Human Genetics

Cincinnati Children's

Division Details

Division Data Summary

Research and Training Details

Number of Faculty	28
Number of Joint Appointment Faculty	6
Number of Support Personnel	125
Direct Annual Grant Support	$3,342,690
Direct Annual Industry Support	$516,321
Peer Reviewed Publications	70

Clinical Activities and Training

Number of Clinical Staff	27
Number of Clinical Fellows	7
Number of Clinical Students	26
Number of Other Students	7
Inpatient Encounters	401
Outpatient Encounters	5,228

Division Photo

Row 1: A Burrow, A Valencia, T Smolarek, K Zhang, G Grabowski
Row 2: S Theru Arumugam, A Hogart-Begtrup, L Martin, H Saal, R Hopkin, G Zhang
Row 3: S Ware, W Nichols, Y Sun, S Oh, R Li, L Bao, P Goldenberg
Row 4: R Stottmann, M Keddache, D Prows, M Pandey, D Neilson, I Sageser, M Myers

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

Raimundo, N., Song, L., Shutt, T.E., McKay, S.E., Cotney, J., **Guan, M.X**., Gilliland, T.C., Hohuan, D., Santos-Sacchi, J., and Shadel, G.S. **Mitochondrial stress engages E2F1 apoptotic signaling to cause deafness**. *Cell.* 148:716-726. 2012.

This article defines a new mechanism for deafness causation.

Martin, L.J., Gupta, J., Jyothula, S.S., Butsch Kovacic, M., Biagini Myers, J.M., Patterson, T.L., Ericksen, M.B., He, H., Gibson, A.M., Baye, T.M., et al. **Functional variant in the autophagy-related 5 gene promotor is associated with childhood asthma.***PLoS One.* 7:e33454. 2012.

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

Mazzulli, J.R., **Xu, Y.H**., **Sun, Y**., Knight, A.L., McLean, P.J., Caldwell, G.A., Sidransky, E., **Grabowski, G.A**., and Krainc, D.. **Gaucher disease glucocerebrosidase and alpha-synuclein form a bidirectional pathogenic loop in synucleinopathies**. *Cell.* 146:37-52. 2011.

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

Sivakumaran, T.A., Igo, R.P., Jr., Kidd, J.M., Itsara, A., Kopplin, L.J., Chen, W., Hagstrom, S.A., Peachey, N.S., Francis, P.J., Klein, M.L., et al. **A 32 kb critical region excluding Y402H in CFH mediates risk for age-related macular degeneration.** *PLoS One* 6:e25598. 2011.

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

Zhang, K., Jordan, M.B., Marsh, R.A., Johnson, J.A., Kissell, D., Meller, J., Villanueva, J., Risma, K.A., Wei, Q., Klein, P.S., et al. **Hypomorphic mutations in PRF1, MUNC13-4, and STXBP2 are associated with adult-onset familial HLH**. *Blood.* 118:5794-5798. 2011.

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**

transient embryonic zones of the cerebral cortex defined by high-resolution mRNA sequencing. *Proc Natl Acad Sci U S A*. 2011; 108:14950-5.

2. Baye TM, He H, Ding L, Kurowski BG, Zhang X, Martin LJ. **Population structure analysis using rare and common functional variants**. *BMC Proc*. 2011; 5 Suppl 9:S8.
3. Bookman LB, Melton KR, Pan BS, Bender PL, Chini BA, Greenberg JM, Saal HM, Taylor JA, Elluru RG. **Neonates with tongue-based airway obstruction: a systematic review**. *Otolaryngol Head Neck Surg*. 2012; 146:8-18.
4. Chartier-Harlin MC, Dachsel JC, Vilarino-Guell C, Lincoln SJ, Lepretre F, Hulihan MM, Kachergus J, Milnerwood AJ, Tapia L, Song MS, Le Rhun E, Mutez E, Larvor L, Duflot A, Vanbesien-Mailliot C, Kreisler A, Ross OA, Nishioka K, Soto-Ortolaza AI, Cobb SA, Melrose HL, Behrouz B, Keeling BH, Bacon JA, Hentati E, Williams L, Yanagiya A, Sonenberg N, Lockhart PJ, Zubair AC, Uitti RJ, Aasly JO, Krygowska-Wajs A, Opala G, Wszolek ZK, Frigerio R, Maraganore DM, Gosal D, Lynch T, Hutchinson M, Bentivoglio AR, Valente EM, Nichols WC, Pankratz N, Foroud T, Gibson RA, Hentati F, Dickson DW, Destee A, Farrer MJ. **Translation initiator EIF4G1 mutations in familial Parkinson disease**. *Am J Hum Genet*. 2011; 89:398-406.
5. Chen H, Zheng J, Xue L, Meng Y, Wang Y, Zheng B, Fang F, Shi S, Qiu Q, Jiang P, Lu Z, Mo JQ, Lu J, Guan MX. **The 12S rRNA A1555G mutation in the mitochondrial haplogroup D5a is responsible for maternally inherited hypertension and hearing loss in two Chinese pedigrees**. *Eur J Hum Genet*. 2012; 20:607-12.
6. Cotney J, Leng J, Oh S, Demare LE, Reilly SK, Gerstein MB, Noonan JP. **Chromatin state signatures associated with tissue-specific gene expression and enhancer activity in the embryonic limb**. *Genome Res*. 2012; 22:1069-80.
7. Ding L, Baye TM, He H, Zhang X, Kurowski BG, Martin LJ. **Detection of associations with rare and common SNPs for quantitative traits: a nonparametric Bayes-based approach**. *BMC Proc*. 2011; 5 Suppl 9:S10.
8. Ding L, Wiener H, Abebe T, Altaye M, Go RC, Kercsmar C, Grabowski GA, Martin LJ, Hershey GK, Chakorborty R, Baye TM. **Comparison of measures of marker informativeness for ancestry and admixture mapping**. *BMC Genomics*. 2011; 12:622.
9. Epstein TG, LeMasters GK, Bernstein DI, Ericksen MB, Martin LJ, Ryan PH, Biagini Myers JM, Butsch Kovacic MS, Lindsey MA, He H, Reponen T, Villareal MS, Lockey JE, Bernstein CK, Hershey GK. **Genetic variation in small proline rich protein 2B as a predictor for asthma among children with eczema**. *Ann Allergy Asthma Immunol*. 2012; 108:145-50.
10. Grabowski GA, Charnas LW, Du H. (2012) **Lysosomal Acid Lipase Deficiencies: The Wolman Disease/Cholesteryl Ester Storage Disease Spectrum**. The Metabolic and Molecular Bases of Inherited Disease. New York, McGraw-Hill. .
11. Grabowski GA, Hopkin RJ. **Lysosomal Storage Diseases**. *Harrison's Principles of Internal Medicine*. New York: McGraw-Hill; 2012:3191-3197.
12. He H, Zhang X, Ding L, Baye TM, Kurowski BG, Martin LJ. **Effect of population stratification analysis on false-positive rates for common and rare variants**. *BMC Proc*. 2011; 5 Suppl 9:S116.
13. He X, Galpin JD, Tropak MB, Mahuran D, Haselhorst T, von Itzstein M, Kolarich D, Packer NH, Miao Y, Jiang L, Grabowski GA, Clarke LA, Kermode AR. **Production of active human glucocerebrosidase in seeds of Arabidopsis thaliana complex-glycan-deficient (cgl) plants**. *Glycobiology*. 2012; 22:492-503.
14. Kanetzke EE, Lynch J, Prows CA, Siegel RM, Myers MF. **Perceived utility of parent-generated family health history as a health promotion tool in pediatric practice**. *Clin Pediatr (Phila)*. 2011; 50:720-8.
15. Karns R, Zhang G, Sun G, Rao Indugula S, Cheng H, Havas-Augustin D, Novokmet N, Rudan D, Durakovic Z, Missoni S, Chakraborty R, Rudan P, Deka R. **Genome-wide association of serum uric acid concentration: replication of sequence variants in an island population of the Adriatic coast of Croatia**. *Ann Hum Genet*. 2012; 76:121-7.

16. Kovacic MB, Myers JM, Wang N, Martin LJ, Lindsey M, Ericksen MB, He H, Patterson TL, Baye TM, Torgerson D, Roth LA, Gupta J, Sivaprasad U, Gibson AM, Tsoras AM, Hu D, Eng C, Chapela R, Rodriguez-Santana JR, Rodriguez-Cintron W, Avila PC, Beckman K, Seibold MA, Gignoux C, Musaad SM, Chen W, Burchard EG, Hershey GK. **Identification of KIF3A as a novel candidate gene for childhood asthma using RNA expression and population allelic frequencies differences**. *PLoS One*. 2011; 6:e23714.
17. Krone N, Reisch N, Idkowiak J, Dhir V, Ivison HE, Hughes BA, Rose IT, O'Neil DM, Vijzelaar R, Smith MJ, MacDonald F, Cole TR, Adolphs N, Barton JS, Blair EM, Braddock SR, Collins F, Cragun DL, Dattani MT, Day R, Dougan S, Feist M, Gottschalk ME, Gregory JW, Haim M, Harrison R, Olney AH, Hauffa BP, Hindmarsh PC, Hopkin RJ, Jira PE, Kempers M, Kerstens MN, Khalifa MM, Kohler B, Maiter D, Nielsen S, O'Riordan SM, Roth CL, Shane KP, Silink M, Stikkelbroeck NM, Sweeney E, Szarras-Czapnik M, Waterson JR, Williamson L, Hartmann MF, Taylor NF, Wudy SA, Malunowicz EM, Shackleton CH, Arlt W. **Genotype-phenotype analysis in congenital adrenal hyperplasia due to P450 oxidoreductase deficiency**. *J Clin Endocrinol Metab*. 2012; 97:E257-67.
18. Latourelle JC, Hendricks AE, Pankratz N, Wilk JB, Halter C, Nichols WC, Gusella JF, Destefano AL, Myers RH, Foroud T. **Genomewide linkage study of modifiers of LRRK2-related Parkinson's disease**. *Mov Disord*. 2011; 26:2039-44.
19. Leon L, Tatituri RV, Grenha R, Sun Y, Barral DC, Minnaard AJ, Bhowruth V, Veerapen N, Besra GS, Kasmar A, Peng W, Moody DB, Grabowski GA, Brenner MB. **Saposins utilize two strategies for lipid transfer and CD1 antigen presentation**. *Proc Natl Acad Sci U S A*. 2012; 109:4357-64.
20. Liou B, Grabowski GA. **Is E326K glucocerebrosidase a polymorphic or pathological variant?**. *Mol Genet Metab*. 2012; 105:528-9.
21. Lu TX, Sherrill JD, Wen T, Plassard AJ, Besse JA, Abonia JP, Franciosi JP, Putnam PE, Eby M, Martin LJ, Aronow BJ, Rothenberg ME. **MicroRNA signature in patients with eosinophilic esophagitis, reversibility with glucocorticoids, and assessment as disease biomarkers**. *J Allergy Clin Immunol*. 2012; 129:1064-75 e9.
22. Lu Z, Chen H, Meng Y, Wang Y, Xue L, Zhi S, Qiu Q, Yang L, Mo JQ, Guan MX. **The tRNAMet 4435A>G mutation in the mitochondrial haplogroup G2a1 is responsible for maternally inherited hypertension in a Chinese pedigree**. *Eur J Hum Genet*. 2011; 19:1181-6.
23. Lynch J, Parrott A, Hopkin RJ, Myers M. **Media coverage of direct-to-consumer genetic testing**. *J Genet Couns*. 2011; 20:486-94.
24. Martin LJ, Gupta J, Jyothula SS, Butsch Kovacic M, Biagini Myers JM, Patterson TL, Ericksen MB, He H, Gibson AM, Baye TM, Amirisetty S, Tsoras AM, Sha Y, Eissa NT, Hershey GK. **Functional variant in the autophagy-related 5 gene promotor is associated with childhood asthma**. *PLoS One*. 2012; 7:e33454.
25. Martin LJ, Hinton RB, Zhang X, Cripe LH, Benson DW. **Aorta Measurements are Heritable and Influenced by Bicuspid Aortic Valve**. *Front Genet*. 2011; 2:61.
26. Martin LJ, Kissebah AH, Olivier M. **Accounting for a quantitative trait locus for plasma triglyceride levels: utilization of variants in multiple genes**. *PLoS One*. 2012; 7:e34614.
27. Martin LJ, Lee SY, Couch SC, Morrison J, Woo JG. **Shared genetic contributions of fruit and vegetable consumption with BMI in families 20 y after sharing a household**. *Am J Clin Nutr*. 2011; 94:1138-43.
28. Mazzulli JR, Xu YH, Sun Y, Knight AL, McLean PJ, Caldwell GA, Sidransky E, Grabowski GA, Krainc D. **Gaucher disease glucocerebrosidase and alpha-synuclein form a bidirectional pathogenic loop in synucleinopathies**. *Cell*. 2011; 146:37-52.
29. Mendell JR, Shilling C, Leslie ND, Flanigan KM, al-Dahhak R, Gastier-Foster J, Kneile K, Dunn DM, Duval B, Aoyagi A, Hamil C, Mahmoud M, Roush K, Bird L, Rankin C, Lilly H, Street N, Chandrasekar R, Weiss RB. **Evidence-based path to newborn screening for Duchenne muscular dystrophy**. *Ann Neurol*. 2012;

71:304-13.
30. Miller EM, Hopkin R, Bao L, Ware SM. **Implications for genotype-phenotype predictions in Townes-Brocks syndrome: case report of a novel SALL1 deletion and review of the literature**. *Am J Med Genet A*. 2012; 158A:533-40.
31. Mushaben EM, Hershey GK, Pauciulo MW, Nichols WC, Le Cras TD. **Chronic allergic inflammation causes vascular remodeling and pulmonary hypertension in BMPR2 hypomorph and wild-type mice**. *PLoS One*. 2012; 7:e32468.
32. Myers K, Davies SM, Harris RE, Spunt SL, Smolarek T, Zimmerman S, McMasters R, Wagner L, Mueller R, Auerbach AD, Mehta PA. **The clinical phenotype of children with Fanconi anemia caused by biallelic FANCD1/BRCA2 mutations**. *Pediatr Blood Cancer*. 2012; 58:462-5.
33. Myers KC, Bleesing JJ, Davies SM, Zhang X, Martin LJ, Mueller R, Harris RE, Filipovich AH, Kovacic MB, Wells SI, Mehta PA. **Impaired immune function in children with Fanconi anaemia**. *Br J Haematol*. 2011; 154:234-40.
34. Myers M, Baugh C. **Genetic contribution to health in Appalachia**. *Appalachian Health and Well-Being*. Lexington, KY: University Press of Kentucky; 2012.
35. Myers MF. **Health care providers and direct-to-consumer access and advertising of genetic testing in the United States**. *Genome Med*. 2011; 3:81.
36. Myers MF, Bernhardt BA. **Direct-to-Consumer Genetic Testing: Introduction to the Special Issue**. *J Genet Couns*. 2012; 21:357-60.
37. Pankratz N, Dumitriu A, Hetrick KN, Sun M, Latourelle JC, Wilk JB, Halter C, Doheny KF, Gusella JF, Nichols WC, Myers RH, Foroud T, DeStefano AL. **Copy number variation in familial Parkinson disease**. *PLoS One*. 2011; 6:e20988.
38. Patek KJ, Kline-Fath BM, Hopkin RJ, Pilipenko VV, Crombleholme TM, Spaeth CG. **Posterior fossa anomalies diagnosed with fetal MRI: associated anomalies and neurodevelopmental outcomes**. *Prenat Diagn*. 2012; 32:75-82.
39. Prada CE, Al Jasmi F, Kirk EP, Hopp M, Jones O, Leslie ND, Burrow TA. **Cardiac disease in methylmalonic acidemia**. *J Pediatr*. 2011; 159:862-4.
40. Prada CE, Rangwala FA, Martin LJ, Lovell AM, Saal HM, Schorry EK, Hopkin RJ. **Pediatric plexiform neurofibromas: impact on morbidity and mortality in neurofibromatosis type 1**. *J Pediatr*. 2012; 160:461-7.
41. Prada CE, Sellars EA, Spaeth CG, Kline-Fath BM, Crombleholme TM, Hopkin RJ. **Severe cervical scoliosis in the fetus**. *Prenat Diagn*. 2011; 31:1198-202.
42. Prada CE, Zarate YA, Hopkin RJ. **Genetic causes of macroglossia: diagnostic approach**. *Pediatrics*. 2012; 129:e431-7.
43. Prochniak CF, Martin LJ, Miller EM, Knapke SC. **Barriers to and motivations for physician referral of patients to cancer genetics clinics**. *J Genet Couns*. 2012; 21:305-25.
44. Prows DR, Gibbons WJ, Jr., Burzynski BB. **Synchronizing allelic effects of opposing quantitative trait loci confirmed a major epistatic interaction affecting acute lung injury survival in mice**. *PLoS One*. 2012; 7:e38177.
45. Qian Y, Zhou X, Liang M, Qu J, Guan MX. **The altered activity of complex III may contribute to the high penetrance of Leber's hereditary optic neuropathy in a Chinese family carrying the ND4 G11778A mutation**. *Mitochondrion*. 2011; 11:871-7.
46. Raimundo N, Song L, Shutt TE, McKay SE, Cotney J, Guan MX, Gilliland TC, Hohuan D, Santos-Sacchi J, Shadel GS. **Mitochondrial stress engages E2F1 apoptotic signaling to cause deafness**. *Cell*. 2012; 148:716-26.
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. *Pediatrics*. 2012; 129:832-8.

48. Saldana SN, Hooper DK, Froehlich TE, Campbell KM, Prows CA, Sadhasivam S, Nick TG, Seid M, Vinks AA, Glauser TA. **Characteristics of successful recruitment in prospective pediatric pharmacogenetic studies**. *Clin Ther*. 2011; 33:2072-81.
49. Saltzman RW, Monaco-Shawver L, Zhang K, Sullivan KE, Filipovich AH, Orange JS. **Novel mutation in STXBP2 prevents IL-2-induced natural killer cell cytotoxicity**. *J Allergy Clin Immunol*. 2012; 129:1666-8.
50. Sardi SP, Clarke J, Kinnecom C, Tamsett TJ, Li L, Stanek LM, Passini MA, Grabowski GA, Schlossmacher MG, Sidman RL, Cheng SH, Shihabuddin LS. **CNS expression of glucocerebrosidase corrects alpha-synuclein pathology and memory in a mouse model of Gaucher-related synucleinopathy**. *Proc Natl Acad Sci U S A*. 2011; 108:12101-6.
51. Sheridan R, Lampe K, Shanmukhappa SK, Putnam P, Keddache M, Divanovic S, Bezerra J, Hoebe K. **Lampe1: an ENU-germline mutation causing spontaneous hepatosteatosis identified through targeted exon-enrichment and next-generation sequencing**. *PLoS One*. 2011; 6:e21979.
52. Sivakumaran TA, Igo RP, Jr., Kidd JM, Itsara A, Kopplin LJ, Chen W, Hagstrom SA, Peachey NS, Francis PJ, Klein ML, Chew EY, Ramprasad VL, Tay WT, Mitchell P, Seielstad M, Stambolian DE, Edwards AO, Lee KE, Leontiev DV, Jun G, Wang Y, Tian L, Qiu F, Henning AK, LaFramboise T, Sen P, Aarthi M, George R, Raman R, Das MK, Vijaya L, Kumaramanickavel G, Wong TY, Swaroop A, Abecasis GR, Klein R, Klein BE, Nickerson DA, Eichler EE, Iyengar SK. **A 32 kb critical region excluding Y402H in CFH mediates risk for age-related macular degeneration**. *PLoS One*. 2011; 6:e25598.
53. Stottmann RW, Moran JL, Turbe-Doan A, Driver E, Kelley M, Beier DR. **Focusing forward genetics: a tripartite ENU screen for neurodevelopmental mutations in the mouse**. *Genetics*. 2011; 188:615-24.
54. Stottmann RW, Turbe-Doan A, Tran P, Kratz LE, Moran JL, Kelley RI, Beier DR. **Cholesterol metabolism is required for intracellular hedgehog signal transduction in vivo**. *PLoS Genet*. 2011; 7:e1002224.
55. Sun Y, Liou B, Xu YH, Quinn B, Zhang W, Hamler R, Setchell KD, Grabowski GA. **Ex vivo and in vivo effects of isofagomine on acid beta-glucosidase variants and substrate levels in Gaucher disease**. *J Biol Chem*. 2012; 287:4275-87.
56. Tariq M, Belmont JW, Lalani S, Smolarek T, Ware SM. **SHROOM3 is a novel candidate for heterotaxy identified by whole exome sequencing**. *Genome Biol*. 2011; 12:R91.
57. Tonkin E, Calzone K, Jenkins J, Lea D, Prows C. **Genomic Education Resources for Nursing Faculty**. *J Nurs Scholarsh*. 2011; 43:330-340.
58. Urbina EM, Gao Z, Khoury PR, Martin LJ, Dolan LM. **Insulin resistance and arterial stiffness in healthy adolescents and young adults**. *Diabetologia*. 2012; 55:625-31.
59. Wagner LM, Smolarek TA, Sumegi J, Marmer D. **Assessment of minimal residual disease in ewing sarcoma**. *Sarcoma*. 2012; 2012:780129.
60. Wang C, Wang Z, Prows DR, Wu R. **A computational framework for the inheritance pattern of genomic imprinting for complex traits**. *Brief Bioinform*. 2012; 13:34-45.
61. Williams JK, Prows CA, Conley YP, Eggert J, Kirk M, Nichols F. **Strategies to prepare faculty to integrate genomics into nursing education programs**. *J Nurs Scholarsh*. 2011; 43:231-238.
62. Woo JG, Guerrero ML, Guo F, Martin LJ, Davidson BS, Ortega H, Ruiz-Palacios GM, Morrow AL. **Human milk adiponectin affects infant weight trajectory during the second year of life**. *J Pediatr Gastroenterol Nutr*. 2012; 54:532-9.
63. Xu YJ, Wang J, Xu R, Zhao PJ, Wang XK, Sun HJ, Bao LM, Shen J, Fu QH, Li F, Sun K. **Detecting 22q11.2 deletion in Chinese children with conotruncal heart defects and single nucleotide polymorphisms in the haploid TBX1 locus**. *BMC Med Genet*. 2011; 12:169.

64. Yadav JS, Pradhan S, Kapoor R, Bangar H, Burzynski BB, Prows DR, Levin L. **Multigenic control and sex bias in host susceptibility to spore-induced pulmonary anthrax in mice**. *Infect Immun*. 2011; 79:3204-15.
65. Yan X, Wang X, Wang Z, Sun S, Chen G, He Y, Mo JQ, Li R, Jiang P, Lin Q, Sun M, Li W, Bai Y, Zhang J, Zhu Y, Lu J, Yan Q, Li H, Guan MX. **Maternally transmitted late-onset non-syndromic deafness is associated with the novel heteroplasmic T12201C mutation in the mitochondrial tRNAHis gene**. *Journal of Medical Genetics*. 2011; 48:682-90.
66. Zhang G, Karns R, Sun G, Indugula SR, Cheng H, Havas-Augustin D, Novokmet N, Rudan D, Durakovic Z, Missoni S, Chakraborty R, Rudan P, Deka R. **Extent of height variability explained by known height-associated genetic variants in an isolated population of the Adriatic coast of Croatia**. *PLoS One*. 2011; 6:e29475.
67. Zhang K, Jordan MB, Marsh RA, Johnson JA, Kissell D, Meller J, Villanueva J, Risma KA, Wei Q, Klein PS, Filipovich AH. **Hypomorphic mutations in PRF1, MUNC13-4, and STXBP2 are associated with adult-onset familial HLH**. *Blood*. 2011; 118:5794-8.
68. Zhang X, He H, Ding L, Baye TM, Kurowski BG, Martin LJ. **Family- and population-based designs identify different rare causal variants**. *BMC Proc*. 2011; 5 Suppl 9:S36.
69. Zheng J, Ji Y, Guan MX. **Mitochondrial tRNA mutations associated with deafness**. *Mitochondrion*. 2012; 12:406-13.
70. Zhou X, Fang M, Li J, Prows DR, Yang R. **Characterization of genomic imprinting effects and patterns with parametric accelerated failure time model**. *Mol Genet Genomics*. 2012; 287:67-75.

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 neurofribromatosis; 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		Annual Direct
GRABOWSKI, G		
Cincinnati Regional Genetics Center		
Health Resources & Services Administration(Ohio Department of Health)		
03130011GS0310	07/01/04-06/30/12	$349,000
Lysosomal Disease Network: Epidemiology and Natural History of Wolman Disease and Cholesteryl Ester Storage Disease		
National Institutes of Health(University of Minnesota)		
U54 NS 065768	09/30/09-08/31/12	$40,000
Studies of Gaucher Disease: A Prototype Lipidosis		
National Institutes of Health		
R01 DK 036729	09/27/07-08/31/12	$283,879
Oxley Grant		
The Oxley Foundation		
	12/1/2011-11/30/2012	$93,946
Cincinnati Center for Excellence in Molecular Hematology (Genomics Core)		
National Institutes of Health		
P30 DK 090971	09/30/10-06/30/15	$63,000
KEDDACHE, M		
Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease - Sequencing Core		
Ntl Inst of Diab & Digest & Kidney Dis		
P30 DK 078392	6/1/2012-5/31/2017	$34,790
KNAPKE, S		
Hereditary Breast & Ovarian Cancer Syndrome		
Komen Breast Cancer Foundation		
	04/01/10-03/31/13	$31,750
LESLIE, N		
Inborn Errors of Metabolism Collaborative: Defining the Natural History		
National Institutes of Health(Michigan Public Health Institute)		
R01 HD 069039	04/15/11-03/31/16	$26,292
MARTIN, L		
Epithelial Genes in Allergic Inflammation		
Ntl Inst of Allergy & Infections Dis		
U19AI070235	9/1/2011-8/31/2012	$89,000
MYERS, M		
Professional Service Contract - Type 2 Diabetes and Social Networks		
National Institutes of Health		
HHSN26820110029IP	07/01/11-06/30/12	$30,000
Social Influence of Family Networks on T2D Risk Perceptiions and Health Behavior		
National Institutes of Health		
K18 DK 095473	09/19/11-09/18/12	$67,578
NICHOLS, W		
Genetic Analysis of Murine Chronic Hypoxia-Induced Pulmonary Hypertension		
National Institutes of Health		
R01 HL 102107	04/01/10-03/31/14	$436,572
National Biological Sample and Data Repository for PAH		

National Institutes of Health
R24 HL 105333 03/03/12-02/28/17 $1,455,419

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

SCHORRY, E

Genetic & Epigenetic Diffencese 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 Pulmomary 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