2013 Research Annual Report

Immunobiology

Cincinnati Children's

Division Details

Division Data Summary

RESEARCH AND TRAINING DETAILS	
Number of Faculty	15
Number of Joint Appointment Faculty	0
Number of Research Fellows	10
Number of Research Students	21
Number of Support Personnel	26

CLINICAL ACTIVITIES AND TRAINING	
Number of Clinical Staff	0
Number of Clinical Fellows	3
Number of Clinical Students	0
Number of Other Students	0
Inpatient Encounters	0
Outpatient Encounters	0

Division Photo

Row 1: H Singh, J Aliberti, C Chougnet
Row 2: E Janssen, S Divanovic, J Koehl, J Katz
Row 3: M Jordan, K Hoebe, I Lewkowich, F Finkelman, HL Grimes, D Hildeman

Significant Accomplishments

Studies Break Ground in Controlling Inflammation

Investigators in our Division published four important papers that suggest improved ways to control dangerous disease-related inflammation.

In a paper published in *Nature Medicine*, Jörg Kohl, PhD, and colleagues reported discovering an important and potent anti-inflammatory mechanism: the immune complex-mediated association of the inhibitory receptor, FcgRIIb, with a C-type lectin-like receptor, dectin-1, inhibits signaling through the proinflammatory receptor for the complement-derived anaphylatoxin, C5a. Because immune complex binding to the dectin-1 receptor depends heavily on galactosylation of the IgG in these complexes, the observations reported in this paper suggest that artificially galactosylated IgG can be used to inhibit the many inflammatory diseases that are mediated by C5a.

Marat Khodoun, PhD, Fred Finkelman, MD, and colleagues published findings in *the Journal of Allergy and Clinical Immunology* that demonstrate a novel approach that safely suppresses IgE-mediated allergy in a mouse model. Mice were injected with rising doses of a monoclonal antibody until inducing anaphylaxis. This approach gradually removed all IgE from these cells, without causing any apparent signs of disease. As a result, the approach eliminated sensitivity to IgE-mediated anaphylaxis. A similar approach could be used to treat human allergic disorders, including food and drug allergies, insect venom sensitivities, allergic skin disease, allergic rhinitis and asthma.

In a paper published in the journal *Blood*, Michael Jordan, MD, and C.E. Terrell explained how humans and mice with impaired perforin-dependent cytotoxic function can develop excessive T-cell activation and the fatal

inflammatory disorder hemophagocytic lymphohistiocytosis (HLH) after infection. Using a mouse model of HLH, they defined a feedback loop that is critical for immune homeostasis. This endogenous feedback loop involves perforin-dependent elimination of antigen-presenting dendritic cells (DCs) by $CD8^-$ T cells; the abnormal persistence of antigen presentation in perforin-deficient mice drove T-cell activation well beyond normal limits, leading to the inflammatory disease. These new findings suggest that interventions to limit DC antigen presentation may be useful to treat HLH.

Julio Aliberti, MS, PhD, and colleagues published findings in *PLoS One* demonstrating that exogenous administration of anti-inflammatory lipoxins can protect against lethal inflammation in experimental malaria by inhibiting the production of the cytokines IL-12 and IFN-γ in the brain. Malaria-infected mice that lack the ability to produce lipoxins developed accelerated mortality, while treatment of wild-type mice with lipoxins as late as 3 days after malaria inoculation prevented early mortality. This suggests that lipoxins may be useful for treating cerebral malaria, a form of malaria that causes mortality and disability, particularly in children.

Regulating the Growth of Leukemia Cells

James Phelan, H. Leighton Grimes, PhD, and colleagues published findings in *Cancer Cell* showing that leukemic cells depend on growth factor independence 1 (Gfi1) for survival. Acute lymphoblastic leukemia (ALL) cells rely on Gfi1 to escape the tumor-suppressing capabilities of another protein, p53, which normally initiates DNA repair that involves apoptosis, or programmed cell death, of cancer cells. . Removal of Gfi1 in lymphoid tumors in mice caused ALL to regress through p53-induced apoptosis. Furthermore, removal of Gfi1 from human T-cell ALL cells implanted into mice again stopped the progression of leukemia in the mice, without any harmful effects. This suggests an approach that might be useful for the suppression of human ALL and, possibly, other malignancies.

Administrative Accomplishments

After an 18-month search, Harinder Singh, PhD, was chosen to direct the Division of Immunobiology. He joins us after having led Immunology programs at the University of Chicago and at Genentech. David Hildeman, PhD, Edith Janssen, PhD, and Fred Finkelman, MD, were active participants in the search. Meanwhile, the German Federal Republic approved funding for a large, integrated immunology graduate program between the University of Lübeck and Cincinnati Children's. Hildeman and Jörg Köhl, MD, led the effort with participation from several Division members. Graduate students from each institution are already rotating in labs at the other institution. This program promises to improve the quality of our future graduate students and post-doctoral fellows and could enhance recognition of Cincinnati Children's in Europe.

Research Highlights

Claire Chougnet, PhD

Claire Chougnet was awarded a Burroughs-Wellcome grant to study the immunological responses elicited by intra-amniotic Ureaplama parvum. Her application as a MPI NIH grant, with Louis Muglia, the Director for the Center for Prevention of Preterm Birth, also received a 5th percentile and should be funded. This multidisciplinary effort will study the connections between stress, infections and the immune response, with the hypothesis that infection and stress during pregnancy synergize to lead to preterm birth.

Fred Finkelman, MD

Fred Finkelman was awarded a 3 year Department of Defense grant for studying the pathogenesis of food allergy. He gave a plenary talk about mechanisms and prevention of anaphylaxis at the World Allergy Organization meeting in Milan.

David Hildeman, PhD

David Hildeman was elected a Fellow of the University of Cincinnati Graduate School.

Michael Jordan, MD

Michael Jordan received new research funding from the Histiocytosis Foundation of America.

Ian Lewkowich, PhD

Ian Lewkowich received an American Lung Association Biomedical Research Grant to address the role of TRAF3 in regulating IL-17A mediated enhancement of IL-13-driven STAT6 phosphorylation. He was an invited speaker at the 2013 AAAAI annual meeting in San Antonio and the 3rd International Forum on Respiratory Disorders in Chonqing, China and was invited to join the Editorial board of Allergy, Asthma and Clinical Immunology, the journal of the Canadian Society of Clinical Immunology.

Significant Publications

Karsten CM, Pandey MK, Figge J, Kilchenstein R, Taylor PR, Rosas M, McDonald JU, Orr SJ, Berger M, Petzold D, Blanchard V, Winkler A, Hess C, Reid DM, Majoul IV, Strait RT, Harris NL, Köhl G, Wex E, Ludwig R, Zillikens D, Nimmerjahn F, **Finkelman FD**, Brown GD, Ehlers M, **Köhl J**. **Anti-inflammatory activity of IgG1 mediated by Fc galactosylation and association of FcγRIIB and dectin-1**. *Nat Med*. 2012. 18:1401-6.

This paper reported the discovery of a previously recognized important and potent anti-inflammatory mechanism: the immune complex-mediated association of the inhibitory receptor, FcγRIIb, with a C-type lectin-like receptor, dectin-1, inhibits signaling through the proinflammatory receptor for the complement-derived anaphylatoxin, C5a. Because immune complex binding to the dectin-1 receptor depends on heavily galactosylation of the IgG in these complexes, the observations reported in this paper suggest that artificially galactosylated IgG can be used to inhibit the many inflammatory disease that are mediated by C5a.

Khandanpour C*, **Phelan JD***, Vassen L, Schütte J, Chen R, Horman SR, Gaudreau MC, Krongold J, Zhu J, Paul WE, Dührsen U, Göttgens B, **Grimes HL**, Möröy T. **Growth factor independence 1 antagonizes a p53-induced DNA damage response pathway in lymphoblastic leukemia**. *Cancer Cell*. 2013. 23:200-14. *co-first authors

Observations reported in this paper showed that leukemic cells depend on growth factor independence 1 (Gfi1) for survival. Acute lymphoblastic leukemia (ALL) cells rely on Gfi1 to escape the tumor-suppressing capabilities of another protein, p53. p53 normally initiates DNA repair that involves apoptosis, or programmed cell death, of cancer cells, but Gfi1 restricts p53 activity. Removal of Gfi1 in lymphoid tumors in mice caused ALL to regress through p53-induced apoptosis. Furthermore, removal of Gfi1 from human T-cell ALL cells implanted into mice again stopped the progression of leukemia in the mice, without any harmful effects. This suggests an approach that might be useful for the suppression of human ALL and, possibly, other malignancies.

Khodoun MV, Kucuk ZY, Strait RT, Krishnamurthy D, Janek K, **Lewkowich I**, **Morris SC**, **Finkelman FD**. **Rapid polyclonal desensitization with antibodies to IgE and FcεRIα**. *J Allergy Clin Immunol*. 2013. 131:1555-64.

This paper demonstrated a novel approach that safely suppresses IgE-mediated allergy in a mouse model. Mice were injected with a monoclonal antibody to FcεRI, the high affinity IgE receptor on mast cell and basophils, starting with a dose too small to induce disease and building over several hours to a dose that induces anaphylaxis in naïve mice. This approach eliminated basophils and initially made mast cells refractory

to FcεRI-mediated stimulation, then more gradually removed all IgE from these cells, without causing any apparent signs of disease. As a result, the approach eliminated sensitivity to IgE-mediated anaphylaxis; a similar approach could be used to treat human allergic disorders, including food and drug allergies, insect venom sensitivities, allergic skin disease, allergic rhinitis and asthma.

Terrell CE, Jordan MB. Perforin deficiency impairs a critical immunoregulatory loop involving murine CD8$^+$ T cells and dendritic cells. *Blood.* 2013.121:5184-91.

Humans and mice with impaired perforin-dependent cytotoxic function may develop excessive T-cell activation and the fatal inflammatory disorder hemophagocytic lymphohistiocytosis (HLH) after infection. This paper showed how this can happen by using a mouse model of HLH to define a feedback loop that is critical for immune homeostasis. This endogenous feedback loop involves perforin-dependent elimination of antigen-presenting dendritic cells (DCs) by CD8$^-$ T cells; the abnormal persistence of antigen presentation in perforin-deficient mice drove T-cell activation well beyond normal limits, leading to the inflammatory disease. This suggests that interventions that limit DC antigen presentation may be useful to treat HLH.

Hung LY*,**Lewkowich IP*,** Dawson L, Downey J, **Yang Y**, Smith DE, Herbert D. **IL-33 drives bi-phasic IL-13 production for non-canonical Type 2 immunity against hookworms**. *Proc. Nat. Acad. Sci.* 2012. 110:282-287.
*co-first authors

This report demonstrated that the cytokine IL-33 makes important contributions to host defense against infection with the hookworm, *Nippostrongylus brasiliensis*. Mice lacking IL-33 have profound defects in the ability of pulmonary type 2 innate lymphoid cells (ILC2s) to produce IL-13, but no defect in the development of IL-4- and IL-13-producing T cells. Despite the lack of a T cell defect, worm clearance was impaired in IL-33 KO mice. These data stress the importance of IL-33 in promoting the development of functional ILC2s in worm-infected mice, and highlights the importance of ILC2s in the clearance of these parasites.

Division Publications

1. Arnold CN, Barnes MJ, Berger M, Blasius AL, Brandl K, Croker B, Crozat K, Du X, Eidenschenk C, Georgel P, Hoebe K, Huang H, Jiang Z, Krebs P, La Vine D, Li X, Lyon S, Moresco EM, Murray AR, Popkin DL, Rutschmann S, Siggs OM, Smart NG, Sun L, Tabeta K, Webster V, Tomisato W, Won S, Xia Y, Xiao N, Beutler B. **ENU-induced phenovariance in mice: inferences from 587 mutations**. *BMC Res Notes*. 2012; 5:577.
2. Barger JF, Gallo CA, Tandon P, Liu H, Sullivan A, Grimes HL, Plas DR. **S6K1 determines the metabolic requirements for BCR-ABL survival**. *Oncogene*. 2013; 32:453-61.
3. Bochner BS, Rothenberg ME, Boyce JA, Finkelman F. **Advances in mechanisms of allergy and clinical immunology in 2012**. *J Allergy Clin Immunol*. 2013; 131:661-7.
4. Borges M, Barreira-Silva P, Flórido M, Jordan MB, Correia-Neves M, Appelberg R. **Molecular and cellular mechanisms of Mycobacterium avium-induced thymic atrophy**. *J Immunol*. 2012; 189:3600-8.
5. Cashman S, Lampe K, Sheridan R, Hoebe K. **An ENU mutagenesis approach to dissect "self"-induced immune responses: Unraveling the genetic footprint of immunosurveillance**. *Oncoimmunology*. 2012; 1:856-862.
6. Chougnet C, Shacklett BL. **T Cell Responses during Human Immunodeficiency Virus (HIV)-1 Infection**. In: J Aliberti, ed. *Control of innate and adaptive immune responses during infectious diseases*. New York: Springer; 2012:141-169.
7. Currier MA, Eshun FK, Sholl A, Chernoguz A, Crawford K, Divanovic S, Boon L, Goins WF, Frischer JS, Collins MH, Leddon JL, Baird WH, Haseley A, Streby KA, Wang PY, Hendrickson BW, Brekken RA, Kaur

B, Hildeman D, Cripe TP. **VEGF blockade enables oncolytic cancer virotherapy in part by modulating intratumoral myeloid cells**. *Mol Ther*. 2013; 21:1014-23.

8. Danzer C, Mattner J. **Impact of microbes on autoimmune diseases**. *Arch Immunol Ther Exp (Warsz)*. 2013; 61:175-86.
9. Finkelman FD. **Worming their way into the pharmacy: use of worms and worm products to treat inflammatory diseases**. *Arthritis Rheum*. 2012; 64:3068-71.
10. Hogan SP, Wang YH, Strait R, Finkelman FD. **Food-induced anaphylaxis: mast cells as modulators of anaphylactic severity**. *Semin Immunopathol*. 2012; 34:643-53.
11. Horwitz MS, Corey SJ, Grimes HL, Tidwell T. **ELANE mutations in cyclic and severe congenital neutropenia: genetics and pathophysiology**. *Hematol Oncol Clin North Am*. 2013; 27:19-41, vii.
12. Huber AK, Finkelman FD, Li CW, Concepcion E, Smith E, Jacobson E, Latif R, Keddache M, Zhang W, Tomer Y. **Genetically driven target tissue overexpression of CD40: a novel mechanism in autoimmune disease**. *J Immunol*. 2012; 189:3043-53.
13. Hung LY, Lewkowich IP, Dawson LA, Downey J, Yang Y, Smith DE, Herbert DR. **IL-33 drives biphasic IL-13 production for noncanonical Type 2 immunity against hookworms**. *Proc Natl Acad Sci U S A*. 2013; 110:282-7.
14. Jordan MB, Filipovich AH. **Histiocytic Disorders**. In: R Hoffman, ed. *Hematology: basic principles and practice*. Philadelphia, PA: Saunders/Elsevier; 2013:686.
15. Karsten CM, Köhl J. **Cross-talk between antibodies, IgG Fc receptors and the complement system**. In: F Nimmerjahn, ed. *Molecular and Cellular Mechanisms of Antibody Activity*. New York: Springer; 2013:159-87.
16. Karsten CM, Köhl J. **The immunoglobulin, IgG Fc receptor and complement triangle in autoimmune diseases**. *Immunobiology*. 2012; 217:1067-79.
17. Karsten CM, Pandey MK, Figge J, Kilchenstein R, Taylor PR, Rosas M, McDonald JU, Orr SJ, Berger M, Petzold D, Blanchard V, Winkler A, Hess C, Reid DM, Majoul IV, Strait RT, Harris NL, Kohl G, Wex E, Ludwig R, Zillikens D, Nimmerjahn F, Finkelman FD, Brown GD, Ehlers M, Köhl J. **Anti-inflammatory activity of IgG1 mediated by Fc galactosylation and association of FcgammaRIIB and dectin-1**. *Nat Med*. 2012; 18:1401-6.
18. Kasperkiewicz M, Nimmerjahn F, Wende S, Hirose M, Iwata H, Jonkman MF, Samavedam U, Gupta Y, Möller S, Rentz E, Hellberg L, Kalies K, Yu X, Schmidt E, Häsler R, Laskay T, Westermann J, Köhl J, Zillikens D, Ludwig RJ. **Genetic identification and functional validation of FcγRIV as key molecule in autoantibody-induced tissue injury**. *J Pathol*. 2012; 228:8-19.
19. Khandanpour C, Krongold J, Schütte J, Bouwman F, Vassen L, Gaudreau MC, Chen R, Calero-Nieto FJ, Diamanti E, Hannah R, Meyer SE, Grimes HL, van der Reijden BA, Jansen JH, Patel CV, Peeters JK, Löwenberg B, Dührsen U, Göttgens B, Möröy T. **The human GFI136N variant induces epigenetic changes at the Hoxa9 locus and accelerates K-RAS driven myeloproliferative disorder in mice**. *Blood*. 2012; 120:4006-17.
20. Khandanpour C, Phelan JD, Vassen L, Schütte J, Chen R, Horman SR, Gaudreau MC, Krongold J, Zhu J, Paul WE, Dührsen U, Göttgens B, Grimes HL, Möröy T. **Growth factor independence 1 antagonizes a p53-induced DNA damage response pathway in lymphoblastic leukemia**. *Cancer Cell*. 2013; 23:200-14.
21. Khodoun MV, Kucuk ZY, Strait RT, Krishnamurthy D, Janek K, Lewkowich I, Morris SC, Finkelman FD. **Rapid polyclonal desensitization with antibodies to IgE and FcεRIα**. *J Allergy Clin Immunol*. 2013; 131:1555-1564 e7.
22. Klarquist JS, Janssen EM. **Melanoma-infiltrating dendritic cells: Limitations and opportunities of**

mouse models. *Oncoimmunology*. 2012; 1:1584-1593.
23. Kong L, Cardona Maya W, Moreno-Fernandez ME, Ma G, Shata MT, Sherman KE, Chougnet C, Blackard JT. **Low-level HIV infection of hepatocytes**. *Virol J*. 2012; 9:157.
24. Korfhagen TR, Kitzmiller J, Chen G, Sridharan A, Haitchi HM, Hegde RS, Divanovic S, Karp CL, Whitsett JA. **SAM-pointed domain ETS factor mediates epithelial cell-intrinsic innate immune signaling during airway mucous metaplasia**. *Proc Natl Acad Sci U S A*. 2012; 109:16630-5.
25. Kumar S, Xu J, Perkins C, Guo F, Snapper S, Finkelman FD, Zheng Y, Filippi MD. **Cdc42 regulates neutrophil migration via crosstalk between WASp, CD11b, and microtubules**. *Blood*. 2012; 120:3563-74.
26. Kurtulus S, Hildeman DA. **Assessment of CD4+ and CD8+ T cell responses using Class I and Class II MHC tetramers**. In: AL Snow, M Lenardo, eds. *Immune homeostasis methods and protocols*. New York: Humana Press; Springer; 2013:71-79.
27. Lages CS, Simmons J, Chougnet CA, Miethke AG. **Regulatory T cells control the CD8 adaptive immune response at the time of ductal obstruction in experimental biliary atresia**. *Hepatology*. 2012; 56:219-27.
28. Lampe K, Cashman S, Aksoylar H, Hoebe K. **ENU Mutagenesis in Mice–Genetic Insight into Impaired Immunity and Disease**. In: R Mishra, ed. *Mutagenesis*. Rijeka, Croatia: InTech; 2012:179-94.
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33. Lutfi R, Lewkowich IP, Zhou P, Ledford JR, Page K. **The role of protease-activated receptor-2 on pulmonary neutrophils in the innate immune response to cockroach allergen**. *J Inflamm (Lond)*. 2012; 9:32.
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Bhardwaj N, Collins S, Divanovic S, Endele M, Finan B, Gao Y, Habegger KM, Hembree J, Heppner KM, Hofmann S, Holland J, Küchler D, Kutschke M, Krishna R, Lehti M, Oelkrug R, Ottaway N, Perez-Tilve D, Raver C, Walch AK, Schriever SC, Speakman J, Tseng YH, Diaz-Meco M, Pfluger PT, Moscat J, Tschöp MH. **p62 links beta-adrenergic input to mitochondrial function and thermogenesis**. *J Clin Invest*. 2013; 123:469-78.

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Faculty, Staff, and Trainees

Faculty Members

Fred Finkelman, MD, Professor

Leadership Interim Director, Division of Immunobiology; McDonald Professor, UC Department of Internal Medicine, Division of Rheumatology and Immunology

Research Interests Allergy/Asthma, Intestinal Parasites

Julio Aliberti, PhD, Associate Professor

Research Interests Induction and regulation of immune responses to intracellular pathogens

Claire A. Chougnet, PhD, Associate Professor

Research Interests Mechanisms of immune dysregulation in HIV and aging; ontgeny of immune responses in early life

Senad Divanovic, PhD, Assistant Professor

Research Interests Role of the innate immune system in obesity and its sequelae. Role of innage immune system in induction of preterm labor

H. Leighton Grimes, PhD, Associate Professor

Leadership Director Cancer Pathology Program

Research Interests Leukemia/Lymphoma

David A. Hildeman, PhD, Associate Professor

Leadership Director, Immunobiology Graduate Program

Research Interests T-cell Biology

Kasper Hoebe, PhD, Assistant Professor

Research Interests Forward genetic analysis of the host immune response using ENU mutagenesis

Edith M. Janssen, PhD, Assistant Professor

Research Interests Mechanistic analysis and translational exploitation of adaptive immune responses to antigens expressed by apoptotic cells

Michael B. Jordan, MD, Associate Professor

Research Interests Childhood Immunodeficiency Diseases

Christopher Karp, MD, Adjunct

Research Interests Molecular mechanisms underlying regulation and dysregulation of inflammatory responses in infectious, allergic, and genetic metabolic diseases

Jonathan Katz, PhD, Professor

Research Interests The immunology of Type 1 Diabetes Mellitus

Joerg Koehl, MD, Adjunct

Research Interests Regulation of innate and adaptive immune responses by the complement system

Ian Lewkowich, PhD, Assistant Professor

Research Interests The role of PD-1 family members in differential control of immune responses/Mechanisms of severe allergic asthma

Jochen Mattner, MD, Assistant Professor

Research Interests Autoimmune Liver Diseases

Marsha Wills-Karp, PhD, Adjunct

Research Interests Immunopathogenesis of asthma

Trainees

Halil Aksoylar, BS, GSY-6, Middle East Technical University, Ankara, Turkey
Maha Almanan, BS, GSY-1, University of Khartoum, Khartoum, Sudan
Nicholas Boespflug, BS, GSY-4, Seattle University, Seattle, Washington
Stacey Burgess, BS, GSY-5, Marietta College, Marietta, Ohio
Monica Cappelletti, PhD, PGY-2, University of Milan, Milan, Italy
Shan Chandrakasan, MD, PGY-2, Children's Hospital of Michigan, Detroit, Michigan
Jordan Downey, BS, GSY-4, Hendrix College, Conway, Arkansas
Changhu Du, PhD, PGY-9, Guangzhou Medical School, Guangzhou, China
Mehari Endale Mengistu, PhD, PGY-2, Kyungpook National University, Daegu, Korea
Maria Fields, BS, GSY-4, Universidad de Antioquia, Medellin, Antioquia, Colombia
Daniel Giles, BS, GSY-2, Case Western Reserve University, Cleveland, Ohio
Naina Gour, BS, GSY-4, University of Delhi, Delhi, India
Isaac Harley, BS, GSY-5, University of Oklahoma, Norman, Oklahoma
Jared Klarquist, BA, GSY-2, Dartmouth College, Hanover, New Hampshire
Sema Kurtulus, BS, GSY-6, Sabanci University, Istanbul, Turkey
Kun-Po Li, MS, GSY-2, Graduate Institute of Immunology, National Taiwan University, Taiwan
Andrew Lindsley, MD, PhD, PGY-6, Indiana University, Indianapolis, Indiana
Jaclyn McAlees, PhD, PGY-4, The Ohio State University, Columbus, Ohio
Cortez McBerry, BS, GSY-6, Southern Illinois University, Carbondale, Illinois
Jonathan McNally, BS, GSY-4, St. Mary's College, St. Mary's City, Maryland
Sara Meyer, PhD, PGY-4, University of Cincinnati, Cincinnati, Ohio
Scott Millen, PhD, PGY-2, University of Cincinnati, Cincinnati, Ohio
Edward Muench, MEng, GSY-1, University of Louisville, Louisville, Kentucky
Omar Niss, MD, PGY-6, University of Nebraska Medical Center
Samet Oksuz, BS, GSY-1, Middle East Technology University, Ankara, Turkey
Andre Olsson, PhD, PGY-7, Lund University, Lund, Sweden
James Phelan, BS, GSY-7, The Ohio State University, Columbus, Ohio
Jana Raynor, BS, GSY-5, North Georgia College and State University, Dahlonega, Georgia
Cesar Rueda Rios, PhD, PGY-2, Universidad de Antioquia, Medellin, Antioquia, Colombia
Rosa Maria Salazar-Gonzalez, PhD, PGY-4, Emory University, Atlanta, Georgia
Hesham Shehata, BA, GSY-3, Transylvania University, Lexington, Kentucky
Sara Stoffers, MS, GSY-2, University of Cincinnati, Cincinnati, Ohio
Robert Thacker, PhD, PGY-6, University of Cincinnati, Cincinnati, Ohio
Mark Webb, BS, GSY-5, Brigham Young University, Provo, Utah

Division Collaboration

Allergy and Immunology » Patricia Fulkerson, MD, PhD

Regulatory of Eosinophil production by TLRs (Hoebe).

Allergy and Immunology » Simon Hogan, PhD

The role of C5a in food allergy (Koehl).

Allergy and Immunology » Kimberly Risma, MD, PhD

The biology of cytotoxicity: Genotype/phenotype correlations (Jordan).

Asthma Research » Gurjit Khurana Hershey, MD, PhD

Experimental asthma (Finkelman).

Bone Marrow Transplantation and Immune Deficiency » Rebecca Marsh, MD

Immune profiling in Hemophagocytic Lymphohistiocytosis (Jordan).

Center for Autoimmune Genomics and Etiology » Nan Shen, MD

CD244 as a path to SLE (Janssen).

Developmental Biology » Timothy Weaver, MS, PhD

StarD7 - a novel inhibitor of allergic lung disease (Lewkowich).

Experimental Hematology & Cancer Biology » Marie-Dominique Filippi, PhD

Neutrophil midgation (Finkelman.)

Experimental Hematology & Cancer Biology » Matthew Flick, PhD

Role of coagulation factors in development and progression of obesity and obesity-associated NAFLD (Divanovic).

Experimental Hematology & Cancer Biology » Punam Malik, MD

Novel methods to promote stem cell engraftment (Jordan).

Experimental Hematology & Cancer Biology » James Mulloy, PhD

NSGS Tg mice as a humanized model for in vivo infectious diseases (Aliberti).

Suppression of IgE-mediated disease by polyclonal rapid desensitization (Finkelman).

Prosurvival role for RUNX1 in acute myeloid leukemia (Grimes).

Experimental Hematology & Cancer Biology » Yi Zheng, PhD

Role of Cdc42 in development and progression of obesity and obesity-associated sequelae (Divanovic).

Experimental Hematology & Cancer Biology; Allergy and Immunology » Punam Malik, MD and Kimberly Risma, MD, PhD

Gene correction strategies for Hemophagocytic lymphohistiocytosis (Jordan).

Gastroenterology, Hepatology & Nutrition » Jorge Bezerra, MD

Dysfunction in biliary atresia (Chougnet).

Forward genetic analysis of immune-mediated liver disease using ENU mutagenesis (Hoebe).

NKT cells and autoimmune liver disease (Mattner).

Gastroenterology, Hepatology & Nutrition » Ted Denson, MD

Human IgG-mediated anaphylaxis (Finkelman).

Gastroenterology, Hepatology & Nutrition » Alex Miethke, MD

Treg in biliary atresia (Chougnet).

Gastroenterology, Hepatology & Nutrition » Greg Tiao, MD

Viral determinants in biliary atresia (Chougnet).

Hematology » Joseph Palumbo, MD

DC in tumorgenesis (Janssen).

Human Genetics; Bone Marrow Transplantation and Immune Deficiency. » Kejian Zhang, MD, MBA and

Rebecca Marsh, MD

Discovery and characterization of new primary immune deficiencies (Jordan).

Immunobiology » Julio Aliberti, PhD

The role of CD244 and Slp76 in Toxoplasma gondii infections (Hoebe).

Immune sensing of T. gondii infection by C5aR and CCR5 pairing (Koehl)

Immunobiology » Claire Chougnet, PhD

Assessing host-microbe cross-talk and determine the role of innate immune pathways on pregnancy outcomes (Hoebe).

Effect of aging on NK function (Hoebe).

Mapping of Ureaplasma signaling pathways (Hoebe).

Effect of aging on DC function (Janssen).

Human DC subsets (Janssen).

Immune sensing of HIV infection by C5aR and CCR5 pairing (Koehl).

Immunobiology » Senad Divanovic, PhD

Characterization of inflammatory pathways driving hepatic steatosis and steatohepatitis in *Acox-1*-deficient mice (Hoebe).

Immunobiology » Fred Finkelman, MD

Lipoxygenases and modulation of immune response to helminthic infections (Aliberti).

IL-4 and memory T cell homeostasis (Hildeman).

C5aR and IgG Fc receptor cross-talk in autoimmunity (Koehl).

NKT cells and TH2 responses (Mattner).

Immunobiology » David Hildeman, PhD

Regulatory T cells in aging (Chougnet).

Assessment of NK cells and their role in CD4+ T cell responses following LCMV infection (Hoebe).

Eliminating diabetogenic T cells by targeting Bcl-2 family members (Katz).

Immunobiology » Kasper Hoebe, PhD

Effect of aging on NK cell function and homeostasis (Chougnet).

Role of Acox-1 (*Lampe1*) in NAFLD progression (Divanovic).

Modulation of viral-specific CD4+ T cell responses by NK cells (Hildeman).

The role of C5a-mediated cross-talk between NK cells and dendritic cell in T.gondii infection (Koehl).

ENU mutagenesis and NKT cells (Mattner).

Immunobiology » Edith Janssen, PhD

Effect of aging on merocytic dendritic cell function (Chougnet).

The role of CD244 in DC function (Hoebe).

Antigen presentation and NKT cells (Mattner).

Immunobiology » Michael Jordan, MD

Exploiting the DNA damage response to selectively sculpt the TCR repertoire (Hildeman).

Gene therapy for Hemophagocytic Lymphohistiocytosis (Hoebe).

Elimination of encephalitogenic T cells without harming protective immunity (Katz).

Immunobiology » Christopher Karp, MD

RP105/BAFF axis in obesity (Divanovic).

Regulation of immune responses by 5-LO during L. major infection (Divanovic).

Therapeutic enhancement of protective immunity during experimental Leishmania major infection (Divanovic).

Immunobiology » Jonathan Katz, PhD

Control of diabetes by manipulation of Bcl-2 family members (Hildeman).

Role of Merocytic DC in Type 1 diabetes (Janssen).

Immunobiology » Joerg Koehl, MD

Suppression of complement-mediated inflammation (Finkelman).

The role of Slp76 and C5AR in NK/NKT cell function (Hoebe).

Immunobiology » Ian Lewkowich, PhD

Experimental asthma (Finkelman).

C5a regulates Th17 development in experimental allergic asthma (Koehl).

Immunobiology » Jochen Mattner, MD

The role of Slp76 and NKT cell function (Hoebe).

Immunobiology » Julio Aliberti, PhD and Joerg Koehl, MD

CCR5-C5aR heterodimers and cell signaling (Chougnet).

Immunobiology » Claire Chougnet, PhD and Joerg Koehl, MD

CCR5 and C5aR heterodimers in microbial recognition (Aliberti).

Immunobiology » David Hildeman, PhD and Jonathan Katz, PhD

Exploiting the DNA damage response for selective immunomodulation (Jordan).

Immunobiology; Biomedical Informatics » David Hildeman, PhD and Bruce Aronow, PhD

Growth factor independent-1 maintains Notch1-dependent transcriptional programming of lymphoid precursors (Grimes).

Immunobiology; Infectious Diseases » Claire Chougnet, PhD and Rhonda Cardin, PhD

Homeostasis and Function of Regulatory T cells in aging (Hildeman).

Immunobiology; Pathology » Senad Divanovic, PhD and Rachel Sheridan, MD

Modeling development and progression of NAFLD (Hoebe).

Immunobiology; Reproductive Sciences » Christopher Karp, MD, Edith Janssen, PhD, and SK Dey, PhD

Role of type I IFN/IFNAR axis in TLR-driven induction of preterm birth (Divanovic).

Immunobiology; Reproductive Sciences » Christopher Karp, MD, Senad Divanovic, PhD, Edith Janssen, PhD, and SK Dey, PhD

Defining the mechanisms underlying inflammation-driven preterm birth (Hoebe).

Infectious Diseases » Joseph Qualls, PhD

Citrulline and intracellular microbial killing mechanisms (Aliberti).

Molecular Cardiovascular Biology » Jeffery Molkentin, PhD

Identification of ENU germline mutants with heart defects (Hoebe).

Neonatology » Alan Jobe, MD, PhD, Paul Kingma, MD, PhD, and Jim Greenberg, MD

Biomarkers of immunologic function and preterm respiratory outcomes (Chougnet).

Neonatology » Suhas Kallapur, MD and Alan Jobe, MD, PhD

Late preterm birth, Ureaplasma species and childhood lung disease (Chougnet).

Neonatology and Center for Prevention of Preterm Birth » Louis Muglia, MD, PhD

Maternal temperament, stress, and inflammation in preterm birth (Chougnet).

Neonatology and Pulmonary Biology; Experimental Hematology & Cancer Biology » Jeffrey Whitsett, MD and Jose Cancelas-Perez, MD, PhD

Kruppel-like-factor 5 (Klf-5) controls bone marrow homing of hematopoietic stem cells and progenitors through Rab5-mediated membrane β1/β2-integrin expression (Grimes).

Reproductive Sciences » SK Dey, PhD

Role of cannabinoids/endocannabinoids in regulation of immune responses and preterm birth (Divanovic).

Recombineering-based dissection of flanking and paralogous Hox gene functions in mouse reproductive tracts (Grimes).

Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
ALIBERTI, J		
Long-Term Immunity Against Toxoplasmosis		
National Institutes of Health(George Washington University)		
R01 AI 033325	07/01/08-06/30/13	$19,608
CHOUGNET, C / HILDEMAN, D (MPI)		
Homeostasis and Function of Regulatory T Cells in Aging		
National Institutes of Health		
R01 AG 033057	08/01/12-07/31/17	$280,311
CHOUGNET, C / JOBE, A (MPI)		
Biomarkers of Immunologic Function and Preterm Respiratory Outcomes		
National Institutes of Health		
U01 HL 101800	05/01/10-04/30/14	$364,354
DIVANOVIC, S		
Better Mouse Models of Disease: Humanizing Experimental Atherosclerosis		
National Institutes of Health		
R21 HL 113907	04/01/12-03/31/14	$145,279
GRIMES, L		
RNA Therapeutics for Leukemia		
The Leukemia and Lymphoma Society		
	10/01/12-09/30/15	$180,018

Targeting an Oncorequisite Factor in Leukemia
Children's Leukemia Research Association
07/01/12-06/30/13 $30,000

MicroRNA in Acute Myeloid Leukemia
National Institutes of Health
R01 CA 159845 07/01/11-04/30/16 $195,050

HILDEMAN, D

Regulation of Apoptosis in Activated Primary T Cells
National Institutes of Health
R01 AI 057753 12/01/08-11/30/13 $239,134

HOEBE, K

Functional Analysis of NK Cells and Their Potential to Generate CTL Responses
National Institutes of Health
R01 AI 074743 07/10/09-06/30/13 $245,025

T-Cell Specific Lysosome Dysfunction as a Primary Cause of IBD in Gimap5sph/sph Mice
Crohn's & Colitis Foundation of America
07/01/12-06/30/15 $105,300

Immunobiology of IFRD1, a Gene Modifying CF Lung Disease
National Institutes of Health
R01 HL 094576 08/01/09-07/31/13 $256,786

CFF Research Development Program (P&F Study)
Cystic Fibrosis Foundation
R457-CR11 03/01/12- 06/30/15 $65,000

JANSSEN, E

Activating Robust Immunity to Tumor-Associated Antigens: Mechanisms and Biology
National Institutes of Health
R01 CA 138617 04/01/09-02/28/14 $90,574

JORDAN, M

CD8 T Cell Mediated Disruption of Blood Brain Barrier Tight Junction
National Institutes of Health(Mayo Clinic)
R01 NS 060881 09/04/10-07/31/14 $16,869

Focused Screening of Novel Therapies for HLH Using an Animal Model
Histiocytosis Association of America
01/01/13-12/31/13 $50,000

Hybrid ImmunoTherapy (ATG/Dexamethasone/Etoposide) for Hemphagocytic Lymphohistiocytosis
National Institutes of Health
R34 HL 107801 03/15/12-02/28/15 $135,000

FINKELMAN, F

Allergenicity Resulting from Functional Mimicry of the TLR Complex
National Institutes of Health
R01 AI 088372 | 03/01/10-02/28/15 | $269,488

LEWKOWICH, I

Mechanisms of Steroid Resistance in Severe Asthma
American Thoracic Society
10/01/11-09/30/13 | $40,000

Synergistic Roles of IL-17 in Asthma Susceptibility
Parker B. Francis Fellowship Program
07/01/10-06/30/13 | $54,000

MATTNER, J

Primary Biliary Cirrhosis: Molecular Genetics and Microbial Pathogenesis
National Institutes of Health
R01 DK 084054 | 06/01/09-05/31/14 | $165,515

MCALEES, J

Der p 2-Driven TLR4 Signaling in Allergic Asthma
National Institutes of Health
F32 HL 110497 | 09/01/11-02/28/13 | $13,943

MEYER, S

Environmental Carcinogenesis and Mutagenesis
National Institutes of Health(University of Cincinnati)
T32 ES 007250 | 02/01/13-06/30/13 | $20,895

The Role of Specific MicroRNAs Associated with Oncongenic Translocations in Acute Myeloid Leukemia
Ladies Auxilliary VFW National HQ
06/01/11-05/31/13 | $50,000

NISS, O

Primary Immune Deficiency Treatment Consortium
National Institutes of Health(The Regents of the University of California)
U54 AI 082973 | 09/01/12-08/31/13 | $25,000

Current Year Direct **$3,057,149**

Total **$3,057,149**

Additional Information

Immunobiology Graduate Program

The Immunobiology Graduate Program is an inter-departmental program within the University of Cincinnati that offers PhD and MS degrees in Immunology. The Division of Immunobiology serves as the administrative home of the Graduate Program. The program is governed by Director Dr. David Hildeman, and a Steering Committee composed of members of several departments/divisions at CCHMC and UC. Dr. Jonathan Katz is the Director of the Foundations in Immunology Course.

The Immunobiology Graduate Program provides broadly based instruction in immunology, along with rigorous research training that emphasizes modern approaches to understanding the function of the immune system in health and disease. To this end, the program currently has 48 faculty members from 5 departments and 15 divisions within the University of Cincinnati College of Medicine and CCHMC. We currently have a total of 45 outstanding students (39 PhD students and 6MS students) from around the country and abroad. This academic year we celebrated the graduation of 8 PhD students. Our students have distinguished themselves already by receiving several travel and research awards (AAAAI, Yates Scholarship Award, Albert J Ryan Fellowship Award, Distinguished Dissertation Fellowship, and an NIH F30 Award).

The Program is supported financially by a variety of sources. This year, tuition support was provided through University Graduate Scholarships awarded by the University of Cincinnati. Student stipends were supported through a variety of sources including funds from the University of Cincinnati, NIH training grants, external grants to their advisors, and funds from Cincinnati Children's Research Foundation. Thanks to a fantastic review for UC2019, the Immunobiology Graduate Program received funding from UC and CCHMC to support two new pilot projects. The first is a student research grant proposal award in which students will compete for a research grant supporting a novel and innovative project for their work. The second is a travel award in which students can use to go to another lab to learn a technique not already existing at UC/CCHMC. After 7 years of continued growth, the program is now focused on maintaining its size, planning on a target class size of 6-8 students per year.

This fall the Immunobiology Graduate Program has established an International Research Training Group (IRTG) with the University of Lübeck/Research Center Borstel in Lübeck, Germany.

The research focus of the IRTG is

1. Humoral and Cellular Pathways of Allergic Inflammation
2. Immuno-regulation of infection-driven inflammation

Students interested in research projects encompassed by these areas may have the opportunity to study and perform research in the beautiful city of Lübeck in north-central Germany for a 3-6 month period.

The Immunobiology Graduate Program (ImmGP), anticipates having between 2-4 doctoral students from our program to participate in the IRTG per year. Last fall 2 students spent 2-3 months each at the University of Lübeck working with collaborating faculty. And this summer the Immunobiology Graduate Program is hosting 3 students from the University of Lübeck.

Immunobiology Graduate Program Students

Doctoral Students

Student	Faculty Mentor	Admission Year
Jill Fritz	Timothy Weaver	2006

Ibrahim Aksoylar	Kasper Hoebe	2007
Sema Kurtulus	David Hildeman	2007
Cortez McBerry	Julio Aliberti	2007
Rachael Mintz-Cole	Neeru Hershey	2007
Mark Webb	Marsha Wills-Karp	2007
Stacey Burgess	Marsha Wills-Karp	2008
Samuel Vaughn	John Harley	2008
Isaac Harley	Christopher Karp	2008
Jana Raynor	David Hildeman	2008
Bo Liu	Yui-Hsi Wang	2008
Nick Boespflug	Christopher Karp	2009
Jordan Downey	Marsha Wills-Karp	2009
Naina Gour	Marsha Wills-Karp	2009
Jonathan McNally	Jonathan Katz	2009
Maria Fields	Claire Chougnet	2009
Harini Raghu	Matthew Flick	2009
Akash Verma	George Deepe	2009
Olivia Ballard	Ardythe Morrow	2010
Kyle Bednar	William Ridgway	2010
Roger Fecher	George Deepe	2010
Wenting Huang	William Ridgway	2010
Jennifer Leddon	Timothy Cripe	2010
Ke Liu	John Harley	2010
Hesham Shehata	Claire Chougnet	2010
Rahul D'Mello	Marc Rothenberg	2011
Dan Giles	Senad Divanovic	2011
Mike Horwath	George Deepe	2011
Jared Klarquist	Edith Janssen	2011

Kun-Po Li	David Hildeman	2011
Sara Stoffers	Ian Lewkowich	2011
Maha Almanan	David Hildeman	2012
Laura Brungs	Sue Thompson	2012
Jeremy Kinder	Sing Sing Way	2012
Xioaming Lu	John Harley	2012
Samet Oksuz	Lee Grimes	2012
Carolyn Rydyzinski	Stephen Waggoner	2012
Kristi Weage	Sean Moore	2012

Master Students

Student	Faculty Mentor	Admission Year
Kristina Bielewicz	Non-Thesis MS	2011
Lindsay Dunn	Non-Thesis MS	2011
Yuan Li	John Harley	2011
Yi Ting Tsai	Simon Hogan	2011
Upansana Parthasarathy	Andrew Herr	2012
Stuart Tinch	Non-Thesis MS	2012

Student Honors

Kyle Bednar (2010) - University of Cincinnati's 33rd Graduate Student Research Forum Honorable Mention 2012

Kristina Bielewicz (2011) - Editorial Assistantship Award for the Journal of Allergy and Clinical Immunology has been awarded an editorial assistantship for 2013-14 by the graduate school

Benjamin Davis (2012) - American Academy of Allergy, Asthma and Immunology Fellow-In-Training Travel Grant 2012

Rahul D'Mello (2011) - 2012 Cincinnati Youth Collaborative Mentor of the Year Award

Maria Fields (2009)

- Dissertation Completion Fellowship 2012
- Albert Ryan Fellowship. University of Cincinnati 2012
- Millipore Amnis Travel Award, 99th Annual Meeting of the American Association of Immunologist

Jared Klarquist (2011) - Travel Award by the Pan-American Society for Pigment Cell Research, to present work at the 21st International Pigment Cell Conference. Sept 2011, Bordeaux, France

Cortez McBerry (2007) - 2013-Present NIH Intramural Research Training Award (IRTA) Fellowship

Harini Raghu (2009) - Graduate student summer research fellowship, University of Cincinnati Research council. Acceptance rate 13%. (May- June 2013)

Hesham Shehata (2010) - 1st place poster at the Annual Immunological Research Retreat CCHMC

Samuel Vaughn (2008) - American Society for Clinical Investigation/Association of American Physicians Joint Annual Meeting

Student Publications

Maha Almanan (2012)

Kano G, **Almanan M**, Bochner BS, Zimmermann N., Mechanism of Siglec-8-mediated cell death in IL-5-activated eosinophils: Role for reactive oxygen species-enhanced MEK/ERK activation.J Allergy Clin Immunol. 2013 May 16.

Olivia Ballard (2010)

Lemay DG, **Ballard OA**, Hughes MA, Morrow AL, Horseman ND, Nommsen-Rivers LA. RNA sequencing of the human milk fat layer transcriptome reveals distinct gene expression profiles at three stages of lactation. PLoS One. 2013 Jul 5;8(7):e67531. doi:10.1371/journal.pone.0067531. Print 2013. PMID:23861770

Ballard OA & Morrow AL. Human Milk Composition: Nutrients and Bioactive Factors. Pediatr Clin North Am. 2013 Feb;60(1):49-74. doi: 10.1016/j.pcl.2012.10.002. Review. PMID: 23178060

Kyle Bednar (2010)

Kachapati, K., Adams, D., **Bednar, K.** & Ridgway, W.M. The Non-Obese Diabetic (NOD) Mouse as a Model of Human Type 1 Diabetes. Methods Mol Biol. 2012;933:3-16. doi: 10.1007/978-1-62703-068-7_1. PMID: 22893397

Hofmann, C.M., **Bednar, K**.J., Anderson, J.M. & Marchant, R.E. Disruption of Staphylococcus epidermidis biofilm formation using a targeted cationic peptide. J Biomed Mater Res A. 2012 Apr;100(4):1061-7. doi: 10.1002/jbm.a.33273. Epub 2012 Feb 8. PMID:22318906

Nicholas Boespflug (2009)

McBerry C, Egan CE, Rani R, Yang Y, Wu D, **Boespflug N**, Boon L, Butcher B, Mirpuri J, Hogan SP, Denkers EY, Aliberti J, Herbert DR. Trefoil factor 2 negatively regulates type 1 immunity against Toxoplasma gondii. J Immunol. 2012 Sep 15;189(6):3078-84. PMID:22896633

Stacey Burgess (2008)

Harley ITW, Giles DA, Pfluger PT, **Burgess SL**, Walters S, Hembree J, Raver C, Rewerts CL, Downey J, Flick LM, Stankiewicz TE, McAlees JW, Wills-Karp M, Sartor RB, Divanovic S, Tschoep MH, Karp CL Differential colonization with Segmented Filamentous Bacteria and Lactobacillus murinus do not drive divergent development of diet-induced obesity in C57BL/6 mice: Microbiome variation and diet-induced obesity. In press at Molecular Metabolism (Elsevier) http://dx.doi.org/10.1016/j.molmet.2013.04.004

Benjamin Davis (2012)

Davis BP, Rothenberg ME. Emerging Concepts in Dietary Therapy of Eosinophilic Esophagitis. Expert Reviews of Clinical Immunology. 2013 Apr;9(4):285-7. doi: 10.1586/eci.13.15. PMID: 23557262

Davis BP, Rothenberg ME. Commentary on "Antigen presentation by eosinophils in eosinophilic esophagitis?". J Pediatr Gastroenterol Nutr. Pediatr Gastroenterol Nutr. 2013 Mar;56(3):242. doi: 10.1097/MPG.0b013e31827ab8d3. PMID: 23132165

Davis BP, Rothenberg ME. 2012. The Roles of Eosinophils in Human Disease: Eosinophils and GI Disease. In: Lee JJ, Rosenberg HF, ed. Eosinophils in Health and Disease. Elsevier.

Bernstein JA, **Davis BP**, Picard JK, Cooper JP, Zheng S, Levin LS. A randomized, double-blind, parallel trial comparing capsaicin nasal spray with placebo in subjects with a significant component of nonallergic rhinitis. Ann Allergy Asthma Immunol. 2011 Aug;107(2):171-8. doi: 10.1016/j.anai.2011.05.016. Epub 2011 Jun 29. PMID: 21802026

Jordan Downey (2009)

Hung LY, Lewkowich IP, Dawson LA, **Downey J**, Yang Y, Smith DE, Herbert DR. IL-33 drives biphasic IL-13 production for noncanonical Type 2 immunity against hookworms. Proc Natl Acad Sci U S A. 2013 Jan 2;110(1):282-7. PMID:23248269

Maria Fields (2009)

Presicce P; **Moreno-Fernandez ME**; Rusie LK; Fichtenbaum C; Chougnet CA. In Vitro HIV Infection Impairs the Capacity of Myeloid Dendritic Cells to Induce Adaptive Regulatory T Cells. PLoS One. 2012;7(8):e42802. doi: 10.1371/journal.pone.0042802. Epub 2012 Aug 13. PMID:22912740

Kong L, Cardona Maya W, **Moreno-Fernandez ME**, Ma G, Shata MT, Sherman KE, Chougnet C, Blackard JT. Low-level HIV infection of hepatocytes. Virol J. 2012 Aug 9;9:157. doi: 10.1186/1743-422X-9-157. PMID: 22877244

Moreno-Fernandez ME, Presicce P, Chougnet CA. Homeostasis and function of regulatory T cells in HIV/SIV infection. J Virol. 2012 Oct;86(19):10262-9. doi: 10.1128/JVI.00993-12. Epub 2012 Jul 18. Review. PMID: 22811537

Dan Giles (2011)

Harley ITW, **Giles DA**, Pfluger PT, Burgess SL, Walters S, Hembree J, Raver C, Rewerts CL, Downey J, Flick LM, Stankiewicz TE, McAlees JW, Wills-Karp M, Sartor RB, Divanovic S, Tschoep MH, Karp CL Differential colonization with Segmented Filamentous Bacteria and Lactobacillus murinus do not drive divergent development of diet-induced obesity in C57BL/6 mice: Microbiome variation and diet-induced obesity. In press at Molecular Metabolism (Elsevier) http://dx.doi.org/10.1016/j.molmet.2013.04.004

Naina Gour (2009)

Edith M. Janssen, Ed E. Lemmens**, Naina Gour**, Rachel A Reboulet, Douglas R. Green, Stephen P. Schoenberger, and Michael J. Pinkoski. Distinct Roles of Cytolytic Effector Molecules for Antigen-restricted Killing by CTL in vivoImmunol Cell Biol. 2010 Oct;88(7):761-5. doi: 10.1038/icb.2010.37. Epub 2010 Mar 23. PMID:20309009

Isaac Harley (2008)

Harley ITW, Karp CL Obesity and the Gut Microbiome: Striving for Causality. Molecular Metabolism (Elsevier) 1:21-31 (2012) http://dx.doi.org/10.1016/j.molmet.2012.07.002

Harley ITW, Giles DA, Pfluger PT, Burgess SL, Walters S, Hembree J, Raver C, Rewerts CL, Downey J, Flick LM, Stankiewicz TE, McAlees JW, Wills-Karp M, Sartor RB, Divanovic S, Tschoep MH, Karp CL Differential colonization with Segmented Filamentous Bacteria and Lactobacillus murinus do not drive divergent development of diet-induced obesity in C57BL/6 mice: Microbiome variation and diet-induced obesity. In press at Molecular Metabolism (Elsevier) http://dx.doi.org/10.1016/j.molmet.2013.04.004

Wenting Huang (2010)

Ando Y, Yang GX, Kenny TP, Kawata K, Zhang W, **Huang W**, Leung PS, Lian ZX, Okazaki K, Ansari AA, He XS, Invernizzi P, Ridgway WM, Lu Q, Gershwin ME. Overexpression of microRNA-21 is associated with elevated pro-inflammatory cytokines in dominant-negative TGF-β receptor type II mouse. J Autoimmun. 2013 Mar;41:111-9. doi: 10.1016/j.jaut.2012.12.013. Epub 2013 Feb 8. PMID:23395552

Jeremy Kinder (2012)

Lambert SE, **Kinder JM**, Then JE, Parliament KN, Bruns HA. 2013. Erythromycin treatment hinders the induction of oral tolerance to fed ovalbumin. Front Immunol. 2012;3:203. doi: 10.3389/fimmu.2012.00203. Epub 2012 Jul 18. PMID: 22826710

Jared Klarquist (2011)

Klarquist JS, Janssen EM. Melanoma-infiltrating dendritic cells: Limitations and opportunities of mouse models. Oncoimmunology. 2012 Dec 1;1(9):1584-1593. PMID:23264904

Mehrotra S, Al-Khami AA, **Klarquist J**, Husain S, Naga O, Eby JM, Murali AK, Lyons GE, Li M, Spivey ND, Norell H, Martins da Palma T, Onicescu G, Diaz-Montero CM, Garrett-Mayer E, Cole DJ, Le Poole IC, Nishimura MI. A coreceptor-independent transgenic human TCR mediates anti-tumor and anti-self immunity in mice. J Immunol. 2012 Aug 15;189(4):1627-38.

Gilbert ER, Eby JM, Hammer AM, **Klarquist** J, Christensen DG, Barfuss AJ, Boissy RE, Picken MM, Love RB, Dilling DF, Le Poole IC. Positioning ganglioside d3 as an immunotherapeutic target in lymphangioleiomyomatosis. Am J Pathol. 2013 Jul;183(1):226-34. doi:10.1016/j.ajpath.2013.04.002. Epub 2013 May 10. PMID: 23665200

Sema Kurtulus (2007)

Kurtulus S, Tripathi P, Hildeman DA Protecting and rescuing the effectors: roles of differentiation and survival in the control of memory T cell development. Front Immunol. 2012 PMID:23346085

Kurtulus S, Hildeman D. Assessment of CD4(+) and CD8 (+) T Cell Responses Using MHC Class I and II Tetramers. Methods Mol Biol. 2013;979:71-9. PMID:23397390

Jennifer Leddon (2010)

Currier MA, Eshun FK, Sholl A, Chernoguz A, Crawford K, Divanovic S, Boon L, Goins WF, Frischer JS, Collins MH, **Leddon JL**, Baird WH, Haseley A, Streby KA, Wang PY, Hendrickson BW, Brekken RA, Kaur B, Hildeman D, Cripe TP. 2013. VEGF Blockade Enables Oncolytic Cancer Virotherapy in Part by Modulating Intratumoral Myeloid Cells. Mol Ther. 2013 May;21(5):1014-23. doi: 10.1038/mt.2013.39. Epub 2013 Mar 12. PMID: 23481323

Browne, A.W., **J.L. Leddon**, M.A. Currier, J.P. Williams, J.S. Frischer, M.H. Collins, C.H. Ahn, and T.P. Cripe. 2011. Cancer screening by systemic administration of a gene delivery vector encoding tumor-selective secretable biomarker expression. PLoS One. 2011 May 11;6(5):e19530. doi: 10.1371/journal.pone.0019530. PMID:21589655

Cortez McBerry (2007)

Shryock N, **McBerry C**, Salazar Gonzalez RM, Janes S, Costa FT, Aliberti J. Lipoxin A_4 and 15-epi-lipoxin A_4 protect against experimental cerebral malaria by inhibiting IL-12/IFN-γ in the brain. PLoS One. 2013 Apr 16;8(4):e61882. doi: 10.1371/journal.pone.0061882. Print 2013. PMID:23613965

McBerry, C., Egan, C. E., Rani, R., Yang, Y., Wu, D., Boespflug, N., Boon, L., Butcher, B., Mirpuri, J., Hogan, S. P., Denkers, E. Y., Aliberti, J. & Herbert, D. B. R. (2012). Trefoil Factor 2 Negatively Regulates Type 1 Immunity against Toxoplasma gondii. J Immunol. 2012 Sep 15;189(6):3078-84. doi: 10.4049/jimmunol.1103374. Epub 2012 Aug 15. PMID:22896633

McBerry, C., Gonzalez, R. M. S., Shryock, N., Dias, A. & Aliberti, J. SOCS2- Induced Proteasome-Dependent TRAF6 Degradation: A Common Anti-Inflammatory Pathway for Control of Innate Immune Responses. PLoS One. 2012;7(6):e38384.doi:10.1371/journal.pone.0038384. Epub 2012 Jun 5. PMID:22693634

Jonathan McNally (2009)

McNally, J.P., Elfers, E.E., Terrell, C. E., Grunblatt, E., Hildeman, D. A., Jordan, M. B., Katz, J. D., Eliminating encephalitogenic T cells without undermining protective immunity, 2013, JEM, Accepted

Mintz-Cole (2007)

Mintz-Cole RA, Brandt EB, Bass SA, Gibson AM, Reponen T, Khurana Hershey GK. Surface availability of beta-glucans is critical determinant of host immune response to Cladosporium cladosporioides. J Allergy Clin Immunol. 2013 Jul;132(1):159-169.e2. doi: 10.1016/j.jaci.2013.01.003. Epub 2013 Feb 10. PMID:23403046

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 β-glucan surface exposure. J Immunol. 2012 Oct 1;189(7):3609-17. Epub 2012 Sep 7. PMID:22962686

Harini Raghu (2009)

Flick MJ, Du X, Prasad JM, **Raghu H**, Palumbo JS, Smeds E, Hook M, Degen JL. Genetic elimination of the binding motif on fibrinogen for the S.aureus virulence factor ClfA improves host survival in septicemia. Blood. 2013 Mar 7;121(10):1783-94. doi: 10.1182/blood-2012-09-453894. Epub 2013 Jan 8. PMID:23299312

Jana Raynor (2008)

Raynor J, Sholl A, Plas DR, Bouillet P, Chougnet CA, Hildeman DA. IL-15 Fosters Age-Driven Regulatory T Cell Accrual in the Face of Declining IL-2 Levels. Front Immunol. 2013 Jun 24;4:161. doi: 10.3389/fimmu.2013.00161. Print 2013. PMID:23805138

Raynor J, Lages CS, Shehata H, Hildeman DA, Chougnet CA. Homeostasis and function of regulatory T cells in aging Curr Opin Immunol. 2012 Aug;24(4):482-7. doi: 10.1016/j.coi.2012.04.005. Epub 2012 May 5. Review. PMID:22560294

Sara Stoffers (2011)

Lewkowich IP, Lajoie S, **Stoffers SL**, Suzuki Y, Richgels PK, Dienger K, Sproles AA, Yagita H, Hamid Q, Wills-Karp M. PD-L2 modulates asthma severity by directly decreasing dendritic cell IL-12 production. Mucosal Immunol. 2013 Jul;6(4):728-39. doi: 10.1038/mi.2012.111. Epub 2012 Nov 14. PMID:23149662

Yi Ting Tsai (2011)

Waddell A, Ahrens R, **Tsai YT**, Sherrill JD, Denson LA, Steinbrecher KA, Hogan SP. Intestinal CCL11 and eosinophilic inflammation is regulated by myeloid cell-specific RelA/p65 in mice. J Immunol. 2013 May 1;190(9):4773-85. doi: 10.4049/jimmunol.1200057. Epub 2013 Apr 5. PMID:23562811

Samuel Vaughn (2008)

Vaughn SE, Kottyan LC, Munroe, ME, and Harley, JB. Genetic susceptibility to lupus: the biological basis of genetic risk found in B cell signaling pathways. Journal of Leukocyte Biology, 2012 Sep;92(3):577-91. doi: 10.1189/jlb.0212095. Epub 2012 Jun 29. Review. PMID:22753952

Alum publications resulting from graduate work

Katie Groshowitz (2005)

Groschwitz KR, Wu D, Osterfeld H, Ahrens R, Hogan SP. Chymase-mediated intestinal epithelial permeability is regulated by a protease-activating receptor/matrix metalloproteinase-2-dependent mechanism. Am J Physiol Gastrointest Liver Physiol. 2013 Mar 1;304(5):G479-89. doi: 10.1152/ajpgi.00186.2012. Epub 2013 Jan 10. PMID:23306080

James Phelan (2006)

Khandanpour C, **Phelan JD**, Vassen L, Schütte J, Chen R, Horman SR, Gaudreau MC, Krongold J, Zhu J, Paul WE, Dührsen U, Göttgens B, Grimes HL, Möröy T. Growth factor independence 1 antagonizes a p53-induced DNA damage response pathway in lymphoblastic leukemia. Cancer Cell. 2013 Feb 11;23(2):200-14. doi: 10.1016/j.ccr.2013.01.011. PMID:23410974

Guo F, Li J, Zhang S, Du W, Amarachintha S, Sipple J, **Phelan J**, Grimes HL, Zheng Y, Pang Q. mTOR kinase inhibitor sensitizes T-cell lymphoblastic leukemia for chemotherapy-induced DNA damage via suppressing FANCD2 expression. Leukemia. 2013 Jul 15. doi: 10.1038/leu.2013.215.PMID:23852546

Joni Prasad (2006)

Flick MJ, Du X, **Prasad JM,** Raghu H, Palumbo JS, Smeds E, Hook M, Degen JL. Genetic elimination of the binding motif on fibrinogen for the S.aureus virulence factor ClfA improves host survival in septicemia. Blood. 2013 Mar 7;121(10):1783-94. doi: 10.1182/blood-2012-09-453894. Epub 2013 Jan 8. PMID:23299312

Amanda Waddell (2006)

Waddell A, Ahrens R, Tsai YT, Sherrill JD, Denson LA, Steinbrecher KA, Hogan SP. Intestinal CCL11 and eosinophilic inflammation is regulated by myeloid cell-specific RelA/p65 in mice. J Immunol. 2013 May 1;190(9):4773-85. doi: 10.4049/jimmunol.1200057. Epub 2013 Apr 5. PMID:23562811

Hogan SP, **Waddell A,** Fulkerson PC. Eosinophils in infection and intestinal immunity. Curr Opin Gastroenterol. 2013 Jan;29(1):7-14. doi: 10.1097/MOG.0b013e32835ab29a. Review. PMID:23132211

Lampinen M, **Waddell A,** Ahrens R, Carlson M, Hogan SP. CD14+CD33+ myeloid cell-CCL11-eosinophil signature in ulcerative colitis. J Leukoc Biol. 2013 Jul 31. PMID:23904440

Student Oral Presentations

Nicholas Boespflug (2009)

- South-Central Regional M.D./Ph.D. Conference, invited oral presentation, Louisville, KY, 2012

Jared Klarquist (2011)

- **Klarquist J**, Li M, Wainwright DA, Luiten RM, Nishimura MI, Le Poole IC. Functional cloning of a gp100-reactive TCR from depigmenting vitiligo skin. 21st International Pigment Cell Conference. Sept 2011, Bordeaux, France, Pigment Cell Melanoma Res. 24: 4 (2011)
- **KlarquistJ**, Eby J, Longley BJ, Nishimura MI, Mehrotra S, Le Poole IC. Spontaneous epidermal depigmentation in mice – a model for vitiligo. 21st International Pigment Cell Conference. Sept 2011, Bordeaux, France, Pigment Cell Melanoma Res. 24: 4 (2011)
- Mosenson J, Zloza A, **Klarquist J**, Mehrotra S, Nishimura MI, Guevara-Patino JA, Le Poole IC. A hot finding: mutant HSP70i to treat vitiligo. 21st International Pigment Cell Conference. Sept 2011, Bordeaux, France, Pigment Cell Melanoma Res. 24: 4 (2011)

Cortez McBerry (2007)

- 16th Annual Woods Hole Immunoparasitology Meeting Marine Biological Laboratory, Woods Hole, MA April 24. Oral Presentation, Trefoil Factor 2regulates Type-1 Inflammation to *Toxoplasma gondii*.

Jonathan McNally (2009)

- AA1 2013
- Block symposia and poster: An immuno-protective treatment strategy for autoimmune diseases

Harini Raghu (2009)

- Harini Raghu, Malinda D. Frederick, Alice Jone, Kathryn E. Talmage, Keith W. Kombrinck & Matthew J. Flick. Plasminogen mediates both positive and negative effects on TNFα-driven arthritis through fibrinogen-dependent mechanisms. Gordon Research Seminar on "Plasminogen activation and extracellular proteolysis". Ventura, CA. Feb 2012

Akash Verma (2009)

- **Akash Verma**, and George S. Deepe Jr. "IL-33, a novel downstream target of IL-4 during *Histoplasma capsulatum* infection". Gordon Research Seminars on Immunology of Fungal Infections, Galveston, TX, Jan 2013.

Student Poster Presentations

Nicholas Boespflug (2009)

- Keystone Symposium, "Myeloid Cells: Regulation and Inflammation," poster presentation, Keystone, CO, 2013
- University of Cincinnati Graduate Student Research Forum, poster presentation, Cincinnati, OH, 2012

Maria Fields (2009)

- Moreno-Fernandez ME, Joedicke. JJ, Chougnet CA.. 2th Imaging and Cytometry Research Day, September 12, 2012. Cincinnati Children's Hospital

Roger Fecher (2010)

- Poster: *Histoplasma capsulatum* induces HIF-1a accumulation in murine macrophages

Presented at the Internal Medicine Trainees' Research Grand Rounds at UC May 2013

- Poster: *Histoplasma capsulatum* induces HIF-1a accumulation in bone marrow derived macrophages

Presented at the Graduate Student Research Foundation at UC November 2012

Naina Gour (2009)

- Naina Gour, Marsha Wills-Karp. Carbohydrates in dust mite allergen modulate HDM-induced Th2 immune responses. American Thoracic Society Annual Conference San Francisco, CA. 2012
- Naina Gour, Marsha Wills-Karp. Carbohydrates in dust mite allergen modulate HDM-induced Th2 immune responses. Pathogenic Processes in Asthma and COPD, Keystone Symposia on Molecular and Cellular Biology, Santa Fe, NM 2013
- Naina Gour, Marsha Wills-Karp. Carbohydrates in dust mite allergen modulate HDM-induced Th2 immune responses. American Association of Immunologists Annual meeting, Honolulu, Hawaii 2013

Wenting Huang (2010)

- Huang, W. T. et al., Genetics and immunological characterization of NOD.*Abd3* as a model for human primary biliary cirrhosis. 41st Annual Autumn Immunology Conference – Chicago Marriott Downtown (November 16 – 19, 2012)

Kun-Po Li (2011)

- **KP Li**, S Lajoie, IP Lewkowich, K Dienger, AA Sproles and M Wills-Karp. IL-17A expression in steroid refractory mice is associated with differential HDAC expression. The 40th Autumn Immunology Conference. Nov 2011. Chicago, IL. USA

Cortez McBerry (2007)

- Keystone Symposium: Innate Immunity: Sensing the Microbes and Damage Signals, Keystone, CO, March 4-9. Poster Presentation, "PD-1 Signaling Drives Immune-Protective IL-10 production in Naïve Mice."

Jonathan McNally (2009)

- AA1 2013
- Block symposia and poster: An immuno-protective treatment strategy for autoimmune diseases

Jana Raynor (2008)

- **Jana Raynor,** Nathan Shock Aging Center Conference on Aging, 2011, *Mechanisms of regulatory T cell*

homeostasis in aging

Hesham Shehata

- Autumn Immunology Conference, Chicago November 2012- " Aging has a complex effect on NK cells in mice, clearly affecting their homeostasis, but only partially affecting their function."

Samuel Vaughn (2008)

- American Society for Clinical Investigation/Association of American Physicians Joint Annual MeetingPresented poster describing fine-mapping of PXK locus and genotypic changes in B cell receptor internalization phenotype
- Imaging and Cytometry Research Day, Ohio River Valley Cytometry Association
- Presented poster describing fine-mapping of PXK locus and the influence of PXK genotypes on B cell antigen receptor functions. Answered questions from judges regarding my poster and work

Akash Verma (2009)

- **Akash Verma**, and George S. Deepe Jr. "CCR2 regulates IL4-IL33 axis during *Histoplasma capsulatum* infection". Gordon Research Conference on Immunology of Fungal Infections, Galveston, TX, Jan 2013

Kristi Weage (2012)

- Digestive Health Center Annual Scientific Retreat 2013, CCHMC Poster Session "Undernutrition by a regional basic diet increases serum interferon-gamma levels and enhances tolerance to oral lipopolysaccharide in weanling mice"
- Digestive Disease Week 2013, Poster Session "Undernutrition by a regional basic diet increases serum interferon-gamma levels and enhances tolerance to oral lipopolysaccharide in weanling mice"