

2015 Research Annual Report

Neurology

RESEARCH AND TRAINING DETAILS



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Faculty	43
Joint Appointment Faculty	3
Research Fellows	5
Research Students	45
Support Personnel	35
Direct Annual Grant Support	\$3,691,614
Direct Annual Industry Support	\$1,818,692
Peer Reviewed Publications	105

CLINICAL ACTIVITIES AND TRAINING

Clinical Staff	90
Staff Physicians	1
Clinical Fellows	3
Other Students	44
Inpatient Encounters	2,628
Outpatient Encounters	27,478

Research Highlights

Myotonic Dystrophy Research and Clinical program

The Division of Neurology has established a Clinical and Research Program to better understand and treat patients with myotonic dystrophies. The clinical program is led by [Dr. Cuixia Tian](#) and the research program is led by [Dr. Lubov Timchenko](#). Myotonic dystrophies type 1 and type 2 are neuro-muscular diseases caused by CTG and CCTG expansions in the 3' UTR of the DMPK gene (DM1) and in the intron 1 of ZNF9 gene (DM2). The most severe form of DM1 is congenital DM1, caused by very long expansions of CTG repeats. The mutant CUG and CCUG repeats form toxic aggregates disrupting RNA metabolism in patients' cells. To improve degradation of these toxic aggregates, Dr. Timchenko's lab searched for RNA-binding proteins with reduced activity during degradation of the mutant RNAs. One of these proteins was purified to homogeneity and found to be RNA helicase DDX5/p68. It appears that the levels of p68 RNA helicase are reduced in muscle tissue samples from patients with DM1 and DM2. Correction of p68 in skin fibroblasts and myoblasts from patients with DM1/2 reduces the number of CUG and CCUG aggregates due to improved degradation of the mutant RNAs. The injection of p68 in skeletal muscle of DM1 mice causes significant reduction of DM1 muscle histopathology. These findings show that the maintenance of the physiological level of p68 in DM1/2 cells leads to degradation of toxic RNAs and to the reduction of DM pathology. This work identifies p68 RNA helicase as a new therapeutic target in congenital and adult DM1 and in DM2. The findings, describing the role of RNA helicase p68 in DM biopathogenesis, were recently published in the [Proceedings National Academy of Sciences \(USA\)](#) and presented on the [International Myotonic Dystrophy Symposium](#) in Paris, France.

Jones K, Wei C, Schoser B, Meola G, Timchenko N, Timchenko L. [Reduction of toxic RNAs in Myotonic Dystrophies type 1 and type 2 by the DEAD-5 RNA-helicase](#). *Proc Natl Acad Sci U S A*. 2015 Jun 30;112(26):8041-5.

Movement Disorder and Tourette Syndrome

The Cincinnati Children's Movement Disorder and Tourette Syndrome program continues to be recognized as a leader in both research and patient care. The [Movement Disorders](#) and [Tourette Syndrome](#) Clinic sees children with tics, stereotypies, dystonia, tremor, chorea, ataxia, functional movement disorders and drug induced movement disorders at the base and several satellite locations. The program has a regional and national reputation, as well as regular referrals from other states for second opinions. The [Dystonia and Complex Movement Disorder Clinic](#) provides pharmacological treatment, botulinum toxin and deep brain stimulation. Pre-operative and post-operative management are multidisciplinary. The Transcranial Magnetic Stimulation (TMS) program includes ADHD/ Tourette syndrome. There are two ongoing National Institutes of Health (NIH) funded studies of motor cortex physiology as a biomarker of behavioral control impairments, and of pharmacological treatment responses in ADHD. Neuroplasticity: Long Term Potentiation/Depression is a series of exciting studies piloting new methods of using transcranial magnetic stimulation to study long term potentiation, and long term depression in motor cortex. Tourette Syndrome Genetics: this is a site in a new, international, National Institute of Mental Health (NIMH) funded collaborative study of genetics of Tourette syndrome. Clinical Trials in Tourette Syndrome: completion of a phase 2a study of a new pharmacological treatment for Tourette syndrome, as well as participation in an ongoing study.

In the past year, their work on quality of life and on neurosensory-adaptation deficits in Tourette syndrome were presented at the first [World Congress on Tourette Syndrome](#), June 24-26 in London, UK. [Dr. Gilbert](#) was selected as a plenary speaker for a session on behavioral therapy in Tourette syndrome. The dystonia treatment and deep brain stimulation (DBS) program has grown and is now co-directed by [Dr. Steve Wu](#) in the Division of Neurology and [Dr. Sudhakar Vadivelu](#) in the [Division of Neurosurgery](#). The motor control and brain stimulation/transcranial magnetic stimulation laboratory has expanded with the addition of a new faculty member, [Dr. Ernest Pedapati](#) in the [Division of Psychiatry](#) within the UC College of Medicine, who is using TMS to study autism and depression in children. The [TMS Lab](#) continues to do important work in motor cortex inhibition and neuroplasticity in children with ADHD and Tourette syndrome and recently published

the largest pediatric safety study of TMS in children.

Tuberous Sclerosis Clinic

Growth of the Tuberous Sclerosis Complex Clinic (TSC) at Cincinnati Children's continues in both clinical care and research. The TSC Clinic continues to be the largest, most comprehensive clinic in the world attracting patients from all over the United States, Central and South America, Europe and Asia. In research, Dr. Brian Siroky joined the TSC team with joint faculty appointment in the Divisions of Nephrology and Neurology. The TSC program+ is a primary site for a large, five-year study that represents a crucial step forward in the treatment of autism spectrum disorder and intellectual disability. The study will enroll patients ages 3 to 21 with tuberous sclerosis complex (TSC), Phelan-McDermid syndrome and PTEN Hamman-Richards syndrome who also have an autism spectrum disorder and/or intellectual disability. The five-year study is funded by the National Institute of Neurological Disorders and Stroke (NINDS). Darcy Krueger, MD PhD, director of the Tuberous Sclerosis Complex Clinic at Cincinnati Children's, is principal investigator for the TSC component of the study, titled "Autism Spectrum Disorder and Intellectual Disability Determinants in Tuberous Sclerosis Complex." Cincinnati Children's opened enrollment to patients with TSC in April 2015. Children participating in the TSC study will be evaluated longitudinally at baseline, 6 months, 12 months, 18 months and 24 months. At each time point, they will undergo standardized observational assessments using cognitive and adaptive measures for autism spectrum disorder and intellectual disability. Investigators will collect clinical data, including medication use, seizure history, interventional therapies and medical comorbidities, to determine if specific clinical factors independently modify the course of autism spectrum disorder and intellectual disability development in TSC. This study expands areas of investigation in the underlying mechanisms of autism disorder spectrum and intellectual disability, which utilized the same advanced MRI and EEG technology and comprehensive autism and cognitive assessment tools in patients with TSC. This includes studies sponsored by the TSC Autism Center of Excellence Network, which is still recruiting TSC patients between 3 and 12 months of age.

Down Syndrome

Differences in neural activation were previously shown during language processing in adolescents and young adults with Down syndrome in comparison with typically developing individuals matched for chronological age. Activation is now shown in the adolescents and young adults with Down syndrome differs significantly in magnitude and spatial extent when compared with both chronological and mental age-matched typically developing control groups during a story listening task. These results provide additional support for an atypical pattern of functional organization for language processing in this population.

Headache Center

The Cincinnati Children's Headache Center will start its 20th year this upcoming year and continues to promote the improved understanding of children, adolescents and young adults with headaches and migraines. Enrollment was concluded this past year in the National Institutes of Health (NIH) sponsored CHAMP study. The CHAMP study is the largest, multi-site study comparing the effectiveness of amitriptyline, topiramate and placebo in preventing childhood and adolescent migraine. The Cincinnati Children's Headache Center is the lead site of 34 sites across the United States. The final results will be analyzed and published the next year and includes not only detailed characterization of these children and their response to treatment, but will also analyze their genetic basis and mRNA expression analysis of these subjects. Additional ongoing significant research includes the further characterization of cognitive behavioral therapy in children with chronic migraine, detailed characterization of more than 10,000 children with migraine, acute and inpatient management of status migrainosus, characterization/evolution and management of adolescents with post-concussive migraine, transition to young adulthood, and the neurophysiological basis of acute, chronic and post-traumatic migraine using magnetic encephalography. This full scale approach from disease characterization and underlying pathophysiology to treatment assessment and long-term outcome should continue to improve the outcomes of children everywhere.

Pediatric Neuroimaging Research Center

The Pediatric Neuroimaging Research Consortium (PNRC) is an interdisciplinary group of 10 principal scientists (including four faculty members appointed in the Division of Neurology within the UC College of Medicine, as well as the Department of Radiology, the Division of Biostatistics and Epidemiology, and the Department of Anesthesiology) who focus on neuroimaging research. Researchers make use of fMRI, MEG, and EEG to study brain development in typically-developing children and those with neurological disorders or injuries. The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) funded Cincinnati MR Imaging of Neurodevelopment (C-MIND) study, led by Drs. Scott Holland and Jennifer Vannest, will be completed in September 2015. The most important result of the study is the C-MIND database, which includes imaging and behavioral data from over 200 typically developing children for a cross-sectional look at the differences in brain function throughout the age range from infancy to adulthood. Additionally, C-MIND contains longitudinal imaging and behavioral data on 40 infants and toddlers (ages 0 to 3 years) as well as 30 children between the ages of 7 and 9 years. The database is publicly available for use by the neuroimaging community, now with over 70 users, at C-MIND. Methods and results from the C-MIND study have been published in the following:

Sroka MC, Vannest J, Maloney TC, Horowitz-Kraus T, Byars AW, Holland SK; CMIND Authorship Consortium.

Relationship between receptive vocabulary and the neural substrates for story processing in preschoolers. *Brain Imaging Behav.* 2015 Mar;9(1):43-55.

Vannest J, Rajagopal A, Cicchino ND, Franks-Henry J, Simpson SM, Lee G, Altaye M, Sroka C, Holland SK; CMIND Authorship Consortium. Factors determining success of awake and asleep magnetic resonance imaging scans in non-sedated children. *Neuropediatrics.* 2014 Dec;45(6):370-7.

Schmithorst VJ, Vannest J, Lee G, Hernandez-Garcia L, Plante E, Rajagopal A, Holland SK; CMIND Authorship Consortium. Evidence that neurovascular coupling underlying the BOLD effect increases with age during childhood. *Hum Brain Mapp.* 2015 Jan;36(1):1-15.

Significant Publications

Franz DN, Belousova E, Sparagana S, Bebin EM, Frost M, Kuperman R, Witt O, Kohman MH, Flamini JR, Wu Y, Curatolo P, de Vries PJ, Berkowitz N, Anak O, Niolat J, Jozwiak S. Everolimus for subependymal giant cell astrocytoma in patients with tuberous sclerosis complex: 2-year open-label extension of the randomised EXIST-1 study. *Lancet Oncol.* 2014 Dec;15(13):1513-20.

mTOR inhibitors have been demonstrated to shrink and control subependymal giant cell astrocytomas in patients with TSC. One concern is whether this treatment can be extended for prolonged periods to prevent regrowth. These results support the longer-term use of everolimus in patients who have few treatment options and who need continued treatment for tuberous sclerosis complex and its varied manifestations. Reduction or stabilisation of tumour volume with everolimus will hopefully provide long-term clinical benefit in patients with SEGA.

Jain SV, Horn PS, Simakajornboon N, Beebe DW, Holland K, Byars AW, Glauser TA. Melatonin improves sleep in children with epilepsy: a randomized, double-blind, crossover study. *Sleep Medicine.* 2015 May;16(5):637-44.

This was a class I study evaluating the effects of melatonin on sleep in children with epilepsy. The study showed that melatonin significantly improved sleep latency and WASO as compared to placebo. No worsening of seizures and epileptiform discharges was seen.

Modi AC, Wu YP, Rausch JR, Peugh JL, Glauser TA. Antiepileptic drug nonadherence predicts pediatric epilepsy seizure outcomes. *Neurology.* 2014 Nov 25;83(22):2085-90.

Adherence to medication recommendations is a significant contributor to outcomes. The aim of the study was to

determine sociodemographic, biological epilepsy-specific, and adherence predictors of long-term pediatric seizure outcomes. The results demonstrated adherence trajectories and two biological epilepsy-specific variables explain a similar proportion of the variability in longitudinal seizure outcomes. The relationship between AED nonadherence and seizure outcomes is not linear. Early adherence interventions could change the course of seizure outcomes, particularly if variability in adherence was minimized postdiagnosis.

Pedapati EV, Gilbert DL, Horn PS, Huddleston DA, Laue CS, Shahana N, Wu SW. Effect of 30 Hz theta burst transcranial magnetic stimulation on the primary motor cortex in children and adolescents. *Front Hum Neurosci.* 2015 Feb;9:91.

Intermittent theta burst transcranial magnetic stimulation (iTBS) is an additional technique to study neurophysiological effects on patients with neurological diseases. This was developed to begin to assess the safety and variability of this technique. The results demonstrated that although iTBS300 (stimulation duration of 92 s at 70% RMT) delivered over M1 in typically developed children was well-tolerated and produced on average significant facilitatory changes in cortical excitability, the post-iTBS300 neurophysiologic response was variable in our small sample. iTBS300-induced changes may represent a potential neuroplastic biomarker in healthy children and those with neuro-genetic or neuro-psychiatric disorders. However, a larger sample size is needed to address safety and concerns of response variability.

Division Publications

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2. Arya R, Greiner HM, Horn PS, Turner M, Holland KD, Mangano FT. **Corpus callosotomy for childhood-onset drug-resistant epilepsy unresponsive to vagus nerve stimulation.** *Pediatr Neurol.* 2014; 51:800-5.
3. Arya R, Greiner HM, Lewis A, Horn PS, Mangano FT, Gonsalves C, Holland KD. **Predictors of response to vagus nerve stimulation in childhood-onset medically refractory epilepsy.** *J Child Neurol.* 2014; 29:1652-9.
4. Arya R, Peariso K. **Status Epilepticus.** In: P Gupta, P Menon, S Ramji, R Lodha, eds. *PG Textbook of Pediatrics.* New Delhi: Jaypee Brothers Medical Publishers; 2015:2112-2119.
5. Arya R, Tenney JR, Horn PS, Greiner HM, Holland KD, Leach JL, Gelfand MJ, Rozhkov L, Fujiwara H, Rose DF, Franz DN, Mangano FT. **Long-term outcomes of resective epilepsy surgery after invasive presurgical evaluation in children with tuberous sclerosis complex and bilateral multiple lesions.** *J Neurosurg Pediatr.* 2015; 15:26-33.
6. Arya R, Wilson JA, Vannest J, Byars AW, Greiner HM, Buroker J, Fujiwara H, Mangano FT, Holland KD, Horn PS, Crone NE, Rose DF. **Electrocorticographic language mapping in children by high-gamma synchronization during spontaneous conversation: comparison with conventional electrical cortical stimulation.** *Epilepsy Res.* 2015; 110:78-87.
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8. Brahimaj B, Greiner HM, Leach JL, Horn PS, Stevenson CB, Miles L, Byars A, Holland K, Sutton M, Mangano FT. **The surgical management of pediatric brain tumors causing epilepsy: consideration of the epileptogenic zone.** *Childs Nerv Syst.* 2014; 30:1383-91.
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- maze performance while sparing allocentric Morris water maze learning. *Neurobiol Learn Mem.* 2015; 118:55-63.
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 12. Chen TH, Wu SW, Welge JA, Dixon SG, Shahana N, Huddleston DA, Sarvis AR, Sallee FR, Gilbert DL. **Reduced short interval cortical inhibition correlates with atomoxetine response in children with attention-deficit hyperactivity disorder (ADHD).** *J Child Neurol.* 2014; 29:1672-9.
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 14. Connolly B, Matykiewicz P, Bretonnel Cohen K, Standridge SM, Glauser TA, Dlugos DJ, Koh S, Tham E, Pestian J. **Assessing the similarity of surface linguistic features related to epilepsy across pediatric hospitals.** *J Am Med Inform Assoc.* 2014; 21:866-70.
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 21. Euro E-RESC, Epilepsy Phenome/Genome P, Epi KC. **De novo mutations in synaptic transmission genes including DNM1 cause epileptic encephalopathies.** *Am J Hum Genet.* 2014; 95:360-70.
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Consortium Report. *Clin Cancer Res.* 2015; 21:1558-65.

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Faculty, Staff, and Trainees

Faculty Members

Andrew Hershey, MD, PhD, FAHS, Professor

Leadership Endowed Chair of Neurology; Director, Headache Center

Research Interests Migraine, blood genomics.

Todd Arthur, MD, Assistant Professor

Research Interests Brain concussion.

Ravindra Arya, MD, DM, Assistant Professor

Research Interests Language mapping; electrocorticography; epilepsy surgery; clinical epidemiology.

Eileen Broomall, MD, Assistant Professor

Research Interests Neurocritical care.

Anna W Byars, PhD, Associate Professor

Research Interests Cognitive effects of epilepsy.

Jamie Capal, MD, Assistant Professor

Research Interests Child neurology; developmental pediatrics; autism; tuberous sclerosis.

James Collins, MD, PhD, Assistant Professor

Research Interests Congenital muscular dystrophy; neuromuscular disease.

Allen DeSena, MD, MPH, Assistant Professor

Research Interests Multiple sclerosis; transverse myelitis; neuromyelitis optica; autoimmune encephalitis; anti-NMDA receptor antibody encephalitis; opsoclonus-myoclonus syndrome; antibody mediated CNS disorders.

Thomas Dye, MD, Assistant Professor

Research Interests Child neurology; sleep medicine.

David Franz, MD, Professor

Leadership Director, Tuberous Sclerosis program

Research Interests Tuberous sclerosis.

Donald Gilbert, MD, MS, Professor

Leadership Director, Movement Disorders program; Director, Neurology Residency Program

Research Interests Tourette syndrome; transcranial magnetic stimulation (TMS).

Tracy A Glauser, MD, Professor

Leadership Director, Comprehensive Epilepsy program

Research Interests Epilepsy; pharmacology.

Hansel Greiner, MD, Assistant Professor

Leadership Co-Director, Epilepsy Surgery Program

Research Interests Epilepsy.

Christina Gross, PhD, Assistant Professor

Research Interests Molecular mechanisms of fragile X syndrome, epilepsy and autism spectrum disorders.

Barbara Hallinan, MD, PhD, Assistant Professor

Research Interests Infantile spasms; neurometabolic disorders; genetic causes of epilepsy.

Katherine Holland-Bouley, MD, PhD, Associate Professor

Leadership Co-Director, Clinical Neurophysiology Laboratory

Research Interests Ion channels and epilepsy.

Sejal Jain, MD, Assistant Professor

Leadership Associate Director of the Sleep Center; Director, Epilepsy & Clinical Neurophysiology Fellowship Programs

Research Interests Epilepsy, sleep.

Marielle A Kabbouche, MD, Associate Professor

Leadership Director, Inpatient & Acute Headache Units

Research Interests Migraine.

Joanne Kacperski, MD, Assistant Professor

Research Interests Pediatric headaches; chronic post-traumatic headaches.

Darren Kadis, PhD, Assistant Professor

Research Interests Neuroimaging and MEG of language.

Darcy Krueger, MD, PhD, Associate Professor

Leadership Director, Tuberous Sclerosis Clinic; Associate Director, Research & Neurosciences

Research Interests Tuberous sclerosis.

Diego Morita, MD, Assistant Professor

Leadership Medical Director, New Onset Seizure Program; Co-Medical Director, Neuroscience Unit

Research Interests Epilepsy; pharmacology.

Hope O'Brien, MD, Assistant Professor

Leadership Director, Headache Medicine Fellowship Program; Director, Young Adult Headache Clinic

Research Interests Headaches.

Douglas Rose, MD, Professor

Leadership Director, MEG lab

Research Interests Magneto-encephalography (MEG).

Mark Schapiro, MD, Professor

Research Interests Neurodevelopmental disorders.

Matthew Skelton, PhD, Assistant Professor

Research Interests Neurobehavioral and neurometabolic.

Shannon Standridge, DO, MPH, Assistant Professor

Leadership Co-Director, Rett Syndrome Clinic; Director, UC Medical Student Clerkship in Child Neurology

Research Interests Outcomes study; epilepsy.

Mary Sutton, MD, Associate Professor

Leadership Clinical Co-Director, Brain & Spinal Tumor Program

Research Interests Neuro-oncology.

J. Michael Taylor, MD, Assistant Professor

Leadership Director, Neurocritical Care Fellowship Program

Research Interests Arteriopathy and outcomes in pediatric stroke.

Jeffrey Tenney, MD, PhD, Assistant Professor

Research Interests Neurophysiology and genesis of absence epilepsy.

Cameron Thomas, MD, MS, Assistant Professor

Research Interests Fetal and neonatal neurology.

Cuixia Tian, MD, Assistant Professor

Research Interests Duchenne's muscular dystrophy.

Lubov Timchenko, PhD, Professor

Research Interests Translate knowledge of the molecular pathobiology into development of the therapeutic treatments for diseases caused by non-coding RNA repeats.

Jennifer Vannest, PhD, Associate Professor

Leadership Assistant Director, Pediatric Neuroimaging Research Consortium

Research Interests Speech and language development.

Charulata Venkatesan, MD, PhD, Assistant Professor

Research Interests Fetal and neonatal neurology.

Charles Vorhees, PhD, Professor

Leadership Co-Director, Animal Neurobehavior Core; Director, Teratology Training Program

Research Interests Drugs/toxicants and brain development.

Kristen Wesselkamper, MD, Assistant Professor

Leadership Director, Neurology Acute Care

Research Interests Improvement science.

Michael Williams, PhD, Associate Professor

Leadership Co-Director, Animal Behavior Core

Research Interests Drugs/toxicants and brain development.

Jonathan Wilson, PhD, Assistant Professor

Research Interests Neurophysiology and engineering.

Brenda Wong, MD, MBBS, Professor

Leadership Director, Pediatric Neuromuscular Program MDA clinic; Director, Interdisciplinary Comprehensive Neuromuscular Program; Director, Pediatric Neuromuscular Fellowship Program

Research Interests Duchenne's muscular dystrophy; spinal muscular atrophy.

Steve Wu, MD, Assistant Professor

Research Interests Movement disorder; transcranial magnetic stimulation (TMS).

Jing Xiang, MD, PhD, Associate Professor

Leadership Director, MEG Research Program

Research Interests MEG.

Joint Appointment Faculty Members

Paul Horn, PhD, Professor (Division of Neurology)

Research Interests Robustness; nonparametrics; statistical computing; simulations; reference intervals.

Ernest Pedapati, MD, MS, FAAP, Assistant Professor (Division of Psychiatry)

Research Interests Neurodevelopmental disorders; autism spectrum disorders; fragile X; schizophrenia; TMS; TDCS; eye tracking; electrophysiology.

Brian Siroky, PhD, Instructor (Division of Nephrology & Hypertension)

Research Interests Tuberous sclerosis complex; polycystic kidney disease; primary cilia.

Clinical Staff Members

- **Irina Rybalsky, MD**

Trainees

- **Haneul Lee, MD**, PGYVI, Yonsei University
- **Sarah Weatherspoon, MD**, PGYVI, University of Texas Southwestern
- **Katrina Peariso, MD**, PGYVI, University of New Mexico
- **Gewalin Aungaroon, MD**, PGYV, Faculty of Medicine Ramathibodi
- **Dror Kraus, MD, PhD**, PGYV, Hebrew University

- **Vinita Knight, MD, MPH**, PGYV, Eastern Virginia Medical School
- **Kelly Kremer, MD**, PGYV, University of Cincinnati
- **Michael Sweeney, MD**, PGYV, Medical College of Wisconsin
- **Marissa Vawter, MD**, PGYV, Indiana University
- **Andrew Knox, MD, MS**, PGYIV, Rush University College of Medicine
- **Staci King, MD**, PGYIV, University of Illinois - Chicago
- **Robert Blake, MD**, PGYIV, Baylor College of Medicine
- **Jennifer O'Malley, MD, PhD**, PGYIV, University of Cincinnati
- **Monica Arroyo, MD**, PGYIII, University of Puerto Rico
- **Christopher Carosella, MD**, PGYIII, Drexel University
- **Rose Gelineau-Morel, MD**, PGYIII, Baylor University
- **Alexandria Lutley, MD**, PGYIII, University of Connecticut
- **Elora Pattanaik, MD**, PGYIII, University of Alabama

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct

Gilbert, D

2/2-Anomalous Motor Physiology in ADHD

National Institutes of Health

R01 MH095014	5/1/2012-4/30/2017	\$175,000
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Movement-Based Training for Children with ADHD: A Feasibility Study

National Institutes of Health (Kennedy Krieger Research Institute)

R21 MH104651	8/5/2014-6/30/2019	\$11,591
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Collaborative Genomic Studies of Tourette Disorder

The University of California, San Francisco

7/1/2014-3/31/2015	\$37,500
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Glauser, T

Cincinnati Neuroscience Clinical Trials Research Center (CinciNEXT)

National Institutes of Health (University of Cincinnati)

U10 NS077311	9/30/2011-8/31/2018	\$100,000
Impact of Initial Therapy and Response on Long Term Outcome in Children with CAE		
National Institutes of Health		
U01 NS045911	9/1/2010-8/31/2015	\$15,318
Gross, C		
Testing the Ribosomal Protein S6 as Treatment Target and Biomarker in Autism Spectrum Disorders		
Autism Speaks Grant Administration		
	7/1/2014-2/28/2015	\$31,355
The Effect of Genetic Background n Kv4.2 Expression in FXS Mouse Models		
National Fragile X Foundation		
	5/25/2015-5/24/2016	\$2,500
Selective Targeting of PI3K to Restore Higher Cognitive Function in FXS		
National Institutes of Health		
R21 MH103748	6/24/2014-4/30/2016	\$155,971
Targeting the PI3K Enhancer PIKE to Reverse FXS-associated Phenotypes		
National Institutes of Health (Emory University)		
R21 MH105353	9/1/2014-8/31/2016	\$75,000
The PI3K Catalytic Subunit p110delta as Biomarker and Therapeutic Target in Autism and Schizophrenia		
The Brain & Behavior Research Foundation		
	6/1/14-1/14/16	\$51,744
Hershey, A / Powers, S		
Amitriptyline and Topiramate in the Prevention of Childhood Migraine		
National Institutes of Health		
U01 NS076788	9/30/2011-8/31/2015	\$1,111,884
Hufgard, J		
Role of Pde1b in Depression: A Mouse Model		
University of Cincinnati		
	1/12/2015-5/31/2015	\$1,650
Krueger, D		

Potential EEG Biomarkers and Antiepileptogenic Strategies for Epilepsy in TSC		
National Institutes of Health (University of Alabama-Birmingham)		
P20 NS080199	9/1/2012-8/31/2015	\$10,606
Early Biomarkers of Autism Spectrum Disorders in Infants with Tuberous Sclerosis		
National Institutes of Health(Children's Hospital Boston)		
U01 NS082320	9/1/2012-8/31/2017	\$101,866
Early Biomarkers of Autism Spectrum Disorders (per patient)		
National Institutes of Health(Children's Hospital Boston)		
U01 NS082320	9/1/2012-8/31/2017	\$37,111
Developmental Synaptopathies Associated with TSC, PTEN and SHANK3 Mutations		
National Institutes of Health (Children's Hospital Boston)		
U54 NS092090	9/30/2014-7/31/2019	\$61,459
TSC Natural History Database Project		
Tuberous Sclerosis Alliance		
	1/1/2015-12/31/2015	\$48,682
Topical Rapamycin Therapy to Alleviate Cutaneous Manifestations of Tuberous Sclerosis Complex		
US Army Medical Research Acquisition (University of Texas Health Science Center)		
W81XWH-11-1-0240	8/31/2012-8/31/2014	\$2,550
Advance an Innovative Translational Approach in Tuberous Sclerosis Complex Research		
Van Andel Research Institute (Michigan Economic Development Corporation)		
	-	\$35,099
Morita, D		
Cognitive AED Outcomes in Pediatric Localization Related Epilepsy (COPE)		
Patient-Centered Outcome Research Institute (Emory University)		
	8/1/2013-8/31/2016	\$8,516
Perna, M		
Mitochondrial Dysfunction in the Hippocampus in Bipolar Disorder		
Brain & Behavior Research Foundation		
	1/15/2015-1/14/2017	\$65,000

Timchenko, L

Molecular Mechanisms of Myotonic Dystrophy

National Institutes of Health

R01 AR044387	8/12/2014-2/28/2015	\$10,032
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Myotonic Dystrophy Type 2

National Institutes of Health

R01 AR052791	6/1/2014-5/31/2016	\$224,759
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Inhibition of GSK3 Beta as Potential Therapy for DM1

National Institutes of Health

R21 AR064488	9/20/2014-8/31/2016	\$110,000
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Vannest, J

Imaging the Effect of Centrotemporal Spikes and Seizures on Language in Children

National Institutes of Health

R01 NS065840	9/15/2011-6/30/2016	\$390,718
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Presurgical Application of FMRI in Epilepsy

Medical College of Wisconsin (National Institutes of Health)

R01 NS035929	6/1/15-5/31/16	\$28,071
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Vorhees, C

Prenatal Antidepressants and Autism Spectrum Disorder

Department of Defense

W81XWH-13-1-0306	9/1/2013-8/30/2015	\$50,000
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Annual Meeting of the Neurobehavioral Teratology Society

Food and Drug Administration

R13 FD004852	7/1/2013-6/30/2018	\$5,000
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Latrophilin-3 and ADHD: A New Potential Mechanism

National Institutes of Health

R21 MH101609	7/1/2013-6/30/2015	\$150,000
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Training Grant in Teratology

National Institutes of Health

T32 ES007051	7/1/2012-6/30/2017	\$293,702
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Transgenerational Inheritance of Epigenetic Effects of Polychlorinated Biphenyls

University of Cincinnati

R21 ES023319	8/29/2013-7/31/2016	\$79,130
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Xiang, J

Aberrant Neuromagnetic Signatures with Chronic Migraine

National Institutes of Health

R21 NS081420	9/30/2013-8/31/2015	\$148,500
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Wong, B

Correlation of Upper Extremity (PUL scores) and Pulmonary Function with MRI Findings in Non-Ambulatory Subjects with Duchenne Muscular Dystrophy

Foundation to Eradicate Duchenne

1/1/15-12/30/15	\$61,300
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Current Year Direct	\$3,691,614
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Industry Contracts

Franz, D

Novartis Pharmaceuticals	\$330,744
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Gilbert, D

AstraZeneca Pharmaceuticals	\$63,203
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Psyadon Pharmaceuticals, Inc	\$32,535
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Hershey, A

Palm Beach Neurology, PA	\$1,155
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Kabbouche, M

Allergan, Inc.	\$14,957
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Krueger, D

Novartis Pharmaceuticals	\$171,972
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Upsher-Smith	\$13,500
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Novartis Pharmaceuticals/Children's Hospital Boston	\$48,682
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Miles, M

Tishcon Corp.	\$231,000
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Morita, D

Eisai Medical Service	\$3,512
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UCB Biosciences, Inc.	\$6,500
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O'Brien, H

Labrys Biologics, Inc.	\$8,000
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Teva Pharmaceuticals	\$31,194
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Skelton, M

Lumos Pharma Inc.	\$49,755
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Leidos Biomedical Research, Inc	\$15,335
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Vorhees, C

Council for the Advancement Pyrethroid Human Risk Assessment, LLC	\$173,644
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Wong, B

Eli Lilly and Company	\$138,769
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GlaxoSmithKline	\$197,512
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Halo Therapeutics, Inc.	\$57,101
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PTC Therapeutics, Inc	\$37,437
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Prosensa Therapeutics	\$24,347
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Pfizer, Inc	\$59,574
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Quintiles, Inc	\$94,064
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Sarepta Therapeutics Headquarters	\$14,200
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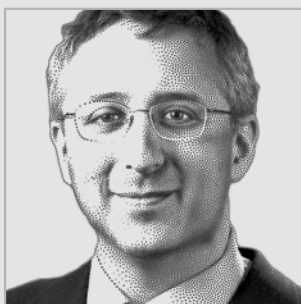
Current Year Direct Receipts	\$1,818,692
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Total	\$5,510,306
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Variable Adherence Has Significant Impact on Seizure Outcomes



Avani Modi, PhD



Tracy Glauser, MD

RESEARCH AND TRAINING DETAILS

Faculty	43
Joint Appointment Faculty	3
Research Fellows	5
Research Students	45
Support Personnel	35
Direct Annual Grant Support	\$3.6M
Direct Annual Industry Support	\$1,818,692
Peer Reviewed Publications	105

Modi AC, Wu YP, Rausch JR, Peugh JL, Glauser TA. Antiepileptic drug nonadherence predicts pediatric epilepsy seizure outcomes. *Neurology*. 2014;83(22):2085-2090.

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Neurology

A two-year collaborative study provides solid scientific backing to the age-old parents' admonition: "It's important to take your medicine."

Avani Modi, PhD, Director of the Center for Adherence and Co-Director of the New Onset Seizure Clinic, led a research team including colleagues from the divisions of Neurology and Behavioral Medicine and Clinical Psychology, who tracked drug adherence and seizure outcomes in children with epilepsy for two years. Findings appeared online Oct. 29, 2014, in *Neurology*.

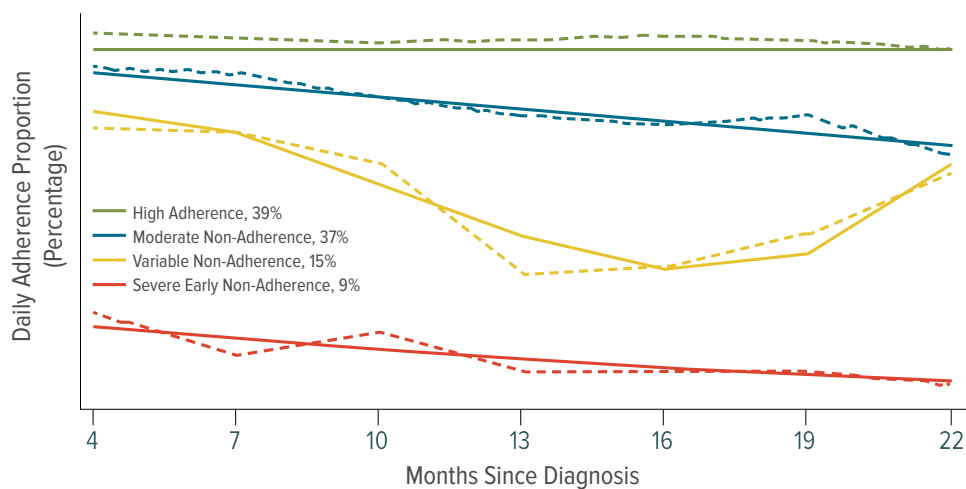
The study used electronic monitoring devices to track adherence patterns and seizure patterns in 109 children. The researchers found that patients fell into four distinct adherence groups: severe early non-adherence (9 percent), variable non-adherence (15 percent), moderate non-adherence (37 percent) and high adherence (39 percent). Children with epilepsy also fell into two distinct seizure groups: high or low seizure probability. Overall, children whose adherence patterns changed significantly had the worse seizure outcomes.

Children in the variable non-adherence group were more likely to be in the high seizure probability group, even after accounting for important medical characteristics such as seizure type and brain abnormalities. Their drug adherence started at 71 percent, dropped to 32 percent and then improved to 58 percent by the end of the study — a variability rate that put them at high risk for ongoing seizures.

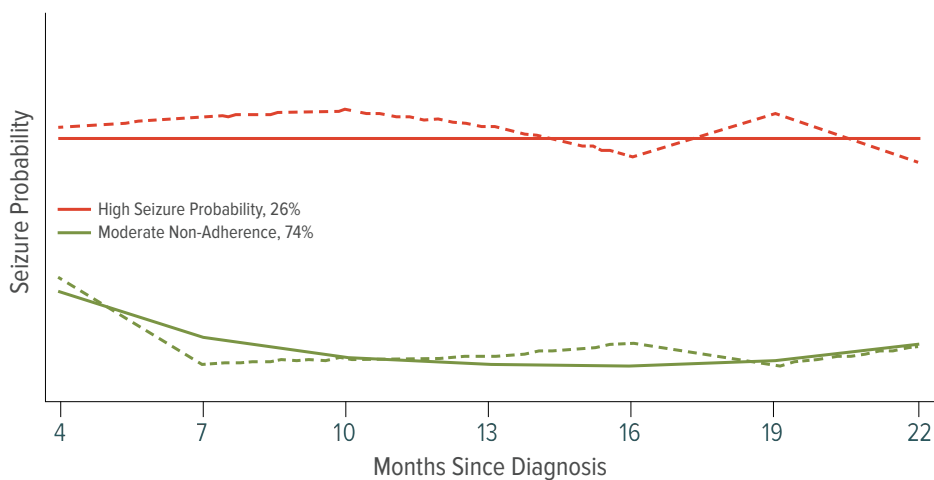
"What was previously unrecognized," Modi says, "is that monitoring and addressing drug adherence is a highly important, modifiable variable that can impact long-term seizure outcome."

This new understanding of the role of drug adherence "empowers the family to really contribute to the child's outcome in a way that no one previously understood," says co-author Tracy Glauser, MD, Director of the Comprehensive Epilepsy Center at Cincinnati Children's.

"Now," Modi says, "we can say with more confidence to families, 'Our job is to give you the best medications and treatments for your child's particular epilepsy diagnosis, and your job is to take the medications.'"



These figures show four distinct adherence patterns among children with pediatric epilepsy (shown here) and two distinct seizure patterns. Researchers at Cincinnati Children's have found that children who have Variable Non-Adherence are more likely to have a High Seizure Probability. These data demonstrate that the relationship between non-adherence and seizures is not linear.



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