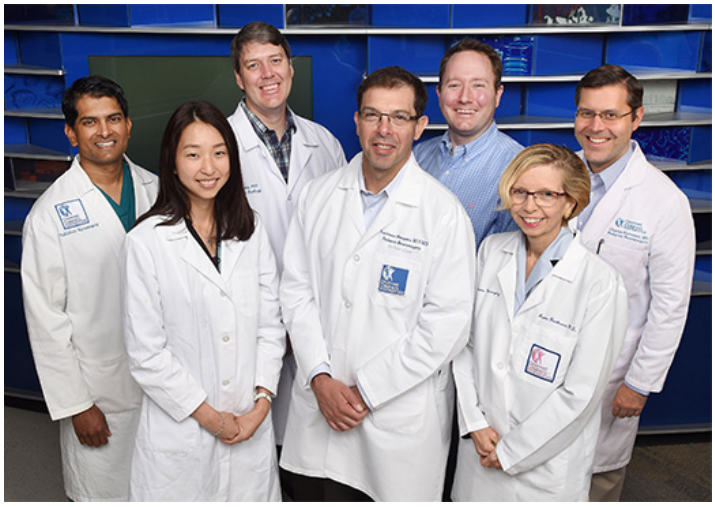
Cincinnati Children's

2015 Research Annual Report

Neurosurgery

RESEARCH AND TRAINING DETAILS



Click to view members

Faculty	7
Joint Appointment Faculty	4
Research Fellows	1
Research Students	2
Support Personnel	11
Direct Annual Industry Support	$292,544
Peer Reviewed Publications	20

CLINICAL ACTIVITIES AND TRAINING

Clinical Staff	8
Staff Physicians	7
Clinical Fellows	2
Inpatient Encounters	716
Outpatient Encounters	3,908

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Research Highlights

Diverse, Collaborative Clinical and Research Activities

The surgical treatment of intractable epilepsy in children, and finding new ways to improve outcomes, remains our division's primary focus. Division Chief Francesco Mangano, DO, FACS, FACOS, is co-principal investigator with Weihong Yuan, PhD, Department of Radiology, on a study of advanced MR imaging techniques in the field of hydrocephalus. Work from this multi-institutional study was published internationally.

Collaborating with physicians in medical neuro-oncology and radiation oncology, Charles Stevenson, MD, leads the division's brain tumor program. As a member institution of the Pediatric Brain Tumor Consortium (PBTC), Cincinnati Children's continues to innovate in clinical trials related to brain cancer. In one recent trial sponsored by the National Cancer Institute and PBTC, a special virus designed to kill tumor cells but not affect normal cells was injected into malignant brain tumors that defy chemotherapy and radiation therapy. Cincinnati Children's is the only pediatric hospital in the U.S. approved for this treatment.

Stevenson, with colleagues in the Divisions of Pediatric Physical Medicine and Rehabilitation and Physical Therapy, launched a multi-disciplinary surgical spasticity clinic which focuses on early identification of patients with cerebral palsy and spinal cord injury. As part of the Fetal Care Center, Stevenson continues to perform in utero repair of myelomeningocele defects. Surgeons are investigating more minimally invasive procedures for both mother and child.

Karin Bierbrauer, MD, collaborates with other institutions to further our understanding of complex injuries and diseases, and is the site principal investigator for a national registry of children with Chiari I malformations and syringomyelia. She performs clinical research on spina bifida and neurologic conditions detected in utero and in 2014 co-authored a chapter about monitoring for dorsal rhizotomy and ablative spinal procedures in a textbook on intraoperative monitoring.

Dr. Sudhakar Vadivelu, DO, focuses on the surgical and endovascular treatment of children with vascular disorders of the brain and spine, complex craniocervical anomalies and spinal disorders, skull and scalp lesions, and neurostimulation for children with movement disorders.

Focus on Hydrocephalus

Timothy Vogel, MD, heads a developmental neuroscience laboratory that studies primary and motile ciliary signaling related to hydrocephalus, a common neurological condition occurring in one in 1,000 children. The lab, along with collaborators Kenneth Campbell, PhD and Masato Nakafuku, MD, PhD, is studying signaling pathways related to ciliary signaling.

Instructor June Goto, PhD, collaborating in Mangano's lab, facilitates basic and translational research in hydrocephalus, cooperating with Drs. Yuan and Campbell they are studying the molecular and cellular basis of hydrocephalus. In the past year, she performed shunt surgeries, immunohistochemistry, and whole genome sequencing using rodent models of hydrocephalus.

Studying our brains to improve breathing

Dr. Steven Crone, PhD heads a laboratory studying how neural circuits in our brain and spinal cord control movements such as breathing and locomotion and how they are affected by disease and injury. Dr. Crone's laboratory uses unique mouse models to find new ways to improve motor function in Amyotrophic Lateral Sclerosis (ALS), spinal muscular atrophy (SMA), and spinal cord injury. In the past year his laboratory has demonstrated that muscles other than the diaphragm are used for breathing in ALS models. Further, they have identified a neuron class in the spinal cord and brainstem whose activity can improve the function of these muscles and improve breathing. Research is currently underway to assess the impact of this novel treatment strategy on disease progression and survival in animal models of ALS. The goal of this work is to prevent ventilator dependence and improve the duration and quality of life of patients with neuromuscular disorders or

spinal cord injury.

Division Publications

1. 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.
2. 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.
3. 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.
4. 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.
5. Bixenmann BJ, Kline-Fath BM, Bierbrauer KS, Bansal D. **Prenatal and postnatal evaluation for syringomyelia in patients with spinal dysraphism**. *J Neurosurg Pediatr*. 2014; 14:316-21.
6. 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.
7. Di Nardo A, Wertz MH, Kwiatkowski E, Tsai PT, Leech JD, Greene-Colozzi E, Goto J, Dilsiz P, Talos DM, Clish CB. **Neuronal Tsc1/2 complex controls autophagy through AMPK-dependent regulation of ULK1**. *Hum Mol Genet*. 2014; 23:3865-3874.
8. Gass D, Dewire M, Chow L, Rose SR, Lawson S, Stevenson C, Pai AL, Jones B, Sutton M, Lane A, Pruitt D, Fouladi M, Hummel TR. **Pediatric tectal plate gliomas: a review of clinical outcomes, endocrinopathies, and neuropsychological sequelae**. *J Neurooncol*. 2015; 122:169-77.
9. Hawasli AH, Beaumont TL, Vogel TW, Woo AS, Leonard JR. **Acalvaria**. *J Neurosurg Pediatr*. 2014; 14:200-2.
10. Korostenskaja M, Wilson AJ, Rose DF, Brunner P, Schalk G, Leach J, Mangano FT, Fujiwara H, Rozhkov L, Harris E, Chen PC, Seo JH, Lee KH. **Real-time functional mapping with electrocorticography in pediatric epilepsy: comparison with fMRI and ESM findings**. *Clin EEG Neurosci*. 2014; 45:205-11.
11. Kosnik-Infinger L, Gendron C, Gordon CB, Pan BS, van Aalst JA, Vogel TW. **Enzyme replacement therapy for congenital hypophosphatasia allows for surgical treatment of related complex craniosynostosis: a case series**. *Neurosurg Focus*. 2015; 38:E10.
12. Kosty J, Vogel TW. **Insights into the development of molecular therapies for craniosynostosis**. *Neurosurg Focus*. 2015; 38:E2.
13. Leach JL, Miles L, Henkel DM, Greiner HM, Kukreja MK, Holland KD, Rose DF, Zhang B, Mangano FT. **Magnetic resonance imaging abnormalities in the resection region correlate with histopathological type, gliosis extent, and postoperative outcome in pediatric cortical dysplasia**. *J Neurosurg Pediatr*. 2014; 14:68-80.
14. Manjila S, Vogel TW, Chen Y, Rodgers MS, Cohen AR. **Hypothalamic hamartoma simulating a suprasellar**

arachnoid cyst: resolution of precocious puberty following microsurgical lesion resection. *J Neurosurg Pediatr*. 2014; 14:101-7.

15. Prabhakar S, Zhang X, Goto J, Han S, Lai C, Bronson R, Sena-Esteves M, Ramesh V, Stemmer-Rachamimov A, Kwiatkowski DJ, Breakefield XO. **Survival benefit and phenotypic improvement by hamartin gene therapy in a tuberous sclerosis mouse brain model**. *Neurobiol Dis*. 2015; 82:22-31.

16. Ragan DK, Cerqua J, Nash T, McKinstry RC, Shimony JS, Jones BV, Mangano FT, Holland SK, Yuan W, Limbrick DD, Jr.. **The accuracy of linear indices of ventricular volume in pediatric hydrocephalus: technical note**. *J Neurosurg Pediatr*. 2015; 15:547-51.

17. Salloum R, DeWire M, Lane A, Goldman S, Hummel T, Chow L, Miles L, Sutton M, Stevenson C, Fouladi M, Leach J. **Patterns of progression in pediatric patients with high-grade glioma or diffuse intrinsic pontine glioma treated with Bevacizumab-based therapy at diagnosis**. *J Neurooncol*. 2015; 121:591-8.

18. Sayama C, Vadivelu S, Livingston A, Ho A, Izaddoost SA, Briceno V, Luerssen TG, Jea A. **Soft-tissue defects after spinal instrumentation in 5 children: risk factors, management strategies, and outcomes**. *J Neurosurg Pediatr*. 2014; 14:644-53.

19. Vadivelu S, Stewart TJ, Qu Y, Horn K, Liu S, Li Q, Silver J, McDonald JW. **NG2+ progenitors derived from embryonic stem cells penetrate glial scar and promote axonal outgrowth into white matter after spinal cord injury**. *Stem Cells Transl Med*. 2015; 4:401-11.

20. Yuan W, Holland SK, Shimony JS, Altaye M, Mangano FT, Limbrick DD, Jones BV, Nash T, Rajagopal A, Simpson S, Ragan D, McKinstry RC. **Abnormal structural connectivity in the brain networks of children with hydrocephalus**. *Neuroimage Clin*. 2015; 8:483-92.

Faculty, Staff, and Trainees

Faculty Members

Francesco T. Mangano, DO, Associate Professor
Leadership Director Pediatric Neurosurgery

Karin S. Bierbrauer, MD, Associate Professor

Kerry Crone, MD, Professor

Charles Stevenson, MD, Assistant Professor

Sudhakar Vadivelu, DO, Assistant Professor

Timothy Vogel, MD, Assistant Professor

Joint Appointment Faculty Members

Ellen Air, MD,PhD, Assistant Professor (Neurosurgery)

Kennth Campbell, PhD, Professor (Developmental Biology and Neurosurgery)

Steven Crone, PhD, Assistant Professor (Neurosurgery)

June Goto, PhD, Instructor (Neurosurgery)

Clinical Staff Members

- **Brian Crowley, MSN, RN, CFNP**
- **Cristina Carone, PA-C, MSPA**
- **Kelly Clapp, MSN, RN, CPNP**
- **Michelle Haimowitz, MSN, RN, CPNP**
- **Candace Sturm, MSN, RN, CPNP**
- **Mary Miller, MSN, RN, CPN**
- **Rodolfo Canos, MSN, RN, CPN**
- **Rachel Griffiths, MSN, RN, CPN**
- **Allie Mains, MSN,RN,CPN**
- **Vicky Minning, MSN,RN,CPN**

Trainees

- **Kaveh Asadi-Moghaddam, MD, Fellow**, 2012, Ohio State University PGY6
- **Mohan S., MD, Resident**, 2012, Henry Ford Hospital PGY5
- **Paul Mazaris, MD, Resident**, 2012, Henry Ford Hospital PGY5
- **Michael Sawvel, DO Resident**, 2013, West Virgina University PGY4
- **Daniel Harwell, MD, Resident**, 2012, University of Cincinnati PGY3
- **Ryan Tackla, MD, Resident**, 2012, University of Cincinnati PGY3
- **Jennifer Kosty, MD, Resident**, 2013, University of Cincinnati, PGY1
- **Mohammed Alsaidi, MD, Resident**, 2013, Henry Ford Hospital PGY5
- **Jonathan York, MD Resident**, 2013, University Of Cincinnati PGY3
- **Christopher Carroll, MD Resident**, 2013, University of Cincinnati PGY1
- **Shawn Vuong, MD Resident**, 2013, University of Cincinnati PGY1
- **Lauren Ostling, MD Resident**, 2012, University of Cincinnati PGY4

Grants, Contracts, and Industry Agreements

Grant and Contract Awards **Annual Direct**

Bierbrauer, K

Park-Reeves Syringomyelia Registry (PRSR)

Washington University

	3/22/2012-3/21/2016	$14,544

Vogel, T

Role of Neural Progenitor Cells in the Development of Neonatal Hyrocephalus

Hydrocephalus Association

	9/1/2013-8/31/2016	$133,000

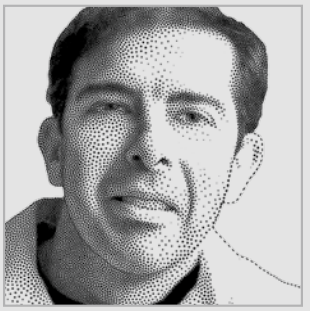
Primary Cilia Signaling in CNS Progenitor Cells and their Role in Neonatal Hydrocephalus

National Institutes of Health (Massachusetts General Hospital)

K12 NS080223	1/1/2014-12/31/2015	$145,000

	Current Year Direct	**$292,544**
	Total	**$292,544**

Novel Surgical Protocol Helps Eliminate Seizures for Some Children With TSC-Related Epilepsy



Francesco Mangano, DO, FACS

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PUBLISHED JANUARY 2015
Journal of Neurosurgery: Pediatrics

Some children with a form of epilepsy that previously made them poor candidates for surgery are now able to live without seizures, experience drastically reduced seizure episodes and symptoms, or take fewer anti-seizure medications as the result of a novel pre-surgical evaluation protocol developed by researchers in the Pediatric Epilepsy Surgery Program at Cincinnati Children's.

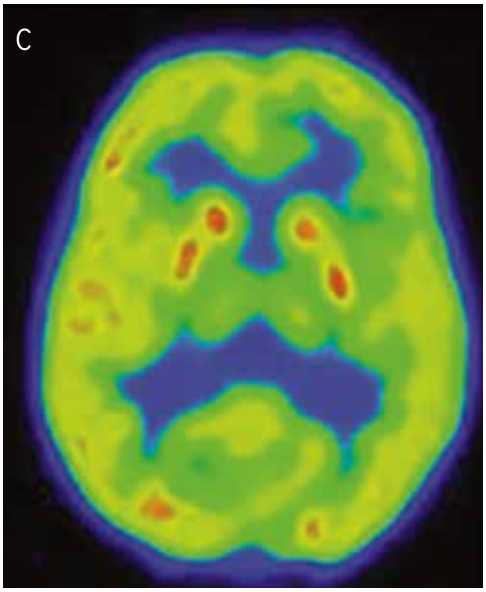
A research team led by Francesco Mangano, DO, FACS, FACOS, Chief of the Division of Pediatric Neurosurgery, studied 37 children who developed epilepsy as a result of tuberous sclerosis complex (TSC), a genetic disorder in which non-malignant tumors form in different organs, including the brain. More than 80 percent of children with TSC develop epilepsy that involves multi-focal brain abnormalities that vary from child to child. Their epilepsy symptoms vary as well.

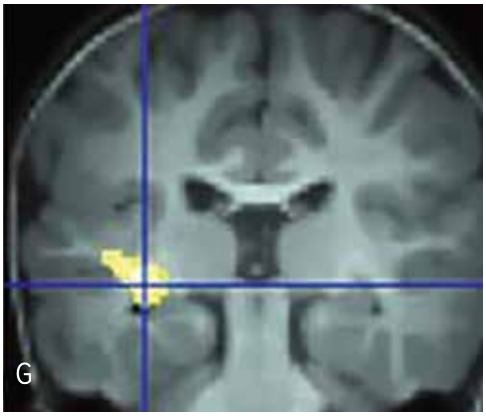
The study, thought to be the largest single-center study in this pediatric epilepsy population, appeared in the January 2015 issue of the *Journal of Neurosurgery: Pediatrics*.

Pre-surgery evaluations relied on non-invasive and invasive brain mapping to identify the origin of seizure patterns in each patient. Neurosurgeons then decided which types of resective surgery to pursue — craniotomy to remove tuberous tissue, lobar resections, and even hemispherectomy in some cases.

After five years, 56 percent of the children were seizure-free, and 87 percent had far fewer seizures and significantly less severe seizures, based on a scale developed by the International League Against Epilepsy (ILAE).

"In those children who were not seizure-free, we were able to decrease the number of anti-epileptic drugs needed to continue to control their disease, and we were able to reduce their medication frequencies and doses to improve their side effect profiles," Mangano says.





Neurosurgeons at Cincinnati Children's employed a novel surgical protocol to help a 5-year-old girl with tuberous sclerosis complex (TSC) who developed multiple types of seizures. At the time of surgical referral, four anti-seizure medications had failed and she had mild global delay. Among several diagnostic scans, FDG-PET showed multiple focal areas of decreased metabolism (image C). SPM imaging revealed a prominent area of hypometabolism involving the left frontal, temporal, and anterior parietal lobes (image G). Subdural grids and interhemispheric strips were placed for invasive monitoring (Image M) in preparation for a right occipital lobectomy. At the two-year follow-up, the child was completely seizure-free.

More than 80 percent of children with TSC develop epilepsy involving multi-focal brain abnormalities that vary from child to child. Their epilepsy symptoms vary as well.