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Asthma Research Annual Report, 2009-10

Division Photo

T. Mersha, M. Butsch Kovacic, G. Khurana Hershey, W. Chen, U. Sivaprasad

Division Data Summary

Research and Training Details	
Number of Faculty	5
Number of Joint Appointment Faculty	2
Number of Research Fellows	4
Number of Research Students	3
Number of Support Personnel	12
Direct Annual Grant Support	$2,988,335
Peer Reviewed Publications	11

Clinical Activities and Training	
Number of Clinical Staff	1
Number of Other Students	3
Inpatient Encounters	28
Outpatient Encounters	233

Significant Publications

Weiguo Chen, Umasundari Sivaprasad, Yasuhiro Tabata, Aaron M. Gibson, Matthew T. Stier, Fred Finkelman, Gurjit K. Khurana Hershey. IL-13 Receptor Alpha 2 Membrane and Soluble Isoforms Differ in Human and Mouse. J Immunol. 2009 Dec 15;183(12):7870-6

Use of a humanized mouse model that expresses IL-13Ra2 in the same way that it is expressed in humans may improve the human applicability of studies of *in vivo* IL-13 and IL-13Ra2 function.

Jocelyn M. Biagini Myers, Ning Wang, Grace LeMasters, David I. Bernstein, Tolly Epstein, Mark Lindsey, Mark Ericksen, Ranajit Chakraborty, Patrick Ryan, Manuel Villareal, Jeff Burkle, James Lockey, Tiina Reponen, and Gurjit K. Khurana Hershey. Genetic and Environmental Risk Factors for Childhood Eczema Development and Allergic Sensitization in the CCAAPS Cohort. J Invest Dermatol. 2010 Feb;130(2):430-7. Epub 2009 Sep 17

Eczema is a chronic inflammatory disorder of the skin that affects as much as 30% of children. Recent results from birth cohort studies have uncovered novel information about genetic and environmental factors that promote the development of eczema. Birth cohort studies provide an optimal study design to elucidate these associations and prospectively track longitudinal data including exposure assessment and health outcomes from birth into early life and childhood.

Division Highlights

Gurjit Khurana Hershey, MD,PhD

Dr. Khurana Hershey is the PI of the NIH funded U19 Asthma and Allergic Diseases Cooperative Research Centers. In addition, she has several ongoing NIH funded projects focused on elucidating the genetic and environmental factors that contribute to the development of asthma and dissecting the mechanisms by which they confer their contributions. The Division of Asthma Research was selected by the Kindervelt organization for a 4 year commitment of support and Dr. Khurana Hershey was named the Kindervelt Endowed Chair in Asthma Research. Dr. Khurana Hershey was also appointed as the new Associate Director of Physician Scientist Training Program at the University of Cincinnati. She serves on a regular NIH Study section panel. This year, Dr. Khurana Hershey has worked on several research projects leading to several new collaborations, including Pulmonary Biology, Immunobiology, Emergency Medicine,and General and Community Pediatrics. In addition, Dr. Khurana Hershey is a graduate from the Executive Leadership in Academic Medicine Program.

Melinda Butsch Kovacic, PhD

As part of her NIH R21, Dr. Butsch Kovacic is evaluating the association between exposure to diesel exhaust particles and products of systemic oxidative stress among children with asthma with Dr. Tianying Wu at UC. Identifying fluorescent plasma oxidation products as biomarkers that can predict asthma severity is highly innovative, as these findings could suggestpreventive interventions to reduce asthma morbidity and mortality. Dr. Butsch Kovacic was appointed a KL2 Scholar. Dr. Butsch Kovacic is also a collaborator with Drs. Susanne Wells and Stella Davies on a grant from the Fanconi Anemia Research Foundation. The goal of this study is better understand the role of human papillomavirus infection in Fanconi anemia patients. She serves on the national AAAAI Genetics,Molecular Biology & Epidemiology Committee.

Weiguo Chen, MD, PhD

Dr. Chen's current research involves: 1) the biological role ofinterleukin-13 receptor alpha2 in the development of allergic asthma 2) Asymmetric dimethylarginine (ADMA)/dimethylarginine dimethylaminohydrolase (DDAH) pathway and allergic asthma. Dr. Chen is also participating incollaborative research with Immunobiology and Pulmonary Biology.

Tesfaye Mersha, PhD

Dr. Mersha's Research focuses on research in the area of Human Genetics. His current research projects include: 1) the study of Admixture mapping in African American asthmatic population with Dr. Ranajit Chakraborty at UC. The overall purpose of this project is to develop and evaluate an efficient approach to localize asthma liability genes in an admixed African American population; 2) a comprehensive expression profiling study to identify the genes and regulatory networks that impact the atopic dermatitis (AD) phenotype. Dr. Mersha Baye recently received a travel award and two NIH grants to support his research.

Umasundari Sivaprasad, PhD

Dr. Sivaprasad's current research projects include: 1) Elucidating the role of serpins in asthma 2) Elucidating the role of IL-13R alpha2 in atopic dermatitis. She has ongoing collaborations including with investigators at the University of of IL-13R alpha2 in atopic dermatitis. She has ongoing collaborations including with investigators at the University

of Pittsburgh, as well as investigators at CCHMC in Pulmonary Biology, Immunobiology, and Pathology. Her work has been submitted for publication and for additional funding. Uma gave several presentations to various Kindervelt local chapters on her current research on asthma this year and has participated in judging several scientific poster sessions at CCHMC, UC, and various high schools.

Division Collaboration

Collaboration with Allergy/Immunology; Immunobiology; Epidemiology and Biostatistics; Pathology

Collaborating Faculty: 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.

Collaboration with Immunobiology

Collaborating Faculty: Fred Finkelman, PhD

Biology of IL-13 Receptor Alpha 2

Collaboration with Emergency Medicine; Pulmonary Medicine; General and Community Pediatrics; Adherence Psychologoy; Biomedical Informatics ; Allergy/Immunology

Collaborating Faculty: Richard Ruddy, MD; Rick Strait, MD; Laurie Johnson, MD; Carolyn Kercsmar, MD; Jeffrey Simmons, MD; Rob Kahn, MD; Dennis Drotar, PhD; Bruce Aronow, PhD; Kelly Metz, MD

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.

Collaboration with Pulmonary Medicine

Collaborating Faculty: Carolyn Kercsmar, 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 area.

Collaboration with Pulmonary Biology

Collaborating Faculty: Tim Le Cras, PhD

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

Collaboration with Hematology/Oncology

Collaborating Faculty: Susanne Wells, PhD

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

Collaboration with Dermatology; Allergy/Immunology; Immunobiology; Hematology/Oncology

Collaborating Faculty: Anne Lucky, MD; Marc Rothenberg, MD, PhD; Fred Finkelman, PhD; Susanne Wells, PhD

Role of IL-13 Receptors in Atopic Dermatitis

Faculty Members

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

Melinda Butsch Kovacic, MPH, PhD, Research Assistant Professor

Weiguo Chen, MD, PhD, Research Assistant Professor

Tesfaye Mersha, PhD, Research Assistant Professor

Umasundari Sivaprasad, PhD, Research Assistant Professor

Trainees

- **Kathy Schroer, PhD,** PL-5, University of Cincinnati
- **Kelly Metz, MD,** PGY4, University of Cincinnati
- **Tolly Epstein, MD,** PGY4, University of Cincinnati
- **Rachael Mintz-Cole, BS,** PL-2, University of Cincinnati
- **Jayanta Gupta, MD/PhD,** PGY2, University of Cincinnati
- **Gerald Lee, MD,** PGY2, University of Cincinnati
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Significant Accomplishments

Cooperative Research Center Grant

This year, the Division of Asthma Research and Khurana Hershey, MD, PhD, received one of only 14 NIH-funded Asthma and Allergic Diseases Cooperative Research Center grants. As part of this grant, we are working to identify epithelial genes important in allergic inflammation.

Epithelial cells have been implicated as critical initiators of allergic inflammation and asthma. However, relevant epithelial candidate genes for asthma have not been identified. We identified six candidate genes and customized an assay that included their non-synonymous and tagging SNPs. We then genotyped 1,152 children enrolled in the Greater Cincinnati Pediatric Clinic Repository. Through this work, we identified the combination of SNPs within all six genes that best predicts asthma risk.

Biomarkers of Oxidative Stress

Melinda Kovacic, MPH, PhD, is using an NIH grant to identify biomarkers of diesel exhaust particle-induced oxidative stress in asthma. Although oxidative stress is generally accepted as a determinant of asthma, there are no reliable and consistent methods to quantify biologically relevant products of oxidative stress. Our preliminary data suggest that fluorescent plasma oxidation products may provide a relevant way to identify the pathways activated by diesel exhaust particles.

SERPINB4 as a Key Regulator of Mucus Production

Excessive mucus production and mucus plugging are key pathologic features of asthma, yet the mechanisms responsible for them remain largely unknown. We recently found that the serine protease inhibitor, SERPINB4, is strongly induced in respiratory epithelial cells of children with asthma.
Microarray analysis revealed that SERPINB3A modulates the expression of multiple genes that regulate mucus production. SERPINB4 may be an important new target for therapeutic intervention.

Division Publications

1. :

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 University of Cincinnati		
T32 ES 10957	07/01/09 - 03/31/11	$38,277 / $38,277
Butsch.Kovacic, M		
Cincinnati Center for Clinical and Translational Sciences and Training University of Cincinnati (National Institutes of Health)		
KL2 RR 026315	07/01/09 - 03/31/11	$90,380 / $90,380
Exposure-Induced Systemic Oxidative Stress in Children with Asthma National Institutes of Health		
R21 ES 016830	06/01/09 - 05/31/11	$125,000 / $275,000
Hershey, G		
Role of IL-13 Receptors in Atopic Dermatis National Institutes of Health		
R01 AR 054490	09/01/07 - 07/31/12	$241,067 / $1,096,767
Biology of IL-13 Receptor Alpha-2 in Asthma National Institutes of Health		
R56 AI 084414	09/15/09 - 08/31/10	$250,000 / $250,000
Allergies and Asthma Research Luther Foundation		
	01/01/10 - 12/31/10	$200,000 / $200,000
Diesel, Allergens and Gene Interactions and Child Atopy University of Cincinnati (National Institutes of Health)		
R01 ES 011170	09/17/09 - 08/31/10	$146,731 / $146,731
Epithelial Genes in Allergic Inflammation National Institutes of Health		

U19 AI 070235	09/15/06 - 08/31/11	$704,169 / $3,478,285
Hershey, G	Administrative Core	33,817
Hershey, G	Project #1	203,845
Rothenberg, M	Project #2	182,955
Wills-Karp, M	Project #3	196,078
Martin, L	Scientific Core	87,474

Epithelial Genes in Allergic Inflammation
National Institutes of Health

U19 AI 070235	08/13/09 - 07/31/11	$300,000 / $300,000
Hershey, G	Project #1	100,000
Rothenberg, M	Project #2	100,000
Wills-Karp, M	Project #3	100,000

Development of an Asthma Research Core Center
National Institutes of Health

P30 HL 101333	09/30/09 - 08/31/11	$399,183 / $696,291

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 / $703,977

Pathogenesis of Neonatal Lung Disease
American Heart Association

0740069N	01/01/07 - 12/31/11	$90,909 / $454,545

Current Year Direct	**$2,988,335**
Total	**$2,988,335**