Faculty Members

Marc E. Rothenberg, MD, PhD, Professor; Division Director
Research Interests: Elucidating the mechanisms of allergic responses especially in mucosal tissues such as the lung and the gastrointestinal tract

J. Pablo Abonia, MD, Research Assistant Professor
Research Interests: The role of mast cells in eosinophilic esophagitis

Amal H. Assa'ad, MD, Professor Clinical; Clinical Director

Division Data Summary

<table>
<thead>
<tr>
<th>Research and Training Details</th>
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<tbody>
<tr>
<td>Number of Faculty</td>
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<tr>
<td>Number of Joint Appointment Faculty</td>
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<tr>
<td>Number of Research Fellows</td>
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<tr>
<td>Number of Research Students</td>
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<tr>
<td>Number of Support Personnel</td>
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<tr>
<td>Direct Annual Grant Support</td>
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<tr>
<td>Direct Annual Industry Support</td>
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<tr>
<td>Peer Reviewed Publications</td>
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<tr>
<th>Clinical Activities and Training</th>
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<tr>
<td>Number of Clinical Staff</td>
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<tr>
<td>Number of Clinical Fellows</td>
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<tr>
<td>Number of Other Students</td>
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<tr>
<td>Inpatient Encounters</td>
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<tr>
<td>Outpatient Encounters</td>
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</table>

**Research Interests:** The occult effect of allergic sensitization to foods on the bronchial hyper-responsiveness seen in asthmatic and the genetic basis of food allergy

**Robert Ausdenmoore, MD, Adjunct Professor Clinical**

- Research Interests: To study food allergy; eosinophilic esophagitis; asthma

**Thomas J. Fischer, MD, Adjunct Professor Clinical**

- Research Interests: The pharmacologic management of asthma, immune deficiency diseases

**Simon P. Hogan, PhD, Assistant Professor**

- Research Interests: To study allergies, food allergies, eosinophil biology & gastrointestinal inflammation

**Michelle B. Lierl, MD, Adjunct Associate Professor**

- Research Interests: To reduce environmental tobacco smoke exposure in children with asthma

**Anil Mishra, PhD, Research Assistant Professor**

- Research Interests: Understanding the mechanism of aeroallergen-induced allergic responses in the lung and lower gastrointestinal tract

**Kimberly A. Risma, MD, PhD, Research Assistant Professor**

- Research Interests: The molecular and cellular bases of primary disorders of immune deficiency and dysregulation, especially as it relates to lymphocyte cytotoxicity

**Manoj Warrier, MD, Research Instructor**

- Research Interests: To understand the molecular pathogenesis involved in food allergy related disorders.

**Nives Zimmermann, MD, Research Assistant Professor**

- Research Interests: The molecular understanding of eosinophil survival in allergic inflammation and asthma

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**Joint Appointment Faculty Members**

**Gurjit Khurana Hershey, MD, PhD, Professor**

- Asthma Research
- Genetics of allergy and asthma; cytokines; and signaling pathways

**Alexandra Filipovich, MD, Professor**

- Hematology/Oncology Diagnostic Laboratory
- Primary immunodeficiencies; BMT for primary immunodeficiencies; Hemophagocytic lymphocytosis; Post-BMT immune reconstruction

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**Clinical Staff Members**

- Kalra Harpinder, MD

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**Trainees**

- Carine Blanchard, PhD, Laboratoire de Gastroenterologie INSERM U45 Lyon, France
- Julie Caldwell, PhD, University of Cincinnati, Ohio
- Eun Jin Lim, PhD, University of Kentucky, Kentucky
- Kelly Metz, MD, University of Cincinnati, Ohio
- Ariel Munitz, PhD, Hebrew University of Jerusalem, Israel
- Miguel Stein, MD, University of Chile Medical School, Chile
- Zeenath Unnisa, PhD, Osmania University, Hyderabad, India
- Li Zuo, MD, Zunyi Medical College, China
- Katherine Groschwitz, Xavier University, Ohio
- Hongyan Zhu, Hubei College of Traditional Medicine, China
- Amanda Beichler, Ohio Northern University, Ohio
- Tom Lu, University of Cincinnati, Ohio
- Leah Kottyan, Huntington College, Alabama

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**Significant Accomplishments in FY08**

The Cincinnati Center for Eosinophilic Disorders (CCED)

The Cincinnati Center for Eosinophilic Disorders (CCED), a joint effort between the Divisions of Allergy and Immunology...
and Gastroenterology, Hepatology and Nutrition, has had a year of tremendous growth both in staffing and in clinical services. There was a 7% growth in the number of new families that came to the CCED, and indeed, the CCED drew patients from around the world with 80% of the 380 patients seen coming from outside the Children's Hospital catchment area. This multidisciplinary, collaborative center utilizes eosinophilic specialists from the Divisions of Allergy, Gastroenterology, Nutrition, Social Work, and Psychology, and Otolaryngology who see these patients and their families in their initial week-long evaluation.

Sean Jameson, as the Program Coordinator, along with Bridget Buckmeier, the Lead Research Coordinator, managed the growth of six new CCED staff, taking the group to ten full-time members. The CCED successfully recruited Dr. James Franciosi, a pediatric gastroenterologist trained at Children's Hospital of Philadelphia, who has expertise in eosinophilic gastrointestinal disorders; this allows expansion of the CCED's capabilities. The CCED has enhanced the services provided to its families with the development of The Eddy project (a patient traveling journal) that is tracked on our website, as well as the development of a weekly “patient education day” for new and existing patients. The CCED has developed the framework for a local family support group which begins in 2008.

During the past fiscal year, the CCED published 17 articles on eosinophils. A recent publication (Clinical Gastroenterology and Hepatology, Collins, M., et al. 2008) reported the clinical, pathologic, and molecular characterization of familial Eosinophilic Esophagitis (EE) in 59 members of 26 families. Further, the initial results on the effect of a new biological therapy (Anti-IL-5) for eosinophilic disorders revealed positive findings which has prompted the pharmaceutical industry to conduct large scale clinical trials. This resulted in a recent publication (New England Journal of Medicine, Rothenberg, M. et al. 2008) on the treatment of patients with Hypereosinophilic Syndrome with Mepolizumab. The group continues to work on two investigator initiated studies in which Dr. Marc Rothenberg, CCED Director, holds the Investigational New Drug (IND) file with the Food and Drug Administration; these studies concern mepolizumab and fluticasone). In addition, the CCED has expanded its comprehensive longitudinal database to >1900 patients, including detailed phenotypic data and biologic samples. This database supports a variety of research projects focused on genetics, natural history, molecular pathogenesis, and outcomes research.

**Food Allergy Program**

Our outstanding Food Allergy Program in the Division of Allergy and Immunology is comprised of experienced faculty, nurses and nutritionists. The number of patients seen in the outpatient clinics, with a diagnosis of food allergy, has dramatically increased 10-fold over the past five years from 161 individual patient visits in 2003 to an anticipated 1,686 in 2008.

This dramatic rise in patients not only reflects the food allergy epidemic locally but also the attraction of national and international patients to our center. Amal Assa’ad, MD, Director of the Food Allergy Clinic, is internationally recognized, recently speaking at the International Food Allergy Symposium of the World Allergy Organization in Bangkok. Dr. Assa’ad has led a team of national experts writing a manual for the gold standard diagnostic procedure in food allergy entitled “The Oral Food Challenge”. The procedure of oral food challenge is performed routinely at the Food Allergy Clinic, and provides the basis for diagnosing food allergy in many children as well as a method of removing an unfounded diagnosis of food allergy from even more children.

The leading research efforts of our Food Allergy Program were recognized by two new NIH awards in 2008; Dr. Simon Hogan for “The Interleukin-9 in Experimental Intestinal Anaphylaxis” (award period 2008-2011 for $1,500,000) and Dr. Carine Blanchard for “TSG6 in IgE Mediated Food Allergy” (award period 2008-2010 for $375,000).

**Significant Publications in FY08**


The long-term use of an investigational antibody-based medication, mepolizumab, designed to target a type of white blood cell, has resulted in steroid-sparing treatment for patients with the devastating blood disorder, hypereosinophilic syndrome (HES), that can lead to heart failure and death, according to a Phase III study published in the March 20 The New England Journal of Medicine. The current standard treatment for the majority of HES patients is the chronic, systemic use of corticosteroids, such as prednisone, which can have considerable side effects. The study found that mepolizumab enabled study patients to significantly reduce their doses of steroids and, often, even withdraw from steroid use.

Munitz A, Brandt EB, Mingler M, Finkelman FD, Rothenberg ME. Distinct roles for IL-13 and IL-4 via IL-13
receptor alpha1 and the type II IL-4 receptor in asthma pathogenesis. Proc Natl Acad Sci U S A 2008; 105:7240-5.

The specific IL-4 and IL-13 receptor in the lung has been identified.


The development of eosinophil remodeling is shown to be IL-5 and eosinophil dependant.


A novel pathway for food allergic responses is identified.

Division Highlights

Experimental Modeling of Allergic Diseases

The Division of Allergy and Immunology research program focuses on defining the molecular basis underlying the development and exacerbation of diseases including asthma, food allergy and eosinophilic gastrointestinal diseases, and hypereosinophilic syndrome (chronic eosinophilic leukemia). The group has developed an array of innovative experimental animal (murine) models of allergic diseases to define the contribution of cytokines, receptors, chemokines, inflammatory cells including eosinophils, CD4+ T-cells and mast cells in the pathophysiological manifestations of allergic diseases. For example, Dr. Simon Hogan's laboratory recently reported a novel mouse model of oral antigen hypersensitivity allowing him to define an essential role for mast cells and the cytokine interleukin-9 in gastrointestinal allergy. (Forbes, E. E. et al. IL-9- and mast cell-mediated intestinal permeability predisposes to oral antigen hypersensitivity. J. Exp. Med. 31 March 2008 [doi:10.1084/jem.20071046])

Division Collaboration

Collaboration with Adherence Psychology; Behavioral Medicine & Clinical Psychology; Gastroenterology, Hepatology and Nutrition; Pathology; Pediatric Otolaryngology

Collaborating Faculty: Dennis Drotar, PhD; Kevin Hommel, PhD; Phillip Putnam, MD; James Franciosi, MD; Margaret Collins, MD; Alessandro deAlarcon, MD

The Cincinnati Center for Eosinophilic Disorders (CCED) is a multidisciplinary, collaborative center utilizes eosinophilic specialists from the Divisions of Allergy, Gastroenterology, Nutrition, Social Work, and Psychology, and Otolaryngology who see these patients and their families in their initial week-long evaluation. (Rothenberg, Albonia, Risma)

Collaboration with Immunobiology; Pathology; Personalized and Predictive Medicine

Collaborating Faculty: Marsha Wills-Karp, PhD; Fred D. Finkelman, MD; David Witte, MD; Keith Stringer, MD; Gurjit K. Khurana Hershey, MD, PhD

Program Project Grant to elucidate the mechanisms by which Interleukin-13 (IL-13) is produced and by which it induces the pathophysiological features of asthma. (Rothenberg)

Collaboration with University of Cincinnati, Molecular Genetics

Collaborating Faculty: Andrew B. Herr, PhD

University Research Council Interdisciplinary Grant entitled "Biophysical Consequences of Missense Mutations in Perforin". (Risma)

Mentions in Consumer Media

- These Benefactors Do Homework As Charities Fawn Wall Street Journal, Newspaper
- Plainville Boy Suffering from Extreme Allergy News Channel 8's Jocelyn Maminta, Television
- The Order of Health Prevention, Magazine
- High Season for Allergies The Windsor Star, Newspaper
- Food Allergy Sufferers Must be on Alert at Fairs The Detroit News, Newspaper
New Drug Eases Asthma Symptoms

Food Allergies Stir a Mother to Action

Food Allergens Show up in Unexpected Places

Halloween and Food Allergy Safety

Breastfeeding is One Way to Reduce Food Allergy Risk

Subway Sued Over Fatal Allergic Reaction

Tri-State Under Fourth Smog Alert Of 2007

Division Publications


Grants, Contracts, and Industry Agreements

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct / Project Period Direct</th>
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<tr>
<td>Blanchard, C</td>
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</table>
Periostin Expression in Inflammatory Contexts 07/01/06 - 06/30/08 $44,000 / $86,000

Filaggrin Expression is Decreased in Pediatric Eosinophilic Esophagitis Patients 02/01/07 - 01/31/09 $13,000 / $25,000

Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease 06/01/08 - 05/31/09 $25,000 / $25,000

TSG6 in IgE-mediated Food Allergy 06/18/08 - 05/31/10 $125,000 / $250,000

Hogan, S
Mast Cell PAF-Dependent Intravascular Leakage in Food-induced Anaphylaxis 07/01/07 - 06/30/09 $55,000 / $110,000

Eosinophils and Pediatric Inflammatory Bowel Disease 01/01/07 - 12/31/09 $90,000 / $179,480

Interleukin-9 in Experimental Intestinal Anaphylaxis 04/01/08 - 03/31/12 $250,000 / $1,000,000

Mishra, A
Mechanistic Analysis Of Eosinophilic Esophagitis 04/01/05 - 03/31/10 $152,392 / $820,000

Munitz, A
Machiah Fellowship 07/01/06 - 06/30/08 $50,000 / $100,000

Risma, K
The Pathophysiologic Basis of Perforin Misfolding in Cytotoxic Granules 07/01/07 - 06/30/09 $50,000 / $100,000

Mechanisms of Altered Lymphocyte Cytotoxicity 08/01/06 - 07/31/09 $125,000 / $375,000

Rothenberg, M
Regulation Of Gastrointestinal Eosinophils 01/15/04 - 12/31/08 $186,033 / $960,000

The Hypereosinophilic Syndromes And Mepolizumab 06/15/04 - 05/31/08 $8,054 / $91,456

Interleukin-13 in Experimental Asthma - Breeding and Genotyping Core 07/01/04 - 06/30/09 $109,971 / $679,922

Interleukin-13 in Experimental Asthma - Component 3 07/01/04 - 06/30/09 $273,182 / $1,327,285

Epithelial Genes in Allergic Inflammation
<table>
<thead>
<tr>
<th>Project Title</th>
<th>Principal Investigator</th>
<th>Funding Agency</th>
<th>Start Date - End Date</th>
<th>Budget</th>
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<tbody>
<tr>
<td>Molecular Analysis of Eosinophilic Esophagitis</td>
<td>Food Allergy and Anaphylaxis Network</td>
<td>National Institutes of Health</td>
<td>02/01/07 - 01/31/09</td>
<td>$69,444 / $138,888</td>
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<tr>
<td>Novel Genetic and Therapeutic Approaches Focusing on Siglec-8 for the Diagnosis and Treatment of Human Idiopathic Eosinophilic Disorders</td>
<td>The Dana Foundation</td>
<td>National Institutes of Health</td>
<td>10/01/07 - 09/30/10</td>
<td>$100,000 / $300,000</td>
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<td>Pediatric Center For Gene Expression &amp; Development</td>
<td>Strauss/Rothenberg</td>
<td>National Institutes of Health</td>
<td>12/01/06 - 11/30/11</td>
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<td>AAAAI Young Faculty Support Award</td>
<td>Warrier, M</td>
<td>American Academy of Allergy, Asthma and Immunology</td>
<td>01/01/08 - 12/31/08</td>
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<td>The Role of Arginine Transport in the Development of Inflammatory Homeostasis in the Lung</td>
<td>Zimmermann, N</td>
<td>March of Dimes - National</td>
<td>06/01/06 - 05/31/09</td>
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**Current Year Direct** $2,451,303

**Industry Contracts**

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<th>Investigator</th>
<th>Company</th>
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<tr>
<td>Assa'ad, A</td>
<td>GlaxoSmithKline</td>
<td>$ 129,661</td>
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<tr>
<td>Rothenberg, M</td>
<td>GlaxoSmithKline</td>
<td>$ 1,060</td>
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<tr>
<td></td>
<td>Merck &amp; Company, Inc</td>
<td>$ 80,850</td>
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**Current Year Direct Receipts** $211,571

**Total** $2,662,874