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Mission Statement

The Sandler Asthma Basic Research Center (SABRE Center) at UCSF is an investigative unit dedicated to basic discovery in asthma research. The SABRE Center is nucleated by a small group of basic scientists who are supported by advanced technology cores. Regular seminars promote integration of the SABRE Center into the more extended UCSF research community to facilitate collaboration and to increase awareness for needs in fundamental discovery in asthma research. Founded in 1999, the SABRE Center is made possible by the generous support of the Sandler Foundation.

Summary of Accomplishments over the Past Year

We have just finished our third year with a full complement of SABRE Center Investigators in place on the Parnassus campus at UCSF. We have organized an efficient scientific unit and our relatively small cadre of scientists and collaborators are beginning to make important contributions to the basic understanding of allergy and asthma. Despite the difficult funding environment, our young investigators are attracting individual awards in support of their work. Integration with the clinical Asthma Center has strengthened such that our first SABRE Center Program Project could be submitted to the NIH. Seed funds from our innovative grants program led to the discoveries at UCSF of the biochemical pathway underlying the biology of ORMDL proteins, which remain the strongest risk for childhood asthma in multiple genome-wide association studies in human patients, and for optimization of biomarkers to define subsets of asthma patients that are being used in clinical trials to guide novel therapies. We look forward to continued successes in the coming year as we continue with our mission to conquer asthma.
Overview – 2011  
Richard M. Locksley, M.D.

The SABRE Center completed hiring the core research scientists and relocating them to UCSF in the first quarter of 2008 and spent much of the next 15 months upgrading and organizing the laboratories, installing equipment, hiring support personnel and generally turning the space into a productive research laboratory. Major equipment additions included the establishment of an LSRII analytical instrument for flow cytometry, a Fluidigm Dynamic Array multi-channel station for rapid 96-well quantitative PCR analyses, and establishing two-photon video microscopy for imaging of lung inflammatory cells \textit{in vivo}. The Center now consists of the Director, Dr. Locksley, three full-time faculty, Drs. Ansel, Liu and Shin, and one UCSF Fellow, Dr. Allen. In turn, these investigators now support eleven postdoctoral trainees, eight graduate students in Immunology and Biomedical Sciences, and three professional staff. Dr. Chapman, the former head of the Pulmonary Division at UCSF, works in contiguous space. His interests focus on lung inflammation and fibrosis, which overlap the interests of the SABRE Center, and his experience at UCSF continues to be an important resource for the young faculty. The Center has transformed into a vibrant new research addition to the UCSF campus that has succeeded in attracting graduate students and establishing itself as a productive investigative center.

Dr. Ansel is working to understand the role of small RNAs in regulating the functions of immune cells involved in asthma. He received a three-year award from the Dana Foundation as a Human Immunology Scholar to investigate microRNAs in asthma. Since arriving at UCSF he has published a methods paper on construction of small RNA libraries, co-authored a manuscript examining effects of an enhancer on the expression of IL-4 by T cells, and submitted two senior author papers describing the expression and effects of microRNAs on cytokine expression by T cells and, in an important contribution, on the development of technologies enabling the discrimination of a microRNA signature profile associated with asthma as revealed by studies in human patients. The first of these papers included Chris Allen of the SABRE Center as a co-author, while the second included Drs. Prescott, Fahy and Erle of the SABRE Center. He has participated in a number of national and international meetings presenting his work. Three additional manuscripts are in preparation. Dr. Ansel’s first R01 submission missed the funding payline, but he was awarded a one-year bridging R56 grant from NIAID to examine the regulation of microRNAs in T cell differentiation. He submitted a second R01 on an independent project examining small RNAs and genome-scale epigenetic profiling in immune cells from patients with human asthma. This R01 was scored in the funding range but has not been formally awarded as yet. He participated with Dr. Fahy, Woodruff and Locksley in a PPG pursuing basic research in human asthma patients that was favorably reviewed but missed the funding payline. He is participating in collaborative work with these investigators for a resubmission planned in the next 6 months. He has worked with the Functional Genomics core (David Erle) to develop technologies at UCSF, including deep sequencing of small RNAs with linkage to downstream bioinformatic analysis and development of ChIP-chip using an ultra high-density Nimblegen array platform, and with the Allen lab to develop robust technology
for transfecting small RNAs into primary T cells. He has established quarterly laboratory meetings with the Woodruff lab, and is working closely with the Asthma Clinical Center to test the feasibility of microRNA signatures that can be used as relatively noninvasive biomarkers for subsets of asthma patients. Dr. Ansel participated in shared equipment grants that resulted in the purchase of an Aria II flow cytometer and a Fluidigm Biomark Dynamic Array instrument for multi-channel quantitative PCR analyses. Both of these instruments are heavily used on campus. He also utilizes the Flow Cytometry Core. His laboratory consists of 1 postdoctoral fellow and 4 graduate students, of which 2 are in the combined MSTP, and a technician. His newest postdoc was awarded a Swiss National Fellowship to support his work in Dr. Ansel’s lab, and his newest graduate student received a National Science Foundation fellowship to support her work. His first two postdoctoral trainees, P. Vijayanand and G. Seumois will be returning to the University of Southampton to establish an independent laboratory pursuing human asthma research, and his first laboratory technician entered graduate school at UC Santa Barbara.

Dr. Liu is examining mechanisms controlling the targeting and turnover of nitric oxide, an important airway and blood vessel relaxant. Work in his postdoctoral training identified the enzyme GSNOR as an important molecule regulating nitrosylation and nitric oxide turnover in tissues, and this molecule has become an important target in asthma, although it will be critical to first identify potential toxicities that might be associated with inhibiting this pathway. In an important contribution in *Science Translational Medicine*, Dr. Liu described the role of GSNOR in mediating nitrosylation and turnover of a major hepatic DNA repair enzyme. In its absence, as occurs in a substantial fraction of human hepatic carcinomas, hepatic cancers can be more readily induced in mice. Thus, targeting of GSNOR may require strategies for local inhibition in the lung and airways to avoid potential off-target effects. Dr. Liu also collaborated with Dr. Burchard in the Genetics Core as a co-author on a manuscript describing gene-gene interactions between GSNOR and the beta-adrenergic receptor in determining the responsive of patients to bronchodilator therapies in asthma. He published a senior author paper with Dr. Locksley describing effects of GSNOR deficiency in lymphocyte development. He also followed up his original manuscript detailing the effects of GSNOR deficiency in predisposing to hepatic cancer by uncovering the mechanism, which involves nitrosylation of a DNA alkyltransferase that protects hepatocytes from genotoxic stress. In pursuit of these findings, Dr. Liu was awarded an R01 from the NCI to examine the role of GSNOR in liver cancer. He is also a co-PI on another R01 and a PPG examining the pathogenesis of chronic hepatitis B infection and liver cancer, and is involved in a pharmaceutical company-sponsored drug screen to find inhibitors of the GSNOR and other targets in the pathway. He presented his work at 7 national and international meetings as an invited speaker in 2010. He continues his work trying to delete GSNOR conditionally in specific tissues in mice in order to delineate genetically which tissues in the lung are the relevant targets for bronchodilation. He utilizes the Animal Physiology Core, the Flow Cytometry Core, the Genetics Core and the Functional Genomics Core in the SABRE Center. His laboratory consists of one postdoctoral fellow, one technician and two research specialists.
Dr. Shin studies dendritic cell maturation and antigen processing and in her postdoctoral training described a novel pathway affecting the turnover of surface complexes of major histocompatibility-peptide complexes at the surface of the dendritic cells, which was regulated by ubiquitination. She is continuing studies of dendritic cells with an emphasis on cells collected from the human lung. She has submitted a manuscript, currently under review, describing the inhibitory role of IL-10 on dendritic cell maturation via a pathway involving upregulation of MARCH1 activity, resulting in ubiquitination of MHC class II and CD86, and was invited to present this work at a Keystone meeting. An R01 seeking to understand this pathway was not funded in its initial evaluation, and a re-submission has recently been completed. Her second area of research involves understanding the role of the high-affinity IgE receptor, FcεRI, in human dendritic cell biology. She has established a close collaboration with pulmonary physicians in the Asthma Clinical Center – Drs. Paul Wolters, Prescott Woodruff and John Fahy – to obtain freshly dissected human lung tissues from transplant procedures and samples of biopsies and cell lavages from asthma patients. She is also using humanized transgenic mice containing human FcεRI expressed on mouse cells in a pattern resembling its expression in humans (developed in the Kinet lab at Harvard). Her initial findings that human lung dendritic cells express FcεRI and her ability to localize these cells in human tissues led to a successful 4-year American Heart Association Scientist Development Award in July 2010. Her initial findings indicate that bound IgE is rapidly endocytosed and cleared in terminal lysosomes of dendritic cells, and in contrast to its persistent residence on the surface on basophils and mast cells, suggesting the dendritic cells may contribute to IgE turnover. She is also examining the possibility that allergic asthma is exacerbated by altered trafficking of dendritic cell FcεRI as compared to cells in healthy lungs. Dr. Shin is preparing these findings for submission as a manuscript and is planning another R01 grant submission in June 2011. Dr. Shin has worked closely with the Asthma Clinical Center, the Flow Cytometry Core and the Imaging Center, and is increasing her use of the Mouse Physiology Core and the Genomics Core. She currently has a graduate student, a postdoc and a technician in her laboratory.

Dr. Allen is a UCSF Fellow and is the first member of the UCSF Fellows Program (http://biochemistry.ucsf.edu/~ucsffellows/current.html) who has been selected to work on any specific human disease, in this case, asthma. He brings expertise in optical imaging of the immune system to a passion for understanding the pathogenesis of allergic inflammation in the lung that causes asthma. Chris participated in the shared instrumentation grant that resulted in the purchase of an Aria II flow cytometer. He submitted a Gates Foundation Challenges grant, but it was not funded. He has generated sensitive IgE reporter mice that detect switched B cells and allows dynamic imaging of IgE-committed cells in live tissues. He has made a number of technologic innovations that are in use in his own laboratory and in other SABRE laboratories, including optimizing methods for simultaneous 5-color labeling of cells in tissue sections, thus approaching flow cytometry in the capacity to discriminate cell types in their native setting. He devised a new method for spectral separation of fluorophors by 2-photon microscopy. He worked with the Ansel laboratory to optimize delivery of small RNAs into primary lymphocytes. He worked with the Locksley laboratory to enable the first
imaging of basophils in living tissues during immune responses, and is a co-author on a submitted manuscript. Chris works closely with the Flow Cytometry, Imaging and Small Animals Physiology Cores in the SABRE Center. He oversees the maintenance and training of the LSRII in the SABRE Center facility. Dr. Allen currently has one senior postdoc in his laboratory.

An important component of the SABRE Center has been support and guidance for advanced technology cores that enhance the ability to move scientific advances quickly. The SABRE Center contributes to cores in Animal Physiology (which provide mouse models of allergic lung inflammation, including challenge with model antigens, fungal antigens and dust mite antigens), Functional Genomics, Genetics, Flow Cytometry and Imaging, including video, confocal and total internal reflection instruments. Our largest monetary support goes to the Small Animals Physiology and Genetics cores, addressing small animal models and the collection of cohorts of carefully phenotyped families with asthma, respectively, in order to meet the needs of special interests to asthma investigators. These cores continue to attract substantial use among asthma investigators as well as scientists in related fields, including inflammation, genetics and stem cell biology. The Animal Core now supports nine AAF studies from non-UCSF investigators. The Genetics Core has developed among the largest cohorts of Latino and African American families afflicted with asthma for genetic studies, and has been awarded two NIH R01’s and a PPG to support these studies. The remaining cores are supported by smaller amounts of funding, typically to core directors and operators, to meet costs that are difficult to recover through recharge or other mechanisms. Despite our successes, the fiscal constraints driven by the current difficult economic downturn will necessitate trimming our support levels, a process that will be driven by the levels of use for individual cores by SABRE, AAF and community investigators, the ability to meet costs from alternative sources, such as recharge, and the input from the executive committee and the outside scientific advisory board. The Imaging Core has made large technical strides in providing optical support for lung and lymph node imaging studies and has grown to support over 140 users involving 45 PI’s and 16 Department or Organized Research Units at UCSF. A technical report on optimizing live lung imaging in the mouse was published and has received substantial attention by the scientific community, and the Center is collaborating with investigators at HHMI Janelia Farms to improve issues related to adaptive optics and tissue penetration. In the Imaging Core, SABRE Center support has been leveraged into two intramural technology grants and two NIH submissions for shared instrument grants and core support. The Imaging Core also organizes a seminar series dedicated to technical advances in imaging that has become a major resource on campus. SABRE support for technology cores has been leveraged to attract NIH funding: the Animal Physiology Core is additionally now supported by technical core funds supported by NIAID Asthma and Allergic Disease Cooperative Research Center (Sheppard, Locksley, Burchard, Fahy) and the Imaging Core is additionally supported by technical core funds supported by a PPG from NHLBI to assess the microenvironments induced by lung inflammation (Caughey, Krummel, McDonald). In each case, funds from SABRE Innovative Grants program initiated projects that led to the organization and support for these programmatic awards,
indicative of the leverage enabled by a focused efforts from relatively small groups of investigators.

A second area of importance to the SABRE Center has been the emergence of the Clinical Asthma and Inflammatory Lung Disease Center (Asthma Clinical Center) on the Parnassus campus for clinical translational studies in asthma. The Center, under the directorship of Dr. John Fahey, a prior Innovative grants awardee, is expanding its presence in human lung disease translational research on the UCSF campus. SABRE Center core scientists and the Director meet quarterly with Dr. Fahey and colleagues to further communication, planning and collaborative investigations of human asthma patients. Each of the core scientists is already involved in ongoing or planned investigations with translational physician scientists in the Asthma Clinical Center, confirming that this will serve as an important integrative unit for translational interests of the SABRE Center. The monthly SABRE Center conferences have been merged with the Pulmonary research conferences to begin a research seminar format entirely integrated between SABRE Center laboratories, pulmonary scientists and interested investigators at UCSF from other disciplines. The conferences, which are alternated between the Parnassus and Mission Bay campuses, have proven extremely well attended, and have spurred a number of collaborative interactions by bringing scientists from different areas together. SABRE Center scientists submitted a joint PPG with translational physician scientists from the Asthma Clinical Center at the end of 2010 that was well scored but just missed the funding range. A re-submission is in progress. Joint publications have already been published between SABRE investigators and pulmonary physicians in the Asthma Clinical Center and one joint NIH R01 grant received a fungible score (Ansel-Woodruff).

The administrative costs of the Center remain steady at ~8% of costs and reflect efficient management and leveraging with Departmental resources in personnel and grants management. We completed installation of environmentally improved water-saver units on our dishwasher/autoclaves in 2010. These units were inherited from the School of Medicine and are over 20 years old. Upgrades will further improve their environmental profiles through increased efficiency and lowering of electric, water and maintenance costs. The School of Medicine, largely based on data procured by the SABRE Center, is beginning to evaluate a system-wide upgrade to the campus dishwashing/autoclave enterprise. We have also recently begun to explore upgrades of the fans that generate airflow in the facility in order to improve the quality and balance of airflow control in a more energy-efficient way. The existing fans are more than 30 years old and are not optimal from either an engineering or efficiency standard. Thus, the SABRE Center has expanded its footprint into both academic and structural elements of the campus. We are grateful to the professionalism and dedication of our core administrative staff in improving the physical plant and the working environment.

We appreciate that evidence-based metrics for success will be important in leveraging continuing support in the future, including from philanthropic entities. SABRE Center investigators have participated in successful fund-raising initiatives spearheaded by the American Asthma Foundation and have begun exploratory
considerations regarding the best mechanisms for instituting a SABRE Center philanthropic outreach. Fund-raising will require evidence for metrics of success, including our capacity to attract extramural research dollars to the community, to contribute high-impact papers that establish novel paradigms in the asthma research arena, to attract new investigators into the field and, ultimately, to drive the discovery of new therapies that affect the disease. Although therapeutic discoveries will take time, we believe we can already point to successes in these evidence-based metric achievements over this past year, despite the fact that this period of time was largely devoted to organization, renovation and startup issues of importance to our new scientists.

Summary of extramural funding and manuscripts by core SABRE Center faculty since prior SRB review (2009-11)

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<th>Grants Submitted</th>
<th>Manuscripts Submitted</th>
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<td>Locksley: NIH R37, NIHR01, NIH PPG x 2, Hillblom Fdn Award HHMI re-appointment</td>
<td>18</td>
<td>NIH PPG</td>
<td>4</td>
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<tr>
<td>Allen (Fellow): NIH Shared Equipment</td>
<td>Gates Fdn</td>
<td>-</td>
<td>1</td>
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<tr>
<td>Ansel: Dana Fdn, NIH R01 (fungible score)</td>
<td>NIH R01, NIH PPG</td>
<td>3</td>
<td>2</td>
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<tr>
<td>Liu: NIH R01 x 2</td>
<td></td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Shin: Cancer Research Institute Award, American Heart Association Scientist Development Award</td>
<td>NIH R01, NIH R21</td>
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In addition, activities related to the SABRE Center cores resulted in publication of over 30 manuscripts and contributions to 11 successfully awarded grants of various types to investigators at UCSF.

Highlighted SABRE Center-supported papers with impact on asthma-related research in 2010-11

This paper uses an unbiased functional genomic screen in yeast to determine the function of Orm family proteins as negative regulators of sphingolipid biosynthesis through a process mediated by phosphorylation-dependent feedback affecting their interaction with the rate-limiting enzyme in sphingolipid production. Although ORMDL3 has been linked with childhood asthma risk in multiple genome-wide association studies, there was no understanding of what these proteins did or how they functioned in the cell. This paper has received widespread recognition in the scientific and lay press, and has uncovered a completely unsuspected new area for intervention in the pathogenesis of human asthma. This study was carried out at UCSF and begun entirely by funding provided to Dr. Weissman with an innovative research grant from the SABRE Center to uncover the function of these proteins.


This study demonstrated that genetic determinations of ancestry improved estimates of lung function, thus preventing mis-identification of patients as having lung dysfunction. The high incidence of asthma in patients of Puerto Rican and African ancestry makes understanding the influence of genetic ancestry important in following and enrolling patients in clinical trials.


This commentary is a wide-ranging essay on the state of research in asthma, the needs for the future and speculation regarding the origins of this type of immune response to environmental allergens.


This paper identifies a role for GSNOR, an S-nitrosoglutathione reductase, as an important regulator of the turnover of a DNA repair protein in the liver, leaving GSNOR-deficient mice as risk for chemically-induced hepatic carcinoma. Further, almost 50% of patients with hepatic carcinoma have diminished activity of liver GSNOR. GSNOR inhibition remains a verified target for control of airway hyperreactivity in asthma, and this study suggests caution be taken to avoid inhibition of the enzyme in the liver.

Eosinophils are highly associated with allergic asthma. Their role in homeostasis is unknown but will be important to understanding potential implications of targeting these cells or interfering with their normal biologic processes in a therapeutic way. In this paper, eosinophils were shown to migrate into white fat and to be necessary for maintaining macrophages in a status optimal for normal metabolic homeostasis. Elevating eosinophils through model helminth infections improved insulin sensitivity in mice on high-fat diet, demonstrating that eosinophils have a role in optimizing metabolic programs in vertebrates. The authors speculate that this biology may have arisen to compete against ubiquitous intestinal parasites for nutrients.


Using whole-genome microarray and quantitative PCR analyses of endobronchial biopsies of moderate-to-severe asthmatics and controls, the investigators describe the genetic spectrum of ‘Th2-associated’ asthma, and define a matrix of 79 co-expressed genes involved in inflammation, cell migration and tissue remodeling that comprise the signature of the response. Inspired by such studies, genetically determined subsets of asthma patients are being used to stratify patients to receive targeted therapeutics. These studies were carried out on patients in the UCSF Asthma Clinical Center in collaboration with investigators at Genentech, including Joe Arron, who was previously funded as a postdoc while at UCSF in the DeRisi lab by SABRE Innovative Grants.


In studies performed in the Imaging Core, the authors devise a new technology for stabilized imaging of video-rate, two photon imaging of the intact, living mouse lung that was able to capture movement of live cells during induction of lung inflammation. Improvements are continuing to enable deeper tissue penetration to levels of small bronchioles that are involved sites in allergic inflammatory diseases like asthma.

Attracting new investigators to the field

We have merged the SABRE monthly conference with a weekly Pulmonary Research Conference, and alternated the conferences between the Parnassus and Mission Bay campuses. This has resulted in a popular conference – usually attended by 50-75 people at both sites – that has increased the outreach of lung basic science biology into the greater UCSF community. Approximately one-third of the conferences directly concern asthma, and the rest revolve around aspects of lung biology and inflammation of
relevance to asthma. We also contribute to targeted speakers in the Immunology seminars that bring investigations of relevance to asthma biology to the greater Immunology community at UCSF. We are beginning to seed individuals from this program, including Joe Arron at Genentech (trained with DeRisi and Fahy), P. Vijayanand and G. Seumois at the University of Southampton (trained with Ansel), and Max Siebold (trained with Burchard) at National Jewish in Colorado, who have dedicated themselves to asthma research.

As in prior years, we will organize this report by reviewing the SABRE Center activities and updating the core technologies that focus on asthma-related research. We continue to believe that these cores help facilitate interest in asthma research and create a stimulating scientific environment for integrating the SABRE Center with other UCSF investigators. Although forced to curtail support for the Innovative Grants Program due to financial considerations, we are looking for ways to resurrect support of this valuable Program after the period of startup support ends after the next year. We will also update the last funding of this Program to facilitate research in the Weissman laboratory investigating the biology of the ORMDL pathway and its potential link to asthma. Already, these investigators have identified the kinases that modify ORMDL activity and have provided evidence that ORMDL is a key sensor of sphingolipid homeostasis in mammalian cells that is involved in ER morphology and lipid biosynthetic pathways. We will summarize our interactions with other campus asthma-oriented research projects and provide listings of the seminar speakers of conferences to which we lend support. We will follow this with a listing of the newly funded, pending or submitted grants and publications since the prior annual reports that reflect support from the many SABRE Center activities. We will summarize the Financial Report for the Program. Finally, we will outline the strategies for the coming year and append the current biographical summaries of the members, awardees and participants in the SABRE Center at UCSF.

We wish to thank the Sandler family for their vision and support in creating and sustaining the SABRE Center. Support for high-risk, open-ended, basic science is difficult to procure in the current funding and fiscal climate. As noted in the overview above, we can identify many examples where support from the SABRE Center has been leveraged greatly to achieve substantial gains for the scientific and academic study of asthma at UCSF. We are most grateful for the Sandler’s continued support.
The goals of the SABRE Center are to drive innovation in basic asthma research. We approach this goal by establishing a core basic science group dedicated to the study of asthma, by enhancing their access to state-of-the-art technologies required to drive the research, by integrating their accomplishments across the greater UCSF campus, and by creating opportunities for interactions with translational and clinical investigators studying asthma patients. The Executive Committee, chaired by Dr. Locksley, was established to develop the strategy and directives to achieve these working objectives. The Executive Committee is specifically constituted to provide the Director with counsel regarding issues of scope, direction and execution. The Executive Committee played a major role in the recruiting faculty to the SABRE Center and provides oversight in sustaining progress towards the overall goals of the Center.

SABRE Center Executive Committee Members

Richard Locksley, M.D., Professor
Director, SABRE Center
 Departments of Medicine and Microbiology/Immunology

Dean Sheppard, M.D., Professor
Associate Director, SABRE Center
Department of Medicine

Homer Boushey, M.D., Professor
Department of Medicine

Hal Chapman, M.D., Professor
Department of Medicine

William Seaman, M.D., Professor
Department of Medicine

Art Weiss, M.D., Ph.D., Professor
Departments of Medicine and Microbiology/Immunology

Zena Werb, Ph.D., Professor
Department of Anatomy
SCIENTIFIC ADVISORY BOARD
Mitchell Kronenberg, Ph.D.
President and Scientific Director
LIAI - La Jolla Institute for Allergy & Immunology

Mitchell Kronenberg was appointed President of the La Jolla Institute for Allergy and Immunology in September 2003. He is responsible for the overall administration of physical resources, finances and space at the Institute; and works with the Institute’s board of directors, faculty, and executive management to develop and implement strategic plans for shaping the Institute’s future. In addition to his duties as LIAI’s chief executive officer, Dr. Kronenberg serves as Scientific Director of the Institute and Head of the Division of Developmental Immunology. He conducts an active research program on the development of the immune system and the pathogenesis of autoimmune disease, and is a world-renowned expert in the fields of mucosal and innate immunity.

Dr. Kronenberg graduated with a bachelor’s degree in biochemistry from Columbia University, and earned his Ph.D. from the California Institute of Technology (Caltech) in 1983. He stayed on at Caltech as a postdoctoral fellow, and joined the faculty of the UCLA School of Medicine in 1986, serving first as Assistant, and later as Associate and full Professor. In 1997, he moved to LIAI to head the Division of Developmental Immunology. He also is an Adjunct Professor of Biology at the University of California, San Diego.

Dr. Kronenberg is the co-author of more than 215 scientific publications and holds six research grants from the U.S. National Institutes of Health (NIH). He has served on a number of grant review panels for NIH and other private medical research agencies, and is on the editorial board of four scientific journals. He is the winner of the Richard Dwyer award for cancer research (UCLA) and has been the Kroc Professor of Medicine at the University of California, Davis, and the Wellcome Foundation visiting Professor at Harvard University.
Philippa (Pippa) Marrack, Ph.D.
Professor of Molecular Biology and Immunology
Vice Chair, Department of Immunology
National Jewish Medical and Research Center, Denver
Professor at the Health Sciences Center, University of Colorado
Research Investigator at the Howard Hughes Medical Institute, USA

As one of the world’s leading research scientists investigating T cells, the family of cells that help the body fight off disease, Dr. Marrack’s work has led to a greater understanding of their role in the immune system.

Born in the United Kingdom, Philippa Marrack earned her undergraduate and doctoral degrees in biological sciences from the University of Cambridge. She left the UK in 1971 to do postdoctoral work in the USA, where she has lived and worked ever since, initially at the University of California, and then at the University of Rochester. Since 1979, she has been based in Denver, Colorado, where she is now a research investigator at the Howard Hughes Medical Institute, Vice Chair of the Department of Immunology and Professor at National Jewish Medical and Research Center, and Professor at the University of Colorado’s Health Sciences Center.

During her career, Philippa Marrack has published more than 300 peer-reviewed journal articles and she has served on the editorial boards of numerous journals, including Cell, Science, and the Journal of Immunology. Amongst her many honors are the Royal Society’s Wellcome Foundation Prize (1990), the Paul Ehrlich and Ludwig Darmtsädter Prize (1993) and the Louisa Gross Horwitz Prize (1995). She has served on various panels and boards for the American Cancer Society, the U.S. National Institutes of Health, and the Burroughs Wellcome Fund. She was the President of the American Association of Immunologists in 2000-2001, and is currently the President of the International Union of Immunological Societies.
Christopher Wilson, M.D.
Director, Global Health Discovery Program, Gates Foundation

Dr. Chris Wilson, Director of the Global Health Discovery program, leads a team that targets fundamental scientific and technological advances in global health that could lead to new ways to prevent, treat, and diagnose disease.

Wilson joined the foundation in 2009 as Deputy Director, Vaccine Discovery and Human Biology, Global Health Discovery.

Wilson is a pediatrician and immunologist. He joined the faculty at the University of Washington in 1979 in the Infectious Diseases Division of the Department of Pediatrics and later served as head of the Division of Infectious Diseases, Immunology and Rheumatology. In 1989, he became one of the founding faculty members in the new Department of Immunology, and served as Chairman of the Department of Immunology and head of the graduate program in immunology from 1999-2009.

He has also served on a number of national advisory panels, including the Institute of Medicine Vaccine Safety Review Committee (2001-2004) and the National Advisory Council on Child Health and Human Development, NICHD, NIH, and he co-chaired the NIAID US Immunodeficiency Network Pilot Grant Review Committee. He is an elected fellow of the American Association for the Advancement of Science.

Wilson received a bachelor’s degree from the University of California, Irvine and a medical degree from UCLA. He trained in pediatrics at Boston Children’s Hospital /Harvard Medical School, served in the US Public Health Service, and then was a post-doctoral fellow in infectious diseases while performing immunology research at Stanford University.
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Howard Hughes Medical Institute
Virology & Microbial Pathogenesis

Dr. Locksley is the Director of the Sandler Asthma Basic Research Center (SABRE) and a Howard Hughes Medical Institute Investigator. He is a Professor in the Departments of Medicine and Microbiology & Immunology. He received his undergraduate degree in biochemistry from Harvard and his M.D. degree from the University of Rochester. After completing his residency at UCSF, he trained in infectious diseases at the University of Washington. Prior to his position as director of the SABRE Center, Dr. Locksley served 18 years as the Chief of the Division of Infectious Diseases at UCSF Medical Center. Dr. Locksley is a fellow of the American Academy of Arts and Sciences.

Dr. Locksley's laboratory focuses on mechanisms by which the immune system becomes organized in stereotyped ways to attack discrete types of challenges. This involves the differentiation of naïve helper T cells to distinct types of cells, termed subsets, that produce different kinds of cytokines, key effector molecules of the immune system. In turn, these different subsets of T cells work with different types of innate cells, including neutrophils, eosinophils, macrophages and others, to mediate the immune response. Properly executed, such responses mediate protection against infectious organisms or repair of damaged tissues, but, when dysregulated, these immune responses lead to disease, including asthma.

Dr. Locksley’s laboratory investigates disease in animal models using mice genetically engineered to report the expression of the cytokines implicated in the different types of immune responses. This approach reveals the shared expression of important cytokines by cells of both the innate and adaptive type. Using mice with various reporter and/or deletion cytokine alleles, the laboratory has been able to implicate key cell types involved in mediating the tissue response. Animal models of helminth and protozoa infection, fungal challenge and allergen challenge are used to investigate mechanisms underlying allergic immunity of the type associated with asthma. Using these models, the laboratory
Sandler Asthma Basic REsearch Center  SABRE Investigators

has discovered a role for chitin, a structural component of a number of allergens – including dust mites, cockroaches, shellfish and molds – as well as helminthes, in inducing infiltration of cells involved in allergy into tissues. The laboratory is actively pursuing the molecular mechanisms underlying chitin recognition as well as the contributions by individual cell types to the expression of cytokines implicated in allergic pathology.

**Representative Publications**


Dr. Christopher Allen is the first Sandler-Newmann Foundation UCSF Fellow in Asthma Research. The UCSF Fellows Program allows exceptionally promising young scientists to attain principal investigator status early in their careers in order to develop novel independent research programs with the sole mandate to do their best science. Dr. Allen first came to UCSF for the Biomedical Sciences Graduate Program in 2001 after completing his B.S. in Biology at MIT. He was funded by a UC Regents Scholarship and a Howard Hughes Medical Institute Predoctoral Fellowship. He was awarded his Ph.D. in 2007 for thesis research in Dr. Jason Cyster’s laboratory focused on the organization and cellular dynamics of germinal centers, which are structures in lymphoid organs that orchestrate the maturation of antibody responses.

Dr. Allen’s research in the SABRE center focuses on the cellular immune response in asthma. He is using his expertise in cutting-edge two-photon microscopy to visualize interactions among cells in the lungs as well as in lymphoid organs that ‘prime’ cells for immune responses in the respiratory tract. A particular emphasis of his research is on the development of IgE antibodies that contribute to allergic responses. IgE has been shown to be important in human asthma, yet little is known about the events leading to IgE production after inhaling allergen. The major goals of the research are to:

1) Develop innovative new mouse models of asthma that will be useful for studies of IgE antibody responses to inhaled allergens.
2) Define the early events leading to allergic sensitization and IgE antibody production after inhalation of allergen.
3) Characterize the interactions between immune effector cells that contribute to disease in the lung in chronic asthma models.

Publications


K. Mark Ansel, Ph.D.
Assistant Professor, Department of Microbiology & Immunology
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Immunology Graduate Program [http://www.ucsf.edu/immuno/faculty/ansel.html]

Dr. Mark Ansel is an Assistant Professor in the Department of Microbiology & Immunology. He completed a B.S. in biochemistry at Virginia Tech, a Ph.D. in Biomedical Sciences at UCSF, and postdoctoral training at the Immune Disease Institute at Harvard Medical School. His laboratory in the Sandler Asthma Basic Research Center focuses on the regulation of gene expression in the immune system.

MicroRNAs, transcription factors, and epigenetic regulation shape the gene expression programs that determine cell identity and function. The Ansel lab studies how these molecular mechanisms work together to control lymphocyte development, differentiation, and function in immunity. We use in vitro cell differentiation systems, mouse genetics, disease models, and gene expression analyses in cells from human clinical samples to unravel the regulatory networks that underlie immunity and immune pathology, especially allergy and asthma.

Lymphocyte lineage decisions are critical for the development of protective immunity against a great diversity of pathogens, but improper or exaggerated responses also contribute to the development and pathology of autoimmune diseases, chronic inflammation, allergy, and asthma. We use in vitro cell differentiation systems, mouse genetics, disease models, and gene expression analyses in cells from human clinical samples to unravel the regulatory networks that underlie immunity and immune pathology.

Our primary experimental system is the differentiation of the central coordinators of adaptive immune responses -- helper T cells. Their distinct cellular identities (Th1, Th2, Th17, etc.) and associated functions are defined by characteristic gene expression programs. We and many others have documented how these programs are controlled by transcription factors, the cis-regulatory DNA elements to which they bind, and epigenetic modifications that constrain chromatin accessibility at those sites.

More recently, we have become very interested in the roles played by microRNAs (miRNAs). Naive CD4+ T cells that cannot produce any miRNAs exhibit reduced cell division and survival in response to immune stimuli. Surprisingly, they also undergo rapid unrestrained differentiation into effector cells. One of the goals of our research is to determine which specific miRNAs regulate each of these T cell behaviors, and which
protein coding mRNAs the miRNAs target to exert their effects. In addition, we learned that T cells rapidly reset their miRNA repertoire upon activation. This rapid change in miRNA expression may be important to allow T cells to change their gene expression programs and develop effector functions.

**Lab Objectives**

1) To define the molecular mechanisms that control miRNA homeostasis, and determine how the miRNA repertoire is so dramatically remodeled during T cell activation.
2) To characterize the function of individual miRNAs that regulate T cell differentiation and immune effector functions.
3) To extend our work beyond in vitro and mouse models to explore how regulatory RNAs contribute to the pathogenic properties of T cells in human asthma.

**Selected Publications**

Dr. Limin Liu is an Assistant Professor in the Department of Microbiology & Immunology. He obtained his B.S. in Biology from University of Science and Technology of China and his Ph.D. in Molecular Biology from University of Missouri. He did postdoctoral research on the biology of nitric oxide (NO) at Duke University Medical Center.

Dr. Liu’s laboratory focuses on enzymatic deactivation of NO bioactivity and its role in asthma and other diseases. NO plays important roles in virtually every biological system. NO regulates functions of numerous proteins through S-nitrosylation, the covalent addition of NO to cysteine thiol. Through the study of S-nitroso-glutathione reductase (GSNOR), the key protein for de-nitrosylation in cells, Dr. Liu and colleagues have demonstrated that S-nitrosylation and its deactivation exert critical functions in systematic inflammation, asthma, cancer, and many other physiological and pathological processes.

**GSNOR and asthma**  It has been demonstrated with GSNOR-deficient (GSNOR<sup>−/−</sup>) mice that increased S-nitrosylation from GSNOR deficiency in a model of allergic asthma does not affect immune responses but abolishes airway hyperresponsiveness. Dr. Liu’s laboratory is investigating the mechanism of S-nitrosylation-dependent protection to understand a key question in asthma: How do allergic immune responses cause airway hyperresponsiveness?

**GSNOR and carcinogenesis**  NO is implicated in tumorigenesis by much circumstantial evidence, but little is known definitively about the mechanisms through which endogenous NO might regulate the behavior of pre-cancerous or cancerous cells. Using GSNOR<sup>−/−</sup> mice Dr. Liu’s laboratory has discovered that dysregulated S-nitrosylation from GSNOR deficiency inactivates a key DNA repair system and promotes liver cancer (Science Translational Medicine 2:19ra13, 2010). Investigation is underway to expend the findings and to further elucidate molecular mechanisms.

**New pathways in NO deactivation**  Dr. Liu and colleagues have demonstrated that GSNOR and flavohemoglobin, the major NO-consuming enzyme, operate together to regulate NO bioactivities and to protect against NO-related toxicity in the yeast.
Saccharomyces cerevisiae. They are employing the yeast model to elucidate the roles of additional, novel genes that are required for protection against NO-related toxicity. Homologue proteins are also investigated in animals.

Selected Publications


Dr. Jeoung-Sook Shin is an Assistant Professor in the Department of Microbiology & Immunology. She completed her B.S. and M.S. in Chemistry at Seoul National University, Korea. She received her Ph.D. from Duke University and her postdoctoral training at Yale University as a Jane Coffin Childs Memorial Fund Postdoctoral Fellow.

The Shin laboratory’s research is at the intersection of cell biology and immunology. Her laboratory is interested in understanding how ubiquitin-mediated regulation of membrane protein expression influences immunologic functions of dendritic cells. Additionally, her laboratory is interested in understanding the role of FcεRI (high affinity IgE receptor) expression on dendritic cells in asthma.

Dendritic cells are professional antigen presenting cells playing an important role in initiating antigen-specific immune responses by stimulating naive T cells. Being localized at various peripheral body sites, dendritic cells continuously endocytose extracellular antigens to monitor the challenge of any foreign agents. Upon contact with inflammatory foreign agents, dendritic cells undergo dramatic biochemical and functional changes termed maturation. Maturing dendritic cells cease endocytosis but increase T cell activating capacity by upregulating the surface expression of antigen-presenting molecules such as MHCII and costimulatory molecules such as CD86. Concurrently, maturing dendritic cells migrate to draining lymph nodes to present the peptide antigen/MHC complexes and activate antigen-specific naive T cells. Dr. Shin has found that the surface expression of MHCII is controlled by regulated ubiquitination. In immature dendritic cells, MHCII is covalently modified by a chain of small proteins called ubiquitins, which leads endocytosis and lysosomal sorting of MHCII. When dendritic cells mature however, MHCII is no longer ubiquitinated, thus not endocytosed but instead accumulated on the surface of the cells. Since Dr. Shin’s group has further found that the surface expression of CD86 is also modulated by ubiquitination and that the ubiquitination of MHCII and CD86 is mediated by the same ubiquitin ligase named MARCH-1. More recently, Dr. Shin’s group has found that MARCH-1-mediated ubiquitination of MHCII and CD86 plays an important role in the regulation of antigen presentation functions of dendritic cells by IL-10, an immune suppressive cytokine. Current research is focused on the understanding of the role of MARCH1-mediated ubiquitination in dendritic cell function in vivo.
Dr. Shin’s group runs another research program investigating the role of FcεRI expression on human dendritic cells in asthma. Many asthma patients have high levels of IgE antibodies against specific allergens to which patients are sensitive. Most of the IgE antibodies in the body are fixed on specific cells that express high-affinity IgE receptors called FcεRI. While its expression is limited to mast cells and basophils in rodents, FcεRI is also expressed on dendritic cells in humans. However, dendritic cell responses to FcεRI/IgE-bound antigen and its role in the pathogenesis of asthma have been poorly investigated. To unveil the role of FcεRI expressed in dendritic cells in asthma, Dr. Shin has taken two complementary approaches. One approach is to characterize IgE/FcεRI-mediated responses of human lung dendritic cells. In collaboration with Drs. Wolters, Fahy, and Woodruff at UCSF, Dr. Shin’s laboratory has localized FcεRI-expressing dendritic cells in human lung tissues by fluorescence microscopy and further verified FcεRI expression in the dendritic cells by flow cytometry. They also established a protocol to isolate lung dendritic cells from the human tissues. These cells will be specifically activated through FcεRI and examined for the phenotypic and functional changes by examining gene expression profile and the T cell activating ability. The other approach is to examine the in vivo functional role of FcεRI-expressing lung dendritic cells by using the human FcεRI-transgenic mice generated by Dr. Kinet at Harvard University. Dr. Shin’s group found that these mice, similarly to humans, express human FcεRI in CD11b+ lung dendritic cells. Further studies will elucidate the functional role of FcεRI expressed by CD11b+ lung dendritic cells in mouse asthma models.

Dr. Shin’s research programs are greatly benefited by many of the excellent core facilities supported by SABRE. Flow cytometry core has been used in a daily basis for most projects. Microscopy facility has been utilized to image dendritic cells in human lung tissues as well as to localize intracellular proteins in subcellular compartments within dendritic cells. Mouse physiology core has provided an initial important technical assistance to develop a mouse model to examine IgE-mediated immune responses in the lungs. These core facilities will continuously support many of her research projects.

**Selected Publications**


CORE FACILITIES
Mouse Physiology and Morphology Core  
*Director: Xiaozhu Huang, M.D.*

**Objective**

Asthma is a chronic inflammatory disease of the airways that is characterized by reversible airway obstruction and airway hyperresponsiveness. Phenotype characterization of animal models has helped us understand the mechanisms behind allergen-induced asthma. It is the objective of the mouse physiology and morphology core to facilitate the research of this devastating disease by providing a centralized laboratory for high-quality quantitative analysis of physiologic and morphologic studies in models of allergic asthma. In addition, the core provides training to students, technicians and post-doctoral fellows in techniques relevant to the animal models and their analysis.

**Accomplishments**

During the year of 2010, the Animal Physiology and Morphology Core provided assistance to many UCSF investigators, including Drs Kamran Atabai, Rosemary Akhurst, Jason Cyster, John Fahy, James Frank, Xiaozhu Huang, Lili Jan, Max Krummel, Limin Liu, Rich Locksley, Dean Sheppard, Thiennu Vu and Art Weiss, in their projects studying airway physiology, immunology, cell and molecular biology, lung development and other related areas. A few representative studies are described below:

Dr. James Frank has been interested in biological function of tight junction protein claudin 18 (CDLN18) in the lung. CLDN18 is specifically expressed in lung epithelia. This protein is required for maintenance of normal paracellular permeability. Mice deficient in claudin 18 are viable and do not have an obvious respiratory phenotype; however, they have measureable defects in the epithelial barrier. The leakier epithelial barrier may increase exposure to environmental antigens and stimulate a Th2 immune response. This inflammation may then lead to fibrosis. The lab hypothesizes that the asthma phenotype in CLDN18 mutant mice may be attenuated as a consequence of impaired epithelial barrier function. The core thus conducted the experiments using Aspergillus (Asp) model based on potential defect in immune response and fibrosis formation in ko mice. Wild type control and CLDN18 deficient mice were sensitized and challenged with Asp followed by airway hyperresponsiveness, lung inflammation and allergic IgE analysis. Surprisingly, CLDN18 knockout mice challenged with allergen developed significantly higher allergic IgE production and lung inflammation which is opposite as what was expected. Furthermore, we observed significant lung fibrotic lesions at the baseline level in CDLN18 ko mice that has not been noticed by the investigator previously. The group is now working on understanding the mechanisms that caused baseline lung fibrosis and enhanced lung inflammation after allergen challenge. The results from this study lead to a preparation of AAF grant application by Dr. Frank.

The core has been assisting Dr. John Fahy’s group in studying role of Periostin, a molecule that has been found to be strongly induced by IL-13 in lungs of asthma patient, in asthma.
development. The core conducted allergen sensitization and challenge studies in periostin ko and littermate control mice. Compared to wild-type controls, periostin deficient mice developed increased airway hyperresponsiveness and serum IgE levels following allergen challenge but lung inflammation response was not significantly altered. Further studies have suggested that these changes were associated with decreased expression of TGF-β and Foxp3 in the lungs of periostin deficient mice. The results from this study demonstrate a regulatory role for periostin on allergen-induced IgE production and hyperresponsiveness and lead to a manuscript submission and a KO8 grant preparation by Dr. Gordon, a pulmonary fellow in Dr. Fahy’s lab.

There is a significant increase of service demand from AAF awardees in the year of 2010. By performing either complete allergic animal model experiments or help with part of their experiments, the core assisted projects of Drs. Mark Anderson, Mathew Bogyo, Andrea Fleig, LiLy Jian, Jean P Kinet, Jeffrey C. Rathmell, Kenneth Rock, Jennifer Whistler and Rui Wang. For AAF funding related projects, the core often needs to put extra effort in helping experimental design and protocol testing since many of these laboratories have not worked with asthma or even lung disease models before. Dr. Jennifer Whistler at Galo center has been studying the role of Neuropeptide S receptor 1 (NPSR1) in the brain and wondered if NPSR1 also contributes to respiratory regulation by modulating airway response through direct effects on epithelium and smooth muscle cells. To explore the potential roles of NPSR1 in the lung, core staff worked closely with the group testing various protocols as well as different routes of NPSR1 ligand delivery so that an appropriate protocol could be finally chosen to produce clear answers.

**Protocol improvement for murine allergic model**

Applying appropriate allergic model is one of the keys to guarantee the success of murine asthma studies. The ovalbumin model used extensively by the core has broadened our understanding of the mechanisms behind allergen-induced asthma but patients with asthma are frequently exposed to environmental allergen such as house dust mite (HDM) but not OVA. More and more investigators are interested in using models that are closer to human exposures. However, the application of widely used HDM model has been limited to be used as the core routine protocol due to the high price of purchasing purified HDM. In communicating with Dr. Locksley’s group, we learned that a side product of HDM that normally is discarded by the company can cause eosinophilia lung inflammation. After a couple of rounds testing, we now show that this crude fecal product is able to induce airway hyperresponsiveness, lung inflammation, allergic IgE and mucous production with substantial reduction of the experimental cost. Further work will be conducted to improve the consistency and potency.

Also the core has developed a much shorter OVA protocol for investigators who are interested in mast cell dependent effects. Previously, it takes ~3 months to induce a mast cell dependent murine allergic model and it needs only five weeks now with this modified protocol. Drs. Atabai and Sheppard have been able to use this modified model to further study the mast cell related effects of MFGE8 and integrin β8 in asthma development. The modified protocol not only significantly shortens the period of obtaining experimental results but also reduce the experimental cost dramatically.


Training and Integration with Sandler Program

It has been one of the major tasks of the core to provide training for post-doctoral fellows, students and research associates whose labs have asthma related projects. In general, the core director will discuss and explain the regimens that core can provide to help with project design and planning. Each of the personnel who are involved in the project is offered the opportunity to learn how to perform the sensitization, challenge, lung function measurement, sample collection and data analysis. During past year, investigators from multiple laboratories (Labs from Andrea Fleig at University of Hawaii, Jennifer Whistler at Galo Center and Sven-Erik Dahlén at Karolinska) have spent days obtaining direct training from core lab members. Dr. Andrea Fleig at The Queen’s Medical Center and University of Hawaii is interested in the role of an ion channel, TRPM2, in asthma development. While sending transgenic mice to the core for induction and characterization of allergic asthma model, a post-doc from lab, Adriana Sumoza-Toledo, also traveled to San Francisco and participated the key parts of the experiment. Dr. Adriana Sumoza-Toledo not only observed the performance of the entire experiment in the core lab but also get hands on experience using the equipment and detail protocols. She has been able to apply the techniques and protocols to her studies after returning to her university.

Grants and Publications

Grants

The animal physiology and morphology core has been providing support letters for many grant applications each year and working with investigators funded by NIH, AAF and other grants. The core provides consultations in helping AAF and SABRE applicants for their grant application and has made commitments to collaborate with investigators if they are funded. The core staffs receive direct salary support from Sandler foundation, NIAID and recharge system.

Publications


Erin D. Gordon, Sukhvinder S. Sidhu, Prescott G. Woodruff, Shaopeng Yuan, Margaret Solon, Simon J. Conway, Xiaozhu Huang, John V. Fahy. Airway allergen challenge in periostin deficient mice reveals a protective role for periostin in allergen-induced eosinophilic inflammation and airway hyperresponsiveness. Submitted to Clinical and Experimental Allergy 2010
Functional Genomics Core

*Director:* David J. Erle, M.D.
*Associate Director:* Andrea Barczak

**Objective**

To make functional genomics technology readily available for investigators researching questions relevant to basic biology of asthma.

**Accomplishments**

*Supported projects:* We continue to support many investigators studying immunology, airway cell biology, lung development, and other relevant areas. These include faculty with primary affiliations with SABRE (Locksley and Ansel), many other faculty who participate actively in a range of SABRE activities (including Krummel, Sheppard, and Woodruff), and an AAF-funded investigator (Keoki Williams, at Henry Ford Hospital). Here is a partial listing of relevant projects that have been completed this year or are still in progress:

<table>
<thead>
<tr>
<th>PI</th>
<th>Project (status)</th>
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<tbody>
<tr>
<td>Mark Ansel</td>
<td>Identifying miR-29 targets by miRNA mimic and inhibitor transfection. <em>Completed.</em></td>
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<tr>
<td>Kamran Atabai</td>
<td>Gene expression during the remodeling phase of bleomycin-induced fibrosis. <em>Completed.</em></td>
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<tr>
<td>Pedro Avila¹</td>
<td>Nasal Mucosal Transcriptome. <em>Completed.</em></td>
</tr>
<tr>
<td>Pedro Avila¹</td>
<td>Transcriptomes in asthma exacerbation. <em>Completed.</em></td>
</tr>
<tr>
<td>Carolyn Calfee</td>
<td>Prognostic gene signatures in early sepsis, acute lung injury (ALI) and acute kidney injury (AKI). <em>In Progress</em></td>
</tr>
<tr>
<td>Harold Chapman</td>
<td>Integrin regulation of EMT in Type II Alveolar Epithelial Cells. <em>Completed.</em></td>
</tr>
<tr>
<td>Harold Chapman</td>
<td>Identification of Epithelial Progenitor Cells by Integrin Profile. <em>In Progress.</em></td>
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<tr>
<td>Anthony Gerber²</td>
<td>Effect of KLF15 deletion on pulmonary gene expression in ovalbumin asthma model. <em>Completed</em></td>
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<tr>
<td>Anthony Gerber²</td>
<td>Effect of KLF15 over-expression on pulmonary gene expression. <em>In Progress.</em></td>
</tr>
<tr>
<td>Nigel Killeen</td>
<td>Transcriptional analysis of memory T cell populations based on amount of prior OX40 expression. <em>Completed.</em></td>
</tr>
<tr>
<td>Investigator</td>
<td>Project Description</td>
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<tr>
<td>Matthew Krummel</td>
<td>Inhibition of T cell responses by tumor associated dendritic cells.</td>
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<tr>
<td>Matthew Krummel</td>
<td>Transcriptional Profile of Dendritic Cell Populations.</td>
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<tr>
<td>Jeroen Roose</td>
<td>Tonic signaling controls gene expression in T lymphocytes.</td>
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<tr>
<td>Richard Locksley</td>
<td>Determining gene expression of enigmaticytes/innate Th2 cells.</td>
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<tr>
<td>Dean Sheppard</td>
<td>Role of integrin alpha(v)beta8 in Th17 differentiation.</td>
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<tr>
<td>Keoki Williams*</td>
<td>Pharmacogenomics of Asthma.</td>
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<tr>
<td>Paul Wolters</td>
<td>Analysis of gene expression in type II cells isolated from normal and fibrotic lung.</td>
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<tr>
<td>Asa Wheelock</td>
<td>Effects of subway exposure on healthy and asthmatic populations.</td>
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<tr>
<td>Asa Wheelock*</td>
<td>COPD and Gender.</td>
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<tr>
<td>Prescott Woodruff</td>
<td>Targeting microRNAs for asthma treatment using next gen sequencing analysis.</td>
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<tr>
<td>Prescott Woodruff</td>
<td>miRNA profiling in asthma patients.</td>
</tr>
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</table>

1 Northwestern University, 2 National Jewish Health, 3 Henry Ford Health, 4 Karolinska Institutet, *AAF awardee

**Personnel**

Andrea Barczak (manager) and Rebecca Barbeau (SRA) continue to provide outstanding service to core users. In June 2010, our staff biostatistician, Christopher Eisley left his position at the core to enter graduate school. We were very fortunate to hire Joshua Pollack as his replacement. Mr. Pollack has a background in statistics and integrative biology and his previous work on the Neanderthal Genome Project with Dr. Svante Paabo at the Max-Planck Institute makes him well suited to take on a key role in analyzing next generation sequence data.

**New technologies**

SABRE support is critical for development and implementation of new methods. Priority is given to development of methods required for studies requested by SABRE investigators. We have focused on 2 areas this year: 1) small sample mRNA analysis and 2) next generation sequencing.
1) Small sample mRNA analysis: Our standard protocols can be used with a minimum of 50ng of total RNA. Alternate protocols that we have adapted from NuGen and Sigma are typically used for projects where the RNA is limiting (laser capture microdissection and cell sorting are two common examples). These whole transcript amplification methods work with as little as 1ng of RNA. Often times, RNA extraction can be problematic when working with very limiting amounts of material; common issues are inadequate purity, and loss of sample. We have implemented a new small sample amplification method (Nugen One-Direct technology) that eliminates the requirement for RNA isolation and the subsequent purification steps. This method prepares targets suitable for microarray analysis with as little as 10 cells. Over the past year, we successfully completed a project with Dean Sheppard using approximately 200 sorted cells for each sample (“Gene expression in MOG35-55 T cell receptor-specific CD4 T cells from mice lacking integrin β8 on dendritic cells”). This method is now offered as a service to all of our users, and offers the opportunity to perform array experiments using very pure cell populations. Hal Chapman’s group is planning to take advantage this new technology for transcriptional profiling of highly enriched, sorted alveolar epithelial stem cells with the goal of finding additional markers that can be used to isolate a more pure population of epithelial stem/progenitor cells.

2) Next generation sequencing: This past year we worked closely with Prescott Woodruff and Dean Sheppard to utilize next generation sequencing methods to assess global small RNA expression in airway epithelial cells from asthmatic and control subjects. The core generated 17 small RNA libraries and the data from these analyses are currently being compared with previous miRNA array data that were generated from the same sample set.

**Plans for the coming year**

We will continue to offer mRNA and miRNA profiling and ChIP-chip services. Investigators submit total RNA (or ChIP samples) and we perform the labeling, hybridization, quality control and data analysis. We will continue to work on approaches for improving sample throughput to allow us to maintain efficient turnaround times even during periods of peak demand. SABRE support allows us to provide a substantial discount to SABRE investigators and in recognition of this support SABRE projects receive higher priority than non-SABRE projects. We anticipate that there will be increasing interest in high throughput sequencing as the technology continues to advance. The latest generations of sequencing systems (e.g., the Illumina HiSeq 2000 and the latest ABI SOLiD systems) offer increased data output and multiplexing capabilities, thereby decreasing the overall cost per sample. We are planning to offer library preparation services and data analysis support to investigators, with a focus on ChIP-Seq, RNA-Seq, and small RNA discovery. We are currently assessing library preparation methods, workflow challenges, and equipment requirements. We expect that SABRE investigators will have an increasing need for next generation sequencing in coming years, and we intend to explore various approaches to making this technology more available. This might involve working in partnership with other groups at UCSF or acquiring additional equipment for our core. We would like to offer RNA extraction services in the coming year, and are currently surveying available automation options. We anticipate that this service would be quite desirable for clinical researchers who lack...
expertise in RNA isolation methods and/or may have limited access to required laboratory equipment. We will continue to process human samples from asthmatic and control subjects in conjunction with projects enrolling subjects in San Francisco, Chicago, Detroit, and Sweden.

**Training and Integration with SABRE and AAF programs**

We provide extensive consultation and training for investigators using the core. We meet with each group (PI and other group members, including students and postdoctoral fellows) to help with project planning. We help with grant preparation, sample size determination, appropriate selection of controls, and RNA extraction protocols. We invite interested investigators to come to our lab to learn how we process samples and hybridize and scan arrays. We meet with each group again after the initial data analysis to discuss the results and provide guidance about further analysis. When work is being readied for publication, we assist with preparation of figures and tables and submission of the results to a public database (NCBI’s Gene Expression Omnibus [GEO]). We are currently involved in collaboration with Asa Wheelock (Karolinska Institutet, Stockholm, Sweden). Her group is working on two large clinical studies with us; the first study investigates the importance of exosome-mediated transfer of specific miRNAs between different cell types in the lung in the observed altered inflammatory response to subway air in asthmatics as compared to healthy subjects, and the second study investigates miRNA and mRNA profiling with respect to gender-related mechanistic differences in the development of COPD (this is part of a larger, ongoing, systems biology study that includes global proteomics and lipidomics profiling of the same sample set). This past year, Dr Wheelock spent a portion of her sabbatical at the core, where she received training on microarray methods and analysis. More recently, her graduate student Bettina Levänen, spent 6 months at the core working side-by-side with core staff to train and perform a large number of miRNA and mRNA array hybridizations. Core staff is currently analyzing these large datasets. Dr Wheelock and Ms. Levänen will return to complete the studies with us in the summer of 2011. The core director attends the monthly UCSF SABRE Research Conference and the annual AAF meeting. This allows many opportunities for raising awareness about the core services among SABRE and AAF investigators. Although we continue to work with other investigators in order to maintain the high volume needed to operate in an economical manner, SABRE projects receive the highest priority.

**Grants and Publications**

**Grants**

We continue to work with many investigators funded by NIH and other grants. We provide support letters for many grants application each year. Most core expenses are offset by recharging grants from users. The core also receives some direct salary support from NIH grants. David Erle and 2 core staff (Andrea Barczak and Josh Pollack) are members of the Biostatistics Program of the UCSF Clinical and Translational Sciences Institute, and are supported in part by a large NIH grant that funds the CTSI (1TL1 RR024129). Unfortunately, the CTSI has elected not to continue to support any core laboratories effective July 2011. This will substantially
reduce our non-recharge funding. Hence continued support from SABRE will be critical in allowing us to develop new technologies for support of SABRE investigators.

**Publications**


*In review*


Wang BT, Ducker GS, Barczak AJ, Barbeau R, Erle DJ, Shokat KM. Transcriptional Profiling of ATP-Competitive mTOR Inhibitors Reveals mTORC1 and mTORC2 Specific Regulatory Networks. Submitted.
Vision

We are building a multidisciplinary research center that will take a comprehensive approach to asthma research. Our comprehensive approach will integrate gene-environment studies with basic biology, population genetics, social and environmental epidemiology. In addition, we are building upon a network of “minority serving” providers to recruit well-phenotyped subjects from throughout the U.S. Finally, we are recruiting leading Ph.D. and physician-scientists who will share in this vision and who are passionate about research in these populations. To accomplish this goal, we are leveraging resources from the Genetics Core with resources from the NIH, the UCSF Schools of Medicine and Pharmacy, the Department of Epidemiology & Biostatistics and the Institute for Human Genetics.

As part of this vision, we have established the Asthma Genetics Core Facility to facilitate asthma genetic research. We offer Sandler sponsored investigators a “full service of genetic testing and analyses.” Specifically, we analyze promising candidate genes identified by investigators using biologic material (DNA and plasma) from large well-phenotyped family-based and case-control asthma populations of racial and ethnically diverse subjects.

This past year the Genetics Core Facility has focused on three main goals: 1) collaboration 2) patient recruitment in new populations of well-phenotyped Latino and African American subjects with asthma and 3) faculty recruitment.

Accomplishments in 2010-2011

Collaboration

In the era of large "Team Science" the value and importance of collaboration cannot be overstated. We have made the existing cohorts widely available to Sandler sponsored investigators (UCSF Sandler Program and the AAF). The Asthma Genetics Core provides all study design, genotyping and expertise with statistical genetic analyses. These services allow investigators to easily test biologically plausible candidate genes and perform replication of novel genetic associations.

We have extracted GWAS data from our population of Latino trios for several Sandler investigators and provided our results as in silico replication to supplement their initial findings. In addition, we have worked closely with asthma investigators throughout the country to advance the field by collectively working towards testing and replicating novel genetic associations identified from basic science models (animal and human) to Genome Wide Association Studies (GWAS). This past year we participated in the NHLBI-sponsored EVE Asthma Consortium. The
main goal of this effort is to pool results from all U.S. genome-wide association studies for asthma. We currently have a paper under review at Nature Genetics.

We also led a multi-center collaboration in which we demonstrated that among African Americans, African ancestry is associated with lower measures of pulmonary function and that inclusion of genetic ancestry provides more accurate measures of lung function and asthma severity than use of self-reported race/ethnicity (New England Journal of Medicine 2010).8 We have demonstrated that among African Americans, African ancestry interacts with tobacco smoke to increase the rate of lung function decline. The later results may suggest that tobacco smoke poses a greater disease risk to African Americans than to Caucasians. We will now extend these results by using admixture mapping to identify causal genetic determinants of normal and abnormal lung function in Latino and African American populations.

Collaborating Faculty - In 2010-11 we have collaborated with the following faculty: Carl Ware (Sanford Burnham), Marsha Wills-Karp and Gurjit (Neeru) K. Khurana Hershey (Univ. of Cincinnati), Mary Sunday (Duke University), Joe “Skip” Garcia (University of Illinois, Chicago), Stephanie London (NIEHS), Keoki Williams (Henry Ford Hospital), Rajesh Kumar (Children’s Memorial, Chicago), David Schwartz (National Jewish), Eran Halperin (Tel Aviv University), Kathleen Barnes (Johns Hopkins), Jenny Ting (UNC), Sven Jordt (Yale), Jim Gauderman (USC), Mehrdad Arjomandi, John Balmes, Robert Nussbaum, Colleen Brown Neil Trevdi, John Fahy, Nadav Ahituv, Rosemary Akhurst, and Jonathan Weissman (UCSF).

Patient Recruitment

We have the largest pediatric asthma genetic study of Latino populations in the U.S. (nearly 5150 children with and without asthma), as well as one of the largest studies among African American children (n=1500). A longitudinal study of asthma treatment and control is ongoing in a subset of the study population (n~1000).

This large recruitment effort is in part supported by an RO1 from the NIEHS, a foundation grant from the FAMRI Foundation and by the Asthma Genetics Core. We have already recruited two patient populations of Latinos and African Americans and we are currently recruiting replicate populations of Latino and African American asthma cases and controls.

The replicate Latino cohort is called Genes-environment & Admixture in Latino Asthmatics (GALA II) and the African American cohort is called the Study of African Americans, Asthma, Genes & Environments (SAGE II). At each center, we are collecting detailed information regarding genetic, social and environmental risk factors for asthma. Compared to prior cohorts, the new cohorts will include environmental assessments and more thorough phenotyping including allergen skin prick testing. We are also collecting Geographic Information System (GIS) coded measures of air pollution and integrating these data with genetic data. The new cohorts will allow investigators the opportunity to replicate potentially promising genetic targets and to test for complex gene-environment interactions.
Faculty Recruitment

We have recruited two young scientists, who have significant research experience in minority populations and asthma genetics.

Dara Torgerson, Ph.D. started at UCSF on April 1st, 2010. She has training and expertise in population genetics, bioinformatics, and applied statistical genetics, and is presently collaborating on several genome-wide association and re-sequencing studies of asthma, including SHARP (SNP Health Association Resource, Asthma Resource Project), STAMPEED (SNP Typing for Association with Multiple Phenotypes from Existing Epidemiologic Data), and the EVE consortium. We are pleased that she has joined UCSF.

This past year she has been extremely productive, resulting in 4 first-author publications either submitted or in the final stages of preparation from her collaborative research. She led the analysis of the NIH-sponsored effort to pool results from all U.S. genome-wide association studies for asthma, and currently has a first-author paper under review at Nature Genetics. She was invited to speak at two international conferences last year, including the Genetics Society of Canada and the 1st Latin American Pharmacogenomics Congress, and gave a platform presentation at the American Society of Human Genetics Annual Meeting. Overall she is a welcomed addition to our research team. Dr. Torgerson is applying for an institutional K-award.

Ryan Hernandez, Ph.D. started at UCSF on April 1st, 2010. He has specific expertise in statistical genomics, computation biology, and population genetics. He has extensive experience in analyzing next generation sequencing data through his involvement in the 1000 Genomes Project. He is the new co-chair of population genetics in the 1000 Genomes Project and he is actively engaged in generating and discussing cutting edge methods for analyzing complex populations using next generation sequencing technologies.

Financial Support

We have been successful at leveraging Sandler funding with NIH support. The aforementioned efforts are supported by the equivalent of four NIH RO1 grants.

Active Grants


Grants under review

Puerto Rican Childhood Obesity and Asthma STudy (PR COAST).

Publications supported by the Strategic Program for Asthma Research and/or the Sandler Family Foundation.

2010-2011 Publications


Cell Sorting and Analysis Core

Director: Zhien-Wang

Objective

Flow cytometry is central to the ability to characterize, purify and separate cell types based on surface characteristics. The objective of the core is to provide technical support and access to highly sophisticated instruments for persons at UCSF performing asthma-related research. Contributions from SABRE Center have been partnered with the Diabetes Center, individual investigator resources and institutional resources to support the space and maintenance of the core largely through an integrated re-charge system. Students and postdocs participate in training in the core at an area where training can be centralized in order to facilitate maintenance and oversight.

Accomplishments

The Core is located in S1067 in proximity to Dr. Locksley’s laboratory and centrally within the Immunology Program corridor above the SABRE Center space in HSE201. Scheduling is online and suitably trained individuals can access instruments in the core 24 hours a day, 7 days a week.

The space offers an array of instrumentation that offers unique capabilities in data acquisition and enhances the depth of technical capacity:

Two Beckman-Coulter MoFlo XDP High-Speed sorter with 4-laser, 17-color, 15-parameter capability centered around 488 nm, 532 nm, 561 nm and 647 nm multi-line air-cooled lasers. Two side-by-side instruments has enabled operation by a single individual, thus optimizing use and minimizing cost.

Beckman-Coulter/Dako CyAn ADP Flow Cytometer with 3-laser, 9-color, 11-parameter capability centered around 488 nm OPSL (blue) laser, 635 nm (red) diode, and 405 nm (violet) lasers. Total use > 650 hrs.

Becton-Dickinson Biosciences LSR II Flow Cytometer with 4-laser, 10-color, 12-parameter capability centered around 488 nm OPSL, 637 nm (red), 403 nm (violet) and 535 nm (green) lasers. Total use > 1600 hrs.

Becton-Dickinson Biosciences LSR II Flow Cytometer with 4-laser, 10-color, 12-parameter capability centered around 488 nm OPSL, 637 nm (red), 403 nm (violet) and 535 nm (green) lasers is maintained by the core but stationed in HSE201 in the SABRE core space. Total use > 800 hrs.
Training and Integration with Sandler Program

Use of the core has stabilized over the past 2 years. Over the last 19 months, 43 laboratories at the UCSF Parnassus and Mission Bay campuses have used the facility 2 or more times. In turn, the numbers of users per laboratory has also stabilized at 2.3 users/lab, and reflects use by graduate students and postdocs. Eight of the labs are direct participants in the SABRE Center, and a number of the other users are affiliated investigators examining various aspects of inflammation and tissue injury of relevance to asthma. All of the core SABRE Center scientists participate in the Sorting Core.

Grants and Publications

Data acquired in the Cell Sorting and Analysis core has contributed to approximately 18% of the publications listed in the bibliography for the current annual report.
Microscopy Core

Managing Director: Sebastian Peck, B.S.
Faculty Director: Matthew Krummel, Ph.D.

Objective/Mandate

The objective of the SABRE Microscopy Core is to advance light-based imaging of the lung and associated tissues. Our core operates under the premise that a critical understanding of diseased tissues and organs will come with the study of the activities of component players (cell types, effector molecules) in their native environment. We also recognize that many existing imaging methods may require some additional development or elaboration before they can be successfully applied in studies of lung biology. We act both as a repository/resource of imaging technology and expertise and to develop novel technologies.

Strategic Goals

The efforts of this center are being directed toward improved imaging technologies for cells of the normal and allergic lung. In 2011, the core will be trying to advance three specific goals for intra-vital imaging. Note that in the 2010 period, we have succeeded in setting up imaging systems for human lung samples as well as enhancements of the live-imaging capabilities. Our continuing goals, based on these successes are:

1. To provide continuously evolving confocal and 2-photon instrumentation that provides access to normal and diseased mouse lungs in a fashion that coordinates ventilation with image acquisition. This will be achieved in 2010-11 with miniaturization of the lung-stabilization rigs.
2. To develop and elaborate methods for site-specific photoablation and photoactivation in tissues.
3. To improve detection capability at the air-water interfaces comprising the intact lung using adaptive optics (in collaboration with Janelia Farm/HHMI)
4. To extend usage of the human lung imaging method through expanded facility capacity and training/sample processing capabilities.
5. To provide ongoing technical and instrumentation support to the UCSF (and beyond) Asthma community in order to put existing and emerging imaging technologies to practical use in the study of asthma.

Organization

The SABRE microscopy core is contained within the Biological Imaging Development Center (BIDC). The larger BIDC is an interdisciplinary center configured to assemble, test, and apply emerging light microscopy techniques and technologies. The BIDC is designed to serve two roles: a conduit for new optical imaging technology & as a site for new technology development. As part of its role as a conduit for new optical imaging technology the BIDC also houses a ‘incubator’ program that helps investigators who are willing to share equipment to have the
instrument in a setting where sharing of the instrument is simplified. The SABRE center is currently one of the major supporters for this campus-wide imaging initiative and now holds major ‘stakes’ in confocal and 2-photon instruments in addition to driving key development initiatives. SABRE affiliated labs and investigators enjoy privileged access to both the SABRE microscopy core and the larger BIDC. This center is managed by a managing director (Sebastian Peck) under the supervision of a Faculty Director (Max Krummel) and an oversight committee representing many of the key stakeholders on campus.

Current Usage

Currently there are 140 registered users of the BIDC. These users represent 45 principal investigators or labs. These labs are drawn from 16 departments or organization units. In 2010, 43 new users were trained. All users received some degree of training on center instruments or image processing stations. Many users are trained on multiple instruments. Most of this training is done on an individual basis and reflects the differences in each users experience, aptitude and project needs.

Recent Accomplishments

Completion of Gen3, 8-color 2-photon microscope Optimized for Live-Lung Imaging.

The ‘Gen3’ 8-color 2-laser 2-photon microscope was completed in 2010 and incorporated features needed for live-imaging (e.g. timed ventilation) and a virtual mouse intensive care unit (ICU). We worked with members of the ‘Micromanager’ open source software initiative to complete this microscope and are now elaborating further design features including software with up to 12 color capability as well as photoablation.

Update of Gen2 2-photon microscope: We have expanded the capacity of this scope to a 5th detector and electro-optical shuttering which permits less-dispersive and depth-dependent illumination. A pulse compressor was reintegrated for deeper illumination and new software and a PMT-protection circuit were installed.

Imaging of Human Lung: We have obtained lungs from the California Lung Donor network and have validated an agarose filling method that maintains viability in human lung sections. This will permit live-imaging based assessments on lung function. We are currently elaborating this protocol and exploring adaptive optics, as described below.

Addressing Imaging Deep into Lungs via Facility Collaboration with HHMI/Janelia Farm:

Following on the success of the intravital lung imaging implementation of 2010 (described in our previous update, MS published this year), we have continued to push to image directly into ventilated lungs. In doing so, we determined that the lung represents a unique optical challenge for deep fluorescent imaging. This results from numerous air/water interfaces that refract light resulting in poor optical coherence. To begin to address the solution to this, we initiated a collaboration with a group working in adaptive optics at Janelia Farm/HHMI. This has defined the problem and SABRE support will allow us to generate a working solution in 2011_12.
Introduction of new equipment, (see below) and establishment of SOPs and training.
As part of an expanding network of instruments, the facility has established standard operating
protocols (SOPs) for 4 new instruments and has established mechanisms to train new labs in
intravital lung imaging.

New Personnel

In 2010, and concurrent with our expanded operations and augmented portfolio of supported
instruments, we were able to hire a second person to assist in day-to-day training. Jessica Wong
joined the facility in November. A recent electrical engineering BA from SUNY, Jessica
undertakes training on the established instruments. She has also been training in generating
sections for IF and live-sections for live-imaging of the lung. The SABRE-sponsored aim of this
is for Jessica to be able to carry process postdocs and graduate students with lung-based imaging
projects from conception to images. Jessica has already been contributing to our local base of
electronics expertise and has manufactured two protection circuits to protect fragile PMTs.

New Instruments that Entered the Imaging Center in 2010-11

**IVIS:** The facility installed and established and SOPs for an IVIS full-mouse imaging system in
2010. This system was granted as an NIH: S10 to 7 investigators at UCSF and they chose to
integrate the system into the BIDC. Jessica Wong now undertakes weekly maintenance of the
instrument as well as on-demand training for new users. This instrument is housed ‘behind the
barrier’ and is available to SABRE users and others at the PH campus.

**Real-time 3D microscope:** Sensing the need for a central microscope for long-term imaging of
epithelial cultures, the facility took on responsibility for a Zeiss Axiovert100 microscope this
year and has undertaken reconfiguration and optimization of its automation. Jessica Wong
established training protocols, and the scope is available to SABRE users and other users at PH.

**Spinning Disk-FRAP:** Another S10 provided funds for the purchase of a new spinning disk
microscope with photobleaching and photostimulation tools. This instrument was placed into HSW6
space (Wittman) and is currently finishing installation. We will provide SOP and the microscope
will become available through our common scheduler. Once installation is complete, it will
become available to SABRE users and others at the PH campus under our pilot-assist program.

**Alaris 3D Printer:** SABRE resources as well as matching funds from other investigators
permitted the facility to purchase an Objet 3D printer for the purpose of fabricating custom-parts.
Given our success with fitted imaging chambers, this instrument will play a large role in
prototyping and manufacturing custom-parts for lung and organ imaging. We chose a model for
which the parts are also sufficiently rigid to support use in optical constructions in some cases.
Space

In 2010, we renovated a desk space, added an electronics workbench and a solidworks workstation for new parts development. The BIDC continues to have 2 dedicated rooms for instruments but also continues to work with satellite labs, integrating their resources into a common scheduler and oversight.

Funding

Two S10s were obtained by participating labs that led to instruments being place in the center (see above). A third S10 to purchase an additional 2 photon for BSL2 experiments such as mycoplasma in the lung is under preparation with help from the facility. The facility continues to seek additional support for development efforts.

Recent publications

A number of recent and forthcoming publications, both methodological and research-orientated, have been produced with help of the facility during the past year. Some of these include:


Pramparo, T., Youn, Y.H., Yingling, J., Hirotsune, S. and Wynshaw-Boris, A. Novel embryonic neuronal migration and neurogenesis defects in Dcx mutant mice are exacerbated by Lis1


**Plans for the Coming Year**

**Completion of DMM Array for Gen3 for targeted tissues in situ (Peck)** - The goal of this implementation is to allow users to photoconvert or photoablate cells deep within lung and other tissue and subsequently read out the resultant behavior of these cells.

**Enhanced Development of Personnel Expertise to Disseminate Live-Lung Methods (Wong/Peck)** - Both Sebastian and Jessica are being trained to run lung section and whole live lung preparations on 2-photon microscopes so that they can assist postdoctoral fellows from SABRE labs in analyzing real-time dynamics in the context of a variety of asthma models.

**Completion of Adaptive Optics Study for Improved Optical Imaging through Airspaces of the Lung (Peck/Krummel)** - The collaboration with Na Ji’s lab at Janelia farm has been established through a collaborative visit to this facility in November of this year. In the coming months, Na will be modeling the data we produced on-site and setting up an adaptive-optics method that we hope will extend imaging depths by hundreds of microns and compensate for dispersion due to numerous air-water interfaces.

**Generation of a First Generation Stabilized ‘Stick Lens’ for Less-Invasive Intravital Lung Imaging (Peck)** - As the next step in our successful lung immobilization we are having optical holders made for gradient index (GRIN) lenses that also immobilize the tissue in order to provide a less-invasive method for live-imaging. This is part of a long-term goal to be able to image through a biopsy needle-sized aperture.
Onsite parts production via 3D Printing - SABRE contributed approximately 60% toward the purchase of an Alaris 3D printer to print rigs for individual imaging experiments. This capability supports our evolving External Parts Pipeline (highlighted last year that includes development of parts together with Sutter Instruments). We intend to train additional personnel from individual labs in order to make this resource more readily available for optimization of imaging and other biological assays.

**Training and Integration with Sandler Program**

As noted in previous updates, the center aims to provide ongoing technical and instrumentation support to the UCSF (and beyond) Asthma community. Specifically our goal is to put existing and emerging imaging technologies to practical use in the study of asthma. This year, we have specifically undertaken training of Peck and Wong in performing lung-based assays from start to finish so that they may be able to undertake experiments for/with new users that may not have experience with these assays. This is particularly important in some of the more complicated procedures in which technical expertise is critical to the success of the experiment.

To introduce imaging advances within the wider community, the core also sponsors a recurring pizza-talk at which groups from the Bay Area and beyond present novel imaging technology and advances. Details can be seen at [http://pathology.ucsf.edu/BIDC/seminars.html](http://pathology.ucsf.edu/BIDC/seminars.html)

**Current Equipment**

1. Gen1 2-photon: 4 color
2. Gen2 2-photon: 5 color
3. *Gen3 2-photon: 8 color (being elaborated with a DMD array for photoactivation/ablation)
4. *Spectral Confocal (C1Si)
5. Spinning-disk Confocal (Yokogawa 4-laser on a Zeiss 200M base)
6. Inverted widefield microscope set up for Fluorescence Interference Contrast Imaging.
7. Zeiss Axiovert100 timelapse system
8. IVIS live animal imager (animal colony)
9. Nikon spinning-disk with photoablation (Wittman)
10. Zeiss Cell Observer with Apotome (Nystul)
11. Alaris 3D printer

* Indicates SABRE is now a partial owner of this instrument.

**Additional Equipment hosted on-site**

In 2010, the facility hosted instruments from Celligo and 2-photon instruments from Olympus and Leica. Olympus is planning a demo of a whole-organ slide-scanner in 2011.
Analysis Computers and Software Platforms

As part of a cooperative agreement, MDS/Molecular Devices supplied upgraded keys for PC-based analysis stations for image processing. In addition we purchased two 64-bit workstations for processing large datasets. We have partnered with and will support the following commercial partners who supply working copies of their software as part of the sponsorship program:

- MDS/Molecular Devices 'Metamorph' (who are supplying the three offline computers/keys as well as online keys)
- Bitplane 'Imaris' (who have subsidized the purchase of software used in the facility).
- Solidworks who have supplied two, discounted software keys for our manufacturing purposes.
ASTHMA RELATED RESEARCH PROJECTS
Mechanisms of remodeling in chronic airway inflammation
Program Director: George H. Caughey, M.D.
NIH P01 HL024136

Objective

Program Project HL024136 is in its 31st year of supporting asthma-related research. The objective of its projects is to learn the mechanisms and consequences of influx of inflammatory cells and changes in epithelium, vasculature and matrix resulting in airway remodeling.

Accomplishments - Summary of progress over the past year

Project P-1 (Matthew Krummel, Ph.D.)
Imaging T cell Airway Responses during Inflammation

Efficiency of Phagocytosis and Presentation by lung DC. The Krummel lab used real time multiphoton live imaging and FACS approaches to explore mechanisms of antigen presentation in the lung in mouse models of asthma. To quantify differential uptake capacity normalized for cell number, we generated a phagocytic index, representing the capacity of cells to become microsphere-positive as a fraction of their population density. The phagocytic capacity of DCs relative to the total pool was consistently 3 fold higher, a number which likely under represents their ability since they are also present within the bulk $c$-$fms$-EGFP population. Notably, the phagocytic index of both CD11c-EYFP and $c$-$fms$-EGFP pools of monocytes remained unchanged upon allergen challenge, suggesting that the inherent capacity of these cell types was not sensitive to inflammation. Finally, to formally show that the same phagocytic cells were highly stimulatory APCs for T cells, we used flow cytometry to sort bead-positive phagocytes and used them as stimulators for OVA-reactive OTII TCR transgenic T cells. $c$-$fms$-EGFP- and bead-positive phagocytes were incapable of generating proliferation in T cells without added stimulatory peptides and even when pulsed in this way, only gave weak responses. In contrast, significant T cell responses were elicited using bead-positive (phagocytic) DCs from the lung, an effect which could be somewhat augmented by additional antigen. Although bead-positivity serves as a marker for the cells that ingested antigen, it does not appear to specifically demarcate subpopulations of monocytes in the lung since bead negative populations had similar stimulatory capacities. Thus, DCs that ingest model antigens are no better as APCs than those that do not, but both are dramatically better than the remaining phagocytic pool. Again, the rise in numbers of DCs with asthma suggests that this will lead to increasing diversion of antigen into the process of activating T cells. As a large part of the study seeks to determine how T cells actually function in tissue, we initiated studies for visualizing T cell behaviors. As we move forward, this method will be used in conjunction with marking of APC and delineation of Th subsets.
Project P-2 (George H. Caughey, M.D.)
Proteases in airway remodeling and host defense

**Human mast cell tryptase haplotype associations.** By genotyping additional genomes in diverse populations, we have identified the major and minor haplotype pairs of tryptases at the two functional soluble tryptase loci *TPSB2* and *TPSAB1*. We have shown that the classic soluble bI allele, which most closely resembles the ancestral form, is promiscuous in that it pairs with other major types of soluble tryptases, including itself (meaning that there are two copies on the same chromosome), although it most often pairs with bIII. However, bIII itself and its frame-shifted loss-of-function variant, bIII<sup>Fs</sup>, are monogamous in the sense that they pair only with bI. *A major insight from these studies is that deficiency alleles, like a and bIII<sup>Fs</sup>, although common, always pair with an active allele.* Thus, humans are protected from inheritance of fewer than two active genes, which we speculate is because tryptases serve immune functions important for survival. On the other hand, a minority of most populations inherit 4 active alleles. Possibly, inheritance of 4 active alleles is deleterious—causing asthma or over-exuberant inflammation, for example. If so, the apparent tendency for populations to converge on an optimum number (i.e., 3) of active tryptase alleles is an example of “stabilizing” (ambidirectional) natural selection. Note that the observed haplotype associations are a subset of those theoretically possible. This is further evidence that alleles at *TPSB2* and *TPSAB1* are in strong linkage disequilibrium. Overall, these data are essential for the effort to assess links between particular haplotypes—in addition to specific alleles—and asthma susceptibility.

Project P-4 (Donald McDonald, M.D., Ph.D.)
Angiogenesis and lymphangiogenesis in airway inflammation

**Proliferation of lung lymphatic vessels after *M. pulmonis* infection.** To determine whether lymphatics in the lung proliferate in sustained inflammation, as they do in the trachea and main bronchi, we extended our studies to intrapulmonary airways of mice infected with *M. pulmonis*. Strikingly, lung lymphatics, stained for VEGFR-3 immunoreactivity, increased more than 8-fold after infection for 2 weeks. Most new lymphatics were located near bronchial-associated lymphoid tissue (BALT), which contained B and T-cells and high endothelial venules identified by MECA-79. LYVE-1 staining was less useful for staining lymphatics because it was expressed by some pulmonary blood vessels. We are taking advantage of these novel findings to test the hypothesis that, despite the greater abundance of lymphatics in chronic airway inflammation, clearance of extravasated fluid is impaired because of defective lymphatic function. In other recent experiments we sought to determine whether lymphangiogenesis that accompanies *M. pulmonis* infection can be prevented or reversed by treatment with an anti-inflammatory agent. We found that lymphangiogenesis, which was robust after 14 days of infection, was almost completely prevented by dexamethasone administered throughout the infection. However, lymphatic growth was only partially reversed by dexamethasone when it was started 7 days after the onset of infection and continued for as long as 7 days or was started 14 days after infection and continued for as long as 28 days. In search of cytokines that participate in lymphatic growth in the airways and lungs after *M. pulmonis* infection, we found that interleukin 1b (IL-1b) was upregulated 300-fold in the airways of mice after infection. This finding led to recent experiments performed in collaboration with Professor Kristina Bry of Gothenburg University, Sweden, using CCSP-IL-1b transgenic mice, in which human IL-1b is over-expressed under doxycycline regulation of the Clara Cell secretory protein promoter in the airway epithelium. Using these transgenic mice, we found that robust
lymphangiogenesis occurred without *M. pulmonis* infection when IL-1b over-expression was activated by doxycycline. In wild-type mice, lymphatics were restricted to the region of airway mucosa between cartilage rings. By comparison, after IL-1b over-expression in the transgenic mice, lymphatics in the airway proliferated into the region of mucosa over cartilage rings.

Lymphangiogenesis was accompanied by the influx of inflammatory cells. When IL-1b was over-expressed for 28 days and then turned off for a further 28 days, most of the abundant new lymphatics persisted. This result is consistent with our finding of only partial reversal of lymphatic growth in the airways of *M. pulmonis* infected mice treated with dexamethasone. Therefore, unlike newly formed blood vessels, new lymphatics resist regression.

**Training and Integration with the Sandler Program**

The formation of the Sandler Center continues to provide a focus to bring together all of the groups studying fundamental questions relevant to asthma at UCSF. This focus includes a monthly research meeting of investigators with asthma-focused basic research. The Sandler-supported core also provided advice and training in sensitization and challenge protocols for creating mouse models of chronic allergic inflammation and for monitoring changes in airway resistance.

**Selected Publications** (Asthma-related, 2009-present)


Trivedi NN and Caughey GH. Mast cell peptidases: chameleons of innate immunity and host defense.
Objective

The major goal of this multi-project grant is to combine studies in genetically modified mice and in people with asthma to identify the molecular mechanisms underlying the initiation and persistence of allergic asthma.

Projects

This center is composed of 3 projects and 2 cores.

Project 1, directed by Dean Sheppard, is focusing on the mechanisms by which activation of TGF-beta by integrins expressed on epithelial cells or dendritic cells, can both positively and negatively regulate allergic inflammation and its consequences. The project is examining how the αvβ6 integrin, which is expressed on airway epithelial cells, regulates the persistence of airway hyperresponsiveness in a model of chronic asthma. This project is also testing the hypothesis that activation of TGF-beta on dendritic cells by another integrin, αvβ8, plays a major role in the negative regulation of adaptive immunity and allergic airway inflammation. Thus far, we developed a novel murine airway brush and used it to show that αvβ6 on airway epithelial cells regulates expression of proteases in intraepithelial mast cells and that the differentially expressed proteases regulate airway smooth muscle contraction though direct effects on airway epithelial cells and smooth muscle. We have also found that mice lacking αvβ8 on dendritic cells are protected from induction of airway hyperresponsiveness and that T cells from these mice are dramatically defective in expression of IL-17 in response to the immunizing antigen. We found that the released IL-17 itself directly effects airway smooth muscle contraction by inducing expression of RhoA and its downstream effector kinase, ROCK2.

Project 2, directed by Rich Locksley, is focused on the nature of the earliest steps in the initiation of allergic airway inflammation. Specifically, the project is examining how chitin, the major carbohydrate in many allergenic organisms, induces the alternative activation program in macrophages and dendritic cells and ultimately facilitates induction of Th2 immune responses and allergic airway inflammation. The project is utilizing a series of novel lines of reporter and deleter mice to examine how chitin leads to skewing of adaptive immune responses toward a Th2 phenotype and subsequently leads to induction of IL4 and IL13 expression in a variety of cells in the airway wall. By utilizing mice that specifically over-express the chitin-degrading enzyme, AMCase, in the airways, the project will also evaluate the relevance of this pathway in models of allergic asthma.

Project 3 is entirely based in studies of people. This project combines Esteban Burchard’s strengths in human genetics and John Fahy’s strengths in detailed evaluation of mechanisms of asthma in humans. The first aim of this project focuses on identifying and characterizing sequence variants in Chit1 and AMCase, the major enzymes responsible for processing chitin in people, and determining the individual and combinatorial association of variants with allergic sensitization, asthma, asthma severity and drug responsiveness. Thus far, the project has identified AMCase variants with increased enzymatic activity that protect against asthma in African Americans. The project has also identified an AMCase splice variant with no enzymatic activity that appears to be the major form expressed in the human lung, suggesting that the protective
effects of the enzyme with increased activity might be due to effects of AMCase outside the lung. The second aim has identified several modest effects of genes in the TGFbeta signaling pathway on prevalence and severity of asthma in patients from Mexico, Puerto Rico or in both populations. Replication studies are currently ongoing.

The three projects are supported by two cores. Core A, the Administrative Core (Dean Sheppard, Core Director), provides support for each of the individual projects and cores with grants management, preparation and submission of progress reports and compliance with regulatory guidelines, and will organize monthly meetings and an annual retreat with members of our external and internal advisory boards. Core B, the Physiology and Tissue Analysis Core (Xiaozhu Huang, Core Director), performs acute and chronic allergen sensitization and challenge, measures airway responsiveness to acetylcholine in anesthetized and ventilated mice and performs bronchoalveolar lavage, lung tissue harvesting and fixation and tissue embedding, sectioning and staining for all 3 projects. The core also performs real-time PCR for quantitative analysis of gene expression for all 3 projects and facilitates the use of common protocols for stereology-based quantitative assessments of airway morphology.

Training and Integration with Sandler Program

This Center grant provides training in the basic biology and genetics of asthma for approximately 16 post-doctoral fellows and 6 graduate students working in the labs of the project directors. The Asthma SCOR grant that preceded this program has already provided training for several scientists who now lead their own laboratories engaged in asthma-related research and we expect a similar outcome from this new Center. The leaders of each of the Projects and Cores are already actively involved in SABRE, including the SABRE director and Associate Director and the Directors of the SABRE human genetics core and mouse physiology and morphology core. Most of the preliminary data that served as the basis for this successful application was generated at least in part through support from SABRE. The studies using murine models of asthma that supplied preliminary data for projects 1 and 2 were performed in the SABRE mouse physiology and morphology core and the human genetic studies were performed together with the SABRE human genetics core. Drs. Fahy and Burchard, co-leaders of project 3, have each received SABRE Innovative grants that contributed to generation of the preliminary data supporting their project. The infrastructure developed through SABRE funding for the Mouse Physiology and Morphology Core was critical for the success of the proposal for a Mouse Physiology and Tissue Analysis Core for the new Center grant. This Center grant would not have been likely to succeed without this extensive support from SABRE, and thus represents a clear example of leveraging SABRE funds to further enhance research into the basic mechanisms underlying asthma.
CONTRIBUTIONS TO RELEVANT SCIENTIFIC ACTIVITIES
"Cognate Regulators of B Cell Immunity."

Dr. Michael McHeyzer-Williams, PhD
Professor, Department of Immunology and Microbial Science
The Scripps Research Institute

Monday, November 8, 2010
9AM, Parnassus, HSW-302

Hosted by Mark Ansel, Ph.D., SABRE Center

BROADCAST | Mission Bay, Genentech Hall, Room S271 • Also available on-line via Video-On-Demand at 169.230.2.27/presentations/live • Seminars archived at http://saa.ucsf.edu/irts/video/immuno_sem.htm
SPONSORS | Gladstone Institute of Virology & Immunology • Rosalind Russell Medical Research Center for Arthritis
• Sandler Asthma Basic Research Center, SABRE
INFORMATION | (415) 502-1961 or http://www.ucsf.edu/immuno
## Immunology Seminar Series 2010-2011 Schedule

**Mondays, 9am Room: N-217**

<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker</th>
<th>Host</th>
</tr>
</thead>
<tbody>
<tr>
<td>September 6</td>
<td><em>No Seminar</em></td>
<td>Matthias Wabl</td>
</tr>
<tr>
<td>September 13</td>
<td><em>No Seminar</em></td>
<td>Art Weiss</td>
</tr>
<tr>
<td>September 20</td>
<td>John Kappler</td>
<td>Matthias Wabl</td>
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<tr>
<td>September 27</td>
<td>Gary Koretzky</td>
<td>Art Weiss</td>
</tr>
<tr>
<td>October 4</td>
<td>Mitch Kronenberg</td>
<td>Rich Locksley</td>
</tr>
<tr>
<td>October 11</td>
<td>Jane Buckner</td>
<td>Michelle Hermiston</td>
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<tr>
<td>October 18</td>
<td>David Raulet</td>
<td>Lewis Lanier</td>
</tr>
<tr>
<td>October 25</td>
<td>Robert Raulet</td>
<td>Tony DeFranco</td>
</tr>
<tr>
<td>November 1</td>
<td>Kenneth Rock</td>
<td>Abul Abbas</td>
</tr>
<tr>
<td>November 8</td>
<td>Michael McHeyzer-William</td>
<td>Mark Ansel</td>
</tr>
<tr>
<td>November 15</td>
<td>Mark Miller</td>
<td>Max Krummel</td>
</tr>
<tr>
<td>November 29</td>
<td>Andy Chan</td>
<td>Art Weiss</td>
</tr>
<tr>
<td>December 6</td>
<td>Marc Jenkins</td>
<td>Mark Anderson</td>
</tr>
<tr>
<td>January 10</td>
<td>Chen Dong</td>
<td>Jason Cyster</td>
</tr>
<tr>
<td>January 17</td>
<td><em>No Seminar Series</em></td>
<td></td>
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<tr>
<td>January 24</td>
<td>Kevin Tracey</td>
<td>Doug Nixon</td>
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<tr>
<td>January 31</td>
<td>John Lowe</td>
<td>Steve Rosen</td>
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<tr>
<td>February 7</td>
<td>Sasha Rudensky</td>
<td>Bill Seaman</td>
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<tr>
<td>February 14</td>
<td>Shannon Turley</td>
<td>Mark Anderson</td>
</tr>
<tr>
<td>February 28</td>
<td>Ananda Goldrath</td>
<td>Mark Anderson</td>
</tr>
<tr>
<td>March 7</td>
<td>Mark Davis</td>
<td>Max Krummel</td>
</tr>
<tr>
<td>March 14</td>
<td>Dean Sheppard</td>
<td>--</td>
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<tr>
<td>March 21</td>
<td>Shane Crotty</td>
<td>Mark Anderson</td>
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<tr>
<td>March 28</td>
<td>Miriam Merad</td>
<td>Larry Fong</td>
</tr>
<tr>
<td>April 4</td>
<td>Jeffrey Ravetch</td>
<td>Michelle Hermiston</td>
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<tr>
<td>April 11</td>
<td>Sebastian Amigorena</td>
<td>Max Krummel</td>
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<tr>
<td>April 18</td>
<td>TBD</td>
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<tr>
<td>April 25</td>
<td>Mark Ansel</td>
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</tr>
<tr>
<td>May 2</td>
<td>Chyi-Song Hsieh</td>
<td>Mark Anderson</td>
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<tr>
<td>May 9</td>
<td>Rich Lewis</td>
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<tr>
<td>May 16</td>
<td><em>No Seminar Series</em></td>
<td></td>
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<tr>
<td>May 23</td>
<td>Dan Campbell</td>
<td>Max Krummel</td>
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<tr>
<td>Date</td>
<td>Talk 1</td>
<td>Talk 2</td>
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<tr>
<td>09/13/10</td>
<td>Ted Omachi (Blanc)</td>
<td>Leah Smith (Lo)</td>
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<tr>
<td>09/20/10</td>
<td>Rob Winn (Univ of Colorado)(Faculty Candidate)</td>
<td>Kamran Atabai (Faculty)</td>
</tr>
<tr>
<td>09/27/10</td>
<td>Tony Shum (Anderson)</td>
<td>Greg Seumois (Ansel)</td>
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<tr>
<td>10/04/10</td>
<td>David Corry (Visiting Professor)</td>
<td>Matthew Krummel (Faculty)</td>
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<tr>
<td>10/11/10</td>
<td>Thaddeus Allen (Bishop)</td>
<td>Chun Chen (Sheppard)</td>
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<tr>
<td>10/18/10</td>
<td>Suzaynn Schick (Faculty)</td>
<td>Anirban Datta (Mostov)</td>
</tr>
<tr>
<td>10/25/10</td>
<td>Luca Richeldi (Visiting Professor)</td>
<td>Host: Hal Collard</td>
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<tr>
<td>11/01/10</td>
<td>Pulmonary Retreat</td>
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<tr>
<td>11/08/10</td>
<td>Meshell Johnson (Faculty)</td>
<td>Laurence Cheng (Locksley)</td>
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<tr>
<td>11/15/10</td>
<td>Hubert Chen (Faculty)</td>
<td>Sanjeev Datar (Fineman)</td>
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<tr>
<td>11/22/10</td>
<td>NO CONFERENCE</td>
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<tr>
<td>11/29/10</td>
<td>Tamiko Katsumoto (Faculty)</td>
<td></td>
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<tr>
<td>12/06/10</td>
<td>Brad Schroeder (Erle)</td>
<td></td>
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<tr>
<td>12/13/10</td>
<td>Christy Trejo (McMahon)</td>
<td></td>
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<tr>
<td>12/20/10</td>
<td>NO CONFERENCE- Christmas</td>
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<tr>
<td>12/27/10</td>
<td>NO CONFERENCE-Christmas/New Year</td>
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<tr>
<td>01/03/11</td>
<td>Sandeep Sanga (Woodruff) Canceled</td>
<td>Luke Davis (Faculty)</td>
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<tr>
<td>01/10/11</td>
<td>Peter Haggie (Faculty)</td>
<td>Michael LaFemina (Frank)</td>
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<tr>
<td>01/17/11</td>
<td>NO CONFERENCE-MLK Holiday</td>
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<tr>
<td>01/24/11</td>
<td>Peter Baluk (McDonald)</td>
<td>Mark Looney (Faculty)</td>
</tr>
<tr>
<td>01/31/11</td>
<td>Mehrdad Arjomandi (Faculty)</td>
<td>Makoto Kudo (Sheppard)</td>
</tr>
<tr>
<td>02/07/11</td>
<td>Nirav Bhakta (Woodruff)</td>
<td>Erika Yoo (Dudley)</td>
</tr>
<tr>
<td>02/14/11</td>
<td>Skip Garcia (Visiting Professor)</td>
<td>Host: Dean Sheppard</td>
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<tr>
<td>02/21/11</td>
<td>NO CONFERENCE-President's Day</td>
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<tr>
<td>02/28/11</td>
<td>Bilge Reischauer (Metzger)</td>
<td>Dario Barbone (Broaddus)</td>
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<tr>
<td>03/07/11</td>
<td>Il-Jin Kim (Balmain)</td>
<td>Joyce Lee (King/Collard)</td>
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<tr>
<td>03/14/11</td>
<td>Adithya Cattamanchi (Faculty)</td>
<td>Sheena Kerr (Fahy)</td>
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<td>03/21/11</td>
<td>Judith Hellman (Faculty)</td>
<td>Seung-Ick Cha (Wolters)</td>
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<td>03/28/11</td>
<td>Laura Koth (Faculty)</td>
<td>Axelle Caudillier (Looney)</td>
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<td>04/04/11</td>
<td>George Su (Faculty)</td>
<td>Dara Torgerson (Burchard)</td>
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<tr>
<td>04/11/11</td>
<td>Josh Galanter (Burchard)</td>
<td>Andrew Melton (Sheppard)</td>
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<td>04/18/11</td>
<td>Christine Garcia (Visiting Professor)</td>
<td>Host: Paul Wolters</td>
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<tr>
<td>04/25/11</td>
<td>John Metcalfe (Hopewell)</td>
<td>Suil Kim (Faculty)</td>
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<tr>
<td>05/02/11</td>
<td>Erin Gordon (Fahy)</td>
<td>Kirsten Kangelaris (Matthay)</td>
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<td>05/09/11</td>
<td>Yvonne Huang (Boushey)</td>
<td>Mallar Bhattacharya (Sheppard)</td>
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<tr>
<td>05/16/11</td>
<td>NO CONFERENCE-ATS Meeting</td>
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<tr>
<td>05/23/11</td>
<td>Jae Woo Lee (Faculty)</td>
<td>Christine Griffin (Frank)</td>
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<td>05/30/11</td>
<td>NO CONFERENCE-Memorial Day</td>
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<tr>
<td>06/06/11</td>
<td>Eunice Kim (King/Collard)</td>
<td>Hassan Lemjabbar-Alaoui (Rosen)</td>
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<tr>
<td>06/13/11</td>
<td>Binh Diep (Matthay)</td>
<td>Midori Kato-Maeda (Faculty)</td>
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<tr>
<td>06/20/11</td>
<td>Payam Nahid (Faculty)</td>
<td>Jon Koff (Faculty)</td>
</tr>
<tr>
<td>06/27/11</td>
<td>End of year Party</td>
<td></td>
</tr>
</tbody>
</table>
PUBLICATIONS SUPPORTED BY THE Sandler Asthma Basic Research Center (2009-2011)
Christopher C.D. Allen, Ph.D.
Steiner DF, Thomas MF, Yang Z, Babiarz JE, Allen CD, Bleloch R, Ansel KM. miR-29 regulates T-box transcription factors and IFN-γ production in helper T cells. (Submitted)

K. Mark Ansel, Ph.D.


Steiner DF, Thomas MF, Yang Z, Babiarz JE, Allen CD, Bleloch R, Ansel KM. miR-29 regulates T-box transcription factors and IFN-γ production in helper T cells. (Submitted)


Homer Boushey, M.D.


Esteban G. Burchard, M.D., M.P.H.


George Caughey, M.D.


**Harold Chapman, M.D.**


**Anthony DeFranco, Ph.D.**


**David Erle, M.D.**


John Fahy, M.D.

Xiaozhu Huang, M.D.

Matthew Krummel, Ph.D.


Limin Liu, Ph.D.


Richard Locksley, M.D.


Kang S-J, RM Locksley. 2009. The inflammasome and alum-mediated adjuvanticity. Faculty of 1000 Biology Reports 1:15


press).

**William Seaman, M.D.**


**Dean Sheppard, M.D.**


Zhi-En Wang, M.D., M.S.

Arthur Weiss, M.D., Ph.D.

Jonathan Weissman, Ph.D.


**Zena Werb, M.D.**


Egeblad M, N Nakasone, Z Werb. 2010. Tumors as organs: complex tissues that interface with the entire organism. Develop Cell 18:884-901.
Prescott Woodruff
The SABRE Center has completed its third full year with a complete complement of core investigators. We have increasingly strengthened collaborations between the SABRE investigators and the Asthma Clinical Research Center through quarterly meetings, shared seminars and interactive lab meetings. We have achieved recognition as an NIAID Asthma and Allergic Diseases Cooperative Research Center. We submitted our first PPG comprised of investigators from SABRE and the Asthma Clinical Research Center, which just missed the funding payline and is being readied for re-submission. We participated in a joint submission from the Asthma Clinical Research Center to establish UCSF as a center in the nationwide NIH Severe Asthma Research Network. Two of our SABRE investigators have secured R01 funding from the NIH, and our third investigator was recognized with a Scientist Development Grant from the American Heart Foundation. Additional R01’s that missed the payline are in the process of re-submission. SABRE Center faculty contributed to successful NIH shared equipment grants that resulted in addition of a flow cytometer, a robotic quantitative PCR instrument to the facility and a new confocal microscope adapted for imaging of the lung in mouse models of allergic disease. New technologies in software data analysis and hardware imaging instruments were developed by SABRE Center investigators and made available to the scientific community campus-wide. Graduate students and postdocs have been recruited to the laboratories and the Center has been increasingly integrated into the greater UCSF research community. The monthly SABRE Center-Pulmonary conferences remain vibrant and widely attended. Graduates of our program are beginning to seed other institutions. We are confident that the coming year will continue with progress in procuring outside funding, contributing to asthma scientific advances and establishing the SABRE Center as a nationally recognized asthma research center.

Despite the difficult paylines at NIH, it is hard not to be encouraged by the momentum that has been established. An example of the potential for rapid progress engendered by such an intense, focused effort is the unprecedented advance of anti-IL-13 therapies to the clinic underpinned by studies at the SABRE Center. Earlier studies from the Locksley lab had identified a key role for IL-13 in mouse models of allergic lung disease. Innovative grants for $100,000 each to Drs. Erle, the director of the Functional Genomics Core, and Fahy, who would become the director of the Clinical Asthma Research Center, were used to define the effects and targets of IL-13 in mice and mouse epithelial cell lines and subsequently the targets in human cell lines and in bronchoalveolar lavage of asthma patients. Based on these findings, a postdoc trained in analysis of microarray data in the DeRisi lab, himself a participant in the Fahy innovative grant, moved to Genentech (now Roche). Due to intense interest in drug discovery and the need for patient samples, Genentech contributed to the establishment of the Asthma Clinical Research Center at UCSF and Dr. Fahy became the director. Working with colleagues at Genentech led by the former DeRisi postdoc, Joe Arron, Drs. Fahy and Prescott worked with Dr. Erle in the Genomics Center to define a biomarker ‘signature’ in bronchoalveolar lavage that could be used to identify a subset - ~40% - of adult asthma patients who had evidence for an IL-13-associated process as defined by the earlier basic studies. This signature was subsequently validated in a collaborative study between UCSF and Genentech/Roche, and is being used to assess efficacy of anti-IL-13 monoclonal antibody in human patients. The studies are now in
phase 2 studies of the first molecularly ‘subset-guided’ trial of asthma therapy in humans, and are being eagerly followed by the pharmaceutical industry. Thus, a basic science observation in 1998 was followed by innovative grants with an outlay of ~$175,000 between 2004-2006, followed by pilot studies in humans from 2006-2009, drug development and molecularly-informed drug trials in asthma by a major pharmaceutical company in 2011. This is a remarkably short pipeline, and suggests that focused interactions between foundations, tightly organized university centers and industry might overcome roadblocks to getting new therapies into the asthma repertoire.

Despite the achievements of this year, the challenges to make new breakthroughs that create novel therapies that will alter the course of asthma remain. These challenges we take seriously for the future in order to honor the extraordinary vision of the Sandler family in committing resources to asthma basic research at UCSF. We are most grateful for the opportunity to respond to the challenge and look forward to discoveries that will impact this increasingly prevalent disease of humans. Our last innovative grant, to Jonathan Weissman in 2009, resulted in discovery of the function of ORMDL, the gene most commonly associated with asthma risk in multiple genome-wide association studies (GWAS). Our hope is that we will look back in 10 years at the development of drugs attacking this pathway and perhaps changing the landscape of asthma.
BIOGRAPHICAL SKETCHES
BIOGRAPHICAL SKETCHES

Christopher Allen, Ph.D.
K. Mark Ansel, Ph.D.
Homer Boushey, M.D.
Esteban Burchard, M.D., M.P.H.
George Caughey, M.D.
Harold Chapman, M.D.
Anthony DeFranco, Ph.D.
David Erle, M.D.
John Fahy, M.D., M.Sc.
Xiaozhu Huang, M.D., M.S.
Matthew Krummel, Ph.D.
Limin Liu, Ph.D.
Richard Locksley, M.D.
Sebastian Peck, B.S.
William Seaman, M.D.
Dean Sheppard, M.D.
Jeoung-Sook Shin, Ph.D.
Zhi-En Wang, M.D., M.S.
Arthur Weiss, M.D., Ph.D.
Jonathan Weissman, PhD.
Zena Werb, PhD.
Prescott Woodruff, M.D., M.P.H.
## BIOGRAPHICAL SKETCH

**NAME**  
Christopher David Caballero Allen, Ph.D.

**POSITION TITLE**  
Sandler-Newmann Foundation UCSF Fellow in Asthma Research

### EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Massachusetts Institute of Technology</td>
<td>B.S.</td>
<td>2001</td>
<td>Biology</td>
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<tr>
<td>University of California, San Francisco</td>
<td>Ph.D.</td>
<td>2007</td>
<td>Biomedical Sciences</td>
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</table>

### Positions and Honors

- **1998-2000**  
  Summer Research Intern, Department of Molecular and Cellular Pharmacology, Isis Pharmaceuticals

- **2000**  
  Undergraduate Student Researcher, Center for Cancer Research, Massachusetts Institute of Technology

- **2001-2007**  
  Graduate Student Researcher, Biomedical Sciences Graduate Program and Immunology Graduate Program, University of California, San Francisco

- **2007**  
  Postdoctoral Scholar, Department of Microbiology and Immunology, University of California, San Francisco

- **2007–present**  
  Sandler-Newmann Foundation UCSF Fellow in Asthma Research, Sandler Asthma Basic Research Center and the Department of Microbiology and Immunology, University of California, San Francisco

- **1998**  
  San Diego Biotech Employee Development Coalition (BEDC) Scholarship

- **1999, 2000**  
  Academic Excellence Award, Office of Minority Education, Massachusetts Institute of Technology

- **2001**  
  Phi Beta Kappa

- **2001**  
  Whitehead Prize in Biomedical Research

- **2001–2002**  
  University of California Regents Fellowship

- **2002–2007**  
  Howard Hughes Medical Institute Predoctoral Fellow

### Selected peer-reviewed publications (in chronological order)


**Research Support**

Active

UCSF Fellows Program 11/01/2007–10/31/2012

Funding provided by the Sandler Family Supporting Foundation, Lorraine Newmann UCSF Fellows Fund, and UCSF Dean’s Office

Project Title: Cellular interactions *in vivo* leading to allergic sensitization, IgE production, and chronic asthma
BIOGRAPHICAL SKETCH

NAME
K. Mark Ansel, Ph.D.

eRA COMMONS USER NAME
anselm

POSITION TITLE
Assistant Professor of Microbiology and Immunology

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Virginia Tech, Blacksburg, VA</td>
<td>B.S.</td>
<td>1992-1996</td>
<td>Biochemistry</td>
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<tr>
<td>University of California, San Francisco</td>
<td>Ph.D.</td>
<td>1996-2001</td>
<td>Biomedical Sciences</td>
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<tr>
<td>Immune Disease Institute, Harvard Medical School</td>
<td></td>
<td>2001-2007</td>
<td>Immunology</td>
</tr>
</tbody>
</table>

Positions

2001- 2005 Postdoctoral Fellow, Immune Disease Institute (p.k.a. Center for Blood Research), Harvard Medical School, Boston, MA

2005- 2007 Instructor, Department of Pediatrics, Children’s Hospital and Immune Disease Institute (p.k.a. Center for Blood Research), Harvard Medical School, Boston, MA

2008 – Present Assistant Professor, Department of Microbiology and Immunology and Sandler Asthma Basic Research Center, University of California San Francisco

Awards and Honors

1992 National Merit Scholarship
1992 Marshall Hahn Scholarship
1992-1996 Virginia Tech President’s List for Notable Achievement and Dean’s List
1993 Gilbert and Lucille Seay Scholarship
1993 William Burns Downey Memorial Scholarship
1994 Golden Key National Honor Society Outstanding Sophomore Scholarship
1995 Virginia Center for Immunotoxicology Scholarship
1995 Cyrus McCormick Scholarship

Other Experience and Professional Memberships

1998 American Association for the Advancement of Science
2006 American Association of Immunologists
2007 International Cytokine Society
1995  Gamma Sigma Delta Agricultural and Forestry Honor Society Scholarship
1995  American Society for Microbiology Undergraduate Research Fellowship
1996  Phi Kappa Phi Medallion Award
1996  Virginia Tech Department of Biochemistry outstanding senior award
1996  Fiat Award for outstanding college graduates
1996  ARCS Foundation Fellowship
1996–1997  University of California San Francisco Regents Fellowship
1997–2001  Howard Hughes Medical Institute Predoctoral Fellowship
2001–2004  Damon Runyon Cancer Research Fund Postdoctoral Fellowship
2005–2007  Leukemia and Lymphoma Society Special Fellow
2006–2007  Burroughs Wellcome Career Award in Biomedical Sciences
2007  International Cytokine Society Outstanding Postdoctoral Fellow
2009–2011  Dana Foundation Human Immunology Scholar

**Selected Peer-reviewed Publications** (selected from 26 peer-reviewed publications)


**Research Support**

**Ongoing Research Support**

Dana Foundation Human Immunology Scholars Program  **Ansel (PI)**  2/1/09 – 1/31/12

Dana Foundation

MicroRNA regulation of helper T cell function in asthma

The major goals of this proposal are to optimize technology for miRNA profiling by qPCR and perform a pilot study of miRNA expression in a small set of clinical samples, to develop a lentiviral miRNA expression library for studies of miRNA function in T cells, and to develop systems for miRNA inhibitor testing in lung explant cultures.

Role: PI

Career Award in Biomedical Sciences 1006173 Ansel (PI)  9/1/06 – 8/31/12

Burroughs Wellcome Fund

Endogenous RNA interference and gene silencing in T cell differentiation

The major goals of this project are to elucidate mechanisms of cis-regulatory control of T cell differentiation and cytokine gene transcription, and the role of regulatory RNA in these processes.

Role: PI
Regulation of miRNA expression during helper T cell differentiation

The goal of these studies is to dissect the mechanisms that govern changes in miRNA expression during the activation of T lymphocytes, and to define how the global regulation of miRNA homeostasis affects T cell activation and immune function. Bridge funding was awarded, and the full R01 resubmission is under consideration (see pending support, below).

Role: PI

Completed Research Support

Integrative Research Award  Ansel, Woodruff, Erle (co-PIs)  7/1/08 – 6/30/09

Sandler Program in Basic Sciences

Targeting microRNAs for asthma treatment

This seed grant funds the combined efforts of three clinical and basic research laboratories to perform pilot studies of miRNA expression and function in asthmatic airway epithelial cells and T lymphocytes.

Role: Co-PI
BIOGRAPHICAL SKETCH

NAME
Homer A. Boushey, Jr., M.D.

POSITION TITLE
Professor of Medicine

eRA COMMONS USER NAME
Boushey

EDUCATION/TRAINING

<table>
<thead>
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<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tr>
<td>Stanford University, Palo Alto, CA</td>
<td>A.B.</td>
<td>1964</td>
<td>Biology</td>
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<tr>
<td>University of California, San Francisco, CA</td>
<td>M.D.</td>
<td>1968</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td>(residency)</td>
<td>1970</td>
<td>Internal</td>
</tr>
<tr>
<td>Beth Israel Hospital, Boston, MA</td>
<td>(residency)</td>
<td>1971</td>
<td>Internal</td>
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<tr>
<td>Oxford University, Oxford, England</td>
<td>(Fellowship)</td>
<td>1972</td>
<td>Pulmonary</td>
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</tbody>
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Positions and Honors

1974-1981  Assistant Professor of Medicine in Residence, University of California, San Francisco.

1981-1987  Associate Professor of Medicine in Residency, University of California, San Francisco.

1986- Present  Member, Senior Staff, Cardiovascular Research Institute, University of California, San Francisco

1987-1989  Professor of Medicine in Residence, University of California, San Francisco.

1989-Present  Professor of Medicine, University of California, San Francisco.

1989-1995  Vice Chairman for Clinical Affairs, Department of Medicine, University of California, San Francisco

1996-2009  Chief, Allergy/Immunology Division, Department of Medicine, University of California, San Francisco

Medical Licenses and Board Certification

California License Number A 023453
American Board of Internal Medicine, June 1972
Subspecialty Board of Pulmonary Medicine, October 1974

Medical Society Memberships

2003- May 2004  Past-President - American Thoracic Society
California Thoracic Society
American Federation for Clinical Research
American Physiological Society
California Academy of Medicine
Western Society for Clinical Investigation
Western Association of Physicians

Honors and Awards

1964               Phi Beta Kappa
1967               AOA
1964-1968          Regents' Scholar
1968               Gold-Headed Cane Recipient
1977               H. J. Kaiser Award for Excellence in Teaching
1988,  ’90, ’95,  Faculty-Student Teaching Award for "An Outstanding Lecture"
1999, 2000
1993               Clean Air Award (Education/Research), American Lung Association, San Francisco
1993               California Medal, American Lung Association-California
1996               UCSF Alumnus of the Year Award
1997-2000          Bay Area’s Best Physicians, San Francisco Focus Magazine
2000               Medical Student Teaching Award: “An Outstanding Clinical Correlation Lecturer”

Selected peer-reviewed publications (in chronological order)


18. Yawn PB, Enright PL, Lemanske Jr RF, Israel E, Pace W, Wollan P, **Boushey HA**. Spirometry can be done in family physicians’ offices and alters clinical decisions in management of asthma and COPD. *Chest*, 2007 June 5; [Epub ahead of print] DOI:10.1378/chest.06-2722


Research Support

Ongoing Research Support

U10 HL098107 (Boushey, HA) 09/30/09-06/30/16
NIH/NHLBI
UCSF AsthmaNet Clinical Center
The major goals are to serve as a clinical center participating in the conduct of NHLBI-supported multi-center clinical trials of asthma therapies in children and adults with asthma, and to conduct smaller, focused studies of mechanisms of action of asthma therapies, of novel treatments for severe asthma, and of concepts of asthma pathophysiology that could lead to the development of new asthma treatments. Role: Co-Investigator

HHS N272200900052C (Boushey, HA) 09/30/09-09/29/14
NIH/NIAID
Inner-City Asthma Consortium II / UCSF ICAC-II Basic Science Site -
The major goal is to serve as a Basic Science Site for the ICAC, enabling examination of relationships of the microbial environment of inner city households, the development of immune function in infancy, and the development of allergic disease, especially asthma, in
childhood. Role: Principal Investigator

P01 HL070831-06A1                                      (Lemanske, R)                 05/01/08-04/30/13
NIH
Rhinovirus Infection and Childhood Asthma
The major goals of this study are to apply the Virochip microarray to search for novel viruses in respiratory secretions obtained from children with severe clinical illnesses with the features of a respiratory infection but in whom standard PCR tests have not detected a virus, and further to expand the ViroChip to detect regions of the rhinovirus genome associated with virulence. Role: Co-Investigator

5 U10 HL074204-05                                      (Boushey, HA)                   09/15/03-07/31/11
NIH/NHLBI
Asthma Clinical Research Network Center at UCSF
To link the established clinical research group at the University of California, San Francisco with other clinical research groups in an interactive network conducting collaborative studies of novel therapeutic approaches for asthma and disseminating the findings on optimal management of asthmatic patients to practitioners and other health care professionals. Role: Principal Investigator

5 U10 HL074431-05                                      (Lazarus, SC)                   08/15/03-07/31/11
NIH/NHLBI
COPD Clinical Research Network at UCSF
HL-03-002 COPD Clinical Research Network
The purpose of the NIH-sponsored COPD Clinical Research Network is to evaluate new and existing approaches for the management of COPD and to disseminate the findings of this network to the medical community. Role: Co-Investigator

Prot 114878/Ref 014716                                 (Boushey, H.)                   08/01/2010-7/31/2011
GlaxoSmithKline
Effects of Fluticasone-Salmeterol on Airway Epithelium to Rhinovirus Infection
To Examine the effects of pretreatment with Fluticasone and Salmeterol individually and in combination on the previously demonstrated effects of adding IL-13 to airway epithelial cells cultured at all air-liquid interface: the induction of mucoid metaplasia and enhancement of susceptibility to infection of human rhinovirus 16. Role: Principal Investigator
**Completed Research Support**

**R01 HL080414-05**  
(Fahy, JV)  
07/01/05-05/31/10  
NIH  
Histoblood group antigens, viruses & asthma  
The major goals are to understand how expression of histo-blood groups antigens by airway epithelial cells and airway mucins influences susceptibility to asthma exacerbations. Role: Co-Investigator

**R01 HL080074-01**  
(Cabana, M)  
07/01/04-06/30/10  
NIH  
Trial of Infant Probiotic Exposure on Developing Asthma  
This trial will measure the effect of a 6-month daily exposure of Lactobacillus, as an infant formula supplement, on immune system and asthma development during the first 3 years of life. Role: Co-Investigator

**Doris Duke Foundation**  
(Ganem, DE)  
10/01/03-6/30/09  
Genomics-based Approaches to New Pathogen Discovery in Chronic Human Diseases  
To use a DNA microarray designed to detect any known virus to explore whether viruses are associated with liver and lung diseases that are currently of unknown etiology. Role: PI

**AI050496-01**  
(Boushey, HA)  
09/01/01-04/31/06  
NIH  
AI-00-012 Asthma and Allergic Diseases Research Centers -- Rhinoviruses, Epithelial Cells, and Airway Function  
The purpose of this Program Project Grant is to examine the hypothesis that the nature and intensity of the nasal and bronchial responses to Rhinovirus infection is determined by properties inherent to the infecting strain, and/or properties inherent to the epithelial cells infected. Role: PI
**BIOGRAPHICAL SKETCH**

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esteban González Burchard, M.D., M.P.H.</td>
<td>Associate Professor of Bioengineering &amp; Therapeutic Sciences and Medicine, Director, Center on Genes, Environments &amp; Health</td>
</tr>
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</table>

**eRA COMMONS USER NAME**

Eburchard

**EDUCATION/TRAINING**

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>San Francisco State University, San Francisco, CA</td>
<td>B.S.</td>
<td>1984-1990</td>
<td>Cellular and Molecular Biology</td>
</tr>
<tr>
<td>Stanford University School of Medicine, Stanford, CA</td>
<td>M.D.</td>
<td>1990-1995</td>
<td>Medicine</td>
</tr>
<tr>
<td>Harvard School of Public Health, Boston, MA</td>
<td>Certificate</td>
<td>1997</td>
<td>Program in Clinical Effectiveness</td>
</tr>
<tr>
<td>Brigham and Women's Hospital, Boston, MA</td>
<td>Resident</td>
<td>1995-1998</td>
<td>Internal Medicine</td>
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<tr>
<td>University of California, San Francisco, SF, CA</td>
<td>Fellow</td>
<td>1998-2001</td>
<td>Critical Care Medicine</td>
</tr>
<tr>
<td>Stanford University, Stanford, CA</td>
<td></td>
<td></td>
<td>Medicine</td>
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<tr>
<td>University of California, Berkeley</td>
<td>M.P.H.</td>
<td>2005-2006</td>
<td>Epidemiology</td>
</tr>
</tbody>
</table>

**Positions and Honors**

- **2001** - Director, UCSF DNA Bank and Asthma Genetics Core Facility
- **2001** - Assistant Professor of Medicine, Division of Pulmonary and Critical Care, UCSF
- **2008** - Associate Professor of Bioengineering & Therapeutic Sciences and Medicine, UCSF
- **2008** - Director, UCSF Center on Genes, Environments & Health
- **2009** - Director, UCSF Clinical Pharmacology Training Program
- **2010** - Vice Chair, Department of Bioengineering & Therapeutic Sciences, UCSF


2005–2010 RWJ Amos Medical Faculty Development Award

2009 Member - American Society of Clinical Investigation (ASCI)

2009 Guest Speaker, Tavis Smiley Show

2010 Guest Speaker, NPR’s Science Friday, hosted by Ira Flatow
Selected Peer-reviewed Publications (chronologic order & selected from 78 publications)


Research Support

Ongoing Research Support

R01 ES015794 (Esteban González Burchard, PI) Project period: 9/01/08-5/31/13
Source: NIH/NIEHS
Project title: Genes-environments & Admixture in Latino Asthmatics (GALA 2)
The major goal of this project is to identify genetic, social and environmental risk factors for asthma among various Latino groups recruited throughout the U.S.

1RC2 HL101651-01 (Co-PIs: Ober, Nicolae) Project period: 09/30/09-09/29/11
NIH/R01
Role on project: Subcontractor
The EVE Asthma Genetics Consortium: Building Upon GWAS
To replicate the most significant GWAS (meta-analysis) results in >15,000 asthma cases and controls of European American, African American, and U.S. Hispanic ethnicities, re-sequence 5-10 genes associated with asthma in European Americans but not in African Americans or Hispanics, to study additional asthma-associated phenotypes and examine interactions, and develop methods to facilitate gene discovery.

R01 HL088133 (Esteban González Burchard, PI) Project period: 3/01/08-2/28/13
Source: NIH/NHLBI
Project title: Whole Genome Analyses for Asthma in Latino Populations
The major goal of this project is to perform genome-wide association analyses to identify genetic factors associated with asthma and related phenotypes in Puerto Ricans and Mexicans.

(Neal Benowitz, Program PI) Project period: 07/01/07-06/30/12
Role on project: Project 7 PI
Source: Flight Attendants Medical Research Institute (FAMRI)
Program title: UCSF Center of Excellence on Secondhand Smoke
Project title: Tobacco Gene–Environment Interactions in African American and Latino Asthmatics
The goal is to identify gene-environment interactions between asthma and secondhand smoke.
R01 CA120120 (Elad Ziv, PI)  Project period: 08/07/07-05/31/12
Source: NIH/NCI
Role on project: Co-Investigator
Project title: Admixture Mapping for Breast Cancer in Latinas
The goal of this project is to use a whole genome admixture mapping approach to search for novel breast cancer susceptibility genes in Latina women.

U19 AI077439 (Dean Sheppard, Program PI)  Project period: 4/1/08-3/31/13
Source: NIH/NIAID
Role: Project 3 PI
Program title: Mechanisms of Initiation and Persistence of Allergic Asthma
Project 3 title: Chitinases and TGFb in Human Asthma
The goal is to analyze the effects of genetic variation on genes in the TGF beta and Chitinase pathways and their role in the initiation and persistence of asthma across racial and ethnically diverse populations.

Completed Research

U01 GM61390 (Kathleen Giacomini, PI)  Project period: 7/20/05-6/30/10
Role on project: Co-Investigator
Source: NIH/NIGMS
Program title: Pharmacogenetics of Membrane Transporters
Project title: Study of Pharmacogenetics in Ethically Diverse Groups
The goal is develop an ethnically diverse cohort of subjects to participate in pharmacogenetic studies.

R01 HL078885 (Esteban González Burchard, PI)  Project period: 8/15/05-7/31/10
Source: NIH/NHLBI
Project title: Case-control Association Studies and Genetic Confounding
The goal is to test and compare methods of detecting and correcting for population stratification.
BIOGRAPHICAL SKETCH

NAME
George H. Caughey, M.D.

POSITION TITLE
Professor of Medicine
eRA COMMONS USER NAME
gcaughey

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Arizona State University</td>
<td>BS</td>
<td>1975</td>
<td>Chemistry</td>
</tr>
<tr>
<td>Stanford University School of Medicine</td>
<td>MD</td>
<td>1979</td>
<td>Medicine</td>
</tr>
<tr>
<td>Pennsylvania Hospital/University of Penn</td>
<td></td>
<td>1982</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco</td>
<td></td>
<td>1986</td>
<td>Pulmonary Medicine</td>
</tr>
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</table>

Positions

1988-92  Assistant Professor, Dept. of Medicine, UCSF
1988-98  Associate Staff, Cardiovascular Research Institute, UCSF
1992-98  Associate Professor, Dept. of Medicine, UCSF
1992     Molecular Medicine Program Faculty, UCSF
1996     Member of UCSF Graduate Program in Biomedical Sciences
1998     Professor, Dept. of Medicine, UCSF
1999     Investigator, Cardiovascular Research Institute, UCSF
2002     Member, UCSF Cancer Center and Center for Neurobiology of Digestive Disease
2004     Editorial Board, *Current Respiratory Medicine Reviews*
2004     Chief of Pulmonary and Critical Care Medicine Section, San Francisco VA Medical Center
2008-09  Board of Directors, Veterans Health Research Institute

Honors and Awards

1974     American Chemical Society Outstanding Undergraduate Award, ASU
1975     Phi Beta Kappa and Merck Award in Chemistry, ASU
1986     NIH Clinical Investigator Award
1992     American Lung Association Career Investigator Award
1992     Elected to American Society for Clinical Investigation
2000     Elected to American Association of Physicians
2004     Recipient of Julius and Lillian Nadel Endowed Chair of Medicine
2010     Elected to Collegium Internationale Allergologicum
Selected publications (in chronological order)


47. **Caughey GH**. “Mast cell proteases as protective and inflammatory mediators”, in Mast Cell Biology: Contemporary and Emerging Topics, Gilfillan AM and Metcalfe DD, eds., Landes Bioscience, 2011.


**Research Support**

*Transcriptional Profiling of Airway Biopsies*

Principal Investigator: George H. Caughey  
Agency: Diamond Family Foundation  
Type: Bequest; 09/01/2000-present  
This fund supports research on cystic fibrosis-related airway gene expression.

*Evolving Microenvironments in Airway Inflammation*

Project 1: Roles of Peptidases in Chronic Airway Inflammation; and Administrative Core A  
Program Director/Project 1 Leader/Core A Leader: George H. Caughey  
Agency: NIH-NHLBI  
Type: Program Project P01 HL024136 05/11/2010-3/30/2015  
Role: Investigator  
The goals of Project 1 of the Program Project grant are to determine roles of secreted airway proteases and protease receptors in airway inflammation.

Completed Research Support

*Mechanisms of Remodeling in Chronic Airway Inflammation*

Project P2: Proteases in Airway Remodeling and Host Defense; and Core A: Project Administration  
Program Director/Project Leader/Core Leader: George H. Caughey  
Agency: NIH-NHLBI  
Type: Program Project P01 HL024136 07/1/2004-5/10/2010  
Dr. Caughey led Project P2, the goals of which were to determine roles of secreted airway proteases and protease receptors in airway inflammation. His role as Program Director and Core Leader was to supervise administration of the Program Project, which comprised four projects plus Mouse and Administrative Cores.
BIOGRAPHICAL SKETCH

NAME
Harold A. Chapman, M.D.

POSITION TITLE
Professor of Medicine

eRA COMMONS USER NAME
Halchapman

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
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<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Tulane University</td>
<td></td>
<td>1968</td>
<td>Premedical</td>
</tr>
<tr>
<td>University of Alabama School of Medicine</td>
<td>M.D.</td>
<td>1972</td>
<td>Medicine</td>
</tr>
</tbody>
</table>

Positions and Honors

Positions

1972-1975 Residency Training in Internal Medicine, University of Utah Affiliated Hospitals, Salt Lake City, UT
1975-1977 Associate Investigator, V.A. Medical Center, Salt Lake City, UT
1978-1979 Pulmonary Fellow, University of Utah Affiliated Hospitals, Salt Lake City, UT
1979-1985 Assistant Professor of Medicine, University of Utah, Department of Medicine, Salt Lake City, UT
1985 Associate Professor of Medicine, University of Utah, Department of Medicine, Salt Lake City UT
1985-1999 Associate Professor of Medicine, Harvard Medical School, Department of Medicine, Boston, MA
1992-1999 Physician, Brigham and Women's Hospital, Boston, MA
1992-1999 Associate Professor of Environmental Health, Harvard School of Public Health, Boston, MA
2000-2008 Chief, Division of Pulmonary and Critical Care Medicine, University of California, San Francisco
2000-2008 Professor of Medicine, University of California, San Francisco
2000 Senior Member, Cardiovascular Research Institute, University of California San Francisco

Honors

1985-1990 Career Investigator Award, American Lung Association
1987 American Society for Clinical Investigation
1998 American Association of Physicians
2001-2011  MERIT Award, NIH/NHLBI
Ad Hoc member of various NIH study sections
Editorial Board of Journal of Clinical Investigation and Associate Editor, American Journal of Respiratory, Cell, and Molecular Biology.

**Selected Peer-reviewed Publications** (Selected from ~140)

Research Support

Ongoing Research Support

5 R37 HL67204 (Chapman, HA) 6/1/2001 – 5/31/2011
NIH/NHLBI MERIT AWARD
Role of Elastolytic Cathepsins in Emphysema

The major goal of this project is to define the role of cysteine proteases in smoking-related emphysema. The project focuses on pathways of elastase expression in lung mesenchymal cells and on the genetics of emphysema in human subjects with early-onset emphysema and normal alpha-1-antitrypsin.

5 R01 HL44712 (Chapman, HA) 1/1/1991 – 12/31/2014
NIH/NHLBI
Regulation of Integrin Function

The major goals of this project are to understand the molecular basis and importance of integrin function in promoting TGFβ1 signaling and pulmonary fibrosis. The hypothesis that epithelial to mesenchymal transition is an important component of pulmonary fibrosis, and regulated by integrins, is the main idea tested in this grant.

5 R01 CA125564 (Chapman, HA) 7/1/2007 – 5/31/2012
NIH/NHLBI
Urokinase Receptor Integrin Interactions in Lung Cancer

The major goals of this project are to define the physical basis of urokinase receptor integrin interactions and the influence of these interactions on tumor cell signaling and lung tumor progression. Primary tumor cells from human tumors will be examined for their expression and dependence on urokinase receptors for adhesion and migration.

Completed Research Support

5 R01 HL48261 (Chapman, HA) 1/1/2003 – 12/31/2007
NIH/NHLBI
Cysteine Proteases in MHC Class II Antigen Presentation

The major goals of this project are to provide insights into the basic mechanisms central to MHC class II-dependent immunity and to determine whether there is a clear rationale for therapeutic regulation of cathepsin S, and possibly other cysteine proteases, in lung diseases promoted by MHC class II immune responses such as multiple sclerosis and transplant rejection.
Identification, Isolation and Reprogramming Alveolar Epithelial Progenitor Cells

The major goal of this project is to assemble a multi-centered application for larger NIH funding of a consortium focused on progenitor cells of the lung. The RO3 primarily funds travel of investigators among sites and does not overlap with other awards.
# BIOGRAPHICAL SKETCH

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITON TITLE</th>
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<tbody>
<tr>
<td>Anthony L. DeFranco, Ph.D.</td>
<td>Professor, Department of Microbiology &amp; Immunology</td>
</tr>
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</table>

<table>
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<tr>
<th>eRA COMMONS USER NAME</th>
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<td>DeFranco</td>
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## EDUCATION/TRAINING

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<tbody>
<tr>
<td>University of California, Berkeley, CA</td>
<td>Ph.D.</td>
<td>10/79</td>
<td>Biochemistry</td>
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<tr>
<td>National Institutes of Health, Bethesda, MD</td>
<td>Postdoctoral</td>
<td>11/79-8/83</td>
<td>Immunology</td>
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</table>

### Positions and Honors

- **1972-1975**: Undergraduate research, laboratory of Dr. Jack Strominger. HLA antigens.
- **1976-1979**: Graduate research, laboratory of Dr. Daniel E. Koshland, Jr. Bacterial chemotaxis.
- **1983-1988**: Assistant Professor, UCSF, Department of Microbiology & Immunology.
- **1983-1988**: Associate Professor, UCSF, Department of Microbiology & Immunology.
- **1989-1990**: Sabbatical with David Baltimore, Whitehead Institute, MIT, Cambridge, MA.
- **1994-present**: Professor, UCSF, Department of Microbiology & Immunology.
- **1997-1998**: Sabbatical with Suzanne Cory, Walter and Eliza Hall Institute, Melbourne, Australia.
- **1998-2004**: Scientific Advisory Board, Abgenix, Inc. Fremont, CA.
- **1999-2009**: Chairman, Department of Microbiology & Immunology, UCSF.
- **1974**: Dreyfuss Foundation Fellow.
- **1975**: Phi Beta Kappa, Harvard University.
- **1975-1978**: NSF Predoctoral Fellow.
- **1979-1982**: Helen Hay Whitney Postdoctoral Fellow; 2nd Rose Lieberman Lecturer, NIH.
- **10/93 1994**: NIAID Merit Award.
- **1997-1998**: NIH Fogarty Senior International Award.
Professional Service (selected list)


Selected peer-reviewed publications (in chronological order)

Original Research/Peer-reviewed journals (from total of 63)


Research projects ongoing or completed during the last the three years

Active

1. “Regulation of B lymphocyte proliferation by antigen”
   Principal Investigator: Anthony DeFranco
   Agency: National Institute for Allergy and Infectious Disease
   Type: R01 (AI20038-26). Period: 12/1/05-11/30/10 (12/10-11/30/11 no cost extension)
   The major goals of this project are: 1. Define the roles of ezrin and non-muscle myosins in lipid raft coalescence following BCR stimulation. 2. Define the role of B144, Rho-family GTPases, and non-muscle myosin motors in directing outgrowth of long membrane processes in BCR-stimulated B cells. 3. Determine the mechanism of assembly of the NF-kB signalosome at lipid rafts in mature B cells stimulated through the BCR. 4. Characterize the differences between immature B cells and mature B cells with regard to BCR-induced lipid raft coalescence and assembly of the Carma1/Bcl10 signaling complex.

2. “Cell Type-Specific Roles of TLR Signaling in Immune Responses”
   Principal Investigator: Anthony DeFranco
   Agency: NIAID
   Type: R01 (R01AI0720585-3). Period: 12/1/07-11/30/2012
The major goals of this project are: Aim 1: To define the role of TLR signaling in dendritic cells for initiating adaptive T cell immune responses. Aim 2: To define the role of TLR signaling in phagocytic cells for inducing inflammation and promoting microbial killing during bacterial infection. Aim 3: To define the role of TLR signaling in B lymphocytes for amplifying antibody responses.

3. “Innate Immune Regulation of Inflammation and Adaptive Immunity”
Program Director: Anthony L. DeFranco. Project #1 “Cellular Basis of TLR Signaling for Mucosal Immune Responses” (A.L. DeFranco, PI)
Agency: NIAID
Type: P01 (AI078869-02). Period: 7/1/08-6/30/13
The major goals of Project 1 are: Aim 1: To define the role of TLR signaling in dendritic cells for initiating adaptive T cell immune responses to antigen challenge via the airways. Aim 2: To define the role of TLR signaling in immature dendritic cells and in neutrophils and macrophages for innate and adaptive immune responses to fungal cell walls. Aim 3: To define the role of TLR signaling in immature dendritic cells and in neutrophils and macrophages for immune defense against systemic infection with the fungal pathogen Candida albicans.
Completed (last 3 years)

1. “Cytoskeleton and Signal Transduction in Host Defense”
Principal Investigator: Anthony DeFranco Agency: NIAID
Type: R01 (R01 AI35811-11). Period: 12/1/06-1/31/10
The goals of this project are to characterize the functional alterations of L-plastin-deficiency on neutrophil and T cell function (This grant was awarded to Dr. Eric Brown and I became the PI to finish the project when Dr. Brown took a position at Genentech, Inc.).
UL1 RR024131 (McCune) 09/30/06-06/30/11
Role on project: Co-investigator
NIH/NCRR
Clinical and Translational Science Institute
The overall mission of the CTSI will be to create an integrated academic home that transforms research and education in clinical investigation and translational science at UCSF and throughout the community. Dr. Erle is a member of the Bioinformatics unit of the CTSI, which supports clinical and translational research and training at UCSF. CTSI is no longer providing support to Dr. Erle or other core members for this activity after 6/30/2011.

Completed Research Support

R21 HG004665 (Erle) 04/01/08-03/31/10
NIH/NHGRI
Tools for high-throughput functional analysis of 3’ UTR cis-regulatory elements
The major goals of this project are: 1) To optimize the design and implementation of the 3’ UTR high-throughput reporter system. 2) To use the system to identify cis-regulatory elements within a representative group of 3’ UTRs from ENCODE regions of the genome.
BIOGRAPHICAL SKETCH

NAME
David J. Erle, M.D.

POSITION TITLE
Professor of Medicine

eRA COMMONS USER NAME
DJERLE

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
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<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Harvard College, Cambridge, MA</td>
<td>A.B.</td>
<td>1980</td>
<td>Biochemistry</td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td>M.D.</td>
<td>1984</td>
<td>Medicine</td>
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<tr>
<td>University of California, San Francisco, CA</td>
<td>Resident</td>
<td>1984-87</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td>Fellow</td>
<td>1987-90</td>
<td>Pulmonary Disease</td>
</tr>
</tbody>
</table>

Positions

1984-1987  Resident in Internal Medicine, University of California Hospitals, San Francisco
1987-1988  Clinical Pulmonary Fellow, University of California Hospitals, San Francisco
1988-1990  Research Fellow, Lung Biology Center and Cardiovascular Research Institute, UCSF
1990-1992  Adjunct Assistant Professor of Medicine, UCSF
1990-present  Attending Physician, San Francisco General Hospital
1992-1998  Assistant Professor of Medicine in Residence, UCSF
1996-present  Faculty, UCSF Immunology and Biomedical Sciences Graduate Programs
1997-2001  UCSF/SFGH General Clinical Research Center (GCRC) Advisory Committee
1998-2004  Associate Professor of Medicine, UCSF
1999-present  Investigator, Cardiovascular Research Institute, UCSF
2000-present  Director, Functional Genomics Core Facility, UCSF SABRE Center
2004-present  Professor of Medicine, UCSF
2006-present  Associate Director, UCSF Clinical and Translational Sciences Institute Bioinformatics Program

Honors

1977  Detur Prize
1984  Alpha Omega Alpha, elected
1990-1993  Edward Livingston Trudeau Award of the American Lung Association
2008-2012  Member, LCMI Study Section
Selected peer-reviewed publications

Fifteen most relevant to my role as director of the SABRE Center Functional Genomics Core (all include microarray studies):


Research Support

Ongoing Research Support

R01 HL099101 (Erle) 01/01/10-12/31/13
NIH/NHLBI
Specialized molecules with essential roles in mucus production
The major goals of this project are: 1) To analyze AGR2 and AGR3 substrate binding specificity. 2) To determine the in vivo roles of AGR2 and AGR3 in the mouse airway. 3) To analyze the functions of AGR2 and AGR3 in human airway epithelial cells.

R01 HL085089 (Erle) 07/21/06-06/30/11
NIH/NHLBI
Airway Epithelial Responses to Allergic Inflammation
The major goals of this project are: 1) To determine the role of the EGF receptor pathway in the airway epithelial cell response to IL-13. 2) To determine the role of the transcription factor FOXA2 in the airway epithelial cell response to IL-13. 3) To determine how the IL-13-inducible epithelial anion exchanger SLC26A4 (Pendrin) contributes to allergic airway disease. 4) To determine how the IL-13-inducible goblet cell-specific secreted protein anterior gradient 2 (AGR2) contributes to allergic airway disease.
UL1 RR024131 (McCune) 09/30/06-06/30/11
Role on project: Co-investigator
NIH/NCRR
Clinical and Translational Science Institute
The overall mission of the CTSI will be to create an integrated academic home that transforms research and education in clinical investigation and translational science at UCSF and throughout the community. Dr. Erle is a member of the Bioinformatics unit of the CTSI, which supports clinical and translational research and training at UCSF. CTSI is no longer providing support to Dr. Erle or other core members for this activity after 6/30/2011.

Completed Research Support

R21 HG004665 (Erle) 04/01/08-03/31/10
NIH/NHGRI
Tools for high-throughput functional analysis of 3’ UTR cis-regulatory elements
The major goals of this project are: 1) To optimize the design and implementation of the 3’ UTR high-throughput reporter system. 2) To use the system to identify cis-regulatory elements within a representative group of 3’ UTRs from ENCODE regions of the genome.
BIOGRAPHICAL SKETCH

NAME
John Vincent FAHY, M.D., M.Sc.

POSITION TITLE
Professor of Medicine in Residence

eRA COMMONS USER NAME
johnfahy

EDUCATION/TRAINING

INSTITUTION AND LOCATION | DEGREE | YEAR(s) | FIELD OF STUDY
---------------------------|--------|---------|------------------------
University College Dublin | MB BAO  | 1985    | Medicine
University College Dublin | Intern | 1985-1986 | Medicine and Surgery
Trinity College Dublin    | Resident| 1986-1989 | Internal Medicine
University College Dublin | Registrar| 1988-1999 | Respiratory Medicine
University of California, San Francisco| Fellow | 1989-1993 | Pulmonary/Critical Care Medicine
University College Dublin | M.D. (doctorate by thesis) | 1997 | Respiratory Medicine
Trinity College Dublin    | M.Sc.   | Year 2003 (sabbatical) | Molecular Medicine

Positions

Internship and Residencies
1985-1986 Medicine Intern, St Vincent’s Hospital, University College Dublin
1986-1988 Senior House Officer, St James’ Hospital, Trinity College Dublin
1988-1989 Medicine Registrar (pulmonary medicine), St Vincent’s Hospital, University College Dublin
1989-1993 Fellow, Pulmonary and Critical Care Medicine, UCSF

Academic Appointments
1993-1998 Assistant Adjunct Professor of Medicine, UCSF
1999-2005 Associate Professor of Medicine in Residence, UCSF
2005-Present Professor of Medicine in Residence, UCSF

Other Experience and Professional Memberships
1993-Present Member, Steering Committee, NHLBI’s Asthma Clinical Research Network
2005-2006 Member, Executive Planning Committee, NHLBI Strategic Plan
2006-Present Director, Airway Clinical Research Center, UCSF
2007-Present Chair, Data and Safety Monitoring Board for Division of Lung Diseases SCCOR Program
2004-Present Member, Program Committee, Asthma, Inflammation, and Immunology
Assembly, ATS
2009-2010 Chair (elected), Program Committee, Asthma, Inflammation, & Immunology Assembly, ATS
2009-Present Member, Trans NIH Asthma Outcomes Working Group
2010-Present Member, Scientific Committee, Transatlantic Airway Conference

Honors
1984 Kirwan Gold Medal and Prize in Ophthalmology, University College Dublin (UCD)
1985 Graduated fifth in class of 120 students, UCD Medical School (one of 10 to receive an honors degree)
1990 Travelling Studentship in Medicine, National University of Ireland
1994 Physician Scientist Award, American College of Chest Physicians
2006 Michael S. Stulbarg Endowed Chair in Pulmonary Medicine, UCSF

Selected Peer-reviewed Publications


Research Support

5 R01 HL080414-05 (Fahy, JV) 7/01/05-05/31/10
Histoblood group antigens, viruses & asthma exacerbation
The major goals of this project are to establish the role of histoblood group antigens in the pathophysiology of asthma exacerbations.
Role: PI
(The renewal application for this grant receives an impact priority score of 13 (1st percentile) and is highly likely to be funded from April 1, 2011).

1 U19 A1077439-02 (Sheppard, D) 4/01/08-3/31/13
NIH/NIAID
Mechanisms of Initiation & Persistence of Allergic Asthma; Project 3: Chitinases and TGFβ in human asthma.
The goal of this center grant is to examine the role of chitinases and TGFβ pathway genes in asthma. Project 3 specifically focuses on genetic and translational studies of chitinases & TGFβ in asthma.
Role: Co-Leader of Project 3 (with Esteban Burchard, M.D.)

R01 HL095372 (Woodruff, PG) 9/30/08-9/29/12
NIH/NHLBI
Molecular Phenotyping of Asthma
This grant supports our gene profiling work in airway tissue bank samples in asthma.
Role: Co-Investigator

1 R01 HL097591 (Woodruff, PG) 7/01/09-06/30/13
NIH/NHLBI
Role of Th2 and non-Th2 Inflammation in Airway Smooth Muscle Remodeling in Asthma.
This grant supports studies of airway smooth muscle in asthma.
Role: Co-investigator

RC2 (Meyers, D) 9/30/09-9/29/11
NIH/NHLBI (ARRA GO proposal)
Linking Genetics, Genomics and Phenomics to Better Understand Asthma Severity
The major goal is to establish genetic, genomic and phenomic profiles through integrated analyses of GWAS and gene expression data in large cohorts of subjects with a range of asthma severity.
Role: Sub contract Co-investigator.

Pending

1P50HL107191-01 (Fahy, JV)
*Preventing fucose-dependent binding of aspergillus and pseudomonas to lung mucin*
This grant was submitted in response to the RFA for “Centers for Advanced Diagnostics and Experimental Therapeutics (cadet-1)”.
Role: PI

1P01HL107202-01 (Fahy, JV)
*Innate and Adaptive Immune Responses in Th2-high Asthma*
This PPG will comprehensively investigate the molecular underpinning of the Th2-high molecular subtype of asthma
Role: Overall PPG PI (Project leader for project 3 and Core leader for Administrative Core and the Human Subjects Core.

Completed NIH Sponsored Research Support

P50 HL56385 (Sheppard, D) 9/1/01-8/31/06
NIH/NHLBI
SCOR Grant: Interactions of Lymphocytes, Cytokines and Airway Cells; Project 4: “T Cells, Epithelial Cells and Remodeling in Human Asthma”.
Role: Project 4 Leader.

P50 HL56385 (Sheppard, D) 9/1/01-8/31/06
NIH/NHLBI
Stereology Core for SCOR Grant “Interactions of Lymphocytes, Cytokines and Airway Cells”.
Role: Core Director

R01 HL66564 (Fahy, JV) 8/1/01-7/31/05
NIH/NHLBI
T Cell Inflammation and Mucin Hypersecretion in COPD
Role: PI

R01 HL61662 (Fahy, JV) 12/1/98-11/30/02
NIH/NHLBI
Studies of goblet cell dysfunction in human asthma
Role: PI
### BIOGRAPHICAL SKETCH

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xiaozhu Huang, M.D.</td>
<td>Associate Professor</td>
</tr>
</tbody>
</table>

#### EDUCATION

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tongji Medical University, Wuhan, People's Republic of China</td>
<td>M.D.</td>
<td>1983</td>
<td>Medicine</td>
</tr>
<tr>
<td>Tongji Medical University, Wuhan, People's Republic of China</td>
<td>M.S.</td>
<td>1988</td>
<td>Pathology</td>
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#### Positions and Honors

<table>
<thead>
<tr>
<th>Period</th>
<th>Position and Details</th>
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<tbody>
<tr>
<td>6/83 to 7/84</td>
<td>Teaching Assistant, Dept. of Pathology, Tongji Medical University, China</td>
</tr>
<tr>
<td>8/84 to 8/85</td>
<td>Pathology Residence, The First Attached Hospital, Tongji Medical University, China</td>
</tr>
<tr>
<td>9/88 to 1/92</td>
<td>Research Assistant, Dept. of Pathology, Tongji Medical University, China</td>
</tr>
<tr>
<td>1/92 to 12/95</td>
<td>Postdoctoral Fellow, Dept. of Medicine, Lung Biology Center University of California, San Francisco</td>
</tr>
<tr>
<td>1/96 to 6/97</td>
<td>Postgraduate Researcher, Dept. of Medicine, Lung Biology Center University of California, San Francisco</td>
</tr>
<tr>
<td>7/97 to 11/99</td>
<td>Assistant Research Molecular Biologist, Dept. of Medicine, Lung Biology Center University of California, San Francisco</td>
</tr>
<tr>
<td>12/99 – 06/2005</td>
<td>Assistant Professor, Dept. of Medicine, Lung Biology Center University of California, San Francisco</td>
</tr>
<tr>
<td>07/2005-present</td>
<td>Associate Professor, Dept. of Medicine, Lung Biology Center University of California, San Francisco</td>
</tr>
</tbody>
</table>

1989 | "Outstanding Teacher" Honor, Department of Pathology, Tongji Medical University |

1/1992-12/1993 | Cheng Research Scholar Award, |

#### Selected peer-reviewed publications

**Journal Articles**


Kuperman DA, **Huang XZ**, Koth LL, Chang GH, Dolganov GM, Zhu Z, Elias JA, Sheppard D, Erle DJ.


Chen C, **Huang X**, Sheppard D. ADAM33 is not essential for growth and development and does not modulate allergic asthma in mice. *Mol Cell Biol.* 2006, 26:6950-6.


*Equal contribution
# BIOGRAPHICAL SKETCH

<table>
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<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
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<tbody>
<tr>
<td>Matthew Frederick Krummel, Ph.D</td>
<td>Associate Professor</td>
</tr>
<tr>
<td>eRA COMMONS USER NAME</td>
<td>Krummel</td>
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## EDUCATION/TRAINING

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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>University of Illinois at Champaign-Urbana</td>
<td>B.S.+B.S.</td>
<td>1985-1989</td>
<td>Biology and Chemistry</td>
</tr>
<tr>
<td>University of California at Berkeley</td>
<td>Ph.D.</td>
<td>1989-1995</td>
<td>Immunology</td>
</tr>
<tr>
<td>Walter and Eliza Hall Institute, Melbourne Australia</td>
<td></td>
<td>1996-1997</td>
<td>Immunology</td>
</tr>
<tr>
<td>Stanford University</td>
<td></td>
<td>1997-2001</td>
<td>Immunology</td>
</tr>
</tbody>
</table>

## Positions

- **Summer 1987**: Summer Undergraduate Research Fellow, UTHSCD
- **Summer 1988**: Stagiare (Technician) Institut Pasteur, Paris, Unite de Genie Micro-Biologique.
- **1989-1996**: Graduate Student and Postdoctoral Fellow, University of California at Berkeley, Department of Molecular and Cell Biology
- **1996-1997**: Postdoctoral Fellow, Walter and Eliza Hall Institute, Melbourne Australia
- **1997-2001**: Postdoctoral Fellow, Beckman Institute, Stanford University, Stanford, CA
- **2001-2006**: Assistant Professor, Department of Pathology, UCSF
- **July 2006-Present**: Associate Professor, Department of Pathology, UCSF
- **2006-Present**: Faculty Director, Biological Imaging Development Center, UCSF

## Honors

- **2009-2012**: Fellow of the American Asthma Foundation
- **2005-2010**: Leukemia and Lymphoma Foundation, Career Award
- **1997-2000**: NRSA Postdoctoral Fellowship, National Institutes of Health
- **1996-1997**: Postdoctoral Fellowship, Juvenile Diabetes Foundation International


Research support

On going

R01 AI52116 (PI: Krummel) 1/15/08-12/31/12 NIH
Myosin Motors in T cell Synapse Formation and Activation
The major goals of this project are to analyze MyoIIA regulation during T cell motility and synapse formation. This includes mutational analyses as well as generation and analyses of knockout animals.
Role: PI

R01 CA134622 (PI: Krummel) 7/17/09-6/30/11 NIH
Regulation of T cell Functions by the Breast Cancer Microenvironment
The major goals of this project are
Aim 1: Define the Nature of the CD8+ T cell response in the microenvironment of a Spontaneous Breast Tumor.
Aim 2: Define the Nature of Tumor Sampling APCs (TSAPCs), the phenotype and capacity of these cells to activate T cells, and the changes in this population with addition of functional CD8+ T cells.
Aim 3: Define the effects of CD4+ T cell subsets, particularly regulatory cells, on CD8 activity in vivo and upon the quantity and phenotype of TSAPCs.
Role: PI

1U01CA141451 (PI: Krummel) 9/1/09-8/31/14 NIH
Collaborative Innate-Adaptive Immune Regulation of Tumor Progression
The major goals of this project are
Goal 1: Visualize the progression in crosstalk between the innate and adaptive immune response during tumor development using mouse models of luminal and basal breast cancer.
Goal 2: Define the specific attractants that regulate immune cell-cell interactions in the tumor.
Goal 3: Use mouse models to determine mechanisms of existing and putative immuno- and cytotoxic anti-cancer regimens and to design and test combinatorial therapies based upon this information.
Role: PI

AAF Fellow (PI: Krummel) 7/1/09-6/30/12
American Asthma Foundation
Directing Antigens to Specific APC and T cell subsets in the Lung
The major goals of this project are to screen for conditions that bias antigens towards particular antigen presenting cell populations and then to read out, through imaging and functional assays, the resulting T cell responses with the aim of optimizing regulatory interaction pathways.
Role: PI

Completed Research Support

R21AI062899 (PI: Krummel 3/1/05-2/28/07
NIH
Image-Based Analysis of Tolerance Induction Mechanisms
The major goals of this project were
Aim 1. We will develop instrumentation, algorithms and cellular methodologies to screen a GFP-expression library for cellular expression patterns.
Aim 2. We will identify and characterize new T cell molecular targets differentially utilized during tolerance induction.
Role: PI

Fellowship (PI: Krummel) 7/1/05-6/30/10
Leukemia & Lymphoma Society
Tumor Suppressors in T cell Synapse Formation and Signaling
The major goals of this project are
Aim 1. We will determine the role of Septin9/MSF in T cell synapse development, signaling, and proliferative control.
Aim 2. We will determine the role of Igl proteins in T cell synapse development, signaling, and proliferative control.
Role: PI
# BIOGRAPHICAL SKETCH

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limin Liu, Ph.D.</td>
<td>Assistant Professor</td>
</tr>
</tbody>
</table>

| eRA COMMONS USER NAME | LIMINLIU |

## EDUCATION/TRAINING

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
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<tbody>
<tr>
<td>University of Science &amp; Technology of China</td>
<td>B.S.</td>
<td>1986</td>
<td>Biology</td>
</tr>
<tr>
<td>University of Missouri, Columbia, MO</td>
<td>Ph.D.</td>
<td>1995</td>
<td>Molecular Biology</td>
</tr>
<tr>
<td>Duke University Medical Center</td>
<td></td>
<td></td>
<td>Nitric oxide biology</td>
</tr>
</tbody>
</table>

### Positions and Employment

- 1996-1997 Research Associate, Department of Animal Sciences, University of Missouri - Columbia
- 1997-2004 Research Associate, Department of Medicine, Division of Pulmonary Medicine, Duke University Medical Center
- 1998-2003 Research Associate, Howard Hughes Medical Institute, Duke University Medical Center
- 2005-Present Assistant Professor, Sandler Center for Basic Research in Asthma, Department of Microbiology and Immunology, University of California San Francisco

### Honors

- 1989-1990 Scholarship, Division of Biological Sciences, University of Missouri
- 1989-1993 Predoctoral Fellowship, Molecular Biology Program, University of Missouri
- 1994 New Investigator Award (First Place), Society for the Study of Reproduction (Biology of Reproduction, Vol. 52, pp. 261)
- 2005 Stewart Trust Cancer Research Award
- 2006 Sandler Innovative Research Award

### Selected peer-reviewed publications (in chronological order)


25. Wei W, Li B, Hanes MA, Kakar S, Chen X, **Liu L** (2010). Deficiency of S-Nitrosoglutathione Reductase Impairs DNA Repair and Promotes Hepatocarcinogenesis. *Science Translational Medicine* 2: 19ra13. *(This paper has been selected and rated by Faculty of 1000 as “Must Read”)*.


**Research Support**

Ongoing Research Support

1 R01 CA122359-01A2 NIH/NCI Liu (PI) 05/01/09-4/30/14 $933,750

Title: Role of S-nitroso-glutathione Reductase in Hepatocellular Carcinoma

The goal of this study is to determine whether GSNOR protects DNA repair proteins and plays a role in liver cancer.

Role: PI

2. 3 R01 CA055578-14S1 NIH/NCI Pulliam & Liu (PI) 09/30/2009-09/29/2011 $310,115 (Liu)

Title: Role of PreS2 Mutants in Pathogenesis of Chronic Hepatitis B

The goal of this study is to test if GSNOR deficiency functions synergistically with PreS2 Mutants in the pathogenesis of chronic hepatitis B

Role: one PI of the double-PI team.

3. 5P01CA123328 J. Ou (PI) 01/01/2010-05/31/2012 $532,285 (Liu)

Project 2 Title: Hepatic Carcinogenesis Induced By Hepatitis B Virus PreS2 Mutant

This project (part of a program project based at the University of Southern California) examines how the preS2 mutant may interact with other HBV proteins and immunological
factors in causing HCC and the role of the various mutant products of the preS2 mutant in
carcinogenesis
Role: PI of Project 2.

PAST

1. UCSF Cancer Center/ Stewart Trust Cancer Research Award 9/1/05-8/31/06
   $50,000
   UCSF Cancer Center
   Title: Potential Role of GSNOR in Tumorigenesis (PI)

2. Pilot-feasibility funding   Liu (PI) 6/1/06-5/31/07 $20,000
   UCSF Liver Center
   Title: Potential Role of S-nitroso-glutathione Reductase in Liver Tumorigenesis (PI)

3. Innovative Research Award   Liu (PI) 1/1/06-6/30/08 $200,000
   Sandler Center for Basic Research in Asthma, UCSF
   Title: Role of GSNOR in Asthma (PI)

4. Research Award   Liu (PI) 7/1/2007-6/30/2008 $50,000
   Cancer Research Coordinating Committee, UC
   Title: Role of S-nitroso-glutathione reductase in protection against carcinogenic N-
nitrosamines (PI)

5. Research Contract, N30 Pharmaceuticals Liu (PI) 07/01/09-09/30/10 $193,522
   Title: Haplosufficiency of S-nitroso-glutathione Reductase
   The goal of this study is to test if GSNOR is haplosufficient for protection against nitrosative
   stress.
   Role: PI
## BIOGRAPHICAL SKETCH

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
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<tbody>
<tr>
<td>Richard M. Locksley, M.D.</td>
<td>Sandler Distinguished Professor, Department of Medicine, University of California, San Francisco</td>
</tr>
</tbody>
</table>

| eRA COMMONS USER NAME | Locksley |

## EDUCATION/TRAINING

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
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<th>FIELD OF STUDY</th>
</tr>
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<tbody>
<tr>
<td>University of Rochester, Rochester, NY</td>
<td>M.D.</td>
<td>1976</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco, CA</td>
<td></td>
<td>1976-80</td>
<td>Resident, Chief Resident</td>
</tr>
<tr>
<td>University of Washington, Seattle, WA</td>
<td></td>
<td>1980-83</td>
<td>Infectious Diseases Fellow</td>
</tr>
</tbody>
</table>

## Positions and Honors

### Positions

1986-2003 Chief, Division of Infectious Diseases, UCSF Medical Center, San Francisco, CA  
1988-93 Member and Chair (1991-93), Tropical Medicine and Parasitology Study Section, NIH  
1991-94 Co-Director, Immunology Section, Biology of Parasitism Course, Woods Hole, MA  
1994-99 Chair, Parasitology Pathogenesis Committee, WHO, Geneva  
1995-05 Council, Chair (1998), Midwinter Conference of Immunologists, Asilomar  
1995-01 Faculty, Association of American Immunology Annual Course, Advanced Immunology  
1997- Investigator, Howard Hughes Medical Institute, UCSF  
1998-01 Member, Chair (2000-01), US-Japan Immunology Board, NIH  
2002-05 Council, NIAID, National Institutes of Health  
2003- Director, Strategic Asthma Basic Research Center, UCSF

### Editorial Boards


### Honors

1991 American Society for Clinical Investigation
1994   Association of American Physicians
1992-97  Burroughs Wellcome Fund Scholar in Molecular Parasitology
1994   Bailey K Ashford Medal, American Society Tropical Medicine and Hygiene
2001-05       Ellison Medical Foundation Senior Scholar in Global Infectious Diseases
2005   American Academy of Arts & Sciences

Selected Peer-reviewed Publications


Additional Publications (selected from >130 total)


Research Support

Active

Not assigned     Locksley (PI)     10/97 – 9/12 (budgeted annually)
Howard Hughes Medical Institute
Activation of Immunity
The major goals of this project are to provide new strategies to optimize host defense and vaccines and to treat pathologic immune responses associated with autoimmunity and allergy. Support from HHMI pays Dr. Locksley's salary.

R37 AI26918     Locksley (PI)     7/88-3/16
NIH/NIAID
Parasite immunity orchestrated by Th2 cells
The major goal of this project is to identify the role of basophils and eosinophils required for immunity to parasitic helminths.

RO1 AI30663     Locksley (PI)     6/08-5/13
NIH/NIAID
Initiation of allergic immunity by parasites
The major goals of this grant are to understand the mechanism by which chitin in helminthes contributes to eosinophilic inflammation in tissues in response to migrating organisms and eggs.

U19 AI077439    Sheppard (PI)     3/08-2/13
NIH/NIAID
Mechanisms of initiation and persistence of allergic asthma
The major goals of this grant are to understand mechanisms of allergic lung inflammation induced by fungi in murine models and human studies.
Role: PI Subproject 1

U19 AI          DeFranco (PI)     7/08-6/13
NIH/NIAID
Cross-talk between innate and adaptive immune cells in inflammation and autoimmunity
The major goals are to assess the role of innate signaling pathways in the induction of mucosal responses to pathogens.
Role: PI Subproject 4

Larry L. Hillblom Center for the immunobiology of type 2 diabetes (Chawla PI, Locksley co-PI)     1/09-12/12
The goal of this project is to understand the interface between immune cell activation and metabolic disorders.
Completed

5-2008-214  Locksley (PI)  12/07-12/08
Juvenile Diabetes Research Foundation Innovative Grants
Functional immune cell activation in type 1 diabetes
The major goal of this project was to use mice with marker alleles in informative cytokine
genes to identify evidence for functionally important cytokine elaboration in mediating
peripheral insulin sensitivity.
NAME
Sebastian Peck, B.S.

POSITION TITLE
Associate Specialist

eRA COMMONS USER NAME

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
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<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>University of California, Berkeley</td>
<td>B.S.</td>
<td>2005-2008</td>
<td>Microbial Biology</td>
</tr>
</tbody>
</table>

Positions and Honors

Positions

Summers 2005–2007  Summer Undergraduate Research Fellow, UC San Francisco
Aug. 2006–May 2007 Research Assistant, Department of Plant and Microbial Biology
University of California, Berkeley
Sep. 2007–Jul. 2008 Research Assistant, Department of Bioengineering
University of California, Berkeley

Mar. 2009–Feb. 2010 Manager, Nikon Imaging Center
University of California, San Francisco
Jan. 2010–Present Director, Biological Imaging Development Center
University of California, San Francisco

Honors

2006 and 2007  Summer Undergraduate Research Fellowship
Howard Hughes Medical Institute

Selected publications

BIOGRAPHICAL SKETCH

NAME
William E. Seaman, M.D.

POSITION TITLE
Professor of Medicine and of Microbiology and Immunology, UCSF

eRA COMMONS USER NAME
BSEAMAN

EDUCATION/TRAINING

<table>
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<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Princeton University, Princeton, NJ</td>
<td>A.B.</td>
<td>1964</td>
<td>English</td>
</tr>
<tr>
<td>Harvard Medical School, Boston, MA</td>
<td>M.D.</td>
<td>1969</td>
<td>Medicine</td>
</tr>
<tr>
<td>Massachusetts General Hospital, Boston, MA</td>
<td>Resident</td>
<td>1969-1971</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>Arthritis and Rheumatism Branch, NIAMDD, NIH Bethesda, MD</td>
<td>Fellow</td>
<td>1971-1974</td>
<td>Immunology and Rheumatology</td>
</tr>
<tr>
<td>Massachusetts General Hospital, Boston, MA</td>
<td>Chief Resident</td>
<td>1974-1975</td>
<td>Medicine</td>
</tr>
<tr>
<td>Massachusetts General Hospital, Boston, MA</td>
<td>Fellow</td>
<td>1976</td>
<td>Rheumatology</td>
</tr>
</tbody>
</table>

Positions and Honors

Academic Positions

1976 - 1984 Assistant Professor of Medicine, University of California San Francisco
1978 - Present Staff Physician, San Francisco VA Medical Center
1981 - 1992 Chief, Arthritis/Immunology Section, San Francisco VA Medical Center
1984 - 1988 Associate Professor of Medicine, UC San Francisco
1988 - Present Professor of Medicine and of Microbiology and Immunology, University of California San Francisco
1992 - 1999 Chief, Medical Service, San Francisco VA Medical Center
1999 - Present Chief, Immunology Section, San Francisco VA Medical Center

Other Recent Positions

1999 - Present Research Director, American Asthma Foundation
1999 - 2003 NIH Study Section, Experimental Immunology
2000 - 2008 Director, Macrophage Biology Laboratory, Alliance for Cellular Signaling
2002 - 2005 President, Society for Natural Immunity
Honors

1964   AB cum laude
1969   MD cum laude
2007   Master, American College of Rheumatology
       Medical and Research Society Memberships and Board Certifications

1973 to Present American College of Rheumatology
1974    American Board of Internal Medicine
1978    American Board of Rheumatology
1979 to Present American Federation for Clinical Research
1980 to Present American Association of Immunologist
1984 to Present American Society for Clinical Investigation
1994 to Present American Association of Physicians
1998 to Present Society for Natural Immunity
2001 to Present American Association for Cancer Research
2007 to Present International Bioiron Society
2007 to Present International Society of Neuroimmunology

Editorships

1985-1989    Associate Editor, Journal of Immunology
1989-1993    Section Editor, Journal of Immunology
2005 to Present Faculty of 1000

15 Selected Peer-Reviewed Publications (of 93)


Research Support

Ongoing Research Support

Title: The Role of Microglial Subsets in Regulating Brain Injury
Agency/Type: Department of Defense PTO75679 PI: WE Seaman 7/1/06 to 6/30/2012
Role: Principal Investigator
Program: These studies examine the role of microglial subsets in the response to TBI. They examine the hypothesis that microglia, like macrophages may be divided into pro-inflammatory
vs. reparative subsets, and that injury following TBI may be improved by driving microglia from
the former to the latter. Key persons are Christine Hsieh, a postdoctoral fellow, my colleague,
Mary Nakamura, MD, and Jialing Liu, PhD, a colleague in Neurosurgery who is expert in TBI.

Title: Role of the Tim-2 Receptor in Immunity and Autoimmunity
Agency/Type: NIH RO1 AI061164-01A1 PI: WE Seaman 7/1/05 to 3/31/2011
(extended)
Role: Principal Investigator
Program: These studies examine the role in immunity and autoimmunity of Tim-2, a receptor
expressed on mouse lymphocytes and on liver cells and renal tubule cells. We previously
discovered that Tim-2 is a receptor for H-ferritin in mice, and this led us to the recent discovery
that transferrin receptor-1 is receptor for ferritin in humans. Key persons are Celia Fang, a
postdoctoral fellow, and Mary Nakamura, a colleague. Suzy Torti, at Wake Forest University, is
a major collaborator.

Ongoing Mentored Grant

Title: The role of CCR2 and Macrophages in Traumatic Brain Injury
Agency/Type: Department of Veterans Affairs PI: Christine Hsieh 1/1/2011 to 12/31/2013
Role: Mentor
Program: This is a VA Career Development Award to Christine Hsieh, PhD, a postdoctoral
fellow in my laboratory for whom I am the mentor on this award. Dr. Hsieh has been studying
traumatic brain injury as part of my DoD grant (above). As part of this work, she showed that
TBI results in an influx of macrophage to the brain, and that this influx is primarily dependent on
the chemokine receptor, CCR2. This grant will allow her to study the functional consequences
of this response and to develop as an independent investigator. Key persons in addition to Dr.
Hsieh and myself include our colleague, Mary Nakamura.

Completed support (last 3 years)

Title: Alliance for Cellular Signaling – Phase II
Agency/Type: NIH 5U54GM062114-05 9/1/00-12/31/2008
Role: Director, Macrophage Biology Laboratory PI: A Gilman
Program: The Alliance for Cellular Signaling was a consortium of scientists and laboratories
dedicated to the elucidation of signaling pathways in mammalian cells.

Title: Role of TREM-2 in the Microglial Response to Brain Injury
Agency/Type: DoD & VA W81XWH-05-2-0094 PI: WE Seaman 5/1/06-4/30/2008
Role: Principal Investigator
Program: These studies examined the expression of TREM-2 TREM 2 ligands on cortical
neurons and the consequent ability of cortical neurons to stimulate phagocytosis by cortical
microglia. (Additional studies looked at the influence of TREM 2 on signaling by LPS in
cortical microglia.)
Title: Biology of a New DAP12-associated receptor family
Agency/Type NIH RO1 CA87922 PI: WE Seaman 4/1/01 to 3/31/2009 (by extension)
Role: Principal Investigator
Program: These studies examined the TREM receptor family, in particular TREM 2, which is expressed on immature dendritic cells and on microglia.

Title: SHPS-1 as a Regulator of Innate Immunity in Arthritis
Agency/Type: NIH R21 AR051751 PI: WE Seaman 9/1/04 to 8/31/2007
Role: Principal Investigator
Program: These studies examined the role of an inhibitory cell-surface receptor, SHPS-1 (SIRPa1) in a mouse model for rheumatoid arthritis, the SKG mouse.
**BIOGRAPHICAL SKETCH**

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dean Sheppard, M.D.</td>
<td>Professor of Medicine</td>
</tr>
</tbody>
</table>

| eRA COMMONS USER NAME | sheppard |

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harvard College, Cambridge, MA</td>
<td>AB</td>
<td>1972</td>
<td></td>
</tr>
<tr>
<td>SUNY at Stony Brook, Stony Brook, NY</td>
<td>MD</td>
<td>1975</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of Washington, Seattle, WA</td>
<td>Resident</td>
<td>1975-1978</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco</td>
<td>Fellow</td>
<td>1978-1981</td>
<td>Pulmonary</td>
</tr>
</tbody>
</table>

**Positions and Employment**

- **2009-Present**: Chief, Pulmonary, Critical Care, Allergy and Sleep Division, University of California, San Francisco
- **1986 to Present**: Director, Lung Biology Center, University of California, San Francisco
- **1999-2004**: Founding Director, Sandler Basic Asthma Research Center, University of California, San Francisco
- **1981-1987**: Assistant Professor of Medicine, University of California, San Francisco
- **1987-1992**: Associate Professor of Medicine, University of California, San Francisco
- **1992 to Present**: Professor of Medicine, University of California, San Francisco
- **1997 to 2009**: Associate Chair for Biomedical Research, Department of Medicine, University of California San Francisco

**Other Experience**

- **1998-2002**: Member, NHLBI Program Project Review Committee
- **2000-2002**: Chair 2000-2002
- **2004-2008**: Member, Lung Injury and Repair Study Section
- **2006-2008**: Chair
- **2006-2009**: Scientific Advisory Board, Parker B. Francis Foundation
- **2003-Present**: Editorial Board, Journal of Clinical Investigation
- **2008 to Present**: Editorial Board, Clinical and Translational Science
- **1995-2002**: Associate Editor, American Journal of Respiratory Cell and Molecular Biology
- **1996-2007**: Editorial Board, American Journal of Physiology
- **2004 to Present**: Chair, Oversight Committee, NHLBI Lung Tissue Consortium,
Honors and Awards

1992  Elected Member, American Society for Clinical Investigation
1995  Elected Member, Association of American Physicians
1995  Clean Air Award, American Lung Association of California
1996  Parker B. Francis Lecturer, Aspen Lung Conference
1998  Lifetime Scientific Achievement Award, American Thoracic Society
2000  Jerome I. Flance Visiting Professor, Washington University
2001  Roger Mitchell Lecturer, Aspen Lung Conference
2004-14 NIH Merit Award
2005  Robert Johnston Lecturer, Drexel University
2006  McClement Lecturer, New York University
2007  Kass Medal, University of Nebraska
2010  Amberson Lecturer, American Thoracic Society

Selected Relevant Publications (Total 239)


Research Support

Ongoing

R01 HL102292 (Sheppard) 12/03/10-11/30/14
NIH
Integrin-mediated regulation of airway smooth muscle
The major goals of this project are to determine the mechanisms by which the alpha9beta1 integrin inhibits the sensitivity of airway smooth muscle to contraction induced by agonists of G protein coupled receptors.

R37 HL53949 (Sheppard) 4/1/04-3/31/14 (merit award)
NIH
In Vivo Functions of Pulmonary Integrins
The major goals of this project are to determine the roles of TGFb1 activation in the induction of lung inflammation and protection from pulmonary fibrosis in integrin b6 subunit null mice.
Regulations of Pulmonary Vascular Permeability by Integrin AlphaVbeta5
The major goals of this project are: 1) To identify the pathways by which avb5 facilitates RhoA activation and contributes to pulmonary vascular permeability. 2) To determine how the integrin b5 subunit contributes to the formation of multi-protein signaling complexes that regulate endothelial permeability. 3) To determine whether the pathways examined in aims 1 and 2 are broadly important in in vivo models of non-cardiogenic pulmonary edema.

Mechanisms of Initiation and Persistence of Allergic Asthma
The major goals of this project are to determine the roles of integrin-mediated TGFb activation in regulating auto-immunity, regulatory T cells and airway hyperresponsiveness after chronic allergen challenge in mice.

This administrative supplement to our U19 grant has three goals – to develop an assay for measurement of environmental chitin, to replace our outdated tissue processor and process our backlog of fixed murine and human tissues, and to develop multi-plexed, bead based assays for measurements of multiple secreted proteins in small volume samples from human and murine airways.

The subcontract is to support a postdoctoral fellow, Neil Henderson, to work in Dr. Sheppard’s laboratory for two years. Dr. Henderson will be working on the mechanisms of activation of TGF beta in the liver.

Novel Leukocyte Integrins
The major goal of this project is to understand how glycan phosphoatidly inositol anchored proteins influence the function of Fc and complement receptors on macrophages and dendritic cells.
Integrin-mediated Development of the Thoracic Duct
The major goals of this project were to determine the mechanisms by which the integrin α9β1 contributes to normal lymphatic development.

U01 HL66600 (Sheppard) 9/30/00-8/31/08
NIH/NHLBI/
Program title: The NHLBI-Bay Area Functional Genomics Consortium
Project title: Mouse Resource for Pulmonary Disease
The overall project inactivated 2,500 genes in murine embryonic stem cells each year and determined their expression pattern in the heart and lungs during development and in models of cardiopulmonary disease. Dr. Sheppard’s project generated tissue for in situ hybridization and gene array analysis from murine models of asthma and pulmonary fibrosis and produced 3 lines of mice/year from targeted ES cells for analysis in these models.
**BIOGRAPHICAL SKETCH**

**NAME**

**Jeoung-Sook Shin, Ph.D.**

**POSITION TITLE**

Assistant Professor

**eRA COMMONS USER NAME**

SHINJS

**EDUCATION/TRAINING**

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Seoul National University, Seoul, Korea</td>
<td>BS</td>
<td>1988-1993</td>
<td>Chemistry</td>
</tr>
<tr>
<td>Seoul National University, Seoul, Korea</td>
<td>MS</td>
<td>1993-1995</td>
<td>Biochemistry</td>
</tr>
<tr>
<td>Duke University, Durham, NC</td>
<td>Ph.D.</td>
<td>1997-2002</td>
<td>Pathology</td>
</tr>
<tr>
<td>Duke University, Durham, NC</td>
<td>Postdoc</td>
<td>2002-2003</td>
<td>Pathology</td>
</tr>
<tr>
<td>Yale University, New Haven, CT</td>
<td>Postdoc</td>
<td>2003-2008</td>
<td>Cell Biology</td>
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**Professional Positions**

<table>
<thead>
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<th>Year</th>
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<tbody>
<tr>
<td>1996</td>
<td>Research Associate, Cheong-Am Biotech, Seoul, Korea</td>
</tr>
<tr>
<td>2002 – 2003</td>
<td>Research Associate, Duke University</td>
</tr>
<tr>
<td>2003 – 2008</td>
<td>Postdoctoral Associate/Fellow, Yale University</td>
</tr>
<tr>
<td>2008</td>
<td>Assistant Professor, University of California San Francisco, Dept. of</td>
</tr>
<tr>
<td></td>
<td>Microbiology Immunology and, Sandler Asthma Basic Research Center</td>
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**Honors and Awards**

<table>
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<tr>
<th>Year</th>
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<tr>
<td>1999</td>
<td>The Best Research Student Award in the Department of Pathology, 9th</td>
</tr>
<tr>
<td></td>
<td>Graduate Student Symposium, Duke University</td>
</tr>
<tr>
<td>2004</td>
<td>The Jane Coffin Childs Memorial Fund Research Fellowship Award</td>
</tr>
<tr>
<td>2009</td>
<td>Strategic Innovative Award in Asthma Research</td>
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<td>2009</td>
<td>Cancer Research Institute Investigator Award</td>
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**Professional Memberships**

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<tr>
<td>2008 - 2010</td>
<td>American Thoracic Society, member</td>
</tr>
<tr>
<td>2011 -</td>
<td>American Society of Cell Biology, member</td>
</tr>
</tbody>
</table>
Selected peer-reviewed publications


Research Support

Research Projects Ongoing

Cancer Research Institute Investigator Award (PI) 7/1/2009 – 6/30/2013
Cancer Research Institute
Mechanism and function of ubiquitin-mediated membrane traffic in dendritic cells

American Heart Association National Scientist Development Award (PI) 7/1/2010 – 6/31/2014
American Heart Association
IgE-mediated activation of dendritic cells in the lungs

Research Projects Completed During the Last 3 Years

Strategic Innovative Award (PI) 1/1/2009 – 12/31/2009
UCSF Sandler Asthma Basic Research Center
Characterization of FceRI-Mediated Activation of Human Dendritic Cells

American Thoracic Society Role of FceRI expression on dendritic cells in asthma
BIOGRAPHICAL SKETCH

NAME
Zhi-En Wang, M.D., M.S.

POSITION TITLE
Research Specialist

eRA COMMONS USER NAME

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tbody>
<tr>
<td>Xian Medical University, Xian, China</td>
<td>M.D.</td>
<td>12/82</td>
<td>Medicine</td>
</tr>
<tr>
<td>Xian Medical University, Xian, China</td>
<td>M.S.</td>
<td>12/85</td>
<td>Immunology</td>
</tr>
</tbody>
</table>

Positions and Honors

1986-1987 Research and Teaching Associate, Department of Microbiology and Immunology, Xian University, Xian, China
1987-1989 Assistant Researcher and Lecturer, Xian University, Xian China
1989-1990 Cheng Scholar and Visiting Scientist, University of California, San Francisco, CA
1990-1991 Research Fellow, Temple University School of Medicine, Philadelphia, PA
1991-1994 Research Fellow, University of California, Department of Medicine, San Francisco, CA
1994-1997 Senior Research Associate, Cell Genesys Inc., Foster City, CA
1997- Research Specialist II, HHMI, San Francisco, CA

Selected Peer-reviewed Publications


BIOGRAPHICAL SKETCH

NAME
Arthur Weiss, M.D., Ph.D.

POSITION TITLE
Professor of Medicine and of Microbiology and Immunology

eRA COMMONS USER NAME
weissa

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
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<tbody>
<tr>
<td>University of Chicago</td>
<td>Ph.D.</td>
<td>1978</td>
<td>Immunology</td>
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<tr>
<td>University of Chicago</td>
<td>M.D.</td>
<td>1979</td>
<td>Medicine</td>
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</table>

Positions and Employment

1979-1980  Postdoctoral Fellow, Swiss Institute for Experimental Cancer Research, Lausanne, Switzerland
1980-1982  Resident, Department of Medicine, University of California, San Francisco (UCSF)
1982-1984  Fellow in Rheumatology/Clinical Immunology, UCSF
1982-1985  Associate, Howard Hughes Medical Institute, UCSF
1984-1985  Instructor, Department of Medicine, Division of Rheumatology/Clinical Immunology, UCSF
1985-1989  Assistant Investigator, Howard Hughes Medical Institute, UCSF
1985-1989  Assistant Professor of Medicine, Microbiology and Immunology, UCSF
1987-      Chief, Division of Rheumatology/Clinical Immunology, Department of Medicine, UCSF
1989-1993  Associate Professor or Medicine, Microbiology and Immunology, UCSF
1989-1994  Associate Investigator, Howard Hughes Medical Institute, UCSF
1991-      Ephraim P. Engleman Distinguished Professor of Rheumatology, UCSF
1992-      Professor of Medicine, Microbiology and Immunology, UCSF
1993-      Investigator, Howard Hughes Medical Institute, UCSF
1998-2005  Associate Director, The Rosalind Russell Medical Research Center for Arthritis, UCSF
2002-2006  Director, Medical Scientist Training Program (MSTP), UCSF
2007-2010  Co-Director, Institute for Molecular Medicine, UCSF
Other Experience and Professional Memberships

1986-1991 Councilor, American Federation for Clinical Research
1991 President, Western Region of the American College of Rheumatology
1998-2002 Member, Allergy and Immunology Study Section (NIH)
1999- Chair, Scientific Advisory Board, American Asthma Foundation
2000-2002 Chair, Allergy and Immunology Study Section (NIH)
2003-2010 Council, American Association of Immunologists
2008-2009 President, American Association of Immunologists
2005- Advisory Council, RIKEN Research Center for Allergy & Immunology
         Yokohama, Japan
2010- Board of Directors, Immune Tolerance Institute

Honors

1990 Young Investigator Award, Western Society for Clinical Investigation
1990 Henry Kunkel Young Investigator Award, American College of Rheumatology
1993 Junior Investigator Award, American Association of Immunologists
1997 Lee C. Howley Prize, Arthritis Foundation
1998 Forty-First Faculty Research Lecturer, University of California, San Francisco
2001 American Association of Immunologist-Huang Foundation Meritorious Career Award
2003 Fellow, American Academy of Arts and Sciences
2004 Member, National Academy of Sciences
2004 Fellow, American Academy of Microbiology
2004 Member, Institute of Medicine
2004 Distinguished Investigator Award, American College of Rheumatology
2004 Walter Bauer Visiting Professor in Rheumatology, Massachusetts General Hospital
2004 Bridget Ogilvie Lecture, University of Dundee, Scotland
2004 Sue Kim Hansen Lecture, Boston University School of Medicine
2005 Dan H. Campbell Memorial Lecture, Midwinter Conference of Immunologists, Asilomar, CA
2005 Visiting Professor, Harvard Medical School Rheumatology Division
2005 Beirne B. Carter Lecture in Immunology, University of Virginia
2005 Dan H. Campbell Memorial Lecture, Midwinter Conference of Immunologists, Asilomar, CA
2006 Keynote Speaker, American Association of Immunologists, Advanced Immunology Course
2009 Ishizaka Lecture, La Jolla Institute for Allergy and Immunology
2009 46th Charles A. Stuart Memorial Lecture, Brown University
2010 Dorothy Baugh Harmon Endowed Lectureship, Oklahoma Medical Research Foundation
Selected Peer-reviewed Publications (from a total of 194)


BIOGRAPHICAL SKETCH

NAME
Jonathan S. Weissman, Ph.D.

POSITION TITLE
Professor, University of California San Francisco
Investigator, Howard Hughes Medical Institute

eRA COMMONS USER NAME
WEISSMAN

EDUCATION/TRAINING

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
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<th>FIELD OF STUDY</th>
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<tr>
<td>Massachusetts Institute of Technology</td>
<td>Ph.D.</td>
<td>1988-1993</td>
<td>Physics</td>
</tr>
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</table>

Positions and Honors

1993-1996  Postdoctoral Fellow, Yale University, Structural and Biochemical Studies of GroEL
1996-2000  Assistant Professor, University of California San Francisco, Departments of Cellular & Molecular Pharmacology, and Biochemistry & Biophysics
2000-2005  Assistant Investigator, Howard Hughes Medical Institute
2000-2003  Associate Professor, University of California San Francisco, Departments of Cellular & Molecular Pharmacology, and Biochemistry & Biophysics
2003-Present  Professor, University of California San Francisco, Departments of Cellular & Molecular Pharmacology, and Biochemistry & Biophysics
2005-Present  Investigator, Howard Hughes Medical Institute

Other Experience and Professional Memberships

1999  Keynote Speaker at Scripps Research Institute Society of Fellows Annual Symposium
2001 to Present  Associate Editor of Molecular Cell
2001-2003  Ad hoc reviewer for CDF-2 NIH study section
2002  Organizer Second International Yeast Prion Symposium
2002 to Present  Organizer, Cold Spring Harbor Heat Shock Meeting
2003 to Present  Editorial Board, BMC Cell Biology
2003  Burroughs Wellcome Visiting Scholar, University of Chicago
2003 to Present  Editorial Board, Public Library of Science (PLoS) Biology
2004  Organizer, FASEB meeting on Amyloid and Diseases of Misfolding
2005  Co-organizer, The Protein Society 19th Annual Meeting
2004-2008  Permanent Member, NIH Molecular Biology & Protein Processing Study Section
2005-2008  Editorial Board, Molecular Biology of the Cell
2005  External Reviewer, Lawrence Berkeley National Lab Physical Biosciences Division
2005-2007  Advisory Board member for NIH on Amyloid Diseases

165
2005 Organizer, Mini-symposium of Quality Control for the Annual American Society of Cell Biology (ASCB) Meeting
2006 to Present Member, Yeast Genetics & Molecular Biology Meeting Program Committee
2006 to Present Editorial Board member, Journal of Molecular Biology
2007 to Present Board of Reviewing Editors, Science
2007 to Present Scientific Advisory Board member for GlycoFi (Merck & Company, Inc.)
2008 to Present Scientific Advisor, Merck Research Labs
2008 to Present Editorial Board, Cell
2009 Program Committee Member, ASCB
2009 to Present Editorial Board, Current Opinion in Cell Biology
2009 Keynote address at the annual retreat of the Genentech Research Organization
2009 Keynote lecture at the annual International Conference on Systems Biology
2009 to Present Scientific Advisory Board Member Proteostasis Therapeutics
2009 Member, NAKFI Steering Committee on Synthetic Biology
2010 Member, NIH College of CSR Reviewers

Honors and Awards

1987 Phi Beta Kappa, Harvard University
1988 Summa cum laude in Physics, Harvard University
1988 Karl Taylor Compton Pre-doctoral Fellowship
1988 National Science Foundation Pre-doctoral Fellowship
1996 David and Lucile Packard Fellowship
1997 Searle Scholars Program Fellowship
2000 Chosen as an Assistant Investigator of the Howard Hughes Medical Institute
2004 Protein Society’s Irving Sigal Young Investigator’s Award
2008 Raymond & Beverly Sackler International Prize in Biophysics
2009 Alexander M. Cruikshank Lecturer, Gordon Research Conference on Stress
2009 Elected to the National Academy of Sciences
2010 David Perlman Award Lecturer of the ACS Division of Biochemical Technology (BIOT)

Selected Peer-reviewed Publications (Selected from 95 peer-reviewed publications)


*corresponding authors


*corresponding author


*corresponding authors


proteasome and regulates histone methylation. Proc Natl Acad Sci USA, 104:5836-41. PMCID: 1851578


**Research Support**

Ongoing Research Support

No Project Number (Weissman) 10/01/2000-8/31/2017

Howard Hughes Medical Institute
Prion-Based Inheritance, Protein Folding, and Analysis of Cellular Systems
This grant supports our studies of how cells insure that proteins fold into their correct shape, as well as the role of protein misfolding in disease and normal physiology. We are also developing experimental and analytical approaches for exploring the organizational principles of biological systems.

P0032295 (Weissman) 12/01/09 - 11/30/2010

AFAR (Glenn Foundation for Medical Research)
Monitoring the Effects of Aging on Protein Translation
Using a ribosome profiling approach pioneered in our lab, we will investigate the impact of aging and the accumulation of misfolded proteins on protein synthesis in a yeast model system.

RFA-RM-08-019 (Stroud; Weissman - Key Personnel) 08/01/09 – 07/31/2014

NIH/NIGMS
Centers for Innovation in Membrane Protein Production for Structure Determination
The goals are to develop approaches that will make the solution of simple membrane protein structures routinely achievable and develop novel methods that can be applied to more complicated membrane proteins containing multiple subunits of the same (homo-oligomers) and different (hetero-oligomers) structure; and to produce and determine structures for complexes that are formed between membrane proteins and their soluble protein partners, small ligands and/or macromolecules.

SABRE Center (Weissman) 07/01/10-06/30/11

Sandler Asthma Basic Research Center Innovative Grant Award
Defining the Function of ORMDL3 and Exploring its Potential Role in Asthma
Specific aims of this project are: 1) Define the function of ORM genes in yeast; 2) Characterize the function of the human ORM homolog ORMDL3; 3) Examine the potential role of ORMDL3 in asthma.
Completed Research Support

P01 AG70770-15 (Prusiner; Weissman Project 5) 07/15/05 - 6/30/10
NIH
Molecular Pathogenesis of Age-Dependent CNS Degeneration
Specific aims of this project are 1) Mechanism of prion growth and replication; 2) Dissection and design of prion elements; and 3) Analysis of the structural basis of prion strains.

Fight for Mike Program (Weissman) 07/23/07-07/22/09
California Institute for Quantitative Biosciences (QB3)
Identification of Factors Important for the Folding of Mammalian Prion Protein
The broad goal of our studies is to identify key factors required for folding of the mammalian prion protein.

SABRE Center (Weissman) 01/01/09-12/31/09
Sandler Asthma Basic Research Center
Defining the Function of ORMDL3 and Exploring its Potential Role in Asthma
Specific aims of this project are: 1) Define the function of ORM genes in yeast; 2) Characterize the function of the human ORM homolog ORMDL3; 3) Examine the potential role of ORMDL3 in asthma.

SABRE Center (Weissman and Fujimori) 01/15/09-01/14/10
Sandler Asthma Basic Research Center
Defining Roles on N-Glycans in Endopasmic Reticulum-Mediated Quality Control
Specific aims of this project are: 1) Biochemical characterization of the putative mannosidase Htm1; and 2) Elucidation of contributions of glycan and mis-folded protein components to substrate recognition in late stages of ERAD-L pathway.
**BIOGRAPHICAL SKETCH**

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zena Werb, Ph.D.</td>
<td>Professor of Anatomy</td>
</tr>
<tr>
<td>eRA COMMONS USER NAME</td>
<td>werbzena</td>
</tr>
</tbody>
</table>

**EDUCATION/TRAINING**

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>University of Toronto, Toronto, Canada</td>
<td>B.Sc.</td>
<td>06/1966</td>
<td>Biochemistry</td>
</tr>
<tr>
<td>Rockefeller University, New York</td>
<td>Ph.D.</td>
<td>06/1971</td>
<td>Cell Biology</td>
</tr>
<tr>
<td>Strangeways Research Laboratory, Cambridge,</td>
<td>Postdoc.</td>
<td>1971-73</td>
<td>Protein Chemistry</td>
</tr>
</tbody>
</table>

**Positions and Honors** (partial list)

**Positions**

1975-1976 Visiting Assistant Prof. of Medicine, Dartmouth Medical School, Hanover, NH
1976-1980 Assist. Prof. Radiobiology, Radiology, Univ. of California, San Francisco;
1979-1980 Assist. Prof. Anatomy, UCSF
1980-1983 Assoc. Prof. of Anatomy and Radiology, UCSF
1983-present Prof. Anatomy, UCSF
1985-1986 Visiting Prof., Sir William Dunn School of Pathology, Univ. of Oxford, U.K.
1998 Visiting Prof., Institut Curie, Paris
1999-present Vice-chair, Dept. Anatomy, UCSF
2006-2008 Visiting Prof., Max-Planck Institute for Biochemistry, Martinsried, Germany

**Honors**

1971-1973 Fellow, Medical Research Council, Canada
1982 R.R. Bensley Memorial Award, American Association of Anatomists
1985-1986 Fellow, John Simon Guggenheim Foundation
1992 Elected Fellow, American Association for the Advancement of Science
1996 FASEB Excellence in Science Award
1998 Rotschild/Mayent Fellowship, Institut Curie
2002 Elected Member, Institute of Medicine
2003 Elected Fellow, American Academy of Arts and Sciences
2003 Doctor of Medicine (honoris causa), University of Copenhagen
2006-2007 Alexander von Humboldt Foundation (Germany) Research Award
2007 E.B. Wilson Medal, American Society for Cell Biology
2009 Colin Thomson Memorial Medal, AICR
2010 Elected Member, National Academy of Sciences
2010 American Society for Cell Biology, Women in Cell Biology Senior Award
Named Lectureships

1986  Muriel Trotter Lecture, Washington University
1992  Lowell Lectures in Biotechnology, Northeastern University, Boston, MA
1993-94  Sigma Xi National Lecturer
1997  Chitra Biswas Memorial Lecture, Tufts Medical School
1998  Earl Benditt Distinguished Lecture, University of Washington
1999  J.L. Melnick Lecture, Baylor College of Medicine
2001  Charlotte Friend Lecture, AACR
2001  44th Faculty Research Lecture Award, UCSF
2004  Schlessinger Lecturer, BIDMC, Harvard Medical School
2004  A. S. Wiener Lecture, NY Blood Center
2005  Maud L. Menten Lecture, University of Pittsburgh
2005  17th Otto Herz Memorial Lecture, Tel Aviv University, Israel
2008  Whitley Lecture, Northwest Developmental Biology Society
2008  ADVANCE Distinguished Lectureship in Academic Careers in Engineering and Science, Case Western Reserve University, Cleveland, OH
2009  Discovery Lecture, Department of Cell Biology, Johns Hopkins University School of Medicine
2009  Friedrich Miescher Lecture, Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland; 2009, Suzanne M. Bernier Lecture in Skeletal Biology, University of Western Ontario, London, Canada.
2010  Keynote Lecture, American Society for Investigative Pathology Annual Meeting, Anaheim CA.
2010  William Larson Distinguished Lecture, Univerisity of Cincinnati, OH

Editorial Boards

1983-1985  Journal of Cell Biology
1982-1987,  American Journal of Physiology
1985-2004  Journal of Experimental Medicine
1990-2001  Science
1999-present  Matrix Biollog
1999-present  Neoplasia
2000-2009  Cell
2001-present  Developmental Cell
2001-present  Cancer Cell
2002-2006  Molecular Biology of the Cell
2007-2009  Genes & Development
2009-present  Current Opinion in Cell Biology

Scientific Leadership

1990-1992  Member, Cell and Molecular Biology Panel, National Cancer Institute of Canada
1991-1995  Member, Board of Scientific Counselors, NIAMS
1992-1995  Council Member, American Society for Cell Biology
1993-1995  Council Delegate, Am. Assoc. for the Advancement of Science
1994-2001  Member, Scientific Advisory Board, Keystone Symposia
2001-2003  Council Member, American Society for Matrix Biology
2001    NIH Oncological SS Boundaries Team
2002    NIH Biochem SS, ad hoc
2003-2005  Council Member, International Society for Matrix Biology
2003-2006  Board of Directors, AACR
2005    President, American Society for Cell Biology
2007-2009  Nominating Committee, AACR
2007    Member, NIH ZRG1 ICI–D01
2008    Reviewer, NIH Pioneer Awards
2008    Chair, NIH ZRG1 MOSS-A (02)
2008-2010  Chair, NIH ICI Study Section

Selected Publications (>430 total full publications)


Cell Stem Cell. 2:90-102. PMCID: PMC2276651


Research Support

Ongoing

NIH/NIEHS U01 ES012801-07 Hiatt (PI), Werb (PI, Collaborative Project 1) 09/29/03 - 07/31/11

NIH/NIEHS U01 ES012801-07S1 Hiatt (PI), Werb (PI, Collaborative Project 1) 09/03/09 - 08/31/11

Bay Area Breast Cancer and the Environment Research Center
This project studies environmental effects on the molecular architecture and function of the mammary gland.

NIH/NIAMS R01 AR046238-10 Werb (PI) 09/01/99 - 01/31/11

Extracellular Remodeling in Bone Development And Repair
This project studies the role of extracellular remodeling in bone development and repair.

NIH/NCI R01 CA129523-03 Werb (PI) 07/01/08 - 04/30/13

R01 CA129523-02S1 Werb (PI) 09/30/09 – 09/29/11

Transcriptional Regulation of Breast Cancer Metastasis
This study addresses how GATA-3 regulates the differentiated state of breast tumors.

NCI R01 CA057621-18 Werb (PI) 04/15/93 - 05/31/13

Role of Metalloproteinases in Mammary Gland Remodeling
This consortium grant between UCSF and LBNL determines functions of ECM-degrading proteinases and inhibitors in mammary epithelium during development.

NIH/NIAID P01 AI053194-08 Mostov (PI), Werb (Leader, Project 4 and Core C) 09/30/02 - 08/31/13

NIH/NIAID P01 AI053194-06A1S1 Mostov (PI), Werb (Leader, Project 4 and Core C) 09/01/09 – 08/31/11

Mucosal Immune Barrier in Infection and Inflammation
This project studies the role of the inflammatory response in mucosal epithelia.

Stand Up To Cancer Gray, Slamon (Dream team leaders) Werb (Team Member) 10/01/09-09/30/12

American Assoc for Cancer Research

Personalizing Treatment of Metastatic Breast Cancer
This project tests the efficacy of individualized treatment of drug-resistant, metastatic breast cancers. 1U01 ES019458-01 (Werb, PI) 09/01/10-04/30/15 Environmental Effect on The
Mammary Gland Across The Lifespan  The major goal of this program is to determine the susceptible times in breast developments and how they are affected by environmental stressors.

Completed

**NCI P01 CA072006-10**  Werb (PI), Werb (Project Leader, Project 3 and Core A)  07/07/03 – 06/30/10
Proteases in Cancer: Biology and Drug Development
This program tested new animal models of invasive cancer with antiprotease therapy.

**NIH/NCI U01 CA105379**  Hanahan (PI), Werb (Co-I)  09/27/04 - 03/31/09
Immune Enhancement and Therapy in Cancer/ Mouse Models of Human Cancer Consortium
This project addressed the immunobiology of carcinogenesis in genetically engineered mouse models

**NIH R01 AG023218**  Werb (PI)  07/01/03 - 06/30/07
Matrix Metalloproteinases Regulate Mesenchymal Stem Cells.
This project studied bone marrow stromal cells that maintain HSC and the role of MMPs.
NAME
Prescott Gurney Woodruff, M.D., M.P.H.

POSITION TITLE
Associate Professor of Medicine in Residence

eRA COMMONS USER NAME
woodruffp

EDUCATION/TRAINING

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wesleyan University, Middletown, CT</td>
<td>B.A.</td>
<td>6/1989</td>
<td>Letters</td>
</tr>
<tr>
<td>Columbia College of Physicians &amp; Surgeons, NY</td>
<td>M.D.</td>
<td>6/1993</td>
<td>Medicine</td>
</tr>
<tr>
<td>Massachusetts General Hospital</td>
<td>Resident</td>
<td>1993-1996</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>Harvard School of Public Health</td>
<td>M.P.H.</td>
<td>6/1998</td>
<td>Epidemiology</td>
</tr>
<tr>
<td>Brigham and Women’s Hospital</td>
<td>Fellow</td>
<td>1997-1998</td>
<td>Resp Epidemiology</td>
</tr>
<tr>
<td>University of California, San Francisco</td>
<td>Fellow</td>
<td>1998-2002</td>
<td>Pulmonary/Critical Care</td>
</tr>
</tbody>
</table>

Positions and Honors

1993-94 Intern in Internal Medicine; Massachusetts General Hospital, Boston, MA
1994-96 Resident in Internal Medicine; Massachusetts General Hospital, Boston, MA
1996-98 Research Fellow, Department of Emergency Medicine; Massachusetts General Hospital, Boston, MA
1997-98 Clinical and Research Fellow, Channing Laboratory, Department of Medicine Brigham and Women’s Hospital, Boston, MA
1998-2002 Clinical and Research Fellow, Pulmonary/Critical Care Medicine & Cardiovascular Research Institute, Department of Medicine, University of California San Francisco, San Francisco, CA
2002-2005 Assistant Adjunct Professor; University of California San Francisco
2005- 2010 Assistant Professor in Residence, Pulmonary/Critical Care Medicine, Department of Medicine and CVRI, University of California San Francisco
2010- Associate Professor in Residence, Division of Pulmonary and Critical Care Medicine, Department of Medicine and CVRI, University of California San Francisco

Other Experience and Professional Memberships

2004- Steering Committee, NIH NHLBI COPD Clinical Research Network
2009- Steering Committee, NIH NHLBI Spiromics Network
2009 NIH Peer Review Committee, RC2 special emphasis panel
Honors

1990  Student Research Fellowship, Columbia College of Physicians and Surgeons, NY, NY
1993  Alpha Omega Alpha, Columbia College of Physicians and Surgeons, NY, NY
1998  Best Fellow Presentation: Society for Academic Emergency Medicine Annual Meeting

Selected peer-reviewed publications (Selected from 44 peer-reviewed publications)


Additional recent publications of importance to the field (in chronological order)

1. Innes AL*, **Woodruff PG***, Ferrando RE, Donnelly S, Dolganov GM, Lazarus SC, Fahy JV. Epithelial mucin stores are increased in the large airways of smokers with airflow obstruction. Chest. 2006 Oct;130(4):1102


**Research Support**

**ACTIVE**

R01 HL097591 (Woodruff PG) 7/1/2009 - 6/30/2013 3.0 Calendar Mo.
NIH/NHLBI $349,139
Role of Th2 and non-Th2 Inflammation in Airway Smooth Muscle Remodeling in Asthma

The goal of this study is to identify pathways linking Th2-driven inflammation to airway smooth muscle remodeling in human tissues.

R01 HL095372-01 (Woodruff PG) 9/24/2008 - 7/31/2012 4.2 Calendar Mo.
NIH/NHLBI $479,121
Molecular Phenotyping of Asthma

The goal of this study is to identify and characterize molecular phenotypes of asthma using gene expression profiling, quantitative morphometry and related imaging techniques.
The goal of this study is to identify sub-populations and intermediate outcome measures in COPD through a large multi-center longitudinal study.

Genentech (Woodruff, PG, Fahy, JV; Co-PIs) 5/15/2007 - 3/31/2011 0.4 Calendar Mo. $129,450
Analysis of Blood Markers in Asthma
The goal of this alliance is to partner with the preclinical asthma research group at Genentech to apply state of the art technology and analysis methods to the study of clinical samples from asthmatic subjects and controls to uncover unsuspected mechanisms of disease in asthma.

RC2 HL101487, NIH/NHLBI (Meyers D) 9/30/2009 - 9/29/2011 1.08 Calendar Mo. $114,849
Linking Genetic, Genomics and Phenomics to better understand Asthma Severity
The major goal is to establish genetic, genomic and phenomic profiles through integrated analyses of GWAS and gene expression data in large cohorts of subjects with a range of asthma severity. Role: Subcontract PI

U10 HL098107, NIH/NHLBI (Boushey HA) 9/30/2009 - 6/30/2016 0.6 Calendar Mo. $25,457
UCSF AsthmaNet Clinical Center
The major goals are to serve as a clinical center participating in the conduct of NHLBI-supported multi-center clinical trials of asthma therapies in children and adults with asthma, Role: Co-Core Leader

U10 HL074431, NIH/NHLBI (Lazarus SC) 9/1/03-8/31/09 0 Calendar Mo $718,506 (no cost extension)
COPD Clinical Research Network
The major goals are to serve as a clinical center participating in the conduct of NHLBI-supported multi-center clinical trials of COPD therapies

ARRA Supplement HL095372 (Woodruff PG) 7/1/2009- 6/30/2011 0 calendar Mo $74,900
NIH/NHLBI
The major goal of this project is to support a post-doctoral fellowship in applied bioinformatics.