Pathology and Laboratory Medicine

RESEARCH AND TRAINING DETAILS

<table>
<thead>
<tr>
<th>Faculty</th>
<th>23</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Fellows</td>
<td>1</td>
</tr>
<tr>
<td>Direct Annual Grant Support</td>
<td>$920,126</td>
</tr>
<tr>
<td>Direct Annual Industry Support</td>
<td>$47,541</td>
</tr>
<tr>
<td>Peer Reviewed Publications</td>
<td>55</td>
</tr>
</tbody>
</table>

CLINICAL ACTIVITIES AND TRAINING

<table>
<thead>
<tr>
<th>Clinical Fellows</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient Encounters</td>
<td>688,474</td>
</tr>
<tr>
<td>Outpatient Encounters</td>
<td>700,537</td>
</tr>
</tbody>
</table>

Division Publications


44. Stanek J, Biesiada J. Relation of placental diagnosis in stillbirth to fetal maceration and gestational age at


---

**Faculty, Staff, and Trainees**

**Faculty Members**

*David Witte, MD, Professor*
Leadership

Mohammad Azam, PhD, Assistant Professor
Research Interests Cancer Biology and Neural Tumors Program

Michael Baker, MD, Assistant Professor
Research Interests Pulmonary pathology, Cardiac pathology

Kevin E Bove, MD, Professor
Research Interests Pediatric liver disease, biliary atresia

Margaret H Collins, MD, Professor
Research Interests Pediatric gastrointestinal pathology, especially pediatric eosinophilic gastrointestinal disorders, pediatric inflammatory bowel disease, pediatric bowel motility disorders

Anita Gupta, MD, Associate Professor
Research Interests Liver tumor pathology, vascular anomalies

Gang Huang, PhD, Assistant Professor
Research Interests Cancer pathology

Robert Lorsbach, MD, PhD, Professor
Leadership Director, Hematopathology Service
Research Interests Hematopathology

Richard L McMasters, MD, Assistant Professor
Research Interests Hematopathology

Lili Miles, MD, Associate Professor
Leadership Director, Training Program
Research Interests Brain tumor, epilepsy research, neuromuscular diseases and NASH liver

Joel E Mortensen, PhD, Associate Professor
Leadership Director, Diagnostic Infectious Disease Lab
Research Interests Microbiology

Lindsey Romick-Rosendale, PhD, Assistant Professor
Research Interests Metabolomics

Kenneth D Setchell, PhD, Professor
Leadership Director, Mass Spec Lab
Research Interests Biochemistry, Bile acids, Sterol and cholesterol metabolism, Steroids, Liver disease, Liver transplantation, Gastroenterology, Nutrition/Diet, Phytochemicals, Isoflavones/Lignans, Breast cancer, Colon cancer, Mass spectrometry – biomedical mass spectrometry, Chromatography, Analytical Biochemistry, Assay development, Therapeutic drug monitoring, Pharmacokinetics and metabolism, Genetics

S. Kumar Shanmukhappa, PhD, Assistant Professor
Research Interests Experimental animal models

Amy Sheil, MD, Assistant Professor

Rachel Sheridan, MD, Assistant Professor
Research Interests Liver pathology, biliary atresia

Jerzy W Stanek, MD, PhD, Professor
Research Interests Pathology and pathomechanisms of in-utero hypoxia, particularly in the placenta; Pathology of perinatal mortality and morbidity
Paul E Steele, MD, Associate Professor
Leadership Medical Director, Clinical Lab
Research Interests Clinical lab medicine

Keith F Stringer, MD, Assistant Professor
Research Interests Microscopic techniques for assessing mRNA expression, protein production and cellular identity in eukaryotic tissues

Peter Tang, PhD, Associate Professor
Research Interests Special chemistry

Dehua Wang, MD, Assistant Professor
Research Interests Hematopathology

Mikako Warren, MD, Assistant Professor
Research Interests Renal pathology

Kathryn Wikenheiser-Brokamp, MD, PhD, Associate Professor
Research Interests Genetic and developmental basis of lung disease, lung cancer and pediatric cystic lung disease

Trainees
- Daniel Leino, MD, PL-6, University of Michigan
- Jessica Hata, MD, PL-5, Vanderbilt University

Grants, Contracts, and Industry Agreements

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azam, M</td>
<td></td>
</tr>
<tr>
<td>Therapeutic Targeting of De Novo and Acquired Resistance in Childhood Leukemia</td>
<td>7/1/2014-6/30/2015 $50,000</td>
</tr>
<tr>
<td>Cancer Free Kids</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved Therapeutic Approaches for Hematological Disorder Treated with Tyrosine</td>
<td>5/1/2012-3/31/2017 $207,500</td>
</tr>
<tr>
<td>National Institutes of Health</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huang, G</td>
<td></td>
</tr>
<tr>
<td>Role of the Hypoxia-Inducible Factor-1alpha in Myelodysplastic Syndromes</td>
<td>3/1/2015-2/29/2020 $225,000</td>
</tr>
<tr>
<td>National Institutes of Health</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Novel Epigenetic Circuit in Acute Leukemia</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Funding Body</td>
<td>Grant No.</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>National Cancer Institute</td>
<td>R21 CA187276</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A Novel Epigenetic Circuit In Acute Leukemia</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wagh, P</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypoxia Signaling and Spontaneous Pulmonary Fibrosis in a Novel Mouse Model</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Witte, D</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Industry Contracts</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>$967,667</td>
</tr>
</tbody>
</table>
Glycocholic Acid Proves Effective Against Newly Identified Amidation Defect

Over the past 30 years, James Heubi, MD, and Kenneth Setchell, PhD, have revolutionized the treatment of liver disease in children, and their novel findings led to the March 2015 FDA approval of the drug Cholbam. This bile acid treatment — when given to children — tricks the liver into thinking it is producing enough of its own healthy bile acid so that it shuts down production of defective bile acids that lead to liver disease.

Now, Heubi and Setchell have identified another liver enzyme irregularity called an amidation defect, in which the liver produces too much unconjugated cholic acid because the amino acids glycine or taurine cannot conjugate it effectively. Normally, cholic acid dissolves fats and helps the body excrete cholesterol.

Heubi and Setchell identified five children with the amidation defect, all of whom showed mutations in the BAAT gene and exhibited failure to grow, vitamin absorption deficiencies or choleostasis. After treatment of up to 92 months with glycocholic acid (GCA), the patients were able to absorb the fat-soluble vitamins D-2 and tocopherol, showed improvement in growth, and experienced no side effects.

This is the sixth of 17 known liver enzyme defects that Heubi and Setchell have identified, and they are working on testing and funding for development of a GCA drug. Their work appeared online Dec. 23, 2014, in Hepatology.

“All of these defects manifest as fatal forms of liver disease if they’re not diagnosed, and there is no other form of liver disease you can reverse like this,” Setchell says. “This is lifelong therapy for all these kids. We believe that GCA should be the standard of care and supplemental fat-soluble vitamins should be the standard of care for affected patients.”

Clinicians and scientists at Cincinnati Children’s have identified and treated five patients with defective bile acid amidation due to a genetically confirmed deficiency in bile acid CoA:amino acid N-acyl transferase (BAAT) with the conjugated bile acid, glycocholic acid (GCA). These charts show changes from baseline in plasma vitamin D2 and tocopherol concentrations in response to a single oral bolus dose of vitamin D2 and tocopherol in patients with BAAT deficiency before and after treatment with glycocholic acid.

“This is lifelong therapy for all these kids. We believe that GCA should be the standard of care and supplemental fat-soluble vitamins should be the standard of care for affected patients.”