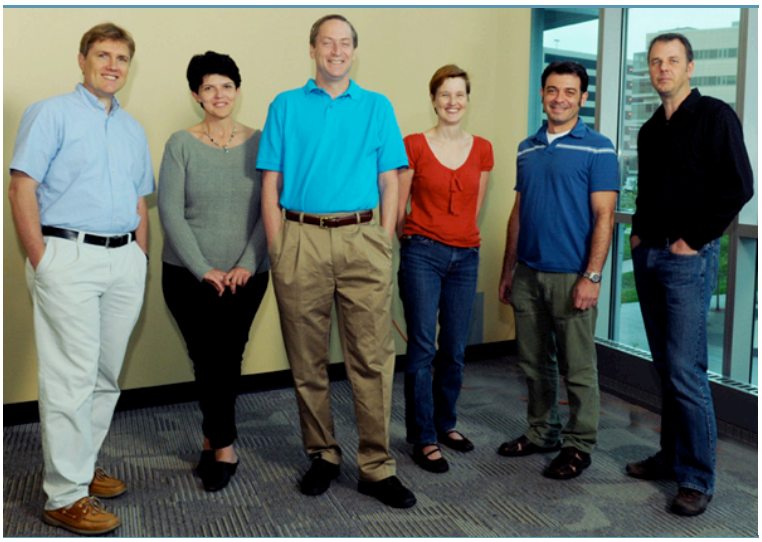
Molecular Immunology

Division Photo



J. Koehl, C. Chougnet, C. Karp, E. Janssen, J. Aliberti, K. Hoebe

Division Data Summary

Research and Training Details	
Number of Faculty	6
Number of Joint Appointment Faculty	1
Number of Research Fellows	5
Number of Research Students	9
Number of Support Personnel	13
Direct Annual Grant Support	$2,956,851
Peer Reviewed Publications	18

Significant Publications

Trompette A, Divanovic S, Visintin A, Blanchard C, Hegde RS, Madan R, Thorne PS, Wills-Karp M, Gioannini TL, Weiss JP, Karp CL. Allergenicity resulting from functional mimicry of a Toll-like receptor complex protein. Nature. 2008. 457:585-588.

Why specific proteins tend to act as allergens in susceptible hosts is a basic mechanistic question that has remained largely unclear. This important paper reports that the major allergen derived from dust mites, Der p 2, tends to be targeted by adaptive immune responses because it behaves as a functional mimic of the ligand-binding component (MD-2) of the innate immune receptor for bacterial lipopolysaccharide, TLR4. The fact that other members of the MD-2-like lipid binding family are allergens, and that more than 50% of defined major allergens are lipid-binding proteins, suggests that intrinsic adjuvant activity by such proteins and their accompanying lipids is likely to have some generality as a mechanism underlying the phenomenon of allergenicity.

Lages CS, Suffia I, Velilla P, Huang B, Warshaw G, Belkaid Y, Chougnet C. Functional regulatory T cells accumulate in aged hosts and promote reactivation of chronic infections. J. Immunol. 2008, Aug; 181(3):1835-48.

Aging is associated with impaired immune function, something that is thought to contribute significantly to disease

burden in the elderly. This seminal paper reports that: (a) there is expansion of regulatory T cells in the blood of elderly humans as well as in lymphoid tissues of aged mice; (b) in vitro depletion of peripheral regulatory T cells from elderly humans leads to increased effector T cell responses; (c) regulatory T cells from old mice exhibit greater suppressive capacity than those from young mice; and (d) the increasing proportion of regulatory T cells correlates directly with spontaneous reactivation of chronic Leishmania major infection in old mice. These data strongly suggest that accumulation of regulatory T cells plays an important role in the frequent reactivation of chronic infections that occurs in the elderly.

Barnes MJ, Krebs P, Harris N, Eidenschenk C, Gonzalez-Quintial R, Arnold CN, Crozat K, Sovath S, Moresco EM, Theofilopoulos AN, Beutler B, Hoebe K. Commitment to the Regulatory T Cell Lineage Requires CARMA1 in the Thymus but Not in the Periphery. PLoS Biology Vol. 7, No. 3, e51 doi:10.1371/journal.pbio.1000051. 2009.

This important paper provides novel mechanistic insight into the development and differentiation of regulatory T cells. Following ENU mutagenesis, mice were identified that had peripheral regulatory T cells in the absence of thymic regulatory T cells. Positional cloning revealed the causative mutation to be in Carma1. Data in this paper provide genetic evidence for two distinct mechanisms controlling regulatory T cell lineage commitment, and demonstrate that peripheral regulatory T cells are a dynamic population that can expand to either limit immunopathology or promote chronic infection.

Krebs P, Barnes MJ, Lampe K, Whitley K, Bahjat KS, Beutler B, Janssen E, Hoebe K. NK cell-mediated killing of target cells triggers robust antigen-specific T cell-mediated and humoral responses. Blood, 113(26):6593-602, 2009.

This seminal publication demonstrates that natural killer (NK) cells can drive robust adaptive immune responses—including CD8+ T cell, CD4+ T cell and B cell responses—through killing of antigen-expressing target cells. This newly-recognized pathway is now being translationally exploited by Dr. Hoebe in order to develop novel vaccines for chronic infectious diseases such HIV/AIDS, as well as for cancer vaccine development.

Gu YY, Harley ITW, Henderson LB, Aronow BJ, Vietor I, Huber LA, Harley JB, Kilpatrick JR, Langefeld CD, Williams AH, Jegga AG, Chen J, Wills-Karp M, Arshad SH, Ewart SL, Thio CL, Flick LM, Filippi MD, Grimes HL, Drumm ML, Cutting GR, Knowles MR, Karp CL. Identification of IFRD1 as a modifier gene for cystic fibrosis lung disease. Nature. 2009. 458:1039-1042,

This important paper reports the results of the first genome-wide single nucleotide polymorphism scan to identify genes that modify the severity of cystic fibrosis lung disease. Polymorphisms in IFRD1, which encodes a histone deacetylase-dependent transcriptional co-regulator, were found (and validated in a second cohort) to contribute to lung disease severity in cystic fibrosis, independent of CFTR genotype. Immunobiological investigation strongly suggests that IFRD1 modulates the pathogenesis of CF lung disease by regulating neutrophil effector function. These data suggest therapeutic utility for targeting neutrophils in cystic fibrosis, and suggest that IFRD1 may provide a useful therapeutic target in this and other diseases in which neutrophilic inflammation plays an important pathogenetic role.

Division Collaboration

Collaboration with Immunobiology

Collaborating Faculty: Michael Jordan, M.D.;

The role of the macrophage IFN-gamma receptor in mediating resistance to Toxoplasma gondii infection (manuscript submitted for publication).

Dissection of cytolytic effector mechanisms.

IFN-g signaling by macrophages in leishmanial infection.

Collaboration with Immunobiology

Collaborating Faculty: Jochen Mattner, M.D.

The role of AhR in mediating resistance to Salmonella oral infection in mice (experiments ongoing).

Collaboration with Immunobiology

Collaborating Faculty: David Hildeman, Ph.D.

Homeostasis of regulatory T cells in aging (R01 funded in 2009; manuscript in revision at PNAS).

Collaboration seeks to obtain a better understanding of the role of NK and NKT cells in CD4 T cell activation upon LCMV infection. In addition, a second project involves the study of Gimap5 in lymphocyte survival (currently submitted for publication).

CD4 and CD8 T cell responses; priming, effector function and memory development. (published in Nature Immunology).
In vivo immunobiology of IL-10 (published in Journal of Immunology).

Collaboration with Immunobiology

Collaborating Faculty: Marsha Wills-Karp, Ph.D.

Role of PD-1 and its ligands in immune suppression associated with aging (manuscript submitted).
Molecular underpinnings of allergy (published in Nature; R01 submitted) Genetic modifiers of cystic fibrosis lung disease (published in Nature; R01 obtained).
The role of complement in allergic asthma (published in Journal of Immunology).

Collaboration with Immunobiology

Collaborating Faculty: Suzanne Morris, Ph.D.; Fred Finkelman, M.D.

Collaboration involves genetic linkage analysis of existing differences in memory CD8 T cell populations observed in mice on a C57BL/6 and BALB/c background.

Collaboration with Immunobiology

Collaborating Faculty: Lee Grimes, M.D.

Collaboration involves studying the role of Gimap5 function in hematopoietic stem cells.
Regulation of neutrophil effector function by the genetic modifier of CF lung disease, IFRD1 (published in Nature; R01 obtained).

Collaboration with Immunobiology

Collaborating Faculty: Fred Finkelman, M.D.

Molecular mechanisms underlying the development of transfusion-related acute lung injury (TRALI). (Manuscript in preparation).
Molecular mechanisms underlying the development of peanut allergy (published in *Journal of Allergy & Clinical Immunology.*
RP105 regulation of B cell function (ongoing R01).
B cell IL-10 production (published in *Journal of Immunology*).

Collaboration with Experimental Hematology

Collaborating Faculty: James Mulloy, Ph.D.

Development of a humanized mouse model for HIV infection.

Collaboration with Experimental Hematology

Collaborating Faculty: Marie-Dominique Philippi, Ph.D.

Regulation of neutrophil effector function by the genetic modifier of CF lung disease, IFRD1 (published in *Nature*; R01 obtained).

Collaboration with Gastroenterology, Hepatology and Nutrition

Collaborating Faculty: Jorge Bezerra, M.D.

Dysfunction in biliary atresia (ongoing R01; published paper in J. Clin. Invest.; second manuscript submitted).
Collaboration involves the characterization of a novel ENU germline mutant designated Lampe1 that develops spontaneous hepatic steatosis.

Collaboration with Gastroenterology, Hepatology and Nutrition

Collaborating Faculty: Kris Steinbrecher, Ph.D.

Collaboration involves studying colitis development in Gimap5-deficient mice.

Collaboration with Gastroenterology, Hepatology and Nutrition

Collaborating Faculty: Lee Denson, M.D.

Collaboration involves studying colitis development in Gimap5-deficient mice.
Regulation of inflammatory bowel disease by TLR signaling (paper submitted).

Collaboration with Pulmonary Biology/Neonatology

Collaborating Faculty: Alan Jobe, M.D., Ph.D.; Suhas Kallapur, M.D.

Late Preterm Birth, Ureaplasma Species and Childhood Lung Disease (R01 funded in 2009).
Biomarkers of immunologic function and preterm respiratory outcomes (U01 submitted, CTSA pilot project submitted).

Collaboration with Developmental Biology

Collaborating Faculty: Jay Degen, Ph.D.

Collaborative efforts involve the ENU mutagenesis program in mice where Dr. Degen seeks to identify non-redundant genes involved in the effective clearance of Listeria monocytogenes from the peritoneum.

Collaboration with Developmental Biology

Collaborating Faculty: Rashmi Hegde, Ph.D.

Molecular underpinnings of allergy (published in Nature; Sandler Foundation Grant; R01 submitted).

Collaboration with Endocrinology

Collaborating Faculty: Jonathan Katz, Ph.D.

Dissection of the role of a novel Dendritic Cell subset in the breaking of T cell tolerance (JDRF Innovative Grant 5-2009-69).

Collaboration with Allergy and Immunology

Collaborating Faculty: Kimberly Risma, M.D., Ph.D.

Dissection of cytolytic effector mechanisms.

Collaboration with Allergy and Immunology

Collaborating Faculty: Carine Blanchard, Ph.D.

IL-10 production by eosinophils.

Collaboration with Hematology/Oncology

Collaborating Faculty: Joe Palumbo, M.D.

Generation of CD8 T cell responses to live tumor cells.

Collaboration with Biomedical Informatics

Collaborating Faculty: Bruce Aronow, Ph.D.

Genetic identification of DC subsets.
Genetic modifiers of CF lung disease allergy (published in *Nature*; R01 submitted), RP105 regulation of B cell function (ongoing R01).

Collaboration with Pulmonary Biology

Collaborating Faculty: Jeffrey Whitsett, M.D.

Pro-resolution lipid mediators in CF lung disease and airway remodeling (ongoing R01).

Collaboration with Pulmonary Biology

Collaborating Faculty: Timothy Weaver, M.S., Ph.D.

Analysis of B cell function in ERdj4-deficient mice.

Collaboration with Pulmonary Biology; Pulmonary Medicine

Collaborating Faculty: Jeffrey Whitsett, M.D.; Henry Akinbi, M.D.; Paul Kingma, Ph.D.; Jamie Wooldridge, M.D.; Carolyn Kercsmar, M.D.

Cystic Fibrosis Foundation Research Development Program Grant.

Collaboration with Infectious Diseases

Collaborating Faculty: Nancy Sawtell, Ph.D.

Role of indolamine 2,3 dioxygenase in HSV infection.

Collaboration with Infectious Diseases

Collaborating Faculty: Rhonda Cardin, Ph.D.

Role of B cell IL-10 production in MCMV infection (published in Journal of Immunology).

Collaboration with Pathology

Collaborating Faculty: Kenneth Setchell, Ph.D.

Molecular underpinnings of allergy; regulation of obesity by the RP105/TLR axis.

Collaboration with Nephrology & Hypertension

Collaborating Faculty: Prasad Devarajan, M.D.

Establishment of a murine congenic kidney transplantation model (published in Clinical & Experimental Immunology).

Faculty Members

Christopher Karp, MD, Professor ; *Associate Director, Immunobiology Graduate Program; Director, CF Research Program; Director, Trustee and Procter Scholar Programs*

Julio Aliberti, PhD, Assistant Professor

Claire A. Chougnet, PhD, Associate Professor

Kasper Hoebe, PhD, Assistant Professor

Edith M. Janssen, PhD, Assistant Professor

Joerg Koehl, MD, Adjunct Professor

Joint Appointment Faculty Members

Jonathan Katz, PhD, Associate Professor
Endocrinology

Trainees

- **Rajat Madan, MD,** GSY-8,
- **Celine Silva-Lages, PhD,** PGY-5,
- **Manoj Pandey, PhD,** PGY-5,
- **Yuan Yuan Gu, MD,** GSY-5,
- **Jessica Allen, BS,** GSY-5,
- **Naonori Uozumi, MD, PhD,** PGY-10, Visiting Scientist, University of Tokyo
- **Senad Divanovic, PhD,** PGY-3,
- **Pietro Pressice, PhD,** PGY-3,
- **Isaac Harley, BS,** GSY-2,
- **Xun Zhang, BS,** GSY-4,
- **Cortez McBerry, BS,** GSY-2,
- **Ibrahim Aksoylar, BS,** GSY-2,
- **Stephanie Walters, BS,** GSY-1,
- **Rebecca Currier, BS,** GSY-1,

Significant Accomplishments

Defining the molecular basis for allergenicity

With the prevalence, morbidity and mortality of allergic asthma continuing its dramatic rise in the Westernized world, it is clear that new therapies are needed. The rational development of novel therapeutic approaches will likely depend upon a better molecular understanding of pathogenesis. Allergic asthma is thought to arise from maladaptive, immune responses to ubiquitous, otherwise innocuous environmental proteins. While the proteins so targeted represent a tiny fraction of the airborne proteins humans are exposed to, the same proteins typically behave as aeroallergens across the human population. Why particular proteins tend to act as allergens in susceptible hosts is a fundamental mechanistic question that has remained largely unclear. The major house dust mite allergen, Der p 2, has structural homology with MD-2, the lipopolysaccharide (LPS)-binding component of the TLR4 signaling complex. Data from the Karp lab have shown that: (a) Der p 2 has functional homology with MD-2 as well, facilitating signaling through direct interactions with the TLR4 complex, and reconstituting LPS-driven TLR4 signaling in the absence of MD-2; (b) Der p 2 facilitates LPS signaling in primary antigen presenting cells, with or without MD-2 being present; and (c) the in vivo allergenic activity of Der p 2 mirrors its in vitro functional and biochemical activity: Der p 2 efficiently drives airway Th2 inflammation in vivo in a TLR4-dependent manner, retaining this ability in the absence of MD-2. These data suggest that Der p 2 tends to be targeted by adaptive immune responses because of its auto-adjuvant properties. The fact that other members of the MD-2 lipid-binding domain family are major allergens and, more broadly, that more than 50% of defined major allergens are lipid-binding proteins, suggests that intrinsic adjuvant activity by such proteins and their accompanying lipid cargo is likely to have some generality as a mechanism underlying the phenomenon of allergenicity.

Exploiting novel pathways of immune activation for vaccine development

Dr. Janssen's laboratory focuses on mechanistic analysis and translational exploitation of newly recognized pathway of activation of antigen-specific adaptive immune responses involving a novel class of dendritic cells (DC) and directed towards detection of antigens expressed by apoptotic cells. Seminal studies by Dr. Janssen have shown that the phagocytosis of apoptotic cells by such DCs can robustly induce the activation and expansion of effector and memory CD4+ and CD8+ T cells specific for cell-associated antigens. The Janssen laboratory aims at translational exploitation of these insights into the development of effective therapeutic and preventive cancer vaccines. In a related vein, Dr. Hoebe recently identified an "endogenous adjuvant" pathway mediated by NK cells. NK cells detect and kill pathogen-infected host cells, as well as neoplastic cells and tissue allografts. However, studies from the Hoebe laboratory have shown that they discharge another duty as well: one that establishes a strong tie between NK cells and the adaptive immune system. Of key importance in this pathway is the recognition and killing of antigen expressing target cells by NK cells. Subsequently, NK cell-induced cell death is recognized by DCs, leading to antigen cross-presentation and to strong cellular and humoral immune responses. Dr. Hoebe's laboratory aims to exploit the knowledge obtained on NK cell-driven adaptive immune responses for the generation of novel vaccines for chronic infectious diseases such HIV/AIDS, as well as for cancer vaccine development.

Identifying genetic modifiers of cystic fibrosis lung disease, and the biological pathways that they regulate

Cystic fibrosis (CF) is the most common, lethal autosomal recessive disorder in the U.S. Novel therapeutic approaches to CF lung disease, the major cause of morbidity and mortality, are clearly needed. Published studies indicate significant heritability of lung disease severity in CF, independent of CFTR genotype. To search for genes modifying CF lung disease, the Karp lab performed a genome-wide association scan in one cohort of CF patients, with replication of top candidates in an independent cohort. Using this approach, genetic variation in IFRD1 was identified and replicated as a modifier of lung disease severity in CF. IFRD1 is a transcriptional co-regulator. In vivo and in vitro analysis has indicated that IFRD1 modulates the pathogenesis of airway disease in CF through regulation of neutrophil effector function. These data suggest therapeutic utility for targeting neutrophils in cystic fibrosis, and suggest that IFRD1 may provide a useful therapeutic target in this and other diseases in which neutrophilic inflammation plays an important pathogenetic role. In addition to continuing to define the molecular mechanisms underlying IFRD1-mediated modulation of neutrophil function, with the goal of developing novel therapeutic approaches to CF lung disease, the Karp lab continues to work on novel CF modifier genes with collaborators from Johns Hopkins (Garry Cutting), the University of North Carolina (Michael Knowles) and Case Western Reserve University (Mitch Drumm).

Division Publications

1. Hoebe K. Genetic dissection of Toll-like receptor signaling using ENU mutagenesis. *Methods Mol Biol.* 2009; 517: 239-51.
2. Tschop MH, Hugenholtz P, Karp CL. Getting to the core of the gut microbiome. *Nat Biotechnol.* 2009; 27: 344-6.
3. Zhang X, Lewkowich IP, Kohl G, Clark JR, Wills-Karp M, Kohl J. A protective role for C5a in the development of allergic asthma associated with altered levels of B7-H1 and B7-DC on plasmacytoid dendritic cells. *J Immunol.* 2009; 182: 5123-30.
4. Gu Y, Harley IT, Henderson LB, Aronow BJ, Vietor I, Huber LA, Harley JB, Kilpatrick JR, Langefeld CD, Williams AH, Jegga AG, Chen J, Wills-Karp M, Arshad SH, Ewart SL, Thio CL, Flick LM, Filippi MD, Grimes HL, Drumm ML, Cutting GR, Knowles MR, Karp CL. Identification of IFRD1 as a modifier gene for cystic fibrosis lung disease. *Nature.* 2009; 458: 1039-42.
5. Khodoun M, Strait R, Orekov T, Hogan S, Karasuyama H, Herbert DR, Kohl J, Finkelman FD. Peanuts can contribute to anaphylactic shock by activating complement. *J Allergy Clin Immunol.* 2009; 123: 342-51.
6. Trompette A, Divanovic S, Visintin A, Blanchard C, Hegde RS, Madan R, Thorne PS, Wills-Karp M, Gioannini TL, Weiss JP, Karp CL. Allergenicity resulting from functional mimicry of a Toll-like receptor complex protein. *Nature.* 2009; 457: 585-8.
7. Krebs P, Barnes MJ, Lampe K, Whitley K, Bahjat KS, Beutler B, Janssen E, Hoebe K. NK cell-mediated killing of target cells triggers robust antigen-specific T cell-mediated and humoral responses. *Blood.* 2009; 113: 6593-602.
8. Sun J, Madan R, Karp CL, Braciale TJ. Effector T cells control lung inflammation during acute influenza virus infection by producing IL-10. *Nat Med.* 2009; 15: 277-84.
9. Barnes MJ, Krebs P, Harris N, Eidenschenk C, Gonzalez-Quintial R, Arnold CN, Crozat K, Sovath S, Moresco EM, Theofilopoulos AN, Beutler B, Hoebe K. Commitment to the regulatory T cell lineage requires CARMA1 in the thymus but not in the periphery. *PLoS Biol.* 2009; 7: e51.
10. Chaix J, Tessmer MS, Hoebe K, Fuseri N, Ryffel B, Dalod M, Alexopoulou L, Beutler B, Brossay L, Vivier E, Walzer T. Cutting edge: Priming of NK cells by IL-18. *J Immunol.* 2008; 181: 1627-31.

11. Byrnes AA, Harris DM, Atabani SF, Sabundayo BP, Langan SJ, Margolick JB, Karp CL. Immune activation and IL-12 production during acute/early HIV infection in the absence and presence of highly active, antiretroviral therapy. *J Leukoc Biol.* 2008; 84: 1447-53.
12. Kim-Saijo M, Janssen EM, Sugie K. CD4 cell-secreted, posttranslationally modified cytokine GIF suppresses Th2 responses by inhibiting the initiation of IL-4 production. *Proc Natl Acad Sci U S A.* 2008; 105: 19402-7.
13. Nebert DW, Karp CL. Endogenous functions of the aryl hydrocarbon receptor (AHR): intersection of cytochrome P450 1 (CYP1)-metabolized eicosanoids and AHR biology. *J Biol Chem.* 2008; 283: 36061-5.
14. Lewis AG, Kohl G, Ma Q, Devarajan P, Kohl J. Pharmacological targeting of C5a receptors during organ preservation improves kidney graft survival. *Clin Exp Immunol.* 2008; 153: 117-26.
15. Bensinger SJ, Bradley MN, Joseph SB, Zelcer N, Janssen EM, Hausner MA, Shih R, Parks JS, Edwards PA, Jamieson BD, Tontonoz P. LXR signaling couples sterol metabolism to proliferation in the acquired immune response. *Cell.* 2008; 134: 97-111.
16. Hildeman D, Janssen E. IFN-gamma and self-absorbed CD4+ T cells: a regulatory double negative. *Nat Immunol.* 2008; 9: 1210-2.

Grants, Contracts, and Industry Agreements

Grant and Contract Awards — Annual Direct / Project Period Direct

ALIBERTI, J

Control of Immune Response by Lipoxins During Tuberculosis
National Institutes of Health
R01 AI 075038 — 02/01/08 - 01/31/13 — $200,000 / $1,000,000

Control of Immune Response by Lipoxins During Tuberculosis
National Institutes of Health
R01 AI 075038 (supplement) — 04/01/09 - 01/31/13 — $26,850 / $129,167

Long Term Immunity Against Toxoplasmosis
National Institutes of Health (George Washington University)
R01 AI 033325 — 07/01/08 - 06/30/13 — $33,464 / $167,320

CHOUGNET, C

CD40 Ligand Dysregulation and HIV Pathogenesis
National Institutes of Health
R01 AI 056927 — 01/01/05 - 12/31/09 — $209,287 / $1,250,000

Role of Regulatory T Cells in HIV Infection
National Institutes of Health
R01 AI 068524 — 08/01/06 - 07/31/11 — $246,093 / $1,294,683

HOEBE, K

A Novel NK Cell Mediated Adjuvant Approach to Generate Robust CD8+T Cell Responses
International AIDS Vaccine Initiative
05/01/08 - 12/31/09 — $222,731 / $412,934

Sphinx: A New Cause of Hepatic Neoplasia
National Institutes of Health
R21 CA 133649 — 07/01/08 - 06/30/10 — $130,500 / $239,250

Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease
National Institutes of Health
P30 DK 078392 — 06/01/09 - 05/31/10 — $30,000 / $30,000

Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease
National Institutes of Health
P30 DK 078392 (supplement) — 06/01/09 - 05/31/10 — $20,000 / $20,000

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 — $207,500 / $1,007,500

T Cell Memory to Cell-Associated Antigens by a New DC Subset
National Institutes of Health
R21 AI 079545 08/01/08 - 07/31/10 $150,000 / $275,000

KARP, C

Lipid Mediators And Dysregulated Inflammation In CF
National Institutes of Health
R01 HL 079312 04/01/05 - 02/28/10 $325,278 / $1,635,205

Regulation of TLR Signaling and Innate Immunity by RP105
National Institutes of Health
R01 AI 075159 07/01/07 - 06/30/12 $242,250 / $1,250,000

Cystic Fibrosis Foundation Research Development Program
Cystic Fibrosis Foundation
09/01/07 - 06/30/12 $370,000 / $1,850,000

Karp, C	Project 4/Core2	150,000
Whitsett, J	Transgenic Core	50,000
Kercsmar, C	Core 3a	30,000
Kingma, P	Project 1	50,000
Woolridge, J	Project 2	50,000
Akinbi, H	Project 3	40,000

Role of Aeroallergen Mimics of TLR Complex Proteins in Asthma Pathogenesis
American Asthma Foundation
06-0284 07/01/06 - 06/30/10 $250,000 / $1,000,000

Hepatitis C Pathogenesis and the Human Genome
National Institutes of Health (Johns Hopkins University)
R01 DA013324 09/01/04 - 08/31/09 $10,357 / $51,785

Cincinnati Rheumatic Diseases Center
National Institutes of Health
P30 AR 047363 07/01/08 - 06/30/09 $50,000 / $50,000

KOEHL, J

Molecular Regulation of Immune Complex Disease
National Institutes of Health
R01 AI 059305 12/15/04 - 11/30/09 $232,541 / $1,162,705

Current Year Direct 2,956,851

Total $2,956,851