

Neurosurgery

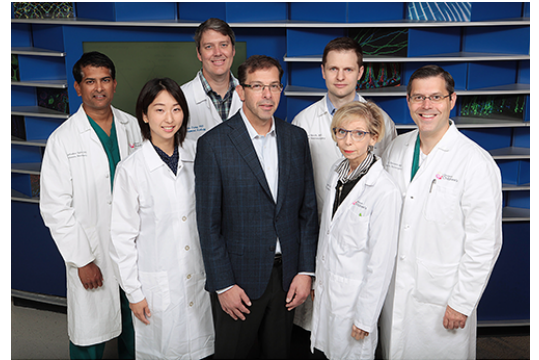
Division Details

RESEARCH AND TRAINING DETAILS

Faculty	7
Joint Appointment Faculty	1
Research Fellows and Post Docs	1
Research Graduate Students	1
Total Annual Grant Award Dollars	\$98,588

CLINICAL ACTIVITIES AND TRAINING

Staff Physicians	5
Clinical Fellows	1
Inpatient Encounters	1,555
Outpatient Encounters	4,438



Row 1: J Goto, F Mangano, K Bierbrauer, C Stevenson

Row 2: S Vadivelu, S Crone, J Skoch

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Division Highlights

Francesco Mangano, DO, and June Goto, PhD

The [Mangano/Gotto lab](#) conducted genetic and functional analysis of ependymal cell development to get insight into the pathogenesis of congenital hydrocephalus. The lab identified a new gene mutation causing severe hydrocephalus in early postnatal stage in rodents, and created both mouse and rat models representing similar hydrocephalus development to human congenital hydrocephalus. The group identified that the gene mutation affects motility of ependymal cilia, which results in retardation of CSF in the cerebral ventricles. The group also developed a new rat model of X-linked hydrocephalus, and performed diffusion tensor imaging focusing on the periventricular white matter tracts. The pilot data showed different water anisotropic values in the mutant, which is similar to the previous study in human hydrocephalus cases. Presented these findings at the [Society for Research into Hydrocephalus and Spina Bifida](#) (St. Louis, MO). One manuscript is currently under review.

Karin Bierbrauer, MD

[Dr. Karin Bierbrauer, MD](#), and [Dr. Francesco Mangano, DO, FACS, FAAP, FACOS](#), as site PIs, along with the other faculty, continue their involvement in furthering the study of pediatric patients with Chiari I malformations by participation in the national multi-site [Park Reeves Registry](#). Cincinnati Children's Hospital Medical Center has also recently become one of the centers that is participating in a prospective trial looking at optimizing neurosurgical intervention to improve outcomes for this condition.

Dr. Bierbrauer continues her ongoing collaboration with colleagues in neuroradiology and the [Cincinnati Fetal Center](#) coauthoring publications focusing on fetal imaging and outcomes in patients prenatally diagnosed with spinal dysraphism.

Sudhakar Vadivelu, DO

The [Vadivelu laboratory](#) conducts translational studies to better understand the complexity of the neurovascular niche as it related to neural development and stroke. One emphasis is to evaluate neurovascular signaling in the development of the cerebral vasculature and its effects on neural cell injury, birth, and regeneration. As an example from bedside to bench, the lab is currently studying cerebrovascular patterning and cerebral reserve in transgenic Notch ligand signaling in mice while in parallel conducting multicenter evaluation of progressive stroke disease in patients with various developmental syndromes including Alagille syndrome. The lab's focus is the neurovascular relationship within the brain, and spinal cord, that predetermines particular patients as having a higher predilection towards cerebral stroke, while also discovering strategies towards not only recovery, but regeneration.

Concurrently, the researchers are studying the role of neurostimulation strategies as it relates to systemic inflammation and stroke. To accomplish lab goals, researchers use models incorporating transgenic mice, small and large animal neuroimaging, and cadaveric studies specifically to understand white matter pathways and its relationship to human vascular development.

There is a relation between the goals of these translational studies and developing innovative therapeutics for cerebrovascular disorders in children.

Jesse Skoch, MD

Epilepsy:

Live Brain Imaging—

Researchers in the division have been utilizing transgenic mice with cortical neurons that express jellyfish protein that fluoresce dependent on intracellular calcium influx. Using high speed confocal or multiphoton microscopy, researchers monitor cell populations spatiotemporally for calcium channel changes that are indicative of neuronal firing. Researchers modified a high speed microscope to allow imaging of these neurons during seizures, and are comparing this data to simultaneously acquired reflected light imaging. By learning how the reflected light images relate to the fluorescent images, the team hopes to then apply the reflected light imaging to detect seizures in normal, wild-type brains.

Multi-center review of Rasmussen's encephalitis data—

In order to better understand the significance of MRI and pathologic features of Rasmussen's encephalitis, an aggressive inflammatory brain disease, researchers are analyzing data from three institutions systematically to determine which patients may best benefit from a radical hemispherotomy surgery.

Craniofacial:

Coagulation labs and transfusion—

A systematic review of outcome data for patients undergoing minimal access surgery for craniosynostosis is underway with a focus on the relevance of pre-operative coagulopathy labs. Researchers hope to determine key factors which may predict a need for blood transfusion, and therefore potential targeted interventions to minimize bleeding.

Steven Crone, PhD

The [Crone lab](#) is investigating how amyotrophic lateral sclerosis (ALS) alter respiratory circuits in an effort to improve breathing and motor function in this deadly neurodegenerative disease. The Crone lab developed a novel physiological system to determine how often the use of the accessory respiratory muscles are for breathing in mouse models of disease, an important indicator that the diaphragm is not functioning properly (*Journal of Visualized Experiments*). Further, they identified a class of neuron in the spinal cord (the V2a class) and brainstem that is able to activate these muscles and improve ventilation, and determined that this class of neuron degenerates in ALS model mice prior to an abrupt decline in respiratory function (*Experimental Neurology*). The Crone lab is currently investigating whether breathing and survival of ALS model mice can improve by preventing degeneration of V2a neurons, improving the function of surviving V2a neurons, or replacing degenerated V2a neurons with healthy embryonic or stem-cell derived neurons. Using the results of these studies may help improve breathing in patients with neuromuscular disorders such as ALS, spinal muscular atrophy (SMA), muscular dystrophy, and multiple sclerosis, or in patients with spinal cord injury.

Division Publications

1. Arya R; Wilson JA; Fujiwara H; Rozhkov L; Leach JL; Byars AW; Greiner HM; Vannest J; Buroker J; Milsap G. **Presurgical language localization with visual naming associated ECoG high- gamma modulation in pediatric drug-resistant epilepsy.** *Epilepsia*. 2017; 58:663-673.
2. Skoch J; Adelson PD; Bhatia S; Greiner HM; Rydenhag B; Scavarda D; Mangano FT. **Subdural grid and depth electrode monitoring in pediatric patients.** *Epilepsia*. 2017; 58 Suppl 1:56-65.
3. Romer SH; Seedle K; Turner SM; Li J; Baccei ML; Crone SA. **Accessory respiratory muscles enhance ventilation in ALS model mice and are activated by excitatory V2a neurons.** *Experimental Neurology*. 2017; 287:192-204.
4. Garzon MC; Epstein LG; Heyer GL; Frommelt PC; Orbach DB; Baylis AL; Blei F; Burrows PE; Chamlin SL; Chun RH. **PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations.** *The Journal of Pediatrics*. 2016; 178:24-33.e2.
5. Infinger LK; Stevenson CB. **Re-examining the need for tissue diagnosis in pediatric diffuse intrinsic pontine gliomas: A review.** *Current neuropharmacology*. 2017; 15:129-133.
6. Gallek MJ; Skoch J; Ansay T; Behbahani M; Mount D; Manziello A; Witte M; Bernas M; Labiner DM; Weinand ME. **Cortical gene expression: prognostic value for seizure outcome following temporal lobectomy and amygdalohippocampectomy.** *neurogenetics*. 2016; 17:211-218.
7. Nagaraj UD; Bierbrauer KS; Zhang B; Peiro JL; Kline-Fath BM. **Hindbrain Herniation in Chiari II Malformation on Fetal and Postnatal MRI.** *American Journal of Neuroradiology*. 2017; 38:1031-1036.
8. Salloum R; Hummel TR; Kumar SS; Dorris K; Li S; Lin T; Daryani VM; Stewart CF; Miles L; Poussaint TY. **A molecular biology and phase II study of imetelstat (GRN163L) in children with recurrent or refractory central nervous system malignancies: a pediatric brain tumor consortium study.** *Journal of Neuro-Oncology*. 2016; 129:443-451.
9. Skoch J; Zoccali C; Zaninovich O; Martirosyan N; Walter CM; Maykowski P; Baaj AA. **Bracing After Surgical Stabilization of Thoracolumbar Fractures: A Systematic Review of Evidence, Indications, and Practices.** *World Neurosurgery*. 2016; 93:221-228.
10. Nagaraj UD; Bierbrauer KS; Peiro JL; Kline-Fath BM. **Differentiating Closed Versus Open Spinal Dysraphisms on Fetal MRI.** *American Journal of Roentgenology*. 2016; 207:1316-1323.
11. Maynard LM; Leach JL; Horn PS; Spaeth CG; Mangano FT; Holland KD; Miles L; Faist R; Greiner HM. **Epilepsy prevalence and severity predictors in MRI-identified focal cortical dysplasia.** *Epilepsy Research*. 2017; 132:41-49.
12. Giridharan N; Horn PS; Greiner HM; Holland KD; Mangano FT; Arya R. **Acute postoperative seizures as predictors of seizure outcomes after epilepsy surgery.** *Epilepsy Research*. 2016; 127:119-125.
13. Fujiwara H; Leach JL; Greiner HM; Holland-Bouley KD; Rose DF; Arthur T; Mangano FT. **Resection of ictal high frequency oscillations is associated with favorable surgical outcome in pediatric drug resistant epilepsy secondary to tuberous sclerosis complex.** *Epilepsy Research*. 2016; 126:90-97.
14. Zoccali C; Skoch J; Patel AS; Walter CM; Maykowski P; Baaj AA. **Residual neurological function after sacral root resection during en-bloc sacrectomy: a systematic review.** *European Spine Journal*. 2016; 25:3925-3931.
15. Arya R; Leach JL; Horn PS; Greiner HM; Gelfand M; Byars AW; Arthur TM; Tenney JR; Jain SV; Rozhkov L. **Clinical factors predict surgical outcomes in pediatric MRI-negative drug-resistant epilepsy.** *Seizure: European Journal of Epilepsy*. 2016; 41:56-61.
16. Merhar SL; Kline-Fath BM; Nathan AT; Melton KR; Bierbrauer KS. **Identification and management of neonatal skull fractures.** *Journal of Perinatology*. 2016; 36:640-642.

17. Carosella CM; Greiner HM; Byars AW; Arthur TM; Leach JL; Turner M; Holland KD; Mangano FT; Arya R. **Vagus Nerve Stimulation for Electrographic Status Epilepticus in Slow-Wave Sleep.** *Pediatric Neurology.* 2016; 60:66-70.
18. Schaffzin JK; Simon K; Connelly BL; Mangano FT; Infect P-OSS. **Standardizing preoperative preparation to reduce surgical site infections among pediatric neurosurgical patients.** *Journal of neurosurgery. Pediatrics.* 2017; 19:399-406.
19. Radhakrishnan R; Leach JL; Mangano FT; Gelfand MJ; Rozhkov L; Miles L; Greiner HM. **Prospective detection of cortical dysplasia on clinical MRI in pediatric intractable epilepsy.** *Pediatric Radiology: roentgenology, nuclear medicine, ultrasonics, CT, MRI.* 2016; 46:1430-1438.
20. Qualmann KJ; Spaeth CG; Myers MF; Horn PS; Holland K; Mangano FT; Greiner HM. **Pediatric Epilepsy Surgery: The Prognostic Value of Central Nervous System Comorbidities in Patients and Their Families.** *Journal of Child Neurology.* 2017; 32:467-474.
21. Fard SA; Avila MJ; Johnstone CM; Patel AS; Walter CM; Skoch J; Sattarov KV; Baaj AA. **Prognostic factors in traumatic atlanto-occipital dislocation.** *Journal of Clinical Neuroscience.* 2016; 33:63-68.
22. Wang LL; Bierbrauer KS. **Congenital and Hereditary Diseases of the Spinal Cord.** *Seminars in Ultrasound, CT and MRI.* 2017; 38:105-125.
23. Alvarado E; Leach J; Caré M; Mangano F; O Hara S. **Pediatric Spinal Ultrasound: Neonatal and Intraoperative Applications.** *Seminars in Ultrasound, CT and MRI.* 2017; 38:126-142.
24. Yuan W; Harpster K; Jones BV; Shimony JS; McKinstry RC; Weckherlin N; Powell SS; Barnard H; Engsborg J; Kadis DS. **Changes of White Matter Diffusion Anisotropy in Response to a 6-Week iPad Application-Based Occupational Therapy Intervention in Children with Surgically Treated Hydrocephalus: A Pilot Study.** *Neuropediatrics: journal of pediatric neurobiology, neurology and neurosurgery.* 2016; 47:336-340.
25. Arya R; Sivaganesan S; Holland KD; Greiner HM; Mangano FT; Horn PS. **A probabilistic approach for lateralization of seizure onset zone in drug-resistant epilepsy with bilateral cerebral pathology.** *Mathematical Biosciences.* 2016; 277:136-140.

Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
Francesco Mangano, DO	Posterior Fossa Decompression with or without Duraplasty for Chiari Type I Malformation with Syringo	Patient-Centered Outcome Research Inst. (Washington University)	CER-1503-29700	12/01/2015 - 11/30/2018	\$3,000
Steven Allen Crone, PhD	Developing a Neuron Replacement Therapy to Improve Breathing, Motor Function and Survival in Neurodegenerative Disease	The Local Initiative for Excellence Fdtn	LIFE - Crone,Steven	07/01/2016 - 06/30/2018	\$50,000
Jun Nakamura, PhD	Identification of Molecular Therapeutic Targets in Choroid Plexus using a Novel Mouse Model of Communicating Hydrocephalus	Mayfield Education and Research Foundati (University of Cincinnati)	GOTO_MERF	07/01/2016 - 06/30/2017	\$45,588
Total Annual Grant Award Dollars					\$98,588
