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 |

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 Bifda (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 relates 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, researcher 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.


6. Gallek MJ; Skoch J; Ansay T; Bebahanani M; Mount D; Manziello A; Witte M; Bernas M; Labine DM; Weinand ME. Cortical gene expression: prognostic value for seizure outcome following temporal lobectomy and amygdalohippocampectomy. *Neurogenetics.* 2016; 17:211-218.


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.


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.


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.


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.


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.


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.


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.

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Grants, Contracts, and Industry Agreements

**Annual Grant Award Dollars**

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Title</th>
<th>Sponsor</th>
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<tr>
<td>Francesco Mangano, DO</td>
<td>Posterior Fossa Decompression with or without Duraplasty for Chiari Type I Malformation with Syringo</td>
<td>Patient-Centered Outcome Research Inst. (Washington University)</td>
<td>CER-1503-29700</td>
<td>12/01/2015 - 11/30/2018</td>
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<tr>
<td>Steven Allen Crone, PhD</td>
<td>Developing a Neuron Replacement Therapy to Improve Breathing, Motor Function and Survival in Neurodegenerative Disease</td>
<td>The Local Initiative for Excellence Fdtn (LIFE - Crone,Steven)</td>
<td>LIFE - Crone,Steven</td>
<td>07/01/2016-06/30/2018</td>
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<td>Jun Nakamura, PhD</td>
<td>Identification of Molecular Therapeutic Targets in Choroid Plexus using a Novel Mouse Model of Communicating Hydrocephalus</td>
<td>Mayfield Education and Research Foundati (University of Cincinnati)</td>
<td>GOTO_MERF</td>
<td>07/01/2016-06/30/2017</td>
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