In Memoriam

We are deeply saddened by the loss of Marion O. Sandler, whose vision and support led to the establishment of the Sandler Asthma Basic Research Center at UCSF. Her passion for excellence continues to foster our commitment to the understanding, control and cure of asthma.
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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

The SABRE Center is maturing into a successful research enterprise embedded within the greater UCSF scientific community. Notable benchmarks achieved this year include: (1) promotion of our first recruit, Dr. Liu, to tenure at UCSF, establishing the center as a successful base for academic advancement; (2) procurement of the first SABRE Center Program Project grant devoted to human asthma research and integration of basic investigators in the SABRE Center with translational investigators in the Airway Clinical Research Center; and (3) a fifth straight year with a continued rise in extramural funds secured by SABRE Center scientists. Investigators have published in competitive and scientifically visible journals and continue to open up novel lines of inquiry into the understanding of asthma and allergy pathogenesis. Interactions with our clinical colleagues in the Pulmonary Division who care for asthma patients are increasing in robust ways. We look forward to further successes in the coming year as we continue with our mission to conquer asthma.
The SABRE Center 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 11 postdoctoral trainees, 8 graduate students in Immunology and Biomedical Sciences, and 3 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 SABRE Center has established close working relationships with the Airway Clinical Research Center (ACRC) under the leadership of Dr. John Fahy, who has joined the Executive Board. The fruits of this collaborative effort resulted in the first NIH Program Project Grant awarded to SABRE investigators, with a major focus centered on human tissues obtained through the ACRC. The SABRE Center is beginning to mature into a self-standing research addition to the UCSF campus with the capacity to contribute to our understanding of an important human disease. We will review the individual investigators and their progress, followed by an overview of the constituents of the Center, a brief discussion of achievements and finally a look at the increasing ability to obtain extramural support for these activities.

**Investigators**

Dr. Ansel is working to understand the gene expression pathways that underpin differentiation and regulation of cell fate and function in allergy, particularly asthma. His focus remains on microRNAs, transcription factors and epigenetics as critical executioners of these pathways. He is building increasing excitement over his discoveries in the field as evidenced by recognition of his early achievements through solid publications and enhanced amounts of extramural grant support. He published 3 manuscripts in 2011-12 as senior author, including two in *Immunity*, that describe aspects of T cell differentiation pathways as elucidated through studies of transcriptional control and microRNA expression. He discovered a role for microRNA-29 in regulating Th1 cell differentiation through regulation of T-bet, an important downstream transcriptional activator of this effector pathway. He has two additional manuscripts addressing the role of specific microRNAs in lymphocyte function that are being revised after favorable reviews at competitive peer-reviewed journals. He is actively pursuing studies using materials collected from patients with asthma in the Airway Clinical Research Center. He is collaborating in studies with the Functional Genomics Core, the Animal Physiology Core and the Flow Cytometry Core. He collaborates with multiple other investigators in the SABRE Center.

Dr. Ansel is finishing the last year of a 3-year Dana Foundation Award as a Human Immunology Scholar to support his investigations of microRNAs in human asthma. Based on studies completed with this Award, he received his first R01 funded grant from the National Heart, Lung and Blood Institute of the NIH to pursue collaborations with Dr. Prescott Woodruff.
in the Airway Clinical Research Center, bringing in $1,796,403 in direct research dollars over a five year period. Dr. Ansel also was a participant Principal Investigator as part of the first Program Project Grant among SABRE Investigators from the NIH. This grant, which includes Drs. Ansel, Fahy, Woodruff and Locksley, received an overall priority score of 1.1, and is scheduled to begin funding in July 2012 at a total level of approximately $1,575,000 per year over the next 5 years. In recognition of his outstanding accomplishments as a young investigator, Dr. Ansel was recently awarded a Leukemia & Lymphoma Society Scholar Award, which will begin July 1, 2012, resulting in approximately $525,000 in direct costs over the next 5 years. Dr. Ansel participated in increasing numbers of national and international scientific conferences related to his expertise. He was invited to speak in Japan and Finland over the past year.

Personnel in the Ansel laboratory include 4 graduate students, with 2 supported by National Science Foundation Predoctoral Research Fellowships and 1 a recipient of an HHMI Graduate Education in Medical Science (GEMS) Training Program Award to pursue translational studies in asthma patients in collaboration with Dr. Fahy in the Airway Clinical Research Center. The postdoctoral fellow is supported by a Swiss National Fellowship. Dr. Ansel’s first laboratory manager/technician was accepted into the Harvard Immunology Program to begin this fall.

Dr. Liu is pursuing the mechanisms that control 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. During his studies at UCSF, Dr. Liu identified an important role for GSNOR in protecting liver cells from genotoxic stress. He went on to identify the mechanism as linked to the nitrosative inactivation of a DNA alkyltransferase involved in DNA repair. He published 5 peer-review manuscripts over the past 2 years addressing roles for GSNOR-mediated nitrosylation in DNA damage in the liver related to oncogenic stress or hepatitis B virus infection and in the regulation of T cell function. He continues to address the role of GSNOR in immune pathways related to asthma in a collaborative publication with Dr. Krummel in the Imaging Core and in on-going but incomplete studies addressing cell-specific deletion of GSNOR in different lung cell populations in order to pinpoint the origin of GSNOR amenable to therapeutic intervention in asthma. Dr. Liu is working collaboratively with individuals in the Functional Genomics, Animal Physiology, Genetics and Flow Cytometry Cores. He presented his work at both national and international scientific meetings.

Dr. Liu is supported by an R01 and P01 on which he participates. These grants, which contribute over $475,000 direct costs per year, are from the National Cancer Institute of the NIH and study aspects of oncogenesis mediated by GSNOR deficiency, an important issue that must be addressed in order to sustain interest in this enzyme as a viable asthma therapeutic target. He is working to develop sufficient preliminary and published information on the role of GSNOR in smooth muscle contraction in order to pursue this as an asthma-related source of NIH funding. In recognition of his accomplishments, Dr. Liu was promoted to Associate Professor, effective
Dr. Shin studies dendritic cell maturation and antigen processing, which represents an extension of her postdoctoral training where she described a novel pathway affecting the turnover of surface complexes of major histocompatibility-peptide complexes at the surface of the dendritic cells, a process which was regulated by ubiquitination. She is continuing studies of dendritic cells with an emphasis on cells collected from the human lung. She published two peer-reviewed manuscripts in the past year addressing the role of ubiquitination in controlling not only MHC class II but also surface CD86, an important co-stimulatory molecule, on dendritic cells. A third manuscript describing the unexpected finding that IgE receptor on dendritic cells promotes serum IgE clearance, was reviewed positively at the Journal of Experimental Medicine and is under revision. Dr. Shin supports her laboratory with two young investigator awards from the Cancer Research Institute and from the American Heart Association. She re-submitted an R01 to the NIH after missing the payline on her first submission. She also submitted an NIH Director’s New Innovator Award grant. She was invited to an Allergy Drug Discovery and Development Conference and attends prominent national meetings.

Dr. Shin has established close collaborations with pulmonary physicians in the Airway Clinical Research 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 with human FcεRI expressed on mouse cells in a pattern resembling its expression in humans (developed in the Kinet lab at Harvard). Dr. Shin works closely with the Airway Clinical Research 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 was selected to work on a specific human disease, in this case, asthma. He brings expertise in optical imaging of the immune system and a passion for understanding the pathogenesis of allergic inflammation in the lung that causes asthma. Dr. Allen’s interests address the mechanisms by which high-affinity IgE-producing B cells and plasma cells are produced. Surprisingly, this remains a poorly understood pathway of fundamental importance to the pathogenesis of allergy and asthma. He published 5 manuscripts in peer-reviewed journals over the past 2 years, including collaborative co-publications with Drs. Locksley and Ansel in the SABRE Center, where his technological innovations were critical to these successful publications. He published his first manuscript as senior author in Immunity, describing his important discovery that IgE heavy chains inherently drive movement of B cells out of germinal centers, a process that may serve to limit somatic hypermutation and thus affinity. This finding will drive new hypotheses regarding mechanisms by which some allergic individuals develop high-affinity IgE, and constitute major efforts of his laboratory. His construction of an IgE reporter mouse that permits the efficient tracking of IgE-switched B cells constitutes an important technical advance for the field.
Dr. Allen participated in the shared instrumentation grant that resulted in the purchase of an Aria II flow cytometer and continues to oversee the sorting and flow activities of the SABRE Center. Now in his 5th year as a UCSF Fellow, Chris submitted his first R01 in February, and submitted an NIH New Innovator Award that has been selected for the second round of review (fewer than 20% were selected for further consideration). Chris works closely with the Flow Cytometry, Imaging and Small Animals Physiology Cores in the SABRE Center, and participates actively with the Airway Clinical Research Center is discussions regarding translational research. Dr. Allen has a senior postdoctoral trainee in his laboratory. As this is his last year of support by the UCSF Fellows’ Award, Chris has already been pursuing recruitment possibilities at several institutions, including at UCSF.

Core Activities

An important component of the SABRE Center has been support and guidance for advanced technology cores. The specific workings of these Cores and their achievements are detailed elsewhere in this report. The SABRE Center contributes to cores in Mouse Physiology (which provides both acute and chronic mouse models of allergic lung inflammation, including challenge with model antigens, fungal antigens and house dust mite antigens), Functional Genomics, Genetics, Flow Cytometry and Imaging, including video, two-photon, confocal and total internal reflection instruments. Our largest monetary support goes to the Mouse Physiology and the Genetics Cores, which support small animal models and the collection of cohorts of carefully phenotyped families with asthma, respectively, in order to meet specialized needs of importance 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 contributed to 9 AAF studies from non-UCSF investigators over the past year. The Genetics Core has procured the largest cohorts of Latino and African American families afflicted with asthma for use in genetic studies, and continues to participate in a number of multi-institutional studies for genome-wide investigations. The remaining cores are supported by smaller amounts of funding, typically to core directors and operators or to help support maintenance contracts for equipment, costs that are difficult to recover through recharge or other mechanisms. The Imaging Core has made large technical strides in providing optical support for live lung and lymph node imaging. SABRE funding is concentrated on developing novel technologies to enhance live imaging capacity, to establish site-specific photo-ablation technology and to extend imaging capacity to sections of human lung. Participation in the Imaging Center has grown to support over 166 users involving 66 Principle Investigators from 26 different Department or Organized Research Units at UCSF. Substantial training of new users and software development to support these new technologies is an ongoing part of the mission. Thus, in a relatively short time, the Imaging Core has become an integral and productive component of the scientific community at UCSF. The Functional Genomics Core, led by Dr. David Erle, has used SABRE support to enable improved technologies for high throughput sequencing, CHIP-seq and microRNA profiling.
SABRE support for these technology cores has been leveraged to attract NIH funding: the Animal Physiology Core is additionally supported by technical core funds from 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 the 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. Support for the Flow Cytometry Core, which is largely self-supported and self-operated, is restricted to financial help with maintenance contracts, data base management and emergency laser failure, issues that are incompletely covered through recharge or grant-based mechanisms.

These Cores achieve substantial leverage of resources, and over the past 2 years contributed to at least 12 successfully funded extramural grants, 7 postdoctoral fellowships and over 40 peer-reviewed manuscripts. Despite these successes, the fiscal constraints driven by the current difficult economic downturn has necessitated trimming 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. Recharge systems have been set in place for the Functional Genomics Core, the Mouse Physiology Core and the Flow Cytometry Core, and these are constantly reassessed to ensure that fiscal accountability is maintained such that these services are not only sustained, but enhanced by upgrading and enabling new technologies.

Airway Clinical Research Center

A major area of importance to the SABRE Center has been establishment of the Airway Clinical Research Center (ACRC) at UCSF Medical Center at Parnassus. The founding aim was to create a Center that was human subject centered, mechanism oriented and linked to strong basic research programs in lung disease, including the SABRE Center. After a $3 million renovation funded from the Cardiovascular Research Institute, the Department of Medicine and industry contributions, the Center opened in 2008. The ACRC occupies 3500 square feet of space and includes 5 separate patient testing rooms. Capacity exists to take histories and perform physical exams, collect blood and bronchoscopy specimens, do pulmonary function testing and airway provocation with methacholine or allergen, and to apply allergy skin tests. Specimen processing and tissue storage also occur in the Center. The space is dedicated to human research – no clinical activities occur. Approximately 1200 subjects were evaluated at the Center in the past year.

Activities in the ACRC support the clinical research activities of several multicenter network studies of importance to asthma, including NIH AsthmaNet (PI: Homer Boushey); NIH Severe Asthma Research Program (PI: Fahy) and the NIH Asthma and Allergic Diseases Clinical Research Centers (PI: Sheppard). The Director of SABRE, Dr. Locksley, participates as a
consultant or participant on all of these network grants. The emergence of the ACRC as a vibrant center for translational asthma research was a major contributor to the first Program Project grant awarded to SABRE Investigators (Locksley, Fahy, Ansel, Woodruff), which will start in July of 2012. 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 Airway Clinical Research Center, confirming that this will serve as an important integrative unit for translational interests of the SABRE Center. There is also a monthly research conference for SABRE/ACRC investigators at the Parnassus site to promote interactions and collaborations.

Successful competition for extramural support

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.

Since the initial recruitment of Dr. Liu and the additions of Drs. Ansel, Shin and Allen, we have seen a steady climb in the amounts of external funds accrued by SABRE investigators in support of their research efforts. This has occurred despite the difficult funding climate, and attests to the capacity of the Center to serve as a nidus for successful research. As demonstrated by our ability to obtain a Program Project this year by capitalizing on the access and expertise of colleagues in the Airway Clinical Research Center, we believe that building multicomponent research teams to take on difficult problems associated with asthma will prove a successful strategy for maintaining this funding momentum.
Growth in accumulated extramural funds by core SABRE investigators.

In addition, activities related to the SABRE Center 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 2011-12


*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.


The role of IL-17, a cytokine that serves to attract neutrophils to sites of inflammation, in asthma is of increasing interest as clinicians begin to understand non-allergic forms of asthma. Using both mouse and human tissues, the authors here show that IL-17A produced by CD4 T cells in the lung can directly mediate airway smooth muscle hyper-contractionality and expose a mechanism related to smooth muscle myosin responsiveness. This study will drive much interest in understanding whether targeting this cytokine or these cells may comprise a therapeutic strategy in some patients with non-allergic asthma.


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.


The authors developed new technologies to interrogate microRNA expression in samples of mouse and human T cells and discover that microRNA-29 is highly associated with inflammatory Th1 CD4 T cells. They go on to find that microRNA-29 directly regulates T-bet expression, thus defining a pathway by which differentiation of Th1 cells is regulated. The fine-tuning of cell differentiation by microRNAs may enable new technologies for targeting inflammatory pathways in disease, an opportunity which the authors hope to exploit in ongoing studies.


Basophils remain poorly studied with efforts hampered by the availability of robust reagents that allow tracking these cells in situ. In this paper, a novel mouse strain was generated in which basophils are fluorescently labeled, thus allowing their recovery by flow cytometry or their identification in tissues using immunohistochemistry. In a collaboration between the Locksley and Allen labs in the SABRE Center, this paper provides the first intravital imaging of basophils moving through living tissues during allergic immune responses. The mice have been
deposited at Jackson Laboratories where they will be made available to the general scientific community for studies in basophil biology of importance to asthma research.


Despite the importance of IgE in mediating manifestations of atopy, methods for studying the B cells that produce IgE were lacking, thus precluding the examination of this pathway as a potential strategy for intervention. The authors devised a knockin reporter mouse strain that reveals cells that have productively switched the immunoglobulin locus to produce IgE. After confirming that they can now isolate and image IgE-producing B cells in vitro, the authors make the unexpected observation that IgE B cells mature in germinal centers, in contrast to prior dogma, but that expression of a successfully rearranged IgE BCR leads to immediate upregulation of Blimp-1 and egress from the germinal center to become a memory B cell or plasma cell. This study reveals a cell-intrinsic mechanism that serves to limit the extent of somatic hypermutation, and hence affinity maturation, that occurs once a B cell expresses IgE. The possibility that patients with severe atopy might dysregulate this highly controlled pathway is being explored.

Organization of the body of this Annual Report

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 hoping to resurrect partial support of this valuable Program for the most promising internal UCSF proposals. 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 Sandlers’ 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 promoting 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. Dr. John Fahy, the Director of the Airway Clinical Research Center at UCSF, has joined the Executive Committee to facilitate interactions between SABRE members and the activities of the Clinical Research Center. The Executive Committee is 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

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

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

John V. Fahy, M.D., Professor
Department of Medicine

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

Dean Sheppard, 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 Darmsädter 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.
SABRE CENTER INVESTIGATORS
Richard M. Locksley, M.D.
Professor, Departments of Medicine and Microbiology & Immunology
Investigator, Howard Hughes Medical Institute

UCSF
513 Parnassus Avenue
Medical Sciences, S-1032B, Box 0795
San Francisco, CA 94143-0795

Tel: 415-476-3087
Fax: 415-502-5081
Website: Cancer Center
Immunology Graduate Program
Pulmonary & Critical Care Division
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 against 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 immunity 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 these methods, 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 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

TIM-2 is expressed on B cells and in liver and kidney and is a receptor for H-ferritin endocytosis. The Journal of Experimental Medicine, 202(7), 955-965.


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.

Our primary experimental system is the differentiation of the central coordinators of adaptive immune responses -- helper T cells. Upon immune activation, naïve CD4+ T cells can differentiate into several different helper T cell effectors subtypes (e.g. Th1, Th2, Th17, iTreg, Tfh, etc.). These lineages are defined by their characteristic gene expression programs and mediate distinct immune functions. As such, proper regulation of the lineage decisions of helper T cells critically determines the development of protective immunity against a great diversity of pathogens, and improper or exaggerated responses contribute to the development and pathology of autoimmune diseases, chronic inflammation, allergy, and asthma. We and many others have documented how these gene expression programs are controlled by external factors from other cells and the environment, inducible and lineage-specific 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). Naïve 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 examine the helper T cells in the blood and inflamed lungs of asthma patients for differences in functional effector subset representation and the expression of miRNAs that may contribute to their pathogenic properties 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 systemic inflammation, asthma, cancer, and many other physiological and pathological processes.

**GSNOR and asthma** It has been demonstrated with GSNOR-deficient (GSNOR-/-) 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-/- 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


   a. †co-senior author; *Corresponding author; ‡Deceased August 31, 2009.

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
Objective

The objective of the Sandler animal physiology and morphology core facility is to provide support to investigators at UCSF and other research institutes for their asthma related research. The core facility has extensive experience in generating and analyzing variety of allergic animal models. Investigators gain insight to the molecular mechanisms of asthma development through either full or partial service provided by the core laboratory. The core also provides training to students, technicians and post-doctoral fellows in techniques relevant to the animal models and their analysis.

Accomplishments

During the year of 2011, the core laboratory has provided support to many investigators at UCSF (Drs. Mark Ansel, Jason Cyster, David Erle, Xiaozhu Huang, Limin Liu, Dean Sheppard, Art Weiss) and at other institutes (Drs. Anthony Gerber, National Jewish Hospital of Denver and Gisli Jenkins from University of Nottingham) for their projects studying airway physiology, immunology, cell and molecular biology and other related areas. The service provided by the core lab has significant impact on many asthma related research projects. Dr. Dean Sheppard has been interested in studying biologic role of integrins and focused on TGF-β mediated protection from persistent airway hyperresponsiveness (AHR) as influenced by the αvβ6 and αvβ8 integrins. For αvβ6 study, the core lab tested multiple allergic models and finally decided to apply a mast cell dependent model to the study. When mice lacking αvβ6 integrin were sensitized and challenged to OVA, they were protected from exaggerated airway narrowing but no obvious reduction of lung inflammation, mucous production and sub-epithelial fibrosis were observed. Further investigation suggests that intra-epithelial activation of TGF-β by the αvβ6 integrin regulates airway responsiveness by modulating mast cell protease expression, and that these proteases and their proteolytic substrates could be novel targets for improved treatment of asthma. The work is currently published in Journal of Clinical Investigation. For the αvβ8 study, we found that mice lacking αvβ8 on dendritic cells were protected from AHR in response to house dust mite and ovalbumin sensitization and challenge. These mice failed to generate Th17 cells in the lung after OVA sensitization and challenge, and the diminished contraction of tracheal rings from these mice was reversed by IL-17A. These data indicate that IL-17A produced by T17 cells contributes to allergen-induced AHR through direct effects on airway smooth muscle and the manuscript has been accepted by Nature Medicine.

The animal physiology core also provided great assistance to many AAF awardees in 2011. The core supported projects of Drs. Dan Dumon, Christopher Garcia, Lily Jane, Dean Li, Max Krummel, Kenneth Rock, Jennifer Whistle and Eric Xu. Most of these are full service support including experimental design, allergic animal model establishment, functional analysis, sample collections and final report. Sometimes the core lab needs to help with animal purchase as some of the investigators do not have animal study protocol due to their primary study interest. Many exciting results have been generated that lead to further related studies.
To address our user’s need optimally, the core lab has been constantly testing and modifying the protocol to comply with the experiments proposed by investigators. Designing different treatment regimen is the most common request by investigators. We sometimes change drug/inhibitor delivery multiple times/ways for a single experiment upon researcher’s request. This way we make sure the best outcome can be achieved and the time and cost can be reduced. We have also been continuing our effort improving the existing house dust mite model, a more clinically relevant model that has become more popular. Dr. Dean Sheppard’s group submitted their original manuscript to *Nature Medicine* with data using OVA model and reviewers requested a validation using house dust mite model for the revision. The core lab performed HDM experiment that showed a similar outcome as the OVA model. The verified findings significantly improved the strength of the paper.

In 2011, the animal core lab experienced significant change due to a personnel reduction as result of financial tightness. We re-organized our routine assignment based on the current personnel structure. Each core lab member has been assuming extra duties on top of their assigned work. There is slight delay in results to investigators but so far no significant impact on the quality of the service.

**Training and Integration with Sandler Program**

In addition to general education from the experiments performed by the core, many labs benefit from free of charge hands-on training service provided by the core facility. In 2011, investigators from multiple laboratories (Labs from UCSF- Drs. Cliff Lower and David Erle; other research institutes - Dr. Donata Vercelli at University of Arizona, Dr. Peter Dube at University of Texas Health Science Center and Dr. Gisli Jenkins at University of Nottingham) sent lab members to the core lab to observe the routine performance and get hands-on experience using equipment and protocols. Sara Mobley from University of Arizona made a special trip to visit us last year. She spent time observing core lab performing experiments and processing routine samples, and obtained protocols used routinely by the core lab. Sara has been able to run lung function analysis in the studies of murine models of allergic asthma at her own lab and continue to contact the core lab whenever necessary. Amanda Atler from Jenkins’s lab, worked closely with the core lab members to examine role of integrin beta5 in Aspergillus allergic model. The final results have helped her manuscript be published in the *Journal of Immunology*.

Additionally, the core lab also tested a fee-based training last year for a company (FivePrime Inc.), which may not be the ideal format for the future reference. The core lab director and senior physiologist made great efforts in planning and training up to four employees from the FivePrime Inc., that helped the company initiate their own pulmonary physiology unit. However, it was not cost effective for the university and the core lab.

The animal core director attends weekly UCSF pulmonary conference, monthly SABRE meeting and the AAF annual meeting. This provides direct interaction between the animal core and investigators who are interested in using core service. Potential experiments can be discussed and oftentimes can be arranged during the interaction.
Future Activities

Some protocol and method developments, such as regular OVA chronic model, are currently in progress. We need to improve the consistency and reduce the variability of our house dust mite model. We have been paying close attention to our key equipment; FlexiVent that makes the lung function measurement available, as the machine model we are using has been discontinued and technical service will soon be no longer available. With the continuing support from the SABRE Foundation, the animal physiology and microscopy core facility will continue to provide the UCSF community with the high quality service that is critical in our research environment.

Grants and Publications

Grants

The animal physiology and morphology core continues to work with many investigators to provide consultations and support letters for their grant applications. The core director either meets in person (local investigators) or has phone conversations (outside institutes) with grant applicants in helping them understand the principles of allergic animal models and carefully discusses the experimental protocols, animal numbers and final outcomes. The AAF funding has gained growing popularity but applicants often have not worked with asthma before, nor even with lung diseases. So for applicants who propose in vivo animal experiment, a brief description of allergic animal model will be usually provided so investigators can incorporate it into the proposals. We not only help investigators funded by NIH, AAF and other grants but also make commitments to collaborate with investigators who submit proposals if they are funded. The core staff receive direct salary support from Sandler Foundation, NIAID and recharge the system.

Publications


Makoto Kudo, Andrew C. Melton, Chun Chen, Mary B. Engler, Katherine E. Huang, Xin Ren, Yanli Wang, Xin Bernstein, John T. Li, Kamran Atabai, Xiaozhu Huang*, Dean Sheppard. IL-17A produced by ab T cells drives airway hyper-responsiveness in mice and enhances mouse and human airway smooth muscle contraction. Nature Medicine. Accepted 1/2012 (in press)
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 (Ansel and Shin), many other faculty who participate actively in a range of SABRE activities (including Chapman, Erle, Krummel, Seaman, 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>Effect of Eri1 on mRNA profile and translation in natural killer cells. In Progress.</td>
</tr>
<tr>
<td>Pedro Avila¹</td>
<td>Mucosal gene expression in respiratory infections. Completed.</td>
</tr>
<tr>
<td>Harold Chapman</td>
<td>Assessing the transcriptional profile of Integrin β4 on alveolar epithelial cells. Completed.</td>
</tr>
<tr>
<td>Harold Chapman</td>
<td>Identification of epithelial progenitor cells by integrin profile. Completed.</td>
</tr>
<tr>
<td>David Erle</td>
<td>IL-13 and IL-17 responsive microRNAs in the airway epithelium. In Progress.</td>
</tr>
<tr>
<td>James Frank</td>
<td>Claudin-18 regulation of alveolar barrier function. Completed.</td>
</tr>
<tr>
<td>Anthony Gerber²</td>
<td>Glucocorticoid-KLF15 targets in mouse in lung. Completed.</td>
</tr>
<tr>
<td>Matthew Krummel</td>
<td>Transcriptional profile of dendritic cell populations. Completed.</td>
</tr>
<tr>
<td>Ross Metzger</td>
<td>Early left/right asymmetry in developing mouse lung. In Progress.</td>
</tr>
<tr>
<td>Dean Sheppard</td>
<td>The role of the αβ8 integrin in liver regeneration. Completed.</td>
</tr>
</tbody>
</table>
Jeoung-Sook Shin mRNA analysis of mouse thymic dendritic cell subsets.  
*Completed*

Keoki Williams\textsuperscript{3}* Pharmacogenomics of asthma. *Completed.*

Asa Wheelock\textsuperscript{4} COPD and gender. *Completed.*

Asa Wheelock\textsuperscript{4} Effects of subway exposure on healthy and asthmatic populations. *Completed.*

Prescott Woodruff miRNA profiling in asthma patients. *Ongoing.*

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

**Personnel:**
Andrea Barczak (manager) and Rebecca Barbeau (SRA), and Joshua Pollack (biostatistician) continue to provide outstanding service to core users.

**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. This past year, we have focused the majority of our efforts on implementing next generation sequencing services. Although microarrays continue to be a very useful and cost effective method for genome-wide profiling of mRNAs and miRNAs, next generation sequencing technologies offer advantages in terms of sensitivity and specificity. Results from our first mRNA-seq pilot experiment (Fig. 1) showed that RNA-Seq had a substantially greater dynamic range than microarrays when comparing two samples with modest differences in gene expression. This is consistent with other studies showing that RNA-Seq increases the ability to detect differential expression, especially for genes expressed at a low level.

\textbf{Figure 1.} Whole transcriptome expression analysis using RNA-Seq versus microarrays. Lung RNA from Agr\textsuperscript{3/-} versus control mice were analyzed by RNA-Seq (Illumina HiSeq 2000) or microarrays (Agilent). Each dot represents one transcript (~20000 transcripts were represented on both platforms). Note that fold-differences estimated by RNA-Seq were generally greater than those estimated by arrays.
During the past year, we have prepared 32 RNA-Seq libraries, established working relationships with 3 UC-affiliated facilities (The UCSF Center for Advanced Technology, the UCSF Institute for Human Genetics Genomic Core Facility, and the UC Davis Genome Core) that have run our samples on Illumina HiSeq 2000 instruments, and installed a new high-end workstation for analysis of next generation sequencing data.

**Plans for the coming year**

We will continue to offer assistance with whole-genome analysis of mRNA and miRNA expression and ChIP analysis. In addition to the array-based analyses offered in previous years, we intend to encourage investigators to employ next generation sequencing-based approaches (RNA-Seq, ChIP-Seq) where appropriate. As detailed above, we have already implemented methods for RNA-Seq but further work is planned to implement protocols that will allow for analysis of very limited amounts of starting material and for strand-specific sequencing and analysis of non-coding RNAs.

There have been significant barriers to the use of these new approaches and we will continue to work to lower those barriers for our users. The three major barriers have been cost, technical issues, and data analysis. Technical advances have reduced costs and we are now able to offer RNA-Seq at a cost that is only ~50% higher than an array-based approach. We have optimized protocols for library generation and other steps in the process and now offer comprehensive RNA-Seq services (including library preparation), which alleviates investigators of the need to develop and optimize protocols in their own laboratories. Joshua Pollack, our core biostatistician, will continue to implement state-of-the-art methods for analyzing next generation sequencing data.

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.

**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 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]). 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

The core is now supported by SABRE and by a recharge mechanism, which covers labor and reagent costs for projects performed by the core. Core staff members work closely with investigators as they apply for NIH funding via R01 and other mechanisms. The following list includes asthma-related projects supported by the core that received new NIH funding during the last year and projects now applying for additional funding from NIH:

<table>
<thead>
<tr>
<th>PI</th>
<th>Project Number</th>
<th>Title</th>
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<tr>
<td>Ansel, Karl Mark</td>
<td>1R01HL109102-01</td>
<td>Role of miRNAs In Th2-driven Inflammation in Asthma</td>
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<tr>
<td>Chapman, Harold A</td>
<td>1U01HL111054-01</td>
<td>Epithelial Progenitor Cells in Lung Repair and Regeneration</td>
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<tr>
<td>Gerber, Anthony N</td>
<td>1R01 HL109557-01A1</td>
<td>Role of Klf15 in Airway Smooth Muscle and the Response to Glucocorticoids</td>
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<td>Pending:</td>
<td></td>
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<tr>
<td>Frank, James A</td>
<td>R21 HL111707-01A1</td>
<td>A Claudin-18 Deficiency in the Pathogenesis of Asthma</td>
</tr>
<tr>
<td>Renewal of:</td>
<td></td>
<td></td>
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<tr>
<td>Sheppard, Dean</td>
<td>5U19AI077439</td>
<td>Mechanisms of Initiation and Persistence of Allergic Asthma</td>
</tr>
</tbody>
</table>

The UCSF Clinical and Translational Sciences Institute provided some core funding until July 2011, when CTSI elected not to continue to support any core laboratories. This reduced our non-recharge funding. Hence continued support from SABRE is critical in allowing us to maintain services and develop new technologies for support of SABRE investigators.

Publications

Core-supported projects led by SABRE-affiliated faculty:


Other core-supported projects:


**Genetics Core**  
*Director: Esteban González Burchard, M.D., M.P.H.,*  
*Professor of Bioengineering & Therapeutic Sciences and Medicine*

**Vision**

We built a multidisciplinary research center and we are taking a comprehensive approach to asthma research. Our approach integrates gene-environment studies with basic biology, population genetics, social and environmental epidemiology. We built a network of “minority serving” providers to recruit well-phenotyped subjects from throughout the U.S. As a result of our efforts we have the largest populations of well characterized minority children with and without asthma in 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. 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 2011-2012**

1) **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 generated GWAS data from our study populations 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 which was published in Nature Genetics. The lead author, Dara Torgerson, was recently recruited to UCSF as an Assistant Professor in the Lung Biology Center.
Admixture Mapping Meta-analysis Through our work with the EVE Consortium we are currently working on a follow-up to the original GWAS to find additional loci via ancestry association or admixture mapping. We have combined data from the African-American and Hispanic/Latino studies within EVE (9 studies in total), comprising over 7,000 individuals. For all individuals we have estimated local ancestry using LAMP algorithms to have locus-specific ancestry calls for all individuals across the genome. The studies comprise a diverse group of designs including case-control, trio-based, and pedigrees. Within this project we have developed novel ancestry imputation methods as well as methods for admixture mapping on large datasets. For replication we have leveraged GALA II as it is the largest study of asthma with genome-wide data. Currently we are assessing multiple methods of meta-analysis as well as analyzing permutation data to calculate the adjusted multiple testing threshold. We anticipate this project to be completed in the next few months.

2) Collaborating Faculty In 2011-12 we have collaborated with the following faculty: Carl Ware (Sandford Burnham Medical Research Institute), Marsha Wills-Karp and Gurjit (Neeru) K. Khurana Hershey (Univ. of Cincinnati), Stephanie London (NIEHS), Keoki Williams (Henry Ford Hospital), Rajesh Kumar (Children’s Memorial, Chicago), Eran Halperin (Tel Aviv University), Kathleen Barnes (Johns Hopkins), Jim Gauderman (USC), Mehrdad Arjomandi, John Balmes, Robert Nussbaum, Neil Trevdi, Kamran Atabai, John Fahy, Nadav Ahituv, Rosemary Akhurst, Ryan Hernandez, and Jonathan Weissman (UCSF). We are also in discussions with investigators at Genentech.

Patient Recruitment We recruited three study populations: 1) the Genetics of Asthma in Latino Americans (GALA I) Study (parent-child trios), a family-based study of Puerto Rican and Mexican children with asthma 2) the Genes-environments & Admixture in Latino Asthmatics (GALA II) Study and 3) the Study of African Americans Asthma, Genes & Environments (SAGE). Combined we now have the largest pediatric asthma genetic study of Latino and African American pediatric populations in the U.S. (nearly 6750 children with and without asthma). A longitudinal study of asthma treatment and control is ongoing in a subset of the study population (n~1000). All subjects are extensively well phenotyped. We have detailed clinical measurements (spirometry, maximal bronchodilator response testing, methacholine challenge, skin prick testing, and IgE measurements), biologic specimens (serum, RNA, DNA and nasal epithelia), geocoded air pollution measures and questionnaire-based information regarding environmental and social risk factors. We have genome-wide data available for all GALA I and II participants.

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. These large cohorts will allow investigators the opportunity to test and replicate potentially promising genetic targets and to test for complex gene-environment interactions.

3) Faculty Recruitment We have recruited two young scientists, who have significant research experience in minority populations and asthma genetics.
Dara Torgerson, Ph.D. was at Genentech but we were able to recruit her back to UCSF as of January 5th, 2012. She has training and expertise in population genetics, bioinformatics, and applied statistical genetics, and has collaborated 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), the NHLBI funded asthma resequencing project, GALA (Genetics of Asthma in Latinos), and the EVE consortium.

This past year she has been extremely productive, resulting in five first-author manuscripts either published, in press, or in the final stages of peer review from her collaborative research. Notably, she led the analysis of the NIH-sponsored effort to pool results from all U.S. genome-wide association studies for asthma, resulting in a first-author paper that was published in Nature Genetics.

Ryan Hernandez, Ph.D. started at UCSF on April 1st, 2010. He has specific expertise in statistical genomics, computation biology, and population genetics. He was recently appointed the new co-chair of population genetics in the 1000 Genomes Project and is actively engaged in generating and discussing cutting edge methods for analyzing complex populations using next generation sequencing technologies. His preliminary work on pilot data from the 1000 Genomes Project resulted in a first author Publication in Science last year. Ryan has become an active member of the UCSF faculty, and has multiple collaborative projects underway.

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

1. RO1 Admixture Mapping of Obesity and Asthma
2. K24 Admixture Mapping of Lung Disease
3. RO1 Exome sequencing of extreme bronchodilator drug response among minority children with asthma.
4. Foundation Proposal: In utero SHS in Latino and African American Children
Publications supported by the Strategic Program for Asthma Research and/or the Sandler Family Foundation.

2011-2012 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 on-line 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 sorters 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 have enabled operation by a single individual, thus optimizing use and minimizing cost.

Becton-Dickinson Biosciences LSR II Flow Cytometer with 4-laser, 10-color, 12-parameter capability centered around 488 nm OPL, 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 OPL, 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 18 months, 41 laboratories at the UCSF Parnassus and Mission Bay campuses have used the facility 2 or more times, with 29 labs over 3 times. In turn, the numbers of users per laboratory has also stabilized at 2.2 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 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 16% of the publications listed in the bibliography for the current annual report.
Microscopy Core
Managing Director: Sebastian Peck.
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 such as the asthmatic lung 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 2012, the core will be trying to advance three specific goals for intravital imaging. Note that in the 2011 period, we have enhanced our efforts in subcellular-level imaging of human lungs and have extended our technologies in the imaging of mouse asthmatic lungs. 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 2012 with miniaturization of the lung-stabilization rigs and with high-speed 3D volume surveying capacity software and automation code to speed up the detection and mapping of ‘rare’ but significant events in lung tissues.

2. To continue to elaborate methods for site-specific photoablation and photoactivation in tissues, through the use of light-sensitive conjugates and refinement of digital micromirror arrays.

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 and through collaboration with asthma researchers with access to primary biopsy material.

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 and 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 166 registered users of the BIDC. These users represent 66 principal investigators or labs. These labs are drawn from 26 departments or organizational units. In 2011, 59 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. After initial trainings BIDC staff continue to consult and assist with projects on an individual basis. Since we don’t charge for our time through recharges, users are able to ask questions and get assistance as needed. We have specifically trained users from the following labs:

Alliston       Looney
Beggs          Margeta
Bickler        Nishimura
Bishop         Nystul
Bluestone      Roose
Chapman        Rosen
Coussens       Rowitch
Debnath        Rubenstein
DeFranco       Sall
Engel          Schneider
Evan           Sheppard
Fahy           Springer
Harris         Stratmann
Koliwad        Szoka
Krummel        Vexler
Kubes          Weaver
Lanier         Werb
Locksley       Wynshaw-Boris
ASTHMA RELATED RESEARCH PROJECTS
Evolving Microenvironments in Airway Inflammation
Program Director:  George H. Caughey, M.D.

Program Project Grant HL.024136 is nearing completion of its 32nd year, the second of a planned five years of interdisciplinary study of airway inflammation competitively renewed on May 11, 2010. Each of the component projects focuses on different populations of airway cells and molecules mediating structural changes in the airway accompanying chronic airway inflammation. The Projects are supported by two Cores, one administrative and one scientific (Tools for Analysis of Airway Inflammation).

Summary of Advances this Year

The following paragraphs summarize major advances by the component projects over the past year.

Project 1: Roles of Peptidases in Chronic Airway Inflammation (Project Leader: G.H. Caughey)

One of Project 1’s major achievements in the second year of this competitive cycle was the discovery that some strains of the gram-negative bacterium Pseudomonas aeruginosa, which is a common cause of airway infections in cystic fibrosis and pneumonia in immunocompromised patients, stimulate histamine synthesis and secretion in neutrophils. This effect is relatively selective for neutrophils, in that it is not seen in Pseudomonas-exposed mast cells, which are the best known cellular source of histamine and are the major source of histamine in lung tissues at baseline. The effect is also strain-selective, in that it was not seen in a cytotoxic strain of Pseudomonas. Our work established that stimulatory effects of the PA01 strain of P. aeruginosa on neutrophil histamine production are mediated by stimulation of mRNA and protein corresponding to histamine decarboxylase, which catalyzes the rate-limiting step in histamine synthesis. The effects were identified first in vitro and confirmed in vivo in mice with airway and lung infection with P. aeruginosa. These findings raise the possibility that Pseudomonas-stimulated neutrophils enhance airway inflammation by producing histamine and are relevant to the pathophysiology of airway obstruction and inflammation in cystic fibrosis, where chronic airway infection with Pseudomonas is associated with high lumenal concentrations of neutrophils. A second major achievement was identification of roles for mast cell proteases as determinants of airway hyperresponsiveness in a mouse model of chronic allergic airway inflammation. Specifically, this work, which was carried out in collaboration with the Sheppard lab, showed that two mast cell secretory granule proteases, namely mMCP-1 and mMCP-4, which for the most part are expressed by different subsets of mast cells, have opposing effects on the development of hyperresponsiveness. Furthermore, the development of airway hyperresponsiveness in mice lacking avb6 integrin appears to be due to recruitment of mMCP-1-expressing mast cells into airway epithelium. Furthermore, hyperresponsiveness in these models appeared to be largely unrelated to degree of airway inflammation and extent of remodeling, suggesting that these models may be able to reveal something fundamental about airway hyperresponsiveness, which is the physiological sine qua non of asthma but lacks an adequate pathophysiological explanation.
Project 2: Imaging T cell Airway Responses during Inflammation (Project Leader: M. Krummel)

Over the past year, we demonstrated a two-phase process of antigen presentation in mouse models of asthma. Contrary to the conclusions drawn from live-imaging of tracheal sections, we do not observe significant particle transport directly at the site of asthma inflammation (e.g., at branching airways). Two-photon microscopy of the lung parenchyma revealed accumulation of CD11b+ dendritic cells (DCs) around the airway after allergen challenge but very limited access of these airway-adjacent DCs to the contents of the airspace. In contrast, we observed prevalent transepithelial uptake of particulate antigens by alveolar DCs. These distinct sites are temporally linked with early uptake in alveoli giving rise to asthma-specific DCs and antigen retention in the airway region. A hyper-reactive lung thus results from selective retention of allergen-presenting cells in airway-adjacent interaction zones, not variation in the abilities of individual cells to survey the lung. The location and function of these zones in allergy--sites that also attract reactive T cells--may be similar to the more profound bronchial-associated lymphoid tissue (BALT) generated in response to pathogens. We have begun to address the site of Th2, Th17 and Treg function at these sites using newly acquired reporter strains specific for these cells.

Project 3: Lymphangiogenesis and Angiogenesis in Airway Inflammation (Project Leader: D.M. McDonald)

Studies of Project 3 during the past year focused on the mechanisms and consequences of lymphangiogenesis and angiogenesis in inflammatory conditions of the airways and lungs. Our underlying hypothesis is that changes in the structure and function of lymphatics and blood vessels contribute to the inflammatory response and are therefore therapeutic targets. We found that Mycoplasma pulmonis infection of the lungs of mice was accompanied by remodeling of blood vessels and lymphatics associated with bronchus-associated lymphoid tissue (BALT), similar to what we found previously in the trachea. Our goal now is to determine whether mucosal edema is sustained because the remodeled blood vessels are abnormally leaky, and the remodeled lymphatics are less efficient at draining the extravasated fluid. We found that remodeled blood vessels in regions of BALT acquired the functional properties of high endothelial venules of lymph nodes. Inhibition of neutrophil influx by treatment with either of two anti-neutrophil antibodies abolished much of the blood vessel remodeling, but reduction of macrophage recruitment had little effect. To examine effects that specific cytokines contribute to the remodeling of blood vessels and lymphatics in airway inflammation, we used transgenic mouse models. In one, interleukin-1, and in the other, VEGF-C, was overexpressed in airway and lung epithelial cells, driven by the Clara Cell Secretory Protein (CCSP) promoter under doxycycline regulation. Unlike M. pulmonis infection, transgenic over-expression of interleukin-1 was accompanied by largely irreversible lymphangiogenesis but no angiogenesis or remodeling of blood vessels. This finding revealed the independence of the responses of blood vessels and lymphatics in inflammation. Transgenic over-expression of VEGF-C in the airways also proved promising because the mice developed chylothorax and lymphangiectasia when VEGF-C was switched on in late gestation or at birth, but not in the adult. This is the first mouse model of the poorly understood and untreatable condition of congenital pulmonary
lymphangiectasia in human newborns and infants and makes it possible to study the underlying mechanism and potential treatments.

Core Activities

Administration Core (A). This core, supervised by Dr. Caughey, coordinated a three-project enterprise involving labs in diverse locations and multiple investigators, consultants and staff, with varying technical backgrounds. Core A administrative personnel organize conference and seminar schedules, coordinate Program Project-related projects and collaborations within the Cardiovascular Research Institute as well as with other research units and institutions, including the Northern California Institute for Research and Education at the San Francisco Veterans Affairs Medical Center site. They organize travel schedules, prepare progress reports and oversee management of budgets and other matters pertaining to the Program Project.

Scientific Core (B). This core facility, supervised by Dr. Krummel and co-directed by Dr. Baluk, has Mycoplasma production, Mouse Genetics, and Imaging components. During the past year, our supply of highly virulent M. pulmonis organisms was re-established through a collaboration with Dr. Mary Brown at the University of Florida- Gainsville, titered and validated by the Core personnel. A major core service provided by the Mouse Genetics component was genotyping via PCR, blotting and FACS. The imaging core principally provided 2-photon intravital microscopy services to personnel associated with individual projects.

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.

P01 HL024136-supported selected publications (2011-2012)


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 TGFbeta 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 TGFbeta on dendritic cells by another integrin, αvβ8, plays a major role in the negative regulation of adaptive immunity and allergic airway inflammation. 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. This work was recently published in the Journal of Clinical Investigation. 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, and that a similar pathway operates in human bronchi. The work was recently published in Nature Medicine and identifies the αvβ8 as an attractive therapeutic target for patients with severe asthma, many of whom do not respond to current therapies.

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 deletor mice to examine how chitin leads to skewing of adaptive immune responses toward a Th2 phenotype and subsequently leads to induction of IL5 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. We have succeeded in identifying a role of innate lymphoid cells, termed iH2 cells, in secreting IL-5 and IL-13 in the airways after chitin challenge, and we have started to sort out the roles of upstream...
cytokines implicated in this process, including IL-33 and TSLP. We have also succeeded in deleting AMCase from the mouse genome and have begun experiments with these mice to assess the role of AMCase in modulating the chitin response by degradation of the challenge particles. These phenotypes are very promising in early experiments that should be completed within the last year of the studies.

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 SMAD2 as a risk factor for asthma using an ancestry mapping strategy from genome-wide SNP data in approximately 8,000 patients from Mexico and Puerto Rico that replicates across multiple study arms. Fine mapping of the SMAD2 region is 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
## Immunology Seminar Series
### 2011-2012 Schedule
**Mondays, 9 a.m. Room: N-217**

<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker</th>
<th>Host</th>
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<tbody>
<tr>
<td>September 26</td>
<td>Riitta Lahesmaa</td>
<td>Mark Ansel</td>
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<tr>
<td>October 3</td>
<td>Harinder Singh</td>
<td>Abul Abbas</td>
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<td>Luis Sigal</td>
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<td>October 17</td>
<td>Kristin Hogquist</td>
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<td>Jenny Ting</td>
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<td>Eric Long</td>
<td>Matija Peterlin</td>
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<td>Christophe Benoist</td>
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<td>Paul Kubes</td>
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<td>Michael Brenner</td>
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<td>Steve Ziegler</td>
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<td>Mark Jay Shlomchik</td>
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<td>Herbert W. Virgin</td>
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<td>Troy Randall</td>
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<td>June 4</td>
<td>Qizhi Tang</td>
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<tr>
<td>Date</td>
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<td>Talk 2 (Basic)</td>
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<td>09/19/2011</td>
<td>Kelly Wong McGrath (Fahy)</td>
<td>Marrah Lachowicz-Scroggins</td>
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<td>Steven M. Rowe, M.D., UAB</td>
<td>John Li (faculty)</td>
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<td>Visiting Professor &amp; Ruprecht Lecturer</td>
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<td>Hui-Ju Tsai (Burchard)</td>
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<td>Neil Trivedi (faculty)</td>
<td>Antonio Gomez (faculty)</td>
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<td>Carolyn Calfee (faculty)</td>
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<td>University of Manchester</td>
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<td>11/21/2011</td>
<td>Jon Singer</td>
<td>Wenxue Zhao (Erle)</td>
</tr>
<tr>
<td>11/28/2011</td>
<td>Sara Arron (faculty)</td>
<td>Mike LaFemina (Frank)</td>
</tr>
<tr>
<td>12/05/2011</td>
<td>Brad Schroeder (Erle)</td>
<td>Chun Chen (Sheppard)</td>
</tr>
<tr>
<td>12/12/2012</td>
<td>Erin Gordon (Fahy)</td>
<td>Sailaja Battula (Broadus)</td>
</tr>
<tr>
<td>12/19/2011</td>
<td>Winter holiday (no conference)</td>
<td></td>
</tr>
<tr>
<td>12/28/2011</td>
<td>Winter holiday (no conference)</td>
<td></td>
</tr>
<tr>
<td>01/02/2012</td>
<td>Winter holiday (no conference)</td>
<td></td>
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<tr>
<td>01/09/2012</td>
<td>Katherine Drake (Burchard)</td>
<td>Collin Blakely (Coussens)</td>
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<tr>
<td>01/16/2012</td>
<td>MLK holiday (no conference)</td>
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<tr>
<td>01/23/2012</td>
<td>Luke Davis (faculty)</td>
<td>Allison Landman (McMahon)</td>
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<tr>
<td>01/30/2012</td>
<td>Lorraine Ware (visiting Professor)</td>
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<tr>
<td>02/06/2012</td>
<td>Jesse Nussbaum (Locksley)</td>
<td>Makoto Kudo (Sheppard)</td>
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<tr>
<td>02/13/2012</td>
<td>Moshe Zutler (Blanc)</td>
<td>Aparna Sundaram (Sheppard)</td>
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<td>02/20/2012</td>
<td>President’s holiday (no conference)</td>
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<tr>
<td>02/27/2012</td>
<td>Timothy Blackwell (visiting Prof.)</td>
<td></td>
</tr>
<tr>
<td>03/05/2012</td>
<td>Joanne Engle (faculty)</td>
<td>Christina Yoon (Huang)</td>
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<tr>
<td>03/12/2012</td>
<td>Charles Everett (Huang/Hopewell)</td>
<td>Chris Gignoux (Burchard)</td>
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<tr>
<td>03/19/2012</td>
<td>Xiang Xu (Caughey)</td>
<td>Jae-Woo Lee (faculty)</td>
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<tr>
<td>03/26/2012</td>
<td>Ric Boucher (visiting Prof.)</td>
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<tr>
<td>04/02/2012</td>
<td>Joyce Lee (Collard/King)</td>
<td>Mallar Bhattacharya (Sheppard)</td>
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<tr>
<td>04/09/2012</td>
<td>Narva Bhakta (Woodruff)</td>
<td>David Sayah (Looney)</td>
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<tr>
<td>04/16/2012</td>
<td>Sam Oh (Burchard)</td>
<td>John Metcalfé (Hopewell)</td>
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<tr>
<td>04/23/2012</td>
<td>Axelle Caudrillier (Looney)</td>
<td>Adithva Cattamanachi (faculty)</td>
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<tr>
<td>04/30/2012</td>
<td>Mehrdad Arjomandi (faculty)</td>
<td>Laura Simpson (Ansel)</td>
</tr>
<tr>
<td>05/07/2012</td>
<td>Edwin Ostrin (Erle)</td>
<td>Ying Wei (faculty)</td>
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<tr>
<td>05/14/2012</td>
<td>Sheena Kerr (Fahy)</td>
<td>Eric Seeley (Wolters)</td>
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<tr>
<td>05/21/2012</td>
<td>ATS (no conference)</td>
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<tr>
<td>05/28/2012</td>
<td>Memorial Day (no conference)</td>
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<tr>
<td>06/04/2012</td>
<td>Rajarshi Ghosh (Papa)</td>
<td>Laura Koth (faculty)</td>
</tr>
<tr>
<td>06/11/2012</td>
<td>Katherine Sutherland (Frank)</td>
<td>Josh Galanter (Burchard)</td>
</tr>
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</table>
### SABRE Asthma Research Conference Schedule

Location: 513 Parnassus Avenue, HSE-1303  
Time: 4PM – 5PM  
Day: 2nd Thursday of each month

<table>
<thead>
<tr>
<th>Date</th>
<th>Presenter</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/10/2011</td>
<td>Mark Ansel, PhD</td>
</tr>
<tr>
<td>12/8/2011</td>
<td>Jeoung-Sook Shin, PhD</td>
</tr>
<tr>
<td>1/12/2012</td>
<td>Richard Locksley, MD</td>
</tr>
<tr>
<td>2/16/2012</td>
<td>Jonathan Weissman, PhD</td>
</tr>
<tr>
<td>3/8/2012</td>
<td>Dean Sheppard, MD</td>
</tr>
<tr>
<td>4/12/2012</td>
<td>Mike McCune, MD, PhD</td>
</tr>
<tr>
<td>5/10/2012</td>
<td>John Fahy, MD</td>
</tr>
<tr>
<td>6/14/2012</td>
<td>David Erle, MD</td>
</tr>
<tr>
<td>7/12/2012</td>
<td>Linda Lee</td>
</tr>
<tr>
<td>8/9/2012</td>
<td>Prescott Woodruff, MD, MPH</td>
</tr>
<tr>
<td>9/13/2012</td>
<td>Limin Liu, PhD</td>
</tr>
<tr>
<td>10/11/2012</td>
<td>Chris Allen, PhD</td>
</tr>
<tr>
<td>11/8/2012</td>
<td>Max Krummel, PhD</td>
</tr>
<tr>
<td>12/8/2012</td>
<td>Esteban Burchard, MD, MPH</td>
</tr>
</tbody>
</table>
Immunology Seminar Series

"Molecular mechanisms of human Th cell differentiation"

Riitta Lahesmaa, PhD
Professor, Director
Molecular Immunology Group and Turku Centre for Biotechnology
University of Turku, Finland

Monday, September 26, 2011
9am, Parnassus, HSW-303
Host: Mark Ansel, Ph.D., SABRE Center

BROADCAST | Mission Bay, Genentech Hall, Room S271 • /presentations/live • Now available Video streaming into SFGH, Building 3, room 505. 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
RECENT AND NEW PUBLICATIONS
SUPPORTED BY THE SANDLER ASTHMA BASIC RESEARCH CENTER
(2010-2012)
**Christopher C.D. Allen, Ph.D.**


**K. Mark Ansel, Ph.D.**


**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.**


**William Seaman, M.D.**


Sandler Asthma Basic REsearch Center       Recent and New Publications

Dean Sheppard, M.D.


Jeoung-Sook Shin

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


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


Limnander A, Depeille P, Freedman TS, Liou J, Leitges M, Kurosaki T, Roose JP, and


Jonathan Weissman, Ph.D.


Zena Werb, M.D.


Prescott Woodruff


Trail of Zileuton for Treatment of COPD Exacerbations Requiring hospitalization. 


Looking to the Future

Richard M. Locksley, M.D.

Much has come to fruition during the creation of the SABRE Center at UCSF. Fully staffed with 4 full-time faculty and a UCSF Fellow and firmly aligned with the UCSF Airway Clinical Research Center, the SABRE Center is increasingly acknowledged as a prominent site for asthma research. The Center received recognition as an NIAID Asthma and Allergic Diseases Cooperative Research Center and as a participant in the NIH Severe Asthma Research Program, or SARP, Network. UCSF is an AsthmaNet participant, and continues to study clinical trials in asthma patients under the leadership of Homer Boushey. The SABRE Center’s first PPG among faculty participants was funded from the NIH National Heart, Lung and Blood Institute after receiving a near perfect score. Each of our faculty has secured extramural funding, and all but one of our four faculty now has NIH R01 funding. The UCSF Fellow and the remaining faculty individuals have submitted R01 grants. New technologies have been secured through NIH shared equipment grants, and infrastructure improvements have been completed to ensure a vibrant working environment. The monthly SABRE Center-Pulmonary conferences remain vibrant and widely attended. The first graduate students will complete their Ph.D. degrees in SABRE Center laboratories, and postdoctoral trainees are beginning to move onto new careers at other institutions. Our first UCSF Fellow is exploring the job market as he begins to transition to a full-time faculty position. Finally, SABRE Center investigators were involved in aspects of both basic and clinical research that laid the foundation for the successful institution of therapies targeting IL-13 in patients with asthma at Genentech/Roche. Although the SABRE Center is a young research institute, maturation is apparent, and has been accompanied by increasing research support, recognition by the UCSF research community and, increasingly, recognition by both academic and industry leaders.

Our Mission Statement defines the SABRE Center as ‘an investigative unit dedicated to basic research in asthma’. Despite all of the studies of allergy and asthma over the past century, the past year has witnessed the discovery of a new cell type – variously designated innate lymphoid cells, nuocytes, innate helper cells and iH2 cells – involved in allergic disease, including asthma. The Locksley lab was one of the laboratories (the other two were in Japan and the United Kingdom) involved in this discovery. Extraordinarily, 5 of the 9 validated genes identified in multiple asthma GWAS studies are highly expressed or involved in the functions of these novel cells. As a small and nimble research organization, the SABRE Center investigators moved quickly to work towards a deeper understanding of these cells in human asthma. Working with information obtained in the mouse system from the Locksley lab, the Ansel and Fahy labs were able to confirm the presence of these cells in humans with asthma. The Locksley lab used the Imaging Core to position these cells in lung. Armed with this information, the Locksley and Ansel labs teamed with the Fahy and Woodruff clinical research labs in the ACRC to plan and submit a Program Project Grant to the NIH. The team met every 2-4 weeks for over a year to integrate findings and develop a strong and focused research plan. This PPG grant received an extremely high score (1.1) at the NIH and begins funding in July, 2012. This is a testimony to the capacity of the SABRE Center to
capitalize quickly on new findings, to move opportunities into human populations with remarkable speed, and to work together across the basic science – clinical research divide to create new opportunities for discovery. We look forward to new findings and continuing discoveries.

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.
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

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Christopher David Caballero Allen, Ph.D.</td>
<td>Sandler-Newmann Foundation UCSF Fellow in Asthma Research</td>
</tr>
</tbody>
</table>

## 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>
</tr>
<tr>
<td>University of California, San Francisco</td>
<td>Ph.D.</td>
<td>2007</td>
<td>Biomedical Sciences</td>
</tr>
<tr>
<td>University of California, San Francisco</td>
<td>Postdoc</td>
<td>2007</td>
<td>Immunology</td>
</tr>
</tbody>
</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

2010  
*Seminars in Immunology* Top Cited Article 2008-2010
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

cERA COMMONS USER NAME
anselm

POSITION TITLE
Assistant Professor of Microbiology and Immunology

EDUCATION/TRAINING

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
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<th>FIELD OF STUDY</th>
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<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>
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<td>2001-2007</td>
<td>Immunology</td>
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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

Other Experience and Professional Memberships

1998 American Association for the Advancement of Science
2006 American Association of Immunologists
2007 International Cytokine Society

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
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   Burroughs Wellcome Career Award in Biomedical Sciences
2007   International Cytokine Society Outstanding Postdoctoral Fellow
2009   Dana Foundation Human Immunology Scholar

Selected Peer-reviewed Publications


Research Support

Ongoing Research Support

<table>
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<th>Project ID</th>
<th>Applicant</th>
<th>Start Date</th>
<th>End Date</th>
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<td>1R01HL109102-01</td>
<td>Ansel (PI)</td>
<td>8/1/11 – 6/30/16</td>
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<tr>
<td>NIH/NHLBI</td>
<td>Role of miRNAs in Th2-driven inflammation in asthma</td>
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The major goals of this project are to discover asthma-associated T cell miRNA expression patterns in clinical samples, and to identify and characterize the in vivo activity of miRNAs that regulate helper T cell functions relevant to asthma. The project will be conducted in collaboration with co-investigator Dr. Prescott Woodruff, co-director of the UCSF Airway Clinical Research Center.

<table>
<thead>
<tr>
<th>Program Name</th>
<th>Applicant</th>
<th>Start Date</th>
<th>End Date</th>
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<tr>
<td>Dana Foundation Human Immunology Scholars Program</td>
<td>Ansel (PI)</td>
<td>2/1/09 – 1/31/12</td>
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<tr>
<td>Dana Foundation</td>
<td>MicroRNA regulation of helper T cell function in asthma</td>
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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.
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.

Pending Research Support
1P01HL107202  Ansel (Project 2 Leader)  6/1/12 – 5/31/17
NIH/NHLBI Innate and adaptive immune responses in Th2-high asthma (PI Dr. John Fahy, co-director UCSF ACRC)
Project 1: Innate helper type II cells in allergic lung (Project leader Dr. Rich Locksley, SABRe director)
Project 2: Role of miRNAs in Th2-Driven inflammation in Asthma (Project Leader Ansel)
Project 3: Mechanisms of airway Th2 inflammation in asthma (Project Leader Fahy, Co-project Leader Ansel)
The major goal of this PPG is to elucidate cellular and molecular mechanisms underlying the initiation and maintenance of Th2-high asthma. We received near-perfect scores of 10, 10, and 12 on the three projects that comprise the full grant, and await a funding decision. The goals of Project 2 are to identify miRNAs that regulate helper T cell functions relevant to asthma, to discover asthma associated T cell miRNA expressions patterns in clinical samples, and to determine the mRNA targets and in vivo role of miR-29 in a mouse model of asthma. My role in aim 3 is immunophenotyping of innate helper type II cells in human asthma.

LLS Scholar Award  Ansel (PI)  7/1/12 – 6/30/2016
Leukemia & Lymphoma Society
MicroRNA regulation of lymphocyte growth and effector functions
This career development program award would support our research program focus on miRNAs that regulate essential helper T cell functions that contribute to immunity, immuopathology, and immune malignancies. In particular, we aim to identify and characterize miRNAs that regulate helper T cell growth, survival, and cytokine production.

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.

1R56AI089828-01  Ansel (PI)  9/1/10 – 7/31/11
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.
# BIOGRAPHICAL SKETCH

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
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</thead>
<tbody>
<tr>
<td>Homer A. Boushey, Jr., M.D.</td>
<td>Professor of Medicine</td>
</tr>
</tbody>
</table>

| eRA COMMONS USER NAME | Boushey |

## 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>
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<tr>
<td>Stanford University, Palo Alto, CA</td>
<td>A.B.</td>
<td>1964</td>
<td>Biology</td>
</tr>
<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, (residency)</td>
<td>Internal Medicine</td>
<td>1970</td>
<td></td>
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<tr>
<td>Beth Israel Hospital, Boston, MA</td>
<td>Internal Medicine (residency)</td>
<td>1971</td>
<td></td>
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<tr>
<td>Oxford University, Oxford, England</td>
<td>Pulmonary Medicine (Fellowship)</td>
<td>1972</td>
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## Positions and Honors

- University of California, San Francisco
- 1974-1981 Assistant Professor of Medicine in Residence
- 1981-1987 Associate Professor of Medicine in Residency
- 1986-Present Member, Senior Staff, Cardiovascular Research Institute
- 1987-1989 Professor of Medicine in Residence
- 1989-Present Professor of Medicine
- 1989-1995 Vice Chairman for Clinical Affairs, Department of Medicine
- 1996-2009 Chief, Allergy/Immunology Division, Department of Medicine

## 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)


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 microbiobial 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
COPD Clinical Research Network at UCSF

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

NAME  
Esteban González Burchard, M.D., M.P.H.

POSITION TITLE  
Professor, Bioengineering & Therapeutic Sciences and Medicine  
Director, Center on Genes, Environments & Health

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 &amp; 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>
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<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>
</tr>
<tr>
<td>University of California, San Francisco, SF, CA</td>
<td>Fellow</td>
<td>1998-2001</td>
<td>Pulmonary &amp; Critical Care Medicine</td>
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<td>Stanford University, Stanford, CA</td>
<td>M.P.H.</td>
<td>2001-2002</td>
<td>Genetic Epidemiology</td>
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<td>University of California, Berkeley</td>
<td></td>
<td>2005-2006</td>
<td>Epidemiology</td>
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</table>

Positions and Honors

2001 - 2010  
Director, UCSF DNA Bank and Asthma Genetics Core Facility

2008 -  
Director, UCSF Center on Genes, Environments & Health

2009 -  
Director, UCSF Clinical Pharmacology Training Program

2010 -  
Vice Chair, Department of Bioengineering & Therapeutic Sciences, University of California, San Francisco

2011 -  
Professor, Bioengineering & Therapeutic Sciences and Medicine, University of California, San Francisco

1988, 1989  
National Collegiate Athletic Association (NCAA) Div. II Academic All-American, Wrestling

2005 – 2010  
RWJ Amos Medical Faculty Development Award

2008  
NIH Study Section Member, Genetics of Health and Disease (GHD)

2009  
American Society of Clinical Investigation (ASCI) Inducted member

2009  
Guest Speaker, Tavis Smiley Show

2010  
Guest Speaker, NPR’s Science Friday, hosted by Ira Flatow
Selected Peer-reviewed Publications (selected from 86 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.

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.

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

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.
The goal was to develop an ethnically diverse cohort of subjects to participate in pharmacogenetic studies.
BIOGRAPHICAL SKETCH

NAME
George H. Caughey

eRA COMMONS USER NAME
gcaughey

POSITION TITLE
Professor of Medicine

EDUCATION/TRAINING

<table>
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<tr>
<th>INSTITUTION AND LOCATION</th>
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<tr>
<td>Arizona State University</td>
<td>BS</td>
<td>1975</td>
<td>Chemistry</td>
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<td>Stanford University School of Medicine</td>
<td>MD</td>
<td>1979</td>
<td>Medicine</td>
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<tr>
<td>Pennsylvania Hospital/UPenn</td>
<td></td>
<td>1982</td>
<td>Internal Medicine</td>
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<td>University of California, San Francisco</td>
<td></td>
<td>1986</td>
<td>Pulmonary Medicine</td>
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Positions and Honors

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
1999- 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

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- Julius and Lillian Nadel Endowed Chair of Medicine
2010 Elected to Collegium Internationale Allergologicum
Publications in chronological order (selected from 135)


**Research Support**

Ongoing 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
Project 1 goals are to determine roles of secreted airway proteases and protease receptors in airway inflammation.
BIOGRAPHICAL SKETCH

NAME
Harold A. Chapman, M.D.

POSITION TITLE
Professor of Medicine

eRA COMMONS USER NAME
Halchapman

EDUCATION/TRAINING

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<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>
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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      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)

1. Kim KK, Kugler MC, Wolters PJ, Robillard L, Galvez MG, Brumwell AN, Sheppard D, 
2. Kim KK, Wei Y, Szekeres C, Kugler MC, Wolters PJ, Hill ML, Frank JA, Brumwell AN, 
10. Wei Y, Lukasev M, Simon DI, Bodary SC, Rosenberg S, Doyle MV, Chapman HA, 
    required for normal MHC class II peptide loading and germinal center development.  Immunity, 10:196-206.


Research Support

Ongoing Research Support

5 R37 HL67204 (Chapman, HA) 6/1/2001 – 5/31/2012
NIH/NHLBI MERIT AWARD
Role of Elastolytic Cathepsins in Emphysema

The major goal of this project is 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 urokiinase receptor beta1 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.
The major goals of this project are (1) To define the transcriptional program of heretofore uncharacterized distal airway and alveolar progenitors and test the hypothesis that differential expression of adhesion receptors underlies the capacity of epithelial subtypes to self-organize and promote repair. (2) Define the requirement for neuroendocrine cells (PNECS) and alveolar progenitor cells in maintenance and reconstitution of distal airway and alveolar cells following lung injury. (3) Analyze and further develop a novel, single cell in vivo lung organoid assay in kidney capsules in order to optimize the capacity of adult epithelial progenitor cells to generate functional respiratory units de novo.
BIOGRAPHICAL SKETCH

NAME
Anthony L. DeFranco, Ph.D.

eRA COMMONS USER NAME
DeFranco

POSITION TITLE
Professor,
Department of Microbiology & Immunology

EDUCATION/TRAINING

<table>
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<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
1979-1983 Postdoctoral research, laboratory of Dr. William E. Paul, B cell activation
1983-1988 Assistant Professor, UCSF, Department of Microbiology & Immunology
1988-1994 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
1993 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.).
BIOGRAPHICAL SKETCH

NAME
David J. Erle, M.D.

POSITION TITLE
Professor of Medicine

eRA COMMONS USER NAME
DJERLE

EDUCATION/TRAINING

<table>
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<tr>
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<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>
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<tr>
<td>University of California, San Francisco, CA</td>
<td>Fellow</td>
<td>1987-90</td>
<td>Pulmonary Disease</td>
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**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
2006-2011  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)**

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)**

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.

**R21 HL108596 (Erle)**

NIH/NHLBI

Micro-RNAs in airway epithelial differentiation and asthma
The major goal of this project is to develop tools to determine how selected miRNAs affect airway epithelial cell differentiation and function.
Completed Research Support

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.

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

<table>
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<tr>
<td>University College Dublin</td>
<td>MB BAO BCH</td>
<td>1985</td>
<td>Medicine</td>
</tr>
<tr>
<td>University College Dublin</td>
<td>Intern</td>
<td>1985-1986</td>
<td>Medicine and Surgery</td>
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<tr>
<td>Trinity College Dublin</td>
<td>Resident</td>
<td>1986-1989</td>
<td>Internal Medicine</td>
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<tr>
<td>University College Dublin</td>
<td>Registrar</td>
<td>1988-1999</td>
<td>Respiratory Medicine</td>
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<td>University of California, San Francisco</td>
<td>Fellow</td>
<td>1989-1993</td>
<td>Pulmonary/Critical Care Medicine</td>
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<tr>
<td>University College Dublin</td>
<td>M.D. (doctorate by thesis)</td>
<td>1997</td>
<td>Respiratory Medicine</td>
</tr>
<tr>
<td>Trinity College Dublin</td>
<td>M.Sc. (Sabbatical year)</td>
<td>2003</td>
<td>Molecular Medicine</td>
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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**

1P50HL107191 (Fahy, JV)  5/01/11-04/30/13
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

1U10HL109146 (Fahy JV)  8/1/2011-7/31/2017
Clinical and Molecular Phenotypes of Severe Asthma
This grant was submitted in response to the RFA for Clinical Centers for the Severe Asthma Research program) – a 6-center national program for research into mechanisms of severe asthma.
Role: PI

5 R01 HL080414 (Fahy, JV)  7/01/05-05/31/15
Protein carbohydrate interactions in the pathophysiology of acute asthma exacerbations
The major goals of this project are to investigate how lectins interact with mucin glycans to cause airway mucus obstruction in acute severe asthma.
Role: PI

1 U19 A1077439 (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

Pending

1P01HL107202 (Fahy, JV)       7/1/12 - 6/30/17  
NIH/NHLBI  
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 the 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

RO1 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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</table>

## Positions

- **6/83 to 7/84**  
  Teaching Assistant, Dept. of Pathology, Tongji Medical University, China
- **8/84 to 8/85**  
  Pathology Residence, The First Attached Hospital, Tongji Medical University, China
- **9/88 to 1/92**  
  Research Assistant, Dept. of Pathology, Tongji Medical University, China
- **1/92 to 12/95**  
  Postdoctoral Fellow, Dept. of Medicine, Lung Biology Center, University of California, San Francisco
- **1/96 to 6/97**  
  Postgraduate Researcher, Dept. of Medicine, Lung Biology Center, University of California, San Francisco
- **7/97 to 11/99**  
  Assistant Research Molecular Biologist, Dept. of Medicine, Lung Biology Center, University of California, San Francisco
- **12/99 to 6/2005**  
  Assistant Professor, Dept. of Medicine, Lung Biology Center, University of California, San Francisco
- **07/2005 to present**  
  Associate Professor, Dept. of Medicine, Lung Biology Center, University of California, San Francisco

## Honors

- **1989**  
  "Outstanding Teacher" honor, Department of Pathology, Tongji Medical University
- **1/1992 to 12/1993**  
  Cheng Research Scholar Award,
Selected peer-reviewed publications


and hyperreactivity in asthma. Proc Natl Acad Sci USA, Jun 2;106(22):9099-104.

*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>
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</table>

| eRA COMMONS USER NAME | Krummel |

<table>
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<th>EDUCATION/TRAINING</th>
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<tr>
<td>INSTITUTION AND LOCATION</td>
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<tr>
<td>University of Illinois at Champaign-Urbana</td>
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<tr>
<td>University of California at Berkeley</td>
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<tr>
<td>Walter and Eliza Hall Institute, Melbourne Australia</td>
</tr>
<tr>
<td>Stanford University</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

1987 Summer Undergraduate Research Fellowship, Howard Hughes Medical Institute

**Selected Peer-reviewed Publications** (out of 51)


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 lgl proteins in T cell synapse development, signaling, and proliferative control.
Role: PI
**BIOGRAPHICAL SKETCH**

**NAME**  
Limin Liu, Ph.D.

**POSITION TITLE**  
Assistant Professor

**eRA COMMONS USER NAME**  
LIMINLIU

**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>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>
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</table>

**Positions**

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)


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. 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
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.
BIOGRAPHICAL SKETCH

NAME
Richard M. Locksley, M.D.

eRA COMMONS USER NAME
Locksley

POSITION TITLE
Sandler Distinguished Professor, Department of Medicine, University of California, San Francisco

EDUCATION/TRAINING

<table>
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<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 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>
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</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.
BIOGRAPHICAL SKETCH

NAME
Sebastian Peck, B.S.

POSITION TITLE
Specialist and Managing Director of the Biological Imaging Development Center

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>
</tr>
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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

Summers 2005–2007    Summer Undergraduate Research Fellow
University of California, 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

2006 and 2007    Summer Undergraduate Research Fellowship
Howard Hughes Medical Institute

Selected publications


# BIOGRAPHICAL SKETCH

**NAME**  
*William E. Seaman, M.D.*

**eRA COMMONS USER NAME**  
*BSEAMAN*

<table>
<thead>
<tr>
<th>POSITION TITLE</th>
</tr>
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<tbody>
<tr>
<td>Professor of Medicine and of Microbiology and Immunology, UCSF</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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</thead>
<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>
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</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, University of California, 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

2011 -- Present  
Associate Chair of Medicine for Research, UCSF
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 PT075679 PI: WE Seaman  
**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**

**NAME**

Dean Sheppard, M.D.

**POSITION TITLE**

Professor of Medicine

eRA COMMONS USER NAME

sheppard

**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>
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<tr>
<td>Harvard College, Cambridge, MA</td>
<td>AB</td>
<td>6/72</td>
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<tr>
<td>SUNY at Stony Brook, Stony Brook, NY</td>
<td>MD</td>
<td>6/75</td>
<td>Medicine</td>
</tr>
<tr>
<td>University of Washington, Seattle, WA</td>
<td>Resident</td>
<td>7/75-6/78</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>University of California, San Francisco, San</td>
<td>Fellow</td>
<td>7/78-6/81</td>
<td>Pulmonary</td>
</tr>
</tbody>
</table>

**Positions**

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

**Other Experience**

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

**Honors and Awards**

Elected Member, American Society for Clinical Investigation, 1992
Elected Member, Association of American Physicians, 1995
Selected Relevant Publications (from a total 252)


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 TGFβ1 activation in the induction of lung inflammation and protection from pulmonary fibrosis in integrin β6 subunit null mice.

U19 AI077439 (Sheppard) 3/1/08-2/28/13
NIH/NIAID-Project 1 and Core A
Mechanisms of Initiation and Persistence of Allergic Asthma
The major goals of this project are to determine the roles of integrin-mediated TGFβ activation in regulating auto-immunity, regulatory T cells and airway hyperresponsiveness after chronic allergen challenge in mice.

Recently completed

R01 HL083950 (Sheppard) 4/1/06-3/31/11
NIH/NHLBI
Regulations of Pulmonary Vascular Permeability by Integrin AlphaVbeta5
The major goals of this project were: 1) To identify the pathways by which αvβ5 facilitated RhoA activation and contributed to pulmonary vascular permeability. 2) To determine how the integrin β5 subunit contributed to the formation of multi-protein signaling complexes that regulated endothelial permeability. 3) To determine whether the pathways examined in aims 1 and 2 were broadly important in in vivo models of non-cardiogenic pulmonary edema.

U19 AI077439-02S1 (Sheppard) 8/15/09-7/31/11
NIH/NIAID (Administrative Supplement Award)
Mechanisms of Initiation and Persistence of Allergic Asthma
This administrative supplement to our U19 grant had 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.

R01 AI024674 (Sheppard) 3/1/06-2/28/10
NIH/NIAID
Novel Leukocyte Integrins
The major goal of this project was to understand how glycan phosphoatidly inositol anchored proteins influenced the function of Fc and complement receptors on macrophages and dendritic cells.

R01 HL64353 (Sheppard) 12/1/03-11/30/09
NIH
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.
University of Edinburgh (Subcontract)
The Role of the Alphavbeta8 Integrin in Hepatic Inflammation and Fibrosis
The subcontract is to support a postdoctoral fellow, Neil Henderson, to work in Dr. Sheppard’s laboratory. Dr. Henderson will be working on the mechanisms of activation of TGF beta in the liver.
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>
</tr>
</thead>
<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>
</tr>
</tbody>
</table>

Professional Positions

1996      Research Associate, Cheong-Am Biotech, Seoul, Korea
2002 – 2003 Research Associate, Duke University
2003 – 2008 Postdoctoral Associate/Fellow, Yale University
2008 Assistant Professor, University of California San Francisco, Dept. of Microbiology Immunology & Sandler Asthma Basic Research Center

Honors and Awards

1999 The Best Research Student Award in the Department of Pathology
9th Graduate Student Symposium, Duke University
2004 The Jane Coffin Childs Memorial Fund Research Fellowship Award
2009 Strategic Innovative Award in Asthma Research
2009 Cancer Research Institute Investigator Award

Professional Memberships

2008 - 2010 American Thoracic Society, member
2011 American Society of Cell Biology, member
2011 American Association of Immunologists, member
Selected peer-reviewed publications


Research Support

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

Pilot Research Award for Junior Investigators (PI) 1/15/2012– 1/14/2013
UCSF Academic Senate
Exploring dendritic cell presentation of IgE-bound antigens in vivo

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

cRA 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>
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</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, San Francisco Department of Medicine
- 1994-1997 Senior Research Associate, Cell Genesys Inc., Foster City, CA
- 1997 Research Specialist II, Howard Hughes Medical Institute (HHMI) San Francisco, CA

Selected Peer-reviewed Publications


## BIOGRAPHICAL SKETCH

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthur Weiss, M.D., Ph.D.</td>
<td>Professor of Medicine and of Microbiology and Immunology</td>
</tr>
</tbody>
</table>

| eRA COMMONS USER NAME | weissa                                                              |

### 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 Chicago</td>
<td>Ph.D.</td>
<td>1978</td>
<td>Immunology</td>
</tr>
<tr>
<td>University of Chicago</td>
<td>M.D.</td>
<td>1979</td>
<td>Medicine</td>
</tr>
</tbody>
</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, University of California, San Francisco
- **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

<table>
<thead>
<tr>
<th>Year</th>
<th>Position</th>
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<tbody>
<tr>
<td>1986-1991</td>
<td>Councilor, American Federation for Clinical Research</td>
</tr>
<tr>
<td>1991</td>
<td>President, Western Region of the American College of Rheumatology</td>
</tr>
<tr>
<td>1998-2002</td>
<td>Member, Allergy and Immunology Study Section (NIH)</td>
</tr>
<tr>
<td>1999-</td>
<td>Chair, Scientific Advisory Board, American Asthma Foundation</td>
</tr>
<tr>
<td>2000-2002</td>
<td>Chair, Allergy and Immunology Study Section (NIH)</td>
</tr>
<tr>
<td>2003-2010</td>
<td>Council, American Association of Immunologists</td>
</tr>
<tr>
<td>2008-2009</td>
<td>President, American Association of Immunologists</td>
</tr>
<tr>
<td>2005-</td>
<td>Advisory Council, RIKEN Research Center for Allergy &amp; Immunology</td>
</tr>
<tr>
<td></td>
<td>Yokohama, Japan</td>
</tr>
</tbody>
</table>

Honors

<table>
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<tr>
<th>Year</th>
<th>Award</th>
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<tbody>
<tr>
<td>1990</td>
<td>Young Investigator Award, Western Society for Clinical Investigation</td>
</tr>
<tr>
<td>1990</td>
<td>Henry Kunkel Young Investigator Award,</td>
</tr>
<tr>
<td></td>
<td>American College of Rheumatology</td>
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<tr>
<td>1993</td>
<td>Junior Investigator Award, American Association of Immunologists</td>
</tr>
<tr>
<td>1997</td>
<td>Lee C. Howley Prize, Arthritis Foundation</td>
</tr>
<tr>
<td>1998</td>
<td>Forty-First Faculty Research Lecturer, University of California,</td>
</tr>
<tr>
<td></td>
<td>San Francisco</td>
</tr>
<tr>
<td>2001</td>
<td>American Association of Immunologist-Huang Foundation Meritorious Career</td>
</tr>
<tr>
<td>2003</td>
<td>Fellow, American Academy of Arts and Sciences</td>
</tr>
<tr>
<td>2004</td>
<td>Member, National Academy of Sciences</td>
</tr>
<tr>
<td>2004</td>
<td>Fellow, American Academy of Microbiology</td>
</tr>
<tr>
<td>2004</td>
<td>Member, Institute of Medicine</td>
</tr>
<tr>
<td>2004</td>
<td>Distinguished Investigator Award, American College of Rheumatology</td>
</tr>
<tr>
<td>2004</td>
<td>Walter Bauer Visiting Professor in Rheumatology, Massachusetts General</td>
</tr>
<tr>
<td></td>
<td>Hospital</td>
</tr>
<tr>
<td>2004</td>
<td>Bridget Ogilvie Lecture, University of Dundee, Scotland</td>
</tr>
<tr>
<td>2004</td>
<td>Sue Kim Hansen Lecture, Boston University School of Medicine</td>
</tr>
<tr>
<td>2005</td>
<td>Dan H. Campbell Memorial Lecture, Midwinter Conference of Immunologists,</td>
</tr>
<tr>
<td></td>
<td>Asilomar, CA</td>
</tr>
<tr>
<td>2005</td>
<td>Visiting Professor, Harvard Medical School Rheumatology Division</td>
</tr>
<tr>
<td>2005</td>
<td>Beirne B. Carter Lecture in Immunology, University of Virginia</td>
</tr>
<tr>
<td>2005</td>
<td>Dan H. Campbell Memorial Lecture, Midwinter Conference of Immunologists,</td>
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<td></td>
<td>Asilomar, CA</td>
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<tr>
<td>2006</td>
<td>Keynote Speaker, American Association of Immunologists, Advanced</td>
</tr>
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<td></td>
<td>Immunology Course</td>
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<tr>
<td>2009</td>
<td>Ishizaka Lecture, La Jolla Institute for Allergy and Immunology</td>
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<tr>
<td>2009</td>
<td>46th Charles A. Stuart Memorial Lecture, Brown University</td>
</tr>
<tr>
<td>2010</td>
<td>Dorothy Baugh Harmon Endowed Lectureship, Oklahoma Medical Research</td>
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<tr>
<td></td>
<td>Foundation</td>
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<tr>
<td>2012</td>
<td>Lifetime Achievement Award, American Association of Immunologists</td>
</tr>
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</table>
Selected Peer-reviewed Publications (from a total of 203)


**Research Support**

Ongoing Research Support

Howard Hughes Medical Institute Weiss (PI) 07/01/85-08/31/12
Cell surface molecules and molecular events involved in human T cell activation
The goal is to study cell surface molecules and molecular events involved in T cell activation. HHMI personnel (3 postdocs and 4 technicians) focus on structure of the TCR and the ZAP-70 protein tyrosine kinase.
Role: Principal Investigator

RO1 AI066120 Weiss (PI) 02/15/06-01/31/12 No Cost Extension
NIH/NIAID
Function of the RPTP CD148 in the Hematopoietic Lineage
The goals in this research 1) characterize the developmental, functional, and biochemical consequences of CD148 loss on the T cell lineage, with emphasis on TCR signaling pathways; 2) characterize the developmental, functional and biochemical consequences of the loss CD148 on the B cell lineage, with emphasis on the antigen receptor signaling pathways; and, 3) characterize the biochemical, functional and immunological consequences of inactivating the CD148 gene in myeloid cells on integrin and Fc-receptor dependent pathways.
Role: Principal Investigator

RC2 AR058947-01 (A.Weiss) 09/25/09-08/31/12 No Cost Extension
NIH/NIAMS
An allosteric inhibitor of ZAP-70 as a novel therapeutic for autoimmune disease
The goals of this project are develop and allosteric inhibitor of ZAP-70 and determine the preclinical utility of a model catalytic inhibitor of ZAP-70 in preclinical models of disease.
Role: Principal Investigator

PO1 AI091580-01 07/15/11-06/30/16
NIH/NIAID (Program Leader A. Weiss)
Deconstructing and Reconstructing the T Cell Signaling Network
The goals of this project are to understand the molecular mechanisms that operate at the plasma membrane to control the specificity, activity and regulation of the TCR signaling mechanisms that lead to protein tyrosine phosphorylation and Ras activity.
Completed Research

PO1 AI35297 Abbas (PI) 08/01/06-07/31/11
NIH/NIAID
Peripheral Tolerance and Autoimmunity
Project #3
Regulation of CD45 signaling in tolerance and autoimmunity
The goals of this project are to exploit a newly discovered model of autoimmunity caused by a genetic disruption that prevents CD45 dimerization as a model for defects in signaling receptors that interfere with self-tolerance. T cell lineages responsible for autoimmunity and the role of antigen will be defined, and the molecular basis of CD45 regulation of lymphocyte responses and self-tolerance will be examined.
Role: Co-Investigator

PN2 EY016546 Lim (PI) 09/01/08-08/30/09
NIH
Cellular Control: Synthetic Signaling/Motility (RMI)
The goals of this project are to engineer cells or cell-like molecular assemblies that perform “smart” therapeutic functions: tasks such as tissue repair or “search and deliver” actions to treat microscopic tumors or cardiovascular lesions.
Role: Project Principal Investigator

RO1 AI52127 Goodnow (PI) 09/15/02-06/30/07
NIH/NIAID
Genes for Tolerance and Immunity Consortium
A consortium of investigators will develop and validate screening tests to identify mice with altered immune regulation, and then define the mutant gene, molecular pathways, and cellular processes revealed by each new mouse strain.
Role: Co-Investigator

U54 GM62114 (NIH/NIGMS) Gilman (PI) 09/01/00-08/31/05
Alliance for Cellular Signaling
The goal for this collaborative effort is to understand G protein-regulated and related cellular signaling systems, qualitatively and quantitatively. The Alliance will study signaling in two cells from the mouse: the cardiac myocyte and the B lymphocyte.
Role: Co-Investigator

5 R01 CA72531-06 (NIH/NCI) Weiss (PI) 02/01/98-01/31/05
Function of the Vav Proto-oncogene
The goals in this application will build on these observations to further explore the mechanism by which Vav1 contributes to TCR signaling. Our specific aims are: 1) to understand the mechanism by which Y174 negatively regulates Vav1 function; 2) to define the relative roles of Vav1 and PIX in activating Pak1 and understand how Pak regulates TCR signal transduction pathways; 3) to identify the domain(s) and
mechanism(s) responsible for the GEF-independent Vav1 function that regulates NFAT-regulated transcriptional responses; and 4) To define the mechanism for LAT-dependent Rac activation. These studies will provide a comprehensive view of how Vav1 and Pak1 are regulated and contribute to TCR signaling.

Role: Principal Investigator
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>
<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>Harvard University</td>
<td>A.B.</td>
<td>1984-1988</td>
<td>Physics</td>
</tr>
<tr>
<td>Massachusetts Institute of Technology</td>
<td>Ph.D.</td>
<td>1988-1993</td>
<td>Physics</td>
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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, Molecular Cell
2001-2003 Ad hoc reviewer, 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 NIH on Amyloid Diseases
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, Journal of Molecular Biology
2007 to Present Board of Reviewing Editors, Science
2007 to Present Scientific Advisory Board, 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, 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 Assistant Investigator, 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)
2010 Fellow, American Academy of Microbiology

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


**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.

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 (homooligomers) 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.

P50 GM073210 (Stroud; Weissman - Key Personnel) 09/01/09 – 08/31/2014
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 for Drug Discovery (Weissman) 11/01/11 - 10/31/2012
Identifying and Characterizing Asiatic Cholera Host Factors
Specific aims of this project are: develop a quantitative functional reporter assay for action of cholera toxin in cell culture; conduct a comprehensive genome-wide screen for factors affecting cholera toxin action; validate and characterize the targets in physiological assays for cholera activity.

Completed Research Support

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.

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.
Defining Roles on N-Glycans in Endoplastic Reticulum-Mediated Quality Control

Specific aims of this project are: biochemical characterization of the putative mannosidase Htm1; and elucidation of contributions of glycan and mis-folded protein components to substrate recognition in late stages of ERAD-L pathway.
BIOGRAPHICAL SKETCH

NAME
Zena Werb, Ph.D.

POSITION TITLE
Professor of Anatomy

eRA COMMONS USER NAME
werbzena

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>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

1973-1975 Research Scientist, Strangeways Res. Lab., Cambridge, United Kingdom
1975-1976 Visiting Assistant Professor of Medicine, Dartmouth Medical School, Hanover, NH
1976-1980 Assistant Professor Radiobiology, Radiology University of California, San Francisco
1979-1980 Assistant Professor Anatomy, University of California San Francisco
1980-1983 Associate Professor of Anatomy and Radiology University of California, San Francisco
1983-Present Professor Anatomy, UCSF
1985-1986 Visiting Professor, Sir William Dunn School of Pathology University of Oxford, United Kingdom
1998 Visiting Professor, Institut Curie, Paris
1999-Present Vice-chair, Dept. of Anatomy, University of California, San Francisco
2006-2008 Visiting Professor, 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
2011  Zero Breast Cancer 2011 Community Breast Cancer Research Award

Named Lectureships

1986  Muriel Trotter Lecture, Washington University
1992  Lowell Lectures in Biotechnology, Northeastern University, Boston, MA
1993-1994  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, University of California, San Francisco
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
2010  Keynote Lecture, American Society for Investigative Pathology Annual Meeting, Anaheim, CA
2010  William Larson Distinguished Lecture, University 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
2010-Present  Guest Editor, Proc. National Academy Science, USA
2010-Present  Member, Editorial Board, Disease Models and Mechanisms
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
2009-2012  Chair, American Academy of Arts and Sciences, Membership Selection Committee Class II, section
2010      Co-organizer, CNIO Cancer Symposium on Frontiers in Invasion and Metastasis, Madrid
2011-Present Member, Steering Committee, AACR Council of Scientific Advisors
2011-2016  Member, Scientific Advisory Board, Max Planck Institute for Biology of Ageing, Cologne, Germany

Selected Publications (>440 total full publications)


Research Support

Ongoing

NIH/NCI R01 CA129523-04 Werb (PI) 07/01/08 - 04/30/13
Transcriptional Regulation of Breast Cancer Metastasis
This study addresses how GATA-3 regulates the differentiated state of breast tumors.

NCI R01 CA057621-19 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 AI053194-09 Mostov (PI), Werb (Leader, Project 4 and Core C) 09/30/02 - 08/31/13
Mucosal Immune Barrier in Infection and Inflammation
This project studies the role of the inflammatory response in mucosal epithelia.

Stand Up To Cancer SU2C-AACR-DT0409-03 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.

**SU01 ES019458-02 (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 environmental stressors affect them.

**SP50 CA058207-17 van ‘t Veer (PI), Werb (PI on Developmental Project)**
05/01/11-04/30/12

**NIH/NCI Bay Area Breast Cancer SPORE and Bay Area Physical Sciences-Oncology Center. Modifying the Stromal Microenvironment to Reduce Breast Cancer Metastasis**
The goal of this Developmental Research Program Award is to test agents that modify the fibrotic response on progression of basal type breast cancer.

**17UB-8705 California Breast Cancer Research Program (Werb, PI)** 09/01/11-08/31/13
Biomarkers for environmental exposures in breast cancer
The major goal of this project is to find glycan biomarkers that are induced by exposure to environmental stressors.

Completed

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

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

**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 CA105379-05 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/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 studied environmental effects on the molecular architecture and function of the mammary gland.
BIOGRAPHICAL SKETCH

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>
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<tr>
<td>Wesleyan University, Middletown, CT</td>
<td>B.A.</td>
<td>6/1989</td>
<td>Letters</td>
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<tr>
<td>Columbia College of Physicians &amp; Surgeons, NY</td>
<td>M.D.</td>
<td>6/1993</td>
<td>Medicine</td>
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<tr>
<td>Massachusetts General Hospital</td>
<td>Resident</td>
<td>1993-1996</td>
<td>Internal Medicine</td>
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<tr>
<td>Harvard School of Public Health</td>
<td>M.P.H.</td>
<td>6/1998</td>
<td>Epidemiology</td>
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<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

1993-96 Intern and 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
2009-2011 NIH Peer Review Committee, RC2 special emphasis panel ZHL1 CSR-D (O1), ZHL1 CSR-W (S1), XRG1-N
2011- Co-Chairperson, Section on Genomics, American Thoracic Society
2012- Associate Editor, American Journal of Respiratory and Critical Care Medicine

Honors

1993 Alpha Omega Alpha, Columbia College of Physicians and Surgeons, NY, NY
2012 Elected to membership, American Society of Clinical Investigation

Selected peer-reviewed publications (Selected from 49 peer-reviewed publications)


**Research Support**

**ACTIVE**

R01 HL095372-01 (Woodruff PG) 9/24/2008 - 7/31/2012

NIH/NHLBI “Molecular Phenotyping of Asthma”

To identify and characterize molecular phenotypes of asthma using gene expression profiling, quantitative morphometry and related imaging techniques.
R01 HL097591 (Woodruff PG) 7/1/2009 - 6/30/2013
NIH/NHLBI “Role of Th2 and non-Th2 Inflammation in Airway Smooth Muscle Remodeling in Asthma”
To identify pathways linking Th2-driven inflammation to airway smooth muscle remodeling in human tissues.

N01-08-08 (Woodruff PG) 2/1/2009 - 1/31/2016
NIH/NHLBI “The Spiromics Project: Clinical Center”
To identify sub-populations and intermediate outcome measures in COPD through a large multi-center longitudinal study.

1U10HL109146 (PI: Fahy, Co-I: Woodruff) 7/1/2011-6/30/17
NIH/NHLBI “Severe Asthma Research Program”
To identify sub-populations in severe asthma through a multi-center longitudinal study.

R01 HL109102-01 (PI: Ansel, Co-I: Woodruff) 8/01/11 –6/30/16
NIH/NHLBI “Role of miRNAs in Th2-Driven inflammation in Asthma”
To identify the role of miRNAs in T-cell differentiation and effector function in asthma.

NIH/NHLBI “UCSF AsthmaNet Clinical Center Clinical Research Skills Development Core”
To promote clinical research skill development in trainees in the context of NHLBI-supported multi-center clinical trials of asthma therapies in children and adults with asthma.

N01 AI90052 (PI: Busse) 9/30/2009- 9/29/14
NIH/NIAID “Inner City Asthma Consortium (ICAC): Immunologic Approaches to Reduce Asthma”
To identify immunological approaches to reduction in asthma prevalence and severity in inner city populations.

PENDING

U10 RFA-HL-12-013 (PI: Koth) 4/012012 – 3/31/15
NIH/NHLBI “Genomic Phenotyping and Mechanisms in sarcoidosis and AAT”
To perform human studies to elucidate the genomic underpinnings of sarcoidosis and AAT.

R01HL110883 (PI” Kheradmand) 2/01/2012 – 1/31/16
NIH/NHLBI “Ancillary T Cell Based Studies in SPIROMICS”
To determine whether T-cell based autoimmunity is associated with early and progressive emphysema.

P01 HL107202 (PI: Fahy)