJ. Host Microbiome Controls Behavioral Responses to Cocaine. Under Revision at *Scientific Reports*.
- **Kiraly DD**, Sher L. Low testosterone in a young combat veteran with dual diagnosis and suicidal behavior: a case study. *Int J Adolesc Med Health*. 2015 May;27(2):235-7.
- **Kiraly DD**, Sher L. Suicidal behavior in a medical professional with comorbid depression and substance use disorder: an educational case report. *Int J Adolesc Med Health*. 2015 May;27(2):231-3.
- **Kiraly DD**, Nemirovsky NE, LaRese TP, Tomek SE, Yahn SL, Olive MF, Eipper BA, Mains RE. Constitutive knockout of Kalirin-7 leads to increased rates of cocaine self- administration. *Mol Pharmacol*. 2013 Oct;84(4):582-90.

##### *Book Chapters*

- **Kiraly DD**, Sher L. Suicidal behavior in men with comorbid depression and substance use disorders: Roles of active substance use, exposure to combat in the military, and alterations in testosterone levels. Chapter in *Neurobiology of Men's Mental Health*. Leo Sher & Tim Rice Eds. Nova Science, 2015.
- **Kiraly DD**, Sher L. Dual diagnosis and suicidal behavior in combat veterans. Chapter in *Forensic Psychiatry: A Public Health Perspective*. Leo Sher & Joav Merrick Eds. Nova Science, 2015.
- **Kiraly DD**, Sher L. Health professionals and suicidal behavior. Chapter in *Forensic Psychiatry: A Public Health Perspective*. Leo Sher & Joav Merrick Eds. Nova Science, 2015.