

ANNUAL REPORT  
DEPARTMENT OF  
MICROBIOLOGY &  
IMMUNOLOGY

JEFFERSON MEDICAL COLLEGE OF  
THOMAS JEFFERSON UNIVERSITY

JULY 1, 2007 THROUGH JUNE 30, 2008

TIM L. MANSER, PH.D.  
PLIMPTON-PUGH PROFESSOR AND CHAIR



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**FACULTY OF THE DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY**

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<b>Name</b>	<b>Faculty Academic Rank</b>	<b>Joint Appointment or Affiliation</b>
Tim L. Manser, B.A., Ph.D.	<b>Plimpton Pugh Professor and Chair</b>	
David Abraham, Ph.D.	Professor	
David Berd, B.S., M.D.*	Professor	Dept Medical Oncology
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 Professor	
Neal Flomenberg, B.S., M.D.	Professor	Dept of Medical Oncology
Richard R. Hardy, Ph.D.	Adjunct Professor	Fox Chase Cancer Center
Donald L. Jungkind, B.S., Ph.D.	Professor Anatomy & Cell Biology	Department of Pathology,
W. Edward Mercer, B.S., Ph.D.	Professor	
Jeffrey V. Ravetch, M.D., Ph.D.	Adjunct Professor	Rockefeller University
Matthias Schnell, Ph.D.**	Professor	
Linda D. Siracusa, B.Sc., Ph.D.	Professor	
J. Bruce Smith, M.S., M.D.*	Professor	Department of Medicine
Algarsamy Srinivasan, Ph.D.	Professor	Terminated, June 2008
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
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	

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**FACULTY OF THE DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY (CONTINUED)**

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<b>Name</b>	<b>Faculty Academic Rank</b>	<b>Joint Appointment or Affiliation</b>
James P. McGettigan, B.S., M.S., Ph.D.	Research Assistant Professor	
Fabienne Paumet, Ph.D.	Assistant Professor	
S.M. Ziaur Rahman, M.D., Ph.D.	Research Assistant Professor	
Jianke Zhang, Ph.D.	Assistant Professor	
W. Paul Havens, Jr., A.B., M.D.	Honorary Professor	Department of Medicine
Susan E. Rittenhouse, B.A., Ph.D.	Professor Emeritus	
Jussi Saukkonen, M.D.	Honorary Professor	
Charles Panos, Ph.D.	Professor Emeritus	
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*

\*\* *Jefferson Vaccine Center, Director*

\*\*\* *Jefferson Vaccine Center, Associate Director*

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

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**INTRODUCTION**

The Department of Microbiology and Immunology continues to deliver outstanding education and training to medical students, graduate students and postdoctoral research fellows. The Department's primary goals remain education and building and maintaining internationally recognized research programs in the areas of immunology, infectious disease and genetics. Departmental faculty maintain active research programs while providing for the education of Jefferson Medical College second year students and the College of Graduate Studies (CGS) students at all levels. Departmental faculty research efforts are reflected in scholarly publications in high impact journals as well as faculty contributions to scientific meetings. Faculty research accomplishments and goals for the coming year are found in Appendix C. We rank 14<sup>th</sup> in NIH funding among medical college departments of microbiology and immunology. Considerable effort is put forth by faculty in writing grant applications in a highly competitive funding arena. With the establishment of the School of Pharmacy (Fall 2009), the Department is now responsible for teaching the Immunology Section of this program. Dr. Jerome Buescher, Assistant Professor, will direct this course.

**ADMINISTRATION**

Effective July 1, 2008 the Department's post-award administration changed to a shared resource with the Department of Biochemistry & Molecular Biology. Rosemarie Fleming-Troendle is our head administrator. It is anticipated the Departmental Office (Chair and Assistant, Kathy Reinermann) will relocate to the third floor of the Bluemle Life Sciences Building (BLSB) pending renovations. The Department continues to share pre-award administration with the Department of Biochemistry & Molecular Biology and the Kimmel Cancer Center. This central office is located in BLSB and is under the direction of Jan Rago. Graduate Education continues to be managed by Joanne Balitzky.

**JEFFERSON VACCINE CENTER**

Jefferson Vaccine Center (JVC) at Thomas Jefferson University was established in October 2007 to unify various researchers under the umbrella of a University-based Center. The Jefferson Vaccine Center is headed by Dr. Matthias Schnell as the director, Dr. Laurence Eisenlohr as the associate director and Dr. Christopher Chambers as the clinical director. The Center currently has 39 members from 10 different Departments at TJU. The Center's mission is to concentrate and enhance existing interests and expertise in vaccine research and related areas of immunology and microbial pathogenesis. The JVC held its first annual retreat on March 27-28 2008 with speakers from academia and industry. Internationally recognized clinical physicians and basic science researchers presented the latest advances in vaccine development in HIV, RSV, TB, Malaria as well as cancer vaccines.

## FACULTY

### NEW APPOINTMENTS

Dr. Fabienne Paumet, Assistant Professor, academic investigator and tenure track joined the Department in December 2007. Dr. Paumet comes to us from Columbia University.

### PROMOTIONS

Dr. Linda D. Siracusa was promoted to Professor in December 2007. Dr. S.M. Ziaur Rahman was promoted to Research Assistant Professor in August 2008.

### RECRUITMENT

The Department is currently in the process of recruiting a new faculty member. We hope to select a candidate by the end of 2008. The Department is particularly interested in candidates with research interests in the areas of the immunobiology of host defense and host-pathogen interactions.

## MEDICAL EDUCATION

### *Immunity, Infection and Disease (MMI200), 2<sup>nd</sup> Year Medical School Course*

Departmental faculty teaches the course Immunity, Infection and Disease (*MMI200*) which is presented to second year medical students. *MMI200* is under the direction of Dr. David Abraham. This 9-week course was taught to 255 students during this reporting period. 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 points throughout the course. It is the objective of this course to introduce the students to the diagnosis, treatment and prevention of infectious diseases as well as autoimmune pathogenesis and allergy. 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., Assistant Professor.

The 2008 Robert J. Mandle Memorial Graduation Award was presented to Louis H. Stein. 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.

### **GRADUATE PROGRAMS – DEPARTMENTAL AND INTER-DEPARTMENTAL**

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 are sponsored by the Kimmel Cancer Center. In addition, entry via the Flexible-Entry Pathway allows a student to complete the first year of coursework while sampling research in any of the eight Ph.D. Programs within the College of Graduate Studies. 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 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.

### **SCHOOL OF PHARMACY**

In the fall of 2009 our Departmental faculty under the direction and organization of Dr. Jerome Buescher will be responsible for teaching the Immunology section in the newly established School of Pharmacy.

### **SEMINARS**

The Department has established the Annual Bice Perussia Memorial Immunology Symposium. This is a yearly event held in the spring of each year in collaboration with investigators from the Fox Chase Cancer Center. The Department together with the Departments of Biochemistry & Molecular Biology and the Kimmel Cancer sponsor the Joint Research Seminar Series. This weekly seminar series hosts speakers from outside the Jefferson Community and is held each Thursday at 12:00 Noon.

### **FACULTY SCHOLARLY MISSION**

#### **RESEARCH**

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.

#### **GRANT SUPPORT**

The Department has an impressive record of grant support despite the ongoing flat NIH budget. Faculty in the Department submitted approximately 45 grant applications within the reporting period. Appendix B contains a list of each investigator's grants, funded and pending.

### **PUBLICATIONS**

In the reporting period, faculty published 42 articles in peer-reviewed journals. This number does not include 'in press' articles or articles submitted for publication. (See Appendix A).

## **TEACHING**

Departmental faculty provides the Medical College and the College of Graduate Studies with teaching assistance. In the fall of 2009 the Department faculty will also assume responsibility for teaching the Immunology Section in the School of Pharmacy. Each faculty member provides teaching in his/her area of expertise. Teaching commitments vary per faculty member. (see Appendix C).

## **UNIVERSITY AND MEDICAL COLLEGE SERVICE**

In addition to teaching responsibilities faculty also serve on various committees within the University and Medical College.

## **EDITORIAL SCHOLARSHIP**

A number of faculty serve on editorial boards of professional journals – including the American Journal of Tropical Medicine and Hygiene (David Abraham), Mammalian Genome (Buchberg), Journal of NeuroVirology (Dietzschold), Antigen Processing and Recognition (Eisenlohr), BioMed-Central Immunology (Manser), Cell Biology International Reports (Mercer) and Journal of Virology (Schnell). Faculty also serves as frequent reviewers for other peer-reviewed journals.

## **CLINICAL MISSION**

The Department does not have clinical responsibilities. Many of our faculty have collaborations with physicians and translational scientists in clinical departments; however, we do not maintain any specific clinical activities.

## **CHAIR'S SUMMARY**

All things considered, this was a successful year for the Department of Microbiology and Immunology. Despite the abysmal ongoing NIH pay lines, we maintained our extramural funding portfolio and some of our Faculty Members actually increased their personal portfolios. Nonetheless, several of our faculty members continue to be significantly under funded, and I will be working diligently with these individuals over the next year in an attempt to correct this situation. Our overall publication productivity also diminished somewhat last year, probably due to the fact that our Faculty was focusing more of their time and effort on grant writing. I am confident that this situation will be reversed once NIH pay lines become more favorable.

The Department continues to expend much energy on its educational mission. The second year JMC course Immunity Infection and Disease has improved dramatically over the last three years, as evidenced by substantially higher approval ratings from the students. Dr. David Abraham, the Director of this course and a Professor in our Department deserves much of the credit for this improvement. Our graduate curriculum has been streamlined to allow Ph.D. students to spend more time doing research after the first two years of their didactic education. These changes were championed by Dr. Laurence “Ike” Eisenlohr, a Professor in our Department, and he is to be commended for these efforts.

Finally, the institution of monthly meetings of all of the Chairs of the Basic Sciences Departments has greatly facilitated the implementation of unified policies of action and oversight in these Departments. In addition, these meetings have become an invaluable means in which to express our collective opinions to the Dean and President on changes in existing policies and new courses of action needed for the support of Basic Research and Education at Jefferson. I look forward to continuing to work with these dedicated individuals in these challenging, yet interesting times.

APPENDIX A  
PUBLICATIONS (JULY 1, 2007 TO JUNE 30, 2008)

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**DAVID ABRAHAM, PH.D.**

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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 G $\alpha$ i2 protein is required for recruitment of neutrophils for antibody mediated elimination of larval *Strongyloides stercoralis* in mice. *Journal of Leukocyte Biology*. 81:1120-1126.

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 *Leishmania (Viannia) braziliensis*. *American Journal of Tropical Medicine*. 77:640-646.

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*. 196:1844-1851.

Sinagra, A., C. Luna, D. ABRAHAM, M. C. Iannella, A. Riarte and A.J. Krolewiecki. 2007. The activity of azithromycin against *Leishmania (Viannia) braziliensis* and *Leishmania (Leishmania) amazonensis* in the golden hamster model. *Revista da Sociedade Brasileira de Medicina Tropical* 40: 627-630.

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**KISHORE R. ALUGUPALLI, PH. D.**

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O'Brien K., Fitzgerald D. C., Naiken K., Alugupalli K. R., Rostami A. M., Gran B. 2008. Role of the innate immune system in autoimmune inflammatory demyelination. *Curr Med Chem*. 15:1105-1115.

Colombo M. J. & Alugupalli K. R. 2008. Complement Factor H-Binding protein, a putative virulence determinant of *Borrelia hermsii*, is an antigenic target for protective B1b lymphocytes. *Journal of Immunology*. 180:4858-4864.

Alugupalli K. R. 2008. A distinct role for B1b lymphocytes in T cell-independent immunity. *Current Topics in Microbiology and Immunology*. 319:105-130.

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**BERNHARD DIETZSCHOLD, D.V.M.**

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Faber, M., Faber, M.-L., Li, J., Preuss, M. A., M. J. Schnell, M. J., Dietzschold, B. Dominance of a non-pathogenic over a pathogenic glycoprotein gene in rabies virus. *J Virol.* 81: 7041–7047, 2007

Li, J.; McGettigan, J.P.; Faber, M., M.J.; Dietzschold B. Infection of monocytes or immature dendritic cells (DCs) with an attenuated rabies virus results in DC maturation and a strong activation of the NFkB signaling pathway. *Vaccine*, 26, 419-26, 2008.

Pulmanusahakul1, R., Li, J., Schnell, M.J., Dietzschold, B. The glycoprotein and matrix protein of rabies virus affect pathogenicity by regulating viral replication and facilitating cell-to-cell spread. *J. Virol.*, *J Virol* 82, 2330-8, 2008.

Dietzschold, B., Li, J., Faber, M., and Matthias Schnell, M.J. Concepts in the pathogenesis of rabies. *Future Medicine*. In press. 2008.

Faber, M., Dietzschold, B., Li, J. Immunogenicity and safety of recombinant rabies viruses used for oral vaccination of stray dogs and wildlife. *Zoonoses and Public Health*. In press, 2008.

Cenna, J., Tan G.S., Papaneri, A.B., Dietzschold, B., Schnell, M.J., and McGettigan, J.P. "Immune Modulating Effect by a Phosphoprotein-deleted Rabies Virus Vaccine Vector Expressing Two Copies of the Rabies Virus Glycoprotein Gene". *Vaccine*, Accepted, 2008.

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

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Plesa, G., A.E. Snook, S.A. Waldman, and L.C. Eisenlohr, 2008. Derivation and Fluidity of Acutely Induced Dysfunctional CD8<sup>+</sup> T Cells. *J. Immunol.* 180:5300-5308.

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**TIM L. MANSER, PH.D.**

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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, T., Z.S.M.Rahman and T. Manser "Quantitatively reduced participation of anti-nuclear antigen B cells that down regulate BCR during primary development of the germinal center/memory B cell response to foreign antigen" (2007) *J. Immunol.*, 178: 56623-5634.

Rahman, Z.S.M., H. Niu, D. Perry, E. Wakeland, T. Manser, and L. Morel "The autoimmune Fcg2b NZW allele fails to up-regulate its expression in germinal center B cells and leads to increased IgG production" (2007) *J. Immunol.* 179: 6663-6672.

Alabyev, B.R., Vuyruru and T. Manser, "Influence of Fas on the regulation of the response to an anti-nuclear antigen B cell clonotype to foreign antigen" (2008) *Int. Immunol.*, in press.

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**JAMES P. MCGETTIGAN, PH.D.**

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McKenna P.M., Koser M.L., Carlson K.R., Montefiori D.C., Letvin N.L., Papaneri A.B., Pomerantz R.J., Dietzschold B., Silvera P., McGettigan J.P., Schnell M.J. (2007) "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.* 2007 195(7):980-8.

Li, J., McGettigan J.P., Faber, M., Schnell, M.J., and Dietzschold, B. "Infection of monocytes or immature dendritic cells (DCs) with an attenuated rabies virus results in DC maturation and a strong activation of the NFkappaB signaling pathway". (2008)*Vaccine*, 26(3):419-26.

Cenna, J., Tan G.S., Papaneri, A.B., Dietzschold, B., Schnell, M.J., and McGettigan, J.P. "Immune Modulating Effect by a Phosphoprotein-deleted Rabies Virus Vaccine Vector Expressing Two Copies of the Rabies Virus Glycoprotein Gene". (2008)*Vaccine*, Accepted.

Faul, E.J., Wangalla, C.N., McGettigan, J.P. and Schnell, M.J. "Interferon-beta expressed by a rabies virus-based HIV-1 vaccine vector serves as a molecular adjuvant and decreases pathogenicity". (2008) *Virology*, Accepted

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**FABIENNE PAUMET, PH.D.**

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C. Delevoye, M. Nilges, P. Dehoux, F. Paumet, S. Perrinet, A. Dautry-Varsat, A. Subtil "SNARE protein mimicry by an intracellular bacterium" (2008) *PLOS Pathogens* 4:e1000022

J. Shen, D. Tareste, F. Paumet, J.E. Rothman, T.J. Melia "Selective activation of cognate SNAREpins by Sec1/Munc18 (SM) proteins" (2007) *Cell* 128: 183-195

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

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Chun X, Z.S. M. Rahman, S. Xie, J. Zhu, Y. Du, X. Qin, H. Zhou, X.J. Zhou, and C. Mohan "Strain distribution pattern of immune nephritis—a follow-up study" (2008) *Int. Immunol.*, 20: 719-728.

Rahman Z.S.M., H. Niu, D. Perry, E. Wakeland, T. Manser, and L. Morel "Expression of the autoimmune Fcgr2b NZW allele fails to be up-regulated in germinal center B cells and is associated with increased IgG production" (2007) *Genes and Immunity.*, 8: 604-612.

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**MATTHIAS J. SCHNELL, PH.D.**

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- Faul, E. J., Celestine, N. W., McGettigan, J. P., and Schnell, M. J. (2008). "Interferon- $\beta$  expressed by a rabies virus-based HIV-1 vaccine vector serves as a molecular adjuvant and decreases pathogenicity". *Virology*, accepted.
- Wirblich, C., Tan, G. S., Papaneri, A., Godlewski, P. J., Orenstein, J. M., Harty, R. N., and Schnell, M. J. (2008). "PPEY motif within the rabies virus (RV) matrix protein is essential for efficient virion release and RV pathogenicity". *J Virol.*, in press
- Cenna, J., Tan, G. S., Papaneri, A. B., Dietzschold, B., Schnell, M. J., and McGettigan, J. P. (2008). "Immune Modulating Effect by a Phosphoprotein-deleted Rabies Virus Vaccine Vector Expressing Two Copies of the Rabies Virus Glycoprotein Gene". *Vaccine*, accepted.
- Weihe, E., Bette, M., Preuss, M. A., Faber, M., Schafer, M. K., Rehnelt, J., Schnell, M. J., and Dietzschold, B. (2008). "Role of virus-induced neuropeptides in the brain in the pathogenesis of rabies". *Dev Biol (Basel)* **131**, 73-81.
- Li, J., McGettigan, J. P., Faber, M., Schnell, M. J., and Dietzschold, B. (2008). "Infection of monocytes or immature dendritic cells (DCs) with an attenuated rabies virus results in DC maturation and a strong activation of the NFkappaB signaling pathway". *Vaccine* **26**(3), 419-26.
- Pulmanausahakul, R., Li, J., Schnell, M. J., and Dietzschold, B. (2008). "The glycoprotein and the matrix protein of rabies virus affect pathogenicity by regulating viral replication and facilitating cell-to-cell spread". *J Virol* **82**(5), 2330-8.
- Snook, A. E., Stafford, B. J., Li, P., Tan, G., Huang, L., Birbe, R., Schulz, S., Schnell, M. J., Thakur, M., Rothstein, J. L., Eisenlohr, L. C., and Waldman, S. A. (2008). "Guanylyl cyclase C-induced immunotherapeutic responses opposing tumor metastases without autoimmunity". *J Natl Cancer Inst* **100**(13), 950-61.
- Faber, M., Faber, M. L., Li, J., Preuss, M. A., Schnell, M. J., and Dietzschold, B. (2007). "Dominance of a nonpathogenic glycoprotein gene over a pathogenic glycoprotein gene in rabies virus". *J Virol* **81**(13), 7041-7.
- McKenna, P. M., Koser, M. L., Carlson, K. R., Montefiori, D. C., Letvin, N. L., Papaneri, A. B., Pomerantz, R. J., Dietzschold, B., Silvera, P., McGettigan, J. P., and Schnell, M. J. (2007). "Highly Attenuated Rabies Virus-Based Vaccine Vectors Expressing Simian-Human Immunodeficiency Virus89.6P Env and Simian Immunodeficiency Virus<sub>mac239</sub> Gag Are Safe in Rhesus Macaques and Protect from an AIDS-Like Disease". *J Infect Dis* **195**(7), 980-8.
- Tan, G. S., Preuss, M. A., Williams, J. C., and Schnell, M. J. (2007). "The dynein light chain 8 binding motif of rabies virus phosphoprotein promotes efficient viral transcription". *Proc Natl Acad Sci U S A*. **104**(17), 7229-34]

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**LINDA D. SIRACUSA, PH.D.**

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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.

McCorkell, K.A., R. Mancini, Z. Siprashvili, B.L. Barnoski, D. Iliopoulos, L.D. Siracusa, N. Zanesi, C.M. Croce, L.Y.Y. Fong, T. Druck and K. Huebner. “Influence of a nonfragile *FHIT* transgene on murine tumor susceptibility” (2007) *Cytogenetic & Gen Res.* 118: 196-203.

Rossi, S., C. Seignani, S.C. Nnadi, L.D. Siracusa\*\* and G.A. Calin\*\* “Cancer-associated genomic regions (CAGRs) and non-coding RNAs: Bioinformatics and therapeutic implications” (2008) *Mammalian Genome* (published ahead of print on-line). \*\* = co-corresponding authors

Databases: Developed and On-line: The MUSMIRSUS Database, Version 2 - 2007, Developed by C. Seignani, S. Nnadi, and L.D. Siracusa, [www.kimmelcancercenter.org/siracusa/musmirsus.htm](http://www.kimmelcancercenter.org/siracusa/musmirsus.htm)

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**YURI SYKULEV, M.D., PH.D.**

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Tsatsanis, C., Vaporidi, K., Zacharioudaki, V., Androulidaki, A., Sykulev, Y., Andrew N. Margioris, A. N., and P.N., Tschlis Tpl2 and ERK transduce antiproliferative T cell receptor signals and inhibit transformation of chronically-stimulated (2008) T cells. *Proc. Natl. Acad. Sci. USA*, 105: 2987-92.

Anikeeva, N., Mareeva, T., Liu, W. and Y. Sykulev Can Oligomeric T-cell receptor be used as a tool to detect viral peptide epitopes on infected cells? (2008) *Clinical Immunology*, in press

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**JIANKE ZHANG, PH.D.**

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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 under revision for *J. Immunol.*

Zhang, H., Hou, Y-J., Han, S., E. Zhang, Huebner, K., and Zhang, J. The mammalian nitrilase homologue Nit1 is negative regulator of proliferation in T lymphocytes. Submitted to *MCB*, 2008.

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 and lymphocyte proliferation” (2008) re-Submitted to *J. Biol. Chem.*

Zhang, H., Rosenberg, S., Coffey, F. J., He, Y-W., Manser, T., Hardy, R. R., and Zhang, J. A role for cFLIP in B cell proliferation and stress MAP kinase regulation. Resubmitted to *Jl.*

MICROBIOLOGY DIRECT COSTS

APPENDIX B  
FACULTY RESEARCH SUPPORT SUMMARY  
MICROBIOLOGY DIRECT COSTS 07/01/07-06/30/08

Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. ABRAHAM	080	03000	A97501	0.00	2008	3/1/2007	2/29/2008		Jefferson Intramural Research Award
DR. ABRAHAM	080	03000	N00501	23,000.00	2008	8/7/2007	8/6/2010		Pfizer, Inc.
DR. ABRAHAM	080	03000	X11801	4,652.49	2008	10/1/2007	9/30/2008		Centers For Disease Control
DR. ABRAHAM	080	03000	X12001	2,241.51	2008	11/1/2007	3/31/2009		NIH/NIAD
<b>DR. ABRAHAM</b>				<b>29,894.00</b>					
DR. ALUGUPALLI	080	03000	R82601	226,391.33	2008	7/15/2006	6/30/2009	6/30/2010	5R01AI065750-03
<b>DR. ALUGUPALLI</b>				<b>226,391.33</b>					
DR. BUCHBERG	080	03000	R69501	186,360.87	2008	7/1/2003	12/31/2008	12/31/2008	5R01AI055842-05
<b>DR. BUCHBERG</b>				<b>186,360.87</b>					
DR. BUCHBERG	080	03000	T04911	0.00	2008	7/30/2004	5/31/2005	5/31/2009	08TCA009678C
DR. BUCHBERG	080	03000	T04912	(7,600.51)	2008	6/4/2005	5/31/2006	5/31/2009	2T32CA09678-12
DR. BUCHBERG	080	03000	T04913	188,157.39	2008	6/21/2006	5/31/2007	5/31/2009	5T32CA09678-13
DR. BUCHBERG	080	03000	T04914	175,485.73	2008	6/1/2007	5/31/2008	5/31/2009	5T32CA009678-14
DR. BUCHBERG	080	03000	T04915	1,557.29	2008	6/1/2008	5/31/2009	5/31/2009	5T32CA009678-15
<b>DR. BUCHBERG</b>	<b>TRAINING GRANTS</b>			<b>357,599.90</b>					

MICROBIOLOGY DIRECT COSTS

Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. CALKINS	080	03000	A87301	0.00	2008	12/1/2005	5/31/2007		Jeff Intramural Research AWDS
DR. CALKINS	080	03000	R87301	25,080.49	2008	9/5/2007	8/31/2009	8/31/2009	5R03I064636-02
DR. CALKINS	080	03000	Z49001	36,088.11	2008	12/15/2007	6/30/2008		NIH Thru Temple University
<b>DR. CALKINS</b>				<b>61,168.60</b>					
DR. DIETZSCHOLD	080	03000	A42201	13,426.57	2008	2/11/2000	12/31/2050		Various Sponsors
DR. DIETZSCHOLD	080	03000	R49404	12,194.20	2008	9/15/2003	12/31/2007	12/31/2007	5R01AI045097-08
DR. DIETZSCHOLD	080	03000	R76301	155,594.94	2008	3/1/2005	2/28/2009	2/28/2010	5R01AI060686-04
DR. DIETZSCHOLD	080	03000	R76401	39,344.70	2008	3/10/2005	2/29/2008	2/29/2008	5R21AI062964-02
DR. DIETZSCHOLD	080	03000	X10204	14,682.99	2008	4/1/2006	7/31/2007		US Dept of Agriculture (USDA)
DR. DIETZSCHOLD	080	03000	X10205	20,113.29	2008	10/1/2007	9/30/2008	9/30/2008	US Dept of Agriculture (USDA)
DR. DIETZSCHOLD	080	03000	Z47201	47,977.68	2008	9/1/2007	8/31/2009	8/31/2009	USDA Thru Molecular Targeting
<b>DR. DIETZSCHOLD</b>				<b>303,334.37</b>					
DR. EISENLOHR	080	03000	R04108	148,253.14	2008	5/1/2004	4/30/2009	4/30/2009	5R01AI036331-13
DR. EISENLOHR	080	03000	R40005	(4,537.46)	2008	6/1/2001	5/31/2007	5/31/2007	5R01AI039501-09
DR. EISENLOHR	080	03000	R40006	79,707.75	2008	1/1/2008	12/31/2008	12/31/2011	2R01AI039501-10A2
DR. EISENLOHR	080	03000	R81501	82,788.74	2008	4/1/2006	3/31/2009	3/31/2009	5R21AI063065-02
DR. EISENLOHR	080	03000	R84201	237,950.04	2008	1/8/2007	12/31/2008	12/31/2010	1R01AI069192-01A1
DR. EISENLOHR	080	03000	R87201	97,607.22	2008	9/1/2007	8/31/2009	8/31/2009	5R21AI077053-02

MICROBIOLOGY DIRECT COSTS

Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. EISENLOHR	080	03000	R90701	150,000.00	2008	6/20/2008	5/31/2010	5/31/2009	1R21AI079526-01
DR. EISENLOHR	080	03000	R92001	135,000.00	2008	7/1/2008	6/30/2009	6/30/2010	1R21CA135602-01
<b>DR. EISENLOHR</b>				<b>926,769.43</b>					
DR. EISENLOHR	080	03000	T05013	6,242.47	2008	8/1/2005	7/31/2006	7/31/2008	5T32CA009683-13
DR. EISENLOHR	080	03000	T05014	104,512.94	2008	8/1/2006	7/31/2007	7/31/2008	5T32CA009683-14
DR. EISENLOHR	080	03000	T05015	104,206.62	2008	8/1/2007	7/31/2009	7/31/2009	5T32CA009683-15
DR. EISENLOHR	080	03000	T11701	35,033.40	2008	8/1/2007	7/31/2009	7/31/2010	5F31NS054444-02
DR. EISENLOHR	080	03000	T12201	32,432.01	2008	9/20/2007	9/30/2009	9/30/2012	5F31AG031666-02
<b>DR. EISENLOHR</b>	<b>TRAINING GRANTS</b>			<b>282,427.44</b>					
DR. MANSER	080	03000	R04507	181,903.67	2008	12/15/2006	11/30/2008	11/30/2011	5R01AI038965-11
DR. MANSER	080	03000	R50104	180,075.79	2008	2/1/2005	1/31/2009	1/31/2010	5R01AI046806-09
DR. MANSER	080	03000	R76501	0.00	2008	3/15/2005	2/28/2007	2/28/2007	5R03AI059730-02
DR. MANSER	080	03000	R76601	0.00	2008	3/15/2005	2/28/2007	2/28/2007	5R03AI57510-02
<b>DR. MANSER</b>				<b>361,979.45</b>					
DR. MANSER	080	03000	T06410	8,804.55	2008	7/1/2005	6/30/2007	6/30/2007	5T32AI007429-10
<b>DR. MANSER</b>	<b>TRAINING GRANTS</b>			<b>8,804.55</b>					

MICROBIOLOGY DIRECT COSTS

Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. MCGETTIGAN	080	03000	F78801	28,815.28	2008	7/1/2007	6/30/2009		National Foundation for Infectious Diseases
DR. MCGETTIGAN	080	03000	R82401	105,177.36	2008	7/15/2006	6/30/2009	6/30/2009	5R21AI070252-02
DR. MCGETTIGAN				133,992.64					
DR. MERCER	080	03000	R48904	123,949.76	2008	4/1/2006	2/28/2009	2/28/2011	5R01CA079756-08
<b>DR. MERCER</b>				<b>123,949.76</b>					
DR. RAHMAN	080	03000	F77801	50,245.06	2008	6/1/2007	5/31/2008		Arthritis National Research Foundation
DR. RAHMAN	080	03000	F77802	2,543.21	2008	6/1/2008	5/31/2009		Arthritis National Research Foundation
DR. RAHMAN	080	03000	R92801	50,000.00	2008	8/1/2008	5/31/2009	5/31/2011	1R03AR055701-01A1
<b>DR. RAHMAN</b>				<b>102,788.27</b>					
DR. SCHNELL	080	03000	N01101	32,828.80	2008	9/24/2007	7/1/2009		Crucell Holland B.V.
DR. SCHNELL	080	03000	R58104	478,285.95	2008	6/1/2005	2/28/2009	2/28/2009	5R01AI049153-07
DR. SCHNELL	080	03000	R77801	33,191.57	2008	7/5/2005	6/30/2008	6/30/2008	5R21AI062807-02
DR. SCHNELL	080	03000	Z34103	(1,395.62)	2008	6/1/2006	5/31/2007		NIH/University of Pittsburgh
DR. SCHNELL	080	03000	Z34104	67,481.51	2008	6/1/2007	5/31/2008		NIH/University of Pittsburgh
DR. SCHNELL	080	03000	Z34105	3,152.48	2008	6/1/2008	5/31/2009		NIH/University of Pittsburgh
DR. SCHNELL	080	03000	Z41901	121,246.17	2008	4/15/2006	3/31/2009	3/31/2009	NIH/Molecular Targeting Tech
DR. SCHNELL	080	03000	Z50301	103,206.00	2008	4/1/2008	3/31/2009	3/31/2009	NIH/Molecular Targeting Tech
<b>DR. SCHNELL</b>				<b>837,996.86</b>					

MICROBIOLOGY DIRECT COSTS

Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. SIRACUSA	080	03000	R67401	175,271.75	2008	2/1/2005	1/31/2009	1/31/2009	5R01CA089560-05
DR. SIRACUSA	080	03000	R86601	154,320.73	2008	7/1/2007	5/31/2009	5/31/2012	1R01CA120243-01A2
<b>DR. SIRACUSA</b>				<b>329,592.48</b>					
DR. SYKULEV	080	03000	R63501	18,134.17	2008	7/1/2002	6/30/2007	6/30/2007	5R01A0I52812-05
DR. SYKULEV	080	03000	R63502	87,982.03	2008	7/1/2007	11/30/2007	11/30/2007	2R56AI052812-06A1
DR. SYKULEV	080	03000	R63503	109,291.68	2008	12/1/2007	11/30/2008	11/30/2012	2R01AI052812-06A2
DR. SYKULEV	080	03000	R75001	11,450.76	2008	9/30/2004	8/31/2007	8/31/2007	5R21AI058755-02
DR. SYKULEV	080	03000	Z26202	(859.12)	2008	9/1/2002	3/31/2007		NIH Thru Vanderbilt University
<b>DR. SYKULEV</b>				<b>225,999.52</b>					
DR. ZHANG	080	03000	R62501	64,424.15	2008	7/1/2002	6/30/2008	6/30/2008	5R01CA095454-05
DR. ZHANG	080	03000	R90801	50,000.00	2008	7/1/2008	6/30/2009	6/30/2010	1R03AI076788-01A2
<b>DR. ZHANG</b>				<b>64,424.15</b>					
<b>TOTAL DIRECT COSTS FY 08</b>				<b>4,563,473.63</b>					

MICROBIOLOGY INDIRECT COSTS

**MICROBIOLOGY INDIRECT COSTS 07/01/07-06/30/08**

Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. ABRAHAM	080	03000	N00501	5,750.00	2008	8/7/2007	8/6/2010		PFIZER, INC.
<b>DR. ABRAHAM</b>				<b>5,750.00</b>					
DR. ALUGUPALLI	080	03000	R82601	102,631.60	2008	7/15/2006	6/30/2009	6/30/2010	5R01AI065750-03
<b>DR. ALUGUPALLI</b>				<b>102,631.60</b>					
DR. BUCHBERG	080	03000	R69501	37,489.85	2008	7/1/2003	12/31/2008	12/31/2008	5R01AI055842-05
<b>DR. BUCHBERG</b>				<b>37,489.85</b>					
DR. BUCHBERG	080	03000	T04912	(3,433.76)	2008	6/4/2005	5/31/2006	5/31/2009	2T32CA09678-12
DR. BUCHBERG	080	03000	T04913	12,244.24	2008	6/21/2006	5/31/2007	5/31/2009	5T32CA09678-13
DR. BUCHBERG	080	03000	T04914	12,225.81	2008	6/1/2007	5/31/2008	5/31/2009	5T32CA009678-14
DR. BUCHBERG	080	03000	T04915	124.58	2008	6/1/2008	5/31/2009	5/31/2009	5T32CA009678-15
<b>DR. BUCHBERG</b>	<b>TRAINING GRANTS</b>			<b>96,140.57</b>					
DR. CALKINS	080	03000	R87301	13,794.27	2008	9/5/2007	8/31/2009	8/31/2009	5R03I064636-02
DR. CALKINS	080	03000	Z49001	19,664.00	2008	12/15/2007	6/30/2008		NIH THRU TEMPLE UNIVERSITY
<b>DR. CALKINS</b>				<b>33,458.27</b>					
DR. DIETZSCHOLD	080	03000	A42201	0.00	2008	2/11/2000	12/31/2050		VARIOUS SPONSORS
DR. DIETZSCHOLD	080	03000	R49404	7,850.73	2008	9/15/2003	12/31/2007	12/31/2007	5R01AI045097-08
DR. DIETZSCHOLD	080	03000	R76301	85,577.22	2008	3/1/2005	2/28/2009	2/28/2010	5R01AI060686-04
Principal Investigator	Unit	Dept	Product	Sum Total Amt (\$)	Fiscal Year	Begin Date	End Date	Project End Date	Agency
DR. DIETZSCHOLD	080	03000	R76401	22,384.24	2008	3/10/2005	2/29/2008	2/29/2008	5R21AI062964-02

MICROBIOLOGY INDIRECT COSTS

DR. DIETZSCHOLD	080	03000	X10204	3,181.82	2008	4/1/2006	7/31/2007		US DEPT OF AGRICULTURE (USDA)
DR. DIETZSCHOLD	080	03000	X10205	2,011.32	2008	10/1/2007	9/30/2008	9/30/2008	US DEPT OF AGRICULTURE(USDA)
DR. DIETZSCHOLD	080	03000	Z47201	26,387.72	2008	9/1/2007	8/31/2009	8/31/2009	USDA THRU MOLECULAR TARGETING
<b>DR. DIETZSCHOLD</b>				<b>147,393.05</b>					
DR. EISENLOHR	080	03000	R04108	81,842.22	2008	5/1/2004	4/30/2009	4/30/2009	5R01AI036331-13
DR. EISENLOHR	080	03000	R40005	(2,677.10)	2008	6/1/2001	5/31/2007	5/31/2007	5R01AI039501-09
DR. EISENLOHR	080	03000	R40006	41,270.60	2008	1/1/2008	12/31/2008	12/31/2011	2R01AI039501-10A2
DR. EISENLOHR	080	03000	R81501	45,533.82	2008	4/1/2006	3/31/2009	3/31/2009	5R21AI063065-02
DR. EISENLOHR	080	03000	R84201	121,162.66	2008	1/8/2007	12/31/2008	12/31/2010	1R01AI069192-01A1
DR. EISENLOHR	080	03000	R87201	51,115.32	2008	9/1/2007	8/31/2009	8/31/2009	5R21AI077053-02
<b>DR. EISENLOHR</b>				<b>338,247.52</b>					
DR. EISENLOHR	080	03000	T05014	7,132.94	2008	8/1/2006	7/31/2007	7/31/2008	5T32CA009683-14
DR. EISENLOHR	080	03000	T05015	5,676.77	2008	8/1/2007	7/31/2009	7/31/2009	5T32CA009683-15
DR. EISENLOHR	080	03000	T05013	(281.22)	2008	8/1/2005	7/31/2006	7/31/2008	5T32CA009683-13
<b>DR. EISENLOHR</b>	<b>TRAINING GRANTS</b>			<b>12,528.49</b>					
DR. MANSER	080	03000	R04507	84,092.45	2008	12/15/2006	11/30/2008	11/30/2011	5R01AI038965-11
DR. MANSER	080	03000	R50104	99,041.68	2008	2/1/2005	1/31/2009	1/31/2010	5R01AI046806-09
<b>DR. MANSER</b>				<b>183,134.13</b>					
<b>Principal Investigator</b>	<b>Unit</b>	<b>Dept</b>	<b>Product</b>	<b>Sum Total Amt (\$)</b>	<b>Fiscal Year</b>	<b>Begin Date</b>	<b>End Date</b>	<b>Project End Date</b>	<b>Agency</b>
DR. MANSER	080	03000	T06410	(6,053.60)	2008	7/1/2005	6/30/2007	6/30/2007	5T32AI007429-10
<b>DR. MANSER</b>	<b>TRAINING GRANTS</b>			<b>360,214.66</b>					
DR. MCGETTIGAN	080	03000	R82401	57,847.55	2008	7/15/2006	6/30/2009	6/30/2009	5R21AI070252-02

MICROBIOLOGY INDIRECT COSTS

<b>DR. MCGETTIGAN</b>				<b>57,847.55</b>					
DR. MERCER	080	03000	R48904	68,172.37	2008	4/1/2006	2/28/2009	2/28/2011	5R01CA079756-08
<b>DR. MERCER</b>				<b>68,172.37</b>					
DR. RAHMAN	080	03000	F77801	0.00	2008	6/1/2007	5/31/2008		ARTHRITIS NATL RESRCH FDN
<b>DR. RAHMAN</b>				<b>0.00</b>					
DR. SCHNELL	080	03000	N01101	18,187.37	2008	9/24/2007	7/1/2009		CRUCCELL HOLLAND B.V.
DR. SCHNELL	080	03000	R58104	127,841.20	2008	6/1/2005	2/28/2009	2/28/2009	5R01AI049153-07
DR. SCHNELL	080	03000	R77801	16,777.02	2008	7/5/2005	6/30/2008	6/30/2008	5R21AI062807-02
DR. SCHNELL	080	03000	Z34103	104.52	2008	6/1/2006	5/31/2007		NIH/UNIVERSITY OF PITTSBURGH
DR. SCHNELL	080	03000	Z34104	36,624.31	2008	6/1/2007	5/31/2008		NIH/UNIVERSITY OF PITTSBURGH
DR. SCHNELL	080	03000	Z34105	1,733.86	2008	6/1/2008	5/31/2009		NIH/UNIVERSITY OF PITTSBURGH
DR. SCHNELL	080	03000	Z41901	61,249.76	2008	4/15/2006	3/31/2009	3/31/2009	NIH/MOLECULAR TARGETING TECH
<b>DR. SCHNELL</b>				<b>262,518.04</b>					
DR. SIRACUSA	080	03000	R67401	92,751.38	2008	2/1/2005	1/31/2009	1/31/2009	5R01CA089560-05
DR. SIRACUSA	080	03000	R86601	79,260.99	2008	7/1/2007	5/31/2009	5/31/2012	1R01CA120243-01A2
<b>DR. SIRACUSA</b>				<b>172,012.37</b>					
<b>Principal Investigator</b>	<b>Unit</b>	<b>Dept</b>	<b>Product</b>	<b>Sum Total Amt (\$)</b>	<b>Fiscal Year</b>	<b>Begin Date</b>	<b>End Date</b>	<b>Project End Date</b>	<b>Agency</b>
DR. SYKULEV	080	03000	R63501	1,359.09	2008	7/1/2002	6/30/2007	6/30/2007	5R01A0I52812-05
DR. SYKULEV	080	03000	R63502	48,390.12	2008	7/1/2007	11/30/2007	11/30/2007	2R56AI052812-06A1
DR. SYKULEV	080	03000	R63503	60,110.43	2008	12/1/2007	11/30/2008	11/30/2012	2R01AI052812-06A2
DR. SYKULEV	080	03000	R75001	6,297.92	2008	9/30/2004	8/31/2007	8/31/2007	5R21AI058755-02
<b>DR. SYKULEV</b>				<b>116,157.56</b>					

MICROBIOLOGY INDIRECT COSTS

DR. ZHANG	080	03000	R62501	29,371.84	2008	7/1/2002	6/30/2008	6/30/2008	5R01CA095454-05
<b>DR. ZHANG</b>				<b>29,371.84</b>					
<b>Total Indirects for FY 08</b>				<b>2,023,067.87</b>					

## APPENDIX C

### INDIVIDUAL FACULTY ACCOMPLISHMENTS

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**DAVID ABRAHAM, PH.D.**  
**PROFESSOR**

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#### RESEARCH ACCOMPLISHMENTS AND GOALS FOR THE COMING YEAR

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 protective immune response. Research is focused on the role of eosinophils, neutrophils and macrophages in killing nematode parasites through the innate and adaptive immune response. Emphasis is placed on the molecular mechanisms used by the cells, with and without antibody, to kill the worms. In addition, we are elucidating the role of eosinophils as antigen presenting cells. Knowledge of the immune mechanisms capable of killing the worms has allowed us to develop vaccines against two different nematode infections. Recombinant antigens have been identified which are successful at inducing protective immunity to these infections in mice. Efforts are now directed at determining the optimal way to administer these antigens to induce immune resistance to the infections.

#### PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)

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 G $\alpha$ i2 protein is required for recruitment of neutrophils for antibody mediated elimination of larval *Strongyloides stercoralis* in mice. *Journal of Leukocyte Biology*. 81:1120-1126.

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*. 77:640-646.

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*. 196:1844-1851.

Sinagra, A., C. Luna, D. ABRAHAM, M. C. Iannella, A. Riarte and A.J. Krolewiecki. 2007. The activity of azithromycin against *Leishmania (Viannia) braziliensis* and *Leishmania (Leishmania) amazonensis* in the golden hamster model. *Revista da Sociedade Brasileira de Medicina Tropical* 40: 627-630.

## SCIENTIFIC PRESENTATIONS

### A. MEETING PRESENTATIONS

Krolewiecki, A.J., N. Taranto, A. Sinagra, S. Cajal, C. Luna, M. Juarez, H. Romero, T. Mimori, A. Di Paolo, M. Tamami, A. Riarte and D. ABRAHAM. Azithromycin for the treatment of American Cutaneous Leishmaniasis. Pre-clinical and clinical data. The 56<sup>th</sup> Annual Meeting of the American Society of Tropical Medicine and Hygiene. Philadelphia, PA. November, 2007. (Abstract No.89)

### B. INVITED PRESENTATIONS

“Immunologic control of infection in animal models” in Symposium 125 – Strongyloidiasis: recent clinical and immunologic observations. The 56<sup>th</sup> Annual Meeting of the American Society of Tropical Medicine and Hygiene. Philadelphia, PA. November, 2007.

“Granulocytes in the immune response to a parasitic nematode: Recruitment, killing and antigen presentation”. Joint Faculty Seminar Series. Thomas Jefferson University. January 2008.

“Granulocytes in the immune response to a parasitic nematode: Recruitment, killing and antigen presentation”. University of Texas Medical Branch. Galveston, Texas. June 2008

## TEACHING

Immunity, Infection and Disease (*MICR-200*) - Course Director and 10 lecture hours

Microbiology (*MI -600*) - 4 lecture hours

Research Elective in Microbiology (*MICR-403*) - Course Director

Infection and Immunity (*IMP 530*) 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

**GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

NIH R21, (Abraham, CoPI), Genetic modifiers of innate immunity to *S. stercoralis* infection in mice, \$225,000  
DC/current year, 10% effort

**ACTIVE GRANT AWARDS**

Centers for Disease Control and Prevention, Contract, (Abraham, PI) Development of a multiplex assay for screening patients with eosinophilia- testing candidate antigens for *Strongyloides*. \$20,000

National Institutes of Health, Contract, (Abraham, PI) Identification and testing of antigens for use in a recombinant vaccine against the nematode *Strongyloides stercoralis*. \$10,000

Thomas Jefferson University, Reapplication Enhancement Award. Neutrophil dependant immunity to *Strongyloides stercoralis*. \$35,000

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**KISHORE R. ALUGUPALLI, PH. D.**  
**ASSISTANT PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

The primary focus of my laboratory is 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 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 concurrently 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. We are also interested in understanding the mechanisms involved in humoral responses to polysaccharide antigens in children. Specific mechanisms we focus upon include the role of Toll-like receptor signaling pathway and other cytokine pathways involved in B lymphopoiesis.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

O'Brien K., Fitzgerald D. C., Naiken K., Alugupalli K. R., Rostami A. M., Gran B. 2008. Role of the innate immune system in autoimmune inflammatory demyelination. *Curr Med Chem.* 15:1105-1115.

Colombo M. J. & Alugupalli K. R. 2008. Complement Factor H-Binding protein, a putative virulence determinant of *Borrelia hermsii*, is an antigenic target for protective B1b lymphocytes. *Journal of Immunology.* 180:4858-4864.

Alugupalli K. R. 2008. A distinct role for B1b lymphocytes in T cell-independent immunity. *Current Topics in Microbiology and Immunology.* 319:105-130.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

**INVITED SEMINAR SPEAKER:**

"International Conference of Immunology, Rio de Janeiro, Brazil, August 2007".

"1st annual retreat of Jefferson Vaccine center, March 27, 2008"

"Federation of American Society for Experimental Biology- Summer Conference, Biology of the Immune System, Carefree, Arizona, June 8 - 13, 2008."

"International Workshop on B cells, Oxford, United Kingdom, June 28 - 30, 2008."

**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)

*IMP 505* Immunology and Microbial Pathogenesis – 2 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 Ph.D. student, Stephen Rosenberg, Josephine Fox, James Testa, Elizabeth Faul of Jefferson College of Graduate Studies.

Member, Faculty Search Committee of the Department of Microbiology & Immunology, Jefferson Medical College

## AWARDS/HONORS

2008, January, Ad hoc Reviewer, Medical Research Council, United Kingdom

## EDITORIAL RESPONSIBILITIES

Reviewer, Infection and Immunity

Reviewer, Journal of Immunology

Reviewer, Molecular Immunology

Reviewer, BMC Microbiology

## MEMBERSHIPS

American Society for Microbiology

American Association of Immunologists

American Association for the Advancement of Science

## COLLABORATIONS

Dr. John Kearney – University of Alabama at Birmingham, Birmingham, AL.

Dr. Egil Lien – University of Massachusetts Medical School, Worcester, MA.

Dr. Bernhard Dietzschold, Thomas Jefferson University, Philadelphia, PA

## GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)

1. Howard Hughes Medical Institute Early Career Scientist Award (Kishore Alugupalli, PI)

Project Period: 05/2009-05/2015

Project title: The development of antigen specific protective B1b lymphocyte responses

Project budget: Direct costs \$1,500,000

2. R01 NIAID (Bernhard Dietzschold, PI, 20% effort; Kishore Alugupalli, Co-PI, 20% effort)

Project period: 04/01/09 - 03/31/14

Project title: Intervention of rabies through pattern recognition receptor (PRR) signaling

Project budget: Direct costs \$250,000/year

**ACTIVE GRANT AWARDS**

NIH RO1-AI065750-01 (Kishore Alugupalli, PI, 40% effort)

Project period: 07/15/06 – 06/30/10

Project title: B1b lymphocytes generate T cell-independent IgM memory

Project budget: Total costs \$1,385,678; Direct costs \$900,000

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**ARTHUR M. BUCHBERG, PH.D.**  
**ASSOCIATE PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

My laboratory is focused on studying the molecular genetics of tumor susceptibility and tumor development. Our main goals are to use the mouse as a model to identify genes associated with tumor susceptibility (modifier loci) and tumor initiation and progression (oncogenes and tumor suppressor genes). One project utilizes the *Apc<sup>Min</sup>* mouse model of colon cancer. Crossing the *Apc<sup>Min</sup>* mouse line with different strains of mice reveals the presence of modifier loci that affect tumor multiplicity, size, location and progression. In collaboration with Dr. Linda Siracusa, we have successfully identified the underlying genetic loci responsible for *Mom1* and *Mom2* and are currently studying the genetic and biochemical pathways affected by these loci. Recently, we have initiated a cross to study the effects of *Cav1* dosage on intestinal tumorigenesis, in collaboration with Dr. Michael Lisanti. The results of this cross have identified two new potent modifier loci, *Mom8* and *Mom9* which increases polyp multiplicity throughout the intestinal tract. A recently initiated project in the laboratory is to utilize the Sleeping Beauty transposon system in sensitized screens to uncover genes involved in mammary, pancreatic and intestinal tumorigenesis. Sleeping beauty is a salmonid-derived transposon adapted for use in mammalian systems. These transposons can be engineered to become activated at specific times and in specific tissues. We have constructed several mouse strains harboring the SB system along with initiating oncogenic events. The activation of SB in a tissue specific fashion will potentiate the development and progression of cancer in these mice. The responsible loci can then be identified through genomic techniques. Finally, we have recently initiated a project with Dr. David Abraham that combines our strengths. Dr. Abraham has developed a potent mouse model to study the immune response to *Strongyloides stercoralis* infection. His earlier work revealed that there exists differences between inbred strains in the innate immune response to *S. stercoralis* infection. We have begun to perform a genetic analysis to identify the genes responsible for the differences in the innate immune response between C57BL/6J and C3H mice.

**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, and 2 lecture hours

*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**

American Cancer Society Development, Differentiation and Cancer Study Section Member  
May 2008 Ad hoc Reviewer Cancer Research UK Programme Grant

### **EDITORIAL RESPONSIBILITIES**

Mammalian Genome Associate Editor  
Cancer Research  
Blood  
Molecular Carcinogenesis  
Genome Research  
American Journal of Physiology – Endocrinology and Metabolism

### **MEMBERSHIPS**

International Mammalian Genome Society  
American Association for Cancer Research

### **COLLABORATIONS**

Dr. Linda Siracusa – Jefferson Medical College  
Dr. David Abraham – Jefferson Medical College  
Dr. Michael Lisanti – Jefferson Medical College  
Dr. Scott Waldman – Jefferson Medical College  
Dr. Bruce Boman – Jefferson Medical College  
Dr. David Largaespada – University of Minnesota

### **GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

NIH RO1 (Buchberg, PI) Impact of the Mom2 locus on intestinal biology and cancer, 25%  
NIH R21 (Buchberg, PI) Sensitized screen to identify cooperating genes involved in pancreatic cancer, 15% effort.  
Susan Komen (Buchberg, PI) Use of Genome Tagging Technologies To Identify Genes Involved in Breast Cancer Initiation and Progression.  
AACR PanCan (Buchberg, PI) Finding Cooperating Oncogenic Loci in Pancreatic Cancer  
NIH RO1 (Buchberg, PI) The Study of Caveolin on Apc-Mediated Tumorigenesis Uncovers a Potent Modifier 20% effort.  
NIH R21 (Buchberg, PI) Sensitized screen to identify cooperating genes involved in pancreatic cancer, 15% effort (second time) PENDING  
NIH R21 (Buchberg, PI) Genetic modifiers of innate immunity to *S. stercoralis* infection in mice, 15% effort. PENDING  
NIH RO1 (Siracusa, PI) Genetic Pathways Controlling Intestinal Biology and Tumorigenesis, 15% effort PENDING.

**ACTIVE GRANT AWARDS**

NIH RO1 CA89560 (Siracusa, PI), Molecular Genetics of Cancer Susceptibility, \$210,000 2/03- 1/09 (no cost extension). 10% effort,

NIH T32 CA09678 (Buchberg) Training Program in Molecular Genetics of Cancer, \$339,000 7/04 – 5/09, 5 % effort.

NIH 5 P30 CA 56036-07 (Pestell, PI), Translational Research in Cancer Institutional Cancer Core Grant, \$224,000 6/95-11/13, Laboratory Animal Facility Director, 5% effort

NIH RO1 AI055842 (Buchberg/Perussia) Activation of Innate Immunity Effector Cells, \$238,000 7/03 – 12/09 (no cost) 5% effort

NIH RO1 CA120243 (Siracusa, PI), Susceptibility genes and colorectal cancer, \$190,000, 7/07 – 6/12, 15% effort

PRA Pilot Research Award (Buchberg) Identification of genetic modifiers underlying resistance to *Strongyloides stercoralis* infection. \$20,000, 4/08 – 3/09.

**JEROME G. BUESCHER, PH.D.**  
**ASSISTANT PROFESSOR**

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**TEACHING**

*MI 500* Immunity, Infection and Disease – 20 lecture hours, 48 laboratory hours

*MI 521* Introduction to Immunology – 24 lecture hours

*MI 582* Diagnostic Microbiology – 12 lecture hours, 24 laboratory hours

*GC 550* Foundations in Biomedical Science – 2 lecture hours

*MI 590* Introduction to Clinical Virology – 24 lecture hours

*MI 682* Advanced Diagnostic Microbiology – 6 lecture hours

*MI 540* Microbiology of Antimicrobials – 30 lecture hours

*MI 600* Microbiology – 2 lecture hours

*IM 505* Fundamentals of Immunology – 7.5 lecture hours

**COMMITTEES**

Web Advisory Committee, Thomas Jefferson University

Student Affairs Committee, Jefferson Medical College

**MEMBERSHIPS**

American Society for Microbiology

Eastern Pennsylvania Branch, American Society for Microbiology

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**CATHERINE CALKINS, PH.D.**  
**PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

My research program is focused on investigating the normal mechanisms of regulating immune responses to chronic exposure to antigen, both self antigens and persisting viral antigens in chronic viral infections. The viral antigens we are studying are the antigens of the hepatitis B virus (HBV), particularly the role of immune regulating mechanisms in the development of chronic liver disease from hepatitis B virus infection. This is being approached using a transgenic mouse model, developed by Dr. Mark Feitelson (formerly in the Dept. of Pathology, TJU, currently in the Dept. of Biology, Temple University) in which SCID mice transfected with HBV and exhibiting circulating HBV are given adoptive transfer of syngeneic, immunocompetent lymphoid populations in order to determine the control of the functioning of the responding immune cells in an environment with HBV antigens persistently present, especially in the liver. 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 seeking to identify the responses associated with chronic liver disease in order to gain understanding of the mechanisms preventing progression to a chronic disease state. The effects of ethanol, known to be associated with chronic HBV infection in humans, are also being considered in this model.

The self antigen we are studying is mouse erythrocytes (MRBC) in normal BALB/c mice and in NZB mice that spontaneously develop anti-MRBC responses by 6-9 months of age. Similar immune control issues pertain to responses to chronically present self antigens such as RBC as to persistent viral antigens. 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 can be suppressed by CD8 positive regulatory T cells. Studying the response to MRBC is complicated by the complex and particulate nature of the MRBC antigen. In collaboration with Dr. Srinivasan (Department of Microbiology) and Dr. Shozo Izui (Medical University of Switzerland, Geneva), we are currently seeking to identify the specific target epitope on MRBC that is recognized by NZB autoantibodies by using phage display technology. 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.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

“Learning about Immune Regulation in the NZB Mouse Model of Autoantibody Mediated Disease”,  
Rheumatology Grand Rounds, Thomas Jefferson University, Philadelphia, Pennsylvania. April, 2008.

**TEACHING**

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

*IMP 505* Fundamentals of Immunology – 6 lecture hours

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

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

## INDIVIDUAL FACULTY ACCOMPLISHMENTS

### Ph.D. Immunology and Microbial Pathogenesis Program

Directed Lab Rotation for 1 Ph.D student

Preliminary Examination Committee for 4 Ph.D. students

Final Ph.D. Thesis Committee for 1 student

Student Research Committees for 4 students

### M.S. in Microbiology Program:

Clerkship

Final M.S. Thesis Committee for 1 student

## COMMITTEES

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

Jefferson Medical College, Nominating Committee

KCC Animal Oversight Committee

Wistar Institute Biosafety Committee

## EDITORIAL RESPONSIBILITIES

Journal of Immunology, ad hoc reviewer

Immunology, ad hoc reviewer

## MEMBERSHIPS

American Association of Immunologists

Sigma Xi

## COLLABORATIONS

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

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

Dr. Shozo Izui - Medical University of Switzerland, Geneva

## ACTIVE GRANT AWARDS

NIH RO3 AI064636-01 (Calkins, P.I.), New Assay for MRBC-Specific Autoantibody Responses, 9/07 – 8/09, \$50,000 DC/year, 5% effort

NIH RO1 AA013697 (Calkins, P.I. on subcontract from Feitelson, MA at Temple), HBV-Ethanol Interactions in Liver Disease, 7/03 - 6/08, \$55,420 (direct + indirect/current year), 20% effort

TJU REA (Calkins, P.I.), Immunoregulation in the Pathogenesis of Chronic HBV, 5/08 – 4/09, \$35,000 DC/current year

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**BERNHARD DIETZSCHOLD, D.V.M.**  
**PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

The research conducted in my laboratory focuses primarily on the role of innate immunity in the defense against rabies and B. Development of a safer live rabies vaccine. Our published data suggested that the outcome of a RV infection depends on the magnitude of induction of the NF $\kappa$ B signaling pathways. To investigate whether a potential interaction of RV with pattern recognition receptors could be responsible for the activation of the NF $\kappa$ B signaling pathway, we compared clinical signs and mortality rates following an intramuscular RV infection in mutant mice with those of their normal counterparts. For infection, we used the chimeric SN-BG variant in which the G of the non-neuroinvasive SPBN was replaced by the G of the highly neuroinvasive SB strain. The SN-BG variant is completely non-pathogenic for Balb/c and C57BL6 mice after inoculation by the i.m. route. To examine the role of type I IFNs on the outcome of a peripheral RV infection, IFN- $\alpha/\beta$  R<sup>-/-</sup> mice Balb/c and normal Balb/c mice were infected i.m. with SN-BG (10 mice per group). While 100% of the IFN- $\alpha/\beta$  R<sup>-/-</sup> mice infected SN-BG succumbed to the infection, all their normal counterparts survived and showed no clinical signs of rabies, indicating that type I IFNs play a decisive role in the outcome of this infection. Of note, IFN- $\alpha/\beta$  R<sup>-/-</sup> mice infected with SN-BG produced significantly higher virus-neutralizing antibody (VNA) titer than the normal mice, indicating VNA alone are not able to interfere with an established RV infection. To investigate whether in addition to type I interferons other factors might play a pivotal role in the immune defense against rabies, C57BL6 mice and mutant mice of C57BL6 background deficient in MyD88 were infected i.m. with SN-BG. All of the MyD88<sup>-/-</sup> mice, but none of the wildtype C57BL6 mice, developed a rabies encephalomyelitis and succumbed to the infection. Viral glycoproteins are known to activate TLR2 and TLR4 and the role of these TLR members was revealed in a variety of viral infection systems. Since we hypothesized that the expression of RV G protein directly correlates with the induction protective immune responses, we examined the outcome of an i.m. infection with SN-BG in mice deficient in TLR2 x TLR4, or TLR2 x TLR9. None of the double knockout mice and the wildtype C57BL6 mice developed any clinical signs and all the animals survived the infection. The lack of a role for TLR2 and TLR4 in RV infection *in vivo* was confirmed by *in vitro* experiments employing an NF $\kappa$ B-inducible-luciferase reporter system (expressed in HEK 293 cells) expressing either TLR2 or TLR4. RV G protein was unable to activate TLR2 or TLR4 *in vitro*. The high mortality rate observed in MyD88<sup>-/-</sup> mice points to a role of TLR signaling in the defense against an RV infection. The exclusion of a role for TLR2, TLR4, TLR9 and TLR3 (which signals using Trif but not MyD88) implies a potential role for TLR7 and TLR8 in RV SN-BG induced immune responses. In addition, because MyD88 is also an adaptor molecule for the IL-1 and IL-18 receptor-mediated signaling, it is possible, that the lack of protection seen in MyD88<sup>-/-</sup> mice is due to a defect in IL-1 or IL-18 responses. Of note, infection of MyD88<sup>-/-</sup> mice resulted in a strong induction of IFN- $\alpha$  RNA expression in the brain and in the production of rabies VNA titers similar to those seen in normal C57BL6 mice.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

- Faber, M., Faber, M.-L., Li, J., Preuss, M. A., M. J. Schnell, M. J., Dietzschold, B. Dominance of a non-pathogenic over a pathogenic glycoprotein gene in rabies virus. *J Virol.* 81: 7041–7047, 2007
- Li, J.; McGettigan, J.P.; Faber, M., M.J.; Dietzschold B. Infection of monocytes or immature dendritic cells (DCs) with an attenuated rabies virus results in DC maturation and a strong activation of the NFκB signaling pathway. *Vaccine*, 26, 419-26, 2008.
- Pulmanausahakul<sup>1</sup>, R., Li, J., Schnell, M.J., Dietzschold, B. The glycoprotein and matrix protein of rabies virus affect pathogenicity by regulating viral replication and facilitating cell-to-cell spread. *J. Virol.*, *J Virol* 82, 2330-8, 2008.
- Dietzschold, B., Li, J., Faber, M., and Matthias Schnell, M.J. Concepts in the pathogenesis of rabies. *Future Medicine*. In press. 2008.
- Faber, M., Dietzschold, B., Li, J. Immunogenicity and safety of recombinant rabies viruses used for oral vaccination of stray dogs and wildlife. *Zoonoses and Public Health*. In press, 2008.
- Cenna, J., Tan G.S., Papaneri, A.B., Dietzschold, B., Schnell, M.J., and McGettigan, J.P. "Immune Modulating Effect by a Phosphoprotein-deleted Rabies Virus Vaccine Vector Expressing Two Copies of the Rabies Virus Glycoprotein Gene". *Vaccine*, Accepted, 2008.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

- “Activation of dendritic cell maturation after infection with rabies virus: implications for the development of antiviral immunity”. Rabies in the Americas Conference, Guanajuato, Mexico, October 1-4, 2007
- “Safety and stability of a recombinant canine adenovirus expressing the rabies virus G Protein”, National rabies management program strategic planning session, Mobile, AL, March 31-April 3, 2008.
- “Evolving concepts of rabies pathogenesis”, Graduate Seminar, University of Georgia, Athens GA, March 24, 2008
- “Strategies for the development of attenuated live rabies vaccines” TJU Vaccine Center Presentation, May, 2008
- “Structural basis of the potency of inactivated rabies vaccines”, Conference of the Animal Health Institute, Ames, IA, July 14 -16, 2008.

**TEACHING**

Micro 625 Borna virus – 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 fuer Biochemie und Molekularbiologie

### **COLLABORATIONS**

Dr. Matthias J. Schnell , Department of Microbiology and Immunology, Thomas Jefferson University.  
Dr. Kishore Alugupalli, Department of Microbiology and Immunology, Thomas Jefferson University  
Dr. Jianke Zhang, 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.

### **GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

NIH R01, (Dietzschold, PI), Intervention of rabies through pattern recognition receptor (PRR) signaling, \$250,000 first year, 25% effort.

NIH R21 (M. Faber, PI), Development of a recombinant Nipah virus vaccine for wildlife, \$125,000, 5% effort

### **ACTIVE GRANT AWARDS**

NIH R01 AI 060686-03 (Dietzschold, PI), Generation of Novel Recombinant Rabies Virus Vaccines, 03/01/05-02/28/10, \$165,932, 25% effort

USDA Agreement # 07-7100-4126-CA, (Dietzschold, PI) Development of a Canine Adenovirus-Based Rabies Vaccine, 10/01/07-09/30/08, \$38,000, 1% effort.

USDA , SBIR, Agreement # 2007-33610-18486 (Dietzschold ,PI), Safety and testing of a novel recombinant CAV2-rabies vaccine for oral immunization of wildlife,09/01/07-08/31/09, \$172,358, 5% effort.

NIH R01 NIH AI 049153-06 (Schnell, PI), Rabies-Virus-based Vectors as an HIV-1 Vaccine, 03/15/01-02/28/09, \$554,380, 5% effort.

NIH R41 AI 063822-01A2 (Schnell, PI) A novel rhabdovirus-based anthrax vaccine, A novel rhabdovirus-based anthrax vaccine, 04/15/06-03/31/09, \$157,512, 10 % effort.

NIH RO1 AI38965 (Manser, PI), Negative Selection Of Autoreactive Antibodies, 5/96-4/11, \$225,000 DC/current year, 25% effort

NIH R01 AI46806A1 (Manser, PI), Regulation Of The Persistent Antibody Response By Fc Receptors, 5/99-1/10, \$225,000 DC/current year, 25% effort.

NIH 5 P30 CA 56036-07 (Pestell, PI), Translational Research in Cancer Institutional Cancer Core Grant, 6/95-5/06 \$17,859 (Program) Immunology Program (Program Leader) No Research Support – Salary Only, 7% effort.

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

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

Currently laboratory activities are focused in three areas: 1) Processing and presentation for class I-restricted T cell recognition. This year we made significant process in understanding how antigens are targeted to the class I-restricted processing pathway. Focus has been on the roles of ubiquitylation, exposed hydrophobic domains, ribosome-associated chaperonins, and capped/uncapped proteasome subunits. Two manuscripts will be submitted shortly. In the near future we will probe the processing of endoplasmic reticulum-targeted antigens. 2) Processing and loading compartments involved in presentation of MHC class II-restricted antigenic peptides. Focus here has been on dissecting a proteasome/TAP-dependent processing pathway that we previously described, determining the significance of this “endogenous” pathway plays in protection, and on studying class II-restricted cross-presentation. Key reagents for all three of these projects have been generated and we anticipate a very productive next 12 months. One manuscript on cross-presentation is in preparation. 3) Cancer and autoimmunity. Here there are three separate projects. A) We have generated an inducible transgenic mouse that we are using to better understand the kinetics of and mechanistic basis for tolerance that develops to a surrogate tumor antigen expressed at different times following conception (prenatal, neonatal, adult). The first manuscript from this work will be submitted shortly. Design and generation of second generation transgenic mice are underway. B) In continued collaboration with Dr. Jay Rothstein (Amgen, Seattle, WA), we are probing the mechanistic link between thyroid cancer and autoimmunity. Our focus is on recognition T cells of phosphopeptides uniquely associated with thyroid cancer. C) In collaboration with Dr. Takami Sato (TJU), we are working toward understanding the therapeutic basis of treating melanoma patients with their own haptenated tumor cells. We are currently establishing proof of principle in a mouse model.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

Plesa, G., A.E. Snook, S.A. Waldman, and L.C. Eisenlohr, 2008. Derivation and Fluidity of Acutely Induced Dysfunctional CD8<sup>+</sup> T Cells. *J. Immunol.* 180:5300-5308.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

“The Immunological Mechanisms in Cancer Program at the Kimmel Cancer Center”, Kimmel Cancer Center International Grand Rounds, Philadelphia, PA, October 2007

“How B cells Learn to be Ignorant”, Temple University School of Medicine, Department of Microbiology and Immunology, April 2008

“Using Influenza Glycoproteins to Dissect MHC Class II-Restricted Antigen Processing Pathways”, Staff Seminar at Thomas Jefferson University, Philadelphia, PA, 10 September 2007.

“The Origin of Acutely Presented MHC Class I-Restricted Peptides”, Antigen Presentation 2007 (Our International Meeting), Invited Speaker, Dunk Island, Australia, 9 October 2007

“Using Influenza Glycoproteins to Dissect MHC Class II-Restricted Antigen Processing Pathways”, Speaker at the Walter Gerhard Retirement Symposium, The Wistar Institute, Philadelphia, PA, 30 November 2007.

“The Many Paths to MHC Class II-Restricted Presentation of the Influenza Glycoproteins”, Invited Plenary Speaker at the Keystone Meeting on Viral Immunity, Keystone, CO, 24 January 2008.

“Unconventional Antigen Processing Pathways”, at Amgen Corp., Seattle, WA, 15 February 2008.

## INDIVIDUAL FACULTY ACCOMPLISHMENTS

“Studies in antigen processing with an eye to enhanced vaccine design”, Thomas Jefferson University, Jefferson Vaccine Center Annual Retreat, Philadelphia, PA, 28 March 2008

“Selection of substrates for MHC class I-restricted antigen processing” (Workshop Session, co-chair of session), San Diego, CA, Annual Meeting of the AAI, 9 April 2008

“Probing the antigen processing machinery with influenza glycoproteins”, Tulane University, New Orleans, LA, 14 April 2008

“Origins of MHC bound peptides”, Penn State Medical Center, Hershey, PA, 1 May 2008.

“The dynamics of tolerance to a neoantigen”, 2<sup>nd</sup> Annual Bice Perussia Immunobiology Symposium, Thomas Jefferson University, Philadelphia, PA, 2 May 2008.

### TEACHING

*Program Director*, Immunology and Microbial Pathogenesis

*Program Co-Director*, Md/Ph.D. Program

*MI 200* (Medical College), Basic Medical Microbiology – 4 lecture hours

*IMP 505* Fundamentals of Immunology –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 - 6 graduate students

### COMMITTEES

Search Committee, Chair of the Department of Pathology, Jefferson Medical College

Confocal/Bioimaging Committee, KCC

Graduate Council of TJU CGS

University Appointments and Promotions Committee

University Tenure Committee

University Research Advisory Committee

Microbiology and Immunology Department Appointments and Promotions Committee

University Web Advisory Committee

Search Committee, Department of Microbiology and Immunology

12 Thesis Committees

MD/Ph.D. Steering Committee

MD/Ph.D. Admissions Committee

### **AWARDS/HONORS**

- 2007, July, Reviewer for NIH/NIAID contracted facility (phone review)
- 2007, August, Reviewer of a grant application to US Army Medical Research and Materiel Command (USAMRMC) (mail in)
- 2007, October, Invited Speaker at the Antigen Presentation 2007 (Our International Meeting), Dunk Island, Australia, 9 October 2007
- 2007, October, Special Emphasis Panel/Scientific Review Group 2008/01 ZAI1 TP-M (J2), Cooperative Research Partnerships for Biodefense, Bethesda, MD
- 2007, November, Special Emphasis Panel/Scientific Review Group 2008/01 ZAI1 MP-I (J1), Systems Approach to Immunity and Inflammation, Bethesda, MD
- 2008 January, Invited Plenary Speaker at the Keystone Meeting on Viral Immunity, Keystone, CO, 24 January 2008

### **EDITORIAL RESPONSIBILITIES**

Faculty of 1000 Member, Antigen Processing and Recognition Section

### **MEMBERSHIPS**

American Association of Immunologists  
American Association for the Advancement of Science

### **COLLABORATIONS**

Dr. Scott Waldman – Jefferson Medical College  
Dr. Matthias Schnell – Jefferson Medical College  
Dr. Takami Sato – Jefferson Medical College  
Dr. Phyllis Flomenberg – Jefferson Medical College  
Dr. Jay Rothstein – Amgen, Seattle, WA  
Dr. Michael Howard – University of Utah, Salt Lake City, Utah  
Dr. Luis Sigal – Fox Chase Cancer Center, Philadelphia, Pennsylvania  
Dr. Christopher Norbury, Pennsylvania State University, Hershey Medical Center, Hershey, PA

### **GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

NIH 5R01 AI49153-7 (Schnell, PI) Rabies virus-based vectors as an HIV-1 vaccine 03/01/08-02/28/09 \$571,398 DC/ first year, 5% effort.

NIH R21 (Eisenlohr, PI), Probing the thyroid oncogene RP3 and its substrates for tumor specific antigenicity, \$125,000 DC/ first year., 10% effort

NIH U19 (Sigal, PI; Eisenlohr, Project leader), Immune Mechanisms of Virus Control (Project 3. Processing and presentation of Ectromelia virus to CD4+ T lymphocytes - Sub-award from Fox Chase Cancer Center) \$332,656 DC/ first year, 15% effort

**ACTIVE GRANT AWARDS**

NIH 5 R01 AI 036331-13 (Eisenlohr, PI), Class II Processing Routes Delineated by Flu Glycoproteins, 04/01/95-04/30/09, \$162,779 DC/ current year, 21% effort.

NIH 5 R25 CA 069277-10 (Waldman, PI), Short-term Training Program in Translational Cancer Research, 8/01/97-03/31/08, \$81,649 DC current year, 5% effort

NIH R01 AI 049153-06 (Schnell, PI), Rabies Virus Based Vectors as an HIV Vaccine, 03/15/01-02/28/09, \$552,204 DC/ current year, 5% effort.

NIH 5 R21 AI 063065-02 (Eisenlohr, PI), The role of the RET Receptor in Autoimmune Disease, 04/01/06-03/31/09, (no cost extension), 3% effort

NIH 5 R01 AI 069192-02 (Eisenlohr, PI), The basis for MHC Class II-restricted proteasome-dependent epitopes, 01/08/07-12/31/10, \$160,000 DC/ current year, 16% effort.

NIH 5 T32 CA 009683-15 (Eisenlohr PI), Training Program in Cancer Immunology, 02/05/93-07/31/08, \$231,342 DC current year , 5% effort.

NIH 1 R21 AI 077053-02 (Eisenlohr, PI), Dissecting 3 processing pathways that generate class II-restricted flu epitopes, 09/01/07-08/31/09, \$122,625 DC/ current year, 8% effort

NIH

NIH 2 R01 AI 039501-10A2 (Eisenlohr, PI), Accessing the MHC Class I Antigen Processing Pathway, 01/01/08-12/31/11, \$175,000 DC/ current year, 16% effort

NIH 1 R21 AI079526-01 (Eisenlohr, PI), Non-proteasomal protease(s) that define C-termini of MHC class I epitopes, 06/20/08-05/31/10, \$150,000 DC/ current year, 10% effort

NIH 1 R21 CA135602-01 (Eisenlohr), Dynamics of tolerance induction to tumor associated antigens , 07/01/08-06/30/10, \$135,000 DC current year, 10% effort.

NIH 5 R01 AI 069192-02 (Eisenlohr, PI), NIH The basis for MHC class II-restricted proteasome-dependent epitopes - Equipment Supplement, 01/01/09-12/31/09. \$25,476 DC/current year.

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

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR THE COMING YEAR**

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  $3 \times 10^7$  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**

“Transgenic Animals, Animal Health and Food Safety”, International Embryo Transfer Society, Denver, Colorado, January 2008.

“Cryopreservation of Mouse Sperm”, Advances in Transgenic Animal Research Meeting, MD Anderson Cancer Center, Houston, Texas, January 2008.

**TEACHING**

*GE 550* Foundations in Biomedical Sciences – 2 lecture hours

*GE 612* Molecular Genetics II Course organizer – 12 lecture hours

*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

**COMMITTEES**

Thomas Jefferson University Institutional Animal Care and Use Committee--Chair

KCC Animal Facility Oversight Committee

KCC Transgenic/Knockout Oversight Committee

Thesis Committee Chair for Amy Baran, Stephanie Nnadi and Richard Crist

**MEMBERSHIPS**

International Society for Transgenic Technologies (Secretary)

Society for Cryobiology

**COLLABORATIONS**

Dr. Xugang Xia, Thomas Jefferson University

Dr. Linda Siracusa, Thomas Jefferson University

Dr. Arthur Buchberg, Thomas Jefferson University

Dr. Scott Waldman, Thomas Jefferson University

Dr. Bruce Boman, Christiana Health

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

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

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 micro environmental locales (particularly the germinal center (GC) in which these changes take place. We are particularly interested in the fate of B cells with autoreactive antigen receptors (either pre-existing or acquired via V region hypermutation) during memory B cells development. Additional projects concern the role of Fc receptors, the BAFF (BlyS) pathway, Toll-like receptors (TLRs) and Fas and c-FLIP in the regulation of the B cell response. In the past, we have largely restricted our studies to immune responses to haptens in mouse models. Going forward, we would like to apply the lessons learned from these to a better understanding of the factors that regulate antibody responses to neoplasia and infection in humans. As such, we are currently developing the technology necessary to generate mice that are "hematopoietically humanized".

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

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, T., Z.S.M.Rahman and T. Manser "Quantitatively reduced participation of anti-nuclear antigen B cells that down regulate BCR during primary development of the germinal center/memory B cell response to foreign antigen" (2007) *J. Immunol.*, 178: 56623-5634.

Rahman, Z.S.M., H. Niu, D. Perry, E. Wakeland, T. Manser, and L. Morel "The autoimmune Fcg2b NZW allele fails to up-regulate its expression in germinal center B cells and leads to increased IgG production" (2007) *J. Immunol.* 179: 6663-6672.

Alabyev, B.R., Vuyruru and T. Manser, "Influence of Fas on the regulation of the response to an anti-nuclear antigen B cell clonotype to foreign antigen" (2008) *Int. Immunol.*, in press.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

"The Immunological Mechanisms in Cancer Program at the Kimmel Cancer Center", Kimmel Cancer Center International Grand Rounds, Philadelphia, PA, October 2007

"How B cells Learn to be Ignorant", Temple University School of Medicine, Department of Microbiology and Immunology, April 2008

**TEACHING**

MI 200 Immunity, Infection and Disease – 4 lecture hours

IM 505 Fundamentals of Immunology – 7.5 lecture hours

**COMMITTEES**

Search Committee, Chair of the Department of Pathology, Jefferson Medical College

Executive Council, Jefferson Medical College

### **AWARDS/HONORS**

2007, October, Chair and Ad hoc Reviewer, NIH NIAID ZI11 KS-I (J3) Special Study Section, B cell Immunology for protective HIV-1 Vaccine, Bethesda, MD

2008, January, Ad hoc Reviewer, NIH NIAID ZA11 QV-I M1 1, Special Study Section, B-cell PO1 applications (phone review)

### **EDITORIAL RESPONSIBILITIES**

Editor, BioMedCentral Immunology

### **MEMBERSHIPS**

American Association of Immunologists

American Association for the Advancement of Science

### **COLLABORATIONS**

Dr. Yuri Sykulev – Jefferson Medical College

Dr. Jianke Zhang – Jefferson Medical College

Dr. Takami Sato – Jefferson Medical College

Dr. Jeffrey Ravetch – Rockefeller University, New York

Dr. Lawrence Wysocki – National Jewish Center, Denver

### **GRANT SUPPORT**

#### **ACTIVE FUNDED GRANT AWARDS**

NIH RO1 AI38965 (Manser, PI), Negative Selection Of Autoreactive Antibodies, 5/96-4/11, \$225,000 DC/current year, 25% effort

NIH R01 AI46806A1 (Manser, PI), Regulation Of The Persistent Antibody Response By Fc Receptors, 5/99-1/10, \$225,000 DC/current year, 25% effort.

NIH 5 P30 CA 56036-07 (Pestell, PI), Translational Research in Cancer Institutional Cancer Core Grant, 6/95-5/06 \$17,859 (Program) Immunology Program (Program Leader) No Research Support – Salary Only, 7% effort.

#### **GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008**

NIH R21, (Manser, PI), The Role of TLRs in B Cell Memory, \$150,000 DC first year, 10% effort.

NIH R49, (Rostami, PI), Autoimmunity Center of Excellence, Pilot Project (Manser), \$100,000 DC first year, 5% effort.

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**JAMES P. MCGETTIGAN, PH.D.**  
**RESEARCH ASSISTANT PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

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 are 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 innate immunity, particularly the IFN and NF- $\kappa$ B response, 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, 2007 THROUGH JUNE 30, 2008)**

McKenna P.M., Koser M.L., Carlson K.R., Montefiori D.C., Letvin N.L., Papaneri A.B., Pomerantz R.J., Dietzschold B., Silvera P., McGettigan J.P., Schnell M.J. (2007) "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.* 2007 195(7):980-8.

Li, J., McGettigan J.P., Faber, M., Schnell, M.J., and Dietzschold, B. "Infection of monocytes or immature dendritic cells (DCs) with an attenuated rabies virus results in DC maturation and a strong activation of the NF $\kappa$ B signaling pathway". (2008)*Vaccine*, 26(3):419-26.

Cenna, J., Tan G.S., Papaneri, A.B., Dietzschold, B., Schnell, M.J., and McGettigan, J.P. "Immune Modulating Effect by a Phosphoprotein-deleted Rabies Virus Vaccine Vector Expressing Two Copies of the Rabies Virus Glycoprotein Gene". (2008)*Vaccine*, Accepted.

Faul, E.J., Wangalla, C.N., McGettigan, J.P. and Schnell, M.J. "Interferon-beta expressed by a rabies virus-based HIV-1 vaccine vector serves as a molecular adjuvant and decreases pathogenicity". (2008) Virology, Accepted

### **SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

“Second-generation Post-exposure Prophylaxis for Rabies Virus: Implications for Global Health”; Faculty Seminar Series, Thomas Jefferson University, Departments of Microbiology and Immunology, Biochemistry, and Cancer Biology, Philadelphia PA; 2007

“Novel Global Health Vaccines: Second-generation Human Rabies Virus Vectors in Mice and Non-human Primates”; Jefferson Vaccine Center Yearly Retreat, Thomas Jefferson University, Philadelphia PA; 2008

“Enhanced Anti-viral Immunity Induced by a Phosphoprotein-deleted Rabies Virus Vaccine Vector”; American Society of Virology Annual Meeting, Cornell University, Ithaca, New York; 2008

### **TEACHING**

IMP 712 Current Literature in Immunology, Co-director - 13 hours

IMP 722 Current Literature in Immunology, Co-director - 9 hours

IMP 732 Current Literature in Immunology, Co-director - 10 hours

IMP 655 Advanced Topics in Microbial Pathogenesis - 2 hours

IMP 600 Microbiology - 2 hours

### **COMMITTEES**

Institutional Biosafety Committee, Jefferson Medical College

Institutional Animal Care and Use Committee, Jefferson Medical College

### **AWARDS/HONORS**

Recipient of the Thomas Jefferson University Pilot Research Program Award (2008)

### **MEMBERSHIPS**

American Society for Virology

Graduate Faculty (Associate Member), Jefferson Medical College

Jefferson Vaccine Center, Thomas Jefferson University

### **COLLABORATIONS**

Dr. Matthias J. Schnell, Jefferson Medical College, Philadelphia PA

Dr. Bernhard Dietzschold, Jefferson Medical College, Philadelphia PA

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

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

INDIVIDUAL FACULTY ACCOMPLISHMENTS

Dr. Jeffry A. Mattis - Molecular Targeting Technologies, Inc., West Chester, PA

Dr. Adolfo Garcia-Sastre - Mount Sinai School of Medicine, New York, NY

Dr. Douglas Lyles - Wake Forrest University, Winston-Salem, NC

**GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

NIH R01 (McGettigan, PI), Replication-deficient rabies vectors against rabies virus infection, \$225,000 DC first year, 70% effort

NIH R41 (McGettigan, PI), Human Rabies Virus Vaccine Development, \$108,272 DC one year, (20% effort)

NIH P01 (Schnell, PI), Functional Analysis of NSV-based HIV vectors, Core Director (McGettigan), \$134,000 DC first year, (20% effort)

**ACTIVE GRANT AWARDS**

NIH R21 AI070252 (McGettigan, PI), Second Generation Rabies Vaccines, 7/15/06–NCE, \$121,375 DC year two, 65% Effort

Infectious Disease Society of America (IDSA) and the National Foundation for Infectious Diseases (NFID), Wyeth Young Investigator Award in Vaccine Development (McGettigan, PI), Peripheral inflammation and novel rabies vaccines 8/01/07 - 7/31/09, \$30,000 DC, 10% effort

Tulane National Primate Research Center (TNPRC) Pilot Research Program (McGettigan, PI), Immunogenicity of replication-deficient rabies virus vectors in non-human primates, 9/01/07 -NCE

Jefferson Medical College Research Pilot Program (McGettigan, PI), Vaccine-induced Antibody Effector Functions, 6/01/08-5/31/09, \$20,000

NIH R01 AI049153 (Schnell, PI), Rabies Virus –based Vectors as an HIV-1 Vaccine, 03/15/01-02/28/09, 25% Effort

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**W. EDWARD MERCER PH.D.**  
**PROFESSOR**

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**RESEARCH ACCOMPLISHES AND GOALS FOR THE COMING YEAR**

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 refractile to conventional chemo/radiation therapeutic modalities. The goal for the following year will focus on elucidating the effects that deregulation of Wip1 phosphatase has on DNA damage and genomic instability.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

KCC Molecular Biology and Genetics Program, "Role of PPM1D/Wip1 Phosphatase in Human Breast Cancer".

Department of Radiation Oncology, TJUH, "PPM1D: A p53-dependent oncogene encoding Wip1 Phosphatase".

**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

Genetics Program Preliminary Examination Committee

JMC Committee on Student Promotion

KCC Molecular Biology and Genetic Program Committee

Lennox K. Black Symposium Organizing Committee

**AWARDS/HONORS**

KCC Award for Education and Mentoring.

Susan G. Komen for the Cure, Breast Cancer Grants Program, Scientific Reviewer.

**EDITORIAL RESPONSIBILITIES**

Editorial Board, Cell Biology International Reports

**MEMBERSHIPS**

American Association for Cancer Research

American Society for Cell Biology

American Association for Advancement of Science

New York Acad. Science

International Federation for Cell Biology

**COLLABORATIONS**

Juan P. Palazzo, M.D. Department of Pathology, TJUH

Scott Waldman, MD. Ph.D. Department of Experimental Therapeutics and Pharmacology

**ACTIVE GRANT AWARDS**

NIH 2 R01 CA079756-06A2 (Mercer, PI) P53-Mediated G1/M Checkpoint Controls Altered by PPM1D, 01/01/99-02/28/2011, 158,727 DC/current year, 50% effort.

NIH 5 P30 CA 56036-07 (Pestell, PI), Translational Research in Cancer, Institutional Cancer Core Grant, 6/95-Molecular Biology and Genetics Program, P53 and Its Molecular Targets, No Research or Salary Support.

**FABIENNE PAUMET, PH.D.**  
**ASSISTANT PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

Since my arrival at Jefferson in December 2007 I have dedicated my time to the set-up and staffing of my laboratory with two key hires, a technician and a research assistant. Nevertheless, we managed to generate results on the phagocytic project, for which we obtained a pilot award (\$20,000). I also participated in the submission of an equipment grant (PI: Dr. Keen) for a TIRF microscope. I am now in the process of submitting an article and an RO1 NIH grant on the host-pathogen interaction project for the October 2008 deadline.

In the future, my goals are to continue to develop the phagocytic project in order to apply for a second RO1 grant. I also plan on submitting an article on this project by the end of 2009. An MD/Ph.D. graduate student will join my lab this fall. I anticipate this student will take over a project on host-pathogen interaction. Hopefully, this student will generate results suitable for publishing by the end of 2009.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

C. Delevoye, M. Nilges, P. Dehoux, F. Paumet, S. Perrinet, A. Dautry-Varsat, A. Subtil "SNARE protein mimicry by an intracellular bacterium" (2008) PLOS Pathogens 4:e1000022

J. Shen, D. Taresté, F. Paumet, J.E. Rothman, T.J. Melia "Selective activation of cognate SNAREpins by Sec1/Munc18 (SM) proteins" (2007)  
Cell 128: 183-195

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

"Mechanisms of intracellular membrane fusion", Jefferson University, 2nd Annual Bice Perussia Immunobiology Symposium, Philadelphia, Pennsylvania, May, 2008.

"Intracellular membrane fusion: in sickness and in health", Jefferson University, Joint faculty seminar series, Philadelphia, Pennsylvania, February, 2008

**COMMITTEES**

Thomas Jefferson University - Thesis Committee (Joseph Comber)

Thomas Jefferson University- Faculty Search committee for Microbiology and Immunology Department

Thomas Jefferson University- Preliminary Examination Committee (Melissa Downbrough)

**EDITORIAL RESPONSIBILITIES**

Reviewer for Chemical Reviews

**MEMBERSHIPS**

The American Society of Cell Biology (ASCB)

Kimmel Cancer Center, Thomas Jefferson University, Philadelphia

**COLLABORATIONS**

Dr. David Abraham – Jefferson Medical College

**GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008**

Equipment Grant, NIH, (PI: Jim Keen)

“TIRF microscope”

Pilot Research Award, Jefferson University (PI: Fabienne Paumet)

“Molecular Mechanisms of Phagocytosis”

**ACTIVE GRANT AWARDS**

Pilot Research Award (PI: Fabienne Paumet) “Molecular Mechanisms of Phagocytosis” (\$20,000)

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**S. M. ZIAUR RAHMAN, M.D., PH.D.**  
**RESEARCH ASSISTANT PROFESSOR**

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### **RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

My lab focuses on (1) 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 and (2) mapping and identifying the gene(s) that might play critical role in immune-mediated end-organ damage such as kidney (nephritis).

(1) 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 autoantibodies and autoimmune disease SLE.

(2) The development of immune-mediated kidney disease is a major hallmark of SLE. Deposition of autoantibodies in the form of immune complex (IC) in the kidney glomeruli is believed to be responsible for the immune mediated kidney disease. Recent studies in mice, using rabbit sera reactive to mouse kidney glomerular basement membrane (GBM) to induce nephritis, have suggested that some laboratory strains (such as NZW, 129/svJ and C58/J) are more prone to immune-mediated kidney damage compared with C57BL/6 and BALB/c control strains. Currently, the studies are conducted in our lab to determine whether the kidney intrinsic events or the difference in the properties or the number of infiltrating immune cells is critical for a kidney disease as a consequence of immunological insult. Also, the genetic basis of this immune-mediated kidney disease is poorly understood. Through genetic mapping and gene expression profile studies, our goal is to identify the genetic loci and candidate genes that specifically contribute to immune mediated kidney disease. Once the actual genes playing a pivotal role in immune mediated renal disease are identified in mice, we will continue to study these genes in lupus patients with kidney disease and develop therapeutic approaches by targeting these genes.

### **PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

Chun X, Z.S. M. Rahman, S. Xie, J. Zhu, Y. Du, X. Qin, H. Zhou, X.J. Zhou, and C. Mohan "Strain distribution pattern of immune nephritis—a follow-up study" (2008) *Int. Immunol.*, 20: 719-728.

Rahman Z.S.M., H. Niu, D. Perry, E. Wakeland, T. Manser, and L. Morel "Expression of the autoimmune Fcγ2b NZW allele fails to be up-regulated in germinal center B cells and is associated with increased IgG production" (2007) *Genes and Immunity.*, 8: 604-612.

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

“B cell and Tolerance” Rheumatology grand round, Rheumatology Department, Thomas Jefferson University, Philadelphia, April, 2008

“Loss of B cell Tolerance in a Mouse Model of Systemic Lupus Erythematosus/SLE” Drexel Institute for Biotechnology and Virology Research (DIBVR) and Pennsylvania Biotechnology Center, Doylestown, PA. May, 2008

**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

2008 The Virginia Riddle Memorial Fellowship of the Arthritis National Research Foundation (ANRF)

**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

**ACTIVE GRANT AWARDS**

Arthritis National Research Foundation (Rahman, PI), Impact of lupus susceptibility loci on peripheral B cell tolerance, 06/08-05/09, \$75,000 DC/current year, 50% effort

NIH RO3 AR 055701-01A1 (Rahman, PI), Impact of lupus susceptibility loci on peripheral tolerance and onset of disease, 08/08-06/11, \$ 50,000 DC/current year, 50% effort

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**MATTHIAS J. SCHNELL, PH.D.**  
**PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

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, 2007 THROUGH JUNE 30, 2008)**

- Faul, E. J., Celestine, N. W., McGettigan, J. P., and Schnell, M. J. (2008). "Interferon- $\beta$  expressed by a rabies virus-based HIV-1 vaccine vector serves as a molecular adjuvant and decreases pathogenicity". *Virology*, accepted.
- Wirblich, C., Tan, G. S., Papaneri, A., Godlewski, P. J., Orenstein, J. M., Harty, R. N., and Schnell, M. J. (2008). "PPEY motif within the rabies virus (RV) matrix protein is essential for efficient virion release and RV pathogenicity". *J Virol.*, in press
- Cenna, J., Tan, G. S., Papaneri, A. B., Dietzschold, B., Schnell, M. J., and McGettigan, J. P. (2008). "Immune Modulating Effect by a Phosphoprotein-deleted Rabies Virus Vaccine Vector Expressing Two Copies of the Rabies Virus Glycoprotein Gene". *Vaccine*, accepted.
- Weihe, E., Bette, M., Preuss, M. A., Faber, M., Schafer, M. K., Rehnelt, J., Schnell, M. J., and Dietzschold, B. (2008). "Role of virus-induced neuropeptides in the brain in the pathogenesis of rabies". *Dev Biol (Basel)* **131**, 73-81.
- Li, J., McGettigan, J. P., Faber, M., Schnell, M. J., and Dietzschold, B. (2008). "Infection of monocytes or immature dendritic cells (DCs) with an attenuated rabies virus results in DC maturation and a strong activation of the NFkappaB signaling pathway". *Vaccine* **26**(3), 419-26.

- Pulmanausahakul, R., Li, J., Schnell, M. J., and Dietzschold, B. (2008). "The glycoprotein and the matrix protein of rabies virus affect pathogenicity by regulating viral replication and facilitating cell-to-cell spread". *J Virol* **82**(5), 2330-8.
- Snook, A. E., Stafford, B. J., Li, P., Tan, G., Huang, L., Birbe, R., Schulz, S., Schnell, M. J., Thakur, M., Rothstein, J. L., Eisenlohr, L. C., and Waldman, S. A. (2008). "Guanylyl cyclase C-induced immunotherapeutic responses opposing tumor metastases without autoimmunity". *J Natl Cancer Inst* **100**(13), 950-61.
- Faber, M., Faber, M. L., Li, J., Preuss, M. A., Schnell, M. J., and Dietzschold, B. (2007). "Dominance of a nonpathogenic glycoprotein gene over a pathogenic glycoprotein gene in rabies virus". *J Virol* **81**(13), 7041-7.
- McKenna, P. M., Koser, M. L., Carlson, K. R., Montefiori, D. C., Letvin, N. L., Papaneri, A. B., Pomerantz, R. J., Dietzschold, B., Silvera, P., McGettigan, J. P., and Schnell, M. J. (2007). "Highly Attenuated Rabies Virus-Based Vaccine Vectors Expressing Simian-Human Immunodeficiency Virus89.6P Env and Simian Immunodeficiency Virus<sub>mac239</sub> Gag Are Safe in Rhesus Macaques and Protect from an AIDS-Like Disease". *J Infect Dis* **195**(7), 980-8.
- Tan, G. S., Preuss, M. A., Williams, J. C., and Schnell, M. J. (2007). "The dynein light chain 8 binding motif of rabies virus phosphoprotein promotes efficient viral transcription". *Proc Natl Acad Sci U S A*. **104**(17), 7229-34

## SCIENTIFIC PRESENTATIONS

### INVITED PRESENTATIONS

- July 11-12, 2007, Wadsworth Center, New York State Department of Health, Albany, NY. "Dynein Light Chain (LC8) as a factor for efficient viral replication".
- January 24-26, 2008 Hilleman lecture series, Department of Microbiology, Montana State University, Bozeman, MO "Rhabdoviral vectors as a platform for HIV-1 vaccines".
- July 1, 2008, Department of Microbiology, Mount Sinai School of Medicine, NY. "How to design rhabdoviral based HIV-1 Vaccines – Learning by observation".

### PRESENTATIONS

- 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". American Society for Virology, 26<sup>th</sup> 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". American Society for Virology, 26<sup>th</sup> 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

*IMP 685* Advanced Topics in Virology and Neurovirology – Course coordinator and 3 lecture hours

*IMP 655* Advanced Topics in Microbial pathogenesis – Course coordinator and 14 lecture hours

## **COMMITTEES**

Thomas Jefferson University Institutional Biosafety Committee

## **AWARDS/HONORS**

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)

Member of the “Jefferson Vaccine Center” - TJU (2008-present)

## COLLABORATIONS

### INTERNAL

Dr. Bernhard Dietzschold - Jefferson Medical College

Dr. Rene Daniel – Jefferson Medical College

Dr. Laurence Eisenlohr – Jefferson Medical College

Dr. James McGettigan – Jefferson Medical College

Dr. Lance Simpson – Jefferson Medical College

Dr. Yuri Sykulev - Jefferson Medical College

Dr. Scott Waldman - Jefferson Medical College

### EXTERNAL

Dr. Pyone Pyone Aye – Tulane National Primate Research

Dr. Adolfo García-Sastre, Mount Sinai School of Medicine

Dr. Ronald Harty – University of Pennsylvania

Dr. Andrew Lackner – Tulane National Primate Research

Dr. Monique Lafon, Pasteur Institute, Paris

Dr. Douglas S. Lyles, Wake Forest University School of Medicine

Dr. Jeffery Mattis – MTT Inc.

Dr. Johnny Peterson – University of Texas, Medical Branch

Dr. Christophe Prehaut, Pasteur Institute, Paris

Robert Rudd - Wadsworth Center, New York State Department of Health, Albany, NY

Dr. Peter Strick– University of Pittsburgh

### GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)

NIH R21 (Schnell, PI), Bat rabies virus in its natural host (score 1.38), \$125,000 DC first year, effort 1.2 calendar

NIH RR 018604-03 (Strick, Univ. of Pittsburgh, Schnell – Core Director Rabies), National Center for Experimental Neuroanatomy with Neurotropic Viruses, \$65,578 DC first year, effort 1.2 calendar

NIH U01 AI082289-01 (Schnell, PI), Botulinum neurotoxin HC50 presented by a viral particle \$320,360 DC first year, effort 3.0 calendar

NIH P01 AI082325-01 (Schnell, PI) Functional analysis of NSV-based HIV vectors, \$1,362,108 DC first year, effort 3.0 calendar

NIH R01 AI 079211 (McGettigan, PI) Replication-Deficient Rabies Vectors against Rabies Infection \$193,1461 DC first year, effort 0.6 calendar

**ACTIVE GRANT AWARDS**

- NIH, R01 AI049153-06 (Schnell, PI), Rabies Virus-Based Vectors as an HIV-1 Vaccine, 03/15/01-02/28/09, \$554,380 DC, current effort, 2.4 calendar
- NIH R01 MH 074375-03 (Schnell, PI), Astrocytes and Restricted HIV-1 Replication, 09/15/05-08/31/08, \$225,193 DC, current effort, 1.8 calendar
- NIH 5R41AI073064-02 (Schnell, PI), A novel vaccine: botulinum neurotoxin subunit on a viral carrier, 04/15/06-03/31/08, \$ 103,206.00 DC, current effort, 1.2 calendar
- NIH R41 AI 063822-02 (Schnell, PI via Molecular Targeting Technologies), A novel rhabdovirus-based anthrax vaccine, 157,512\$157,512 DC, current, effort 0.48 calendar
- Crucell Holland (Schnell, PI), Alanine Scanning of the Rabies Virus (RV) Glycoprotein (G) Binding Site for CR4098, 09/24/07-06/24/09 \$166,695 DC, current effort 0.6 calendar  
Using Recombinant Rabies Viruses
- NIH RR 018604-03 (Strick, Univ. of Pittsburgh, Schnell – Core Director Rabies), National Center for Experimental Neuroanatomy with Neurotropic Viruses, 06/01/04-05/31/09, \$68,952 DC, 1.2 calendar
- NIH R01 AI 060686-03 (Dietzschold, PI), Generation of Novel Recombinant Rabies Virus Vaccines, 03/01/05-2/28/10, \$165,932 DC, current effort 1.2 calendar
- NIH R01 AI 069192-02 (Eisenlohr, PI ) The basis for MHC Class II restricted proteasome-dependent epitopes, 01/08/07-12/31/10, \$160,000 DC, current effort, 0.6 calendar

**LINDA D. SIRACUSA, PH.D.**  
**PROFESSOR**

**RESEARCH ACCOMPLISHMENTS AND GOALS FOR THE COMING YEAR**

My laboratory uses a combination of classical genetics and molecular biology to study genes that influence the biology of the gastrointestinal tract and the development of cancer. Mutations in the human the tumor suppressor Adenomatous Polyposis Coli (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 intestinal adenomas. Complex trait analyses have identified modifier loci which impact the phenotype of *Apc* mutations. We were the first to report that the secretory type II Phospholipase A2 (*Pla2g2a*) gene is a strong candidate for the Modifier of Min 1 (*Mom1*) locus. Transgenic mice and gene expression profiling are being used to establish the mechanism by which *Pla2g2a* prevents intestinal adenoma formation. 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. We found a duplication within the ATP synthase (*Atp5a1*) gene that is responsible for the *Mom2* phenotype. Our studies of tumor suppression suggest a novel mechanism of cellular lethality that is specific to the tumor lineage. We have also established reciprocal congenic lines of C3H/HeJ and C57BL/6J mice and completed large-scale backcrosses to identify new modifier loci. A combination of classical genetics and novel genomics technologies are used to assess and prioritize genes (coding and noncoding) for further study, and to determine which pathways are prime candidates for conferring resistance to cancer. Further investigations will lead to insights regarding the role of modifier genes in human cancer risk assessment, tumor prevention, diagnosis, and their predictive value for response to treatment.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

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.

McCorkell, K.A., R. Mancini, Z. Siprashvili, B.L. Barnoski, D. Iliopoulos, L.D. Siracusa, N. Zanesi, C.M. Croce, L.Y.Y. Fong, T. Druck and K. Huebner. “Influence of a nonfragile *FHIT* transgene on murine tumor susceptibility” (2007) *Cytogenetic & Gen Res.* 118: 196-203.

Rossi, S., C. Sevigani, S.C. Nnadi, L.D. Siracusa\*\* and G.A. Calin\*\* “Cancer-associated genomic regions (CAGRs) and non-coding RNAs: Bioinformatics and therapeutic implications” (2008) *Mammalian Genome* (published ahead of print on-line). \*\* = co-corresponding authors

Databases: Developed and On-line: The MUSMIRSUS Database, Version 2 - 2007, Developed by C. Sevigani, S. Nnadi, and L.D. Siracusa, [www.kimmelcancercenter.org/siracusa/musmirsus.htm](http://www.kimmelcancercenter.org/siracusa/musmirsus.htm)

**SCIENTIFIC PRESENTATIONS**

“Genetic Susceptibility to Colorectal Cancer”, Staff Seminar Series, Kimmel Cancer Center, Philadelphia, PA, December 2007

“Susceptibility Genes and Colorectal Cancer”, Targeted Therapies for Gastrointestinal Cancer, New York Academy of Sciences, New York, NY, March, 2008. Invited Speaker

## TEACHING

GC 550 Foundations in Biomedical Sciences - 3 lecture hours

GE 612 Genetics of Model Organisms - Lecturer – 3 lecture hours

## COMMITTEES

JCGS 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

KCC Training Committee, Member

KCC Seminar 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

2007, October Permanent Member, NCI – Cancer Genetics Study Section

2008, February Permanent Member, NCI – Cancer Genetics Study Section

2007, June Permanent Member, NCI – Cancer Genetics Study Section

*Manuscript selected by the Faculty of 1000*

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

## EDITORIAL RESPONSIBILITIES

Associate Editor, Genetics

Editorial Board, Mammalian Genome

## 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. Bruce Boman – Christiana Care Hospital, Delaware  
Dr. George Calin – M.D. Anderson Cancer Center, Texas  
Dr. Peter Demant – Roswell Park Cancer Institute, New York  
Dr. Tina Edmonston– Jefferson Medical College  
Dr. Terry Hyslop – Jefferson Medical College  
Dr. Scott Waldman – Jefferson Medical College

**GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008**

NIH RO1 (Buchberg, PI) Impact of the Mom2 Locus on Intestinal Biology and Cancer, \$250,000, 10% effort.  
NIH RO1 (Buchberg, PI) The Study of Caveolin on Apc-Mediated Tumorigenesis Uncovers a Potent Modifier, \$250,000, 10% effort.  
NIH RO1 (Siracusa, PI) Genetic Pathways Controlling Intestinal Biology and Tumorigenesis, \$250,000, 20% effort.

**ACTIVE GRANT AWARDS**

NIH RO1 CA89560 (Siracusa, PI) Molecular Genetics of Cancer Susceptibility, \$210,000, 2/03-1/09 (no cost extension). 20% effort.  
NIH RO1 CA120243 (Siracusa, PI) Susceptibility Genes and Colorectal Cancer, \$190,000, 7/07 -6/12, 25% effort

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

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

Using cutting edge technologies, we are investigating molecular mechanisms underlying functioning of virus- and cancer-specific cytotoxic lymphocytes. Our goal is to unravel fundamentals of these mechanisms that can be utilized to develop novel immunotherapeutic interventions.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

Tsatsanis, C., Vaporidi, K., Zacharioudaki, V., Androulidaki, A., Sykulev, Y., Andrew N. Margioris, A. N., and P.N., Tschlis Tpl2 and ERK transduce antiproliferative T cell receptor signals and inhibit transformation of chronically-stimulated (2008) T cells. Proc. Natl. Acad. Sci. USA, 105: 2987-92.

Anikeeva, N., Mareeva, T., Liu, W. and Y. Sykulev Can Oligomeric T-cell receptor be used as a tool to detect viral peptide epitopes on infected cells? (2008) Clinical Immunology, in press

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

"A mechanism of effective delivery of a poison pill: lessons from studies of CD4 and CD8 cytotoxic lymphocytes", Invited Speaker, 2nd International Congress "Immune-Mediated Diseases", September 10-14, 2007, Moscow, Russia

"Control of cytotoxic T cell response to HIV", Invited Speaker, 8th John Humphrey Advanced Summer Programme in Immunology, September 10-14, 2007, Moscow, Russia

"On the sensitivity of CTL responses", Invited Seminar Speaker, Cedars Sinai Medical Center, October 11-12, 2007, Los Angeles

"CD8 and cytotoxicity", Speaker, CD8 Club meeting, October 22-25, 2007, Amherst, Massachusetts

"Why responses of CD8 CTL are so sensitive?" Invited Speaker: Cancer and Diabetes Metabolism Seminar, University of Pennsylvania, November 26, 2007, Philadelphia

"Cooperative Binding to Self Antigens revealed by Quantum Dot/Peptide-MHC Biosensors", Invited Speaker, Third Al-Ain International Immunology Meeting IMMUNOREGULATION IN CHRONIC INFLAMMATORY DISORDERS, March 17-20, 2008 Al-Ain, UAE

**TEACHING**

*IM 631* Cellular Immunology – 1 lecture hours

*IM 505* Fundamentals of Immunology – Director

**COMMITTEES**

Search Committee, Faculty of the Department of Microbiology and Immunology, Jefferson Medical College

Academic Protocol Committee, Jefferson Medical College

### **AWARDS/HONORS**

2007, September, Ad hoc Reviewer, Council of Scientific and Industrial Research, India, review submitted in writing

2007, October, Ad hoc Reviewer, NIH NCI CA097296-06, ZCA1 SRC(99), CD8+ T cells and Immunological tumor regression, Bethesda, DC

2007, November, Ad hoc Reviewer, NIH NIAID 1P01AI072677, Special Study Section, The influence of TCR spatial organization on the T cell responses (phone review)

2007, November, Ad hoc Reviewer, Internal Grant Review Committee, KCC, Monoclonal antibody-based prodrugs – new tools for cancer therapy, Philadelphia, PA

### **EDITORIAL RESPONSIBILITIES**

Reviewer of Wellcome Trust, UK

### **MEMBERSHIPS**

American Association of Immunologists

### **COLLABORATIONS**

Dr. Matthias Schnell – Jefferson Medical College

Dr. Jianke Zhang – Jefferson Medical College

Dr. Takami Sato – Jefferson Medical College

Dr. Tim Manser - Jefferson Medical College

Dr. Mike Dustin – New York University, New York

Dr. Erik Martinez-Hackert –Columbia University, New York

### **GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

NIH R21, (Sykulev PI), Proximity between immune receptors on the cell surface and the sensitivity of T-cell, \$150,000 (\$50K subcontract) DC first year, 20% effort.

W. W. Smith Charitable Trust Award (Sykulev, PI), Detection and Targeting of T cells Using Quantum Dot/peptide-MHC Conjugates in Stress Related Heart Disease, \$100K direct cost

DOD, Synergistic idea award (Sykulev, PI), Multimodal biodegradable nanoplatfoms for targeted imaging and treatment of breast cancer, \$125K DC first year, 40% efforts

Nanotechnology Institute, Core Grant (Sykulev, PI), Lipid-based nanoparticles for in vivo imaging and targeting of cancer and virus-infected, \$336,708 (\$99,815 subcontract) DC one year, 40% efforts

NIH, Instrumentation grant, Total Internal Reflection Fluoreecent Microscope (Keen, PI)

### **ACTIVE GRANT AWARDS**

NIH RO1 R01AI052812 (Sykulev, PI), Immune Receptors on Cytotoxic Lymphocytes and Target Cells, 7/2007-12/2012, \$250K (\$70K subcontract) DC/current year

DOD BC076522 (Popov, PI) Development of Lipid-Based Nanoparticles for in Vivo Targeted Delivery of Imaging Agents into Breast Cancer Cells, 9/2008-8/2009, \$24.5K (subcontract)

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**JIANKE ZHANG, PH.D.**  
**ASSISTANT PROFESSOR**

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**RESEARCH ACCOMPLISHMENTS AND GOALS FOR COMING YEAR**

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. Recently, Steve Rosenberg, a graduate student in the lab found evidence that FADD plays role in the NF- $\kappa$ B pathway and also a signaling process involving the death kinase RIP1. To delineate the multiple functions of FADD, we performed reverse genetic studies. Xiaohui Zhou, a postdoctoral fellow showed that fetal liver HSC from death domain mutant embryos failed to develop into lymphocytes in irradiated hosts. Furthermore, the few mutant lymphocytes developed were severely impaired in proliferation. Therefore, it appears that the death domain has a function in mediating both apoptosis and proliferation. A paper on this subject has been submitted to JBC entitled, "TLR regulation by FADD and cFLIP". We have previously shown that FADD-deficient B cells were defective in TLR3- and TLR4-induced proliferation responses. Recently, we have found that B cell-specific FADD knockout mice were compromised in *in vivo* antibodies responses. As cFLIP is a likely signaling protein downstream of FADD, we have performed preliminary analysis of the cFLIP function in the immune system by generating B cell-specific cFLIP deficient. This project is currently supported by an NIH R03 grant. A manuscript prepared by Haibing Zhang, a postdoctoral fellow and Steve Rosenberg has been rerevised and submitted to the Journal of Immunology. To understand the function of Nit1, a putative tumor suppressor in apoptosis, we recently analyzed defects in T cells lacking Nit1. This study revealed that Nit1 is dispensable in apoptosis, but plays a role in negatively regulating T cell proliferation responses. This manuscript with Haibing Zhang as the lead author has been submitted to MCB. In collaboration with Drs. Manser and Sato, we are developing a humanized mice model which is useful for the study of human immunology and cancer.

**PUBLICATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

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 under revision for *J. Immunol.*

Zhang, H., Hou, Y-J., Han, S., E. Zhang, Huebner, K., and Zhang, J. The mammalian nitrilase homologue Nit1 is negative regulator of proliferation in T lymphocytes. Submitted to MCB, 2008.

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 and lymphocyte proliferation" (2008) re-Submitted to *J. Biol. Chem.*

Zhang, H., Rosenberg, S., Coffey, F. J., He, Y-W., Manser, T., Hardy, R. R., and Zhang, J. A role for cFLIP in B cell proliferation and stress MAP kinase regulation. Resubmitted to *J. Immunol.*

**SCIENTIFIC PRESENTATIONS (JULY 1, 2007 THROUGH JUNE 30, 2008)**

"Lymphocyte proliferation and apoptosis signaling mediated by the DISC proteins", University of Wisconsin Madison, School of Veterinary Medicine, August 2007

"Regulation of hematopoietic stem cells by cell death proteins", Jefferson Stem Cell Center Symposium, Philadelphia, PA, June, 2008

## TEACHING

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

*IM 505* Fundamentals of Immunology – 4 lecture hours

*IM 605* Molecular Immunology and Immunogenetics – Course coordinator, and 6 lecture hours

## COMMITTEES

Member, Faculty search committee

Member, Thomas Jefferson University Institutional Animal Care and Use Committee

Member, Thomas Jefferson University Committee for Professionalism

Director, Thomas Jefferson University Flow Cytometry Facilities

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

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

Member, IMP graduate training/preliminary exam Committee

Thesis committee for the following students: Alison Bell, Josephine Fox, Jackie Roth, Jim Testa, Liz Faul, RJ Nelly, Francis Coffey, Yingying Chen, Christine Juliana, Michelle Kraz.

## 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”

2008 (July 1) NIH R03 “The cFLIP function in B lymphocytes”

## EDITORIAL RESPONSIBILITIES

Ad hoc reviewer for *J. Immunol.*, *Mol. Immunol.*, *E. J. Immunol.*, *Biochem.*

## 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)

International Society for Stem Cell Research (ISSCR)

## COLLABORATIONS

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  
 Dr. Bernhard Dietzschol - TJU

**GRANTS SUBMITTED JULY 1, 2007-JUNE 30, 2008 (PENDING)**

R01 CA095454-06 (J. Zhang, PI) competing renewal A1 resubmission Apoptosis and Proliferation Signaling Mediated by FADD, \$125,000 DC first year, 25% effort  
 NIH P30 CA 056036-08 (Pestell, PI; Zhang co-P.I.), Translational Research in Cancer, Cancer Center Support Grant, \$113,783 DC 10% effort Flow Cytometry Facility (Facility Director)  
 R03 AI076788-01A1 (J. Zhang, PI) A1 resubmission, The Function of cFLIP in B Lymphocytes, \$50,000 DC, first year, 15% effort.  
 R03 AI076788-01A2 (J. Zhang, PI) A2 resubmission, The Function of cFLIP in B Lymphocytes, \$50,000 DC, first year, 15% effort.  
 Arthritis Foundation Research Grant (J. Zhang, PI), Death receptor and Toll-like receptor signaling regulation in autoimmunity, \$100,000 DC first year, 20% effort.

**ACTIVE GRANT AWARDS**

NIH R01 CA95454, 7/1/02-6/30/08, Zhang (P.I.), Apoptosis and Proliferation Signaling Mediated by FADD, 25% effort, \$100,000 DC , No cost extension, pending renewal.  
 NIH P30 CA 056036-08, 12/01/05-05/31/09, (Pestel, PI; Zhang co-P.I.), Translational Research in Cancer, Cancer Center Support Grant, 10% effort, Flow Cytometry Facility (Facility Director) Total direct costs: \$113,783 (Facility)  
 Intramural KCC Pilot Award , 10/1/07-9/30/09 Zhang, P.I., Co-PI's Sykulev, Manser, Sato Testing cancer-specific immunotherapeutics in the humanized mouse model, Total direct cost: \$75,000.  
 TJU Pilot grant, 7/1/07-6/30/08, Zhang, PI, The Function of cFLIP in B Lymphocytes, \$20,000 DC,  
 TJU REA grant, 7/1/07-6/30/08, Zhang, PI, Apoptosis and Proliferation Signaling Mediated by FADD, \$35,000 DC.  
 R03 AI076788, 7/1/08-6/30/10 (J. Zhang, PI) The Function of cFLIP in B Lymphocytes, \$50,000 DC, first year, 15% effort.

