## Allergy and Immunology

## **Division Details**

### **Division Data Summary**

#### **Research and Training Details**

Number of Faculty	16
Number of Joint Appointment Faculty	3
Number of Research Fellows	9
Number of Research Students	3
Number of Support Personnel	45
Direct Annual Grant Support	\$2,811,913
Direct Annual Industry Support	\$116,065
Peer Reviewed Publications	44

#### **Clinical Activities and Training**

Number of Clinical Staff	1
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Number of Clinical Fellows	6
Number of Other Students	4
Inpatient Encounters	516
Outpatient Encounters	6,883

## Cincinnati Children's

## **Division Photo**



Row 1: N Zimmermann Row 2: Y Wang, A Barski, K Risma, T Moncrief, P Fulkerson Row 3: J Sherrill, M Rothenberg, T Fischer

## Significant Accomplishments

#### Positive results from monoclonal antibody clinical trial

Amal Assa'ad, MD, clinical director, was lead author for "Antibody Against IL-5 Reduces Numbers of Esophageal Intraepithelial Eosinophils in Children with Eosinophilic Esophagitis," published in *Gastroenterology*. This multicenter, international project showed positive results using an anti-IL-5 antibody to treat eosinophilic esophagitis in children and was the first clinical trial to document the use of a monoclonal antibody in children as young as two years of age. This is promising news for the treatment of eosinophilic disorders as these conditions are chronic and often present at an early age. This clinical trial was based on basic and translational work by Marc Rothenberg, MD, PhD, division director.

#### New faculty member targets home environment in asthma outcomes

Recently appointed faculty member Terri Moncrief, MD, researches the impact of single parenthood, family routines and allergic sensitizations on asthma outcomes. Moncrief, under the direction of Robert Kahn, MD, MPH, is executing a multidimensional analysis of the home environment and its effect on asthma morbidity in disadvantaged populations. Several of her studies were presented at national conferences, and her research will help develop tools to identify at-risk children and guide intervention strategies.

#### MicroRNA biomarkers and regulators of allergic disease

Rothenberg has identified a dysregulated microRNA signature that correlates with disease activity for eosinophilic esophagitis (EoE), a severe food allergy. Promisingly, the most elevated microRNA in the signature, miR-21, regulates T cell polarization and activation in preclinical models. Rothenberg also identified a microRNA, miR-375, that regulates interleukin-13, a key immune hormone in allergic reactions. These findings are proof of principle that microRNAs are involved in fine-tuning interleukin-13-mediated immune responses and show promise for use of microRNAs, such as miR-21 and miR-375, as noninvasive biomarkers and therapeutic targets for allergic disease. The ability to detect and measure the status of EoE with a noninvasive blood test would be a significant benefit to individuals and families.

## **Division Highlights**

#### Division Clinical Director Supports Cincinnati Children's National and Global Mission

Amal H. Assa'ad, MD has exemplified the national and global mission of Cincinnati Children's through her farreaching dedication and valued efforts to improve child health. She has represented Cincinnati Children's as an invited speaker at plenary sessions and international symposia at two national meetings in the USA and three international meetings in South America, Europe and the Middle East. In addition, she was the 2011 Ghory Lecturer at Cincinnati Children's; serves as an elected member of the AAAAI Board of Directors and the chair of the ACAAI Food Allergy Committee; and has published several sequels to the NIH Expert Panel on Food Allergy Guidelines.

### **Division Researcher Dedicated to Fungal Spore Research**

Michelle B. Lierl, MD is conducting a study investigating the role of outdoor fungal and myxomycete spores as aeroallergens; this study involves allergy skin testing with myxomycete and basidiomycete spore extracts to identify whether they are previously unrecognized aeroallergens. As no extracts of these spores were commercially available, Lierl collects the spores herself and makes the extracts for the allergy skin testing. Having discovered the lack of photographs available of these microscopic spores, she also maintains a website to share photographs of spores of basidiomycetes, ascomycetes, and myxomycetes as a reference source for others for fungal species identification. In addition to the fungal research, Lierl is researching the association of exhaled nitric oxide levels with the development of asthma in a birth cohort of children from families with allergies, having completed the final study visits in Fall of 2011, and presented "Problem-based Learning Seminar on Pediatric Anaphylaxis" at the 2012 AAAAI Annual Meeting.

# Division Researcher Forwards Knowledge of Mechanisms of Aeroallergen-Induced Airway Responses

Ariel Munitz, PhD furthered knowledge of IL-13 and resistin-like molecule alpha (RELM-α) in mechanisms of aeroallergen-induced airway responses. He presented "OpITIMixing Eosinophil Activation in Mucosal Inflammation" at the 2012 Research Conferences at the Vall d'Heron Institut de Recerca and "Eosinophil Receptors and Receptor-Mediated Inhibition" at the 7th International Eosinophil Society Biannual Meeting. He published in the *Journal of Allergy and Clinical Immunology*, the *Journal of Immunology*, and the *American Journal of Respiratory Cell and Molecular Biology* and was awarded funding from the Bi-National U.S.-Israel Science Foundation, the Israel Science Foundation, and Israel Cancer Research Fund. The Editor-in-Chief of the *Journal of Allergy and Clinical Immunology* officially nominated him to the journals' reviewer board in recognition of his excellent record of reviewing manuscripts.

#### DIVISION RESEARCHEF MEMANES MECHANISHIS AND DIVINALARES IN OCULAR DISEASES

Santa Ono, PhD contributed several significant research findings this year through his investigations on the transcriptional regulation in the human immune system, mechanisms of mast-cell dependent inflammation on the ocular surface and immune component of age-related macular degeneration. He published his studies in *Experimental and Molecular Pathology* and the *British Journal of Ophthalmology*: "Identification of anti-retinal antibodies in patients with age-related macular degeneration", "Serum autoantibody biomarkers for age-related macular degeneration and possible regulators of neovascularization", "Identification of genes and proteins specifically regulated by costimulation of mast cell Fce Receptor I and chemokine receptor 1", and "The effect of perioperative allergic conjunctivitis on corneal lymphangiogenesis after corneal transplantation". Ono was the invited plenary speaker for the 2012 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting. In addition to his research, Ono continues to serve as the Senior Vice President for Academic Affairs and University Provost at the University of Cincinnati.

#### **Division Researcher Committed to Asthma Morbidity Research**

Terri M. Moncrief, MD forwarded her research to critically analyze the components of the social home environment that contribute to poor asthma morbidity among disadvantaged populations. Her work entitled "Prevalence of Cockroach and Mouse Sensitization among Children Hospitalized for Wheezing and Asthma", was preseTerri M. Moncrief, MD forwarded her research to critically analyze the components of the social home environment that contribute to poor asthma morbidity among disadvantaged populations. Her work entitled "Prevalence of Cockroach and Mouse Sensitization among Children Hospitalized for Wheezing and Asthma", was presented at the 2011 Pediatric Hospitalist Medicine Conference and the 2011 World Allergy Congress; "Single-parenthood: Possible Mechanisms of Increase Pediatric Asthma-Related Morbidity" at the 2011 American College of Allergy, Asthma and Immunology (ACAAI) National Scientific Meeting; and "Effect of a "Home Away from Home' on Children's Adherence to Asthma Medicine" at the 2012 Pediatric Academic Society Scientific Meeting. She published a related research study, "Mouse Sensitization as an Independent Risk Factor for Asthma Morbidity", in the peer-reviewed journal Annals of Allergy, Asthma & Immunology. These studies and her ongoing research will serve as the foundation for forming clinically relevant tools for successful identification of at-risk children and instituting effective intervention strategies.nted at the 2011 Pediatric Hospitalist Medicine Conference and the 2011 World Allergy Congress; "Single-parenthood: Possible Mechanisms of Increase Pediatric Asthma-Related Morbidity" at the 2011 American College of Allergy, Asthma and Immunology (ACAAI) National Scientific Meeting; and "Effect of a "Home Away from Home' on Children's Adherence to Asthma Medicine" at the 2012 Pediatric Academic Society Scientific Meeting. She published a related research study, "Mouse Sensitization as an Independent Risk Factor for Asthma Morbidity", in the peer-reviewed journal Annals of Allergy, Asthma & Immunology. These studies and her ongoing research will serve as the foundation for forming clinically relevant tools for successful identification of at-risk children and instituting effective intervention strategies.

## Significant Publications

**Assa'ad AH**, Gupta SK, Collins MH, Thomson M, Heath AT, Smith DA, Perschy TL, Jurgensen CH, Ortega HG, Aceves SS. **An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis**. *Gastroenterology*. 141(5):1593-604. Nov 2011.

This clinical study establishes the involvement of IL-5 in the pathogenesis of eosinophilic esophagitis in children and the ability of mepolizumab, an anti-IL-5 antibody, to reduce esophageal eosinophilic inflammation in pediatric patients.

DeBrosse CW, Franciosi JP, King EC, Butz BK, Greenberg AB, Collins MH, Abonia JP, Assa'ad A, Putnam PE, Rothenberg ME. Long-term outcomes in pediatric-onset esophageal eosinophilia. *J Allergy Clin Immunol*. 128(1):132-8. Jul 2011.

This study identifies that pediatric-onset esophageal eosinophilia persists into adulthood and is associated with reduced quality of life.

Henderson CJ, **Abonia JP**,King EC, Putnam PE, Collins MH, Franciosi JP, **Rothenberg ME**. **Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis.** *J Allergy Clin Immunol*. 129(6):1570-8. Jun 2012.

This study is a critical step in improving patient care as it evaluates the comparative effectiveness of current dietary therapies (elemental diet, six-food elimination diet, skin test-directed elimination diet) and the utility of skin test-directed diets in food reintroductions for eosinophilic esophagitis, a severe, often painful food allergy that renders children and adults unable to eat a wide variety of foods.

Kucuk ZY, Strait R, Khodoun MV, Mahler A, **Hogan S**, Finkelman FD. **Induction and suppression of allergic diarrhea and systemic anaphylaxis in a murine model of food allergy**. *J Allergy Clin Immunol*. 129(5):1343-8. May 2012.

Using a mouse model of food allergy, this translational study identifies that intestinal immunity and the amount of oral antigen determine whether diarrhea, systemic anaphylaxis, or both are induced.

Lu TX, Sherrill JD, Wen T, Plassard AJ, Besse JA, Abonia JP, Franciosi JP, Putnam PE, Eby M, Martin LJ, Aronow BJ, Rothenberg ME. MicroRNA signature in patients with eosinophilic esophagitis, reversibility with

**glucocorticoids, and assessment as disease biomarkers**. *J Allergy Clin Immunol*. 129(4):1064-75.e9. Apr 2012. This study implicates a dysregulated microRNA signature in eosinophilic esophagitis and its correlation with disease activity, giving promise for its use as a noninvasive biomaker for the diagnosis and treatment of the disease.

## **Division Publications**

- 1. Abonia JP, Putnam PE. Mepolizumab in eosinophilic disorders. Expert Rev Clin Immunol. 2011; 7:411-7.
- Abonia JP, Rothenberg ME. Eosinophilic esophagitis: rapidly advancing insights. Annu Rev Med. 2012; 63:421-34.
- Ahrens R, Osterfeld H, Wu D, Chen CY, Arumugam M, Groschwitz K, Strait R, Wang YH, Finkelman FD, Hogan SP. Intestinal mast cell levels control severity of oral antigen-induced anaphylaxis in mice. *Am J Pathol.* 2012; 180:1535-46.
- 4. Assa'ad AH, Bahna SL. Food allergy: diagnosis and beyond. *Ann Allergy Asthma Immunol*. 2012; 108:289-90.
- Assa'ad AH, Gupta SK, Collins MH, Thomson M, Heath AT, Smith DA, Perschy TL, Jurgensen CH, Ortega HG, Aceves SS. An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis. *Gastroenterology*. 2011; 141:1593-604.
- Aye CC, Toda M, Morohoshi K, Ono SJ. Identification of genes and proteins specifically regulated by costimulation of mast cell Fcepsilon Receptor I and chemokine receptor 1. *Exp Mol Pathol.* 2012; 92:267-74.
- 7. Boyce JA, Bochner B, Finkelman FD, Rothenberg ME. Advances in mechanisms of asthma, allergy, and immunology in 2011. *J Allergy Clin Immunol.* 2012; 129:335-41.
- 8. Burks AW, Jones SM, Boyce JA, Sicherer SH, Wood RA, Assa'ad A, Sampson HA. **NIAID-sponsored 2010** guidelines for managing food allergy: applications in the pediatric population. *Pediatrics*. 2011; 128:955-

65.

- 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.
- DeBrosse CW, Franciosi JP, King EC, Butz BK, Greenberg AB, Collins MH, Abonia JP, Assa'ad A, Putnam PE, Rothenberg ME. Long-term outcomes in pediatric-onset esophageal eosinophilia. J Allergy Clin Immunol. 2011; 128:132-8.
- 11. DeBrosse CW, Rothenberg ME. **Eosinophilia: clinical manifestations and therapeutic options**. *Allergy*. Edinburgh ; New York: Elsevier Saunders; 2012:361-368.
- Dorris K, Fouladi M, Davies SM, Perentesis JP, Lawrence JM, Chow LM, Assa'ad A, Uygungil B, Jodele S. Severe allergic reactions to thiol-based cytoprotective agents mesna and amifostine in a child with a supratentorial primitive neuroectodermal tumor. *J Pediatr Hematol Oncol.* 2011; 33:e250-2.
- 13. Flynn TH, Ohbayashi M, Dawson M, Larkin DF, Ono SJ. **The effect of perioperative allergic conjunctivitis on corneal lymphangiogenesis after corneal transplantation**. *Br J Ophthalmol*. 2011; 95:1451-6.
- Franciosi JP, Hommel KA, DeBrosse CW, Greenberg AB, Greenler AJ, Abonia JP, Rothenberg ME, Varni JW. Development of a validated patient-reported symptom metric for pediatric eosinophilic esophagitis: qualitative methods. *BMC Gastroenterol.* 2011; 11:126.
- Henderson CJ, Abonia JP, King EC, Putnam PE, Collins MH, Franciosi JP, Rothenberg ME. Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis. J Allergy Clin Immunol. 2012; 129:1570-1578.
- 16. Hommel KA, Franciosi JP, Hente EA, Ahrens A, Rothenberg ME. **Treatment adherence in pediatric eosinophilic gastrointestinal disorders**. *J Pediatr Psychol*. 2012; 37:533-42.
- Keller MD, Petersen M, Ong P, Church J, Risma K, Burham J, Jain A, Stiehm ER, Hanson EP, Uzel G, Deardorff MA, Orange JS. Hypohidrotic Ectodermal Dysplasia and Immunodeficiency with Coincident NEMO and EDA Mutations. Front Immunol. 2011; 2:61.
- Kucuk ZY, Strait R, Khodoun MV, Mahler A, Hogan S, Finkelman FD. Induction and suppression of allergic diarrhea and systemic anaphylaxis in a murine model of food allergy. J Allergy Clin Immunol. 2012; 129:1343-8.
- Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, Burks AW, Chehade M, Collins MH, Dellon ES, Dohil R, Falk GW, Gonsalves N, Gupta SK, Katzka DA, Lucendo AJ, Markowitz JE, Noel RJ, Odze RD, Putnam PE, Richter JE, Romero Y, Ruchelli E, Sampson HA, Schoepfer A, Shaheen NJ, Sicherer SH, Spechler S, Spergel JM, Straumann A, Wershil BK, Rothenberg ME, Aceves SS. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol*. 2011; 128:3-20 e6; quiz 21-2.
- 20. Lu TX, Hartner J, Lim EJ, Fabry V, Mingler MK, Cole ET, Orkin SH, Aronow BJ, Rothenberg ME. MicroRNA-21 limits in vivo immune response-mediated activation of the IL-12/IFN-gamma pathway, Th1 polarization, and the severity of delayed-type hypersensitivity. J Immunol. 2011; 187:3362-73.
- Lu TX, Sherrill JD, Wen T, Plassard AJ, Besse JA, Abonia JP, Franciosi JP, Putnam PE, Eby M, Martin LJ, Aronow BJ, Rothenberg ME. MicroRNA signature in patients with eosinophilic esophagitis, reversibility with glucocorticoids, and assessment as disease biomarkers. *J Allergy Clin Immunol.* 2012; 129:1064-75 e9.
- 22. Lykens JE, Terrell CE, Zoller EE, Risma K, Jordan MB. **Perforin is a critical physiologic regulator of T-cell activation**. *Blood*. 2011; 118:618-26.
- 23. Mavi P, Rajavelu P, Rayapudi M, Paul RJ, Mishra A. **Esophageal functional impairments in experimental eosinophilic esophagitis**. *Am J Physiol Gastrointest Liver Physiol*. 2012; 302:G1347-55.

- 24. Moncrief T, Kahn R, Assa'ad A. Mouse sensitization as an independent risk factor for asthma morbidity. *Ann Allergy Asthma Immunol.* 2012; 108:135-40.
- 25. Morohoshi K, Ohbayashi M, Patel N, Chong V, Bird AC, Ono SJ. Identification of anti-retinal antibodies in patients with age-related macular degeneration. *Exp Mol Pathol.* 2012; 93:193-199.
- Morohoshi K, Patel N, Ohbayashi M, Chong V, Grossniklaus HE, Bird AC, Ono SJ. Serum autoantibody biomarkers for age-related macular degeneration and possible regulators of neovascularization. *Exp Mol Pathol.* 2012; 92:64-73.
- Munitz A, Cole ET, Karo-Atar D, Finkelman FD, Rothenberg ME. Resistin-Like Molecule-alpha Regulates IL-13-Induced Chemokine Production but Not Allergen-Induced Airway Responses. Am J Respir Cell Mol Biol. 2012; 46:703-13.
- 28. Munitz A, Foster PS. T(H)9 cells: in front and beyond T(H)2. J Allergy Clin Immunol. 2012; 129:1011-3.
- 29. Pentiuk S, Putnam PE, Rothenberg M. Gastroesophageal reflux disease and eosinophilic esophagitis in children with complex airway disease. *Kendig and Chernick's disorders of the respiratory tract in children*. Philadelphia, PA: Elsevier/Saunders; 2012:966-968.
- Rajavelu P, Rayapudi M, Moffitt M, Mishra A, Mishra A. Significance of para-esophageal lymph nodes in food or aeroallergen-induced iNKT cell-mediated experimental eosinophilic esophagitis. *Am J Physiol Gastrointest Liver Physiol*. 2012; 302:G645-54.
- 31. Rani R, Smulian AG, Greaves DR, Hogan SP, Herbert DR. **TGF-beta limits IL-33 production and promotes the resolution of colitis through regulation of macrophage function**. *Eur J Immunol*. 2011; 41:2000-9.
- 32. Risma K. A loss of naivete. Blood. 2012; 119:3371-2.
- 33. Risma K, Jordan MB. Hemophagocytic lymphohistiocytosis: updates and evolving concepts. *Curr Opin Pediatr.* 2012; 24:9-15.
- 34. Rothenberg ME. **Eosinophilic syndromes**. *Goldman's Cecil medicine*. Philadelphia: Elsevier/Saunders; 2012:1118-1121.
- 35. Rothenberg ME, Wen T, Shik D, Cole ET, Mingler MM, Munitz A. **IL-13 receptor alpha1 differentially regulates aeroallergen-induced lung responses**. *J Immunol*. 2011; 187:4873-80.
- 36. Sherrill JD, Rothenberg ME. **The genetic basis of eosinophilic esophagitis**. *Eosinophilic Esophagitis*. New York: Springer (Humana Press); 2012:97-106.
- 37. Sherrill JD, Rothenberg ME. Genetic dissection of eosinophilic esophagitis provides insight into disease pathogenesis and treatment strategies. *J Allergy Clin Immunol.* 2011; 128:23-32; quiz 33-4.
- 38. Spergel JM, Rothenberg ME, Collins MH, Furuta GT, Markowitz JE, Fuchs G, 3rd, O'Gorman MA, Abonia JP, Young J, Henkel T, Wilkins HJ, Liacouras CA. Reslizumab in children and adolescents with eosinophilic esophagitis: results of a double-blind, randomized, placebo-controlled trial. J Allergy Clin Immunol. 2012; 129:456-63, 463 e1-3.
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- 40. 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.
- Walsh KB, Teijaro JR, Zuniga EI, Welch MJ, Fremgen DM, Blackburn SD, von Tiehl KF, Wherry EJ, Flavell RA, Oldstone MB. Toll-like Receptor 7 Is Required for Effective Adaptive Immune Responses that Prevent Persistent Virus Infection. *Cell Host Microbe*. 2012; 11:643-53.
- 42. Wang YH, Wills-Karp M. The potential role of interleukin-17 in severe asthma. *Curr Allergy Asthma Rep.* 2011; 11:388-94.

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- Zhang K, Jordan MB, Marsh RA, Johnson JA, Kissell D, Meller J, Villanueva J, Risma KA, Wei Q, Klein PS, Filipovich AH. Hypomorphic mutations in PRF1, MUNC13-4, and STXBP2 are associated with adult-onset familial HLH. Blood. 2011; 118:5794-8.

## Faculty, Staff, and Trainees

#### **Faculty Members**

#### Marc E. Rothenberg, MD, PhD, Professor

Leadership Division Director

**Research Interests** Elucidating the mechanisms of allergic responses in mucosal tissues such as the lung and the gastrointestinal tract with a focus on eosinophilic esophagitis

#### J. Pablo Abonia, MD, Assistant Professor

**Research Interests** Investigates the role of mast cells in eosinophilic esophagitis and focuses on informatics analysis of medical records and the Registry of Eosinophilic Gastrointestinal Disorders (REGID)

#### Amal H. Assa'ad, MD, Professor

Leadership Clinical Director

**Research Interests** Investigates food allergy (natural history of IgE-mediated food allergy, diagnostic tools, association with cardiovascular morbidity) and conducts clinical trials of novel therapies for atopic disorders (food allergy, eosinophilic disorders, asthma)

#### Barski Artem, PhD, Assistant Professor

**Research Interests** Investigates chromatin biology and epigenomic and transcriptional regulation of immune responses and uses epigenomic data to augment genome-wide association studies

#### Thomas J. Fischer, MD, Adjunct

Research Interests Focuses on the pharmacologic management of asthma and immune deficiency diseases

#### Simon P. Hogan, PhD, Associate Professor

Research Interests Studies allergies, food allergies, eosinophil biology and gastrointestinal inflammation

#### Michelle B. Lierl, MD, Adjunct

**Research Interests** Investigates the role of basidiomycete fungal spores and myxomycete spores as aeroallergens and conducts allergen component testing for food allergies

#### Anil Mishra, PhD, Associate Professor

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

#### Terri Moncrief, MD, Instructor

**Research Interests** Conducts multidimensional analysis of the home environment and its effect on asthma morbidity, focusing on the impact of single-parenthood, family routines and allergic sensitizations on asthma outcomes

#### Ariel Munitz, PhD, Assistant Professor

Research Interests Investigates cytokine receptor signaling in mucosal inflammation to identify immunological

mechanisms and pharmacological targets

#### Santa Ono, PhD, Professor

**Research Interests** Focuses on the transcriptional regulation in the human immune system, mechanisms of mast cell-dependent inflammation on the ocular surface and the immune component of age-related macular degeneration

#### Kimberly A. Risma, MD, PhD, Assistant Professor

**Research Interests** Develops novel diagnostic/therapeutic approaches to improve outcomes for children with hemophagocytic lymphohistiocytosis, an inflammatory disease caused by genetic defects in the cytotoxic pathways of natural killer cells and cytotoxic T lymphocytes

#### Karl von Tiehl, MD, Assistant Professor

**Research Interests** Conducts clinical research on the relation of egg allergy to the influenza vaccine and on eosinophilic disorders

#### Yui-Hsi Wang, PhD, Assistant Professor

**Research Interests** Investigates the mechanisms of T cell plasticity in the airway and gut and how inflammatory mediators regulate T cell subpopulation development in allergic gastrointestinal inflammation

#### Nives Zimmermann, MD, Associate Professor

**Research Interests** Focuses on deciphering the mechanisms of eosinophilia and eosinophil survival and death in allergic inflammation and asthma

#### Li Zuo, MD, Assistant Professor

**Research Interests** Investigates mechanisms and new therapeutic options for food allergy and food allergyrelated disorders

#### **Joint Appointment Faculty Members**

#### Gurjit Khurana Hershey, MD, Professor (Asthma Research)

Research Interests Asthma genetics

#### Alexandra Filipovich, MD, Professor (Hematology/Oncology Diagnostic Laboratory)

**Research Interests** Primary immunodeficiencies; BMT for primary immunodeficiencies; Hemophagocytic lymphocytosis; Post-BMT immune reconstruction

#### **Clinical Staff Members**

• Kalra Harpinder, MD, Staff Physician

#### Trainees

- Andrew Lindsley, MD, Phd, PGY-5, Indiana University School of Medicine
- Zeynep Yesim Kucuk, MD, PGY-6, Istanbul Universitesi, Istanbul Tip Fakultesi
- Terri Moncrief, MD, PGY-6, Washington University School of Medicine, St. Louis
- Patricia Fulkerson, MD, PhD, PGY-5, University of Cincinnati, College of Medicine, Ohio
- Maya Nanda, MD, PGY-4, Albany Medical College
- Jinzhu Li, MD, PhD, PGY-4, Wayne State University
- Carine Bouffi, PhD, University of Montpellier, France
- Julie Caldwell, PhD, University of Cincinnati, College of Medicine, hio
- Chen Chun-Yu, PhD, University of Rochester, New York
- Gen Kano, PhD, Kyoto Prefectural University of Medicine, Kyoto, Japan
- Hilde Laeremans, PhD, University of Maastricht, The Netherlands

- Eun Jin Lim, PhD, University of Kentucky, Kentucky
- Priya Rajavelu, PhD, University of Madras, India
- Joseph Sherrill, PhD, University of Cincinnati, Ohio
- Lee Jee-Boong, PhD, Ewha Womans University, South Korea
- Ting Wen, PhD, Rutgers University/UMDNJ, New Jersey
- Zhu Xiang, PhD, Nanjing Medical University, Nanjing, Jiangsu Province China
- Amanda Beichler, , Ohio Northern University, Ohio
- Bo Liu, , Tsinghua University, Beijing, China
- Thomas Lu, , University of Cincinnati, Cincinnati, OH
- Svetlana Itskovich, PhD, Tel Aviv University, Israel
- Benjamin Davis, MD, University of Iowa, Iowa
- Rahul D'Mello, , Johns Hopkins University, Baltimore, MD

### **Division Collaboration**

# **Cincinnati Center for Eosinophilic Disorders (CCED)** » Margaret H. Collins, MD, Lisa J. Martin, PhD, Philip E. Putnam, MD, and Nicole E. Zahka, PhD

The Cincinnati Center for Eosinophilic Disorders (CCED) is the international leader in both caring for patients with eosinophilic conditions and researching the best treatments and cure. The CCED was the first center established that brings together experts in allergy / immunology, gastroenterology, social work, nutrition and pathology to evaluate, treat and study these chronic medical problems in children and adults. The CCED's multidisciplinary team has extensive experience with these disorders and aims to provide personalized care and learn from each patient. Several of the faculty of the Division of Allergy and Immunology are physicians and researchers on the CCED's multidisciplinary team: Marc E. Rothenberg, MD, PhD; J. Pablo Abonia, MD; Simon P. Hogan, PhD; Anil Mishra, PhD; Kimberly A. Risma, MD, PhD; and Karl F. von Tiehl, MD.

#### Digestive Health Center » Jorge A. Bezerra, MD and Kasper Hoebe, PhD

The Digestive Health Center (DHC) is focused on bench-to-bedside research in pediatric digestive disease and is one of only 17 Silvio O. Conte Digestive Diseases Research Core Centers in the nation supported by the National Institute of Diabetes and Digestive and Kidney Diseases. Marc E. Rothenberg, MD, PhD, Simon P. Hogan, PhD, and Anil Mishra, PhD, are all investigators of this center, and Nives Zimmermann, MD, and Yui-Hsi Wang, PhD, are associate members.

#### Division of Asthma Research » Gurjit Khurana Hershey, MD, PhD

The Division of Asthma Research at Cincinnati Children's focuses its research efforts on individual variations in asthma presentation, treatment response and outcomes. Faculty of the Division of Asthma Research and the Division of Allergy and Immunology frequently collaborate as evidenced by a shared NIH U19 AADCRC grant. Our Asthma and Allergic Diseases Cooperative Research Center (AADCRC) is one of only 12 such centers in the United States. Marc E. Rothenberg, MD, PhD, is a project principal investigator for this center, which received a renewal of its NIH-funded U19 grant last year. The center's overarching hypothesis is that epithelial cell genes play a central role in the pathogenesis of allergic disorders.

#### Division of Asthma Research » Gurjit Khurana Hershey, MD, PhD

Mechanism of Airway Acidification in Asthma (Nives Zimmermann, MD)

#### Division of Behavioral Medicine and Clinical Psychology » Kevin A. Hommel, PhD

Behavioral Functioning, Treatment Adherence and Symptom Assessment in Pediatric Eosinophilic Gastrointestinal Disorders (Marc E. Rothenberg, MD, PhD)

#### Division of Biomedical Informatics » Bruce J. Aronow, PhD

MicroRNA Analysis of Polarized Macrophages (Ariel Munitz, PhD)

MicroRNA Signatures and Regulation of IL-13 Mechanisms in Eosinophilic Esophagitis (Marc E. Rothenberg, MD, PhD)

Division of Cardiology / Division of Human Genetics / Heart Institute » Stephanie M. Ware, MD, PhD, FACMG Human Genetics and Relationship of Connective Tissue Disorders and Eosinophilic Gastrointestinal Disorders (Marc E. Rothenberg, MD, PhD)

**Division of Gastroenterology, Hepatology and Nutrition** » Jose M. Garza, MD, MS, Philip E. Putnam, MD, and Noah F. Shroyer, PhD

The Division of Gastroenterology, Hepatology and Nutrition at Cincinnati Children's specializes in treatment and research for gastrointestinal, liver and nutritional disorders. Faculty of the Division of Gastroenterology, Hepatology and Nutrition and the Division of Allergy and Immunology, such as Marc E. Rothenberg, MD, PhD and Simon P. Hogan, PhD, frequently collaborate in areas of research including eosinophilic gastrointestinal disorders and inflammatory bowel diseases.

- **Division of Gastroenterology, Hepatology and Nutrition** » Lee A. Denson, MD and Kris A. Steinbrecher, PhD Role of Eosinophils in Pediatric Inflammatory Bowel Diseases (Simon P. Hogan, PhD)
- **Division of General and Community Pediatrics; Division of Biostatistics and Epidemiology** » Andrew F. Beck, MD, Bin Huang, PhD, Robert S. Kahn, MD, MPH, and Jeffrey M. Simmons, MD

Social Home Environment and Asthma Morbidity (Terri M. Moncrief, MD, MS)

Division of Immunobiology » Fred Finkelman, MD

Expression and Function of CMRF35-like Molecule (CLM-1) in Asthma (Ariel Munitz, PhD)

Mechanisms of Allergy, Asthma, and Immunology (Marc E. Rothenberg, MD, PhD)

Mechanisms of Food Allergy and Anaphylaxis (Simon P. Hogan, PhD, Yui-Hsi Wang, PhD)

Intestinal Innate Helper Cells and Food Allergy (Yui-Hsi Wang, PhD)

#### Division of Immunobiology » Fred Finkelman, MD

The Division of Immunobiology at Cincinnati Children's conducts research toward understanding the cellular, molecular and genetic mechanisms that drive immunologically mediated disorders in children. Fred Finkelman, MD, of the Division of Immunobiology actively collaborates, publishes and co-mentors with faculty of the Division of Allergy and Immunology. Two of our faculty serve as directors of admissions for the Immunobiology Graduate Program: Simon P. Hogan, PhD, is the director of PhD admissions, and Nives Zimmermann, MD, is the director of MS admissions.

#### Division of Orthopedics » Charles T. Mehlman, DO, MPH

Metal sensitivity in patients with scoliosis (Michelle B. Lierl, MD)

#### Division of Pathology » Margaret H. Collins, MD

Molecular Mechanism of Eosinophil Cell Death (Nives Zimmermann, MD, Marc E. Rothenberg, MD, PhD)

#### Division of Reproductive Sciences » Satoshi H. Namekawa, PhD

RNF8 directs active epigenetic modifications and escape gene expression from inactive sex chromosomes in male germ cells. (Artem Barski, PhD)

**Division of Rheumatology / Center for Autoimmune Genomics and Etiology (CAGE)** » John B. Harley, MD, PhD, Kenneth M. Kaufman, PhD, and Matthew T. Weirauch, PhD

Epigenomics of Lupus (Artem Barski, PhD)

**Division of Rheumatology / Center for Autoimmune Genomics and Etiology (CAGE)** » John B. Harley, MD, PhD

Consortium of Food Allergy Research (CoFAR) - Eosinophilic Esophagitis and Food Allergy (Marc E. Rothenberg, MD, PhD)

Collaborative Mentoring of Postdoctoral Fellow (Marc E. Rothenberg, MD, PhD)

## **Division of Rheumatology / Center for Autoimmune Genomics and Etiology (CAGE)** » Kenneth M. Kaufman, PhD

Genetics of Eosinophilic Esophagitis (Marc E. Rothenberg, MD, PhD)

## Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
ASSA'AD, A		
Hemodynamic Alterations During Fo	ood Allergy Reactions and Anaphylaxis	
American Academy of Allergy, Asthma	& Immunology	
	07/01/11-06/30/12	\$13,000
BARSKI, A		
Role of Chromatin and Gene Poising	g in T Cell Differentiation and Activation	
National Institutes of Health		
K22 HL 098691	09/12/11-06/30/14	\$249,000
CALDWELL, J		
Molecular Mechanisms of Cadherin-	Like 26 in Inflammation	
American Heart Association		
11POST7440046	07/01/11-06/30/12	\$47,000
FULKERSON, P		
Role of Spi-C in Eosinophil Develop	ment and Functional Responses	
National Institutes of Health		
K08 AI 093673	02/04/11-01/31/16	\$85,122
HOGAN, S		
Eosinophil:M2 Macrophage:CCL11 A Ulcerative Colitis	Axis in Experimental Colitis and Pediatric Corticosteroid Resignation Resignation and Pediatric Corticosteroid Resignation and Pe	stant
National Institutes of Health		
R01 DK 090119	04/01/12-03/31/16	\$217,500
KUO, C		
Roles of CC Chemokine Activity in M	last Cell Responses and Ocular Allergy	
National Institutes of Health(University	of Cincinnati)	
R01 EY 019630	05/01/11-07/31/13	\$255,101
LI, J		
Immunology/Allergy Fellowship Trai		
National Institutes of Health(University	of Cincinnati)	
T32 AI 060515	07/01/11-05/31/12	\$42,977

LINDSLEY, A		
Immunology/Allergy Fellowship Trainin	ng Grant	
National Institutes of Health(University of 0	Cincinnati)	
T32 AI 060516	07/01/10-05/31/12	\$48,655
LU, T		
miR-21 in the Pathogenesis of Asthma		
National Institutes of Health		
F30 HL104892	08/16/10-08/15/13	\$45,364
MISHRA, A		
Mechanistic Analysis of Eosinophilic E National Institutes of Health	sophagitis.	
R01 DK 067255	08/01/11-05/31/15	\$252,651
101 DR 001200		φ202,001
RISMA, K		
Perforin Gene Transfer Into Human Cyt	otoxic Lymphocytes	
Histiocytosis Association of America		
	01/01/12-12/31/12	\$50,000
The Functional Consequences of Incon American Academy of Allergy, Asthma & I		
American Academy of Allergy, Astinna & I	07/01/09-06/30/12	\$100,000
		\$100,000
ROTHENBERG, M		
IL-13 and Eosinophilic Esophagitis		
National Institutes of Health		
R01 DK 076893	09/01/07-06/30/12	\$196,902
IL-13 Associated Eosinophil Lung Resp National Institutes of Health	Donses	
R01 AI 083450	08/20/09-07/31/14	\$245,025
Immunobiology of Peanut Allergy and i		φ2+0,020
National Institutes of Health(Mount Sinai N		
U19 AI 066738	07/01/10-06/30/15	\$341,219
Regulation of Gastrointestinal Eosinop	hils	
National Institutes of Health		<b></b>
R37 Al 045898 Cincinneti Contor for Clinical/Translatio	12/01/10-11/30/14	\$222,750
Cincinnati Center for Clinical/Translatic National Institutes of Health(University of C	-	
UL1 RR 026314	04/03/09-03/31/14	\$39,647
		<b>+ , -</b>
SHERRILL, J		
	Enhances Allergic Sensitization in Eosinophilic Es	ophagitis
Thrasher Research Fund	00/04/40 00/00/44	<b>\$40 500</b>
	03/01/12-02/28/14	\$12,500
WANG, Y		
Regulation of TH2 Memory/Effector Cel	Is During Allergic Inflammation	
National Institutes of Health		
R01 AI 090129	05/01/10-04/30/15	\$247,500
The Roles of IL-17-producing TH2 Mem	ory/Effector Cells in Allergic Asthma	
American Lung Association	07/04/40 00/20/40	*=^ ^^^
AI169584N	07/01/10-06/30/12	\$50,000

ZIMMERMANN, N

Mechanism of Airway Acidification in Asthma American Lung Association

**Current Year Direct** 

	\$46,419
	\$4,620
	\$65,026
Current Year Direct Receipts	\$116,065
Total	\$2,927,978