### Division Data Summary

#### Research and Training Details

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#### Clinical Activities and Training

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### Division Photo

Row 1: G Grabowski, G Zhang, M Myers  
Row 2: T Smolarek, R Hopkin, A Barski, T Burrow, L Bao  
Row 3: C Prows, S Zimmerman, E Schorry, K Komurov, D Neilson, C Atzinger, K Zhang  
Row 4: L Martin, S Oh, I Sageser, S Theru Arumugam, B Tinkle, D Prows, R Stottmann, H Saal, M Pandey

### Significant Publications


The first two publications show the global involvement of the CNS by alpha-synuclein accumulation in Gaucher disease mouse models. They furthermore provide a potential mechanism for the relationship between excess glycosphingolipid deposition in Gaucher disease and neurodegenerative diseases.


This second edition provides a comprehensive evaluative approach to joint examinations for hypermobility. Significantly, this is the only such single source for this such physical examinations in a quantitative manner.


Mitochondrial dysfunction is being increasingly recognized as a component, if not causality of, many complex and maternally inherited/influenced diseases. This paper is the first to demonstrate a specific mitochondrial genomic mutation as directly linked to essential hypertension, a disease that affects millions world-wide.
Division Highlights

**Dr. Grabowski, Dr. Keddachi**

Drs. Grabowski and Keddache, together with the Division of Biomedical Informatics, collaborated with the Institute for Blood Disorders and Cancer to establish two new National Centers at CCHMC, the Center of Excellence in Molecular Hematology (Dr. Y. Zhang, P.I.) and the Progenitor Cell Biology Consortium Characterization Core (Dr. P. Malik, P.I.). These two Centers provide support for the molecular and genetic characterization, and potential new therapies for major disorders of childhood.

Drs. Grabowski and Keddache have upgraded the genotyping and sequencing capabilities and analyses of the Genetic Variation and Gene Discover Core as part of the CCHMC effort to enhance Genomics. These are accomplished in close collaboration with the Division of Rheumatology and Dr. John Harley, and the Division of Biomedical informatics through joint hiring of new faculty, cross-platform development, and combined grant applications. Additional joint hires of faculty with Experimental Hematology and Allergy Research provide enhanced bioinformatic analytic capabilities for CCHMC.

**Dr. K. Zhang**

In addition to Dr. Zhang's research and translational work with Dr. Grom in Rheumatology, she and Dr. Keddache worked closely with Dr. Clint Joiner and Theodosia Kalfa to establish a clinical panel for testing Red Blood Cell Skeleton Disorders. This panel will provide a unique resource for CCHMC, national, and International patients with these types of disorders. Such approaches currently are being extended to the hemoglobinopathies. An additional collaborative program includes the Division of Pediatric Dermatology and is focused on the genomics of Epidermolysis Bullosa.

**Dr. Keddache**

Dr. Keddache is the lead of the Genetic Variation and Gene Discovery Core (GVGDC) of UC/CCHMC. During the past year, he has expanded the Investigator base of this laboratory to >350 that includes CCHMC, UC, regional, governmental, and international clients desiring state-of-the-art genomic characterization by SNP genotyping and Sanger and NextGen massively paralleled DNA and RNA sequencing. The GVGDC provides these services, but also collaboration, design, development, and initial analyses and consultations for large and small projects for UC/CCHMC investigators. Together with our quantitative genomics team (Drs. Lisa Martin, Ge Zhang, Siva Theru-Arumugam, and Sunghee Oh), investigators have interactive access to modern genomic analyses that is supplemented by faculty in bioinformatics and jointly appointed faculty in Experimental Hematology (Dr. K. Komurov).

**Dr. Burrow**

Dr. Burrow has established two major collaborative clinics at CCHMC. Together with Dr. Ton DeGraw and Barbara Hillinan, he established an expanding multidisciplinary neurometabolic clinic to service CCHMC, national, and international patients with such conditions. Similarly, he and Drs. K. Shah and A. Lucky have initiated a Dermatogenetics Clinic that focuses on patients with such conditions, their molecular diagnosis, and developing new therapies.
Faculty Members

Gregory Grabowski, MD, Professor
  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
  Assoc. Director, The Genetic Counseling Program
  Research Interests

Liming Bao, MD, PhD, Associate Professor
  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

Hong Du, PhD, Associate Professor
  Research Interests Understanding the molecular mechanisms of genetic disorders of lipid metabolism and the development of therapeutic treatments for these disorders

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
  Director, Genetic Residency Programs
  Research Interests Fabry Disease; Robin Sequence; 22q11 deletion; Neurofibromatosis; craniofacial genetics; chromosomal anomalies

Mehdi Keddache, PhD, Assistant Professor
  Leader, Genomics Core
  Research Interests DNA Sequencing / Genotyping Core/Linkage and Association analyses

Nancy Doan Leslie, MD, Professor
  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
  Biostatistics and Epidemiology
  Research Interests Focus on common complex diseases including obesity and heart malformations

Melanie Myers, PhD, MS, CGC, Associate Professor
  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, Associate Professor  
Chairman, DHG Research Review Committee  
**Research Interests** The identification of genetic variants contributing to disease susceptibility

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

Xiaoyang Qi, PhD, Associate Professor  
**Research Interests** Translational research focused on the role of saposin C in multivesicular body bioformation and neuropathogenesis and the development of saposin C-containing nanovesicles as a novel anticancer agent

Howard Saal, MD, Professor  
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, Assistant Professor  
Craniofacial Center  
**Research Interests** Multidisciplinary management of individuals affected by craniofacial abnormalities

Elizabeth K Schorry, MD, Associate Professor  
Director, Neurofibromatosis Clinic  
**Research Interests** Psychosocial and orthopedic aspects of neurofibromatosis; Clinical drug trials for NF1

Teresa A Smolarek, PhD, Associate Professor  
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

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

Siva Theru Arumugam, PhD, Assistant Professor  
Assistant Director, Molecular Genetics Laboratory  
**Research Interests** Finding the genes for macular deterioration, Quantitative Genetics

Bradley T Tinkle, MD, Associate Professor  
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

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

Kejian Zhang, MD, Associate Professor
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
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

John Greinwald, MD, Associate Professor
Otolaryngology
Research Interests Genetics of Hearing Loss

Kakajan Komurov, PhD, Assistant Professor

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, Certified Pediatric Nurse, Craniofacial Team
- Patricia Bender, RN, MSN, Craniofacial Team
- Lisa Berry, MS, Genetic Counselor for Lysosomal Disease Center
- Kathleen Collins, MS
- Susan Cordes, MS, Genetic Counselor
- Jennifer Glass, MS
- Carol Hetteburg, RN, MSN
- Judy Johnson, MS
- Sandy Kaiser, LPN
- Sara Knapke, MS, Hereditary Cancer Program
- Betty Leech, MS, VCFS
- Anne Lovell, RN, MSN, APN, Neurofibromatosis Clinic Nurse
- Erin Mundt, MS
- Kimberly Page, RD
- Cynthia Prows, MSN, CNS, Genetics Clinical Nurse Specialist
- Shelly Rudnick, MS
- Jodie Rueger, MS
- Kerry Shooner, MS
- Diana Smith, MS
Christine Spaeth, MS, Fetal Care Genetic Counselor
Kristen Sund, PhD
Martha Walker, MS
Connie Wehmeyer, RN, Nurse Coordinator for Lysosomal Disease Center
Katie Wusik, MS

Trainees
- Sophia Bous, MD, PGY1, Pediatrics/Genetics Combined Residency
- Jaya George-Abraham, MD, PGY5, Medical Genetics Fellowship
- Melissa Maxwell-Stropes, PhD, Clinical Molecular Genetics Fellowship
- Haiying Meng, PhD, Clinical Cytogenetics Fellowship
- Stephanie Peters Santoro, MD, PGY2, Pediatrics/Genetics Combined Residency
- Carlos Prada, MD, PGY5, Pediatrics/Genetics Combined Residency
- Elizabeth Sellars, MD, PGY4, Pediatrics/Genetics Combined Residency
- Dipesh Tamakuwala, PhD, Clinical Cytogenetics Fellowship
- K. Nicole Weaver, MD, PGY2, Pediatrics/Genetics Combined Residency
- Wenying Zhang, MD, PhD, Clinical Molecular Genetics Fellowship

Significant Accomplishments

**Gaucher disease linked with Parkinson’s**
Gregory Grabowski, MD, You-Hai Xu, PhD, and Ying Sun, PhD have collaborated with researchers in Boston and Ottawa to show a mechanistic link between Gaucher disease and Parkinson disease. Based on these results, additional ongoing studies provide a framework for the dissection of the pathogenesis and potential novel treatments of Parkinson disease and other common neurodegenerative diseases.

**Progress in HLH research**
Kejian Zhang, MD, MBA, has collaborated with the National Institutes of Health and Stanford University on studies that have delineated the phenotype and molecular genetic characteristics in the development of familial hemophagocytic lymphohistiocytosis (HLH) and associated lymphoproliferative syndromes. These studies expand basic knowledge about the pathogenic mechanisms of these diseases and point toward targets to improve their treatment outcomes.

**Pulmonary arterial hypertension advancements**
William Nichols, PhD, contributed to significant advancements in understanding the genetic basis of Parkinson’s disease and pulmonary arterial hypertension (PAH). Major efforts focused on the establishment of the National Biological Sample and Data Repository for Pulmonary Arterial Hypertension in conjunction with investigators of the REVEAL registry. This national/international collaborative effort at Cincinnati Children’s will provide basic and clinical data for the analyses of the pathogenic mechanisms and treatment of PAH.

Division Publications


20. Guan MX. Mitochondrial 12S rRNA mutations associated with aminoglycoside ototoxicity.


Global gene expression profile progression in Gaucher disease mouse models. 


Grants, Contracts, and Industry Agreements

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|               | **Current Year Direct Receipts** | **$684,113** |
|               | **Total**                       | **$2,917,435** |