

Division Data Summary

Research and Training Details

Number of Faculty	6
Number of Research Fellows	6
Number of Research Students	1
Number of Support Personnel	13
Direct Annual Grant Support	\$1,472,994
Peer Reviewed Publications	16

Clinical Activities and Training

Number of Clinical Staff	1
Number of Clinical Fellows	1
Number of Other Students	6
Inpatient Encounters	26
Outpatient Encounters	223

Division Photo



Row 1: H Ji, U Sivaprasad, G Khurana Hershey
Row 2: M Butsch Kovacic, T Mersha, W Chen

Significant Publications

Baye TM, **Butsch Kovacic M**, Biagini Myers JM, Martin LJ, Lindsey M, Patterson TL, He H, Ericksen MB, Gupta J, Tsoras AM, Lindsley A, Rothenberg ME, Wills-Karp M, Eissa NT, Borish L, **Hershey GKK**. **Differences in Candidate Gene Association between European Ancestry and African American Asthmatic Children.** *PLoS ONE*. 6(2): e16522. Feb 28, 2011.

Candidate gene case-control studies have identified several single nucleotide polymorphisms (SNPs) that are associated with asthma susceptibility. Most of these studies have been restricted to evaluations of specific SNPs within a single gene and within populations from European ancestry. Recently, there is an increasing interest in understanding racial differences in genetic risk associated with childhood asthma. Our aim was to compare association patterns of asthma candidate genes between children of European and African ancestry.

Sivaprasad U, Askew DJ, Ericksen MB, Gibson AM, Stier MS, Brandt E, Bass SA, Daines MO, Chakir J, Stringer KF, Wert SE, Whitsett JA, Le Cras TD, Wills-Karp M, Silverman GA, **Hershey GKK**. **A non-redundant role for mouse *Serpina3a* in the induction of mucus production in asthma.** *J Allergy Clin. Immunol.* 127(1):254-261.e6. 2010.

Asthma is a major public health burden worldwide. Studies from our group and others have demonstrated that SERPINB3 and SERPINB4 are induced in patients with asthma; however, their mechanistic role in asthma has yet to be determined.

Division Highlights

Asthma Research

A Pyrosequencing Core was approved by Research Administration and will be run by Asthma Research personnel. It is the first core managed by the division. It has a dedicated faculty member and staff member, and is located on the 8th floor of the S Building. There are external and internal marketing and public relations plans to assure that this core is advertised to a regional and national audience.

The two primary core objectives are:

1. To provide services to accurately measure DNA methylation level in a locus specific manner in a 96 well format, suitable for large-scale high-throughput validation analysis.
2. To provide services for mutation analysis and genotyping, suitable for detection, and quantification of genetic variations including insertion-deletions, single nucleotide polymorphisms, single tandem repeats, and variable gene copy number.

Also, the division increased its grant, contract and award volume by 18 percent during the past year. The dollar volume rose by 10 percent. It was a superb year given that NIH and many agencies restricted the volume of grants awarded, as well as the amount of funding per award. Dr. Brandt was awarded a third year of funding on a T32 grant, which originally had a two year award period.

Dr. Melinda Butsch Kovacic was selected to attend the Association Medical Colleges Early Career Women Faculty Professional Development Seminar in Washington, DC.

Dr. Tesfaye Mersha was selected as an editor for the *Frontiers in Applied Genetic Epidemiology*.

Dr. Umasundari Sivaprasad was a recipient of the *University of Cincinnati Research Council* grant.

Division Collaboration

Allergy/Immunology; Immunobiology; Biostatistics and Epidemiology; Human Genetics; Pathology » Marc Rothenberg, MD, PhD; Marsha Wills-Karp, PhD; Lisa Martin, PhD; Keith Stringer, MD

Asthma and Allergic Diseases Cooperative Research Center funded by the NIH.

Emergency Medicine; Pulmonary Medicine; General and Community Pediatrics; Adherence Psychology; Biomedical Informatics; Allergy/Immunology » Richard Ruddy, MD; Rick Strait, MD; Carolyn Kerckmar, MD; Jeffrey Simmons, MD; Rob Kahn, MD; Dennis Drotar, PhD; Bruce Aronow, PhD

Asthma Nasal Epithelial Study: A collaborative study determining the molecular heterogeneity of the gene expression profile in response to the treatment of acute asthma exacerbations in hospitalized children with asthma.

Pulmonary Medicine » Carolyn Kerckmar, MD; Karen McDowell, MD; Gary McPhail, MD

The Division of Asthma Research has partnered with the Asthma Center to form the CCHMC Asthma Program to improve the health of children with asthma by integrating evidence-based clinical care with innovative research that will lead to personalized asthma therapy for the children living in the Greater Cincinnati. Drs. Gurjit Khurana Hershey and Carolyn Kerckmar were recently awarded a \$2.8M grant to participate in a national study aimed at preventing asthma in inner-city children. The asthma research is being done as part of an 11-site group called the "Inner City Asthma Consortium".

Neonatology and Pulmonary Biology » Tim Le Cras, PhD

Impact of Early Life Diesel Exposure on Immune Patterning and Lung Structure/Function grant.

Hematology/Oncology » Susanne Wells, PhD

HPV Replication and Transformation in FA Squamous Cell Carcinomas; HPV Prevalence Studies in Fanconi

Anemia Population.

Dermatology; Allergy/Immunology; Immunobiology; Hematology/Oncology » Anne Lucky, MD; Marc Rothenberg, MD, PhD; Fred Finkelman, MD

Role of IL-13 Receptors in Atopic Dermatitis grant.

Faculty Members

Gurjit Khurana Hershey, MD, PhD, Professor

Division Director

Kindervelt Endowed Chair

Associate Director, Physician Scientist Training Program

Research Interests Elucidating the mechanisms of allergic inflammation and asthma. The research centers on identifying genes important in asthma and allergy.

Melinda Butsch Kovacic, MPH, PhD, Assistant Professor

Research Interests Using classical and molecular epidemiological approaches to evaluate environmental, infectious, genetic, and socioeconomic causes of chronic disease with current focuses on asthma and Fanconi anemia.

Weiguo Chen, MD, PhD, Assistant Professor

Research Interests Mechanisms underlying airway hyperresponsiveness, inflammation and remodeling of allergic asthma.

Hong Ji, PhD, Assistant Professor

Research Interests Epigenetic plasticity of development and disease; asthma epigenetics; genome-wide and locus specific DNA methylation analysis; epigenetic regulation of gene expression

Tesfaye Mersha, PhD, Assistant Professor

Research Interests Integrating and using genomics, statistical genetics, biological profiling and pathway methods to elucidate the genetic architecture of complex diseases of public significance, including asthma.

Umasundari Sivaprasad, PhD, Assistant Professor

Research Interests Allergic inflammation; atopic dermatitis; asthma; development of anti-inflammatory therapies

Trainees

- Rachael Mintz-Cole, BS, PL-4, University of Cincinnati
- Jayanta Gupta, MD/PhD, PGY7, University of Cincinnati
- Eric Brandt, PhD, PGY11, Institut Pasteur de Lille, France
- Hyun-Bae Jie, PhD, PGY10, Harvard Medical School
- Jocelyn Biagini Myers, PhD, PGY3, University of Cincinnati
- Gerald Lee, MD, PGY3, University of Cincinnati
- Lili Ding, PhD, PY1, University of Cincinnati
- Zhouyang Weng, PhD, PY1, University of Cincinnati
- Zonghua Zhang, MD, Vanderbilt University

Significant Accomplishments

Cooperative Research Grant

Our Asthma and Allergic Diseases Cooperative Research Center (AADCRC) is one of only 12 such centers in the United States. Gurjit Khurana Hershey, MD, PhD, is the principal investigator for this center, which received a renewal of its NIH-funded U19 grant this year.

The center's overarching hypothesis is that epithelial cell genes play a central role in the pathogenesis of allergic disorders. Thus far, 10 peer-reviewed papers and five review articles and/or chapters have resulted from this grant.

Hershey, who also serves on the AACRC steering committee, will continue to investigate the genetics of allergy-driven epithelial genes in children with asthma, atopic dermatitis and/or food allergy to identify shared and unique genes and pathways.

Inner City Asthma Consortium

Cincinnati Children's was selected this year to join the NIAID-funded Inner City Asthma Research Consortium (ICAC). The consortium, which includes 11 research centers, is the nation's largest effort to study the factors that promote asthma in an inner city environment. Gurjit Khurana Hershey is the principal investigator for the Cincinnati Children's subcontract.

The consortium's objectives include conducting clinical studies to improve asthma control, prevent asthma among inner city children, and improve asthma phenotyping using validated biomarkers. The group plans to conduct longitudinal birth cohort studies as well as mechanistic studies involving human subjects to gain information on the early immunopathogenesis of asthma, to identify asthma risk factors for inner city children, and to study the differences in the early immunopathogenesis of asthma between inner city and non-inner city children.

Admixture Mapping in African American Asthmatic Children

This study proposes that disease does not affect all populations equally. Therefore, screening the genome of African American mixed ancestry can be an efficient strategy to identify asthma genes. Tesfaye Mersha, PhD, is developing a program of study that would lead to an in-depth understanding of the genome of African American (AA) admixed populations and develop procedures and methods to localize asthma liability genes by utilizing this information and SNP markers for linkage disequilibrium admixture mapping.

Division Publications

1. Baye TM. **Inter-chromosomal variation in the pattern of human population genetic structure.** *Hum Genomics.* 2011; 5:220-40.
2. Baye TM, Abebe T, Wilke RA. **Genotype-environment interactions and their translational implications.** *Per Med.* 2011; 8:59-70.
3. Baye TM, Butsch Kovacic M, Biagini Myers JM, Martin LJ, Lindsey M, Patterson TL, He H, Ericksen MB, Gupta J, Tsoras AM, Lindsley A, Rothenberg ME, Wills-Karp M, Eissa NT, Borish L, Khurana Hershey GK. **Differences in candidate gene association between European ancestry and African American asthmatic children.** *PLoS One.* 2011; 6:e16522.
4. Baye TM, Martin LJ, Khurana Hershey GK. **Application of genetic/genomic approaches to allergic disorders.** *J Allergy Clin Immunol.* 2010; 126:425-36; quiz 437-8.
5. Baye TM, Wilke RA. **Mapping genes that predict treatment outcome in admixed populations.** *Pharmacogenomics J.* 2010; 10:465-77.
6. Biagini Myers JM, Khurana Hershey GK. **Eczema in early life: genetics, the skin barrier, and lessons**

- learned from birth cohort studies.** *J Pediatr.* 2010; 157:704-14.
7. Epstein TG, Bernstein DI, Levin L, Khurana Hershey GK, Ryan PH, Reponen T, Villareal M, Lockey JE, Lemasters GK. **Opposing effects of cat and dog ownership and allergic sensitization on eczema in an atopic birth cohort.** *J Pediatr.* 2011; 158:265-71 e1-5.
 8. Gawrieh S, Baye TM, Carless M, Wallace J, Komorowski R, Kleiner DE, Andris D, Makladi B, Cole R, Charlton M, Curran J, Dyer TD, Charlesworth J, Wilke R, Blangero J, Kissebah AH, Olivier M. **Hepatic gene networks in morbidly obese patients with nonalcoholic fatty liver disease.** *Obes Surg.* 2010; 20:1698-709.
 9. Le Cras TD, Acciani TH, Mushaben EM, Kramer EL, Pastura PA, Hardie WD, Korfhagen TR, Sivaprasad U, Ericksen M, Gibson AM, Holtzman MJ, Whitsett JA, Hershey GK. **Epithelial EGF receptor signaling mediates airway hyperreactivity and remodeling in a mouse model of chronic asthma.** *Am J Physiol Lung Cell Mol Physiol.* 2011; 300:L414-21.
 10. Newcomb DC, Boswell MG, Zhou W, Huckabee MM, Goleniewska K, Sevin CM, Hershey GK, Kolls JK, Peebles RS, Jr.. **Human TH17 cells express a functional IL-13 receptor and IL-13 attenuates IL-17A production.** *J Allergy Clin Immunol.* 2011; 127:1006-13 e1-4.
 11. Reszka KJ, Sallans L, Macha S, Brown K, McGraw DW, Kovacic MB, Britigan BE. **Airway peroxidases catalyze nitration of the {beta}2-agonist salbutamol and decrease its pharmacological activity.** *J Pharmacol Exp Ther.* 2011; 336:440-9.
 12. Sherrill JD, Gao PS, Stucke EM, Blanchard C, Collins MH, Putnam PE, Franciosi JP, Kushner JP, Abonia JP, Assa'ad AH, Kovacic MB, Biagini Myers JM, Bochner BS, He H, Hershey GK, Martin LJ, Rothenberg ME. **Variants of thymic stromal lymphopoietin and its receptor associate with eosinophilic esophagitis.** *J Allergy Clin Immunol.* 2010; 126:160-5 e3.
 13. Sivaprasad U, Askew DJ, Ericksen MB, Gibson AM, Stier MT, Brandt EB, Bass SA, Daines MO, Chakir J, Stringer KF, Wert SE, Whitsett JA, Le Cras TD, Wills-Karp M, Silverman GA, Khurana Hershey GK. **A nonredundant role for mouse Serpinb3a in the induction of mucus production in asthma.** *J Allergy Clin Immunol.* 2011; 127:254-61, 261 e1-6.
 14. Sivaprasad U, Warriar MR, Gibson AM, Chen W, Tabata Y, Bass SA, Rothenberg ME, Khurana Hershey GK. **IL-13Ralpha2 has a protective role in a mouse model of cutaneous inflammation.** *J Immunol.* 2010; 185:6802-8.
 15. Wang N, Drotar D, Khurana Hershey G. **Pediatric Pharmacogenomics.** *Handbook of Genomics and the Family.* New York: Springer; 2010: 437-456. .
 16. Zhang Y, Smith EM, Baye TM, Eckert JV, Abraham LJ, Moses EK, Kissebah AH, Martin LJ, Olivier M. **Serotonin (5-HT) receptor 5A sequence variants affect human plasma triglyceride levels.** *Physiol Genomics.* 2010; 42:168-76.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards

Annual Direct / Project Period Direct

BRANDT, E.

Molecular Epidemiology in Children's Environmental Health Training Program

National Institutes of Health(University of Cincinnati)

T32 ES010957

07/01/09-03/31/12

\$51,555

BUTSCH KOVACIC, M

Exposure-Induced Systemic Oxidative Stress in Children with Asthma

National Institutes of Health

KHURANA HERSHEY, G**Development of an Asthma Research Core Center**

National Institutes of Health

P30 HL 101333

09/30/09-08/31/11

\$297,108

Role of IL-13 Receptors in Atopic Dermatitis

National Institutes of Health

R01 AR 054490

09/01/07-07/31/12

\$301,610

Inner City Asthma Consortium

National Institutes of Health(University of Wisconsin-Madison)

HHSN272200900052C

03/01/11-09/29/14

\$192,198

KHURANA HERSHEY, G/LECRAS, T (MPI)**Impact of Early Life Diesel Exposure on Immune Patterning and Lung Structure/Function**

National Institutes of Health

R01 HL 097135

09/01/09-07/31/14

\$347,205

MERSHA, T**Admixture Mapping in African American Asthmatic Children**

National Institutes of Health

K01 HL 103165

07/14/10-05/31/15

\$124,996

MINTZ-COLE, R**Regulation of Foxp3 Expression by DNA Methylation in Mold-Induced Asthma**

National Institutes of Health

F30 HL 103087

07/01/10-06/30/14

\$33,322

Current Year Direct**\$1,472,994****Total****\$1,472,994**