Asthma Research

Division Photo

Front Row: G. Khurana Hershey, M. Butsch Kovacic, K. Schroer, S. Bass, C. Chappell, G. Butler, T. Patterson, J. Gupta, U. Sivaprasad, H. Jie

Back Row: A. Gibson, A. Tsoras, C. Petitt, M. Lindsey, E. Brandt, M. Ericksen, W. Chen, J. Biagini-Myers

Division Data Summary

Research and Training Details

Number of Faculty	6
Number of Joint Appointment Faculty	2
Number of Research Fellows	3
Number of Research Students	6
Number of Support Personnel	6
Direct Annual Grant Support	$1,578,520
Peer Reviewed Publications	8

Clinical Activities and Training

Number of Clinical Staff	2
Number of Clinical Fellows	2
Number of Clinical Students	1
Number of Other Students	5
Outpatient Encounters	600

Faculty Members

Gurjit Hershey, MD, PhD, Professor ; *Division Director*

Melinda Butsch Kovacic, MPH, PhD, Research Assistant Professor

Umasundari Sivaprasad, PhD, Research Assistant Professor

Ning Wang, PhD, Research Assistant Professor

Manoj Warrier, MD, Instructor

Chen Weiguo, PhD, Research Assistant Professor

Trainees

- **Yasuhiro Tabata, MD/PhD,** PGY6, Kyoto University
- **Alex Masino, PhD,** PGY4, Washington State University
- **Kathy Schroer, PhD,** PGY4, University of Cincinnati

- **Andrew Smith, MD,** PGY3, Northwestern University
- **Jayanta Gupta, MD/PhD,** PGY1, University of Cincinnati
- **Salma Musaad, MD/PhD,** PGY1, University of Khartoum

Significant Accomplishments in FY08

Dr. Hershey

Dr. Hershey delivered the Elliot Ellis lecture at AAAAI in March in Philadelphia, Pennsylvania. The division receives ongoing federal financial support as one of only 11 Asthma and Allergic Diseases Cooperative Research Centers in the country. She was also selected to serve as the Associate Director of the Physician Scientist Training Program at the University of Cincinnati. Recipient of 2008-09 Luther Foundation Award.

Dr. Sivaprasad

Dr. Sivaprasad's research focus since she joined CCHMC in October 2007 has been on elucidating the mechanism by which SerpinB3a, a serine protease inhibitor contributes to the asthma phenotype in murine models. She had demonstrated a novel function for SerpinB3a in mucus production in asthmatic airways and is currently working on elucidating the mechanism for this function of SerpinB3a. Her second research project uses siRNA technology to dissect out the mechanism by which soluble IL-13Ralpha2 expression is induced in human lung epithelial cells. She has demonstrated that, unlike mice, the primary source of souble IL-13Ralpha2 in humans is from the membrane form of IL-13Ralpha2. She was selected to present her work at the Hypersensitivity School in Utah.

Dr. Butsch Kovacic

Dr. Butsch Kovacic led the development of the "New Patient Visit Questionaire", a dual purpose (clinical and research tool) used in allergy and pulmonary clinics. She submitted several NIH grant proposals focusing on environmental exposures and asthma.

Significant Publications in FY08

Warrier MR, Hershey GK. Asthma genetics: personalizing medicine. J Asthma. 2008; 45: 257-64.

Over the past few decades, much effort has been focused on the genetics of asthma, and investigators have identified more than one hundred potential asthma susceptibility genes, of which at least ten have been replicated in numerous independent studies. In parallel, researchers have also identified genetic factors that impact the pharmacotherapeutic responses to the major classes of asthma medications. While the results of the previous studies have been promising, future investigations need to combine genetics, pharmacogenetics, accurate disease genotyping, and environmental exposures to build the foundation for personalized and predictive medicine for the 21st century. The ultimate goal is to enable physicians to identify those at risk for asthma, intervene to prevent or attenuate the disease, and select the optimal medical regimen for each individual patient. If successful, the resulting paradigm shift in medical practice will lead to improved clinical outcomes and decreased health care expenditures.

Division Highlights

Umasundari Sivaprasad

Dr. Sivaprasad was selected to attend and present her work at the Hypersensitivity and Allergic Diseases School held by the Clinical and Immunological Society.

Weiguo Chen

Dr. Chen presented research on the "Role of Interleukin-13 Receptor Alpha2 in Allergic Inflammation" at the Center for Immunological Research, which demonstrated unique biological functions of soluble and membrane forms of interleukin-13 receptor alpha2 in allergic inflammation. He also Collaborated with Dr. Tim LeCras from Division Pulmonary Biology and Dr. William Nichols from Human Genetics on a project to study the relationship between allergen exposure and pulmonary remodeling/pulmonary atery hypertension.

Asthma

Asthma is the most common chronic childhood disease and the most common reason for pediatric hospital admission. Currently in Ohio, asthma is the number one cause of school absenteeism due to chronic illness. CCHMC has made a strong commitment to asthma with the goal of reducing hospital admissions due to asthma by providing evidenced-based care that is individualized to each child's disease, environment, genetics; etc. All of these approaches require further research and the newly established Division of Asthma Research will contribute to new standards for clinical

care through new scientific discoveries and cutting edge research. The mission of the Division of Asthma Research is to create a central base and lead research efforts in asthma around CCHMC, the Cincinnati community, and across the tristate region to effect change and ensure the highest standards for asthma care. There are multiple ongoing federal funded studies that are investigating how asthma develops in early childhood, why asthma attacks occur, and which treatments are most effective.

Division Collaboration

Collaboration with Allergy and Immunology; Immunobiology; Epidemiology and Biostatistics;
Collaborating Faculty: Dr. Rothenberg; Dr. Wills-Karp; Dr. Nick;
Asthma and Allergic Diseases Cooperative Research Centers

Collaboration with Immunobiology; Allergy and Immunology;
Collaborating Faculty: Dr. Wills-Karp; Dr. Finkelman; Dr. Rothenberg
Program Project Grant

Collaboration with Emergency Medicine; General and Community Pediatrics; Biomedical Infomatics; Pulmonary Medicine; Adherence Psychology
Collaborating Faculty: Dr. Strait; Dr. Ruddy; Dr. Simmons; Dr. Kahn; Dr. Aronow; Dr. Kercsmar; Dr. Drotar
Gene Expression Profiles of Acute Asthma

Mentions in Consumer Media

Division Publications

1. Khodoun M, Lewis CC, Yang JQ, Orekov T, Potter C, Wynn T, Mentink-Kane M, Hershey GK, Wills-Karp M, Finkelman FD. **Differences in expression, affinity, and function of soluble (s)IL-4Ralpha and sIL-13Ralpha2 suggest opposite effects on allergic responses**. *J Immunol.* 2007; 179: 6429-38.
2. Warrier MR, Hershey GK. **Asthma genetics: personalizing medicine**. *J Asthma.* 2008; 45: 257-64.
3. Brandt EB, Mingler MK, Stevenson MD, Wang N, Khurana Hershey GK, Whitsett JA, Rothenberg ME. **Surfactant protein D alters allergic lung responses in mice and human subjects**. *J Allergy Clin Immunol.* 2008; 121: 1140-1147 e2.
4. Gupta J, Grube E, Ericksen MB, Stevenson MD, Lucky AW, Sheth AP, Assa'ad AH, Khurana Hershey GK. **Intrinsically defective skin barrier function in children with atopic dermatitis correlates with disease severity**. *J Allergy Clin Immunol.* 2008; 121: 725-730 e2.
5. Iossifova Y, Reponen T, Daines M, Levin L, Khurana Hershey GK. **Comparison of two analyitcal methods for detecting (1-3)-B-D-glucan in pure fungal cultures and in home dust samples**. *Open Allergy J.* 2008; 1: 26-34.
6. Smith AM, Bernstein DI, LeMasters GK, Huey NL, Ericksen M, Villareal M, Lockey J, Khurana Hershey GK. **Environmental tobacco smoke and interleukin 4 polymorphism (C-589T) gene: environment interaction increases risk of wheezing in African-American infants**. *J Pediatr.* 2008; 152: 709-15, 715 e1.
7. Stevenson MD, Sellins S, Grube E, Schroer K, Gupta J, Wang N, Khurana Hershey GK. **Aeroallergen sensitization in healthy children: racial and socioeconomic correlates**. *J Pediatr.* 2007; 151: 187-91.
8. Tabata Y, Khurana Hershey GK. **IL-13 receptor isoforms: breaking through the complexity**. *Curr Allergy Asthma Rep.* 2007; 7: 338-45.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct / Project Period Direct
Hershey, G		
Genetic Susceptibility for Occupational Asthma National Institutes of Health (University of Cincinnati) R01 OH 008795	09/01/06 - 08/31/10	$47,310 / $179,424
Expanding the Genomic Data Analysis Core National Institutes of Health (University of Texas Health Sciences Center-San Antonio) U19 AI 070412	04/01/07 - 09/30/08	$83,000 / $83,000
Biology of IL-13 Receptor Alpha 2		

National Institutes of Health
R01 AI 058157 01/01/04 - 12/31/08 $162,779 / $1,250,000

Expanding the Genomic Data Analysis Core - Supplement
National Institutes of Health (University of Texas Health Sciences Center-San Antonio)
U19 AI 070412 03/01/08 - 02/28/09 $110,000 / $110,000

Diesel, Allergens And Gene Interaction In Child Atopy
National Institutes of Health (University of Cincinnati)
R01 ES 011170 07/01/07 - 06/30/09 $13,681 / $27,574

Epithelial Genes in Allergic Inflammation
National Institutes of Health
U19 AI 070235 09/15/06 - 08/31/11 $673,569 / $3,567,767

Hershey, G	Admin Core	34,503
Nick, T	Scientific Core	67,205
Hershey, G	Project 1	190,620
Rothenberg, M	Project 2	190,620
Wills-Karp, M	Project 3	190,620

Role of IL-13 Receptors in Atopic Dermatitis
National Institutes of Health
R01 AR 054490 09/01/07 - 07/31/12 $215,000 / $1,075,000

Interleukin-13 in Experimental Asthma
National Institutes of Health
P01 HL 076383 06/30/04 - 07/01/09 $273,181 / $273,181

Current Year Direct **$1,578,520**

Total $1,578,520