2013 Research Annual Report

Asthma Research

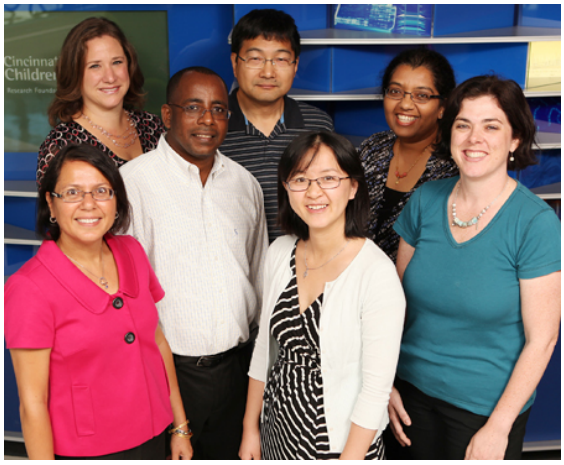
Division Details

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	24
Direct Annual Grant Support	$3,399,272
Peer Reviewed Publications	11

CLINICAL ACTIVITIES AND TRAINING	
Number of Clinical Staff	1
Number of Other Students	11

Division Photo



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

Significant Accomplishments

Ohio Pediatric Asthma Repository Begins Studying Hospital Stays

In 2012, Gurjit Khurana Hershey, MD, PhD and the Division of Asthma Research, working in conjunction with Governor Kasich's office, were awarded a grant from the Ohio Children's Hospital Association (OCHA) and the Ohio Department of Job and Family Services (ODJFS) to develop and lead an asthma research study in conjunction with the five other free-standing children's hospitals in Ohio. Utilizing a new central IRB infrastructure available to research institutions in Ohio, the Ohio Pediatric Asthma Repository (OPAR) began enrollment in December 2012 and now has 905 participants. The six-hospital group will analyze phenotypic, demographic, treatment, and outcome data to look for differences between patients, treatments and site pathways to see what factors impact reutilization and length of hospital stay.

Cincinnati Children's Joins Three Clinical Trials Through 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 the principal investigator for the Cincinnati site. Thus far, Cincinnati Children's has been involved in three clinical trial studies:

- Preventative Omalizumab or Step-up Therapy for Severe Fall Exacerbations, which examines whether the drug therapy decreases autumn-season asthma exacerbations.
- Asthma Phenotypes in the Inner City, which seeks to differentiate easy vs. difficult-to-treat asthma.
- Biomarker-Based Cockroach Sublingual Immunotherapy, which evaluates immunotherapy against exposure to German cockroach, the most common species infesting apartments and other urban buildings.

Cooperative Research Center Studies Epithelial Cell Genes in Allergic Response

Gurjit Khurana Hershey, MD, PhD, is the principal investigator of an NIH-funded Asthma and Allergic Diseases Cooperative Research Center (AADCRC) and serves on the AADCRC steering committee. This Center focuses on characterizing epithelial genes in allergic diseases and delineating the mechanisms by which they contribute to allergic response. The overarching hypothesis is that epithelial cell genes play a central role in the pathogenesis of allergic disorders. The Center provides important insights about genes and pathways that may be important in epithelial-driven allergic inflammation and provides a basis for the design of new therapies aimed at epithelial surfaces, such as the lung in asthma cases, the skin in atopic dermatitis, or the gut in food allergy or eosinophilic esophagitis.

Research Highlights

Melinda Butsch Kovacic, PhD

Dr. Butsch Kovacic's studies have revealed strong associations between health outcomes, biomarkers of oxidative stress and socioeconomic factors. Dr. Butsch Kovacic has partnered with Cincinnati's CoreChange, a grassroots advocacy group, and Seven Hills Neighborhood Houses Center, a full service social service agency and community center in the West End of Cincinnati, to expand her research into the community using a community-based participatory research (CBPR) approach. To this end, we have utilized a $25K gift to implement a community-based research registry, needs assessments using a child-centered PhotoVoice approach and a 7 Health Habits at 7 Hills COACH (Coaching On Achieving Community Health) program. Adult focus groups have also been planned. To support the Seven Hills Center and buttress research efforts, we have partnered with numerous colleges across the University of Cincinnati to form "UCore7H". Some of UCore7H partners include Dr. Gwendolyn Yip-Ono- Community Philanthropist; Dr. Victor Garcia- Division of Pediatric Surgery and Co-founder of CoreChange; Mr. Michael Sharp- Director for UC's Center for Service Learning and Civic Engagment; Dr. Liam Ream - UC's Division of Professional Practice; Dr. Gisela Esco - UC's Vice Provost for Assessment and Student Learning; and Dr. Tina Whalen - Vice Dean of the School of Allied Health.

Hong Ji, PhD

Dr. Ji and her colleagues are actively recruiting children in the Emergency Department who are admitted due to asthma exacerbation. The purpose of this study is to understand the epigenetic basis of different responses to steroid treatment for asthma exacerbation in these children. The identified methylation biomarkers may be used to provide prognostic as well as predictive information to improve patient care for asthmatic children that respond poorly to standard therapy for exacerbation, and may lead to the development of novel therapeutic strategies. Dr. Ji recently received an NIH award to fund the goals of this study.

Tesfaye Mersha, PhD

Dr. Tesfaye Mersha is working on a project focused on examining Ethiopian Jews with asthma living in Israel and in Ethiopia. This study identifies genetically isolated immigrant populations exposed to native and host environments and provides a molecular mechanism to explain the effects of environment on the development and prevalence of asthma phenotypes. Dr. Mersha is collaborating with Dr. Eitan Kerem, Professor and Chairman of Pediatrics of the Hadassah Hebrew University Hospital in Israel, to study Ethopian Jews (living in Israel and in Ethiopia) to answer these important questions: 1) Are there regions of the epigenome that are susceptible to environmental insults occurring before and after immigration? 2) Can epigenetic biomarkers be used to assess the risk of asthma in immigrant populations. The information obtained from this project will contribute to our understanding of these key questions.

Division Publications

1. Amirisetty S, Hershey GK, Baye TM. **AncestrySNPminer: a bioinformatics tool to retrieve and develop ancestry informative SNP panels**. *Genomics*. 2012; 100:57-63.
2. Bienengraeber M, Pellitteri-Hahn M, Hirata N, Baye TM, Bosnjak ZJ, Olivier M. **Quantitative characterization of changes in the cardiac mitochondrial proteome during anesthetic preconditioning and ischemia**. *Physiol Genomics*. 2013; 45:163-70.
3. Brunst KJ, Leung YK, Ryan PH, Khurana Hershey GK, Levin L, Ji H, Lemasters GK, Ho SM. **Forkhead box protein 3 (FOXP3) hypermethylation is associated with diesel exhaust exposure and risk for childhood asthma**. *J Allergy Clin Immunol*. 2013; 131:592-4 e1-3.
4. Brunst KJ, Ryan PH, Lockey JE, Bernstein DI, McKay RT, Khurana Hershey GK, Villareal M, Biagini Myers JM, Levin L, Burkle J, Evans S, Lemasters GK. **Unraveling the relationship between aeroallergen sensitization, gender, second-hand smoke exposure, and impaired lung function**. *Pediatr Allergy Immunol*. 2012; 23:479-87.
5. Hoskins EE, Morreale RJ, Werner SP, Higginbotham JM, Laimins LA, Lambert PF, Brown DR, Gillison ML, Nuovo GJ, Witte DP, Kim MO, Davies SM, Mehta PA, Butsch Kovacic M, Wikenheiser-Brokamp KA, Wells SI. **The fanconi anemia pathway limits human papillomavirus replication**. *J Virol*. 2012; 86:8131-8.
6. Lee GB, Brandt EB, Xiao C, Gibson AM, Le Cras TD, Brown LA, Fitzpatrick AM, Khurana Hershey GK. **Diesel exhaust particles induce cysteine oxidation and s-glutathionylation in house dust mite induced murine asthma**. *PLoS One*. 2013; 8:e60632.
7. Mintz-Cole RA, Gibson AM, Bass SA, Budelsky AL, Reponen T, Hershey GK. **Dectin-1 and IL-17A suppress murine asthma induced by Aspergillus versicolor but not Cladosporium cladosporioides due to differences in beta-glucan surface exposure**. *J Immunol*. 2012; 189:3609-17.
8. Mushaben EM, Brandt EB, Hershey GK, Le Cras TD. **Differential effects of rapamycin and dexamethasone in mouse models of established allergic asthma**. *PLoS One*. 2013; 8:e54426.
9. Newman NC, Ryan P, Lemasters G, Levin L, Bernstein D, Hershey GK, Lockey JE, Villareal M, Reponen T, Grinshpun S, Sucharew H, Dietrich KN. **Traffic-related air pollution exposure in the first year of life and behavioral scores at 7 years of age**. *Environ Health Perspect*. 2013; 121:731-6.
10. Reponen T, Lockey J, Bernstein DI, Vesper SJ, Levin L, Khurana Hershey GK, Zheng S, Ryan P, Grinshpun SA, Villareal M, Lemasters G. **Infant origins of childhood asthma associated with specific molds**. *J Allergy Clin Immunol*. 2012; 130:639-644 e5.
11. Shriner D, Coulibaly I, Ankra-Badu G, Baye T, Allison D. **Genetic contributions to the development of obesity**. In: SR Akabas, SA Lederman, BJ Moore, eds. *Textbook of obesity: biological, psychological, and cultural influences*. Chichester, West Sussex; Ames, Iowa: Wiley-Blackwell; 2013:95-107.

Faculty, Staff, and Trainees

Faculty Members

Gurjit Khurana Hershey, MD, PhD, Professor

Leadership Division Director; Kindervelt Endowed Chair; Director, Medical 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, PY3, University of Cincinnati
Rachael Mintz-Cole, BS, PL-5, University of Cincinnati
Zonghua Zhang, MD, PGY3, Vanderbilt University
Chang Xiao , MD, PhD, PY2, University of Cincinnati

Division Collaboration

Allergy/Immunology; Human Genetics; Pathology » Marc Rothenberg, MD, PhD, Pablo Abonia, MD, Simon Hogan, 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 Cincinnati Children's 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; Human Genetics » Carolyn Kercsmar, MD, Jeffrey Simmons, MD, and Lisa Martin, PhD

Ohio Pediatric Asthma Repository

Hematology/Oncology; Pulmonary Medicine » Susanne Wells, PhD, Stella Davies, PhD, Parinda Mehta, MD, Kasiani Myers, MD, and Daniel Grosseoehme, DMin

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

Neonatology and Pulmonary Biology » Jeffrey Whitsett, MD, Tim Le Cras, PhD, and Susan Wert, PhD

Role of Serpinb3a in goblet cell hyperplasia

Pathology » Keith Stringer

Role of Serpinb3a in mouse model of cutaneous inflammation

Division of Cellular and Molecular Immunology » Ian Lewkowich, PhD

Transcriptional regulation of IL-17 induced genes in the nasal epithelium

Biostatistics and Epidemiology » Patrick Ryan, PhD

Epigenetic Analysis of Individuals with Asthma and Non-Asthmatic Controls; Birth Cohort Study

Biostatistics and Epidemiology » Patrick Ryan, PhD and Rhonda Szczesniak, PhD

Effects of environmental exposures on systemic oxidative stress levels and allergic disease risk and severity in individuals with asthma and allergies

Neonatology and Pulmonary Biology; Biostatistics and Epidemiology » Tim Le Cras, PhD and Patrick Ryan, PhD

Immunologic Basis for Adverse Health Effects of Particulate Exposure on Childhood Asthma

Human Genetics » Lisa Martin, PhD

Nasal Epithelial Cell Study

Molecular Immunology » Edith Janssen, PhD

Human Dendritic Cell Differentiation project

Division of Pediatric General and Thoracic Surgery » Victor Garcia, MD

CoreChange Project

Pulmonary Medicine; Hospital Medicine; Human Genetics » Carolyn Kercsmar, MD, Jeffrey Simmons, MD, and Lisa Martin, PhD

A Multimedia Tool for Asthma study

Neonatology and Pulmonary Biology » Timothy Weaver, PhD

Characterizing the mechanistic basis for the protective function of Stard7 in the lungs

Division of Anesthesiology » Senthil Sadhasivam, MD, MPH

Ancestry informative markers development for *morphine related pain medication*

Human Genetics » Lisa Martin, PhD

Admixture mapping in asthmatic African American children

Pulmonary Medicine » Carolyn Kercsmar, MD

Severe asthmatics and rare variants association in admixed asthmatic children

Biostatistics and Epidemiology » Lili Ding, PhD and Mekibib Altaye, PhD

Rare variants in admixed asthmatic children

Grants, Contracts, and Industry Agreements

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 $265,370

HERSHEY, G

Epithelial Genes in Allergic Inflammation
National Institutes of Health
U19 AI 070235 09/01/11-08/30/16 $1,035,014

Rothenberg, M	Project 2	$267,544
Martin, L	AADCRC Core	$87,789

Ohio Children's Hospitals Asthma Task Force
Ohio Dept of Jobs and Family Services(Nationwide Children's Hospital)
G-1213-07-0561 07/01/12-06/30/14 $846,585

Inner City Asthma Consortium
NIH(University of Wisconsin (Madison))
5/1/2011-4/30/2015 $565,285

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 $332,402

JI, HONG

DNA Methylation in Children Hospitalized with Asthma Exacerbation
National Institutes of Health
R21 AI 101375 08/01/12-07/31/14 $150,000

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 $47,232

ZHANG, Z

Molecular Epidemiology in Children's Environmental Health Training Program

National Institutes of Health(University of Cincinnati)

T32 ES 010957	09/01/12-06/30/14	$38,410

Current Year Direct	**$3,399,272**
Total	**$3,399,272**