**Division Data Summary**

<table>
<thead>
<tr>
<th>Research and Training Details</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of Faculty</td>
<td>19</td>
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<tr>
<td>Direct Annual Grant Support</td>
<td>$631,591</td>
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<tr>
<td>Direct Annual Industry Support</td>
<td>$76,283</td>
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<tr>
<td>Peer Reviewed Publications</td>
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<table>
<thead>
<tr>
<th>Clinical Activities and Training</th>
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<tbody>
<tr>
<td>Number of Clinical Fellows</td>
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<tr>
<td>Inpatient Encounters</td>
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<tr>
<td>Outpatient Encounters</td>
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</table>

**Significant Publications**

**Division Collaboration**

**Human Genetics** » Gregory Grabowski MD

Providing technical and professional support for NIH study to characterize a metabolic disease animal model.

**Gastroenterology, Hepatology and Nutrition** » Mitch Cohen MD; Jorge Bezerra MD; Xiaonan Han PhD; Noah Shroyer PhD

Digestive Health Center: Integrated morphology core lab, provides technical and professional support to members of the DHC involved in basic and translational research in gastrointestinal tract.

**Gastroenterology, Hepatology and Nutrition** » James HEubi MD; John Bucuvalas MD; Jorge Bezerra MD; Kathleen Campbell MD

Director of Pathology Core for multicenter BARC and CLIC studies on biliary atresia and other chronic liver disorders in children.

**Endocrinology** » Stuart Handwerger MD

Providing technical and professional support for NIH placental studies.

**Rheumatology** » John Harley MD; Sue Thompson PhD; Hermine Brunner MD

Providing pathology professional and technical support for establishment of Biorepository service and support for Rheumatology core lab for Cincinnati Rheumatic Diseases Center and multicenter study for lupus.
nephritis.

**Allergy and Immunology** » Marc Rothenberg MD; Pablo Abonia MD

Providing professional support for the Cincinnati Center for Eosinophilic Disorders program and related research.

**Hematology/Oncology** » Maryam Fouladi MD; Richard Dressi PhD

Providing pathology professional and technical support for multicenter referral service for the High Grade Glioma program and basic research program.

**Hematology/Oncology Research** » Yi Zheng PhD; James Mulloy PhD; Jose Cancelas MD, PhD

Joint development of Leukemia Biology program at CCHMC.

**Department of Surgery and Division of Hematology/Oncology** » Denise Adams MD; Richard Azizkhan MD; Anusa Dasgupta MD

Hemangioma/vascular malformation clinical program. Providing professional diagnostic and technical pathology support for multidisciplinary patient care program.

### Faculty Members

**David Witte, MD**, Professor
*Division Director*

**Research Interests**

**Mohammad Azam, PhD**, Assistant Professor

**Research Interests**

**Kevin E Bove, MD**, Professor

**Research Interests**

**J. Todd Boyd, DO**, Assistant Professor

**Research Interests**

**Margaret H Collins, MD**, Professor

**Research Interests**

**Anita Gupta, MD**, Assistant Professor

**Research Interests**

**Gang Huang, PhD**, Assistant Professor

**Research Interests**

**Richard L McMasters, MD**, Assistant Professor

**Research Interests**

**Lili Miles, MD**, Associate Professor
*Director, Training Program*

**Research Interests**

**Michael Miles, PharmD**, Professor

**Research Interests**

**Jun Q Mo, MD**, Associate Professor

**Research Interests**

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

Kenneth D Setchell, PhD, Professor
  Director, Mass Spec Lab

Research Interests

Jerzy W Stanek, MD, PhD, Professor

Research Interests

Paul E Steele, MD, Associate Professor
  Medical Director, Clinical Lab

Research Interests

Keith F Stringer, MD, Assistant Professor

Research Interests

Peter Tang, PhD, Assistant Professor

Research Interests

Kathryn Wikenheiser-Brokamp, MD, PhD, Associate Professor

Research Interests

Hong Yin, MD, Assistant Professor

Research Interests

Trainees

- Rachel Sheridan, MD, PGY-VI, University of Cincinnati
- Amy Sheil, MD, PGY-VI, Medical University of South Carolina
- Matthew Bramlage, MD, PGY-8, Memorial Sloan-Kettering Cancer Center
- Guangju Luo, MD, PGY-V, University of Cincinnati

Significant Accomplishments

Molecular Basis for Lung Disease

Kathryn Wikenheiser-Brokamp, MD, PhD, is a clinical pathologist with research programs in lung development and cancer. Her laboratory studies the genetic and developmental basis of lung disease, with specific interest in identifying the molecular underpinnings of lung cancer and pediatric cystic lung disease. She has identified critical functions for the Rb/p16 and p53 tumor suppressive pathways in pulmonary epithelial cell growth in the context of lung development, injury repair and carcinogenesis. These studies are supported by a National Institutes of Health RO1 grant and funding from the American Cancer Society. Wikenheiser-Brokamp is part of a multi-institutional, interdisciplinary team of physicians and researchers that recently discovered DICER1 mutations in a familial tumor predisposition syndrome that develop pleuropulmonary blastoma (PPB). This work was published in Science in 2009 and represents the first human syndrome associated with DICER1 mutations. She leads the consortium toward elucidating how DICER1, and the microRNAs it generates, controls organogenesis and oncogenesis. In addition to the NIH grant (2011-2015), she received three grants from the St. Baldrick’s Foundation (2009-2016). The most recent St. Baldrick’s Research Consortium Grant supports the basic science studies and development of the International PPB Treatment and Biology Registry.

Targeting Genes for Drug-Resistant Tumors
The introduction of Gleevec (imatinib mesylate) as a targeted therapeutic agent has changed the management of chronic myelogenous leukemia (CML) and played a significant role in developing key concepts for targeting other oncogenic kinases such as EGFR, c-KIT, PDGFR, PDGFRB and BRAF. Targeted inhibition of these oncogenic kinases by small molecule inhibitors induces hematologic remission in leukemias and tumor regression in solid tumors. Despite this success, most patients retain molecular evidence of residual disease, and emergence of drug resistance limits the prospects for cure. Mohammad Azam, PhD, hypothesizes that a clear understanding of oncogene addiction in imatinib-responsive cells will allow strategies to target the intrinsic resistance of leukemia stem cells (LSCs). Recent work in his lab includes a comparative expression profiling studies of imatinib-responsive and -resistant cells, which suggests c-Fos, Dusp1, Dusp10 and mir-279 are critical mediators of imatinib-mediated therapeutic response. Eradication of these cancer stem cells is probably a critical part of any successful anticancer therapy. This work is aimed to target these identified genes using genetic and pharmacological agents in LSCs of CML. He anticipates engineering the oncogene addiction in LSCs either by genetic or pharmacological means to develop a curative response.

Cancer Biology Program
Cincinnati Children’s is a nationally recognized center for diagnostic evaluation and management of children with malignancies of the hematopoietic system. We are also building a world-class research program in cancer biology to support this clinical program. The focus is to dissect hematopoietic and cancer cell signaling networks at the molecular level. The Division of Pathology has joined with the Hematology/Oncology Research Division under the direction of Yi Zheng, PhD, to build a larger comprehensive joint program of research in leukemia and stem cell biology. An example of this successful joint effort includes the work of Gang Huang, PhD, in the Division of Pathology. He has recently obtained funding from the Ohio Cancer Research Associates to study the “Molecular Mechanisms of Leukemogenesis Mediated by MLL-partial tandem Duplication (MLL-PTD).” MLL-related leukemogenesis has been researched for nearly 20 years. There are still many unknown roles in how MLL causes leukemias. Huang, based on his original study, proposes an elegantly designed step-wise approach to investigate the non-Hoxs MLL downstream targets, the MLL/RUNXI/CFB beta/PU.1 network in leukemogenesis. These focuses will potentially provide a scientific foundation in understanding the heterogeneity of MLL-leukemias that may potentially lead to more precise targeting therapy for leukemia patients.

Division Publications


## Grants, Contracts, and Industry Agreements

### Grant and Contract Awards

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<thead>
<tr>
<th>Name</th>
<th>Project Description</th>
<th>Funding Agency</th>
<th>Start Date</th>
<th>End Date</th>
<th>Annual Direct / Project Period Direct</th>
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<tr>
<td>AZAM, M</td>
<td>Molecular and Therapeutic Analysis of Human Leukemia Using Human Induced-Pluripotent Stem Cells</td>
<td>The V Foundation</td>
<td>12/01/09</td>
<td>11/30/11</td>
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<td>BOVE, K</td>
<td>Clinical Center for Cholestatic Liver Disease in Children</td>
<td>National Institutes of Health</td>
<td>09/10/09</td>
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<td>SIMPSON, D</td>
<td>Role of Rb/p16 Pathway in Pulmonary Progenitor Cell Regulation</td>
<td>National Institutes of Health</td>
<td>08/11/09</td>
<td>08/10/13</td>
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<td>WIKENHEISER-BROKAMP, K</td>
<td>Role of Rb Family in Lung Epithelial Response to Injury</td>
<td>National Institutes of Health</td>
<td>04/01/10</td>
<td>03/31/14</td>
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<td>Rb-p16 Regulatory Pathway in Lung Carcinogenesis</td>
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<td>Mouse Model to Elucidate Mechanisms of Pleuropulmonary Blastoma Initiation</td>
<td>St. Baldrick's Foundation</td>
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<td>WITTE, D</td>
<td>Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Health (Integrative Morphology Core)</td>
<td>National Institutes of Health</td>
<td>08/01/07</td>
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### Industry Contracts

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<td>WITTE, D</td>
<td>Ception Therapeutics Inc</td>
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**Current Year Direct Receipts** $76,283

**Total** $707,874