

ANNUAL REPORT

DEPARTMENT OF
MICROBIOLOGY AND
IMMUNOLOGY

JEFFERSON MEDICAL COLLEGE OF
THOMAS JEFFERSON UNIVERSITY

JULY 1, 2006 THROUGH JUNE 30, 2007

TIM L. MANSER, PH.D.
CHAIR



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FACULTY OF THE DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY

Name	Faculty Academic Rank	Joint Appointment or Affiliation
Tim L. Manser, B.A., Ph.D.	Professor and Chair	
David Abraham, Ph.D.	Professor	
David Berd, B.S., M.D.*	Professor	Department of Medicine
Melvin J. Bosma, Ph.D.	Adjunct Professor	Fox Chase Cancer Center
Catherine E. Calkins, B.A., Ph.D.	Professor	
Bernhard Dietzschold, B.S., D.V.M.	Professor	
Laurence C. Eisenlohr, V.M.D., Ph.D.	Professor	
Neal Flomenberg, B.S., M.D.	Professor	Department of Medicine,
	Medical Oncology	
Richard R. Hardy, Ph.D.	Adjunct Professor	Fox Chase Cancer Center
Donald L. Jungkind, B.S., M.D., Ph.D.	Professor	Department of Pathology,
	Anatomy & Cell Biology	
W. Edward Mercer, B.S., Ph.D.	Professor	
Jeffrey V. Ravetch, M.D., Ph.D.	Adjunct Professor	Rockefeller University
Matthias Schnell, Ph.D.	Professor	
J. Bruce Smith, M.S., M.D.*	Professor	Department of Medicine
Algarsamy Srinivasan, Ph.D.	Professor	
Raffaele Baffa, M.D.*	Associate Professor	Department of Urology
Arthur Buchberg, B.Sc., Ph.D.	Associate Professor	
Glen F. Rall, B.A., Ph.D.	Adjunct Associate Professor	Fox Chase Cancer Center
Linda D. Siracusa, B.Sc., Ph.D.	Associate Professor	
Luis J. Sigal, DVM, Ph.D.	Adjunct Associate Professor	Fox Chase Cancer Center
David L. Wiest, B.S., Ph.D.	Adjunct Associate Professor	Fox Chase Cancer Center
Yuri Sykulev, M.D., Ph.D.	Associate Professor	
Kishore Alugupalli, Ph.D.	Assistant Professor	
Jerome G. Buescher, B.A, Ph.D.	Clinical Assistant Professor	
John F. Klement, B.S., M.S., Ph.D.*	Assistant Professor	Department of Dermatology
Carlisle P. Landel, A.B., Ph.D.	Research Assistant Professor	
James P. McGettigan, B.S., M.S., Ph.D.	Research Assistant Professor	
Jianke Zhang, Ph.D.	Assistant Professor	
S.M. Ziaur Rahman, M.D., Ph.D.	Instructor	

* Secondary appointment in the Department of Microbiology and Immunology

FACULTY OF THE DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY

Name	Faculty Academic Rank	Joint Appointment or Affiliation
W. Paul Havens, Jr., A.B., M.D.	Honorary Professor	Department of Medicine
Susan E. Rittenhouse, B.A., Ph.D.	Emeritus Professor	
Jussi Saukkonen, M.D.	Honorary Professor	
Russell W. Schaedler, M.D.	Plimpton-Pugh Professor Emeritus <i>Deceased 2007</i>	
Charles Panos, Ph.D.	Professor Emeritus	
Harry W. Smith, Ph.D.	Professor Emeritus <i>Deceased 2006</i>	
Abbas ar-Rushdi, B.S, Ph.D.	Honorary Research Associate Professor	
Carl F. Clancy, B.S., M.S., Ph.D.	Honorary Associate Professor	

** Secondary appointment in the Department of Microbiology and Immunology*

**STATE OF THE DEPARTMENT
DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY
JEFFERSON MEDICAL COLLEGE**

The Department continues to deliver outstanding education and training to medical students, graduate students and postdoctoral research fellows. Our primary goals remain education, and building and maintaining internationally recognized research programs in the areas of immunology, infectious disease and genetics. The majority of Departmental faculty have active research programs. In addition to full-time research, our faculty spends a great deal of time teaching at both the medical school and graduate school level.

FACULTY NEWS

James McGettigan, Ph.D., was promoted to Research Assistant Professor and S.M. Ziaur Rahman, M.D., Ph.D., was promoted to Instructor. Matthias Schnell, Ph.D., Professor has been awarded tenure. Luis Sigal, VMD, Ph.D. joins the Department as an Adjunct Associate Professor. Dr. Sigal a Member of the Fox Chase Cancer Center (FCCC), and joins our other FCCC adjunct members. Dr. Sigal is a viral immunologist and provides Jefferson with his teaching expertise in the Microbial Pathogenesis Program.

The Department hosted a symposium in honor and memory of Bice Perussia, M.D., a professor in the Department who passed away in April 2006. This symposium, "The Future of Immunology," was held on our Center City Campus on May 8, 2007 and hosted seven internationally recognized scientists and former colleagues of Dr. Perussia. The event was an outstanding scientific meeting and a wonderful tribute to Dr. Perussia's life and research accomplishments. Program participants included Carlo M. Croce, M.D., Marco Colonna, M.D., Paulo Casali, M.D., Jordon Orange, M.D., Ph.D., Jeffrey Miller, M.D., Giorgio Trinchieri, M.D. and Jeffrey Ravetch, M.D., Ph.D. Russell Schaedler, M.D., Professor and Chair Emeritus passed away on May 8, 2007. Dr. Schaedler served as professor and chair of this Department from 1968-1991. Dr. Schaedler remained an active member of the Jefferson Community and continued as a member of our teaching faculty for many years past his retirement.

Harry L. Smith, Jr., Ph.D., Professor Emeritus passed away on December 6, 2006. Dr. Smith served this Department as an educator and researcher for 42 years.

PLANS FOR FUTURE FACULTY

Fabienne Paumet, Ph.D. will join the Department in December 2007 as an Assistant Professor, in the Academic Investigator Track. Dr. Paumet's research area is vesicle trafficking and its inhibition by pathogenic infection. She comes to our Department from Columbia University where she was an Associate Research Scientist. Dr. Paumet's laboratory will be located in 750 Bluemle Life Sciences Building.

EDUCATION

GRADUATE PROGRAMS – DEPARTMENTAL AND INTER-DEPARTMENTAL

Laurence C. Eisenlohr, V.M.D., Ph.D., Chair, Training Committee

The Department offers doctoral programs in Genetics and Immunology & Microbial Pathogenesis. These, along with doctoral programs in Biochemistry & Molecular Biology as well as Molecular Pharmacology & Structural Biology form the Joint Programs of the Kimmel Cancer Center. Joint Programs option allows an entering student to complete the first year of coursework while sampling research in any of the four Ph.D. Programs described above. Each of the programs of study is designed to provide graduating students with outstanding training and research experience to pursue future careers as scientific investigators in academic, biotechnology, government or industrial settings. Students in each program take a core course, GC 550 Foundations in Biomedical Sciences that includes basic biochemistry, molecular biology, cell biology and genetics as well as complete three laboratory research rotations during the first year of study. They then select a mentor in whose laboratory they will complete their studies, while students completing the first year in the Joint Program also select one of the four Ph.D. Programs as their formal course of study.

The Department has been very active in seeking extramural funding for our training programs. We now have two highly competitive NRSA Institutional Training Grants that provide stipend and research expense support for both predoctoral and postdoctoral fellows. Currently, active awards include Training in Molecular Genetics of Cancer and Cancer Immunology.

The Department continued its recruiting and outreach efforts in the past year.

IMMUNITY, INFECTION AND DISEASE (MI200)

David Abraham, Ph.D., Course Coordinator

Immunity, Infection and Disease (MMI200) presented to second year medical students under the direct organization and supervision of Dr. David Abraham was taught this past year to 232 students. The course ran for 9 weeks from the middle of September to the middle of November. The goals of the course are to teach the fundamentals of immunology and the component sections of microbiology, bacteriology, virology, mycology and parasitology. Pharmacology lectures, relevant to immunology and microbiology, are presented at relevant points throughout the course. In addition, it is the objective to introduce the students to the practice of Infectious Diseases. The course consists of 108 lectures, 11 clinical conferences and 9 two-hour laboratories.

The Microbiology Laboratory curriculum is under the direction of Jerome Buescher, Ph.D., Clinical Assistant Professor. The Laboratory Manual is revised yearly to better meet the goal of teaching useful skills to the sophomore medical student and familiarizing them with some of the protocols and techniques currently used in the clinical laboratory to support their diagnostic activities. To satisfy these objectives there is a significant reliance on students actually performing the basic studies and relating them to case studies. Students also present their cases and supporting studies they perform.

This year an additional Clinical Management Conference was added to the laboratory.

The two conferences utilized a Team Learning educational approach to instruct the students how to manage complex infectious disease cases. These conferences were enthusiastically received by both students and faculty.

There were several student initiatives in the course that enhance the ability of the class to understand, appreciate and remember the course content. These included three “movie nights”, where Nova or National Geographic documentaries on Ebola, bioterrorism and plague were shown, the development of a student generated study question bank and the invitation of a faculty member from the University of Pennsylvania to teach the students songs to remember key facts about clinical microbiology.

Students performed very well in the course, achieving class averages comparable to past years. In addition, student evaluations were very enthusiastic about the course expressing general satisfaction with the course material and faculty.

The 2007 Robert J. Mandle Memorial Graduation Award was given to Gary Schienbaum. This award is given each year to the graduating medical student who has shown the greatest proficiency in research in the field of microbiology or related medical sciences as judged by the Department’s faculty.

DEPARTMENTAL RESEARCH

The Department has an impressive record of grant support. Despite the recent dramatic down turn in NIH pay lines, the faculty continue to remain robustly funded for research by extramural sources. Funded programs are detailed in the Research Support Section of this report. (See page 54). The Departments of Microbiology and Immunology, Biochemistry and Molecular Biology, and the Cancer Biology host an active joint Research Seminar Program in which an outstanding scientist presents his/her work and spends the day meeting with faculty, postdoctoral fellows and graduate studies. The seminar series takes place from September through May. The Joint Seminar Series also hosts three named lectureships, which take place during the year. Individual research groups hold journal clubs and special seminars weekly. Faculty present their research at the Monday Staff Seminar Series held jointly with the Departments of Microbiology and Immunology and Biochemistry and Molecular Biology and the Kimmel Cancer Center.

The Department’s strengths rest with the first-class scientists who make up our research program. In addition to establishing and maintaining research programs, these scientists are responsible for the education of postdoctoral fellows, graduate students and medical students. The Department includes a diverse group of scientists studying immunology, infectious diseases, virology and genetics.

JEFFERSON VACCINE CENTER

The Jefferson Vaccine Center (JVC) is a newly established Center administered by the Department of Microbiology and Immunology and directed by two of its faculty. Matthias Schnell, Ph.D., Professor is the director and Laurence C. Eisenlohr, VMD, Ph.D., is the associate director of this new entity. The focus of the Center is to facilitate analysis of the molecular and cellular mechanisms in infectious disease and novel approaches for their prevention to increase human health and quality in developed and developing countries. The Center provides support to members in seeking funding op-

portunities, opens avenues for funding not available to single investigators, assists in the preparation of training and collaborative grants while facilitating collaborations, provides resources advocating for the Center with TJU and mentoring of junior faculty members. The Center will hold a regular seminar series on a monthly basis. The series will alternate speakers internal and external to TJU.

INTERDEPARTMENTAL PROGRAMS

Many faculty members hold secondary appointments in other departments. The Department's faculty interacts closely with faculty members in the Department of Biochemistry and Molecular Biology as well as with members of the Kimmel Cancer Center.

DEPARTMENTAL ADMINISTRATION

Tim L. Manser, Ph.D., Chair

Kathleen A. Reinersmann, Assistant to the Chair and Director, Faculty Career Development and Advocacy

- Andrew Curran, Administrator
- Dorothy Wyszynski, Business Coordinator and Assistant to the Administrator
- Dina Leibowitz, Timekeeper/Personnel Coordinator
- Melissa McDaid, Purchasing Coordinator
- Kathy Wyszynski, Grant Accountant
- Tracy Kajesky, Grant Accountant
- Tina Bergey, Grant Accountant
- * Joanne Balitzky, Graduate Programs
- * Kathleen Keiser, Assistant, Graduate Programs
- * Janice Rago, Grants Administrator
- * Linda Hines, Grants Specialist
- * Nicole Matthews, Grants Specialist
- * Jeannine Voll, Grants Processor
- * Yolanda Crespo, Grants Processor
- * Kate Salmon
- * Kelly Gallagher

◦ Indicates shared with Departments of Cancer Biology, Biochemistry and Molecular Genetics and the Kimmel Cancer Center

Indicates shared with Department of Cancer Biology and the Kimmel Cancer Center

COLLEGE

It is our goal to continually improve our teaching and research performances. Our faculty members are experts in their field and are dedicated to teaching and providing students with the fundamental knowledge of immunology, bacteriology, virology, mycology, parasitology and genetics. It is our expectation to expand our first class research program, thus contributing to Jefferson's reputation as an outstanding medical school and research institution.

DAVID ABRAHAM, PH.D.
PROFESSOR

DESCRIPTION OF RESEARCH

Research in my laboratory is directed at understanding how the immune response eliminates large multicellular parasites and determining how the parasites have evolved to evade the destructive immune response. Two general approaches are being used, the first is to study the immune response from a basic science perspective with the goal of understanding the mechanism by which the parasites are killed. The second approach is to utilize this knowledge to develop vaccines against the infections.

1. FUNCTION OF EOSINOPHILS AND NEUTROPHILS IN THE CONTROL OF HELMINTH INFECTIONS.

Eosinophils have been shown to be associated with the development of allergic responses and the control of helminth infections. The goal of this project is to determine the role of eosinophils in the innate and adaptive immune response of mice to the nematode parasite *S. stercoralis*. We have shown that protective immunity to these parasites is dependent on IL-5 and on eosinophils. The goals of this project are: (1) To determine the role of eosinophils in killing larvae by the innate immune response. The approach taken is to determine if killing of larvae by the innate immune response is dependent on granule release from the eosinophils in the immediate environment of the larvae and which specific mouse eosinophil granule products are capable of killing larvae in vitro and in vivo. (2) To determine the role of eosinophils in the induction of the adaptive immune response. Previous studies have shown that eosinophils are essential for the induction of the adaptive immune response against *S. stercoralis*. The focus of these studies is to assess the capability and potential of eosinophils to function as antigen presenting cells. Previous studies have shown that eosinophils can act as APC to induce Th2 responses. The goal is now to study the mechanisms used by eosinophils to present antigen in comparison to other professional APCs (3) To determine the role of eosinophils and neutrophils in killing parasites through the adaptive immune response. In this section we are studying how granulocytes participate in killing larvae in collaboration with antibody and complement.

2. VACCINE DEVELOPMENT AGAINST HELMINTH INFECTIONS.

The goals of this research project are: (1) to determine the mechanisms used by the immune response to kill the parasites and (2) to utilize the information gained on how the parasites are killed to develop vaccines against these infections. We have demonstrated that antibody is crucial for the immune control of these infections. Protective immunity has been shown to be dependent on IgG or IgM depending on the immunization regimen. Furthermore, we have determined that human antibody will kill the parasites in mice. The anatomical and molecular specificity of the mouse and human protective antibodies are all different, thereby providing tools for identifying a variety of antigens for use in clinically applicable vaccines. Recombinant antigens have been identified and cloned based on their recognition by antibodies. These antigens are then tested using different delivery systems to determine vaccine efficacy. Several recombinant antigens have been identified which are successful at inducing protective im-

immunity to infections in mice. DNA vaccines have also been successfully developed with other antigens. Efforts are now directed to determine the optimal way to administer these antigens to induce immune resistance to the infections.

3. SERODIAGNOSIS OF STRONGYLOIDIASIS.

Human infections with the parasite *Strongyloides stercoralis* remain a challenge to diagnose. Serum samples have been collected from approximately 100 patients with proven *S. stercoralis* infections and 100 normal patients from endemic loci in Argentina. Three different sets of antigens will be tested in two different assays to determine the optimal method for serologically diagnosing strongyloidiasis.

4. TREATMENT OF AMERICAN CUTANEOUS LEISHMANIASIS.

Previous studies in humans, mice and hamsters have shown that treatment with azithromycin will reduce infections with cutaneous leishmaniasis. The objective is to now add another drug, fluconazole, to the treatment regimen of hamsters infected with *Leishmania brasiliensis* to determine if the dual drug treatment will result in a synergized elimination of the infection.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Kerepesi L.A , J.A. Hess, T.J. Nolan, G.A. Schad and D. Abraham. 2006. Complement component C3 is required for protective innate and adaptive immunity to larval *Strongyloides stercoralis* in mice. *Journal of Immunology*. 176:4315-4322.

Padigel, U.M., J. J. Lee, T.J. Nolan, G.A. Schad and D. Abraham. 2006. Eosinophils can function as antigen presenting cells to induce primary and secondary immune responses to *Strongyloides stercoralis*. *Infection and Immunity*. 74:3232-3238.

Galioto, A.M., J. A. Hess, T. J. Nolan, G. A. Schad, J. J. Lee, and D. Abraham. 2006. Role of eosinophils and neutrophils in innate and adaptive protective immunity to larval *Strongyloides stercoralis* in mice. *Infection and Immunity*. 74:5730-5738.

Kerepesi L.A , J.A. Hess, O. Leon, T.J. Nolan, G.A. Schad and D. Abraham. 2007. Toll-like receptor 4 (TLR4) is required for protective immunity to larval *Strongyloides stercoralis* in mice. *Microbes and Infection*. 9:28-34.

Padigel, U.M., L. Stein, K. Redding, J.J. Lee, T.J. Nolan, G.A. Schad, L. Birnbaumer and D. Abraham. 2007. Signaling through *Gai2* protein is required for recruitment of neutrophils for antibody mediated elimination of larval *Strongyloides stercoralis* in mice. *Journal of Leukocyte Biology*. 81:1120-1126.

Padigel, U.M., J.A. Hess, J.J. Lee, J.B. Lok, T.J. Nolan, G.A. Schad, and D. Abraham. 2007. Eosinophils act as antigen presenting cells to induce immunity to *Strongyloides stercoralis* in mice. *Journal of Infectious Diseases*. In Press.

Krolewiecki, A.J., H.D. Romero, S.P. Cajal, D. Abraham, T. Mimori, M. Tamami, M. Juarez and N.J. Taranto. 2007 A randomized clinical trial comparing oral azithromycin and meglumine antimoniate for the treatment of American cutaneous leishmaniasis due to *Leishmaniana (Viannia) braziliensis*. *American Journal of Tropical Medicine*. In Press.

SCIENTIFIC PRESENTATIONS

MEETING PRESENTATIONS

Buescher, J.G. D. Abraham and J. DeSimone. Team-based learning exercises in the laboratory portion of a medical school “Immunity, Infection, and Disease” course. Fifth Annual Team-Based Learning Collaborative Conference. Lubbock TX. March, 2006

O’Connell, A.E., and D. Abraham. Myeloperoxidase is required for protective adaptive immunity to *Strongyloides stercoralis* in mice. The 55th Annual Meeting of the American Society of Tropical Medicine and Hygiene. Atlanta, GA. November, 2006. (Abstract No.1108)

O’Connell A.E and D. Abraham. Macrophages produce a soluble mediator which enables neutrophils to kill the parasitic nematode *Strongyloides stercoralis*. The 94th American Association of Immunologists Annual Meeting, Miami Beach, FL. May, 2007 (J. Immunol., Apr 2007; 178: 51.4).

Abraham, D., L. Stein, U. Padigel, J. Hess and J.J Lee. Eosinophil interaction with a parasitic nematodes: recruitment, killing and antigen presentation. 5th Biennial Symposium of International Eosinophil Society. Snowbird, UT. July 2007

INVITED PRESENTATIONS

“Neutrophils in the immune response to *Strongyloides stercoralis*: Recruitment, activation and killing” University of Pennsylvania Seminar Series in Parasitology. 2007

TEACHING

MICR 200 *Immunity – Infection and Disease* – Course Director and 10 lecture hours

MI 600 *Microbiology* – 4 lecture hours

MICR-403 *Research Elective in Microbiology* – Course Director

IMP 530 *Infection and Immunity* – 6 lecture hours

COMMITTEES

Course Director, Immunity Infection and Disease, Jefferson Medical College

Chairman, Curriculum Committee, Jefferson Medical College

Member, Professorial Advisory Committee, Jefferson Medical College

Member, Immunology and Microbial Pathogenesis Teaching Committee, Kimmel Cancer Center

EDITORIAL RESPONSIBILITIES

Acta Parasitologica

American Journal of Tropical Medicine and Hygiene

Cellular Immunology

Clinical and Diagnostic Laboratory Immunology

Clinical Microbiology Reviews

Experimental Parasitology
FEMS Immunology and Medical Microbiology
Human Gene Therapy
International Journal for Parasitology
Journal of Allergy and Clinical Immunology
Journal of Immunology
Journal of Infectious Diseases
Journal of Leukocyte Biology
Journal of Parasitology
Microbes and Infection
Parasite
Parasitology
Parasite Immunology
Parasitology Research
Proceedings of the National Academy of Sciences, U.S.A.
Transactions of the Royal Society of Tropical Medicine and Hygiene
Vaccine

MEMBERSHIPS

American Society of Parasitologists
American Association of Immunologists
American Society of Tropical Medicine and Hygiene
Helminthological Society of Washington
American Association for Advancement of Science

HONORS/AWARDS

Member of Editorial Board – American Journal of Tropical Medicine and Hygiene
Adjunct Professor of Parasitology, Department of Pathobiology, School of Veterinary
Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

COLLABORATIONS

Dr. Sara Lustigman - New York Blood Center
Drs Gerry Schad, Tom Nolan, Ed. Pearce and Phil Scott - University of Pennsylvania
Drs Jamie and Nancy Lee - Mayo Clinic-Scottsdale
Dr. Tom Nutman - National Institutes of Health
Dr Patrick Lammie – Center for Disease Control
Dr. David Andrew – Department of Neurosurgery
Dr. Alejandro Krolewiecki - Fundación Huésped Buenos Aires

KISHORE R. ALUGUPALLI, PH.D.
ASSISTANT PROFESSOR

DESCRIPTION OF RESEARCH

Overwhelming bacteremia is one of the leading causes of death by infectious disease. A critical factor in preventing bacteremia from evolving into a life-threatening infection is the ability of the host to rapidly generate protective antibodies against the invading pathogens. T cell-independent (TI) responses are highly protective and develop significantly more rapidly than T cell-dependent (TD) responses. However, TI responses have been long considered exclusively short-lived and incapable of conferring long-lasting protection.

To understand the immune mechanisms that are capable for the rapid control of bacteremia, we have been studying *Borrelia hermsii*, a bacterial pathogen that colonizes bloodstream very efficiently. We have utilized a murine model of *B. hermsii* infection to show that this TI response in fact generates long-term protection. This immunity is conferred by B1b lymphocytes, a novel subset of B cells whose functions are not yet well understood. These B1b cells expand concurrent with the resolution of *B. hermsii* infection, persist, and secrete protective IgM. Interestingly, while B1b cells from convalescent mice confer complete protection when transferred to immunodeficient mice, naïve B1b cells provide only partial and short-lived immunity, indicating that the convalescent B1b cells have apparently acquired immunological memory. Understanding the basis of this TI memory-like response, and identification of specific antigen(s) targeted by B1b cells are among the major interests of my laboratory.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Alugupalli K. R., Akira, S., Lien E. and Leong J. M. 2007. MyD88- and Bruton's tyrosine kinase-mediated signals are essential for T cell-independent pathogen-specific IgM responses. *The Journal of Immunology*. 178: 3740-3749.

Wong S. M. S., Alugupalli K. R., Ram. S., Akerley, B. A. 2007. The ArcA regulon and oxidative stress resistance in *Haemophilus influenzae*. *Molecular Microbiology*. 64:1375-1390.

SCIENTIFIC PRESENTATIONS

“Immune Responses and Persistent Bacteremia”, 107th General Meeting of the American Society of Microbiology, Toronto, Canada, May 23 2007.

TEACHING

- IMP 600 *Bacteriology* – 8 lecture hours (for Graduate Students)
 Immunity, Infection and Disease – 3 lecture hours (for Medical Students)
 Advanced Cellular and Molecular Immunology – 2 hours (for Graduate Students)
- IMP 530 *Immunology and Microbial Pathogenesis* – 4 lecture hours (for Graduate Students)

COMMITTEES

Member, Kimmel Cancer Center, Flow cytometry facility oversight Committee
Member, Thomas Jefferson University Institutional Biosafety Committee
Member, Thesis committee of Amy O'Connell, MD/Ph.D. student of Jefferson Medical College
Member, Thesis committee of Ph.D. student, Stephen Rosenberg, Josephine Fox, James Testa of Jefferson College of Graduate Studies.

EDITORIAL RESPONSIBILITIES

Reviewer, Infection and Immunity
Reviewer, Journal of Immunology
Reviewer, Molecular Immunology

MEMBERSHIPS

American Society for Microbiology
American Association of Immunologists
American Association for the Advancement of Science

COLLABORATIONS

Dr. John Leong – University of Massachusetts Medical School, Worcester, MA.
Dr. Egil Lien – University of Massachusetts Medical School, Worcester, MA.
Dr. Tim Manser – Jefferson Medical College
Dr. Jianke Zhang – Jefferson Medical College

ARTHUR M. BUCHBERG, PH.D.
ASSOCIATE PROFESSOR

DESCRIPTION OF RESEARCH

My research is focused on the molecular genetics of tumor predisposition and development. We continue to work in two model systems and are developing additional systems. The first is the characterization of homeobox genes involved in myeloid leukemia. We identified several novel oncogenes involved in myeloid leukemia of BXH-2 mice. Nearly 100% of BXH-2 mice develop an aggressive acute myeloid leukemia (AML) by 1 year of age with an average age of onset of 6 months. This leukemia is caused in part by the insertional alteration of cellular protooncogenes or tumor suppressor genes by an endogenous retrovirus. We isolated a common site of viral integration, *Meis1*, which is activated in 15% of the myeloid tumors. *Meis1* encodes a novel homeobox protein and its homeodomain is closest in homology to the homeodomain of PBX1. Our recent work has focused on the characterization of *Meis1* as both an oncogene and a pro-apoptotic gene. We discovered an apparent paradox concerning the functioning of *Meis1*. It is clear that the overexpression of *Meis1* in conjunction with some Hox proteins induces a rapid and fatal myeloid leukemia; in fact, it has been shown that the overexpression of *Meis1* and *HoxA9* is a direct consequence of MLL fusion proteins resulting from chromosomal translocations in pediatric AMLs. However, we discovered that the overexpression of *Meis1* alone induces a rapid apoptotic response in cells. Our recent studies have focused on exploring the role of *Meis1* expression in contributing to cell-death. We have determined that transient expression of *Meis1* in a variety of cell lines induces a rapid apoptotic death. This death is abrogated through the coexpression of *HoxA9* or *HoxA7* (a key cofactor in the development of leukemia) or through deletion of the *Meis1* domain required for Meis-Pbx interaction. In addition, we determined that the expression of *Bcl2* is also capable of abrogating *Meis1* dependent apoptosis. We are currently dissecting the mechanism of this proapoptotic response of the AML cells and exploring ways to develop this strategy into a new therapeutic regimen to combat AML. *Meis1* is also expressed in a wide array of tissues, so we have started to determine the role of *Meis1* in intestinal development and tumorigenesis.

The second model system we are studying is the influence of genetic modifier loci on the incidence of polyp development in colon cancer. This project is being performed in collaboration with the laboratory of Dr. Linda Siracusa. Mutations in the *Apc* gene are responsible for various familial and sporadic colorectal cancers. *Min* mice carry a mutation in the homolog of the *Apc* gene and develop multiple adenomas throughout their small and large intestine. Mapping studies have identified a locus, *Mom1*, which maps to the distal region of chromosome 4 that dramatically modifies *Min*-induced tumor number. We have identified a candidate gene for *Mom1*. The gene for secretory type II Phospholipase A2 (*Pla2g2a*) maps to the same region that contains *Mom1*, and we have identified a 100% concordance between allele type and tumor susceptibility. Expression analysis revealed that *Mom1* susceptible strains are null for *Pla2g2a* activity. Our results indicate that *Pla2g2a* acts as a novel gene which modifies polyp number by altering the cellular microenvironment within the intestinal crypt. We are in the process of determining the mechanism by which *Pla2g2a* acts to confer resistance to polyp formation as well as to determine the role of *Pla2g2a* in the development of human colon cancer. We have also identified a new modifier locus, *Mom2*. *Mom2* re-

duced polyp load 85-95% when compared with control mice. *Mom2* arose as a spontaneous mutation in the *Apc^{Min}* mouse colony at The Jackson Laboratory. We have recently identified a candidate gene responsible for the *Mom2* mutation. We identified an insertion mutation in one allele of *Atp5a1*, the gene encoding the alpha subunit of ATP synthase. The presence of the mutation in *Atp5a1* suggests a hypothesis for the mechanism of action of the *Mom2* allele, linking the importance of metabolic energy homeostasis with tumor initiation. We are in the process of confirming the role of *Atp5a1* in conferring resistance to tumor development and in identifying the pathway that is altered in tumor development. Work is continuing to identify and characterize additional modifier loci that are present within the C3H and CAST genomes that exert profound influences on polyp development. As we identify these modifier genes in the mouse we are exploring their role in the development of human colorectal cancer as both a predictor of disease incidence as well as response to chemotherapeutic regimen. In addition, the identification of new modifier genes could eventually be used to develop new therapeutic strategies against colorectal cancer.

A new project that was recently initiated was to determine the tumor suppressor role of Caveolin 1 (Cav1) in collaboration with Dr. Michael Lisanti. Cav1 functions as a general negative regulator to inhibit the basal activity of many pro-proliferative and oncogenic proteins. We have begun two projects determining the role of Cav1 in tumorigenesis. The first is to determine the effect of Cav1 has on *Apc^{Min}* induced intestinal tumorigenesis. We have initiated crosses between *Apc^{Min}* mice and the Cav1 null mice to determine the effect of the loss of Cav1 expression in polyp initiation and growth. A more long term project that has begun is to determine the effect of the loss of Cav1 expression in mammary tumorigenesis by initiating a sensitized screen for oncogenes and tumor suppressor involved in mammary cancer. This project involves the use of MMTV induced mammary tumorigenesis as well as the utilization of the recently developed Sleeping Beauty inducible transposon system. Both these projects will reveal a novel set of oncogenes and tumor suppressor genes that specifically cooperate with the loss of Caveolin 1 in mammary tumorigenesis.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Sollars, V.E., Pequinot, E., Rothstein, J.L. and Buchberg, A.M. Analysis of Expansion of Myeloid Progenitors in Mice to Identify Leukemic Susceptibility Genes. (2006). *Mamm. Gen.* 17:808-821..

Baran, A., Silverman, K.A., Zeskand, J., Koratkar, R., Palmer, A., McCullen, K., Curran, W.J. Jr., Edmonston, T.B., Siracusa, L.D., and Buchberg, A.M., The Modifier of *Min 2 (Mom2)* Locus: Embryonic Lethality of a Mutation in the *Atp5a1* Gene Suggests a Novel Mechanism of Polyp Suppression. (2007). *Gen Res.* 17:566-576 (cover).

SCIENTIFIC PRESENTATIONS

“Meis1 Apoptosis or Leukemia: Context determines outcome” Apoptosis Working Group Seminar, Molecular Hematology and Therapy Section, University of Texas, M.D. Anderson Cancer Center Oct 18, 2006

TEACHING

- GC550 *Foundations in Biomedical Sciences* – 2 lecture hours
GE637 *Introduction to Human Genetics II* – 1 lecture hours and course co-
 coordinator
GE652 *Molecular Basis of Cancer* – Course Coordinator
GE710 *Seminar in Genetics I* – 15 lecture hours
GE720 *Seminar in Genetics II* – 12 lecture hours
GE730 *Seminar in Genetics III* – 12 lecture hours

COMMITTEES

Kimmel Cancer Center Shared Computer Facility, Chair
Kimmel Cancer Center Training Committee,
Kimmel Cancer Center Animal Colony Committee,
Kimmel Cancer Center Cancer Genomics Committee
Kimmel Cancer Center Laboratory Animal Shared Resource, Director
Jefferson Medical College Committee on Bylaws and Rules

AWARDS/HONORS

June 2006 American Cancer Society Development, Differentiation and Cancer Study
Section Member

Sept 2007 Faculty of 1000 Biology Citation for Baran et al 2007, Gen Res 17:566-576.

EDITORIAL RESPONSIBILITIES

Mammalian Genome Associate Editor
Cancer Research
Genomics
Oncogene
Blood
Molecular Carcinogenesis
PLoS Genetics
Genetics

MEMBERSHIPS

Delaware Valley Mouse Club

International Mammalian Genome Society

COLLABORATIONS

Dr. Jianke Zhang – Jefferson Medical College

Dr. Scott Waldman – Jefferson Medical College

Dr. Linda Siracusa – Jefferson Medical College

Dr, Michael Lisanti – Jefferson Medical College

Dr. Bruce Boman – Jefferson Medical College

JEROME G. BUESCHER, PH.D.
ASSISTANT PROFESSOR

TEACHING

GC 550	<i>Core Course</i> – 2 lecture hours
MI 200	<i>Basic Medical Microbiology and Immunology</i> – 21 lecture hours, 48 laboratory hours
MI 521	<i>Immunology</i> – 24 lecture hours
MI 582	<i>Diagnostic Microbiology</i> – 12 lecture hours, 24 laboratory hours
MI 590	<i>Introduction to Clinical Virology</i> – 24 lecture hours
MI 682	<i>Topics in Advanced Diagnostic Microbiology</i> – 6 lecture hours
MI 540	<i>Microbiology of Antimicrobials</i> – 12 lecture hours

COMMITTEES

Thomas Jefferson University Web Advisory Committee
Jefferson Medical College Student Affairs Committee

MEMBERSHIPS

American Society for Microbiology
Eastern Pennsylvania Branch American Society for Microbiology

CATHERINE CALKINS, PH.D.
PROFESSOR

DESCRIPTION OF RESEARCH

One project on-going in my laboratory, being done in collaboration with Dr. Mark Feitelson (Dept. of Pathology), is an investigation of the immune responses that cause chronic hepatitis B liver disease. We are studying a mouse model of the disease in which immunodeficient SCID mice, expressing HBV as a transgene, develop signs of liver disease following adoptive transfer of syngeneic, immunocompetent lymphocytes. We are analyzing the immune cells of these adoptively transferred mice to (1) determine the nature of the immune reactivity to HBV antigens in terms of specificity, cytokine production, and requirements for activation and (2) to find mechanisms for reversing and/or blocking development of the chronic disease state. We are also comparing the responses developed during chronic disease with those developed during acute disease in order to gain understanding of the mechanisms preventing progression to a chronic state in the animals exhibiting acute disease that succeed in resolving it. The effects of ethanol, known to be associated with chronic HBV infection in humans, are also being investigated in this model. As a part of these studies, we are investigating the regulatory mechanisms that control the immune responses to the HBV viral antigens.

The second project is an investigation of the normal mechanisms of regulating immune responsiveness to self antigens. Briefly, we are studying the response to self erythrocytes (MRBC) in normal BALB/c mice and in NZB mice that spontaneously develop anti-MRBC responses by 6-9 months of age. We have demonstrated that both T and B cells reactive to self erythrocytes are present in normal as well as autoimmune mice. In culture, development of anti-erythrocyte autoantibody responses depend upon CD4 positive helper T cells and can be suppressed by CD8 positive T cells. Studies in the literature have suggested that the NZB autoantibodies are specific for Band 3 on erythrocyte membranes. In collaboration with Dr. Srinivasan (Department of Microbiology) and Dr. Shozo Izui (Medical University of Switzerland, Geneva), we are currently investigating the specific epitope on the Band 3 molecule that is recognized by NZB autoantibodies and by the autoimmune B cells detectable in normal mice. With this study, we will be able to determine if there are any changes in the fine specificity of the anti-self erythrocyte response throughout the course of the autoimmune disease in the NZB mice. We will be testing peptides predicted from the known sequence of mouse Band 3 and peptides selected by monoclonal autoantibodies in phage display from random peptide libraries. Using the identified target peptides, we will develop cell based assays that will allow us to probe the cellular mechanisms of control and loss of control in this anti-self reactivity.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Chichester, J.A., Feitelson, M.A. and Calkins, C. E. Transient Inhibition of Th1-type cytokine production by CD4+ T cells in HBcAg immunized mice is mediated by regulatory T cells. (2006) *Immunology*, 118:438-448.

Smith, M.E., Koser, M., Xiao, S., Siler, C., McGettigan, J.O., Calkins, C., Pomerantz, R.J., Dietzschold, B., and Schnell, M.J. Rabies Virus Glycoprotein as a carrier for Anthrax protective antigen. (2006) *Virology*, 353:344-356.

SCIENTIFIC PRESENTATIONS

“Immunoregulation in Responses to HBV Antigens”, KCC Staff Seminar Series, Thomas Jefferson University, Philadelphia, Pennsylvania. Nov., 2006.

TEACHING

MI 200 *Basic Medical Microbiology and Immunology* – 4 lecture hours

IMP 505 *Fundamentals of Immunology* – 6 lecture hours

IMP 632 *Advanced Cellular/Molecular Immunology* – Course Director, 36 lecture hours

IMP 712,722,732 *Journal Club* – 8 hours

Ph.D. Immunology and Microbial Pathogenesis Program

Directed Lab Rotation for 1 student

Preliminary Examination Committee for 4 students

Student Research Committees for 2 students

M.S. in Microbiology Program:

Clerkship, 2 credits for 1 student

Clerkship and Thesis Project , 10 credits for 1 student and 12 credits for 1 student, both graduated June, 2007

COMMITTEES

Jefferson Medical College, Student Promotions Committee (Member of ad hoc student subcommittees)

KCC Animal Oversight Committee

Wistar Institute Biosafety Committee

AWARDS/HONORS

Dean’s Citation for Significant Contributions to the Advancement of Education at Jefferson Medical College, June, 2007

MEMBERSHIPS

American Association of Immunologists

Sigma Xi

COLLABORATIONS

Dr. Mark Feitelson – Department of Pathology and Cell Biology, Thomas Jefferson University

Dr. Matthias Schnell – Department of Microbiology and Immunology, Thomas Jefferson University

Dr. Algarsamy Srinivasan – Department of Microbiology and Immunology, Thomas Jefferson University

Dr. Shozo Izui - Medical University of Switzerland, Geneva

BERNHARD DIETZSCHOLD, D.V.M.
PROFESSOR

DESCRIPTION OF RESEARCH

The major themes of the research conducted in my laboratory focus on A) Neuropeptide-mediated subversion of immunity in rabies B) Dominance of a Nonpathogenic Glycoprotein Gene over a Pathogenic Glycoprotein Gene in Rabies Virus, and C) Activation of dendritic cell maturation after infection with rabies virus.

A) The observation that the histopathological changes seen in RV-infected brains of human rabies patients are often limited, as well as the lack of detectable immune responses in most cases of human rabies after onset of clinical signs, support the conclusion that neurological signs of rabies are not caused by neuronal destruction or inflammatory lesions. A possible explanation for the scarcity of immune responses against RV in human rabies patients or animals is that RV infection subverts immunity by taking advantage of mechanisms involved in the maintenance of the immune privilege of the CNS. Although the immune privilege is controlled by multiple factors, including co-stimulatory molecules, cytokines, and neuropeptides, a large body of published data indicates that neuropeptides, in particular calcitonin gene related peptide (CGRP), may play a major role in the control of immune privilege. We have found that the expression of CGRP is strongly upregulated in the brain during RV infection, suggesting that RV has the ability to preserve the immune privilege of the CNS at least in part by stimulating the expression of CGRP. To test this hypothesis, we are studying the effect of the inoculation route and the nature of the RV strain on CGRP expression in the CNS and examining the effect of CGRP gene expression knockdown on immune responses in the CNS and on the outcome of an RV infection. Knowledge regarding the role of neuropeptides in the pathogenesis of RV could have important implications for therapeutic interventions against clinical rabies in humans. Temporary abolishment of the immune privilege of the CNS by blocking the action of immunosuppressive neuropeptides such as CGRP could be one of the strategies by which immune clearance of the virus and thus the prevention of the fatal outcome of the disease could be achieved.

B) The nonpathogenic phenotype of the live rabies virus (RV) vaccine SPBNGAN is determined by an Arg3Glu exchange at position 333 in the glycoprotein, designated GAN. We recently showed that after several passages of SPBNGAN in mice, an Asn3Lys mutation arose at position 194 of GAN, resulting in GAK, which was associated with a reversion to the pathogenic phenotype. Because an RV vaccine candidate containing two GAN genes (SPBNGAN-GAN) exhibits increased immunogenicity in vivo compared to the single-GAN construct, we tested whether the presence of two GAN genes might also enhance the probability of reversion to pathogenicity.

Comparison of SPBNGAN-GAN with RVs constructed to contain either both GAN and GAK genes (SPBNGANGAK and SPBNGAK-GAN) or two GAK genes (SPBNGAK-GAK) showed that while SPBNGAK-GAK was pathogenic, SPBNGAN-GAN and SPBNGAN-GAK were completely nonpathogenic and SPBNGAK-GAN showed strongly reduced pathogenicity. Analysis of genomic RV RNA in mouse brain tissue revealed significantly lower virus loads in SPBNGAN-GAK- and SPBNGAK-GAN-infected brains than those detected in SPBNGAK-GAK-infected brains, indicating the dominance of the non-

pathogenic phenotype determined by GAN over the GAK-associated pathogenic phenotype. Virus production and viral RNA synthesis were markedly higher in

SPBNGAN-, SPBNGAK-GAN-, and SPBNGAN-GAK-infected neuroblastoma cells than in the SPBNGAK- and SPBNGAK-GAK-infected counterparts, suggesting control of GAN dominance at the level of viral RNA synthesis. These data point to the lower risk of reversion to pathogenicity of a recombinant RV carrying two identical GAN genes compared to that of an RV carrying only a single GAN gene.

C) Oral immunization of wildlife with live vaccines is the most effective method to control and eventually eradicate rabies. Although the mechanism by which oral immunization with modified-live rabies virus (RV) vaccines confers protective immunity is not known, a primary site of replication of the RV vaccine strains is the tonsils, a major lymphoid tissue rich in dendritic cells (DCs). To assess the potential role of DCs or monocytes in the development of a protective immune response following oral immunization with live attenuated RV vaccines, we infected human immature DCs or monocytes with non-pathogenic (SPBNGAS-GAS) and pathogenic (DOG4) RVs. Both cell types could be infected with SPBNGAS-GAS and DOG4, although their susceptibility for the non-pathogenic RV was higher and infection with the non-pathogenic RV resulted in higher RV G expression. However, despite the differences in RV G expression levels, both RVs were similarly potent in inducing maturation of immature DCs or CD14-positive monocytes. Since the differentiation of monocytes into mature DCs occurred in the absence of IL-4, we tested whether type 1 interferons induced during RV infection might play a role in the DC maturation. While the non-pathogenic SPBNGAS-GAS induced very high levels of IFN- α 1 mRNA in monocytes and DCs, infection with the pathogenic DOG4 resulted in only marginal IFN- α 1 RNA expression. PCR array analysis revealed up-regulation of the expression of at least 26 genes related to the NF κ B signaling pathway, including IFN- α and IFN- β , in SPBNGAS-GAS-infected DCs, and somewhat increased expression of several of the NF κ B-related genes in DOG4-infected cells. Thus, the extent of upregulation of NF κ B pathway-related genes in DCs infected with the non-pathogenic RV might underlie the protection conferred by live RV vaccines.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Faber, F., Faber, M-L., Jianwei Li, J., Mirjam A. R. Preuss, M.R.J., Schnell, M.J., Bernhard Dietzschold, B. "Dominance of a Nonpathogenic Glycoprotein Gene over a Pathogenic Glycoprotein Gene in Rabies Virus" (2007) *J. Virol*, 81: 7041-7047.

Blanton, J.D., Self, J., Niezgod, M., Faber, M-L., Dietzschold, B., Charles Rupprecht, C.E. "Oral Vaccination of Raccoons (*Procyon lotor*) with a genetically modified rabies virus vaccine" (2007). Vaccine, in press.

McKenna PM, Koser ML, Carlson KR, Montefiori DC, Letvin NL, Papaneri AB, Pomerantz RJ, Dietzschold B, Silvera P, McGettigan JP, Schnell MJ. "Highly attenuated rabies virus-based vaccine vectors expressing simian-human immunodeficiency virus 89.6P Env and simian immunodeficiency virus mac239 Gag are safe in rhesus macaques and protect from an AIDS-like disease" (2007) *J Infect Dis*. 195:980-988.

Blanton JD, Meadows A, Murphy SM, Manangan J, Hanlon CA, Faber ML, Dietzschold B, Rupprecht CE. "Vaccination of small Asian mongoose (*Herpestes javanicus*) against rabies" (2006) *J Wildl Dis.* 42:663-666.

Li J, Faber M, Papaneri A, Faber ML, McGettigan JP, Schnell MJ, Dietzschold B. "A single immunization with a recombinant canine adenovirus expressing the rabies virus G protein confers protective immunity against rabies in mice" (2006) *Virology.* 356:147-54.

Smith ME, Koser M, Xiao S, Siler C, McGettigan JP, Calkins C, Pomerantz RJ, Dietzschold B, Schnell MJ. "Rabies virus glycoprotein as a carrier for anthrax protective antigen" (2006) *Virology.* 353:344-56.

SCIENTIFIC PRESENTATIONS

"New Pathways to B Cell Tolerance", University of California, Seminars in Immunology, UCI Center for Immunology, NCI Cancer Research Institute and the UCI General Clinical Research Center, Irvine, California, April 2007.

"Development of a recombinant canine adenovirus2-rabies virus G protein vaccine (CAV2-RV G)", Rabies in the Americas Conference, Brasilia, October 15 -20, 2006.

"Molecular determinants of rabies virus neuropathogenesis and neuroinvasiveness", NIMH, Section on Molecular Neuroscience, Bethesda, April 19, 2007.

"Progress Report on the development of a recombinant canine adenovirus expressing the rabies virus G Protein", National rabies management program strategic planning session, San Antonio, Texas, March 27-29, 2007.

"The role of the regulation of viral gene expression in the pathogenesis of rabies", Rabies Pathogenesis Meeting, Paris, May 26, 2007:

"Dominance of a non-pathogenic over a pathogenic glycoprotein gene in rabies virus", Joint OIE/WHO/EU International Conference towards the elimination of rabies in Eurasia, Paris, May 27, 2007

"Unraveling the pathogenesis of rabies", Department of Anatomy and Cell Biology, University of Marburg, Germany, May 31, 2007.

TEACHING

NS 625 *The Molecular Biology of Rabies* – 2 lecture hours

Micro 600 *Viral Pathogenesis* – 2 lecture hours

COMMITTEES

Microbiology Curriculum Committee

Microbiology Thesis Committee

EDITORIAL RESPONSIBILITIES

Associate editor, Journal of NeuroVirology

MEMBERSHIPS

Society of Microbiology

International Society for NeuroVirology

American Association for the Advancement of Science

Gesellschaft für Biochemie und Molekularbiologie

COLLABORATIONS

Dr. Matthias J. Schnell – Department of Microbiology and Immunology, Thomas Jefferson University.

Dr. Eberhard Weihe – Institute of Anatomy and Cell Biology, Philipps-University Marburg, Germany.

Dr. Charles E. Rupprecht – Centers for Disease Control, Atlanta, GA.

LAURENCE C. EISENLOHR, V.M.D., PH. D.
PROFESSOR

DESCRIPTION OF RESEARCH

There are currently four major interests in the laboratory, most of which relate to T cell recognition of antigen:

1) Processing and presentation for class I-restricted T cell recognition. Most effort is being expended to understand how antigen is targeted for processing and to identify the cellular elements involved in antigen processing. These issues are mainly being addressed through expression of genetically-manipulated influenza proteins bearing known class I-restricted T cell determinants.

2) Processing and loading compartments involved in presentation of MHC class II-restricted antigenic peptides. We are utilizing two glycoproteins of influenza virus, hemagglutinin (HA) and neuraminidase (NA) 1) to identify the subcellular compartments within the cell where antigen becomes available for binding to class II molecules and the compartments where binding takes place, and 2) to determine the extent to which these processes differ in different cell types and when the antigen is taken up from the extracellular space vs. expressed in the antigen presenting cell itself.

3) The expression and response to "cryptic" MHC class I-restricted epitopes. MHC class I-restricted cytotoxic T lymphocytes (CTL) are exquisitely sensitive to low levels of antigens and we and others have demonstrated that they can be triggered by the products of aberrant gene expression, such as alternative splicing, exon translation, alternative start codon usage and frameshifting. We hypothesize that these aberrant translation products play an important role in defining the world of "self" and may be involved in triggering autoimmunity. In collaboration with the laboratory of Dr. Michael Howard (U. of Utah) we have recently reported on one of these mechanisms, ribosomal frameshifting and have nearly completed characterization of a second, stop codon readthrough.

4) Cancer and autoimmunity. The co-incidence of autoimmunity and neoplasia has been noted for both thyroid and colon cancer. Based upon our experience with T cell recognition, protein engineering and the generation of recombinant vectors, we are collaborating with Dr. Jay Rothstein (formerly of Department of Otolaryngology-HNS, currently Amgen, Inc., Seattle, WA) to determine basis for the link between autoimmune thyroiditis and thyroid neoplasia. We are playing a similar role in collaborating with Dr. Scott Waldman (Chairman, Clinical Pharmacology Department) to investigate inflammatory bowel disease and potential therapies for colon cancer.

Findings related to these four projects will contribute important information to the areas of vaccine design, tissue transplantation, autoimmune therapy, and immune-based anti-cancer strategies.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Plesa, G., McKenna, P. M., Schnell, M. J., and L. C. Eisenlohr, 2006. "Immunogenicity of cytopathic and non-cytopathic viral vectors", *J. Virol.*, 80: 6259-6266.

Eisenlohr, L. C., Huang, L., and T. N. Golovina, 2007. "Rethinking peptide supply to MHC class I molecules", *Nat. Rev. Immunol.*, 7: 403-410.

SCIENTIFIC PRESENTATIONS

Talk Entitled: "The Antigenic World According to T Cells", University of Pennsylvania 20th Anniversary of Biomedical Graduate Studies (1 of 5 invited graduates), University of Pennsylvania, Philadelphia, PA, 13 November 2006.

Talk Entitled: "Three Natural Pathways for the Class II-Restricted Presentation of Influenza Proteins", Cooperative Centers for Translational Research on Human Immunology and Biodefense, Harvard University, Boston MA, 22 March 2007

TEACHING

Program Director, *Immunology and Microbial Pathogenesis*

GC550 Foundations of Biomedical Science – 2 lecture hours (Scientific Writing)

MI 200 (Medical School) Basic Medical Microbiology and Immunology – 4 lecture hours

IMP 505 Fundamentals of Immunology – 2.5 lecture hours

IMP 600 Fundamentals of Microbiology – Course Director, 2.5 lecture hours

IM 530 Infection and Immunity – 2 lecture hours, 24 class hours

IM/MI 610,620,630 Graduate School Research Rotation – 2 rotating students this year

IM/MI 910,920 Graduate School Dissertation – 3 graduate students

COMMITTEES

Member, Confocal/Bioimaging Committee, KCC

Member and Chair, KCC Training Committee

Member, Graduate Council of TJU CGS

Member, University Appointments and Promotions Committee

Member, University Tenure Committee

Member, University Research Advisory Committee

AWARDS/HONORS

One of five Ph.D. graduates invited to deliver a seminar at the symposium marking the 20th Anniversary of Biomedical Graduate Studies at the University of Pennsylvania

EDITORIAL RESPONSIBILITIES

Faculty of 1000, Antigen Processing and Presentation Section

MEMBERSHIPS

American Association of Immunologists

COLLABORATIONS

Jay Rothstein, Amgen Corporation, Seattle WA

Scott Waldman - Department of Pharmacology and Experimental Therapeutics, TJU

Phyllis Flomenberg - Department of Medicine, Infectious Diseases, TJU

Raymond Gesteland and Michael Howard – University of Utah

Matthias Schnell – Department of Microbiology and Immunology, TJU

CARLISLE P. LANDEL, PH.D.
RESEARCH ASSISTANT PROFESSOR

DESCRIPTION OF RESEARCH

Genetics of mouse sperm cryopreservation. Cryopreservation of mouse germplasm is useful because it provides security against loss of valuable mouse strains and because it allows strains not currently under investigation to be removed from the shelf, thus freeing valuable resources (vivarium space and per diem costs) for other efforts. In many cases, sperm cryopreservation would be an optimal approach to this because a single male can provide on the order of 3×10^7 sperm and the methodology is very simple. However, adoption of this method is constrained by the fact that cryopreserved sperm of many inbred strains of mice, including C57BL/6 (the canonical mouse strain), fertilize very poorly after cryopreservation. This loss of function has a genetic basis. The goal of my research is to identify the genes associated with this loss of function in order to facilitate developing better methods for the cryopreservation of valuable inbred mouse strains and predict the viability of cryopreserved semen from individual human or livestock donors.

SCIENTIFIC PRESENTATIONS

“Cryopreservation of Mouse Sperm”, 7th Transgenic Technology Meeting, University of Queensland, Brisbane, Australia, February 2007.

“Mouse IVF and Sperm Cryopreservation Course”, Transgenic Animal Service of Queensland and the International Society for Transgenic Technologies Course, University of Queensland, Brisbane, Australia, February 2007.

TEACHING

GE 636 *Human Genetics* – 2 lecture hours
GE 710 *Seminar in Genetics I* – 12 lecture hours
GE 720 *Seminar in Genetics II* – 12 lecture hours
GE 730 *Seminar in Genetics III* – 12 lecture hours
GE 612 *Molecular Genetics II* – Course organizer
(Not offered this year due to small number of students registered)

COMMITTEES

Thomas Jefferson University Institutional Animal Care and Use Committee
KCC Animal Facility Oversight Committee
KCC Transgenic/Knockout Oversight Committee
Thesis Committee Chair for Amy Baran and Stephanie Nnadi

MEMBERSHIPS

International Society for Transgenic Technologies (Secretary)
Society for Cryobiology

COLLABORATIONS

Dr. Xugang Xia, Thomas Jefferson University
Dr. Robert Mason, Alfred I. DuPont Hospital for Children
Dr. Linda Siracusa, Thomas Jefferson University
Dr. Barbara Schick, Thomas Jefferson University

TIM L. MANSER, PH.D.
PROFESSOR AND CHAIR

DESCRIPTION OF RESEARCH

Our laboratory's interests center on the antigen-dependent stages of B cell differentiation in the mouse, leading to the generation of B cell memory. We are investigating the mechanisms responsible for antigen-driven changes in the structure and function of the antibody repertoire during memory development, as well as the microenvironmental locales (particularly the germinal center (GC)) in which these changes take place. We are predominantly interested in the fate of B cells with autoreactive antigen receptors (either pre-existing or acquired via V region hypermutation) during memory B cell development. Additional projects concern the role of Fc receptors, Toll-like receptors, follicular dendritic cells and T cells in the regulation of the B cell response.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Imtiyaz, H. Z., Rosenberg, S., Zhang., Y., Rahman, Z. S. M., Hou, Y-J., Manser, T. L., and J. Zhang. "The Fas-Associated Death Domain Protein (FADD) is Required in Apoptosis and TLR-induced Proliferative Responses in B Cells" (2006) *J. Immunol.* 176: 6852-6861.

Rahman, Z.S.M., B. Alabyev and T. Manser. "FcγRIIB Regulates Autoreactive Primary Antibody Forming Cell, but not Germinal Center B Cell, Activity" (2007) *J. Immunol.*, 178: 897-907.

Liu, X., L. J. Wysocki and T. Manser "Autoantigen-B Cell Antigen Receptor Interactions that Regulate Expression of B Cell Antigen Receptor Loci" (2007) *J. Immunol.*, 178: 5035-5047.

Alabyev, B. Z.S.M. Rahman and T. Manser "Quantitatively Reduced Participation of Anti-nuclear Antigen B Cells that Down Regulate BCR During Primary Development in the Germinal Center/memory B Cell Response to Foreign Antigen" (2007) *J. Immunol.*, 178: 5623-5634.

Rahman, Z.S.M., H. Niu, D. Perry, E. Wakeland, T. Manser, and L. Morel "Expression of the Autoimmune Fcγr2b NZW Allele Fails to be Up-regulated in Germinal Center B Cells and Leads to Increased IgG Production", (2007) *Genes Immun.*, in press.

Coffey, F., X. Liu and T. Manser, "Toll-like receptor 9 and other MyD88-dependent TLRs are not required for primary and foreign antigen driven development of an anti-chromatin B cell clonotype", *J. Immunol.* in press.

SCIENTIFIC PRESENTATIONS

"B Cell Tolerance via Learned Ignorance", Joint Staff Seminar Series, Departments of Microbiology and Immunology, Biochemistry and Molecular Biology, Cancer Biology and Kimmel Cancer Center, April 2007.

"New Pathways to B Cell Tolerance", University of California, Seminars in Immunology, UCI Center for Immunology, NCI Cancer Research Institute and the UCI General Clinical Research Center, Irvine, California, April 2007.

TEACHING

MI 200 *Basic Medical Microbiology and Immunology* – 4 lecture hours
IM 505 *Fundamentals of Immunology* – 7.5 lecture hours

COMMITTEES

Thomas Jefferson University Professorial Faculty Advisory Committee
Thomas Jefferson University Committee on Research
Kimmel Cancer Center Executive Committee
Jefferson Medical College Executive Council

AWARDS/HONORS

2007 (June, 10, 11) NIH, NIAID A Special Study Section, B Cell Immunology and HIV neutralizing Antibody Projects

EDITORIAL RESPONSIBILITIES

Editor, BMC Immunology
Editor, “Antibodies in Infectious Diseases”, Current Topics, Micro. Immunol., (2007), in press.

MEMBERSHIPS

American Association of Immunologists
American Association for the Advancement of Science

COLLABORATIONS

Dr. Yuri Sykulev – Jefferson Medical College
Dr. Takami Sato - Jefferson Medical College
Dr. Jianke Zhang - Jefferson Medical College
Dr. Laurence Morel - University of Miami

JAMES P. McGETTIGAN, PH.D.
INSTRUCTOR

DESCRIPTION OF RESEARCH

The World Health Organization and the Global Alliance for Vaccines and Immunizations report that almost 27 million people do not receive vaccines that are available and needed. Due to cost, complicated vaccine strategies and lack of availability, over two million deaths occur annually for otherwise preventable disease. Most of these deaths occur in developing countries, where it is clear that novel vaccines are needed. In addition, simple and less expensive vaccination strategies are also desirable for developed countries, where health care costs are becoming a major burden on the medical infrastructure. Therefore, it is our goal to create a new class of vaccines that are simple to administer, inexpensive and effective for use in both developed and developing countries.

Our primary focus to help achieve this goal is the development of improved rabies virus (RV) vaccines for use as post-exposure prophylaxis (PEP). The high incidence of rabies infections in developing countries resulted in an estimated 10 million people receiving PEP after contact with potentially infected animals and an estimated 40,000 to 70,000 deaths world-wide. Most of these occur in children due to the high cost or unavailability of vaccine or rabies immune globulins (RIG). However, recent studies indicate that human rabies deaths may be up to 100 times higher than officially reported. In addition, emerging rabies-related viruses are being discovered where the current PEP is not effective. Our vaccine is based on replication-deficient RV-based vectors, in which one of its five essential genes is deleted. These vectors are very safe and highly immunogenic, and may prove effective alternative vaccines against rabies virus and other infectious diseases.

We are also investigating molecular mechanisms and virus-host interactions that may influence the immunogenicity of our replication-deficient vectors. Areas of interest include the role of apoptosis and innate immunity, particularly the IFN and NF- κ B responses, in rabies virus pathogenicity and immunity. Innate immune response serves as the first line of defense that recognizes and eliminates viruses on its own, and triggers and coordinates subsequent immune functions. Specifically, the induction of innate immune responses leads to the release of chemicals and proteins that serve to attract immune cells to the site of infection. In addition, these responses play an important role in the regulation of immune functions. Taken together, a vaccine that is able to activate innate immune pathways may be the key to the development of new and effective vaccine strategies. This is currently being tested as part of our replication-deficient rabies vaccine program.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Smith, M.E., Koser, M., Xuo, S., Siler, C., McGettigan, J.P., Calkins, C., Pomerantz, R.J., Dietzschold, B., and Schnell, M.J. Rabies virus glycoprotein as a carrier for anthrax protective antigen. (2006)Virology. Sep 30;353(2):344-56

Li, J., Faber, M., Papaneri, A., Faber, M.L., McGettigan, J.P., Schnell, M.J., and Dietzschold, B. A single immunization with a recombinant canine adenovirus expressing the rabies virus G protein confers protective immunity against rabies in mice. (2006) *Virology* Dec 5-20;356(1-2):147-54.

McKenna, P.M., Koser, M.L., Carlson, K.R., Montefiori, D.C., Letvin, N.L., Papaneri, A., Pomerantz, R.J., Dietzschold, B., Silvera, P., McGettigan, J.P., and Schnell, M.J. Highly attenuated rabies virus-based vaccine vectors expressing simian-human immunodeficiency virus89.6P Env and simian immunodeficiency virusmac239 Gag are safe in rhesus macaques and protect from an AIDS-like disease. (2007) *J Infect Dis.* Apr 1;195(7):980-8.

TEACHING

IMP 722 *Current Literature in Immunology* – 9 hours

IMP 723 *Current Literature in Immunology* - 12 hours

AWARDS/HONOR

2007 Infectious Disease Society of America and the National Foundation for Infectious Diseases Wyeth Young Investigator Award in Vaccine Development

2007 Recipient of the Tulane National Research Primate Center Pilot Research Program Award

MEMBERSHIPS

American Society for Virology

COLLABORATIONS

Dr. Charles Rupprecht– Center for Disease Control and Prevention, USA

Dr. Preston A. Marx - Tulane National Primate Research Center, Convington, LA

Dr. Andrew Lackner - Tulane National Primate Research Center, Convington, LA

W. EDWARD MERCER PH.D.
PROFESSOR

DESCRIPTION OF RESEARCH

Research in my laboratory focuses on the p53 tumor suppressor gene product, p53 protein, and the molecular networks it controls. The p53 gene is one of the most frequently mutated genes found to date in human cancers. The p53 protein normally protects us from developing cancer by its action as a major mediator of cell cycle checkpoint control pathways and programmed cell death pathways (apoptosis). Both pathways insure that cell cycle progression; and ultimately, cell division does not occur under suboptimal conditions such as damage to the cellular genome, metabolic perturbations, and other forms of cellular stress that can promote the emergence of neoplastic cells. Our current studies focus on p53 checkpoint control pathways activated in response to DNA damage induced by ionizing radiation (IR), UV-radiation and anticancer drugs that induce DNA damage. Specifically, we are investigating the biochemical mechanisms of action of the recently discovered PPM1D gene. The PPM1D gene encodes a nuclear protein phosphatase of the type 2C class. The PPM1D gene is frequently amplified in human breast carcinoma, ovarian, and neuroblastoma tumors that carry a wild type p53 gene. Ectopic expression of PPM1D blocks cell cycle progression in and abrogates the apoptotic response in cells exposed to DNA damaging agents. The overall goal of this work is to gain insight into the role that Wip1 phosphatase plays in modulating wild type p53-mediated checkpoint controls and apoptosis in human tumor cells exposed to DNA damaging agents and to elucidate the molecular mechanisms by which amplification of the PPM1D gene in the pathogenesis of human cancer. An understanding of these pathways at the molecular level could provide significant insight toward the development of novel therapeutic interventions for the treatment of human cancer retractile to conventional chemo/radiation therapeutic modalities.

SCIENTIFIC PRESENTATIONS

“Down regulation of Wip-1 phosphatase in MCF-7 breast cancer cells enhances doxorubicin-induced apoptosis through p53-mediated transcriptional activation of Bax.” 3rd International Meeting on Tumor Progression and Therapeutic Resistance, Baltimore, MD. October 22-24 2006.

TEACHING

KCC Radiation Biology Course for Residents – 1 lecture hour
GE 652 *Molecular Basis of Cancer – Tumor Suppressor Genes* – 1 lecture hour
GE 651 *Pathobiology of Cancer – Course Director* 10 lectures hours
GE 636 *p53 Tumor Suppressor Gene in Cell Cycle Regulation* – 2 lecture hours

COMMITTEES

Reviewer: JMC REA Committee
Genetics Program Committee

Chairman: Genetics Program Preliminary Examination Committee
JMC Committee on Student Promotion
KCC Molecular Biology and Genetic Program Committee

AWARDS/HONORS

2006 Certificate of Appreciation Thomas Jefferson Medical College, Kimmel Cancer Center
2006 International p53 Research Laboratory, International Agency for Research on Cancer (IARC).

EDITORIAL RESPONSIBILITIES

Editorial Board, Cell Biology International Reports

MEMBERSHIPS

American Association for Cancer Research
American Association for Advancement of Science
New York Acad. Science

COLLABORATIONS

Juan P. Palazzo, M.D. Department of Pathology, TJUH
Alexander Mazo Ph.D. Department of Biochemistry and Molecular Biology
Charles P. Scott, Ph.D. Department of Microbiology and Immunology
Scott Waldman, M.D., Ph.D. Department of Experimental Therapeutics and Pharmacology

MATTHIAS J. SCHNELL, PH.D.
PROFESSOR

DESCRIPTION OF RESEARCH

The research interest of the laboratory is focus on two areas: 1) viral pathogenesis and 2) vaccine development

Viral pathogenicity: We are interested in a detailed understanding of the biochemistry, molecular biology and immunology of rabies virus and its interaction with the infected host. The molecular mechanism of rabies virus pathogenesis is not well understood and our research analyses the different functions the rhabdoviral proteins (e.g. rabies virus) and their interaction with cellular host proteins. Current projects are directed to:

- RV virus neurotropism and neuroinvasiveness: The transport of RV within neurons and the interaction of the RV phosphoprotein (P) with the LC8 of dynein complex.
- The cellular RV receptor(s) for pathogenic and attenuated RV strains, RV entry into cells.
- Immune responses of RV in the infected host (innate and adaptive) Vaccines: The other focus of the laboratory are Rhabdovirus-based vectors as vaccines against other infectious diseases.
- Using different molecular approaches, we perform detailed studies of highly attenuated RV and vesicular stomatitis virus (VSV) expressing HIV-1 or SIV genes and analyze their immunogenicity in mice. The most promising HIV vaccine candidates are currently under investigation to prevent an AIDS-like disease in a monkey model.
- New approaches using genetically modified RV G proteins or RV capsids carrying antigens of other pathogens are developed as novel vaccines against Anthrax and Botulism.
- Development of safer and more potent vaccines for wildlife and human rabies. Publications (July 1, 2006)

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Tang J, Murtadha M, Schnell M, Eisenlohr LC, Hooper J, Flomenberg P: Human T-cell responses to vaccinia virus envelope proteins. *J Virol* 2006, 80:10010-10020.

Tang J, Olive M, Pulmanusahakul R, Schnell M, Flomenberg N, Eisenlohr L, Flomenberg P: Human CD8+ cytotoxic T cell responses to adenovirus capsid proteins. *Virology* 2006, 350:312-322.

McKenna PM, Koser ML, Carlson KR, Montefiori DC, Letvin NL, Papaneri AB, Pomerantz RJ, Dietzschold B, Silvera P, McGettigan JP, Schnell MJ: Highly Attenuated Rabies Virus-Based Vaccine Vectors Expressing Simian-Human Immunodeficiency Virus89.6P Env and Simian Immunodeficiency Virusmac239 Gag Are Safe in Rhesus Macaques and Protect from an AIDS-Like Disease. *J Infect Dis* 2007, 195:980-988.

Tan GS, Preuss MA, Williams JC, Schnell MJ: The dynein light chain 8 binding motif of rabies virus phosphoprotein promotes efficient viral transcription. Proc Natl Acad Sci U S A 2007.

Faber M, Faber ML, Li J, Preuss MA, Schnell MJ, Dietzschold B: Dominance of a non-pathogenic over a pathogenic glycoprotein gene in rabies virus. J Virol 2007.

SCIENTIFIC PRESENTATIONS

Invited presentations:

January 18-19, 2007 From Mice to Monkeys - Rabies Virus as a Vaccine Vector against HIV-1. Tulane National Primate Research Center, Tulane University, Health Sciences Center, Covington, LA.

April 16-17, 2007 Dynein Light Chain (LC8) as a factor for efficient viral replication. MMG Seminar, Emory University, Atlanta

July 11-12, 2007 Dynein Light Chain (LC8) as a factor for efficient viral replication. Wadsworth Center, New York State Department of Health, Albany, NY

Presentations:

McKenna, P.M., M.L. Koser, K.R. Carlson, D. C. Montefiori, N.L. Letvin, A. B. Papaneri, R.J. Pomerantz, B. Dietzschold, Peter Silvera, J.P. McGettigan, and MJ. Schnell. Highly attenuated rabies virus-based vaccine vectors expressing SHIV89.6P Env and SIVmac239 Gag are safe and immunogenic in rhesus macaques and protect from an AIDS-like disease. (Presented at HIV Vaccines: From Basic Research to Clinical Trials 25 to 30 March 2007, Whistler Alberta Canada, Canada)

Faber, M, Faber, M.-L.K., Li, J., Schnell, M. J., and Dietzschold, B.D. Presence of a second glycoprotein gene with an Arg333 to Glu333 mutation (GAN) increases the safety of a live rabies vaccine. (Presented at the American Society for Virology, 26th annual meeting, Oregon State University, July 14-18, 2007)

Li, J., Faber, M., Papaneri, A., Faber, M.-L., McGettigan, J.P., Schnell, M. J., and Dietzschold, B.D. Construction of a recombinant adenovirus 2 expressing rabies virus G protein that confers protective immunity against rabies in mice.

(Presented at the American Society for Virology, 26th annual meeting, Oregon State University, July 14-18, 2007)

TEACHING

MI 200 *Basic Medical Microbiology and Immunology* – 2 lecture hours

IMP 600 *Microbiology* – 2 lecture hours

COMMITTEES

Thomas Jefferson University Institutional Biosafety Committee

AWARDS/HONORS

Several NIH, NIAID Special Study Sections

Member NIH, NIAID MID-B Study Section

EDITORIAL RESPONSIBILITIES

Editorial Board, Journal of Virology

MEMBERSHIPS

National Societies:

Member of American Society for Microbiology (1995-present)

Member of American Association for the Advancement of Science (1998-present)

Member of the Infectious Diseases Society of America (2001-present)

Member of the American Society for Virology (2000-present)

Member of the German Society of Virology (2002-present)

Member International Society for NeuroVirology (2006-present)

Local Societies:

Member of the Farber Institute for Neurosciences - TJU (2004-present)

Member of the Kimmel Cancer Center - TJU (2007-present)

COLLABORATIONS

INTERNAL

Dr. Rene Daniel – Jefferson Medical College

Dr. Bernhard Dietzschold – Jefferson Medical College

Dr. Laurence Eisenlohr – Jefferson Medical College

Dr. James McGettigan – Jefferson Medical College

Dr. Lance Simpson – Jefferson Medical College

Dr. Jianke Zhang – Jefferson Medical College

EXTERNAL

Dr. Pyone Pyone Aye – Tulane National Primate Research

Dr. Ronald Harty – University of Pennsylvania

Dr. Andrew Lackner – Tulane National Primate Research

Dr. Monique Lafon, Pasteur Institute, Paris

Dr. Jeffery Mattis – MTT Inc.

Dr. Johnny Peterson – University of Texas, Medical Branch

Dr. Christophe Prehaut, Pasteur Institute, Paris

Dr. Jack Rose – Yale University

Dr. Peter Strick– University of Pittsburgh

LINDA D. SIRACUSA, PH.D.
ASSOCIATE PROFESSOR

DESCRIPTION OF RESEARCH

The study of genes that influence complex traits is a rapidly evolving field. The power of mouse genetics coupled with the ability to scan entire genomes of individual mammals has led to the discovery of chromosomal regions that harbor genes conferring susceptibility or resistance to different cancers. My laboratory uses a combination of classical genetics and molecular biology to identify and characterize genes that influence the development of cancer along the gastrointestinal tract.

The system we chose involves the tumor suppressor gene adenomatous polyposis coli (*apc*). Mutations in the human *apc* gene are responsible for the majority of inherited and sporadic colorectal cancers. *Apc^{min}* mice have a mutation in the murine homologue of the human *apc* gene and develop multiple adenomas along their intestinal tract. Quantitative trait locus (qtl) studies identified a locus, modifier of min 1 (*mom1*), at the distal end of mouse chromosome 4 which dramatically affects *apc^{min}*-induced tumor number. We were the first to report that the secretory type ii phospholipase a2 (*pla2g2a*) gene is a strong candidate for the *mom1* locus. Inbred mouse strains display 100% concordance between *pla2g2a* allele type and tumor susceptibility. Expression and sequence analysis showed that *mom1* susceptible strains carry null alleles of the *pla2g2a* gene. We developed a fluorescent enzyme activity assay for *pla2g2a* which confirms and extends our molecular and immunohistochemical findings (performed in collaboration with dr. Steve farber, carnegie institute). Transgenic mice and gene expression profiling are being used to establish the mechanism by which *pla2g2a* prevents intestinal polyp formation. We are moving to investigate the role of *pla2g2a* in human neoplasia and intestinal homeostasis.

We discovered a spontaneous dominant mutation, Modifier of Min 2 (*Mom2*), which is a potent suppressor of intestinal and colorectal tumorigenesis in *Apc^{Min}* mice. The resistant *Mom2^R* allele reduces small intestine adenoma numbers and colon adenoma incidence by ~90% in *Apc^{Min}* mice. We localized *Mom2* to the distal end of mouse chromosome 18 using a unique exclusion mapping strategy. Quantitative RT-PCR and sequencing revealed a 4 bp duplication within exon 3 of the ATP synthase (*Atp5a1*) gene that is responsible for the *Mom2* phenotype. Studies of tumor suppression are suggesting a novel mechanism of cellular lethality that is specific to the tumor lineage. Further work is ongoing to understand the full effects of *Mom2* on polyp initiation, growth, and progression. Our research on gastrointestinal tumorigenesis is performed in collaboration with Dr. Arthur Buchberg at the Jefferson Medical College.

We established reciprocal congenic lines of mice between the C3H/HeJ and C57BL/6J inbred strains that have a wildtype *Mom1* locus on an otherwise susceptible background and a susceptible *Mom1* locus on an otherwise resistant background. Testing of these congenic lines demonstrated significant differences in polyp formation in both the small and large intestines. Using these new congenic strains in designer crosses, offspring are aged and analyzed for tumor number, size and position and QTL analyses is performed to identify regions with genes that act to significantly decrease intestinal polyp formation. We completed the first large-scale backcross to identify new modifier loci. Phenotyping of 492 N2 offspring was performed in our laboratory; geno-

typing of 492 N2 offspring was accomplished with a grant from the Center for Inherited Disease Research. Our results identified five loci with significant Lod scores. Reciprocal congenic lines have been established for these regions and we are testing them by crosses to B6 *Apc^{Min}* mice. In addition, microarray analyses will determine gene expression profiles of existing and future congenic lines to determine which pathways are prime candidates for conferring the resistant phenotype.

We used a similar strategy to assess the impact of the evolutionarily divergent *Mus castaneus* background on *Apc^{Min}* tumorigenesis. The CAST/Ei genome confers resistance by significantly decreasing both polyp number and polyp size. We have used a large-scale backcross to identify at least two regions that confer potent resistance to *Apc^{Min}* tumorigenesis in the CAST/Ei genome, and are working to narrow these regions and identify the modifier genes.

We hypothesized that microRNAs can be tumor susceptibility genes. To this end, we established a database comparing the positions of mouse microRNAs across the genome with the positions of loci conferring susceptibility to eight different solid tumors. Statistical analyses revealed a highly significant association between the presence of microRNA genes and the locations of tumor susceptibility loci. Sequence comparisons of microRNAs between inbred strains that are known to differ in their resistance or susceptibility to specific types of tumors has revealed polymorphism, primarily in the regions upstream of the microRNA stem-loop structure. Studies are continuing to assess the level of expression of microRNAs in tissues of the gastrointestinal tract, in both normal and disease states. This research is performed in collaboration with Dr. Carlo Croce and Dr. George Calin at the Ohio State University Medical Center.

The comprehensive examination of novel modifier loci in human tumors will facilitate an understanding of the relationship between the effects of modifier genes on tumor initiation, growth, and progression. The abundance of mouse mutants provides a wealth of heritable alterations useful for defining the molecular basis of tumor phenotypes. Further investigations will lead to insights regarding the role of modifier genes in cancer risk assessment, tumor prevention, diagnosis, and their predictive value for response to treatment.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Sevignani, C., G. Calin, L.D. Siracusa, and C.C. Croce. Mammalian MicroRNAs: A small world for fine-tuning gene expression (2006) *Mammalian Genome* 17: 189-202.

Baran, A.A., K.A. Silverman, J. Zeskand, K.A. Koratkar, A. Palmer, K. McCullen, W. Curran, W.Jr., T. Bocker-Edmonston, L.D. Siracusa, and A.M. Buchberg.

Characterization of the Modifier of Min 2 (Mom2) locus: The embryonic lethality of a mutation in the *Atp5a1* gene suggests a novel mechanism of polyp suppression (2007) *Genome Research* 17: 566-576.

Sevignani, C., Calin, G.A., Nnadi, S.C., Shimizu, M., Davuluri, R.V., Hyslop, T., Demant, P., Croce, C.M. and L.D. Siracusa. MicroRNA genes are frequently located near mouse cancer susceptibility loci (2007) *Proc. Natl. Acad. Sci. USA* 104: 8017-8022.

Li, P., S. Schulz, A. Bombonati, J.P. Palazzo, T.M. Hyslop, Y. Xu, A.A. Baran, L.D. Siracusa, G.M. Pitari and S.A. Waldman. GCC opposes intestinal tumorigenesis by regulating proliferation and genomic integrity (2007) *Gastroenterology* 133: 599-607.

SCIENTIFIC PRESENTATIONS

INVITED SPEAKER

“Novel modifier loci influence intestinal and colorectal polyposis in the C3H/HeJ genome”, Complex Trait Consortium Meeting. Chapel Hill, North Carolina. May 2006.

“Modifier genes and cancer susceptibility”, NCI - International Symposium on Functional Mouse Genomics. Dutch's Daughter Restaurant. Frederick, Maryland. July 2006.

“The Genetics of Gastrointestinal Cancer Susceptibility — Yesterday, Today, and the Promise of Prevention”, Penn Cancer Genetics Seminar. Abramson Pediatric Research Center. March 2007.

“Modifier Genes and Cancer Susceptibility”, Cold Spring Harbor Laboratory - Molecular Embryology of the Mouse Course, 25th Anniversary Symposium. Cold Spring Harbor Laboratory, New York. June 2007.

TEACHING

GC 550 *Foundations in Biomedical Sciences* – 3 lecture hours

GE 637 *Advanced Human Genetics* – Course Coordinator and Lecturer,
6 lecture hours & 6 exam hours

COMMITTEES

ICGS Genetics Ph.D. Program - Director

JCGS Graduate Council

JCGS Graduate Council Student Affairs Subcommittee - Member

JMC Faculty Affairs Committee - Member

JMC Professorial Faculty Advisory Committee – Secretary –Elect

KCC Training Committee – Member

KCC Biostatistics Core Oversight Committee - Member

KCC Transgenic and Gene Targeting Committee - Member

Department of Microbiology and Immunology Faculty Search Committee - Member

AWARDS/HONORS

Invited to speak at the 25th Anniversary of the Cold Spring Harbor Laboratory - Molecular Embryology of the Mouse Course in New York.

EDITORIAL RESPONSIBILITIES

Editorial Board, *Mammalian Genome*

Associate Editor, *Genetics*

MEMBERSHIPS

American Association for Cancer Research
Delaware Valley Mouse Club (member and co-founder)
International Mammalian Genome Society
American Association of University Women
Sigma Xi, The Scientific Research Society

COLLABORATIONS

Dr. Arthur Buchberg – Jefferson Medical College
Dr. Tina Bocker Edmonston – Jefferson Medical College
Dr. George Calin – Ohio State University Medical Center, OH
Dr. Carlo Croce – Ohio State University Medical Center, OH
Dr. Peter Demant – Roswell Park Cancer Institute, NY
Dr. Bruce Herron – Wadsworth Center, NY
Dr. Terry Hyslop – Jefferson Medical College
Dr. Scott Waldman – Jefferson Medical College

A. SRINIVASAN, PH.D.
PROFESSOR

DESCRIPTION OF RESEARCH

HIV-1: STRUCTURE-FUNCTION, PATHOGENESIS, AND VACCINE DEVELOPMENT

RNA viruses are well known for their enormous genetic variation. Retroviruses share this feature with other RNA viruses, and HIV-1 has been extensively investigated in this regard. Based on the DNA sequence analysis, HIV-1 has been classified into three groups: M, N, and O, with viral subtypes in each group. While the genetic variation between viral isolates has been documented throughout the genome, specifically, the env gene exhibits high variation. The variation observed in individual HIV-1 genes in the form of changes at the nucleotide level may lead to changes at the protein level. Hence, it is likely that the variation may impact on the function of the protein, depending on the nature of the mutation. The goal of our research is to analyze the polymorphisms in Vpr and assess their effects on the functions of Vpr from the point of view of its structure. Vpr has been shown to be associated with the induction of programmed cell death (apoptosis) and cell-cycle arrest in cell cultures. To assess the relevance of these observations to HIV-1 neuropathogenesis *in vivo*, we have carried out studies in collaboration using a small animal model. Single-round replication-competent retrovirus vectors expressing Vpr were utilized for this purpose. The results showed that Vpr induces apoptosis in CNS cells *in vivo* implicating a role for Vpr in AIDS pathogenesis. The results from these studies will be useful for developing Vpr-specific therapeutics and also for understanding the molecular basis of Vpr function.

Though antiviral treatment provides a benefit to HIV-1 infected individuals, this seems to be limited by the continued emergence of drug-resistant HIV variants and also by drug toxicity. This situation warrants the development of novel approaches including vaccines to contain HIV-1. Though the correlates of protective immunity are not clear, it is likely that HIV-specific cellular and humoral immune responses to the viral antigens such as Gag, Pol and Env play a role in controlling HIV-1 infections. Given its importance in viral replication and presence on the virion surface, it has been suggested that Env antigen is an ideal candidate for inducing cellular and humoral immune responses. Such a view is strengthened by the protection observed by using monoclonal antibodies against Env and the detection of neutralizing antibodies in the sera of AIDS patients. Of the human monoclonal antibodies identified, 4E10 has been shown to have broadly neutralizing capability against diverse HIV-1 isolates. Interestingly, the peptide corresponding to the epitope of this antibody by itself or in the context of a heterologous protein failed to induce neutralizing antibodies. This has prompted us to consider a modified Env gp140 antigen as a candidate vaccine for inducing broadly neutralizing antibodies. Currently, we are considering several modifications to the Env protein to improve its immunogenicity.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Cui J, P.K. Tungaturthi, V. Ayyavoo, M. Ghafouri, H. Ariga, K. Khalili, A. Srinivasan, S. Amini, and B.E. Sawaya. "The role of Vpr in the regulation of HIV-1 gene expression." (2006) *Cell Cycle*. 22: 2626-2638.

Cheng, X., M. Mukhtar, E. Acheampong, A. Srinivasan, M. Rafi, R.J. Pomerantz, and Z. Parveen.. HIV-1 Vpr potently induces programmed cell death in the CNS *in vivo*. (2007) DNA Cell Biol. 20: 116-131.

Siddiqui, K., L.D.Valle, N. Morellet, J. Cui, M. Ghafouri, R. Mukerjee, K. Urbanska, S. Fan, C.B. Pattillo, S.L. Deshmane, M.F. Kiani, R. Ansari, K. Khalili, B.P. Roques, K. Reiss, S. Bouaziz, S. Amini, A. Srinivasan, and B.E. Sawaya. Molecular mimicry in inducing DNA damage between HIV-1 VPR and the anti-cancer agent, cisplatin. (2007) Oncogene. In press.

TEACHING

IMP 600 *Microbiology*, 6 lecture hours

COMMITTEES

National Center for Research Resources, NIH, Site Visit Committee
Advisory Committee Member, Department of Neuroscience, Temple University

EDITORIAL RESPONSIBILITIES

<i>Editorial Board</i>	J. Virology
DNA and Cell Biology	AIDS Research and Human Retroviruses
<i>Manuscript Review</i>	Virology
Vaccine	
DNA and Cell Biology	

MEMBERSHIPS

American Society for Microbiology

COLLABORATIONS

Dr. Zahida Parveen – Thomas Jefferson University
Dr. Ronald Collmann – University of Pennsylvania
Dr. Phalguni Gupta – University of Pittsburgh
Dr. Bassel Sawaya – Temple University
Dr. Kamel Khalili – Temple University
Dr. Shoreh Amini – Temple University
Dr. David Weiner – University of Pennsylvania
Dr. K. Muthumani – University of Pennsylvania
Dr. S. Kalyanaraman – Advanced Bioscience Labs
Dr. Ramachandram Murali – University of Pennsylvania

YURI SYKULEV, M.D., PH.D.
ASSOCIATE PROFESSOR

DESCRIPTION OF RESEARCH

We want to understand how cytotoxic lymphocytes identify and destroy unwanted cells in the host body. This knowledge is expected to facilitate the development of new immunotherapeutic interventions aiming to eradicate virus-infected and cancer cells from the host.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Anikeeva, N., Lebedeva, T., Clapp, A.R., Goldman, E.R., Dustin, M.L., Mattoussi, H., and Sykulev, Y. (2006) Quantum Dot/Peptide-MHC Biosensors reveal strong CD8-dependent Cooperation Between Self and Viral Antigens that Augment the T Cell Response. *Proc. Natl. Acad. Sci. USA*, 103: 16846-16851.

Anikeeva, N., Martinez-Hackert, E., Kalams, S., Walker, B.D., Hendrickson, W. A. and Sykulev, Y. (2006) Structural basis for degenerate recognition of natural HIV peptide variants by cytotoxic lymphocytes. *J Biol. Chem.*, 281: 20205-20212.

SCIENTIFIC PRESENTATIONS

2006 Annual Meeting of the American Society for Cell Biology, December 9-13, 2006, San Diego, CA, Invited speaker

Blood Systems Research Institute, San Francisco, December 14, 2006, Invited speaker

DiPIA2007 (Developments in Protein Interaction Analysis 2007), May 6-9, 2007, Phoenix, Arizona, Invited speaker

AAI2007 meeting, May 19-22, 2007, Miami Beach, Florida, Invited speaker

Center for Molecular Studies in Digestive and Liver Diseases of the University of Pennsylvania, June 14, 2007, Invited speaker

AAI 2006 Meeting, The structure of a peptide-MHC complex bound to T cell receptor-like antibodies, Poster Presentation

Keystone 2007, Nanotechnology, Nanoparticles as a unique scaffold to mimic close proximity of immune receptors on the cell membrane to elucidate nature of highly sensitive T cell response, Poster Presentation

Keystone 2007 Imaging of Immune System (won award), Lymphocyte-Mediated Cytotoxicity: Understanding effective delivery of a poison pill, Award winning Poster Presentation

TEACHING

IMP505 *Fundamentals of Immunology* – Course Coordinator, 12 lecture hours

IM722 *Current Literature* – Course Coordinator
(second semester of 2005-2006 Academic year)

Advanced Cellular and Molecular Immunology – 2 lecture hours

COMMITTEES

Thomas Jefferson University, Faculty Search Committee of the Department of Microbiology and immunology Committee, Chair

Thomas Jefferson University, Member of the Academic Protocol Committee

AWARDS/HONORS

2007 Faculty of 1000 Recognition, Immunology (Vol. 103: 16846-16851, 2006)

EDITORIAL RESPONSIBILITIES

Ad-hoc reviewer, Special Emphasis Panel RFA-AI-06-041 NIAID International Research in Infectious Diseases Program

Ad-hoc reviewer, Special Emphasis Panel RFP-NIH-NIAID-DMID-07-17 "Tuberculosis Research Unit (TBRU)"

Ad-hoc reviewer, Cancer Research UK

MEMBERSHIPS

American Association of Immunologists

COLLABORATIONS

Dr. Mike Dustin – New York University, USA

Dr. Phillip Norris – Blood System Research Institute, San Francisco, USA

Dr. Wayne Hendrickson – Columbia University, USA

Dr. Spyros Kalams - Vanderbilt University Medical Center, Nashville, USA

Dr. Bruce Walker- Massachusetts General Hospital, Boston, USA

JIANKE ZHANG, PH.D.
ASSISTANT PROFESSOR

DESCRIPTION OF RESEARCH

My laboratory investigates the molecular biology of signal transduction in immune cells. We have been focusing on proteins that appear to have a dual function in mediating apoptosis and proliferation of T and B lymphocytes.

1. Understanding the proliferative function of FADD in TCR induced pathways. The FADD (Fas-associated death domain) protein is an essential component of the death inducing signaling complex (DISC) of Fas, TRAIL-R, and TNF-R1, which can be proapoptotic. Whereas a lack of Fas results in lymphoproliferative and autoimmune diseases, mutations in the FADD gene disrupted embryonic development. By using a viable mutant mouse model in which FADD is deleted specifically in T cells, we previously established that FADD is not only required for Fas-induced apoptosis but also plays an essential role in TCR-induced T cell proliferative responses. In the continued study, we revealed that FADD deficiency impaired the expression of activation associated proteins including CD25 (IL-2R α) and CD69 which are required for optimum proliferation in T cells. Furthermore, FADD is required for the expression of IL-2 which is essential for T cell survival. We further showed that FADD deficiency blunted cell cycle progression by reducing the activity of CDK2. This work has been submitted for publication in the Journal of Immunology.

2. Delineate functional domains of FADD by reverse genetics. The FADD protein contains two protein-protein interaction domains: the death domain (DD) which binds to the DD of Fas and other DRs; and the death effector domain (DED) which interacts with the DED of the downstream Caspase 8. We are interested in identifying mutant forms of FADD which lose some function but retain others. Our results have showed that phosphorylation of FADD at serine 191 is dispensable in apoptotic and proliferation signaling. In contrast, mutations in the death domain replacing arginine 117 or valine 121 with alanine or asparagine (R117A and V121N) disrupted a function of FADD essential for embryonic development. However, these two mutations are distinct in that R117A blocked apoptosis, whereas V121N retains normal apoptotic function. This work was submitted to J. Biol. Chem. For publication.

3. Novel functions of FADD in the innate immunity. To analyze the function of FADD in B lymphocytes, we generated B cell-specific FADD-deficient mice using the CD19-Cre gene. In collaboration with Dr. T. Manser's lab, we demonstrated that early B cell development in the bone marrow was not significantly affected. However, B cell-specific FADD-deficient mice contained increased numbers of peripheral B2 B cells, which may be due to a lack of apoptosis of mature FADD $^{-/-}$ B cells. Unexpectedly, FADD $^{-/-}$ proliferation induced by the antigen receptor (BCR) stimulation was intact, unlike FADD $^{-/-}$ T cells. More interestingly, FADD $^{-/-}$ B cells had defects in proliferation induced by Toll-like receptors, TLR3 and TLR4. Therefore, our study revealed a novel function for FADD in the innate immune responses mediated by TLRs. This studies was carried out in collaboration with Dr. Manser's Lab and the results were published in the J. of Immunology.

4. The function of Nit1 gene in T cells. The mammalian *Nit1* gene is homologous to

bacterial and plant nitrilases. In the fruit fly *D. melanogaster* and worms *C. elegans*, *Nit1* is fused to the *Fhit* gene, whereas in mammals, *FHIT* and *NIT1* are separate genes. *FHIT* is a tumor suppressor gene located at chromosome region 3p14.2, encompassing the common fragile site of the human genome. Somatic loss of *Fhit* in humans is associated with cancers in a wide variety of sites, including lung, kidney, stomach, pancreas, cervix, ovary, head and neck, breast, and hematopoietic cells. Proteins that engage in fusion events are expected to jointly participate in a biochemical or cellular pathway and/or to physically interact. Therefore, *Nit1* may be functionally related to *Fhit*. Overexpression of *Fhit* and *Nit1* can induce apoptosis. There was evidence showing that *Fhit* can induce FADD-mediated cell death. In this study, the *in vivo* function of *Nit1* was analyzed using the *Nit1* knockout mice. Deletion of *Nit1* had no effect on mouse development. *Nit1*^{-/-} mice contains normal lymphocyte populations. *Nit1*^{-/-} deficient cells have no defect in apoptosis induced by a variety of signals. However, *Nit1*^{-/-} T cells had a hyper-proliferative responses induced by TCR stimulation. Furthermore analysis showed there was an enhanced cell cycle entry to the S phase in *Nit1*^{-/-} T cells. These data suggest that *Nit1* may play a role in tumor suppression/surveillance in T cell. This paper is under preparation for submission to J. Immunol.

5. Analysis of the function of the FLIP protein This is a regulatory protein with homology to the casapase 8 protein but lacking protease activities. We have performed embryonic development of FLIP^{-/-} mice. Similar to FADD deficiency, a lack of FLIP blocks early embryonic development. This study is to test the hypothesis that FLIP participate in a signaling pathway that also involves FADD. We showed that heterozygous FLIP^{+/-} mice had a hypomorphic phenotype: reduced T cell proliferation, similar to FADD^{-/-} T cells. We have performed preliminary analysis of the cFLIP function in the immune system by generating B cell-specific cFLIP deficient. The manuscript is to be submitted shortly. An NIH R03 grant has been submitted on February 16, 2007, was scored favorably on the initial review, and was resubmitted on July 16, 2007.

6. We have collaborated with Dr. Alnemri's lab in the study of a molecular complex containing pyrin and related proteins which are involved in inflammatory responses in macrophages. This work has been published in the journal "Cell death and differentiation".

7. In collaboration with Dr. Craig Wash's lab at University of California, Irvine, we showed that FADD-mediated regulation of T cell cycle progression involves a novel mechanism unrelated to phosphorylation of FADD. This study has been submitted for publication in J. Immunology.

8. The Daxx protein was initially identified as a potential Fas-interacting protein. Whereas a role of Daxx in Fas-induced apoptosis may not withstand further test, it's formally established that Daxx is essential for embryonic development. To further understand the function of Daxx, we obtained Daxx^{+/-} and Daxx^{-/-} embryonic stem cells from Dr. P. Leder's lab, and performed biochemical analysis using these mutant cells, in collaboration with Dr. Xiao-Lu Yang's lab at University of Pennsylvania. We showed that Daxx is required for the stability of the tumor suppressor Mdm2 and thus regulate p53 activity. This paper has been published in Nature Cell Biology.

9. Analysis of the FADD functions in innate immunity against influenza and rabies viruses. This study is in collaboration with Dr. M. Schnell and Dr. L. Eisenlohr's labs.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Imtiyaz, H. Z., Rosenberg, S., Zhang, Y., Rahman, Z. S. M., Hou, Y-J., Manser, T. L., and J. Zhang. "The Fas-Associated Death Domain Protein (FADD) is Required in Apoptosis and TLR-induced Proliferative Responses in B Cells" (2006) *J. Immunol.* 176: 6852-6861.

Tang, J., Qu, L., Zhang, J., Wang, W., Michaelson, J. S., Degenhardt, Y. Y., El-Deiry, W. S., and Yang, X. "Critical role for Daxx in regulating Mdm2" (2006) *Nature Cell Biol.* 8:855-862.

Fernandes-Alnemri, T., Wu, J., Yu, J.W., Datta, P., Miller, B., Jankowski, W., Rosenberg, S., Zhang, J., Alnemri, E. S. "The pyroptosome: a supramolecular assembly of ASC dimers mediating inflammatory cell death via caspase-1 activation" (2007) *Cell Death Differ.* 14:1590-1604.

Imtiyaz, H. Z., Rosenberg, S., Zhang, H., Zhang, Y., and J. Zhang. "FADD is essential for induction of activation-associated proteins and cytokines, and cell cycle progression in T lymphocytes" (2007) Submitted and in revision for *J. Immunol.*

Hou, Y-J., Han, S., Zhang, H., Huebner, K., and Zhang, J. Nit1 suppresses proliferation in T lymphocytes. Manuscript in preparation, 2006.

Imtiyaz, H. Z., Zhang, H., Chen, D., Hu., T., and J. Zhang. "An essential role of the death domain of FADD required in mouse development" (2007) Submitted and in revision for *J. Biol. Chem.*

Arechiga, A. F., Bell, B. D., Weist, B. M., Rosenberg, S., Morrissette, N. S., Zhang, J., and Walsh, C. M. 2007. FADD Phosphorylation and Cell Cycle are Unlinked in Primary T cells (2007) submitted to *J. Immunol.*

SCIENTIFIC PRESENTATIONS

"Regulation of Proliferation and Apoptosis by the DISC (death-inducing signaling complex) protein.", Aronson symposium, Department of Biological Sciences, Purdue University, West Lafayette, Pennsylvania, October, 2007

"Regulation of Proliferation and Apoptosis by the DISC (death-inducing signaling complex) protein.", Bortree Lecture Series, Department of Veterinary and Biomedical Sciences, Pennsylvania State University, State College, Pennsylvania, November, 2006.

"Novel aspects of the FADD function in lymphocytes revealed using hypomorphic FADD mutant and conditional FADD-deficient", short talk, Annual meeting of American Association of Immunologists, Miami, Florida, May, 2007

TEACHING

GC 550 *Fundamentals in Biomedical Sciences* – 2 lecture hours

IM 505 *Fundamentals of Immunology* – 4 lecture hours

IM 632 *Molecular Immunology and Immunogenetics* – Course coordinator and 6 lecture hours

GE 652 *Molecular Basis of Cancer* – 2 lecture hours

COMMITTEES

Thomas Jefferson University Institutional Animal Care and Use Committee, member

Thomas Jefferson University Committee for Continuing Evaluation of the Code of Professional Conduct, member

Thomas Jefferson University Flow Cytometry Facilities, Director

Thomas Jefferson University Kimmel Cancer Center Animal Use Advisory Committee, Chair

Thomas Jefferson University Micro/Biochem/Kimmel Cancer Center joint Seminar committee, member

Thomas Jefferson University Kimmel Cancer Center Graduate Preliminary Exam Committee, member

AWARDS/HONORS

2007 (July 1) TJU Pilot award (\$20,000) “The function of cFLIP in B lymphocytes”

2007 (July 1) TJU Resubmission Enhancement Award (REA) (\$35,000) “Apoptosis and Proliferation Signaling Mediated by FADD”

2007 (July 1) KCC Program Project Pilot Award (\$75,000, PI, J Zhang, Co-PI, T. Sato, T. Manser, Y. Sykulev) “Testing cancer-specific immunotherapeutics in the humanized mouse model”

MEMBERSHIPS

American Association of Immunologists (AAI)

American Association for the Advancement of Science (AAAS)

International Society of Analytical Cytometry (ISAC)

Society of Chinese Bioscientists in America (SCBA)

American Society for Biochemistry and Molecular Biology (ASBMB)

COLLABORATIONS

Dr. Xiao-Lu Yang – University of Pennsylvania

Dr. Kay Huebner – Ohio State University

Dr. Hao Shen – University of Pennsylvania

Dr. Craig Walsh – University of California, Irvine

Dr. Emad Alnemri – Jefferson Medical College

Dr. Tim Manser – Jefferson Medical College

Dr. Matthias Schnell – Thomas Jefferson University

Dr. Yuri Sykulev – Jefferson Medical College

Dr. Takami Sato – Jefferson Medical College

Dr. Ike Eisenlohr – Jefferson Medical College

S. M. ZIAUR RAHMAN, M.D., PH.D.
INSTRUCTOR

DESCRIPTION OF RESEARCH

My research interests focus on studying the basic mechanisms of peripheral tolerance notably germinal center (GC) and antibody-forming cell (AFC) pathways and how altered mechanisms might lead to the production of autoantibodies and the development of lupus nephritis under autoimmune conditions such as SLE.

SLE (systemic lupus erythematosus) is a complex polygenic disease. Most of our understanding about the autoimmune disease such as SLE to date has come from the studies of animal models. The New Zealand Black (NZB)/NZ White (NZW)-derived NZM2410 strain develops a disease that resembles human SLE. Three major genomic intervals (Sle1, Sle2 and Sle3) were identified by the Wakeland group in the NZM2410 strain. B6 mice congenic for each of these loci exhibit different component phenotypes. For instance, B6.Sle1 mice spontaneously develop high titers of ANAs but these can mediate high penetrance of severe glomerulonephritis only in combination with other SLE susceptibility loci (Sle2, Sle3/Sle5, Yaa and Ipr). Two of the most potent loci are Sle1 and Sle3. Sle3 in combination with Sle1 mediates severe lupus nephritis. B6.Sle3 has been shown to be associated with ANAs, T cell hyperactivity, elevated ratios of CD4/CD8 T cells and hyperstimulatory antigen-presenting cells (APCs). However, it is not clear whether this process is due to loss of central or peripheral tolerance. Using B cell antigen receptor transgenic mouse line (B6.HKIR) that produces autoreactive (DNA-reactive) B cells, we are investigating how Sle1 and Sle3 might be altering the peripheral B cell tolerance operative during GC and AFC pathways leading to the development of autoimmune disease SLE.

PUBLICATIONS (JULY 1, 2006 THROUGH JUNE 30, 2007)

Rahman, Z.S.M., Alabyev, B. and Manser, T.. "Fc γ RIIB regulates autoreactive primary antibody forming cell, but not germinal center B cell, activity" (2007) *J. Immunol.*, 178: 897-907.

Alabyev, B., Rahman, Z.S.M and Manser, T.. "Quantitatively reduced participation of anti-nuclear antigen B cells that down regulate BCR during primary development in the germinal center/memory B cell response to foreign antigen" (2007) *J. Immunol.*, 178: 5623-5634.

SCIENTIFIC PRESENTATIONS

"The inhibitory Fc receptor Fc γ RIIB (RIIB) regulates autoreactive antibody-forming cell, but not germinal center B cell, activity", Arthritis Foundation Research Conference, Atlanta, Georgia.

TEACHING

IMP 722 *Current Literature in IMP II* – 24 hours

IMP 732 *Current Literature in IMP III* – 19 hours

AWARDS/HONORS

2007 Research award from the Arthritis National Research Foundation (ANRF)

2007 Travel award to attend the Arthritis Foundation Research Conference

MEMBERSHIPS

American Association of Immunologists

COLLABORATIONS

Dr. Tim Manser – Thomas Jefferson University

Dr. Laurence Morel – University of Florida

Dr. Chandra Mohan-Texas University Southwestern Medical Center

DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY

TIMOTHY MANSER, PH.D.

CHAIR

FACULTY RESEARCH SUPPORT SUMMARY

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
MANSER, TIMOTHY	NIH 2 RO1 AI 038965-10	Negative Selection of Autoreactive Antibodies	05/01/96- 11/30/11	200,000	P.I. 20%
	NIH 5 T32 AI 007492-11	TRAINING GRANT: Training Program in Developmental Immunology	07/01/96- 06/30/07	172,811	P.I. N/A
	NIH 5 RO1 AI 046806-08	Regulation of Persistent Antibody Response by FC Receptors	05/15/99- 01/31/10	213,341	P.I. 21%
	NIH 5 P30 CA 56036-08	Translational Research in Cancer (Pestell, R., Program Director) Institutional Cancer Core Grant Immunology Program No Research Support – Salary Only	06/22/95- 05/31/08	19,221	Program Leader 10%
	Commonwealth of PA Department of Health ME-03-184	B Cell Tolerance in Germinal Center Project #9	01/01/05- 12/31/07	155,122	P.I. 20%
	NIH 1RO3 AI 059730-02	A V _H Gene that Fails to Promote Development of Follicular B Cells	03/01/05- 02/28/07	48,825	P.I. 5%
	NIH 1RO3 AI 057510-02	A New Model for Studying Antigen-driven B B Cell Tolerance	03/15/05- 02/28/07	48,825	P.I. 5%
	NIH 5 T32 AI 07492-11 (Pending)	TRAINING GRANT: Training Program in Developmental Immunology	07/01/08- 06/30/13	208,288	P.I. N/A
	NIH 5 P30 CA 56036-09 (Pending)	Translational Research in Cancer (Pestell, R., Program Director) Institutional Cancer Core Grant Immunological Mechanisms in Cancer No Research Support – Salary Only	06/22/08- 05/31/13	23,512	Program Leader 10%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
ABRAHAM, DAVID	GA0660XO Pfizer Buenos Aires	Evaluation of the activity of the combination- azithromycin-fluconazole against Leishmania (V) Braziliensis and Leishmania (L) amazonensis in golden Hamsters determination of the bioavailability of azithromycin In hamsters after oral administration	11/01/06-10/30/07	28,750	P.I. N/A
	Pfizer Argentina GA0660XO	Evaluation of the clinical efficacy of azithromycin in combination with fluconazole or meglumine Antimonite for the treatment of American cutaneous Leishmaniasis (ACL) in Argentina	08/07/07-08/06/10	28.750	P.I. N/A
	200-2007-M-22911 Centers for Disease Control and Prevention	Development of a multiplex assay for screening patients with Eosinophilia-Testing candidate antigens	10/01/07-09/30/08	20,000	P.I. 2%
	NIH R01 (Pending)	The development of recombinant multivalent vaccine against human onchocerciasis (Hotez, P.I., Sub with GU)	07/01/07-06/30/12	179,452	P.I. 20%
	NIH R01 (Pending)	Neutrophil Dependent Immunity to Strongyloides Stercoralis	12/01/07-11/30/12	250,000	P.I. 20%
	NIH R01 (Pending)	The Development of a Recombinant Vaccine Against Onchocerciasis (Sub with NY Blood Ctr, Dr. Lustigman)	04/01/08-03/31/13	\$99,438	Co-Investigator 20%
ALUGUPALLI, KISHORE	NIH 1 R01 AI 065750-02	B1B Lymphocytes Generate T-cell-independent Memory	07/15/06-06/30/10	218,475	P.I. 40%
	American Heart Association (Pending)	Toll-like receptor signaling in the B1b lymphocyte	01/01/08-12/31/13	90,909	P.I. 20%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
BUCHBERG, ARTHUR	NIH 5 RO1 CA 89560-05	Molecular Genetics of Cancer Susceptibility (Siracusa, L., P.I.)	02/01/03-01/31/08	210,970	Co-Investigator 10%
	NIH 5 T32 CA 009678-14	Training Program in Molecular Genetics of Cancer	04/01/92-05/31/09	341,784	Director 5%
	NIH 5 P30 CA 56036-08	Translational Research in Cancer (Pestell , R., Program Director) Institutional Cancer Core Grant Laboratory Animal Facility – No Salary Requested	06/22/95-05/31/08	216,336	Facility Director 5%
	NIH 5 RO1 AI 055842-05	Activation of Innate Immunity Effector Cells	07/01/03-12/31/07	200,095	P.I. 5%
	NIH 1R01 CA 120243-01	Susceptibility Genes and Colorectal Cancer (Siracusa, L., P.I.)	07/01/07-05/31/12	190,000	Co-Investigator 15%
	NIH 5 P30 CA 56036-09 (Pending)	Translational Research in Cancer (Pestell , R., Program Director) Institutional Cancer Core Grant Laboratory Animal Facility	06/01/08-05/31/13	223,548	Facility Director 5%
	DOD (Pending)	Use of genome tagging technologies to identify genes involved in breast cancer initiation and Progression	09/30/08-09/29/11	100,000	P.I. 20%
	NIH (Pending)	Impact of the Mom2 locus on intestinal biology and cancer	04/01/08-03/31/13	250,000	P.I. 25%
CALKINS, CATHERINE E.	NIH 5 RO1 AA 013697-01	Ethanol Interactions in Liver Disease (Feitelson, M., P.I.)	07/01/03-06/30/08	225,000	Co-Investigator 20%
	TJU Intramural Award	New Assay for MRBC-Specific Auto Antibody Responses	12/01/05-11/30/06	20,000	P.I. N/A
	NIH 1 R03 AI 064636-01	New Assay for MRBC-Specific Auto- antibody Responses	09/05/07-08/31/09	50,000	P.I. 15%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
CALKINS, CATHERINE E. (continued)	NIH R01 (Pending)	Immunoregulation in the Pathogenesis of Chronic HBV	07/01/07-06/30/12	250,000	P.I. 30%
DIETZSCHOLD, BERNHARD	NIH 5 RO1 AI 45097-08	Molecular Pathogenesis of Rabies	04/15/99-12/31/07	175,000	P.I. 15%
	NIH 5 RO1 AI 049153-06	Rabies Virus-Based Vectors as an HIV-1 Vaccine (Schnell, M., P.I.)	03/15/01-02/28/09	554,380	Co-Investigator 5%
	NIH 5 RO1 AI 060686-03	Generation of Novel Recombinant Rabies Virus Vaccines	03/01/05-02/28/10	165,932	P.I. 25%
	NIH 1R 21 AI 062964-02	Rhabdovirus-based Recombinant Vaccines against SARS	03/10/05-02/28/10	150,000	P.I. 10%
	NIH 1 R21 AI 062807-01	Killed Rhabdoviruses as Novel Anthrax Vaccines (M. Schnell, P.I.)	07/05/05-06/30/07	151,867	Co-Investigator 5%
	NIH 1R41 AI 063822-01	A Novel rhabdovirus-based Anthrax Vaccine via MOLECULAR TARGETING TECHNOLOGIES, INC. (Schnell, M., P.I.)	04/15/06-03/31/08	157,512	Co-Investigator 10%
	US Dept of Agriculture 2006-33610-16801	Selection and Testing of recombinant CAV-2 Rabies Vaccine for oral immunization of wildlife	05/01/06-12/31/06	15,358	P.I. 5%
	NIH 1 R01 AI 072360 (Pending)	Pathogenesis of Rabies Virus in Bats (Sub with NY State Dept. of Health) (Schnell, M., P.I.)	07/01/07-06/30/12	250,000	Co-Investigator 5%
	NIH SBIR (Pending)	Safety and efficacy of a novel recombinant CAV2 Rabies Vaccine for Oral Immunization of wildlife	09/01/07-08/31/09	110,318	P.I. 17%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
DIETZSCHOLD, BERNHARD (continued)	NIH R21 (Pending)	Rhabdoviral Carrier as a Novel Botulinum Neurotoxin Sub-unit Vaccine (Schnell, M., P.I.) (Sub to MTTI)	03/01/08-02/28/13	397,471	Co-Investigator 10%
	NIH 1 R21 AI 068837-01 (Pending)	Development of a recombinant Nipah virus vaccine for wildlife (Faber, M., P.I.)	04/01/08-03/31/10	125,000	Co-Investigator 5%
	USDA/APHIS (Pending)	Development of a Canine Adenovirus-Based Rabies Vaccine	10/01/07-09/30/08	34,545	P.I. 0%
EISENLOHR, LAURENCE	NIH 5 RO1 AI 039501-09	Accessing the MHC Class I Antigen Processing Pathway	06/01/97-05/31/07	225,000	P.I. 28%
	NIH 5 RO1 AI 036331-12	Class II Processing Routes Delineated by Flu Glycoproteins	04/01/95-04/30/09	165,932	P.I. 25%
	NIH 5 R25 CA 069277-07	Short-term Training Program in Translational Cancer (Waldman, S., P.I.)	08/01/97-03/31/08	80,304	Co-Leader 5%
	NIH 5 RO1 AI 049153-06	Rabies Virus-Based Vectors as an HIV-1 Vaccine (Schnell, M. P.I.)	03/15/01-02/28/09	554,380	Co-Investigator 5%
	NIH 5 R21 AI 063065-02	The Role of the RET Receptor in Autoimmune Disease	04/01/06-03/31/08	121,375	P.I. 25%
	NIH 1 RO1 AI 069192-01	The Basis for MHC Class II-restricted proteasome- dependent epitopes	01/08/07-12/31/10	225,000	P.I. 20%
	NIH 5 T32 CA009683-15	Training Program in Cancer Immunology	02/05/93-07/31/08	231,342	P.I. 5%
	NIH 1 R21 AI 007053-01	Dissecting 3 processing pathways that generate class II-restricted flu epitopes	09/01/07-08/31/09	150,000	P.I. 10%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
EISENLOHR, LAURENCE (continued)	NIH 5 R01 AI 039501-10 (Pending)	Accessing the MHC Class 1 Processing Pathway	12/01/07- 11/30/12	250,000	P.I. 30%
LANDEL, CARLISLE	NIH 5 P30 CA 56036-08	Translational Research in Cancer (Pestell, R., Program Director) Institutional Cancer Core Grant Transgenic/Knockout Mouse Facility	06/22/95- 05/31/08	226,375	Facility Director 50%
	NIH 5 P30 CA 56036-09 (Pending)	Translational Research in Cancer (Pestell, R., Program Director) Institutional Cancer Core Grant Transgenic/Knockout Mouse Facility	06/01/08- 05/31/13	160,672 Facility	Facility Director 50%
McGETTIGAN, JAMES P.	NIH 5 R21 AI 070252-02	Second Generation Rabies Vaccines	07/15/06- 06/30/08	121,375	P.I. 65%
	NIH 5 R01 AI 049153-06	Rabies Virus-based Vectors as an HIV-1 Vaccine (Schnell, M., P.I.)	03/15/01- 02/28/09	554,380	Co-Investigator 25%
	NIH 1P40 RR 018604-02	Experimental Neuroanatomy with Neurotropic Viruses (Strick, P., P.I. - Univ. of Pittsburgh) (Core A Leader – Schnell, M.)	06/01/04- 05/31/09	67,847 (Core A)	Res. Assoc. 0%
	Commonwealth of PA Department of Health SAP# 4100026302	Detection and Targeting of Infected Cells with TCR-like anti- bodies (Y. Sykulev)	01/01/05- 12/31/08	60,128	Co-Investigator 5%
	NIH 1 R21 AI 062807-02	Killed Rhabdoviruses as Novel Anthrax Vaccines (Schnell, M., P.I.)	07/05/05- 06/30/07	151,867	Instructor 0%
	Wyeth Young In- vestigators Award (Pending)	Peripheral Inflammatory Responses and Novel Rabies Vac- cines	07/01/07- 06/30/09	150,000	P.I. 15%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
MERCER, W. EDWARD	NIH 5 RO1 CA 79756-09	p53-Mediated G2/M-Checkpoint Control	01/01/99- 02/28/11	158,727	P.I. 50%
RAHMAN, ZIAUR	NIH 5 RO1 AI 46806-08	Regulation of Persistent Antibody Response by FC Receptors (Manser, T., P.I.)	05/15/99- 01/31/10	213,341	100%
	Arthritis Foundation (Funded)	Impact of lupus susceptibility loci on peripheral B cell tolerance	07/01/07- 06/30/08	50,000	P.I. 50%
	NIH R03 (Pending)	Impact of Lupus Susceptibility Loci on Peripheral Tolerance and Onset of Disease	12/01/07- 11/30/10	50,000	P.I. 50%
SCHNELL, MATTHIAS	NIH 5 RO1 AI 049153-06	Rabies Virus-Based Vectors as an HIV-1 Vaccine	03/15/01- 02/28/09	554,380	P.I. 20%
	NIH 1P40 RR 018604-03	Experimental Neuroanatomy with Neurotropic Viruses (Strick, P., P.I. - Univ. of Pittsburgh)	06/01/04- 05/31/09	69,882	Core Director 10%
	NIH 5 RO1 AI 060686-03	Generation of Novel Recombinant Rabies Virus Vaccine (Dietzschold, B., P.I.)	03/01/05- 02/28/10	165,932	Investigator 10%
	NIH 1 R21 AI 062807-02	Killed Rhabdoviruses as Novel Anthrax Vaccines	07/05/05- 06/30/07	122,062	P.I. 16%
	NIH 1 RO1 AI 069192-01	The Basis for MHC Class II-restricted proteasome- dependent epitopes (Eisenlohr, P.I.)	01/08/07- 12/31/10	225,000	Co-Investigator 5%
	NIH 1R41 AI 063822-01	A Novel rhabdovirus-based Anthrax Vaccine via MOLECULAR TARGETING TECHNOLOGIES, INC.	04/15/06- 03/31/08	157,512	P.I. 16%
	NIH 5 RO1 MH 074375-03	Astrocytes and Restricted HIV-1 Replication	09/15/05- 08/31/08	225,193	P.I. 5%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
SCHNELL, MATTHIAS (continued)	NIH R41 AI 073064-01 (Pending)	Novel Vaccine: Botulinum Neurotoxin Subunit on a Viral Carrier (Sub to TJU with MTTI, Pak, K. P.I.)	11/01/07-10/31/09	102,955	Co-Investigator 10%
	NIH 1 R01 AI 072360 (Pending)	Pathogenesis of Rabies Virus in Bats (Sub with NY State Dept. of Health)	07/01/07-06/30/12	250,000	P.I. 20%
	NIH 1 R21 (Pending)	Can TCR-like antibody help eradicate the virus? (Sykulev, Y., P.I.)	09/01/07-08/31/09	125,000	P.I. 25%
	NIH R21 (Pending)	Rhabdoviral Carrier as a Novel Botulinum Neurotoxin Subunit Vaccine (Sub to MTTI)	03/01/08-02/28/13	397,471	P.I. 20%
	NIH 1 R21 AI 068837-01 (Pending)	Development of a recombinant Nipah virus vaccine for wildlife (Faber, M., P.I.)	04/01/08-03/31/10	125,000	Co-Investigator 5%
SIRACUSA, LINDA	NIH 5 RO1 CA 89560-05	Molecular Genetics of Cancer Susceptibility	02/01/03-01/31/08	210,970	P.I. 25%
	NIH 5 RO1 CA 89560-05S1	Molecular Genetics of Cancer Susceptibility MINORITY SUPPLEMENT (Stephanie Nnadi)	02/01/03-01/31/08	38,421	P.I. N/A
	Commonwealth of PA Department of Health ME-02-177	Proteomics Research on Lung Cancer Alternatives – The Commonwealth Universal Research Enhancement (Cure) Program (Davidson, R., P.I.)	01/01/03-12/31/06	40,000	Proj. P.I. 5%
	TJU Intramural Award	Investigation of pathways for Cancer	03/31/06-02/28/07	20,000	P.I. N/A

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
SIRACUSA, LINDA (continued)	NIH 5 P30 CA 56036-08	Translational Research in Cancer (Pestell , R., Program Director) Institutional Cancer Core Grant Program Developmental Funds	06/22/95- 05/31/08	75,000	2%
	NIH 1RO1 CA 120243-01	Susceptibility Genes and Colorectal Cancer	07/01/07- 05/31/12	190,000	P.I. 20%
	NIH (Pending)	Impact of the Mom2 locus on intestinal biology and cancer (Buchberg, A., P.I.)	04/01/08- 03/31/13	250,000	Co-Investigator 10%
SRINIVASAN, A.	NIH R21 (Pending) (not funded)	Neuropathogenesis by HIV-1 Vpr using a small- animal model (Parveen, P.I.)	02/01/07- 01/31/07	150,000	Co-Investigator 10%
	NIH R21 (Pending) (not funded)	A mouse model for HIV-1 using a Chimeric MuLv/HIV-1	04/01/07- 03/31/09	150,000	P.I. 50%
SYKULEV, YURI	NIH 5 P30 CA 56036-08	Translational Research in Cancer (Pestell, R., Program Director) Institutional Cancer Core Grant Protein/Peptide Chemistry/Molecular Interaction Facility No Research Support – Salary Only	06/22/95- 05/31/08	12,986	Co-Facility Director 10%
	NIH 5 RO1 AI 39966-06	TCR Gene Usage and Quantitation of HIV- Specific CTL (Kalmas, S., P.I., Mass General)	04/01/02- 03/31/07	24,351	Co-Leader 5%
	NIH 2 R56 AI 052812-05	Molecular Assemblies of Immune-Receptors on Cytotoxic Lymphocytes and Target Cells	07/01/02- 06/30/08	301,750	P.I. 30%
	NIH 1 R21 AI 58755-02	Soluble Oligomeric TCR and Antigen Presentation to CTL	09/30/04- 08/31/06	150,000	P.I. 25%

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
SYKULEV, YURI (continued)	Commonwealth of PA Department of Health SAP# 4100026302	Detection and Targeting of Infected Cells with TCR-like antibodies	01/01/05-12/31/08	60,128	P.I. 5%
	NIH 1R01 (Pending)	Quantum dot/peptide MHC conjugates: novel tools for probing T cell responses (sub with MIT)	04/01/07-03/31/12	250,000	P.I. 40%
	NIH 2 R56 AI 052812 (Pending)	Immune-Receptors on Cytotoxic Lymphocytes and Target Cells (sub with Mike Dustin, NYU)	12/01/07-06/30/12	301,750	P.I. 30%
	NIH R21 (Pending)	Proximity between Immune Receptors on the Cell Surface and the Sensitivity of Tcell Responses Sub with Edinburgh Instruments (Gakamsky)	12/01/07-11/30/09	150,000	P.I. 20%
	NIH 1 R21 (Pending)	Can TCR-like antibody help eradicate the virus?	09/01/07-08/31/09	125,000	P.I. 25%
	Philip Morris (Pending)	The influence of the proximity between immune receptors on the sensitivity of CTL response	11/01/07-10/31/10	108,531	P.I. 10%
ZHANG, JIANKE	NIH 5 P30 CA 056036-08	Translational Research in Cancer Institutional Cancer Core Grant (Pestell, R., Program Director) Flow Cytometry Facility	06/22/95-05/31/08	113,783	Facility Director 10%
	NIH 5 RO1 CA 95454-05	Apoptosis and Proliferation Signaling Mediated by FADD	07/01/02-06/30/08	173,817	P.I. 25%
	TJU Pilot Award 920012	Regulation of toll-like receptor signaling by "cell death" proteins	07/01/07-06/30/08	20,000	P.I. N/A

FACULTY RESEARCH SUPPORT

Investigator	Support Source and I.D.	Title of Support	Period	Current Year Direct Costs	Role and % Effort
ZHANG, JIANKE (continued)	TJU REA Award 920011	The function of cFLIP in B lymphocytes	07/01/07- 06/30/08	35,000	P.I. N/A
	NIH RO1 AI 072112 (Pending)	Regulation of toll-like receptor signaling by “cell death” proteins	12/01/07- 11/30/12	250,000	P.I. 25%
	NIH 5 R01 CA 095454-06 (Pending)	Apoptosis and Proliferation Signaling Mediated by FADD	07/01/07- 06/30/12	250,000	P.I. 25%
	NIH R03 AI 076788-01 (Pending)	The Function of cFLIP in B Lymphocytes	12/01/07- 11/30/09	50,000	P.I. 10%
	NIH 1R01 CA 95654-01 (Pending)	Apoptosis and Proliferation Signaling Mediated by FADD	12/01/07- 11/30/09	250,000	PI 25%
	NIH 5 P30 CA 056036-09 (Pending)	Translational Research in Cancer Institutional Cancer Core Grant (Pestell, R., Program Director) Flow Cytometry Facility	06/01/08- 05/31/13	117,196 Facility	Facility Director 10%