Surgery Research Conference

Pediatric Surgery Research Update
February 14, 2018
Research Highlights
Division of Research is LIVE!

https://www.mcw.edu/Surgery-Research.htm

- Faculty
- Surgery Research Conference Notes
- Research Resources
  - Training
  - Submitting Grants
  - Research Affiliates
  - Campus Partnerships
- CME and Funding Opportunity Calendar
- Check out our Twitter page for updates @MCWSurgResearch
Nogo-B receptor increases the resistance of estrogen receptor positive breast cancer to paclitaxel.

**Pediatric Surgery**
- Ying Jin
- Wenquan Hu
- Tong Liu
- Ujala Rana
- Amanda Kong
- Pin Gao
- Xiang Wang
- Yajun Duan
- Qing Robert Miao

*Cancer Letters Journal*

Inhibition of Myeloperoxidase by N-Acetyl Lysyltyrosylcysteine Amide Reduces Oxidative Stress-Mediated Inflammation, Neuronal Damage, and Neural Stem Cell Injury in a Murine Model of Stroke.

**Pediatric Surgery**
- Guoliang Yu
- Ye Liang
- Shikan Zheng
- Hao Zhang

*Journal of Pharmacology & Experimental Therapeutics*

Pannus, thrombus, calcium-Bioprosthetic mitral replacement in young children has it all.

**Pediatric Congenital Cardiac Surgery**
- Ronald K. Woods
- Viktor Hraska

*Journal of Thoracic & Cardiovascular Surgery*

External validation of a smartphone app model to predict the need for massive transfusion using five different definitions.

**General Surgery**
- MJ Cohen
- P Muskat

*Journal of Trauma and Acute Care Surgery*

Muthusamy Kunnimalaiyaan has been asked to serve as an editorial board member for the journal *OncoTargets and Therapy*
Publications

Overall survival after resection of retroperitoneal sarcoma at academic cancer centers versus community cancer centers: An analysis of the National Cancer Data Base.

**Surgical Oncology**
- Nicholas G. Berger
- Jack P. Silva
- Harveshp Mogal
- Callisia N. Clarke
- Kathleen K. Christians
- Susan Tsai
- Clark T. Gamblin

*Surgery Journal*

The effect of prior upper abdominal surgery on outcomes after liver transplantation for hepatocellular carcinoma: An analysis of the database of the organ procurement transplant network.

**Surgical Oncology**
- Jack P. Silva
- Nicholas G. Berger
- Susan Tsai
- Kathleen K. Christians
- Callisia N. Clarke
- Harveshp Mogal
- Clark T. Gamblin

*Surgery Journal*

Inhibition of myeloperoxidase by N-acetyl lysyltyrosylcysteine amide reduces experimental autoimmune encephalomyelitis-induced injury and promotes oligodendrocyte regeneration and neurogenesis in a murine model of progressive multiple sclerosis.

**Pediatric Surgery**
- Guoliang Yu
- Shikan Zheng
- Hao Zhang

*Neuroreport Journal*

Is the venoarterial extracorporeal membrane oxygenation circuit your frenemy.

**Cardiothoracic Surgery**
- David L. Joyce

*Journal of Thoracic & Cardiovascular Surgery*
“The Word on Medicine: where Knowledge is changing life”

Gynecology Oncology  February 17<sup>th</sup> 4:00pm

This airing of “The Word on Medicine” features many individuals who care for patients with uterine, ovarian and other gynecologic cancers. This show will focus on diagnosing, treating and managing these complex diseases.

Dr. Denise Uyar, Gynecologic Oncologist  
Dr. Beth Erickson, Radiation Oncologist  
Jennifer Guerts, Genetic Counselor  
Claudia Bojar, Gynecology Oncology Outpatient Clinic Nurse  
Dr. Erin Bishop, Gynecologic Oncologist  
Dr. Stacy O’Connor, Radiologist  
Jamie Neary, NP, Women’s Health  
Mary Pipkin, Gynecology Oncology Research Program Nurse  
Dr. William Bradley, Gynecologic Oncologist

Women’s Cardiovascular Health  March 3<sup>rd</sup> 4:00pm
Medical College of Wisconsin, Department of Surgery
We Care Fund for Medical Innovation and Research
2018 Faculty Seed Grants

Eligibility

$150,000 Grant
• Full time faculty member in the Department of Surgery
• Interdisciplinary collaboration with another division, department or center at MCW

$50,000 Grant
• Assistant & Associate Professors

Overview

The mission of the We Care Fund is to use contributions made available by the philanthropic community to support Department of Surgery faculty demonstrate the importance of innovation and discovery to advance science and clinical care of patients.

Key Dates

RFA
February 12, 2018
Budget Review:
April 11, 2018
eBridge application to GCO:
April 18, 2018
Emailed We Care:
April 25, 2018
Scientific Committee Review:
June 21, 2018
Award Notifications:
July 16, 2018
Anticipated Start Date:
September 1, 2018
Biostatistical Support Process Updates

• Complete Department form \textit{first} for Tracking ID assignment
• Include tracking ID # in Biostats Consulting online request form
• Share biostats estimate when received
• Projects <$3,000 will be approved
• Average project cost: $1,800
• Continue to bring questions and concerns to Division of Research
NEXT MONTH:

Colorectal Surgery Research Update

Timothy J. Ridolfi, MD
Carrie Y. Peterson, MD, MS

Wednesday, March 14, 2018
5:00-6:00pm
Cancer Center
Conference Room M
Pediatric Surgery Research Update

David Gourlay, MD
Our Team

Melissa Lingongo – Research Manager (0.6FTE)
Michelle Knezevich – Clinical Research Coordinator/Database Specialist (1.0FTE)
Ed Bedjeti – Clinical Research Coordinator (0.2FTE)
Meghann Sytsma – Clinical Research Coordinator (0.2FTE)
Chris Fueger – Clinical Research Coordinator (GOOD Study) (1.0FTE)
TBD – Clinical Research Assistant (1.0FTE)
CLINICAL RESEARCH
Hernia in Premies (HIP) Study
<table>
<thead>
<tr>
<th>HIP Participating Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanderbilt</td>
</tr>
<tr>
<td>Arkansas</td>
</tr>
<tr>
<td>Duke</td>
</tr>
<tr>
<td>Le Bonheur</td>
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<tr>
<td>Iowa</td>
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<tr>
<td>Nationwide</td>
</tr>
<tr>
<td>Kaiser</td>
</tr>
<tr>
<td>Columbia</td>
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<tr>
<td>Erlanger</td>
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<tr>
<td>UVA</td>
</tr>
<tr>
<td>Utah</td>
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<tr>
<td>Albany</td>
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<tr>
<td>MUSC</td>
</tr>
<tr>
<td>UT Houston</td>
</tr>
<tr>
<td>Alabama</td>
</tr>
<tr>
<td>Arkansas</td>
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<tr>
<td>Connecticut Children's</td>
</tr>
<tr>
<td>Akron</td>
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<tr>
<td>Buffalo</td>
</tr>
<tr>
<td>All Children's</td>
</tr>
<tr>
<td>Cardinal Glennon</td>
</tr>
<tr>
<td>UCLA-Harbor</td>
</tr>
<tr>
<td>Dayton Children's</td>
</tr>
<tr>
<td>Washington University</td>
</tr>
<tr>
<td>Rhode Island</td>
</tr>
<tr>
<td>Cincinnati</td>
</tr>
<tr>
<td>Texas Children's</td>
</tr>
<tr>
<td>Tufts</td>
</tr>
<tr>
<td>Valley Children's</td>
</tr>
<tr>
<td>Seattle</td>
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<tr>
<td>Penn State</td>
</tr>
<tr>
<td>UCLA</td>
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<tr>
<td>Wisconsin</td>
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<tr>
<td>Dartmouth</td>
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<td>CHLA</td>
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<td>CMC Dallas</td>
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<tr>
<td>OHSU</td>
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<tr>
<td>Rocky Mountain</td>
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<tr>
<td>Wayne State</td>
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</table>
**HYPOTHESIS**: Late IH repair (5 months after NICU discharge, approx. 55-60 weeks post-menstrual age [PMA]) in premature neonates with an IH will result in a 10% absolute reduction in the proportion of infants with ≥ 1 SAE compared to early IH repair (prior to NICU discharge, approx. 38 weeks PMA).

**DESIGN**: prospective RCT; NIH funded

**CURRENT STATUS**: actively enrolling; 1 patient enrolled at CHW, 197 patients enrolled nationally
### Calkins HIP Study

<table>
<thead>
<tr>
<th>Cardiorespiratory or Anesthesia – related SAE</th>
<th>Inguinal Hernia or Surgery – related SAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>IH incarceration</td>
</tr>
<tr>
<td>Use of extracorporeal membrane oxygenation (ECMO)</td>
<td>IH strangulation</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>IH resuscitation</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation</td>
<td>Reoperation for IH or related to initial operation</td>
</tr>
<tr>
<td>Hypotension treated with vasopressor drugs</td>
<td>Injury to adjacent structure / organ</td>
</tr>
<tr>
<td>Apnea treated with increased respiratory support</td>
<td>Wound disruption (deep)</td>
</tr>
<tr>
<td>Local anesthetic toxicity (e.g. seizure)</td>
<td>Surgical site infection (deep)</td>
</tr>
<tr>
<td>Prolonged intubation / ventilation (&gt;48 hours post op)</td>
<td>Other SAE involving intervention to prevent or address patient harm</td>
</tr>
<tr>
<td>Unplanned reintubation</td>
<td></td>
</tr>
<tr>
<td>Intraoperative unplanned extubation</td>
<td></td>
</tr>
</tbody>
</table>
HIP Study Design

Identify Premature Infant with IH & obtain Informed Consent

~2 weeks prior to anticipated NICU discharge

Early IH Repair
(~38 weeks PMA)

Prospective Measurement of SAEs
~30 Sites
N = 586

Late IH Repair
(~55 weeks PMA)

Randomization
(~36 weeks PMA)
[Study Time Zero]

10 Months After Randomization

Neurodevelopmental Assessment
(22-26mo corrected age)
Pediatric Colorectal and Pelvic Learning Consortium (PCPLC)

- 18 countries
- steering committee and 5 working groups
  - GI & motility
  - gynecology
  - Hirschsprung disease
  - long-term functional outcomes
  - urology
- www.pcplc.org
**AIM**: To characterize pediatric colorectal disease by examining patient demographics, etiology of conditions, diagnostic information, surgical and medical management, and functional outcomes; data from the registry will also be used as a resource for physicians to query and facilitate hypothesis generation for future PCPLC studies.

**DESIGN**: prospective, observational registry

**CURRENT STATUS**: actively collecting data; 43 patients from CHW, 731 patients nationally
• 11 regional children’s hospitals
• Goals:
  – improving patient outcomes
  – developing best practices
  – reducing health care expenditures
• www.mwpsc.org
**AIM:** To determine the success rate of nonoperative management of acute appendicitis, defined as the proportion of patients receiving antibiotic therapy who do not undergo appendectomy at 1 year.

**DESIGN:** prospective, patient choice trial of surgery versus antibiotic therapy; PCORI funded

**CURRENT STATUS:** actively enrolling; 74 patient enrolled at CHW, 737 patients enrolled nationally
**AIM**: To characterize the demographics, management strategies and outcomes in a contemporary multi-institutional cohort of infants diagnosed with EA/TEF to identify potential areas for standardization of care.

**RESULTS**: Largest retrospective cohort study in the literature (N=396); used to develop best practice bundle for prospective QI study.
**DESIGN**: prospective, observation of QI bundle

**BUNDLE**:
- No trans-anastomotic tubes prior to esophagram
- No prosthetic interposition material between esophageal and tracheal suture lines
- Discontinuation of antibiotics used for surgical site infection prophylaxis within 24 hours
- Obtain esophagram POD#5
- Track acid suppression use

**CURRENT STATUS**: CHW is data coordinating center; facilitating IRB/DUA submissions at participating sites for prospective data collection
Lal Primary Spontaneous Pneumothorax Study

**AIM:** To determine success rate of simple aspiration for initial management of primary spontaneous pneumothorax in children; success of aspiration is defined as adequate expansion of the lung without the need for additional intervention during the initial hospitalization for PSP.

**DESIGN:** prospective, patient choice trial of simple aspiration versus surgical management

**CURRENT STATUS:** actively enrolling; 4 patient enrolled at CHW, 29 patients enrolled nationally
**AIM:** To evaluate the natural history of infants who have a patent processus vaginalis (PPV) or inguinal hernia by 1) determining the frequency of the development of symptomatic inguinal hernia in infants who are found to have an opening in their inguinal canal during laparoscopy for pyloric stenosis, and 2) observing the timeframe to develop a symptomatic inguinal hernia in infants who are found to have an opening in their inguinal canal during laparoscopy for pyloric stenosis.

**DESIGN:** prospectively consented observational study of all patients who undergo laparoscopic pyloromyotomy

**CURRENT STATUS:** actively enrolling; 6 patient enrolled at CHW, 61 patients enrolled nationally
**AIM:** To collect clinical information and quality of life assessments (PedsQL™) on patients with select neonatal surgical disease to better understand overall care and health in these patients.

**DESIGN:** prospectively consented, observational registry (CDH, omphalocele, gastroschisis, TEF/EA, Hirschsprung’s, NEC)

**CURRENT STATUS:** actively enrolling; N=478
Can omphalocele ratio predict postnatal outcomes?*

Jason A. Fawley, Erika L. Peterson, Melissa A. Christensen, Lisa Rein, Amy J. Wagner

Abstract

Background: The purpose of this study was to characterize and compare the outcomes of fetuses with omphalocele in utero.

Methods: A retrospective analysis of all patients with omphalocele diagnosed by prenatal ultrasound was performed. Outcomes were compared with a control group of patients without omphalocele.

Results: The study included 10 patients with omphalocele and 10 control patients. The ratio of omphalocele to abdominal circumference (OAC/AC) was significantly higher in the omphalocele group (p < 0.01). The mean OAC/AC ratio was 0.39 ± 0.10 in the omphalocele group and 0.31 ± 0.05 in the control group. The incidence of major anomalies was significantly higher in the omphalocele group (60% vs. 10% in the control group). The mortality rate was 20% in the omphalocele group and 10% in the control group.

Conclusions: The ratio of omphalocele to abdominal circumference is a useful marker for identifying fetuses with omphalocele, and may help predict the need for prenatal intervention. Early intervention may improve outcomes for these fetuses.

The significance of organ prolapse in gastroschisis

Shannon M. Koehler, Aniko Szabo, Matt Loechinger, Erika Peterson, Melissa Christensen, Amy J. Wagner

Abstract

Purpose: The purpose of this study was to evaluate the incidence and importance of organ prolapse in gastroschisis.

Methods: This was a retrospective review of all patients with gastroschisis admitted to our institution between 2000 and 2010. Retrospective chart review was performed to evaluate the incidence and impact of organ prolapse.

Results: Out of 100 patients with gastroschisis, organ prolapse was identified in 60% of cases. Prolapsed organs included the stomach, intestines, and bladder. Patients with organ prolapse had a significantly higher rate of postoperative complications, including sepsis, pneumonia, and reintubation.

Conclusions: Organ prolapse is a significant complication of gastroschisis and should be included in the management strategy for these patients. Early recognition and prompt intervention can help reduce the incidence of complications.
GOOD
Gastroschisis Outcomes of Delivery
GOOD Study Participating Sites
HYPOTHESIS: Delivery at 35 0/7-35 6/7 weeks in stable patients with gastroschisis is superior to observation and expectant management with a goal of delivery at 38 0/7-38 6/7 weeks.

DESIGN: prospective RCT; grant funded; www.thegoodstudy.org

CURRENT STATUS: actively enrolling at CHW; participating site IRB deferrals pending
QUALITY IMPROVEMENT
• **Peds NSQIP**
• ***Pediatric and Infant Case Log and Outcomes***
• REDCap™ database of all pediatric general surgery cases with associated M&M
• automated data pulls from Epic with validation and supplementary entry
• used for OPPE, hospital reporting, quality improvement initiatives
• 2012-present; N=20,414
Operationalizing quality improvement in a pediatric surgical practice
Marjorie J. Arca, Jessica Enters, Melissa Christensen, Paul Jeziorczak, Thomas T. Sato, Robert Thielle, Keith T. Oldham
Division of Pediatric Surgery, Children’s Hospital of Wisconsin, Medical College of Wisconsin, Milwaukee, WI

ARTICLE INFO
Article history:
Received 26 September 2013
Accepted 30 September 2013

Key words:
Quality improvement, Maintenance of certification, Case log, Surgery, Pediatrics

ABSTRACT
Background/Purpose: Quality improvement which QI initiatives are relevant and useful to our team have developed and implemented a streamlining approach. We designed a web-based Pediatric Research Electronic Data Capture (PEDS) QI; a surgeon completes a case log within 5-7 days. Outcomes such as cost, transfers to ICU, ER visit, additional clinic, and follow-up visits from the American College of Surgeons’ National Surgical Quality Improvement Program (NSQIP) database were reviewed.

Original scientific article
Does the American College of Surgeons NSQIP—Pediatric Accurately Represent Overall Patient Outcomes?


Erica R. Gross MD a, Melissa Christensen BS a, Jessica A. Schultz BSN b, Laura D. Cassidy PhD a, Yvonne Anderson BSN a, Marjorie J. Arca MD, FACS a, b, c
Reducing surgical site infections:

- Account for 24% of all hospital-acquired infections
- A source of morbidity
- Prolong hospital stays
- Increase costs

<table>
<thead>
<tr>
<th>Wound Classification</th>
<th>Children’s Hospital</th>
<th>Industry Standards</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>0.7%</td>
<td>1%</td>
</tr>
<tr>
<td>Clean-contaminated</td>
<td>1.8%</td>
<td></td>
</tr>
<tr>
<td>Contaminated</td>
<td>1.1%</td>
<td>10%</td>
</tr>
<tr>
<td>Dirty/Infected</td>
<td>4.8%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Surgical site infection rate by wound classification
Kid Friendly Care

Appendicitis imaging at Children’s

<table>
<thead>
<tr>
<th></th>
<th>Ultrasound</th>
<th>CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>9%</td>
<td>84%*</td>
</tr>
<tr>
<td>2016</td>
<td>91%</td>
<td>16%</td>
</tr>
</tbody>
</table>

*Represents 234 appendix ultrasounds in 2016
Measuring Individual Outcomes

OPPE Dashboard

Dr. Gourlay

<table>
<thead>
<tr>
<th>Median Time (days) to Closed Encounters for Ambulatory</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
</tbody>
</table>

Provider Rating (source: Connect)

<table>
<thead>
<tr>
<th>Provider Rating</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>89.5</td>
<td>88.5</td>
<td>86.6</td>
</tr>
</tbody>
</table>

SSI by Wound Classification

<table>
<thead>
<tr>
<th>SSI by Wound Classification</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean</td>
<td>0.0%</td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td>Clean-Contaminated</td>
<td>0.0%</td>
<td>1.8%</td>
<td></td>
</tr>
<tr>
<td>Contaminated</td>
<td>0.0%</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td>Dirty/Infected</td>
<td>7.5%</td>
<td>4.8%</td>
<td></td>
</tr>
</tbody>
</table>

Rate of Readmission post Appendectomy

<table>
<thead>
<tr>
<th>Rate of Readmission post Appendectomy</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4.9%</td>
<td>1.7%</td>
<td></td>
</tr>
</tbody>
</table>

Rate of ED Visit post Appendectomy

<table>
<thead>
<tr>
<th>Rate of ED Visit post Appendectomy</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.4%</td>
<td>1.1%</td>
<td></td>
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</tbody>
</table>

OR Costs for Appendectomy (median)

<table>
<thead>
<tr>
<th>OR Costs for Appendectomy (median)</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>DR. GOURLAY Acute Median vs Group</td>
<td>$ 6,671</td>
<td>$ 7,187</td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>$ 5,457</td>
<td>$ 5,446</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>$ 9,617</td>
<td>$ 14,941</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OR. GOURLAY Complex Median vs Group</th>
<th>Dr. Gourlay</th>
<th>Group</th>
<th>Organizational Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min</td>
<td>$ 8,772</td>
<td>$ 10,846</td>
<td></td>
</tr>
<tr>
<td>Max</td>
<td>$ 12,931</td>
<td>$ 21,863</td>
<td></td>
</tr>
</tbody>
</table>
AIM: To create a solution for endotracheal intubation that enables clinicians and first responders to manage airways easily and successfully.

DESIGN: Development of a steerable stylet used to place an endotracheal tube (with versions that incorporate video guidance).

CURRENT STATUS: research and development with end-user testing in simulation environment; pending human trials
Upcoming Studies

• Arca Statewide NICU Consortium for NEC
• Gourlay MPSC VTE Study
• Siddiqui Global Health Epidemiology of Pediatric Surgical Disease
QUESTIONS?
• Nogo-B receptor (NgBR) is a cell surface receptor that was identified by Dr. Miao during his postdoctoral training at Yale School of Medicine

• NgBR is a vital gene required for development and loss of NgBR causes early embryonic lethality
NgBR is required for blocking LXRα translocation and preventing hepatic steatosis – NIH R01DK112971

- NgBR levels decrease in the liver of fatty liver patients.
- NgBR loss increases the nuclear translocation of liver X receptor (LXR), which is a nuclear receptor promoting hepatic lipogenesis.
- The funded R01 grant will determine if maintaining the expression of NgBR in the liver is an effective approach to prevent the onset of non-alcoholic fatty liver disease.
Cerebral cavernous malformations (CCMs) consist of clusters of enlarged endothelial channels (‘caverns’) and are common vascular malformations with a prevalence of 1 in 200–250 individuals.

- CCM causes headaches, seizures, cerebral hemorrhages and focal neurological deficits.
- More than 80% of familial CCM is caused by germline mutations in 3 CCM genes: CCM1 (KRIT1), CCM2 (MGC4607), or CCM3 (PDCD10).
- Sporadic CCM are characterized by a lack of family history of the disease. The etiology of sporadic CCM is unclear.
- Dr. Miao’s team demonstrated that NgBR is required for maintaining CCM1/2 expression. NgBR loss in brain capillaries promote the onset of sporadic CCM.
• MPO generates toxic oxidants that increase inflammation and cell death
• Inhibiting MPO will decrease vascular inflammation and improve vascular function.
• Developed novel therapeutic agent N-Acetyl lysyltyrosylcysteine amide (KYC); United States Patent #8673847 B2
KYC Dose-Dependently Decreases Clinical Symptoms in Multiple Sclerosis Mouse Model

KYC treatment significantly attenuates EAE disease. EAE was induced in B6 WT mice at 6-8 wk of age by s.c. immunization with MOG35-55 peptide, and groups of mice were either administered with KYC or PBS daily, starting from day 0. Clinical signs of EAE were evaluated daily starting on day seven and the daily average disease score with 5-15 mice in each group (***p<0.001).
SCD mice were treated with PBS or KYC (0.3 mg/kg/d, 3 weeks). Plasma were isolated for quantification of neutrophil elastase and MPO activity as well as soluble L-Selectin (sL-Selectin), a biomarker of neutrophil vascular infiltration. The bar graph in panel A shows that KYC tends to reduce neutrophil elastase release in SCD mice. The bar graph in panel B shows that KYC significantly inhibits neutrophil MPO release in SCD mice. The bar graph in panel C shows that KYC reduces neutrophil shedding sL-Selectin in SCD mice (n=6). Thus, KYC inhibits neutrophil degranulation and vascular infiltration in SCD mice. Panel D KYC dose dependently inhibits HOCl production by PMA-stimulated neutrophils.