2013 Research Annual Report
Human Genetics

Division Data Summary

RESEARCH AND TRAINING DETAILS

<table>
<thead>
<tr>
<th>Category</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Number of Faculty</td>
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<td>Number of Joint Appointment Faculty</td>
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CLINICAL ACTIVITIES AND TRAINING

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<td>Number of Clinical Staff</td>
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<td>Outpatient Encounters</td>
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Significant Accomplishments

Advance in Genomic Analyses
Lisa Martin, PhD, Co-Director of the Cincinnati Genomic Control Cohort, recently published a methods paper entitled “Variant Impact on Linkage Effect Test.” This paper is a major contribution to the field because it identifies a method for overcoming a critical mismatch in the way linkage results are followed up. Given that linkage and association are expected to overlap only in Mendelian conditions, using such an approach for complex traits may impede our ability to detect disease causing variants.

Progress in Pulmonary Hypertension
William Nichols, PhD, has established the NHLBI-funded National Biological Sample and Data Repository for Pulmonary Arterial Hypertension. Since receiving its first samples in October 2012, biological samples have been collected from more than 600 patients from 24 enrollment centers across the US with a five-year goal of building the cohort to 3,000 patients. Biological samples, clinical data, and genetic data on WHO Group 1 PAH patients will be distributed to researchers worldwide to enhance genetic and other studies of this devastating disease.

Genetics Counseling Program Earns High Rating
The Genetic Counseling Graduate Program (GCP) received an A rating of excellence from the UC Graduate School Review. Reviewers said the program has "achieved national reputation and might be expected to develop as a center of excellence." The GCP also was reaccredited this year by the Accreditation Council for Genetic Counseling for the maximum amount of eight years. Melanie Myers, PhD, Director, and Carrie Atzinger, MS,
CGC, Associate Director, also successfully transitioned the program from quarters to semesters. Close monitoring and frequent meetings with advisors resulted in students meeting academic requirements and finishing research projects on time, despite six weeks less time than previous classes.

Research Highlights

Carrie Atzinger, MS, CGC
Ms. Atzinger was elected to a two year term as Director at Large for the Board of Directors of the National Society of Genetic Counselors.

Liming Bao, MD, PhD
Dr. Bao played an instrumental role in developing the joint international college of medicine between University of Cincinnati College of Medicine and Chongqing Medical University in China. This will be the first such international collaborative program between China and US. The success of the program will significantly elevate UC/Cincinnati Children’s standing in global medical education and facilitate clinical and research collaboration between two institutes.

Thomas Burrow, MD
Dr. Burrow has successfully initiated an industry funded trial evaluating the safety and efficacy of enzyme replacement therapy with recombinant human lysosomal acid lipase in individuals with cholesterol ester storage disease. This provides potential for a new specific therapy for these individuals.

Gregory A. Grabowski, MD, You-Hai Xu, MD, PhD, Ying Sun, PhD
Research efforts were concentrated in three areas: 1) The elucidation of the CNS pathogenesis of the α-synuclein and amyloid protein accumulation in Gaucher disease mouse brains. These studies indicate the disruption of the lysosome/autophagy/mitophagy system leading to complex abnormalities that predispose to Parkinson-like manifestations in Gaucher disease. 2) Comparative whole genome RNA-Seq analyses of the major organs in Gaucher disease before and following enzyme therapy. These analyses show that two highly similar biopharmaceuticals (differ only in oligosaccharide termination) have very different transcriptomic effects and lead to differential correction of the molecular pathology of this disease. 3) Development of neuroprogenitor and differentiated neurons as well as hepatocyte precursors from iPSCs derived from human and mouse fibroblasts. These cells are being used as potential therapeutics as well as for “disease in a dish” analyses for the glycosphingolipid storage diseases and lysosomal acid lipase deficiency, as prototypes.

Amber Hogart-Begtrup, PhD
Dr. Begtrup has spent her first year in the Molecular Genetics Laboratory engaging in the daily operations of the laboratory and laying the groundwork for future collaborations and research. Specifically, together with Dr. Kalfa of the Cancer and Blood Diseases Institute Dr. Hogart is developing comprehensive genetic testing for disorders of the red blood cell; the first in the country to offer functional characterization and comprehensive molecular genetic diagnostics to improve the care of children with RBC disorders. Also, Dr. Hogart together with Anne Lucky, MD and the Epidermolysis Bullosa (EB) Center are developing a rapid, comprehensive, genetic tests, for the diagnosis of this devastating skin disorder. In addition to improving clinical care by expediting a diagnosis, this program will expand our knowledge of the molecular basis of this disease, and ultimately lead to better therapeutic opportunities.

Taosheng Huang, MD, PhD
Dr. Huang has initiated the program of Mitochondrial Medicine at Cincinnati Children’s. The program integrates basic/translational research, genetic testing, and clinical service for mitochondrial diseases. He is an
internationally recognize researcher, and he was appointed as a scientific advisor for Ministry and Health in China.

Mehdi Keddache, PhD
Dr. Keddache developed a nationally available webinar for the U01 “Pluripotent Cell Biology Consortium” funded by the NIH. This educational webinar focused on the genomic technologies at the Cincinnati Cell Characterization Core (C4). Through collaborative projects with the US-EPA, Dr. Keddache developed and implemented new technologies in the Genetic Variation and Gene Discovery facility of the DHG in the fields of metagenomics and bioinformatics.

Nancy Leslie, MD
Dr. Leslie completed a two year collaborative project sponsored by HRSA to create uniform case definitions for all inborn errors included in the Newborn Screening Uniform Panel. This resource will be provided to state newborn screening programs to aid in classification of identified cases, promote future outcomes research, and assure that incidence rates reflect standardized assignments of affected status. A major hurdle to appropriate classification in some states is lack of funding for molecular diagnostic testing. It is hope that this tool will help states advocate for coverage of essential diagnostic testing for these disorders.

Ronghua Li, PhD
Dr. Li began his independent research career to study human mitochondrial diseases using cell-specific models by developing specific trans mitochondrial cybrids to study pathogenesis of maternally transmitted hypertension. His general research is focused on using iPSCs to study tissue specific effects of mitochondrial diseases.

Derek Neilson, MD
Dr. Neilson assumed leadership in developing the greatly expanding Ehlers-Danlos clinic and research program at Cincinnati Children’s. This nationally recognized center is among the few in the nation to provide comprehensive approaches to Ehlers-Danlos syndrome.

Sunghee Oh, PhD
Dr. Oh developed a statistical approach to the analyses of differential expression using RNA-seq profile data. These approaches are being applied to the identification of differential expression of alternative splicing variability, cell cyclic regulation and stimuli-response data, and time course analyses. These methodological accomplishments will significantly contribute to analyzing various types of time-dependent data including, disease progression, age-related gene expression, and integrative analysis with chip-seq and methylation epigenetic factors omics data.

Manoj Pandey, PhD
Dr. Pandey recognized C5a mediated signaling as a positive regulator for immunological inflammation in Gaucher disease mice. This finding may provide an approach to control the inflammatory propagation of Gaucher brain diseases.

Cindy Prows, MSN, CNS
Ms. Prows’ research is aimed at measuring responses (parents and clinicians) to integration of genomic research results into the health care system. Toward this aim, she provides leadership as co-PI on three different studies: DHG Performance of Exome Sequencing with Greg Grabowski, MD; Return of eMERGE Research Results with John Harley, MD (Rheumatology); and Pre-emptive Genotyping of Children and Adolescents with Senthil Sadhasivam, MD (Anesthesia). These data collection phases for the first two projects are ongoing and updates are initiated for Genetic Pharmacology Service test offerings and associated EPIC alerts.
Ms. Prows was an Editorial Advisory Board member and invited author for a Special Genomic Nursing Clinical Issue published the first quarter of 2013 by the Journal of Nursing Scholarship. In conjunction with the special issue, a webinar series was produced in which authors presented additional content and answered questions from a national online audience. Links to the published articles and webinar series can be found on genome.gov. This effort is part of an ongoing national initiative to integrate genetics / genomics into nursing education and practice.

Daniel Prows, PhD
Dr. Prows has successfully propagated a newly discovered mutant mouse that develops severe cardiac fibrosis and right ventricular dilated cardiomyopathy (DCM), with affected mice dying prematurely of heart failure and/or sudden cardiac arrest. Results from exome sequencing of mutants with heart failure combined with ratios of affected-to-unaffected offspring suggest that 2-3 genetic variants interact to produce the DCM and heart failure. Because most cardiomyopathies have only been associated with single gene variants, this mutant may represent a unique multigenic model of DCM with potential to identify and investigate an important gene-gene interaction causal for early-onset right-sided heart failure and premature death.

Howard Saal, MD
Dr. Saal served as President of American Cleft Palate Association (term ended 12/31/12) and served as a member of the AAP Neuromotor Screening panel. In addition, he was named to the top 1% of Clinical Geneticists by US News and World Report and listed in Best Doctors in America.

Elizabeth Schorry, MD
Dr. Schorry was re-funded by the Department of Defense for the NF Clinical Trials Consortium. She is the lead for the internationally recognized NF Clinic and is the PI for Cincinnati Children’s for the NF Consortium, which now includes 13 sites internationally and is funded through 2017 to perform clinical trials for NF1 and NF2. Two trials have been completed, an additional three trials are ongoing and enrolling, and two additional trials will open in the near future. Of particular interest are the trials of agents for treatment of plexiform neurofibromas, which will likely bring in the near future the first reports of drugs (MEK inhibitors) capable of shrinking these tumors. These trials have the potential to significantly impact health outcomes for children and adults with neurofibromatosis.

Teresa Smolarek, PhD
A collaborative effort between Drs. Sund, Zimmerman, Thomas, Mitchell, Prada, Bao, Martin, Smolarek and Grote, showed that SNP microarray will identify copy neutral regions of homozygosity (ROH) and demonstrated the clinical utility of ROH. Genetic information obtained from the array rapidly aided in the diagnosis of autosomal recessive disorders in some cases.

Together with Dr. Christine Phillips, MD of the CBDI, a collaborative study examined the use of low dose decitabine in children and young adults with refractory acute myeloid leukemia and demonstrated that this is an effective therapy for selected patients, thereby establishing a new therapeutic for these patients.

Rolf Stottmann, PhD
Dr. Stottmann, along with investigators from the Divisions of Human Genetics, Developmental Biology, and Hematology/Oncology, is undertaking studies to understand the genetic basis of congenital defects in patients with craniofacial and forebrain malformations. They have recently discovered the cause of two separate syndromes and have begun to uncover the molecular bases for these phenotypes.

Dr. Stottmann characterized a novel mouse mutation in the tubulin, beta 2B gene (Tubb2b) and showed that heterozygous mice for mutations in Tubb2b have behavioral abnormalities and subtle cortical defects.
Homozygous mutants, however, die at birth and have major defects in growth and patterning of the forebrain. This is the first mouse model of a recessive mutation in tubulin genes and adds significantly to recent studies identifying the consequences of tubulin mutations (tubulopathies) for brain development in mouse and human.

Dr. Stottmann was awarded a March of Dimes Basil O'Connor Research Scholar Award.

Ying Sun, PhD
Dr. Sun focuses her research on the glycosphingolipid storage diseases of the CNS in two major areas: 1) A detailed study of the glycosphingolipids in various regions of the brain and in visceral tissues showed that the accumulations of specific types of these lipids are region/organ and mutation dependent, and thereby, demonstrating substrate preference for specific mutations of acid β-glucosidase, the Gaucher disease enzyme. 2) Analysis of double deficiencies of the sphingolipids activator proteins (saposins) A and B showed differential in vivo effects on the sulfatide pathway and regionally specific effects in the CNS. These studies have implications for understanding the roles of glycosphingolipids and sulfated glycosphingolipids in regional brain development and disease as well as their treatment.

C. Alexander Valencia, PhD
Dr. Valencia has led the development of the bioinformatic analysis pipeline and the technical validation of the clinical exome program at Cincinnati Children’s. He has worked with the Division of Human Genetics, Rheumatology, and BMI to coordinate the launch of the two parallel analysis pipelines that meet CLIA/CAP regulatory requirements. The clinical exome will improve the diagnoses and potentially alter patient management, and provide identification of genes related to specific phenotypes which will be essential for addressing functional questions. In addition, his articles have shown that next-generation sequencing panels for congenital muscular dystrophies increases the diagnostic yield when compared to single gene Sanger sequencing testing. In the realm of protein-targeted delivery of cancer biomarkers, he demonstrated that his novel heptamer molecules successfully targeted EGFR and HER2 with high stability and avidity. He presented, “MetaboSeq: A clinical fatty acid oxidation disorders next generation sequencing panel” at the 130th OMICS Group Conference and International Conference on OMICS studies in Orlando, Florida.

Ge Zhang, MD, PhD
Dr. Zhang has conducted multiple genome-wide association (GWA) studies and quantitative genetic analyses of human complex traits and diseases, including 1) metabolic syndrome and related traits; 2) preterm birth and 3) isocyanate-induced occupational asthma. In addition, he has developed computer packages for efficient storage and rapid analysis of massive genomic data and he has conducted multiple genome-wide association (GWA) studies and quantitative genetic analyses of human complex traits. The significant results generated from these studies provided deeper insights into the molecular etiology and genetic architecture of human complex traits.

Kejian Zhang, MD, MBA
Dr. Zhang leads the design, validation and implementation of the next-generation sequencing based testing program including OtoSeq, MetaboSeq, ImmunoSeq, and Clinical Exome Sequencing at Cincinnati Children’s. The successful introduction of these clinical testing programs positions Cincinnati Children’s as a leading pediatric academic institution in genetic diagnoses for rare childhood diseases. It has and will have significance positive impact on clinical and basic research as well as improving children’s health.

**Division Publications**


64. Qiu Q, Li R, Jiang P, Xue L, Lu Y, Song Y, Han J, Lu Z, Zhi S, Mo JQ, Guan MX. Mitochondrial trRNA mutations are associated with maternally inherited hypertension in two Han Chinese pedigrees. Hum Mutat. 2012; 33:1285-93.


Faculty, Staff, and Trainees

Faculty Members

Gregory Grabowski, MD, Professor
Leadership The A. Graeme Mitchell Chair in Human Genetics; Director, Division of Human Genetics; Professor of Pediatrics and Molecular Genetics, Biochemistry and Microbiology
Research Interests Molecular pathogenesis and therapy of human genetic disease

Carrie Atzinger, MS, Assistant Professor
Leadership Assoc. Director, The Genetic Counseling Program

Liming Bao, MD, PhD, Associate Professor
Leadership Associate Director, Clinical Cytogenetics Laboratory
Research Interests Genetic biomarkers of hematological diseases and their underlying pathogenesis and clinical relevance

T. Andrew Burrow, MD, Assistant Professor
Research Interests Lysosomal storage diseases, particularly Gaucher disease; Inborn errors of metabolism,
particularly focusing on development of evidence based medicine

Min-Xin Guan, PhD, Professor

**Research Interests** Mechanisms of mitochondrial disorders, with a focus on maternally transmitted hearing loss and vision loss

Amber Hogart-Begtrup, PhD, Assistant Professor

**Leadership** Assistant Director, Clinical Molecular Genetics Laboratory

**Research Interests** Next Generation Sequencing/ Epigenomics/Molecular Genetic Diagnostics

Robert Hopkin, MD, Associate Professor

**Leadership** Director, Genetic Residency Programs

**Research Interests** Fabry Disease; Robin Sequence; 22q11 deletion; Neurofibromatosis; craniofacial genetics; chromosomal anomalies

Taosheng Huang, MD, PhD, Professor

**Leadership** Director, Program of Mitochondrial Medicine; Associate Director, Molecular Diagnostic Laboratory

**Research Interests** Disease-causing gene discovery with next generation sequencing and iPS cell therapy

Mehdi Keddache, PhD, Assistant Professor

**Leadership** Leader, Genetic Variation and Gene Discovery Laboratory

**Research Interests** DNA Sequencing / Genotyping Core/Linkage and Association analyses

Nancy Doan Leslie, MD, Professor

**Leadership** Director, Biochemical Genetics Laboratory; Director, Medical Biochemical Genetics Fellowship; Program Director, Laboratory Fellowships

**Research Interests** Inborn errors of metabolism, with an emphasis on long term outcome in PKU and in the molecular biology of galactosemia

Ronghua Li, PhD, Instructor

**Research Interests** Cell-specific models of mitochondrial diseases

Xia Li, PhD, Assistant Professor

**Leadership** Assistant Director, Clinical Cytogenetics Laboratory

**Research Interests** The role of molecular markers in hematological disorders for prediction, treatment, and monitoring

Lisa Martin, PhD, Associate Professor

**Leadership** Biostatistics and Epidemiology

**Research Interests** Focus on common complex diseases including obesity and heart malformations

Melanie Myers, PhD, MS, CGC, Associate Professor

**Leadership** Director, The Genetic Counseling Program

**Research Interests** Clinical utility of family health history and other genomic tools in health promotion

Derek Neilson, MD, Assistant Professor

**Research Interests** The genetic contribution to acute necrotizing encephalopathy, a disorder in which children are predisposed to devastating neurologic injury following common infections

William Nichols, PhD, Professor
Leadership  Associate Lab Director; Chairman, DHG Research Review Committee

Research Interests  The identification of genetic variants contributing to disease susceptibility

Sunghee Oh, PhD, Assistant Professor
Research Interests  Development of methodologies in RNA-seq; temporal dynamic profiles; genetic regulatory analysis; Bayesian approaches in RNA-seq and chip-seq

Manoj Pandey, PhD, Instructor
Research Interests  Immunobiology of the lysosomal storage disease

Daniel R Prows, PhD, Associate Professor
Research Interests  Mouse models of complex human diseases, with specific interest in mouse models of acute lung injury; use of quantitative trait locus analysis to identify regions linked to complex traits

Howard Saal, MD, Professor
Leadership  Director, Clinical Genetics; Medical Director, Cytogenetics Laboratory; Director, Cincinnati Children's Craniofacial Center

Research Interests  The natural history of genetic disorders, especially as they relate to craniofacial disorders; developing treatment and management protocols for craniofacial disorders

Iris Sageser, RDH, MS, Associate Professor
Leadership  Craniofacial Center

Research Interests  Multidisciplinary management of individuals affected by craniofacial abnormalities

Elizabeth K Schorry, MD, Associate Professor
Leadership  Director, Neurofibromatosis Clinic

Research Interests  Psychosocial and orthopedic aspects of neurofibromatosis; Clinical drug trials for NF1

Teresa A Smolarek, PhD, Associate Professor
Leadership  Director, Clinical Cytogenetics Laboratory; Director, Clinical Cytogenetics Fellowship Program

Research Interests  Application of SNP microarrays to determine constitutional and acquired DNA copy number changes; the genetic basis of pulmonary lymphangioleiomyomatosis

Rolf W Stottmann, PhD, Assistant Professor
Research Interests  Genetic analysis of congenital malformations affecting the brain and face

Ying Sun, PhD, Associate Professor
Research Interests  The pathological mechanisms of lysosomal storage diseases

Siva Theru Arumugam, PhD, Assistant Professor
Leadership  Assistant Director, Molecular Genetics Laboratory

Research Interests  Finding the genes for macular deterioration, Quantitative Genetics

C. Alexander Valencia, PhD, Assistant Professor
Leadership  Assistant Director, Molecular Genetics Laboratory

Research Interests  Clinical genomics and proteomics: A systems biology view in human genetics

You-hai Xu, MD, PhD, Professor Emeritus
Research Interests  Molecular and pathophysiological mechanisms of Gaucher Disease, particularly of neuronopathic Gaucher Disease

Ge Zhang, MD, PhD, Assistant Professor
Research Interests Genome-wide association studies and mathematical modeling of human genetic variations

Kejian Zhang, MD, MBA, Associate Professor

Leadership Director, Molecular Genetics Laboratory

Research Interests Molecular defects and molecular diagnosis of primary immunodeficiency diseases; Genetic aspects of predictive personalized medicine, eg., Pharmacogenetics; Fanconi Anemia SeqChip development

Sarah Zimmerman, PhD, Assistant Professor

Leadership Assistant Director, Clinical Cytogenetics Laboratory

Research Interests Genome-wide analysis for chromosome aberrations in congenital disorders and cancer using molecular cytogenetic techniques

Joint Appointment Faculty Members

Artem Barski, PhD, Assistant Professor (Allergy & Immunology)

Research Interests Chromatin biology; epigenomic and transcriptional regulation of immune response; use of epigenomic data to augment genome –wide association studies

Paula Goldenberg, MD, Assistant Professor (Cardiology)

Research Interests Application of genomic and clinical research methods in syndromic populations

John Greinwald, MD, Associate Professor (Otolaryngology)

Research Interests Genetics of Hearing Loss

Kenneth Kaufman, PhD, Professor (Center for Autoimmune Genomics and Etiology)

Research Interests Genetics of complex diseases such as systemic lupus erythematosus

Kakajan Komurov, PhD, Assistant Professor (Exp. Hem. & Cancer Bio.)

Research Interests Interested in identifying global molecular network models of cancer progression

Stephanie Ware, MD, PhD, Associate Professor (Molecular Cardiovascular Biology)

Research Interests Genetic disorders of cardiac structure and function

Clinical Staff Members

- Laurie Bailey, MS, Lysosomal Disease Center Coordinator; Clinical Trials Coordinator
- Judy Belli, RN
- Patricia Bender, RN, MSN
- Lisa Berry, MS
- Ashley Brazil, MS
- Anne Burroughs, RN
- Kathleen Collins, MS
- Jessica Connor, MS
- Susan Cordes, MS
- Jennifer Glass, MS
- Carol Hetteburg, RN, MSN
- Judy Johnson, MS
- Sandy Kaiser, LPN
• Emily King, MS
• Sara Knapke, MS,
  Hereditary Cancer Program; Clinical Manager
• Betty Leech, MS
• Anne Lovell, RN, MSN, APN
• Erin Mundt, MS
• Kimberly Page, RD
• Cynthia Prows, MSN, CNS
• Shelly Rudnick, MS
• Jodie Rueger, MS
• Jacqueline Scott, MS
• Krysten Shipley, MS
• Diana Smith, MS
• Christine Spaeth, MS
• Kristen Sund, PhD
• Martha Walker, MS
• Connie Wehmeyer, RN
• Katie Wusik, MS

Trainees
• Sophia Bous, MD, PGY3, Pediatrics/Genetics Combined Residency
• Lisa Dyer, PhD, PGY6, Clinical Fellow Cytogenetics
• Rob Hufnagel, MD, PhD, PGY2, Pediatrics/Genetics Combined Residency
• Harry Lesmana, MD, PGY1, Pediatrics/Genetics Combined Residency
• Haiying Meng, PhD, PGY7, Clinical Cytogenetics Fellowship
• Stephanie Peters Santoro, MD, PGY4, Pediatrics/Genetics Combined Residency
• Carlos Prada, MD, PGY7, Pediatrics/Genetics Combined Residency/Clinical Biochemical Genetics Fellowship
• Yaping Qian, PhD, PGY7, Clinical Fellow Molecular Genetics
• K. Nicole Weaver, MD, PGY4, Pediatrics/Genetics Combined Residency

**Division Collaboration**

**Allergy and Immunology** » Pablo Abonia, MD and Marc Rothenberg, MD, PhD
  Identifying contributions of Ehlers Danlos to eosinophilic esophagitis.

**Allergy and Immunology** » Marc Rothenberg, MD, PhD
  Statistical genetic analyses for Dr. Rothenberg's NIH grant.

**Allergy and Immunology** » Kimberly Risma, MD, PhD
  Characterizing novel granzyme B substrates, through functional assays.

**Anesthesiology; Occupational Therapy and Physical Therapy; Sports Medicine; Rheumatology** » Ken Goldsneider, MD, FAAP, Jason Long, PhD, Paula Melson, PT, MMSc, Stephanie Powell, PT, Greg Myer, PhD, and Tracy Ting, MD
  Clinical studies in Ehlers-Danlos hypermobility.

**Anesthesiology** » Senthil Sadhasivam, MD, MPH
  A research project identify genetic variations influencing pain relief and opioid adverse effects in children.
Anesthesiology » Senthil Sadhasivam, MD, MPH
- Pre-emptive Genotyping of Children and Adolescents.

Anesthesiology » Senthil Sadhasivam, MD, MPH
- Study of “Improving Acute Pediatric Pain Management Using Neurogenomics”.

Anesthesiology » Senthil Sadhasivam, MD, MPH
- The genetics of opioid and morphine related side effects and analgesia.

Asthma Research » Neeru Hershey, MD, PhD
- Providing statistical assistance for grant development, and a biostatistical core for a U19.

Biomedical Informatics » Bruce Aronow, PhD
- Analysis interfaces for NGS data.

Biomedical Informatics » Keith Marsolo, PhD
- eMERGE

Biostatistics and Epidemiology » Jessica Woo, MHSA, PhD
- Statistical analysis on various manuscripts.

Biostatistics and Epidemiology » Rick Ittenbach, PhD
- Planning team for Feb 2013 Empirical Bioethics conference sponsored by CCTST.

Bone Marrow Transplantation and Immune Deficiency » Sonata Jodele, MD
- Research project finding genetic causes of hematopoietic stem cell transplantation-associated thrombotic microangiopathy.

Bone Marrow Transplantation and Immune Deficiency » Stella Davies, MBBS, PhD and Parinda A. Mehta, MD
- Investigating monosomy 7 and its association with pediatric myelodysplastic syndrome or acute myeloid leukemia.

Bone Marrow Transplantation and Immune Deficiency; Experimental Hematology » Stella Davies, MBBS, PhD, Parinda Mehta, MD, Jim Mulloy, PhD, and Jose Cancellas, MD, PhD
- Examining genomic copy number changes in flow sorted cells by SNP microarray analysis.

Bone Marrow Transplantation & Immune Deficiency » Alexandra (Lisa) Filipovich, MD and Stella Davies, MBBS, PhD
- The study of primary immunodeficiency disorders.

Bone Marrow Transplantation & Immune Deficiency » Alexandra (Lisa) Filipovich, MD and Stella Davies, MBBS, PhD
- Molecular diagnoses of patients with immunodeficiency.

Cardiology » Jeffery Molkentin, PhD
- Characterizing mouse model of mitochondrial phosphate carrier disease.

Cardiology » Stephanie Ware, MD, PhD, FACMG
- Database established to look at DNA copy number changes in the genome in patients with congenital heart defects.

Cardiology » Stephanie Ware, MD, PhD, FACMG
- NIH funded project using next generation sequence data

Cardiology ; Molecular Cardiovascular Biology » John Lynn Jefferies, MD and Michael Taylor, MD
- Initial characterization of a new heart failure mutant line.
Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP
   Genetic Pharmacology Services

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP
   Pharmacogenetics of IMPDH in Kidney Transplant Patients which is an extension of our on-going study of
   genetic effect of UGT2B7, 1A8 and 1A9 on the pharmacogenetics of MPA on patients underwent kidney
   transplant.

Clinical Pharmacology » Sander Vinks, PharmD, PhD, FCP
   To evaluate the advantage of pharmacogenetics based Tacrolimus dosing through a clinical trial.

Critical Care Medicine » Hector R. Wong, MD,
   Genetic stratification of clinical septic shock.

Dermatology » Anne Lucky, MD
   Genetic study for Epidermolysis Bullosa.

Dermatology » Anne Lucky, MD
   Developing a clinical assays for the genetic diagnosis of Epidermolysis Bullosa.

Dermatology » Kara Shah, MD, PhD
   Co-directs the genodermatoses clinic which focus on diagnosis, management, and clinical research of
   individuals with genetic disorders having significant dermatologic involvement.

Developmental Biology » Brian Gebelien, PhD
   Developing a drosophila model of a unique dystonia-spastic paraplegia mutation.

Developmental Biology » Jim Wells, PhD and Chris Mayhew, PhD
   Designed and maintains the PSCF ordering website and billing system for the iPSC core.

Developmental Biology » Rulang Jiang, PhD
   Forward genetics to identify novel molecular players in Shh signal transduction.

Developmental Biology » Chris Mayhew, PhD
   Generating induce pluripotent stem cells from human fibroblasts.

Endocrinology » Lawrence M. Dolan, MD
   Genetic test for patients with Diabetes and hypoglycemia.

Environmental Health » Ranjan Deka, PhD
   To conduct a systematic genetic study of metabolic traits involved in metabolic syndrome.

Experimental Hematology and Cancer Biology Research » Dao Pan, PhD
   Neuronopathic Gaucher disease treatment.

Experimental Hematology and Cancer Biology Research » Nancy Ratner, PhD
   Provides basic science expertise as the basis for NF clinical trials.

Experimental Hematology and Cancer Biology Research » Qishen Pang, PhD
   Mouse ES cell characterization and breakage analysis.

Experimental Hematology and Cancer Biology Research » Lionel Chow, MD, PhD
   Characterization of mouse model for oligodendrogloma.

Experimental Hematology and Cancer Biology Research » Punam Malik, MD and Jose Cancelas, MD, PhD
   Helping CEH and C4 researchers with DNA Sequencing experimental designs.
Experimental Hematology and Cancer Biology Research » Marie-Dominique Filippi, PhD
Statistical analysis on RNA-seq transcriptome (and microarray) and Chip-seq with methylation marks.

Gastroenterology, Hepatology and Nutrition Research » Jorge A Bezerra, MD and Alexander Miethke, MD
Neonatal Jaundice testing program.

Gastroenterology, Hepatology and Nutrition Research » Jorge A. Bezerra, MD and Alexander Miethke, MD
Development of a Liver Disease testing center.

Gastroenterology, Hepatology and Nutrition Research » Alexander Miethke, MD
Functional characterization of candidate genes identified by exome sequencing.

Gastroenterology, Hepatology and Nutrition Research » Alexander Miethke, MD
Molecular Basis of mitochondrial depletion syndrome.

Gastroenterology, Hepatology and Nutrition Research » Jorge Bezerra, MD and Cindy Wetzel, PhD
DHC researchers with DNA Sequencing experimental designs.

General and Thoracic Surgery; Hematology/Oncology; Hemangioma and Vascular Malformation Center »
Belinda Dickie, MD, PhD, Denise Adams, MD, Adrienne Hammill, MD, PhD, and Peter Dickie, PhD
Working to identify genes in vascular malformations.

Hematology » Ralph A. Gruppo, MD
Developing of Next-generation sequencing-based molecular screening test for atypical hemolytic uremic syndrome and blood coagulation disorders.

Hematology » Eric Mullins, MD
A potential new bleeding mutant line in the colony; exome sequencing has revealed some interesting candidate genes.

Hematology » Charles Quinn, MD, MS
Launch of the testing program for hemoglobin disorders, e.g. Sickle cell and alpha and beta Thalassemia.

Hematology » Malik Putnam, MD and Theodosia Kalfa, MD, PhD
Develop clinical panel testing for “Red Cell Skeleton” disorders.

Hematology » Theodosia Kalfa, MD, PhD
Developing comprehensive genetic assays for the diagnosis of Hereditary Spherocytosis and other inherited hemolytic anemias.

Hospital Medicine » Armand Antommaria, MD, PhD, FAAP
Student project, interviewer for research ethicist candidates, Bioethics conference planning team.

Infectious Diseases » David Bernstein, MD, MA
To test genome-wide associations for genetic risk factors for isocyanate-induced occupational asthma.

Information Services » Shanti Smith
EPIC – Genetic Pharmacology Services results templates and clinical decision support alerts.

Medical Bioinformatics » Phil Dexheimer, MS
Sorting and reanalysis of exome sequencing data, specifically the heart failure mutant line on the A/J strain.

Molecular Cardiology » Arnold W. Strauss, MD
MetaboSeq genetic testing.

Neurology » Donald Gilbert, MD, MS
Studying dystonia-spastic paraplegia.
Neurology » Steve Danzer, PhD
Evaluating a new mouse model of congenital forebrain malformations that has epileptic seizure activity.

Neurology » Barbara Hallinan, MD, PhD
Co-directs the neurometabolic clinic which focus on diagnosis, management, and clinical research of patients with neurometabolic conditions.

Neurology » Charles Vorhees, PhD, Michael William, PhD, and Matthew Skelton, PhD
Assessment of neurobehavioral in our mouse models with neurologic defect.

Neurology » Matthew R. Skelton, PhD
iPS cell model for creatinine transport defects.

Oncology » John P. Perentesis, MD, FAAP
Genetic changes in pediatric patients with leukemia and lymphoma.

Oncology » John P. Perentesis, MD, FAAP
To develop a new pediatric oncology testing program.

Oncology » John P. Perentesis, MD, FAAP
Test design for tumor genotyping.

Oncology » Bipul DasGupta, PhD and John P. Perentesis, MD, FAAP
Molecular mechanisms underlying a novel, causal mutation in patients with microcephaly identified in DHG human exome analysis protocol.

Oncology » John P. Perentesis, MD, FAAP and Brian Weiss, MD
Development and implementation of the drug trials for plexiform neurofibromas, optic nerve gliomas, and MPNST.

Oncology » Jim Geller, MD
Development of fluorescence in situ hybridization (FISH) probes to more accurately diagnose specific translocations in pediatric renal cell carcinoma.

Ophthalmology » Zubair M. Ahmed, PhD
Developing next-generation sequencing-based molecular screening test for eye disorders.

Ophthalmology » Zubair M. Ahmed, PhD
Eye genetics research and identifying genes for new and rare eye disorders.

Ophthalmology » Richard Lang, PhD
Characterization of Bst mice.

Orthopedics » Alvin Crawford MD, FACS and Viral Jain MD
Clinical studies involving bone complications of NF1.

Otolaryngology » John Greinwald, MD, FAAP and Daniel Choo, MD
Long time collaboration has resulted in nationally recognized molecular diagnostic program.

Pathology and Laboratory Medicine » Joel Mortensen PhD and David Witte MD
Designed CLIA test for clinical microbiology.

Pathology and Laboratory Medicine » David Witte MD
Consultations for mouse and human tissue pathology.

Pathology and Laboratory Medicine » Kevin Bove, MD
Molecular Basis of mitochondrial depletion syndrome
Pathology and Laboratory Medicine » Kenneth D. Setchell, PhD
Role of cholesterol metabolism in the phenotypes in a mouse model with a mutation in a cholesterol biosynthetic enzyme.

Patient Services Center for Professional Excellence » Rita Pickler, PhD, RN, PNP-BC, FAAN
Theses RACs, Divisional Scientific Review.

Pediatric Surgery » Joo-Seop Park, PhD
Statistical analysis on Chip-seq data.

Perinatal Institute » Louis J. Muglia, MD, PhD
To identify genetic variants in human birth timing control by genome-wide analysis in human populations as well as cross-species comparisons and microevolutionary approaches.

Physical Medicine and Rehabilitation » Brad Kurowski, MD, MS
Genetics of recovery from traumatic brain injury.

Plastic Surgery; Developmental Biology » Samantha Brugmann, PhD, Rulang Jiang, PhD, and Steven Potter, PhD
Exome analyses for studies to identify genes important for to craniofacial and brain development.

Plastic Surgery; Developmental Biology » Samantha Brugmann, PhD
Studying the role of primary cilia in regulating growth and patterning of the embryonic forebrain and craniofacial structures.

Psychiatry » Drew Barzman, MD and Melissa Delbello, MD
Genomic research aimed at identifying predisposition to bipolar disorder.

Pulmonary Biology » Steve Glasser, PhD
Assessing lung pathology following several acute injuries, including ozone or hyperoxia inhalation, and lung infection models.

Radiology » Beth M. Kline-Fath, MD
Prenatal diagnosis of skeletal dysplasias.

Reproductive Science » Hosu Sin, PhD
Statistical analysis on RNA-seq and microarray data.

Rheumatology » Matthew T. Weirauch, PhD
Testing whether mRNA-display can identify transcription factors that can bind in the regulatory regions of lupus susceptibility genes.

Rheumatology » John Harley MD, PhD and Ke Liu, BS
Investigating sex chromosome abnormalities and what role they may play in a group of select autoimmune disorders.

Rheumatology » John Harley MD, PhD and Michael Barnes, PhD
Return of eMERGE Research Results.

Rheumatology » Alexei Grom MD
To define genetic defects responsible for the development of MAS in sJIA.

Rheumatology » Alexei Grom MD
The relationship between defects in Munc13-4 gene and Macrophage Activation Syndrome in patients with sJIA.

Rheumatology » John Harley, MD, PhD and Kenneth Kaufman, PhD
Develop and implement the Whole Exome Sequencing technology and analyses for clinical services.

**Rheumatology** » John Harley MD, PhD  
Informatics for emerge projects.

**Rheumatology; Medical Bioinformatics; CCHMC Biobank** » John Harley MD, PhD, Michael Barnes, PhD, and Keith Marsolo, PhD  
Co-Investigators on the National Biological Sample and Data Repository for PAH.

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### Grants, Contracts, and Industry Agreements

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<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
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<td><strong>BURROW, T</strong></td>
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| **Bringing Together Rare Disease: A Conference for Families**  
Genzyme Corporation | $3,000 |
| 06/15/13-06/14/14         |              |
| **Bringing Together Rare Disease: A Conference for Families**  
Shire Human Genetic Therapies | $4,055 |
| 06/15/13-06/14/14         |              |

| **GRABOWSKI, G**          |              |
| **Cincinnati Regional Genetics Center**  
Health Resources & Services Admin (Ohio Department of Health) | $349,000 |
| 03130011GS0310             | 07/01/12-03/31/16 |
| **Improved Diagnosis and Treatment of Pediatric Mood Disorders through Integrated Clinical Genomics**  
The Oxley Foundation | $95,210 |
| 12/01/11-11/30/14         |              |
| **Cincinnati Center for Excellence in Molecular Hematology**  
National Institutes of Health | $63,001 |
| P30 DK 090971             | 07/01/10-06/30/13 |

| **HUANG, T**             |              |
| **Genetic Studies of Optic Atrophy**  
National Institutes of Health | $135,309 |
| R01 EY 018876             | 05/01/13-01/31/14 |

| **KEDDACHE, M**          |              |
| **Digestive Health Center - Sequencing Core**  
National Institutes of Health | $31,790 |
| U01 DK 062497             | 09/10/09-05/31/14 |

<p>| <strong>LEECH, B</strong>             |              |
| <strong>Dempster Family Foundation Grant</strong> |          |</p>
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<tr>
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<td>Use of Serum and Imaging Biomarkers to Evaluate Degree of Myocardial and Coronary Involvement in Patients with Mucopolysaccharidenses</td>
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<td>The Role of the Intraflagellar Transport Gene Ttc21b in Neural Ciliopathic Disease</td>
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