**Division Data Summary**

**Research and Training Details**

<table>
<thead>
<tr>
<th>Description</th>
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<tr>
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<td>Number of Joint Appointment Faculty</td>
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<td>Number of Research Fellows</td>
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<td>Peer Reviewed Publications</td>
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**Clinical Activities and Training**

<table>
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<tr>
<td>Number of Other Students</td>
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**Significant Publications**


Orphan or rare diseases are diseases of low prevalence (affecting fewer than 200,000 in the USA) which pose a major problem for the scientific research and health care. Because they are so rare, spending a large amount of resources studying them is difficult to rationalize. However, there are about 8000 known orphan diseases whose collective impact is on a large number of people. One way of tackling this is to establish connections between orphan diseases and identify shared features among two or more orphan diseases that will in turn facilitate managing a group of diseases together. Additionally, finding such links between different diseases would improve the current understanding of the underlying pathophysiology of the orphan diseases. To this effect, we created a network of orphan diseases (1772) and the genes (2124) that are mutated in them by taking into account functional similarities, protein interactions, and literature co-citations. Analyzing these networks, we found that the genes mutated in orphan diseases tend to serve as essential hubs in their network – a finding that differs vastly from what we know about mutations that have occurred in non-essential genes being drivers of common diseases. Based on the high connectivity between different orphan diseases and the causative gene mutants, we believe that the shared biological processes and pathways implied by this connectivity can serve as potential orphan drug targets.


We had a burst of excellent publications that appeared in FY2011. Two of these publications deserve special mention. One, by Liu and Ma, was published in Nature Cell Biology in January 2011. In this paper, we provide...
the first experimental demonstration that protein stability regulates the formation of a normal concentration gradient (of the morphogen protein Bicoid) in Drosophila embryos. Another paper, by Cheung et al., was published in Development in July 2011. Here we propose a first model for how embryonic patterns in Drosophila can be formed in a proportionate, or scaled, manner.

Division Collaboration

**Allergy & Immunology/Gastroenterology, Hepatology & Nutrition** » Dr. Pabo Abonia; Dr. James Franciosi; Dr. Marc Rothenberg

Keith Marsolo and the i2b2 team are leading the development of a multi-center registry focused on Eosinophilic Esophagitis. This registry takes advantage of functionality developed for Liver Transplant and also allows extracts from other sites to be uploaded into the registry. Another component of this registry is a module that allows for the administration and completion of surveys to collect patient reported outcomes (PROs) on quality of life (QoL) measures.

**Developmental Biology** » Dr. James Lessard; Dr. Steven Potter

Dr. Aronow's group collaborates with Potter and Lessard along with an international consortium on the use of genomics analyses to gain insight into the normal or abnormal development of the kidney and lower urinary tract.

**Gastroenterology, Hepatology & Nutrition** » Dr. Jorge Bezerra

Dr. Jegga collaborates with Bezerra Lab to understand the molecular basis of biliary atresia, a rare condition in newborn infants which if unrecognized could lead to liver failure. He provides bioinformatic support that includes data analysis, data-mining and hypothesis generation using systems biology-based approaches.

**Gastroenterology, Hepatology & Nutrition** » Dr. Jorge Bezerra

In his collaboration with Dr. Bezerra Dr. Aronow serves as the Bioinformatics Core Director on the Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease grant project. His role is to aid or supervise in strategic planning, experimental designs, data analysis, and to generate a data portal for the genomics data and sample characterizations.

**Gastroenterology, Hepatology & Nutrition** » Dr. John Bucuvalas; Dr. Kathleen Campbell

Keith Marsolo and the i2b2 team have developed a research registry for Liver Transplant based on the i2b2 informatics framework. This registry, which is in the final stages of User Acceptance Testing, allows investigators to enter relevant data into the Epic electronic health record, after which it is transferred into i2b2, where it can be augmented, through the use of data entry screens, with research-specific variables not collected in the clinic. This registry is serving as a pilot template for other research registries throughout CCHMC.

**Hematology/Oncology**

Dr. Pestian and his team are collaborating with clinicians and scientists to develop methods to identify the clinical needs of end-of-life patients.

**Human Genetics** » Dr. Daniel Prows

As a leading expert in the design and analysis of DNA microarrays, including Incyte and Affymetrix technologies, Dr. Aronow's collaboration efforts with Dr. Prows include microarray design, oversight in all aspects of microarray analysis, including data sorting, and data analysis. Additionally, Dr. Aronow oversees the in-depth *in silico* analyses and generates appropriate figures, tables, and the related text for manuscript preparation.

**Human Genetics** » Dr. William Nichols

In his collaboration with Dr. Nichols, Dr. Aronow provides complete interaction, and direction for the
interpretation of resulting data including statistically and biologically significant gene expression patterns associated with hypoxia and improved right ventricular function in chronic lung disease in the context of all available information that pertains to understanding of normal, disease, and developmental pathway and gene network based processes. He is also fully involved in the prediction and analysis of strain variant gene polymorphisms that appear to play modifier roles.

**Immunobiology » Dr. H. Lee Grimes**

Dr. Jegga collaborates with Grimes Lab in their continuing pursuits to characterize cancer proteins and understand the underlying regulatory mechanisms of oncogenic transformation of hematopoietic progenitor cells.

**James M. Anderson Center of Excellence »**

Keith Marsolo and the i2b2 team have worked extensively with colleagues in the Anderson Center in their efforts to operationalize hundreds of outcome measures as part of the Epic Outpatient implementation and to implement a system intended to document and operationalize all of the legacy outcome measures, the Performance Measurement and Reporting System (PMRS).

**James M. Anderson Center of Excellence » Dr. Edward Donovan; Dr. Carole Lannon**

Keith Marsolo and the BMI software development group have worked to design an infrastructure for data collection, reporting and analysis that will serve as a template for quality improvement networks that are part of the State of Ohio’s BEACON initiative (Best Evidence for Advancing Childhealth in Ohio Now).

**James M. Anderson Center of Excellence » Dr. Eric Kirkendall; Dr. Stephen Muething; Dr. Uma Kotagal**

Dr. Solti’s collaboration efforts with Dr. Kirkendall include the submission of an NIH grant application (PI: Solti) to develop new modules for cTAKES and the submission of an internal Trustee grant application (PI: Solti) to develop clinical NLP infrastructure.

Dr. Solti is collaborating with Drs. Kirkendall and Muething in preparing the EHR-based medication safety project.

Additionally Dr. Solti is collaborating with Dr. Kotagal of the Anderson Center preparing the EHR-based predictive modeling of clinical outcomes project.

**James M. Anderson Center of Excellence; Emergency Medicine; Emergency Medicine » Dr. Evaline Alessandrini; Dr. Holly Brodzinski; Dr. Judith Dexheimer**

Dr. Solti collaborates with the members of the Anderson Center and Emergency Medicine in the appendicitis risk stratification project. The divisions are developing an automated system to determine the risk of appendicitis in abdominal pain patients.

**James M. Anderson Center of Excellence; Gastroenterology, Hepatology & Nutrition » Dr. Peter Margolis; Dr. Shehzad Saeed**

Keith Marsolo and the i2b2 team are working to develop an i2b2-based registry to support the quality improvement and research efforts of the ImproveCareNow Network, which focuses on improving the outcomes of children with Inflammatory Bowel Disease (IBD). This registry will allow users to enter data directly into i2b2, or collect data directly in the medical record, after which it can be transferred to the registry, either by file upload or a database feed. Also included as part of this registry will be population management and monthly quality reports. These reports can be generated on demand and allow investigators to see data on patients from their own site as well as aggregate numbers from the collaborative as a whole.

**James M. Anderson Center of Excellence; Pulmonary Medicine » Dr. Peter Margolis; Dr. Michael Seid**

Keith Marsolo is helping to lead the design and development of the technical infrastructure needed to support
their growing C3N (Clinical Collaborative Care Network). This infrastructure is expected to include personal health records, the ability to visualize and display patient-specific health and outcomes data, the ability to conduct N of 1 trials, and social networking and data sharing functionality.

**Molecular Immunology** » Dr. Christopher Karp

Dr. Aronow’s collaboration efforts with Dr. Karp and the Division of Molecular Immunology include the use of expression microarray and proteomic techniques for mechanistic definition of disease pathogenesis.

**Neonatology and Pulmonary Biology** » Dr. Yan Xu

Dr. Lu and his team work closely with Dr. Xu in developing statistical models to analyze gene expression during the development of mouse models with the goal of understanding the role of SREBP network in sulfatcaltan lipid homeostasis and lung maturation.

**Neurology** » Dr. Tracy Glauser

Dr. Pestian and his team are collaborating with Dr. Glauser for the ongoing development of CHRISTINE, a clinical decision support system for identifying optimal drug therapy for patients with epilepsy, and ADHD.

**Neurology** » Dr. Anna Weber Byars

Dr. Pestian and his team are collaborating with Dr. Byars on innovations in neuropsychology research.

**Neurology; Neurology; Neuroimaging Research Consortium** » Dr. Tracy Glauser; Dr. Shannon Standridge; Dr. Scott Holland

Dr. Pestian and his team are collaborating with Drs. Glauser, Holland and Standridge to develop the advanced informatics system for The Comprehensive Epilepsy Center.

**Neurology; Neuroimaging Research** » Dr. Jennifer VanNest; Dr. Scott Holland

In his role of informatics lead on an NICHD contract ("Cincinnati MRI Imaging Neuronal Development", Scott Holland, PI), he collaborates with the PI and Dr. Jennifer VanNest (Div. of Neurology) to build and disseminate a database of fMRI images of normally developing brains.

**Oncology** » Dr. John Perentesis

Dr. Solti collaborates with Dr. Perentesis on the clinical trial announcement grant. Their collaboration efforts focus on extracting eligibility criteria for oncology patients.

**Psychiatry** » Dr. Robert Kowatch

Dr. Pestian and his team are collaborating with Dr. Robert Kowatch for the ongoing development of CHRISTINE, a clinical decision support system for identifying optimal drug therapy for patients with mood disorders.

**Psychiatry; Emergency Medicine** » Dr. Robert Kowatch; Dr. Jacqueline Grupp-Phelan

Dr. Pestian and his team are collaborating with Drs. Kowatch & Grupp-Phelan to develop methods to identify the likelihood of repeated suicide attempts.

**Rheumatology** » Dr. Hermine Brunner; Dr. Esi Morgan DeWitt; Dr. Daniel Lovel; Dr. Susan Thompson

Keith Marsolo and the i2b2 team are part of a joint development effort with colleagues at the Children's Hospital Boston to develop a distributed, virtual registry for pediatric rheumatic diseases. Dr. Marsolo and his team have focused on developing functionality to display quality reports and the visualization of patient outcomes.

**Rheumatology** » Dr. Esi Morgan DeWitt

Keith Marsolo and the i2b2 team are working to develop population management and monthly quality reports for a multi-center quality improvement collaborative focused on juvenile idiopathic arthritis. These reports will provide similar functionality to the ones developed for ImproveCareNow, meaning they can be generated on demand and allow investigators to see data on patients from their own site as well as aggregate numbers from
the collaborative as a whole.

Rheumatology » Dr. David Glass; Dr. John Harley; Dr. Susan Thompson
As Director of the Informatics Core of the NIAMS-sponsored Cincinnati Core Center for Rheumatic Diseases (Susan Thompson, PI), Michael Wagner collaborates closely with Rheumatology Investigators David Glass, Susan Thompson and John Harley on genome-wide analyses of variants contributing to juvenile rheumatic disease.

Reproductive Sciences » Dr. Sudhansu Dey
Dr. Jegga collaborates with Dey Lab in their mission to understand the signaling networks that influence uterine biology in the context of embryo-uterine interactions during pregnancy and delivery. He is specifically focusing on the miRNA-based regulation of labor.

Faculty Members

John Hutton, MD, Professor
Director, Division Chief
Research Interests

Bruce Aronow, PhD, Professor
Co-Director, Computational Medicine Center
Research Interests Gene Expression Analysis, Gene Regulation, Clinical Genomics, Functional Genomics of Development and Disease

Anil Jegga, MS, DVM, Assistant Professor
Research Interests Gene Regulatory Networks, Biomedical Ontologies, Integrative Genomics

Michal Kouril, PhD, Assistant Professor
Director, Research IT
Research Interests Computational Support, High-performance computing, Parallel Programming, High-end Data Storage

Long Jason Lu, PhD, Assistant Professor
Research Interests Bioinformatics, Machine Learning, Integrative Genomics, Biological Networks, Computational Modeling, Software Development

Jun Ma, PhD, Professor
Research Interests Development, Transcription, Morphogen Gradient, Embryo, Robustness, Quantitative Studies

Keith Marsolo, PhD, Assistant Professor
Director, Software Development and Data Warehouse
Research Interests i2b2, Data Integration, Data Warehousing and Data Management

John Pestian, PhD, MBA, Associate Professor
Director, Computational Medicine Center
Research Interests Natural Language Processing, Clinical Decision Support, Suicide Research, Pathology Research, Psychiatric Research

S. Andrew Spooner, MD, FAAP, Associate Professor
Chief Medical Information Officer
Research Interests Decision Support, Pharmacy Information Systems

Imre Solti, MD, PhD, MA, Assistant Professor
Research Interests Computational Linguistics
Michael Wagner, PhD, Associate Professor

Faculty Liaison

Research Interests Machine Learning, Proteomics, Genome-wide Association, Parallel Computing, Computational Infrastructure, Bioinformatics

Joint Appointment Faculty Members

Eric Hall, PhD, Instructor
Neonatology & Pulmonary Biology
Research Interests Clinical Informatics, Knowledge Discovery Tools, Data Mining and Warehousing

Mario Medvedovic, PhD, Associate Professor
UC Environmental Health
Research Interests Biostatistics

Jarek Meller, PhD, Associate Professor
UC Environmental Health
Research Interests Protein Modeling

Yan Xu, PhD, Associate Professor
Pulmonary Medicine

Trainees
- Jacek Biesiada, PhD, 2000, University of Silesia, Poland
- Feng He, PhD, 2009, Fudan University, Shanghai, China
- Louise Deleger, PhD, 2009, Pierre et Marie Curie University, Paris, France
- Junbo Liu, PhD, 2000, Fudan University, Shanghai, China
- Mayur Sarangdhar, PhD, 2011, University of Hull, Hull, UK
- Wei Wang, PhD, 2009, University of Cincinnati, Cincinnati, Ohio, USA

Significant Accomplishments

Linking Research Registries and Electronic Health Records

The Division of Biomedical Informatics (BMI) was awarded a three-year, $12 million grant from the Agency for Healthcare Research and Quality (AHRQ) to create a modular registry that can be populated with data directly from electronic health records (EHRs) to support comparative effectiveness and quality improvement research. Collaborating with the ImproveCareNow network, which serves children with inflammatory bowel disease (IBD), our developers are using the open-source SHRINE and i2b2 informatics platforms to create a registry that can be populated with data directly from sites’ EHRs, removing the need for staff to perform the double data entry common to most research registries. Our team also is automating quality and population management reports so they can be generated on demand. Finally, we are enhancing the registries so they can be federated, making it possible for sites to keep their registry data at their own institution, but still share aggregate numbers across institutions. Once these developments are complete, these enhanced registries will be used to compare the effectiveness of alternative treatment strategies for IBD, with a special focus on the timing of biologic agents. John Hutton, MD, is principal investigator on the AHRQ grant and Keith Marsolo, PhD, is co-investigator.

Molecular Mechanisms Underlying Human Diseases
Jason Lu, PhD, is developing network and systems approaches to study of molecular mechanisms underlying human diseases. One focus of his research is identifying subspecies of blood lipoproteins such as HDL and their role in causing human atherosclerosis. So far, he has identified approximately 30 potential HDL subspecies. His approach also has proved useful in mapping transcriptional networks controlling surfactant homeostasis in the lung.

Making Meaningful Use of Electronic Medical Records

Andrew Spooner, MD, chief medical information officer at Cincinnati Children’s, completed the institutional assessment and project team preparation for the federal “Meaningful Use” incentive program, with payments due to arrive in 2012. Spooner also participated as a clinical leader in the design, training and support for 11 ambulatory divisions that have gone live with Epic.

Spooner is leading projects to use electronic medical records to implement population management programs and to maintain compliance with medication reconciliation regulations. He has collaborated on an accepted manuscript report of the STEPSTools pediatric drug dosing clinical decision support project. Spooner actively participated as a clinical leader in the design, training and support for 11 ambulatory divisions that have gone live with Epic.

Division Publications


Grants, Contracts, and Industry Agreements

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<tr>
<th>Grant and Contract Awards</th>
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<td><strong>Exploiting Advances in Biotechnology for Force Protection</strong></td>
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<tr>
<td>Molecular Signatures of Cancer Metastasis</td>
<td>Department of Defense</td>
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<tr>
<td>Nextgen Dissection of the Genomic Basis of Kidney Development</td>
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<td>Risk Stratification &amp; Identification of Immunogenetic and Microbial Markers</td>
<td>Crohn's and Colitis Foundation of America (Emory University)</td>
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<td>Dissecting the Roles of dCBP in the Drosophila</td>
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<td>Building Modular Pediatric Chronic Disease Registries for QI and CE Research</td>
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<td>Cincinnati Center for Clinical and Translational Sciences and Training</td>
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<td>Developing a Statistical Framework to Improve the Accuracy of Essential Gene Assignments by Transposon Mutagenesis</td>
<td>University of Cincinnati</td>
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<td>The Molecular Basis for High Density Lipoprotein Heterogenity</td>
<td>National Institutes of Health (University of Cincinnati)</td>
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<tr>
<td>Evolution of Canalizing Mechanisms in Gene Expression</td>
<td>NIH (University of Chicago)</td>
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<tr>
<td>Probing the Robustness of a Developmental System</td>
<td>NSF</td>
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<td>CARRA: Accelerating Toward an Evidence Based Culture in Pediatric Rheumatology</td>
<td>National Institutes of Health (Duke University)</td>
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<td>Shared Task 2010 Analysis of Suicide Notes for Subjective Information</td>
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Increasing Clinical Trial Enrollment: A Semi-Automated Patient Centered Approach

National Library of Medicine
R00 LM 010227 10/02/10-10/01/13 $163,145

| WAGNER, M | Cincinnati Rheumatic Diseases Core Center (Core 4-Informatics) | National Institutes of Health | P30 AR 047363 09/01/06-06/30/11 | $57,743 |

| Industry Contracts |

| PESTIAN | Eisai Europe Ltd | $78,279 |

| Funded Collaborative Efforts |

| ARONOW, B | Immunobiology of IFRD1, a gene modifying CF lung disease | National Institutes of Health | Karp, C 08/01/09-07/31/13 | 5% |

| Genetic Analysis of Hyperoxia Induced Acute Lung Injury | National Institutes of Health | Prows, D 05/01/09-04/30/13 | 5% |

| Global Gene Expression Atlas of Craniofacial Development | National Institutes of Health | Potter, S 09/21/09-04/30/14 | 5% |

| Cincinnati Ctr for Clinical and Translational Sciences and Training | National Institutes of Health | Heubi, J 04/03/09-03/31/14 | 10% |

| Genetic Analysis of Murine Chronic Hypoxia-Induced Pulmonary Hypertension | National Institutes of Health | Nichols, W 04/01/10-03/31/14 | 5% |

| Glomerulosclerosis in Human FSGS and Animal Models | National Institutes of Health | Potter, S 09/14/09-09/13/11 | 5% |

| Cincinnati Cell Characterization Core | National Institutes of Health | Malik 09/01/10-04/30/12 | 5% |

| Cincinnati Center for Excellence in Molecular Hematology | National Institutes of Health | Zheng, Y 09/30/10-06/30/15 | 5% |

| JEGGA, A | Biological Basis of Phenotypes & Clinical Outcomes | National Institutes of Health | Bezerra, J 09/01/09-08/31/13 | 5% |

| Epigenetic Manipulation of Leukemia | Alex's Lemonade Stand Foundation | Grimes, L 07/01/09-09/06/30/12 | 5% |

| Epigenetic Manipulation of Leukemia | National Cancer Institute | Grimes, L 07/01/09-09/06/30/11 | 5% |

<p>| Molecular Signatures of Cancer Metastasis | Department of Defense | | |</p>
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<td>Comparative Effectiveness of Pediatric Eosinophilic Esophagitis</td>
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<td>Leveraging EPIC for Quality Improvement in Rheumatology</td>
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<td>Perinatal Quality Improvement Project and Data Infrastructure Development Project</td>
<td>Ohio State University</td>
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<td>Impact of Initial Therapy and Response on Long Term Outcome</td>
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Total: $5,036,202