**Division Details**

### Division Data Summary

#### Research and Training Details

<table>
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<tr>
<td>Number of Faculty</td>
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<td>Direct Annual Industry Support</td>
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#### Clinical Activities and Training

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<td>Number of Clinical Staff</td>
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<td>Inpatient Encounters</td>
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<tr>
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### Significant Accomplishments

**National research resource for pulmonary hypertension**

William Nichols, PhD, leads the new National Biological Sample and Data Repository for Pulmonary Arterial Hypertension (PAH). This project is using a five-year, $10 million NHLBI grant to build a biorepository of blood samples obtained from participants in the national REVEAL registry. Twenty four centers nationwide are contributing to the biorepository, which is based here at Cincinnati Children's. Genomic DNA, plasma, lymphocyte cDNA, and transformed lymphoblasts from 3,000 PAH patients will be available to the research community. Whole genome SNP genotypes and DNA sequence data also will be generated and shared.

**Exome sequencing initiative**

Cynthia Prows, MSN, CNS, developed, submitted, and obtained approval for a series of projects that will measure the performance of exome sequencing in clinical settings using a variety of strategies and will access parent’s experiences, and expectations, as well as uses of exome sequencing research results. Similar genetic studies of mood disorder are funded by the Oxley Foundation. These protocols will generate sustainable collaborations between our Division’s clinical and research faculty and faculty from other Cincinnati Children's divisions and the UC College of Medicine.

**Rare disease meets common neurodegenerative diseases**

Ying Sun, PhD, You-Hai Xu, PhD, and Division Director Gregory Grabowski, MD, lead a project to elucidate the
initiating events in the pathogenesis of CNS involvement in Gaucher disease as models for more common chronic brain diseases, including Parkinson and Alzheimer diseases. During the past year pathogenic links have been established between the autophagy and lysosomal systems and the glycosphinoglipid disruption in Gaucher disease mice and these chronic neurodegenerative diseases that could lead to new approaches to therapies for both these disease groups.

Division Highlights

Liming Bao, MD, PhD, Associate Professor
A new mouse cytogenetics core was established to support researchers at CCHMC and UC for studies of mouse disease models and stem cells.

T. Andrew Burrow, MD, Assistant Professor
Dr. Burrow together with Dr. Barbara Hallinan in Neurology has expanded the neurometabolic clinic to include services by physicians from the division of Physical Medicine and Rehabilitation, allowing for enhanced, comprehensive care of children with neurometabolic conditions. Similarly, in collaboration with Dr. Kara Shah in Dermatology, he has successfully initiated the combined genodermatosis clinic for care of individuals with genetic conditions affecting the skin.

Mehdi Keddache, PhD, Assistant Professor
As the leader of the Genetic Variation and Gene Discovery Core, Dr. Keddache together with colleagues in Bioinformatics and Rheumatology, has implemented RNA-Seq data generation and a time saving analysis pipeline, as a part of the standard service. In addition, he has implemented sustainable, cost-effective next generation sequencing services for clinical and research projects.

Nancy Doan Leslie, MD, Professor
Dr. Leslie actively participates in The Inborn Errors of Metabolism Collaborative, an NIH funded national demonstration project. The goal of this registry is to track long term outcomes in individuals with disorders detectable by newborn screening. This registry has over 800 individuals enrolled, and represents 22 distinct disorders detectable by newborn screening.

In addition, she was appointed to a national expert panel, organized by HRSA, charged with the development of epidemiologically solid case definitions for all of the disorders detectable by newborn screening. These definitions will be important for future validation of screening algorithms and evaluation of outcomes of intervention after detection by newborn screening.

Lisa Martin, PhD, Associate Professor
Dr. Lisa J. Martin was appointed co-Director of the Cincinnati Genomic Control Cohort. The directorship of this unique resource is charged with advancing CCHMCs capacity to perform genetic studies by providing a population representative sample from the community.

Melanie Myers, PhD, MS, CGC, Associate Professor & Carrie Atzinger, MS, Assistant Professor: Genetic Counseling Program (GCP):
The GCP celebrated a weekend of events to mark the 30th Anniversary of the Cincinnati GCP, resulting in a commitment of $18,000 for the GCP while fostering alumni relations.
Ms. Atzinger was key to a new online cardiovascular genetics course and updating two existing Teratology and Clinical Embryology courses increasing user participation from 40 users to 85. The online program increased national exposure for the GCP and DHG.

Dr. Myers, GCP Program Director, was the Guest Editor for the Journal of Genetic Counseling's special issue on direct-to-consumer genetic testing (June, 2012). The articles in the special issue will contribute to the previously limited data on the impact of direct-to-consumer genetic testing.

Daniel R. Prows, PhD, Associate Professor
Using a susceptibility mouse model, Dr. Prows previously identified several regions linked to differential acute lung injury susceptibility and has now constructed separate lines of mice for the two major regions of effect. Interestingly, these two loci demonstrated opposing allelic effects, such that alleles for one locus led to increased resistance, whereas the same alleles for the second locus increased sensitivity. These findings strongly support that these two regions contain interacting genes and suggest that these mice will provide a powerful model to identify and characterize the genes acting together to affect acute lung injury susceptibility.

Howard M. Saal, MD, FACMG, Professor
Dr. Saal was elected as President of American Cleft Palate-Craniofacial Association, an organization of 2500 members representing over 15 healthcare specialties, including Pediatrics, Medical Genetics, Plastic Surgery, ENT, Psychology, Speech Pathology and Dentistry. He will be responsible for implementing the strategic plan of the Association, committee organization and assignments, annual review of the ACPA executive director, and presiding over the Annual Meeting and Executive Council meetings.

Iris Sageser, RDH, MS, Associate Professor
Ms. Sageser spearheaded the application that resulted in the Craniofacial Center becoming certified in September 2011. This accomplishment ensures compliance with the Standards for Cleft Palate and Craniofacial Teams by the Commission on Approval of Teams (CAT) of the American Cleft Palate-Craniofacial Association.

Elizabeth K. Schorry, MD, Associate Professor
Dr. Schorry is a participant in the multi-center DOD-funded (2012-2017) Neurofibromatosis Consortium, which currently has 3 ongoing drug trials for NF1. Additional drug trials for NF1 and NF2 treatment are components of the re-funded grant. Dr. Schorry is the head of the bone committee in the Consortium.

Teresa A. Smolarek, PhD, Associate Professor/Cytogenetics:
Dr. Smolarek introduced two new fluorescence in situ hybridization (FISH) panels for myeloproliferative disorders and eosinophilia, and re-established the relationship with UC Hematology/Oncology for genetic testing. In addition, isolation of CD138 positive cells was integrated into FISH testing for multiple myeloma.

Siva Theru Arumugam, PhD, Assistant Professor
In a series of publications, Dr. Theru Arumugam pinpointed the CFH locus as the most common gene associated with Age-related Macular Degeneration (AMD), examined the relationships between cataract/cataract surgery and AMD genes, and the genotype/phenotype associations of a CFH common mutation and disease progression/regression and lifetime risks for AMD. These studies will be important for the diagnosis and prognosis of affected AMD patients, a common form of blindness.
Ge Zhang, MD, PhD, Assistant Professor
Dr. Zhang has reported genome-wide association (GWA) studies of metabolic syndrome and related traits in a relatively isolated population. In addition, he is engaged in a genetic study of preterm birth and received a pilot project funded by the Perinatal Institute. The significant results generated from these studies are providing deeper insights into the molecular etiology and genetic architecture of human complex traits.

Kejian Zhang, MD, Associate Professor
Dr. Zhang led the first large scale, multicenter, retrospective study on genetics in geriatric onset Hemophagocytic Lymphohistiocytosis (HLH) leading to a featured article in “Blood”. This study has and will have major impact in the clinical diagnosis and management of adult patients with HLH. Dr. Zhang received the “Entrepreneurial Achievement Award” at the first annual Cincinnati Children’s Hospital Medical Center (CCHMC) Faculty Awards Program for her outstanding accomplishments in development and growth of the Division of Human Genetics (DHG), Molecular Genetics Laboratory into a regional, national and international resource for genetic testing.

Significant Publications
This article defines a new mechanism for deafness causation.

Shows the connection between intracellular organelle (autosome/lysosome) systems and asthma.

Provides the first direct mechanistic link between Parkinson disease and mutations in the Gaucher disease gene.

Identifies a small genomic region that encodes a gene(s) for the risk of developing a common cause of blindness.

Provides the identification of genes that link HLH diseases in childhood and their adult counterparts.

Division Publications
1. Ayoub AE, Oh S, Xie Y, Leng J, Cotney J, Dominguez MH, Noonan JP, Rakic P. Transcriptional programs in


47. Sadhasivam S, Chidambaran V, Ngamprasertwong P, Esslinger HR, Prows C, Zhang X, Martin LJ, McAuliffe J.
Race and unequal burden of perioperative pain and opioid related adverse effects in children. 


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

**Robert Hopkin, MD**, Associate Professor  
**Leadership** Director, Genetic Residency Programs  
**Research Interests** Fabry Disease; Robin Sequence; 22q11 deletion; Neurofibromatosis; craniofacial genetics;
chromosomal anomalies

Mehdi Keddache, PhD, Assistant Professor
Leadership Leader, Genomics Core
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

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 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 lymphagioleiomyomatosis

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

Bradley T Tinkle, MD, Associate Professor

**Leadership** Clinical Geneticist; Assistant Director, Molecular Genetics Laboratory; Director, Skeletal Dysplasia Center; Co-Director, Marfan/Ehlers-Danlos Syndromes Clinic

**Research Interests** Natural history of connective tissue disorders and outcome studies of various clinical interventions

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, Associate Professor

**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, 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
- Kathleen Collins, MS
- Jessica Connor, MS
- Susan Cordes, MS
- Jennifer Glass, MS
- Carol Hetteburg, RN, MSN
- Judy Johnson, MS
- Jacqueline Kara, 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
- Diana Smith, MS
- Christine Spaeth, MS
- Kristen Sund, PhD
- Martha Walker, MS
- Connie Wehmeyer, RN
- Katie Wusik, MS

Trainees
- Sophia Bous, MD, PGY2, Pediatrics/Genetics Combined Residency
- Anthony Broering, MD, PGY4, Clinical Fellow/Medical Genetics
- Haiying Meng, PhD, PGY6, Clinical Cytogenetics Fellowship
- Stephanie Peters Santoro, MD, PGY3, Pediatrics/Genetics Combined Residency
- Carlos Prada, MD, PGY6, Pediatrics/Genetics Combined Residency
- Yaping Qian, PhD, PGY6, Clinical Fellow Molecular Genetics
- K. Nicole Weaver, MD, PGY3, Pediatrics/Genetics Combined Residency
### Grants, Contracts, and Industry Agreements

#### Grant and Contract Awards

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<td>GRABOWSKI, G</td>
<td>through Health Resources &amp; Services Administration(Ohio Department of Health)</td>
<td>Health Resources &amp; Services Administration(Ohio Department of Health)</td>
<td>07/01/04-06/30/12</td>
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<td>Lysosomal Disease Network: Epidemiology and Natural History of Wolman Disease and Cholesteryl Ester Storage Disease</td>
<td>National Institutes of Health(University of Minnesota)</td>
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<td>Studies of Gaucher Disease: A Prototype Lipidosis</td>
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<td>National Institutes of Health</td>
<td>National Institutes of Health</td>
<td>09/30/10-06/30/15</td>
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<td>KEDDACHE, M</td>
<td>for Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease - Sequencing Core</td>
<td>Ntl Inst of Diab &amp; Digest &amp; Kidney Dis</td>
<td>6/1/2012-5/31/2017</td>
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<td>Inborn Errors of Metabolism Collaborative: Defining the Natural History</td>
<td>National Institutes of Health(Michigan Public Health Institute)</td>
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<td>Epithelial Genes in Allergic Inflammation</td>
<td>Ntl Inst of Allergy &amp; Infections Dis</td>
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<td>09/19/11-09/18/12</td>
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<td>Genetic Analysis of Murine Chronic Hypoxia-Induced Pulmonary Hypertension</td>
<td>National Institutes of Health</td>
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### PROWS, D  
**Genetic Analysis of Hyperoxia Induced Acute Lung Injury**  
National Institutes of Health  
R01 AI 075562  
05/01/09-04/30/13  
$257,548

### SCHORY, E  
**Genetic & Epigenetic Diffenceses in Monozygotic Twins with NF1**  
Department of Defense Army  
W81XWH1010867  
09/15/10-09/14/12  
$16,448  
**Neurofibromatosis Consortium Development Operation**  
Department of Defense Army (University of Alabama-Birmingham)  
W81XWH0510615  
07/01/07-03/31/12  
$26,607

### TOLENTINO, C  
**Graduation Research Supplement - Genetic Analysis of Murine Chronic Hypoxia-Induced Pulmonary Hypertension**  
National Institutes of Health  
R01 HL 102107  
04/01/10-03/31/14  
$40,861  
**Current Year Direct**  
$3,342,690

### Industry Contracts

#### BURROW, T  
Shire Human Genetic Therapies  
$37,227

#### GRABOWSKI, G  
Genzyme Corporation  
$57,896  
Shire Human Genetic Therapies  
$168,518

#### HOPKIN, R  
Amicus Therapeutics, Inc.  
$7,623  
BioMarin Pharmaceutical Inc  
$16,216  
Genzyme Corporation  
$187,995

#### LESLIE, N  
BioMarin Pharmaceutical Inc  
$2,695  
Genzyme Corporation  
$38,151  
**Current Year Direct Receipts**  
$516,321

**Total**  
$3,859,011