Asthma Research

Division Details

Division Data Summary

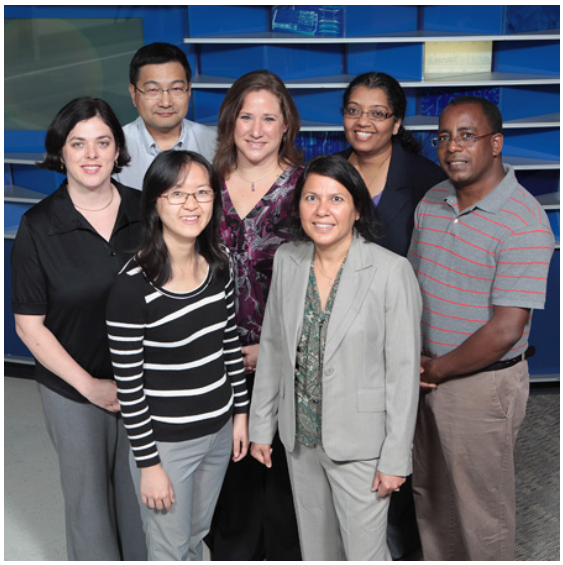
Research and Training Details

Number of Faculty	7
Number of Joint Appointment Faculty	1
Number of Research Fellows	3
Number of Research Students	1
Number of Support Personnel	17
Direct Annual Grant Support	$3,123,602
Peer Reviewed Publications	23

Clinical Activities and Training

Number of Clinical Staff	1
Number of Other Students	5

Division Photo



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

Significant Accomplishments

Pyrosequencing Core

Our Division played a leading role in launching the new Pyrosequencing Core Laboratory for Genomic and Epigenomic Research. This core lab, directed by Hong Ji, PhD, facilitates the study of epigenetic regulation mechanisms underlying normal development and disease pathogenesis. Equipped with a Qiagen PyroMark Q96 system, the core detects and quantifies genetic variation via DNA methylation by pyrosequencing. The core has begun working with several researchers at Cincinnati Children’s and UC. It also helps faculty write grant proposals, two of which have been funded so far.

Inner City Asthma Consortium

Cincinnati Children’s is one of 10 research centers to join the Inner City Asthma Consortium, the nation’s largest effort to study asthma in the inner city. Gurjit Khurana Hershey, MD, PhD, is principal investigator for the Cincinnati site. So far, Cincinnati Children's has been involved in three studies; examining a decrease in fall asthma exacerbations, understanding easy vs. difficult-to-treat asthma, and studying immunotherapy against exposure to German cockroach, the most common species infesting apartments and other urban buildings.

Cooperative Research Grant

Gurjit Khurana Hershey, MD, PhD, also is principal investigator of an NIH-funded Asthma and Allergic Diseases Cooperative Research Center (AADCRC), which focuses on characterizing epithelial genes in allergic diseases.

Hershey also serves on the AADCRC steering committee. Epithelial cell genes play a central role in allergic disorders. The Center's work will provide a basis for developing new therapies aimed at epithelial surfaces in the lung (asthma), on skin (atopic dermatitis), or in the gut (food allergy or eosinophilic esophagitis).

Significant Publications

Hong Ji, **Gurjit K. Khurana Hershey**. **Genetic and Epigenetic Influence on the Response to Environmental Particulate Matter.***J Allergy Clin Immunol.* 129(1):33-41. Jan 2012.

The significance of this review is to summarize recent findings on the genetic and epigenetic regulation of responses to ambient air pollutants, specifically respirable particulate matter, and their association with the development of allergic disorders. Understanding these epigenetic biomarkers and how they integrate with genetic influences to translate the biologic effect of particulate exposure is critical to developing novel preventative and therapeutic strategies for allergic disorders.

Jocelyn M Biagini Myers, **Gurjit K Khurana Hershey**, Prodipto Pal, Ranjan Deka, Jeffrey Burkle, Linda S. Levin, David I. Bernstein, Manuel Villareal, James E. Lockey, Tiina Reponen, Joey Gareri, Angelika Lubetsky, Gideon Koren, Grace K. LeMasters. **Asking the Right Questions to Ascertain Early Childhood Secondhand Smoke Exposures?** *J Pediatr.* 160(6):1050-1. Epub 2012 Apr 10. Jun 2012.

Secondhand smoke is associated with a myriad of adverse health outcomes. Therefore, it is essential for clinicians to ask precise questions about exposures, particularly for children. We present 4 questions that incorporate several locations of exposure and provide a more comprehensive account of children's smoke exposures than maternal smoking alone.

Melinda Butsch Kovacic, Jocelyn Biagini Myers, Ning Wang, Lisa Martin, Mark Lindsey, Mark Erickson, Hua He, Tia Patterson, Tesfaye Mersha, Jayanta Gupta, **Umasundari Sivaprasad**, Aaron Gibson, Anna Tsoras, Donglei Hu, Celeste Eng, Rocio Chapela, Jose Rodriguez-Santa, William Rodriguez-Cintron, Pedro Avila, Kenneth Beckman, Max Seibold, Chris Gignoux, Salma Musaad, **Weiguo Chen**, Esteban Burchard, **Gurjit K. Khurana Hershey**. **A novel unbiased approach identifies the KIF3A gene as an epithelial biomarker of childhood asthma**. *PLoS One* ;6(8):e23714. Epub Aug 30 2011.

Our study demonstrates that KIF3A, a member of the kinesin superfamily of microtubule associated motors that are important in the transport of protein complexes within cilia, is a novel candidate gene for childhood asthma. Polymorphisms in KIF3A may in part be responsible for poor mucus and/or allergen clearance from the airways. Furthermore, our study provides a promising framework for the identification and evaluation of novel candidate susceptibility genes.

Division Publications

1. 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.
2. Bernstein DI, Kissling GE, Khurana Hershey G, Yucesoy B, Johnson VJ, Cartier A, Gautrin D, Sastre J, Boulet LP, Malo JL, Quirce S, Tarlo SM, Langmeyer S, Luster MI, Lummus ZL. **Hexamethylene diisocyanate asthma is associated with genetic polymorphisms of CD14, IL-13, and IL-4 receptor alpha**. *J Allergy Clin Immunol*. 2011; 128:418-20.
3. Biagini Myers JM, Khurana Hershey GK, Deka R, Burkle JW, Levin LS, Bernstein DI, Villareal M, Lockey JE,

Reponen T, Gareri J, Lubetsky A, Koren G, Lemasters GK. **Asking the right questions to ascertain early childhood secondhand smoke exposures**. *J Pediatr*. 2012; 160:1050-1.

4. Butsch Kovacic M, Biagini Myers JM, Lindsey M, Patterson T, Sauter S, Ericksen MB, Ryan P, Assa'ad A, Lierl M, Fischer T, Kercsmar C, McDowell K, Lucky AW, Sheth AP, Hershey AD, Ruddy RM, Rothenberg ME, Khurana Hershey GK. **The Greater Cincinnati Pediatric Clinic Repository: A Novel Framework for Childhood Asthma and Allergy Research**. *Pediatr Allergy Immunol Pulmonol*. 2012; 25:104-113.
5. 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.
6. Ding L, Wiener H, Abebe T, Altaye M, Go RC, Kercsmar C, Grabowski G, Martin LJ, Khurana Hershey GK, Chakorborty R, Baye TM. **Comparison of measures of marker informativeness for ancestry and admixture mapping**. *BMC Genomics*. 2011; 12:622.
7. 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, Khurana 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.
8. Feng Q, Wilke RA, Baye TM. **Individualized risk for statin-induced myopathy: current knowledge, emerging challenges and potential solutions**. *Pharmacogenomics*. 2012; 13:579-94.
9. Ji H, Khurana Hershey GK. **Genetic and epigenetic influence on the response to environmental particulate matter**. *J Allergy Clin Immunol*. 2012; 129:33-41.
10. Kim H, Levin L, LeMasters GK, Villareal M, Evans S, Lockey JE, Khurana Hershey GK, Bernstein DI. **Validating childhood symptoms with physician-diagnosed allergic rhinitis**. *Ann Allergy Asthma Immunol*. 2012; 108:228-31.
11. Koshiol J, Butsch Kovacic M. (2012) **Cytokines and Markers of Immune Response to HPV Infection**. Recent Advances in Immunology to Target Cancer, Inflammation and Infections. Rijeka, Croatia, InTech. 3-22.
12. 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.
13. Kramer EL, Hardie WD, Mushaben EM, Acciani TH, Pastura PA, Korfhagen TR, Hershey GK, Whitsett JA, Le Cras TD. **Rapamycin decreases airway remodeling and hyperreactivity in a transgenic model of noninflammatory lung disease**. *J Appl Physiol*. 2011; 111:1760-7.
14. 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.
15. 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.
16. Mushaben EM, Kramer EL, Brandt EB, Khurana Hershey GK, Le Cras TD. **Rapamycin attenuates airway hyperreactivity, goblet cells, and IgE in experimental allergic asthma**. *J Immunol*. 2011; 187:5756-63.
17. 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.
18. Reponen T, Vesper S, Levin L, Johansson E, Ryan P, Burkle J, Grinshpun SA, Zheng S, Bernstein DI, Lockey J, Villareal M, Khurana Hershey GK, LeMasters G. **High environmental relative moldiness index during**

infancy as a predictor of asthma at 7 years of age. *Ann Allergy Asthma Immunol*. 2011; 107:120-6.

19. Schroer KT, Gibson AM, Sivaprasad U, Bass SA, Ericksen MB, Wills-Karp M, Lecras T, Fitzpatrick AM, Brown LA, Stringer KF, Hershey GK. **Downregulation of glutathione S-transferase pi in asthma contributes to enhanced oxidative stress**. *J Allergy Clin Immunol*. 2011; 128:539-48.
20. Shriner D, Coulibaly I, Ankra-Badu G, Baye TM, Allison DB. **Genetic Contributions to the Development of Obesity**. *Textbook of Obesity: Biological, Psychological and Culture Influences*. New York: John Wiley & Sons, Ltd.; 2012:95-107.
21. Uygungil B, Assa'Ad A, Khurana Hershey GK, Risma K. **Immunodeficiency: a problem with the faucet or the drain?**. *Ann Allergy Asthma Immunol*. 2011; 107:547-9.
22. Wills-Karp M, Rani R, Dienger K, Lewkowich I, Fox JG, Perkins C, Lewis L, Finkelman FD, Smith DE, Bryce PJ, Kurt-Jones EA, Wang TC, Sivaprasad U, Hershey GK, Herbert DR. **Trefoil factor 2 rapidly induces interleukin 33 to promote type 2 immunity during allergic asthma and hookworm infection**. *J Exp Med*. 2012; 209:607-22.
23. 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.

Faculty, Staff, and Trainees

Faculty Members

Gurjit Khurana Hershey, MD, PhD, Professor

Leadership Division Director; Kindervelt Endowed Chair; 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.

Jocelyn Biagini Myers, PhD, Assistant Professor

Research Interests Role of genetics in secondhand smoke-related pediatric asthma.

Melinda Butsch Kovacic, MPH, PhD, Assistant Professor

Leadership Secretary/Treasurer, CCHMC Women's Faculty Association

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

Leadership Director, Pyrosequencing Core

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

- **Eric Brandt, PhD**, PGY12, Institut Pasteur de Lille, France
- **Lili Ding, PhD**, PY2, University of Cincinnati
- **Hyun-Bae Jie, PhD**, PGY10, Harvard Medical School
- **Rachael Mintz-Cole, BS**, PL-5, University of Cincinnati
- **Zonghua Zhang, MD**, PGY2, Vanderbilt University
- **Chang Xiao , MD, PhD**, PY1, University of Cincinnati

Division Collaboration

Allergy/Immunology; ; ; Immunobiology; Human Genetics; Pathology » Marc Rothenberg, MD, PhD, Pablo Abonia, MD, Simon Hogan, PhD, Marsha Wills-Karp, PhD, DeBroski Herbert, PhD, Lisa Martin, PhD, and Keith Stringer, MD

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

Pulmonary Medicine » Carolyn Kercsmar, MD

The Division of Asthma Research partners with the Pulmonary Asthma Center to form the CCHMC Asthma Program to improve the health of children with asthma by integrating the evidence-based clinical care with innovative research that will lead to personalized asthma therapy for children living in the Greater Cincinnati area. Drs. Gurjit Khurana Hershey and Carolyn Kercsmar participate in an NIH-funded study entitled "Inner City Asthma Consortium" aimed at preventing asthma in inner-city children.

Neonatology and Pulmonary Biology » Tim Le Cras, PhD

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

Pulmonary Medicine; Hospital Medicine; Adherence Psychology; General and Community Pediatrics; Emergency Medicine; ; Biomedical Informatics » Carolyn Kercsmar, MD, Jeffrey Simmons, MD, Dennis Drotar, PhD, Rob Kahn, MD, Richard Ruddy, MD, Rick Strait, MD, and 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.

Hematology/Oncology » Susanne Wells, PhD

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

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
BRANDT, E		
Molecular Epidemiology in Children's Environmental Health Training Program National Institutes of Health(University of Cincinnati) T32 ES 10957	07/01/09-03/31/12	$51,681
BUTSCH KOVACIC, M		
Fanconi Anemia as a Model for Susceptibility to Human Papillomavirus Infection		

National Institutes of Health
R01 HL 108102 07/01/11-06/30/16 $265,183

Oxidative Inactivation of ß2-Agonists by Endogenous Peroxidases in the Asthmatic Airway
University of Cincinnati
07/01/11-06/30/12 $39,032

HERSHEY, G

Epithelial Genes in Allergic Inflammation
National Institutes of Health
U19 AI 070235 09/01/11-08/30/16 $999,999

Impact of ADRB2 Polymorphisms on Treatment Response in Children with Acute Asthma Exacerbations
Luther Foundation
01/01/10-12/31/12 $250,000

Inner City Asthma Consortium
National Institutes of Health(University of Wisconsin-Madison)
HHSN272200900052C 03/01/11-09/29/14 $750,249

Role of IL-13 Receptors in Atopic Dermatitis
National Institutes of Health
R01 AR 054490 09/01/07-07/31/12 $257,970

HERSHEY, G / LECRAS, T

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 $356,772

MERSHA, T

Admixture Mapping in African American Asthmatic Children
National Institutes of Health
K01 HL 103165 07/14/10-05/31/15 $118,974

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 $33,742

Current Year Direct $3,123,602

Funded Collaborative Efforts

BUTSCH KOVACIC, M

Community-Based Asthma Intervention Program
The John A Schroth Family Charitable Trust Foundation
Kercsmar, C 01/01/2012-12/31/2012 20%

Total $3,123,602