

The Mindich Child Health and Development Institute

# **MCHDI Developmental Outcomes**

Fall 2017

Research Advancements: Neurobiology

## Dani Dumitriu Becomes the First Female Resident in the U.S. to Secure R01 During Training

In 2014, facing rapid decline of physicianscientists entering academia, the NIH tasked the Physician-Scientist Workforce Working Group (PSW-WG) with root cause analysis of this trend. Around the same time, Dr. Dani Dumitriu, having just completed the MD/PhD program at Mount Sinai, was battling an important career decision. During the previous two years, she had developed a mouse model to tackle her long-term goal of identifying neurocircuits of resilience and was excited about spearheading this research. Simultaneously, she found herself loving clinical medicine and could not imagine leaving her physician-half behind while continuing to advance her scientist-half. The conundrum: going the traditional route of residency followed by fellowship meant being away from the bench for a minimum of 3-5 years. Would the field of Neuroscience wait for her to finish residency? Would she have the stamina to return to this work following prolonged emersion into the clinical realm? The answer to both, according to the PSW-WG: probably not.

To solve this conundrum, Dr. Dumitriu developed a radical third alternative: integrate post-graduate clinical and basic

CreER

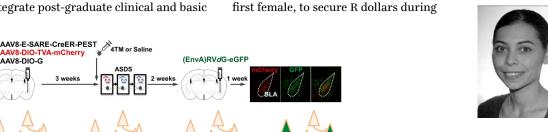
BLA "starter" (yellow) and "input" cells (green)

science training. Following her match into the Pediatric Residency at Mount Sinai, she approached the departments of Pediatrics, Environmental Health, and Neuroscience with an ambitious but clearly outlined plan: interweave residency requirements with a research fellowship in Pediatric Environmental Health over the course of five years, with the goal of developing an independent research program. A faculty position in a non-clinical department would enable applying for funding.

Within a year of this custom-tailored residency, Dr. Dumitriu encountered another major challenge outlined by the PSW-WG: a complete lack of suitable funding mechanisms. Counterintuitively, the only grant she qualified for was an R award, for which "any individual with the skills, knowledge, and resources necessary to carry out the proposed research" is eligible. In contrast, K awards require a minimum of 75% research time, an unrealistic allocation during residency. In year three, Dr. Dumitriu applied for an R01 which was discussed but scored outside the fundable range. In year four, she received the award on resubmission, becoming the second resident in the country, and the

training. This important milestone is underscored by another finding from the PSW-WG: females comprise only 22% of NIH Research Project Grant physicianscientist awardees.

Perhaps not by coincidence—both Dr. Dumitriu and Dr. Kafui Dzirasa (the first resident awarded an R01) study the neurobiological basis of resilience. To date, research has primarily focused on the pathophysiology of disease. Very little is known about the flipside: resistance to developing disease. Yet even highly heritable disorders show incomplete penetrance. In the lab, this can be studied at the mechanistic level. For example, the Dumitriu lab examines differences in the structural connectomes of stressactivated neurons in resilient versus susceptible mice (Fig). Putative pathways can then be tackled at the developmental and environmental levels, with the goal of identifying interventions that subtly nudge the circuit toward resilience. Analogously, post-graduate physician-scientist training programs might benefit from studying index cases of successful nontraditional residencies.



Examples of distal input cells





Dani Dumitriu, MD, PhD Assistant Professor, Neuroscience

Figure legend: (A) Experimental design showing stereotactic viral injections into amygdala and behavioral paradigm.

- (B) Schematic of inducible activity-dependent labeling of activated neurons with subsequent trans-synaptic retrograde labeling.
- (C) Amygdala "starter" (yellow) and local "input" (green) neurons.
- (D) Distal "input" neurons found throughout the brain.

### A Comprehensive Meta-Analysis Shows That Sperm Concentration Has Dropped More Than 50 Percent in 40 Years

In a systematic review and meta-analysis of trends in sperm count published in July 2017¹ in *Human Reproduction Update*, Shanna H. Swan (Department of Environmental Medicine and Pubic Health and member of the Mindich Child health and Development Institute), together with researchers from the Hebrew University-Hadassah Braun School of Public Health and Community Medicine and researchers at the Icahn School of Medicine at Mount Sinai reported a significant decline in sperm concentration and total sperm count among men from Western countries.

Scientists have been debating whether sperm count has been going down ever since researchers in Denmark published a study in 1992 showing a 50 percent drop in sperm count between 1940 and 1990. Shanna Swan and colleagues decided to return to this question 25 years after that alarm by conducting a state-of-the art-review of the subject. To conduct the current review and meta-analysis, they searched PubMed/MEDLINE and EMBASE for English language studies of human sperm count (SC) and total sperm count (TSC) published 1981-2013. To deal with a very large number of potentially relevant articles (7518 abstracts and 2510 articles) reporting primary data on SC they assembled a team of seven researchers and worked with a research librarian and a meta-analysis expert. All selected abstracts and articles were reviewed following a predefined protocol, following PRISMA guidelines. After exclusions of articles not meeting eligibility criteria the meta-analysis included 244 estimates of SC and TSC from 185 studies of 42,935 men who provided semen samples 1973-2011. Slopes were examined within broad geographic groups (North America, Europe

and Australia, called "Western" and within two categories of subjects (those who had proven their fertility and those who were not selected by fertility). The slopes of SC and TSC were estimated as functions of sample collection year using simple linear regression and weighted metaregression models. The latter models were adjusted for covariates and modification by fertility and geographic group. SC declined significantly between 1973 and 2011 (slope in unadjusted models =-0.70 x million/ml/year; 95% CI -0.72 to -0.69; p<0.001; slope in adjusted meta-regression models = -0.64; -1.06 to -0.22; p=0.003). Slopes were modified by fertility and geographic group, with a steeper slope among Unselected Western (-1.38; -2.02 to -0.74; p<0.001; 52.4% overall) vs. Fertile Western (-0.68; -1.31 to -0.05; p=0.033). Trends for TSC were similar to those for SC and results changed minimally in sensitivity analyses. This comprehensive analysis reports a significant decline in sperm count (as measured by SC and TSC) between 1973 and 2011, with a 50-60% decline among men unselected by fertility from North America, Europe and Australia.

In this comprehensive analysis, sperm count (whether measured by SC or TSC) declined significantly among men from North America, Europe and Australia during 1973-2011, with a 50-60% decline among men unselected by fertility. These findings strongly suggest a decline in male reproductive health, plausibly linked to changing environment and modern lifestyle. This major current public health challenge should be addressed. Research on causes and implications of this decline is urgently needed.





Shanna H. Swan, PhD
Professor of Environmental
Medicine and Public Health

1.Levine H, Jorgensen N, Anderson M-A, Mendiola J, Weksler-Derri D, Mindlis I, Pinotto R, Swan S. Temporal trends in sperm count: A systematic review and meta-regression analysis. Human Reproduction Update; 2017.

Niels Skakkebæk, a Danish pediatrician and researcher whose 1992 paper with Elisabeth Carlsen reporting large long-term declines in human sperm count kicked off over 20 years of debate, commented: "Most worryingly [in Denmark] is that semen quality is in general so poor that an average young Danish man has much fewer sperm than men had a couple of generations ago, and more than 90 percent of their sperm are abnormal."

### Amy Kontorovich, MD, PhD

Amy R. Kontorovich, MD, PhD is an Assistant Professor of Medicine in Cardiology and is the Medical Director of Adult Cardiovascular Genetics in the Zena and Michael A. Wiener Cardiovascular Institute. Dr. Kontorovich received a BSE in Bioengineering from the University of Pennsylvania where she studied biomechanical effects on endothelial cells in atherogenesis. She fulfilled the MD and PhD degrees from Stony Brook University. Her doctoral work with Dr. Ira Cohen involved developing a novel quantum-dot nanoparticle-based method for tracking stem cells after delivery to the heart. Dr. Kontorovich completed both the Internal

#### Recent Publications:

Belkaya S, Kontorovich A, Byun M, Bajolle F, Mulero-Navarro S, Josowitz R, Itan Y, Lorenzo L, Boucherit S, Laux D, Poupelin E, Di Filippo S, Abel L, Zhang S-Y, Bonnet D, Gelb B, Casanova J-L. Autosomal recessive cardiomyopathy presenting as acute myocarditis. *Journal of the American College of Cardiology*. 69(13):1653-65, 2017.

Pollack A, Kontorovich AR, Fuster V, Dec GW. Viral myocarditis-diagnosis, treatment options, and current controversies. *Nature Reviews Cardiology*, 12(11):670-80, 2015.

Medicine residency and fellowship in Cardiology at the Icahn School of Medicine at Mount Sinai. Her research is focused on myocarditis, an inflammatory condition of the heart that can lead to sudden cardiac death and cardiomyopathy. She studies genetic factors that mediate this rare and potentially fatal outcome of infection by common viruses.



Amy Kontorovich, MD, PhD Assistant Professor of Medicine, Cardiology Medical Director of Adult Cardiovascular Genetics

### Ke Hao, ScD

Dr. Ke Hao is a tenured Associate Professor in the Department of Genetics and Genomic Sciences, and a member of the Icahn Institute for Genomics and Multiscale Biology. He received his undergraduate degree in Biological Sciences and Technology at Tsinghua University, China. He graduated with a Doctor of Science degree at Harvard University in Environmental Health. He then performed his postdoctoral studies in the Department of Biostatistics at Harvard University, focusing on algorithm development and analysis of genetics and genomics data. In 2012, he was recruited to Icahn School of Medicine at Mount Sinai. His current research activities include: (1) environmental health, (2) genetics of human diseases, and (3) computational biology algorithm development. He invented an integrated system, Bio<sup>3</sup>Air, to measure the amount of ambient  $PM_{2.5}$ inhaled over a long period of time with very high spatial and time resolution. The system is now applied in environment epidemiology studies in China led by Dr. Hao. He was also involved in a large number of genetics studies, including linkage scans, genome-wide association studies (GWAS) and whole-exome/whole genome studies (NGS) on many disease areas (e.g COPD and IBD). Dr. Hao led

#### Recent Publications:

Woo S, Schadt EE and **Hao K.** Bayesian method to predict individual SNP genotypes from gene expression data. *Nat Genet*. 2012;44(5):603-8.

Hao K, Bossé Y, Nickle DC, Paré PD, Postma DS, Laviolette M, Sandford A, Hackett TL, Daley D, Hogg JC, Elliott WM, Couture C, Lamontagne M, Brandsma C, van den Berge M, Koppelman G, Reicin AS, Nicholson DW, Malkov V, Derry JM, Suver C, Tsou JA, Kulkarni A, Zhang C, Vessey R, Opiteck GJ, Curtis SP, Timens W, Sin DD. Lung eQTLs to Help Reveal the Molecular Underpinnings of Asthma, *PLoS Genetics*, 2012 Dec;8(12).

Luo W, Obeidat M, Di Narzo AF, Chen R, Sin DD, Paré PD, **Hao K.** Airway Epithelial Expression Quantitative Trait Loci Reveal Genes Underlying Asthma and Other Airway Diseases. Am J Respir Cell Mol Biol. 2016 Feb;54(2):177-87.

Hong X, Hao K [co-first author], Ladd-Acosta C, Hansen K, Tsai H, Liu X, Xu X, Thornton T, Caruso D, Keet C, Sun Y, Wang G, Luo W, Kumar R, Fuleihan R, Singh A, Kim J, Story R, Gupta R, Gao P, Chen Z, Walker X, Bartell T, Beaty T, 5 Fallin D, Schleimer R, Holt P, Nadeau K, Wood R, Pongracic J, Weeks D, Wang X. Genome-wide Association Study of Food Allergy Identifies Peanut Allergy-Specific Susceptibility Loci and Evidence of Epigenetic Mediation in U.S. Children of European Ancestry. *Nature Communications*. 2015 Feb 24;6:6304

Hong X, Hao K [co-first author], Ji H, Peng S, Sherwood B, Di Narzo A, Tsai HJ, Liu X, Burd I,Wang G, Ji Y, Caruso D, Mao G, Bartell TR, Zhang Z, Pearson C, Heffner L, Cerda S, Beaty TH, Fallin MD, Lee-Parritz A, Zuckerman B, Weeks DE, Wang X. Genome-wide approach identifies a novel gene-maternal pre-pregnancy BMI interaction on preterm birth. *Nature Communications*. 2017 Jun 9;8:15608.

projects to systematically characterize genetic control of transcriptome and proteome (i.e., eQTLs and pQTLs) in human tissues and also construct gene networks. The xQTLs were integrated with GWAS or NGS to provide insight on the molecular mechanism underlying disease genetic predisposition.



Ke Hao, ScD Associate Professor, Genetics and Genomic Sciences

### **Trainee Pilot Projects: 2017 Awardees**

# Project Title: "Cell-type specific transcriptome profiling in umbilical cord blood"

Investigator: Michael S. Breen, PhD, Postdoctoral fellow, Seaver Autism Center for Research and Treatment, Department of Psychiatry and Genetics and Genomic Sciences

**Primary Mentor:** Joseph D. Buxbaum, PhD, Department of Psychiatry and Genetics and Genomic Sciences

**Secondary Mentors:** Dan J. Stein, PhD (University of Cape Town) and Meaghan Jones, PhD (University of British Columbia)

Abstract: Several recent reports, including preliminary data from our large prospective longitudinal mother-infant cohort, the Drakenstein Child Health Study in South Africa, support the utility of gene expression in umbilical cord blood (UCB) to identify the molecular changes associated with prenatal exposures

to adverse in utero environments. However, cellular heterogeneity in UCB has not been fully appreciated. Failure to account for cellular composition in gene expression studies of bulk tissue can result in both widespread false positive and false negative results. Moreover, there is a dearth of studies exploring the gene expression profiles within specific UCB cell subsets, which will enable the identification of UCB cell-type specific markers that could drive the discovery of cellular or molecular differences that are potentially masked by bulk UCB sampling techniques. This project will 1) perform genome-wide RNA-sequencing on seven flow-cytometry sorted UCB cell subsets, including monocytes, NK cells, CD4+ and CD8+ T cells, B cells, neutrophils and nucleated red blood cells. Subsequently, 2) cell-type specific gene expression signatures will be used to develop computational tools for predicting frequencies of multiple cell types in

gene expression profiles of bulk UCB samples, which will be validated using cell frequencies determined by flow cytometry on paired samples. These data will be 3) applied to our already existing motherinfant studies of UCB gene expression and will provide an open-resource for *in silico* estimation of the relative proportion of each cell type in bulk UCB, which will also benefit other researchers.



Postdoctoral Fellow, Department of Psychiatry and Genetics and Genomics Sciences

#### Project Title: "Using long-reads to identify repeat expansions in undiagnosed dominantly-inherited ataxias"

**Trainee Investigator:** Oscar Rodriguez, PhD Candidate, Department of Genetics and Genomics Sciences

**Primary Mentor:** Andrew Sharp, PhD, Department of Genetics and Genomics Sciences

**Secondary Mentor:** Ali Bashir, PhD, Department of Genetics and Genomics Sciences

Abstract: Expansions of tandem repeats (TRs), most commonly triplet repeats, are known to underlie >20 different human neurological diseases. While several of these, e.g. Huntington's disease, are usually adult onset disorders, many repeat expansion disorders such as Friedreich's ataxia, myotonic dystrophy and Spinobulbar muscular atrophy often show childhood onset. Furthermore, expansion

of the FMR1 locus represents the most common cause of congenital intellectual disability in males. Although recent advances enable TR loci to be genotyped from high-throughput sequencing, short-read technologies are limited for the study of TRs. Specifically, only TR tracts that can be completely spanned by a single read can be reliably genotyped. As pathogenic repeat expansions that underlie neurological disease are typically larger than a 150bp Illumina read, the identification of expanded TRs is intractable to short-read sequencing, and therefore this class of mutation remains essentially undetectable with current sequencing technologies.

We have shown that long-read sequencing technology can detect previously missed structural variants such as large TR expansions. Combined with novel algorithms that we developed that allow the accurate genotyping of very large TRs, we propose that the application

of Pacific Biosciences sequencing to carefully selected cohorts has the potential to identify novel pathogenic repeat expansions underlying a number of human neurological diseases.

To generate pilot data for a larger project, this proposal lays out a framework to develop the necessary background datasets and perform long-read sequencing to identify a putative novel tandem repeat expansion using a rare family with a history of dominant ataxia.



Oscar Rodriguez
PhD Candidate, Department of
Genetics and Genomics Sciences

# MCHDI Trainee Leadership Committee in Second Year of Enhancing Training Environment

The Trainee Leadership Committee (TLC), now in its second year, was formed with the goal of building a community of young scientists focused on child health. In the first year, they consolidated a trainee mailing list, hosted a social, organized workshops on negotiation and policy, and established a trainee pilot grant program. The winners of the inceptive pilot grant were Oscar Rodriguez and Michael S. Breen, PhD. Oscar is a PhD candidate in the labs of Ali Bashir and Andrew Sharp. He will perform long-read sequencing to identify novel tandem repeat expansions in a family with a history of dominant ataxia. Michael is a postdoctoral fellow in Joseph Buxbaum's lab and his pilot project will measure cell type specific transcriptome profiles from umbilical cord blood in order to build more effective models for extracting cell subset-specific information directly from heterogenous samples. Congratulations!

This year, the TLC again brought together over 30 predocs and postdocs for our annual kick-off social. In addition to providing a venue where trainees can get to know each other, they also surveyed the attendees on workshops they would like to see in the coming year. In contrast to last year's more focused results, the interests were across the board: how to give a job talk, science "speed dating," accessing the Mount Sinai Data Warehouse, working with the IRB, and science and/ or healthcare policy. Their first official event was on October 3rd-they organized a grant writing panel (featuring trainees with funded grants) as part of the Child Health Research seminar series. The TLC are looking forward to workshops in the winter and spring, and are open to suggestions!

Finally, the committee would like to welcome the two newest TLC members, Allison Kann and Maya Deyssenroth.

Jeanette Stingone, PhD, MPH— Postdoctoral Fellow, Department of Environmental Medicine and Public Health

Maya Deyssenroth—DrPH, Postdoctoral Fellow, Department of Environmental Medicine and Public Health

Felix Richter—MD/PhD Student, Graduate School of Biomedical Sciences

Allison Kann—PhD Student, Graduate School of Biomedical Sciences

Allison is a PhD student in Dr. Rob Krauss's lab, studying the role of cell adhesion proteins in the muscle stem cell niche. Maya is a postdoctoral fellow in Dr. Jia Chen's lab focusing on placental epi/genomic analyses in relation to intrauterine metal exposures and postnatal health effects.



MPH
Postdoctoral Fellow,
Department of
Environmental Medicine and
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Maya Deyssenroth, PhD
Postdoctoral Fellow,
Department of
Environmental Medicine and
Public Health



Felix Richter
MD/PhD Student, Graduate
School of Biomedical
Sciences



Allison Kann
PhD Student, Graduate
School of Biomedical
Sciences

# Save the Date Children's Health Seminars and Workshops hosted by the TLC

February 6, April 3, and May 15, 2018 • 12–1 pm in Room L6-14 of the Icahn Building Feel free to contact Allison, Felix, Jeanette or Maya with suggested topics and/or speakers.

### **Faculty Highlights**

### Grants

**Dani Dumitriu,** MD, PhD, NIMH, R01, "Multiscale Connectomic Principles of Resilience and Susceptibility in Mouse"

**Adolfo Garcia-Ocana,** PhD, NIDDK, R01, "Dextran Sulfate, Beta Cell Preservation, and Immune Regulation in Type 1 Diabetes"

**Dorothy E. Grice,** PhD and Joseph D. Buxbaum, PhD. Stanley Center Foundation. "International Collaborative OCD Network"

Shelley Liu, PhD, Mount Sinai Transdisciplinary Center on Health Effects of Early Environmental Exposures, P30 Pilot Grant, "Statistical methods to assess prenatal exposures to metal mixtures and associations with latent patterns of neurodevelopmental trajectories"

**Ruth Loos**, PhD, NIDDK, R01, "Search for obesity-associated genes with protective effects on metabolic health"

**Ruth Loos,** PhD, NIDDK, R01, "Biological Insights from Genetic Investigation of ANthropometric Traits (GIANT) Across the Allelic Spectrum"

**Hirofumi Morishita,** MD, PhD, NINDS BRAIN Initiative R21, "Integrative Analysis of Long-range Top-down Cortical Circuit for Attentional Behavior"

### **Awards/Honors/Patents**

**Shelley Liu,** PhD, International Society of Environmental Epidemiology, New Researcher Best Abstract Award 2017

Ruth Loos, PhD, Clarivate Analytics, Highly Cited Researcher 2017

**Annemarie Stroustrup,** MD, MPH, Perinatal Research Society, Full Member

**Rupangi Vasavada,** PhD, U.S. Utility Patent, "Use of Osteoprotegerin (OPG) to increase human pancreatic beta cell survival and proliferation"

### **Faculty Highlights**

### **Publications**

Arora M, Reichenberg A, Willfors C, Austin C, Gennings C, Berggren S, ... Bolte S. Fetal and postnatal metal dysregulation in autism. *Nat Commun.* 2017 Jun 01;8:15493.

Goswami R, Blazquez AB, Kosoy R, Rahman A, Nowak-Wegrzyn A, Berin MC. Systemic innate immune activation in food protein-induced enterocolitis syndrome. *J Allergy Clin Immunol.* 2017 Jun;139(6):1885-96.e9.

Gnanapragasam MN, Bieker JJ. Orchestration of late events in erythropoiesis byKLF1/EKLF. Curr Opin Hematol. 2017 May;24(3):183-190.

Jobson J, Brown BD. Micromanaging tolerance in hemophilia a gene therapy. *Mol Ther.* 2017 Aug 02;25(8):1739-40.

Watson CT\*, Cohain AT\*, Griffin RS, Chun Y, Grishin A, Hacyznska H, ... Sicherer S, Sampson HA, Sharp AJ, Schadt EE^, Bunyavanich S^. Integrative transcriptomic analysis reveals key drivers of acute peanut allergic reactions. *Nat Commun.* 2017. [Accepted]

Sims R, van der Lee SJ, Naj AC, Bellenguez C, Badarinarayan N, Jakobsdottir J, ... Buxbaum JD, ... Schellenberg GD. Rare coding variants in plcg2, abi3, and trem2 implicate microglial-mediated innate immunity in alzheimer's disease. *Nat Genet*. 2017 Sep;49(9):1373-84.

Varghese M, Keshav N, Jacot-Descombes S, Warda T, Wicinski B, Dickstein DL, ... **Buxbaum JD,** Hof PR. **Autism spectrum disorder: Neuropathology and animal models.** *Acta Neuropathol.* 2017 Jun 05. Das TK, Cagan RL. Kif5b-ret oncoprotein signals through a multi-kinase signaling hub. *Cell Rep.* 2017 Sep 05;20(10):2368-83.

Zhu Y, Vidaurre OG, Adula KP, Kezunovic N, Wentling M, Huntley GW, Casaccia P. Subcellular distribution of hdac1 in neurotoxic conditions is dependent on serine phosphorylation. *J Neurosci*. 2017 Aug 02;37(31):7547-59.

Deyssenroth MA, Peng S, Hao K, Lambertini L, Marsit CJ, Chen J. Whole-transcriptome analysis delineates the human placenta gene network and its associations with fetal growth. *BMC Genomics*. 2017 Jul 10;18(1):520.

Shtraizent N, DeRossi C, Nayar S, Sachidanandam R, Katz LS, ... Scott DK, ... Chu J. MPI depletion enhances O-GlcNAcylation of p53 and suppresses the Warburg effect. *Elife*. 2017 Jun 23;6.

Poleshko A, Shah PP, Gupta M, Babu A, Morley MP, Manderfield LJ, ... Dubois NC, ... Jain R. Genome-nuclear lamina interactions regulate cardiac stem cell lineage restriction. *Cell.* 2017 Oct 19;171(3):573-87.

Bardot E, Tzavaras N, Benson DL, Dubois NC. Quantitative whole-mount immunofluorescence analysis of cardiac progenitor populations in mouse embryos. *J* Vis Exp. 2017 Oct 12(128).

Takahashi A, Chung JR, Zhang S, Zhang H, Grossman Y, Aleyasin H, ... **Dumitriu D**, ... Russo SJ. **Establishment of a repeated social defeat stress model in female mice.** *Sci Rep.* 2017 Oct 09;7(1):12838. Dunkin D, Berin MC, Mondoulet L, Tobar S Yeretssian G, Tordesillas L, ... Sampson HA. Epicutaneous tolerance induction to a bystander antigen abrogates colitis and ileitis in mice. *Inflamm Bowel Dis.* 2017 Nov;23(11):1972-1982.

Bradley KAL, Case JAC, Freed RD, Stern ER, Gabbay V. Neural correlates of rdoc reward constructs in adolescents with diverse psychiatric symptoms: A reward flanker task pilot study. *J Affect Disord*. 2017 Jul;216:36-45.

Jin SC, Homsy J, Zaidi S, Lu Q, Morton S,... Gelb BD, ... Brueckner M. Contribution of rare inherited and de novo variants in 2,871 congenital heart disease probands. *Nat Genet*. 2017 Nov;49(11):1593-1601.

Bello GA, Arora M, Austin C, Horton MK, Wright RO, Gennings C. Extending the distributed lag model framework to handle chemical mixtures. *Environ Res.* 2017 Jul;156:253-64.

Nissen J, Powell S, Koch SV, Crowley JJ, Matthiesen M, Grice DE, ... Parner E. Diagnostic validity of early-onset obsessivecompulsive disorder in the Danish Psychiatric Central Register: findings from a cohort sample. *BMJ Open*. 2017 Sep 18;7(9).

Peng S, Deyssenroth MA, Di Narzo AF, Lambertini L, Marsit CJ, Chen J, Hao K. Expression quantitative trait loci (eqtls) in human placentas suggest developmental origins of complex diseases. *Hum Mol Genet*. 2017 Sep 01;26(17):3432-41.

## Publications, continued

de Water E, Proal E, Wang V, Medina SM, Schnaas L, Tellez-Rojo MM, Wright RO, ... Horton MK. Prenatal manganese exposure and intrinsic functional connectivity of emotional brain areas in children. Neurotoxicology. 2017 Jun 10.

Felix JF, Joubert BR, Baccarelli AA, Sharp GC, Almqvist C, Annesi-Maesano I, ... Just AC, ... London SJ. Cohort profile: Pregnancy and childhood epigenetics (pace) consortium. Int J Epidemiol. 2017 Sep 13.

Lim ET, Uddin M, De Rubeis S, Chan Y, Kamumbu AS, Zhang X, ... Kolevzon A, ... Buxbaum JD, Walsh CA. Rates, distribution and implications of postzygotic mosaic mutations in autism spectrum disorder. *Nat Neurosci.* 2017 Sep;20(9):1217-24.

Rankine J, Li E, Lurie S, Rieger H, Fourie E, Siper PM, ... Buxbaum JD, Kolevzon A. Language environment analysis (lena) in phelan-mcdermid syndrome: Validity and suggestions for use in minimally verbal children with autism spectrum disorder. *J Autism Dev Disord*. 2017 Jun;47(6):1605-17.

Krauss RS. Regulation of skeletal myoblast differentiation by drebrin. *Adv Exp Med Biol.* 2017;1006:361-73.

Nomura Y, John RM, Janssen AB, Davey C, Finik J, Buthmann J, ... Lambertini L. Neurodevelopmental consequences in offspring of mothers with preeclampsia during pregnancy: Underlying biological mechanism via imprinting genes. *Arch Gynecol Obstet.* 2017 Jun;295(6):1319-29.

Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu NN, ... Zhong M. The lancet commission on pollution and health. *Lancet*. 2017 Oct 17.

Srivastava KD, Song Y, Yang N, Liu C, Goldberg IE, Nowak-Wegrzyn A, Sampson HA, Li XM. B-fahf-2 plus oral immunotherapy (oit) is safer and more effective than oit alone in a murine model of concurrent peanut/tree nut allergy. Clin Exp Allergy. 2017 Aug;47(8):1038-49.

Liu SH, Bobb JF, Lee KH, Gennings C, Henn BC, Bellinger D, Austin C... Wright RO, Arora M, Coull BA. Lagged kernel machine regression for identifying time windows of susceptibility to exposures of complex mixtures. *Biostatistics*. 2017 Sep 06.

Zhao W, Rasheed A, Tikkanen E, Lee JJ, Butterworth AS, Howson JMM, ... Loos RJF, ... Saleheen D. Identification of new susceptibility loci for type 2 diabetes and shared etiological pathways with coronary heart disease. *Nat Genet*. 2017 Oct;49(10):1450-1457.

Zillikens MC, Demissie S, Hsu YH, Yerges-Armstrong LM, Chou WC, Stolk L, ... Loos RJF, ... Kiel DP. Large meta-analysis of genomewide association studies identifies five loci for lean body mass. *Nat Commun.* 2017 Jul 19;8(1):80.

Jiang Y, Loh YE, Rajarajan P, Hirayama T, Liao W, Kassim BS, ... Morishita H, ... Akbarian S. The methyltransferase SETDB1 regulates a large neuron-specific topological chromatin domain. *Nat Genet*. 2017 Aug;49(8):1239-125

Steullet P, Cabungcal J, Coyle J, Didriksen M, Gill K, Grace A, ... Morishita H, ... Do KQ. Oxidative stress-driven parvalbumin interneuron impairment as a common mechanism in models of schizophrenia. *Mol Psychiatr.* 2017 Jul;22(7):936-943.

Agyemang A, Feuille E, Tang J, Steinwandtner I, Sampson H, Nowak-Wegrzyn A. Outcomes of 84 consecutive open food challenges to extensively heated (baked) milk in the allergy office. J Allergy Clin Immunol Pract. 2017 Jun 29.

Ruiz-Martinez J, Azcona LJ, Bergareche A, Marti-Masso JF, **Paisan-Ruiz C.** Whole-exome sequencing associates novel csmd1 gene mutations with familial parkinson disease. Neurol Genet. 2017 Oct;3(5):e177.

Breen MS, Uhlmann A, Ozcan S, Chan M, Pinto D, Bahn S, Stein DJ. Parallel changes in serum proteins and diffusion tensor imaging in methamphetamine-associated psychosis. Sci Rep. 2017 Mar 02;7:43777.

Sandin S, Lichtenstein P, Kuja-Halkola R, Hultman C, Larsson H, Reichenberg A. The heritability of autism spectrum disorder. *Jama*. 2017 Sep 26;318(12):1182-4.

Mollon J, Reichenberg A. Cognitive development prior to onset of psychosis. *Psychol Med.* 2017 Jul 24:1-12.

Fuhrman DY, Schneider MF, Dell KM, Blydt-Hansen TD, Mak R, **Saland JM**, ... Schwartz GJ. **Albuminuria**, proteinuria, and renal disease progression in children with ckd. *Clin J Am Soc Nephrol*. 2017 Jun 07;12(6):912-20.

Tordesillas L, Berin MC, Sampson HA. Immunology of food allergy. *Immunity*. 2017 Jul 18;47(1):32-50.

Masilamani M, Chang LM, Kamalakannan M, Schussler E, Rassbach W, Sampson HA. Dietary isoflavone supplementation for food allergy: A pilot study. *J Allergy Clin Immunol Pract*. 2017 Nov–Dec;5(6):1760-1762.

Wang H, Bender A, Wang P, Karakose E, Inabnet WB, Libutti SK, ... Lambertini L, ... Scott DK, ... Stewart AF. Insights into beta cell regeneration for diabetes via integration of molecular landscapes in human insulinomas. *Nat Commun.* 2017 Oct 03;8(1):767.

Shemesh E, Kleinman LC. Asthma: The past, future, environment, and costs. *J Allergy Clin Immunol*. 2017 Sep;140(3):688-9.

Sicherer SH, Sampson HA, Eichenfield LF, Rotrosen D. The benefits of new guidelines to prevent peanut allergy. *Pediatrics*. 2017 Jun;139(6).

Stroustrup A, Teitelbaum SL, Aschner JA. The value of preterm infant environmental health cohorts: The canary in the coal mine. *JAMA Pediatr.* 2017. [In Press]

Levine H, Jørgensen N, Martino-Andrade A, Mendiola J, Weksler-Derri D, Mindlis I, ... Swan SH. Temporal trends in sperm count: a systematic review and meta-regression analysis. *Hum Reprod Update*. 2017 Jul 25:1-14.

Deierlein AL, Wolff MS, Pajak A, Pinney SM, Windham GC, Galvez MP, ... Teitelbaum SL. Phenol concentrations during childhood and subsequent measures of adiposity among young girls. *Am J Epidemiol*. 2017 Sep 01;186(5):581-92.

Sacaan AI, Thibault S, Hong M, Kondegowda NK, Nichols T, Li R, Rosselot C, ... Garcia-Ocaña A, Khan N, Stewart AF, Vasavada RC. CDK4/6 inhibition on glucose and pancreatic beta cell homeostasis in young and aged rats. *Mol Cancer Res.* 2017. [Epub Ahead of Print]

Huang X, Wang J. Mitotic bookmarking: Maintaining the stem cell identity during mitosis. *Cell Stem Cell*. 2017 Jun 01;20(6):741-2.

Tsuang A, Demain H, Patrick K, Pistiner M, Wang J. Epinephrine use and training in schools for food-induced anaphylaxis among non-nursing staff. *J Allergy Clin Immunol Pract.* 2017 Sept-Oct;5(5):1418-1420.

Torok MR, Winickoff JP, McMillen RC, Klein JD, *Wilson KM*. Prevalence and location of tobacco smoke exposure outside the home in adults and children in the United States. *Public Health*. 2017 Oct;151:149-59.

Meyer JA, Zhou D, Mason CC, Downie JM, Rodic V, Abromowitch M, Wistinghausen B, ... Miles RR. Genomic characterization of pediatric b-lymphoblastic lymphoma and b-lymphoblastic leukemia using formalinfixed tissues. Pediatr Blood Cancer. 2017 Jul;64(7).

Wu S, Gennings C, Wright RJ, Wilson A, Burris HH, Just AC, ... Wright RO, Baccarelli AA. Prenatal stress, methylation in inflammation-related genes, and adiposity measures in early childhood: The progress cohort study. *Psychosom Med.* 2017 Aug 05.

Rodosthenous RS, Burris HH, Sanders AP, Just AC, Dereix AE, Svensson K, ... Wright RO, Baccarelli AA. Second trimester extracellular micrornas in maternal blood and fetal growth: An exploratory study. *Epigenetics*. 2017 Jul 31:1-7.

Rosa MJ, Pajak A, Just AC, Sheffield PE, Kloog I, Schwartz J, ... Wright RO, Gennings C, Wright RJ. Prenatal exposure to pm2.5 and birth weight: A pooled analysis from three north american longitudinal pregnancy cohort studies. *Environ Int.* 2017 Oct;107:173-80.

### 5<sup>th</sup> Annual MCHDI Retreat

# Save the Date 5<sup>th</sup> Annual MCHDI Retreat

Date: November 28, 2017 Time: 8:30 am – 5:15 pm Location: Harmonie Club

Ballroom, 1st Floor

4 E 60th St, New York, NY 10022



Icahn School of Medicine at Mount The Mindich of Child Health and Development Institute



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