BIOGRAPHICAL SKETCH

NAME Peter Hotez MD PhD	POSITION TITLE President, Sabin Vaccine Institute Distinguished Research Professor and Chair Microbiology, Immunology, & Tropical Medicine
eRA COMMONS USER NAME eRA Commons User Name	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Yale University (magna cum laude)	BA	1976 - 1980	Molec. Biophysics
Rockefeller University	PhD	1980 - 1987	Biochemistry (Parasitol.)
Cornell University Medical College	MD	1980 - 1987	Medical Science
Harvard Medical School (Mass. Gen. Hosp)	Residency	1987 - 1989	Pediatrics
Yale University School of Medicine	Fellowship	1989 - 1991	Molecular Parasitology

A. Personal Statement.

Professor Peter Hotez is a laboratory and clinician investigator with a major interest in recombinant protein vaccines for neglected tropical diseases (NTDs). He is an elected member of the Institute of Medicine and founding director of one of the first non-profit public private partnerships (PDP) for developing vaccines to combat NTDs. PDPs use industrial practices but develop products in the non-profit sector because they target diseases of the world's poorest people. Launched in 2000, the PDP of the Sabin Vaccine Institute filed its first Investigational New Drug application for a recombinant vaccine in 2004, with a second IND filed this year. Today the Sabin PDP is also developing recombinant vaccines for schistosomiasis, and other NTDs. These vaccines are engineered in yeast and bacteria. Process development at the 10 liter fermentation scale, followed by protein purification and formulation studies are conducted at Sabin followed by technology transfer to a pilot scale manufacturer either in the U.S. or Brazil, and then clinical testing either in the U.S. or in rural areas of Brazil where the prevalence of these NTDs is close to or exceeds 50%. Sabin's PDP will relocate to Baylor College of Medicine on September 1, 2011 where it will be known as Sabin Vaccine Institute and Texas Children's Center for Vaccine Development.

B. Positions and Honors.

Positions and Employment

1991-92 Instructor, Pediatrics, Yale University
1992-95 Assistant Professor, Pediatrics/Epidemiology & Public Health, Yale University
1995-00 Associate Professor, Epidemiology &Public Health/Pediatrics, Yale University
2000-11 Professor and Chair, Department of Microbiology, Immunology and Tropical Medicine, The George Washington University
2006-11 Walter G. Ross Professor of Basic Science Research, The George Washington University
2008-11 Distinguished Research Professor, The George Washington University
2007- President, Sabin Vaccine Institute
2007- Editor-in-Chief, *PLoS Neglected Tropical Diseases*
2010- President, American Society of Tropical Medicine and Hygiene
2011- Professor and Head of Pediatric Tropical Medicine, Baylor College of Medicine (after 9-1-11)
2011- Dean, National School of Tropical Medicine at Baylor College of Medicine (after 9-1-11)

Honors (after 2005)

2006 Leverhulme Medal, Liverpool School of Tropical Medicine
2006 Ambassador, Paul G. Rogers Society for Global Health Research, ResearchAmerica!
2007 Member of Advisory Board (Council), Fogarty International Center, National Institutes of Health

2008 Science and Technical Advisory Group on Neglected Tropical Diseases, WHO
2008 Member, Institute of Medicine of the National Academies
2009 Science and Technical Advisory Committee on Tropical Disease Research, WHO
2011 Member, National Institutes of Health Council of Councils

C. Selected peer-reviewed publications (in chronological order). (Selected from 218)

1. Hotez PJ, Ferris M. The antipoverty vaccines. Vaccine 2006; 24: 5787-99. (http://www.ncbi.nlm.nih.gov/pubmed/16759763)
2. Hotez PJ, Molyneux DH, Fenwick A, Kumaresan J, Ehrlich Sachs S, Sachs JD, Savioli L. Control of neglected tropical diseases. N Engl J Med 2007; 357: 1018-27. (http://www.nejm.org/doi/full/10.1056/NEJMra064142)
3. Loukas A, Bethony J, Brooker S, Hotez PJ. Hookworm vaccines – past, present and future. Lancet Infect Dis 2006; 6: 733-41. (http://www.ncbi.nlm.nih.gov/pubmed/17067922)
4. Diemert DJ, Bethony JM, Hotez PJ. Hookworm vaccines. Clin Infect Dis 2008; 46: 282-8. (http://ukpmc.ac.uk/abstract/MED/18171264)
5. Hotez PJ, Brindley P, Bethony J, King CH, Pearce E, Jacobson J. Helminth infections: the great neglected tropical diseases. J Clin Invest 2008; 118: 1311-21. PMCID: PMC2276811
6. Hotez PJ, Bethony J, Costa Oliveira S, Brindley PJ, Loukas A. A multivalent anthelminthic vaccine to prevent hookworm and schistosomiasis. Expert Rev Vaccines 2008; 7: 745-52. (http://www.ncbi.nlm.nih.gov/pubmed/18665774)
7. Bethony JM, Simon G, Diemert DJ, Parenti D, Desrosiers A, Schuck S, Fujiwara R, Santiago H, Hotez PJ. Randomized, placebo-controlled, double-blind trial of the Na-ASP-2 hookworm vaccine in unexposed adults. Vaccine 2008; 26: 2408-17. (http://www.ncbi.nlm.nih.gov/pubmed/18396361)
8. Hotez PJ. A plan to defeat neglected tropical diseases. Sci Am 2010; 302: 90-6. (http://www.ncbi.nlm.nih.gov/pubmed/20063641)
9. Hotez PJ, Fenwick A, Savioli L, Molyneux DH. Rescuing the “bottom billion” through neglected tropical disease control. Lancet 2009; 373: 1570-4. (http://www.ncbi.nlm.nih.gov/pubmed/19410718)
10. Pearson MS, Bethony JM, Pickering DA, de Oliveira LM, Jariwala A, Santiago H, Miles AP, Zhan B, Jiang D, Ranjit N, Mulvenna J, Tribolet L, Plieskatt J, Smith T, Bottazzi ME, Jones K, Keegan B, Hotez PJ, Loukas A. An enzymatically inactivated hemoglobinase from Necator americanus induces neutralizing antibodies against multiple hookworm species and protects dogs against heterologous hookworm infection. FASEB J 2009; 23: 3007-19. PMCID: PMC2735369
11. Hotez PJ. Peace through vaccine diplomacy. Science 2010; 327: 1301. PMID : 20223952. (http://www.sciencemag.org/content/327/5971/1301.summary)
12. Pearson MS, Pickering DA, Tribolet L, Cooper L, Mulvenna J, Oliveira LM, Bethony JM, Hotez PJ, Loukas A. Neutralizing antibodies to the hookworm hemoglobinase *Na*-APR-1: implications for a multivalent vaccine against hookworm infection and schistosomiasis. J Infect Dis 2010; 201:1561-9. PMID 20367477. (http://jid.oxfordjournals.org/content/201/10/1561.short).
13. Zhan B, Perally S, Brophy PM, Xue J, Goud G, Liu S, Deumic V, de Oliveira LM, Bethony J, Bottazzi ME, Jiang D, Gillespie P, Xiao SH, Gupta R, Loukas A, Ranjit N, Lustigman S, Oksov Y, Hotez P. Molecular Cloning, Biochemical Characterization and Partial Protective Immunity of the Heme-binding Glutathione S-Transferases from the Human Hookworm Necator americanus. Infect Immun 2010; 78:1552-63. PMCID: PMC2849424
14. Hotez PJ, Pecoul B. “Manifesto” for the control and elimination of the neglected tropical diseases. PLoS Neglect Trop Dis 2010; 4: e718. PMCID: PMC2876053
15. Hotez PJ, Bethony JM, Diemert DJ, Pearson M, Loukas A. Developing vaccines to combat hookworm infection and intestinal schistosomiasis. Nat Rev Microbiol 2010; 8: 814-26. PMID: 20948553 (http://www.nature.com/nrmicro/journal/v8/n11/abs/nrmicro2438.html)

D. Research Support.

Ongoing Research Support

32472 Hotez (PI) 08/01/2000 - 07/31/2011

Human Hookworm Vaccine Initiative 1
Sabin Vaccine Institute is conduit for The Bill & Melinda Gates Foundation
Human Hookworm Vaccine Initiative (HHVI): Clinical Development & Evaluation of the *Na*-ASP-2 Hookworm Vaccine
The goal of this study is to continue product development, including the manufacture of a second pilot lot, and to conduct a global health impact analysis of the human hookworm vaccine with the Sabin Vaccine institute

38988 Hotez (PI) 08/01/2006 - 07/31/2011
Human Hookworm Vaccine Initiative 2
Sabin Vaccine Institute-Human Hookworm Vaccine Initiative (HHVI): To develop and test the Na-APR-1 Hookworm Vaccine
The goal of this study is to conduct the process development, cGMP manufacture and testing, and clinical evaluation of APR-1 in order to develop a bivalent human hookworm vaccine with the Sabin Vaccine Institute

RCA8608 Hotez (PI) 09/30/2009 - 09/30/2011 NCE
(b)(4) -PATH-MVI
Development of a Malaria transmission blocking Vaccine
To develop a feasibility of expression study for the expression and scale-up of the Anopheles-APN-1 target candidate antigen as a malaria transmission blocking vaccine. The goal of this study is to conduct the early feasibility of expression using both yeast and bacterial expression systems.

1UL1RR031988-01 Hotez (GW PI) 07/01/2010 – 06/30/2015
National Institutes of Health
Clinical and Translational Science Institute at Children's National (CTSA)
The goal of the project is to provide highly integrated, cost effective, investigator-focused resources designed to overcome obstacles to investigation, promote collaborative research, and be continuously monitored and evaluated to identify when further adaptation or modification is needed.

Hotez (PI) 01/01/2011-12/31/2014
Dutch Government
Product Development Support of the Human Hookworm Vaccine
The ultimate goal of the project is to conduct Phase 1 studies to assess the safety and immunogenicity of the *Na*-GST-1 and *Na*-APR-1 hookworm antigens in both adults and children.

AI 90577 Hotez (PI) 01/01/2011 – 12/31/2012
National Institutes of Health
Title: Product development of a membrane tetraspanin vaccine against schistosomiasis
The goal of this project is the development of a high-yield, low-cost process for producing and formulating a recombinant Sm-TSP-2 schistosomiasis vaccine (10-liter scale)

Bottazzi/Hotez (MPI) 09/01/2010 - 08/31/2013
Instituto Carlos Slim de la Salud
Slim Initiative for Antipoverty Vaccine Development
The main goal of this project is to build a new generation of urgently needed vaccines for the neglected diseases, and to build capacity for vaccine development in Mexico.

Hotez (PI) 09/01/2011 – 07/31/2016
(b)(4)
Human Hookworm Vaccine Initiative 3

Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.

Completed Research Support (selected support after 2000)

Clinical Research Grant Hotez (PI) 2000 - 2003
Private Source
Cloning and vaccine testing of novel hookworm antigens based on human serologic responses to identify human correlates of immunity against hookworm vaccine antigens in China
Role: Principal Investigator

Parasitology grant 98-674 Wang (PI) 1998 - 2001
China Medical Board of New York
Goals to develop DNA vaccines and diagnostic reagents for malaria, trichinellosis and hookworm and to establish Beijing as a world-class center of molecular parasitology. Role of Dr. Hotez: To establish a China Medical Board Scholars Program between Yale, GW, Peking Union Medical College, Capital University of Medical Sciences, and the Institute of Parasitic Diseases.
Role: Co-Investigator

RO1 AI-32726-09 Hotez (PI) 1996 - 2004
NIAID-NIH
Hookworm Larval Infectivity & Development
The major goals are to understand the mechanism of protection afforded by vaccination with recombinant hookworm antigens
Role: Principal Investigator

5 U54 AI57168 Levine (PI) 09/04/2003 - 02/28/2009
NIH/NIAID
RCE-Biodefense & Emerging Infectious Diseases
GWU Administrative Core and Media Training for Biodefense Scientists
The goals are to provide biodefense scientists the tools to handle media contacts in the case of a biodefense emergency with training that uses educational methods to obtain successful media interviews by focusing on extensive message discipline, delivery, physical appearance, presentation and relaxation techniques.
Role: Co-PI

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Jiang, Shibo	Member & Lab Head
eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
The First Medical University of PLA, China	M.D.	1978	Medicine
The First Medical University of PLA, China	M.S.	1983	Immunology
The Fourth Medical University of PLA, China	Ph.D.	1995	Virology
The Rockefeller University, New York.	Post-doc.	1987-1990	Immunology

A. Personal Statement

The goal of the proposed research is to develop an effective and safe severe acute respiratory distress syndrome (SARS) vaccine based on the receptor binding domain (RBD) of the SARS spike (S) protein for preventing the SARS outbreak or biodefense preparedness, through the selection of the appropriate expressions system, establishment of scalable manufacturing process and cGMP manufacture, as well as the completion of GLP toxicology testing and preparation of a regulatory filing. I, as the PI#2, will be responsible for planning, directing and executing the majority of the studies in Aim 1. I have a broad background in immunology, virology, infectious diseases and biomedicine. As PI on several NIH grants, I have accumulated extensive experience in development of vaccines against SARS-CoV. Since 2004, I have authored and coauthored more than 30 peer-reviewed papers related to SARS and influenza vaccine studies. My team is the first group in the world to show that the RBD of SARS-CoV S protein contains multiple conformation-dependant neutralizing epitopes, and vaccination of animals with recombinant RBD resulted in highly potent neutralizing antibodies and protection against SARS-CoV challenge, suggesting a great potential to develop rRBD-based SARS vaccine. In my lab, a series of techniques have been established for expression of rRBD proteins and evaluation of their antigenicity, functionality and immunogenicity. Most of the facilities, instruments and reagents required for the proposed studies are available. Therefore, my expertise, experience and a strong record of publications and extramural funding will allow me to act as the PI#2 in this project and achieve the goal proposed.

B. Positions and Honors

Positions and Employment

1978-85 Teaching Instructor (1978-82) and Lecturer (1983-85), the 1st Medical University of PLA, China.
1987-90 Postdoctoral Fellow, Laboratory of Cellular Physiology & Immunology, Rockefeller University, NY.
1990- Assistant Member (1990-96), Associate Member (1997-06), Member (2006-), & Lab Head (2002-), Viral Immunology Laboratory, Lindsley F. Kimball Research Institute, New York Blood Center, NY.

Other Experience and Professional Memberships

1998 *Ad hoc* Member, NIID Special Emphasis Panel on Innovative AIDS Vaccines.
2000- Member, International Society for Antiviral Research (ISAR) and International AIDS Society (IAS).
2002 *Ad hoc* Member, NIAID Special Emphasis Panel on *In vitro* Test Systems for Evaluating Chemotherapies against AIDS.
2004 *Ad hoc* Member, NIAID Special Emphasis Panel on Innovative Research Topic in Virology.
2004 External Reviewer for Canadian Institutes of Health Research (CIHR).
2004- Member, Overseas Assessor Board for Chinese Academy of Sciences.
2005- External Reviewer for Chinese National Sciences Foundation (CNSF).
2005- Editorial Consultant for *The Lancet*.

2007-09 Regular Member, AIDS Discovery & Development of Therapeutics (ADDT) Study Section of NIAID.
2008- External Reviewer for Hong Kong Research Grant Council (RGC).
2010 *Ad hoc* Member, NIAID Special Emphasis Panel on SARS-CoV-Host Cell Interactions & Vaccine Development.

Honors

1985 & 86 Research Excellence Award, the First Medical University of PLA.
1985 Young Scientist Award, Guangzhou Youth Medical Worker Association.
1987 World Health Organization (WHO) Fellowship
1988 Cancer Research Institute Fellowship
2003, 06, 09 New York Blood Center President Award for Special Recognition as Investigator in Research.

C. Selected Peer-reviewed Publications (Selected from 244 peer-reviewed publications)

Most relevant to the current application

1. He, Y., Lu, H., Siddiqui, P., Zhou, Y., and **Jiang, S.** (2005). Receptor-binding domain of SARS-CoV S protein contains multiple conformation-dependant epitopes that induce highly potent neutralizing antibodies. *J. Immunol.* 174, 4908-4915. http://www.ncbi.nlm.nih.gov/pubmed/15814718
2. He, Y., Li, J., Li, W., **Lustigman, S.**, Farzan, M., and **Jiang, S.** (2006). Cross-neutralization of human and palm civet SARS-CoV variants by antibodies targeting the receptor-binding domain of spike protein. *J. Immunol.* 176, 6085-6092. http://www.ncbi.nlm.nih.gov/pubmed/16670317
3. **Du, L.**, Zhao, G., He, Y., Guo, Y., Zheng, B.-J., **Jiang, S.**, and Zhou, Y.S., (2007). The receptor-binding domain of SARS coronavirus spike protein induces long-term protective immunity in an animal model. *Vaccine.* 25, 2832-2838. http://www.ncbi.nlm.nih.gov/pubmed/17092615
4. **Du, L.**, Zhao, G., Chan, C., Li, L., Sun, S., Liu, Z., Guo, H., He, Y., Zhou, Y., Zheng, B.J., **Jiang, S.** (2009). Recombinant receptor-binding domain of SARS-CoV spike protein expressed in mammalian, insect and E. coli cells elicits potent neutralizing antibody and protective immunity. *Virology.* 393, 144-150. PMC2753736
5. **Du, L.**, He, Y., Zhou, Y., Liu, S., Zheng, B., **Jiang, S.** (2009). The spike protein of SARS-CoV – a target for vaccine and therapeutic development. *Nature Rev. Microbiol.* 7, 226-236. PMC2750777

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

1. He, Y., Zhou, Y., Liu, S., Kou, Z., Li, W., Farzan, M., and **Jiang, S.** (2004). Receptor-binding domain of SARS-CoV spike protein induces highly potent neutralizing antibodies: implication for developing subunit vaccine. *Biochem. Biophys. Res. Commun.* 324, 773-781. http://www.ncbi.nlm.nih.gov/pubmed/15474494
2. He, Y., Zhou, Y., Wu, H., Luo, B., Chen, J., Li, W., and **Jiang, S.** (2004). Identification of immunodominant domains in the SARS-CoV S protein: implication for developing SARS diagnostics and vaccines. *J. Immunol.* 173, 4050-4057. http://www.ncbi.nlm.nih.gov/pubmed/15356154
3. He, Y., Zhou, Y., Siddiqui, P., and **Jiang, S.** (2004). Inactivated SARS-CoV vaccine elicits high titers of spike protein-specific antibodies that block receptor binding and virus entry. *Biochem. Biophys. Res. Commun.* 325, 445-452. http://www.ncbi.nlm.nih.gov/pubmed/15530413
4. He, Y., Zhu, Q.Y., Liu, S., Zhou, Y.S., Yang, B., Li, J., and **Jiang, S.** (2005). Identification of a critical neutralization determinant of SARS-associated coronavirus: importance for designing SARS vaccines. *Virology* 334, 74-82. http://www.ncbi.nlm.nih.gov/pubmed/15749124
5. He, Y., Li, J., Heck, S., **Lustigman, S.**, **Jiang, S.** (2006). Antigenic and immunogenic characterization of recombinant baculovirus-expressed SARS-CoV S protein: implication for vaccine design. *J.Virol.* 80, 5757-5767. PMC1472569
6. He, Y., Li, J., Yan, X., Hu, G., Zhou, Y. and **Jiang, S.** (2006). Identification and characterization of novel neutralizing epitopes in the receptor-binding domain of SARS-CoV spike protein: revealing the critical

antigenic determinants in inactivated SARS-CoV vaccine. *Vaccine*. 24, 5498-5508. http://www.ncbi.nlm.nih.gov/pubmed/16725238

7. **Du L**, Zhao G, Lin Y, Sui H, Chan C, Ma S, He Y, **Jiang S**, Wu CY, Yuen KY, Jin DY, Zhou Y, Zheng BJ. Intranasal vaccination of recombinant adeno-associated virus encoding receptor-binding domain of severe acute respiratory syndrome coronavirus (SARS-CoV) spike protein induces strong mucosal immune responses and provides long-term protection against SARS-CoV infection. *J Immunol.* 2008;180(2):948-956. PMC2603051
8. **Du, L.**, Zhao, G., Lin, Y., Chan, C., He, Y., **Jiang, S.**, Wu, C. Jing, D., Yuen, K.Y., Zhou, Y., Zheng, B.J. (2008). Priming with rAAV encoding RBD of SARS-CoV S protein and boosting with RBD-specific peptides for T cell epitopes increase T cell responses and provide protection against SRAS-CoV infection. *Vaccine.* 26, 1644-1651. PMC2600875
9. **Du, L.**, Zhao, G., Li, L., He,Y., Zhou,Y., Zheng, B.J., **Jiang, S.** (2009). Antigenicity & immunogenicity of SARS-CoV S protein receptor-binding domain stably expressed in CHO cells. *Biochem. Biophys. Res. Commun.* 384, 486-490. PMC2750803
10. **Du, L.**, Zhao, G., Chan, C., He, Y., Zhou, Y., Zheng, B.J., **Jiang, S.** (2010). A 219-mer recombinant receptor-binding domain of SARS-CoV spike protein induces highly potent immune responses and protection. *Viral. Immunol.* 23, 211–219. PMC2883479

Related patent:

Jiang, S., and He, Y. Neutralizing monoclonal antibodies against severe acute respiratory syndrome-associated coronavirus. *US Patent 7,629,443.* Filed February 7, 2005. Issued December 8, 2009.

D. Research Support

Ongoing Research Support

3R01 AI046221-09S1 Jiang (PI) 6/1/2000 – 5/31/2011
Rational design of HIV fusion inhibitors targeting gp41 (Recovery Act Funds for Administrative Supplements)
The goal of this ARRA project is to determine the binding site of the identified small molecule HIV-1 fusion inhibitors in HIV-1 gp41 coiled coil domain by drug resistance-related mutation studies. **Role**: PI

Completed Research Support

1R01 AI068002-04 Jiang (PI) 3/15/2007 – 2/28/2011
SARS-CoV S protein receptor-binding domain-based vaccines
The goal of this project is to express RBD of SARS-CoV S protein in *E. coli* or yeast systems as subunit vaccines for prevention of SARS. **Role**: PI

2R01 AI046221-09 Jiang (PI) 2/1/2000 – 1/31/2011
Rational design of HIV fusion inhibitors targeting gp41
The goal of this project is to identify lead antiviral compounds targeted to the HIV-1 gp41 coiled coil domain and to optimize the lead compounds for generating most active HIV-1 fusion inhibitors. **Role**: PI

U19 AI076964-05 Jiang (PI) 9/1/04 – 8/31/10 (NCE)
Anti-HIV composite cellulose acetate phthalate film
The major goal of this program project is to evaluate the anti-HIV-1 activity of CAP film in *in vitro* systems, animal models, and phases I clinical trials. **Role**: PI

BIOGRAPHICAL SKETCH

NAME Maria Elena Bottazzi	POSITION TITLE Professor
eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
National University of Honduras, Tegucigalpa, Honduras	BS	1989	Microbiology and Tropical Medicine
University of Florida, Gainesville, FL	Ph.D.	1995	Molecular Biology and Tumor Virology
University of Miami, Miami, FL	Post-doc	1995-1998	Cell Biology, Cell Cycle Genetics
University of Pennsylvania, Philadelphia, PA	Post-doc	1998-2001	Cell Biology and Cell Cycle Genetics

A. Personal Statement

I have extensive experience in the product development activities for recombinant biologics including projects to express proteins derived from hookworm, schistosome and other neglected infectious agents that are vaccine targets. Our studies will involve expression, process development, analytical and formulation development of recombinant expression of the rRBD) antigen of SARS-CoV. I have the expertise, leadership and motivation necessary to successfully carry out the proposed work. I have a broad background in molecular and cellular biology, with specific training and expertise in key research areas for this application. I have over 11 years of molecular/cellular biology experience and have served for the last 10 years as the Program Director for Product Development of a recombinant vaccine product development program. I have ample expertise in managing complex programs and technical units for the process development of recombinant vaccines using the yeast and bacteria expression systems. As PI or co-Investigator on several previous non-federal- and NIH-funded grants, I laid the groundwork for the proposed research by developing feasibility processes for recombinant protein expression as well as how to scale them up. In addition, I successfully administered the projects (e.g. staffing, research protections, budget), collaborated with other researchers, and produced several peer-reviewed publications from each project. As a result of these previous experiences, I am aware of the importance of frequent communication among project members and of constructing a realistic research plan, timeline, and budget. The current application builds logically on my prior work and prior product development and manufacturing collaborations.

B. Positions and Honors

Positions and Employment

1998-1989 Research Assistant Dept of Microbiology, National Univ. of Honduras, Tegucigalpa, Honduras
1989-1995 Graduate Assistant, Dept of Pathology, University of Florida, Gainesville, FL
1995-1998 Post-doctoral Fellow, Dept of Cell biology and Anatomy, Univ. of Miami, Miami, FL
1998-2001 Post-doctoral Fellow, Dept of Pharmacology, Univ. of Pennsylvania, Philadelphia, PA
2001-2004 Assistant Research Professor, Department of Microbiology and Tropical Medicine, The George Washington University, Washington, DC
2004-2007 Associate Research Professor, Department of Microbiology and Tropical Medicine, The George Washington University, Washington, DC
2007-2011 Associate Professor and Department Vice Chair for Administration, Department of Microbiology, Immunology and Tropical Medicine, The George Washington University, Washington, DC
2011-Present Professor and Associate Dean, National School of Tropical Medicine, Division Pediatric Tropical Medicine, Dept. of Pediatrics, Baylor College of Medicine and Texas children's hospital, Houston, TX

Other Experience and Professional Memberships

2001- Member, American Society for Microbiology
2001- Member, American Society for Tropical Medicine and Hygiene
2008- Associate Editor, Public Library of Science –Neglected Tropical Disease

Honors

BS with Honors, 1989
American Association of University Women Educational Foundation Pre-Doctoral Fellowship, 1991
American Heart Association, Florida Affiliate Post-Doctoral Fellowship, 1996

Department of Defense (DOD) Breast Cancer Post-Doctoral Fellowship, 1997

C. Selected Peer-reviewed Publications

Most relevant to the current application

Jariwala AR, Oliveira LM, Diemert DJ, Keegan B, Plieskatt JL, Periago MV, **Bottazzi ME,** Hotez PJ, Bethony JM. Potency testing for the experimental Na-GST-1 hookworm vaccine. Expert Rev Vaccines. 2010 Oct; 9 (10):1219-30. PMID: 20923271 http://www.ncbi.nlm.nih.gov/pubmed/20923271

Zhan B, Perally S, Brophy PM, Xue J, Goud G, Liu S, Deumic V, de Oliveira LM, Bethony J, **Bottazzi ME,** Jiang D, Gillespie P, Xiao SH, Gupta R, Loukas A, Ranjit N, Lustigman S, Oksov Y, Hotez P. (2010). Molecular Cloning, Biochemical Characterization and Partial Protective Immunity of the Heme-binding Glutathione S-Transferases from the Human Hookworm Necator americanus. Infect Immun. 2010 Feb 9. [Epub ahead of print] PMCID: PMC2849424.

Cai S, He F, Samra HS, de la Maza LM, **Bottazzi ME,** Joshi SB, Middaugh CR. (2009). Biophysical and stabilization studies of the Chlamydia trachomatis mouse pneumonitis major outer membrane protein. Mol Pharm. Sep-Oct;6(5):1553-61.PMCID: PMC2757499.

Pearson MS, Bethony JM, Pickering DA, de Oliveira LM, Jariwala A, Santiago H, Miles AP, Zhan B, Jiang D, Ranjit N, Mulvenna J, Tribolet L, Plieskatt J, Smith T, **Bottazzi ME**, Jones K, Keegan B, Hotez PJ, Loukas A. (2009) An enzymatically inactivated hemoglobinase from Necator americanus induces neutralizing antibodies against multiple hookworm species and protects dogs against heterologous hookworm infection. FASEB J. Sep;23(9):3007-19. PMCID: PMC2735369.

Bottazzi, ME and Shah Brown, A.(2008) Model for the product development of vaccines against neglected tropical diseases: a vaccine against human hookworm **Expert Reviews in Vaccines** 7(10):1481-92. PMID: 19053205 http://www.ncbi.nlm.nih.gov/pubmed/19053205

Fujiwara RT, Zhan B, Mendez S, Loukas A, Bueno LL, Wang Y, Plieskatt J, Oksov Y, Lustigman S, **Bottazzi ME,** Hotez P, Bethony JM. Reduction of worm fecundity and canine host blood loss mediates protection against hookworm infection elicited by vaccination with recombinant Ac-16. Clin Vaccine Immunol. 2007 Mar;14(3):281-7. Epub 2007 Jan 31. PMCID: PMC1828853.

Hotez P, Bethony J, **Bottazzi ME,** Brooker S, Diemert D, Loukas A. (2006) New Technologies for the Control of Human Hookworm Infection. Trends in Parasitology 22(7):327-31. http://www.ncbi.nlm.nih.gov/pubmed/16709466

Bottazzi ME*, Miles AP*, Diemert DJ, Hotez, PJ. (2006) An ounce of prevention on a budget: a non-profit approach to developing vaccines against neglected diseases. *co-first authors. Expert Reviews of Vaccines 5(2):189-98. http://www.ncbi.nlm.nih.gov/pubmed/16608419

Williamson AL, Lustigman S, Oksov Y, Deumic V, Plieskatt J, Mendez S, Zhan B, **Bottazzi ME**, Hotez P, Loukas, A (2006). Ac-MTP-1, an astascin-like metalloprotease secreted by infective hookworm larvae, is involved in tissue migration. Infection and Immunity, 74(2):961-7. PMCID: PMC1360348

Fujiwara, R.T., Loukas, A., Mendez, S., Williamson, A.L., Bueno, L.L., Wang, Y., Samuel, A., Zhan, B., **Bottazzi, M.E.,** Hotez, P.J. and Bethony, J.M. (2006). Vaccination with irradiated Ancylostoma caninum third stage larvae induces a Th2 protective response in dogs. Vaccine, 24(4):501-9. http://www.ncbi.nlm.nih.gov/pubmed/16140437

Bottazzi ME*, Goud GN*, Zhan B, Mendez S, Deumic V, Plieskatt J, Liu S, Wang Y, Bueno L, Fujiwara R, Samuel A, Ahn SY, Solanki M, Asojo O, Wen J, Saul A, Bethony JM, Loukas A, Roy M, Hotez PJ (2005) Expression of the Necator americanus hookworm larval antigen Na-ASP-2 in Pichia Pastoris and purification of the recombinant protein for use in human clinical trials. *co-first authors. Vaccine, 23(39):4754-64. http://www.ncbi.nlm.nih.gov/pubmed/16054275

Bethony JM, Loukas A, Smout MJ, Mendez S, Wang Y, **Bottazzi ME,** Zhan B, Williamson A, Correa-Oliveira R, Xiao SH, Hotez PJ. (2005) Antibodies against a secreted protein from hookworm larvae reduce the intensity of hookworm infection in humans and vaccinated laboratory animals. FASEB Journal, 19(12):1743-5. http://www.ncbi.nlm.nih.gov/pubmed/16037096

Loukas A, Bethony JM, Mendez S, Fujiwara RT, Goud GN, Ranjit N, Zhan B, Jones B, **Bottazzi ME,** and Hotez PJ. (2005) Vaccination with recombinant aspartic hemoglobinase reduces parasite load and blood loss after hookworm infection. PLoS Medicine 2(10):e295. PMCID: PMC1240050

D. Research Support

Active

32472 Hotez (PI) 08/01/2000 - 07/31/2011
Human Hookworm Vaccine Initiative 1
Sabin Vaccine Institute is conduit for The Bill and Melinda Gates Foundation
Clinical Development & Evaluation of the *Na*-ASP-2 Hookworm Vaccine

The goal of this study is to continue product development, including the manufacture of a second pilot lot, and to conduct a global health impact analysis of the human hookworm vaccine with the Sabin Vaccine institute.
Role: Director Product Development

38988 Hotez (PI) 08/01/2006 - 07/31/2011
Human Hookworm Vaccine Initiative 2
Sabin Vaccine Institute is conduit for The Bill and Melinda Gates Foundation
Development and testing of the Na-APR-1 Hookworm Vaccine
The goal of this study is to conduct the process development, cGMP manufacture and testing, and clinical evaluation of APR-1 in order to develop a bivalent human hookworm vaccine with the Sabin Vaccine Institute
Role: Director Product Development

RCA 8608 Hotez (PI) 09/30/2009 - 09/30/2011 nce
(b)(4) -PATH-MVI
Development of a Malaria transmission blocking Vaccine
To develop a feasibility of expression study for the expression and scale-up of the Anopheles-APN-1 target candidate antigen as a malaria transmission blocking vaccine. The goal of this study is to conduct the early feasibility of expression using both yeast and bacterial expression systems.
Role: Director Product Development

1UL1RR031988-01 Hotez (GWU-PI) 07/01/2010 – 06/30/2015
National Institutes of Health
Clinical and Translational Science Institute at Children's National
The goal of the project is to provide highly integrated, cost effective, investigator-focused resources designed to overcome obstacles to investigation, promote collaborative research, and be continuously monitored and evaluated to identify when further adaptation or modification is needed.
Role: Associate Co-Principal Investigator for GWU

1R24TW008897-01 Mullan/Frehywot (PD/PI) 9/01/2010 – 9/29/2015
National Institutes of Health
Coordinating Center: Fostering African Medical Education Community of Excellence
The George Washington University will serve as the Coordinating Center for multiple MEPI programs and linked grantees where the project focuses on improving medical education and research in Sub-Saharan Africa.
Role: Co-Investigator

Dutch Government Bottazzi/Bethony (MPI) 01/01/2011-12/31/2014
Product Development Support of the Human Hookworm Vaccine
The ultimate goal of the project is to conduct Phase 1 studies to assess the safety and immunogenicity of the *Na*-GST-1 and *Na*-APR-1 hookworm antigens in both adults and children.

1R56AI090577-01 Bethony/Bottazzi (MPI) 01/01/2011 – 12/31/2011
National Institutes of Health/Sabin
Product development of a membrane tetraspanin vaccine against schistosomiasis
The goal of this project is to establish a manufacturing process for a vaccine target against schistosomiasis and perform technology transfer for cGMP manufacturing.

Bottazzi/Hotez (MPI) 1/1/2011 - 12/31/2013
Instituto Carlos Slim de la Salud
Slim Initiative for Antipoverty Vaccine Development
The main goal of this project is to build a new generation of urgently needed vaccines for the neglected diseases, and to build capacity for vaccine development in Mexico.

Hotez (PI) 09/01/2011 – 07/31/2016
(b)(4)
Human Hookworm Vaccine Initiative 3
Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.

Role: Co-Investigator

Completed

Private Source **Bottazzi (PI)** 11/01/2006 - 10/31/2008 on NCE to 10/31/2009

Ancylostoma Caninum derived antigens as potential veterinary diagnostic tools.
The major goal is to explore the possibility of identifying relevant new tools and develop them for the diagnosis of hookworm disease in dogs.

1 R43 CA123991-01A2 Bonafe 06/01/2008 – 05/31/2009

NIH/NCI Phase I SBIR

Glioma therapeutics targeting glioma pathogenesis-related protein
The major goal is to produce recombinant proteins using the yeast *Pichia* eukaryotic system in order to express and purify the glioma pathogenesis-related protein.

R21 AI071903 Kashanchi (PI) 06/01/2006 – 05/31/2007 on NCE to 05/31/2008

NIH/NIAID
A human stem cell mouse model for HIV expression and inhibition
The major goal of this project is to look for human and mouse surface markers from human Stem cells that will be differentiated into human monocyte and T-cells in double KO animals.

Private Source **Greenberg (PI)** 11/01/2006 – 03/31/2007 on NCE to 10/31/2007

Private Source

The major goal of this project is a collaborative effort with Private Source to plan for the creation of an International Institute for Public Health Laboratory Management in order to provide training to management, leadership and oversight training to administrators of public health laboratories.

NIH U54 AI57168 Levine (PI) 03/01/2006 – 02/28/2007

MARCE New Opportunities Award
Subcontract to University of Maryland, Baltimore
The major goal of this project is to develop and optimize the expression, purification and scale-up pilot production of HeV and NiV sG recombinant proteins and the human mAbs. The successful process development of these molecules will allow for initiation of preclinical and passive protection studies leading to cGMP manufacture and the clinical testing of cGMP material.
Role: Co-PI

Private Source **Kashanchi (PI)** 09/01/2006 – 08/31/2007

The major goal of this project is to identify human immune cells and HIV-1 replication in xenotransplanted $Rag2^{-/-}\gamma_c{}^{-/-}$ mice, and evaluate feasibility of topical anti-HIV microbicide efficacy using NRTI, NNRTI, and entry inhibitors against vaginal challenge. Private Source a 501(c)(3) organization located at Private Source that funds HIV research pertaining to microbicides and AIDS in women,
Role: Co-PI

AI061560 Kashanchi (PI) 06/01/2004 – 05/31/2006

NIH-R21
Title: Alteration of Retinoblastoma tumor suppressor protein in HTLV-1 transformed cells.
The major goal of this project is to understand how tax-dependent perturbation of restriction point regulators leads to leukemogenesis.
Role: Co-PI

Hotez (PI) 08/01/2001-07/31/2003

NIH-NIAID
Hookworm Larval Infectivity and Development.
Role: Research Faculty Supplement for Underrepresented Minorities

DAMD17-97-1-7323 Bottazzi (PI) 10/30/1997 – 07/15/2001

Department of the Army
Anchorage Dependent and Independent control of the cyclin A gene: Implications for breast cancer.
The major goal of this postdoctoral grant was to analyze the regulation of expression of the cyclin A gene in fibroblast as well as mammary epithelial cells leading to the understanding of the progression to breast cancer.

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Sara Lustigman	Member and Laboratory Head
eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Hebrew University of Jerusalem, Israel	BSc	1975	Chemistry/ biochemistry
Hebrew University of Jerusalem, Israel	MSc	1978	Microbiology/Parsitology
Hebrew University of Jerusalem, Israel	PhD	1985	Immunoparasitology
The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia	Postdoc-Fellow	1988	Malaria Studies

A. Personal Statement

The studies of the proposed research will lead to the expression, process development, formulation, technology transfer, cGMP manufacture, GLP toxicology and preparation of a regulatory filing (IND submission) of a recombinant vaccine to prevent severe acute respiratory distress syndrome (SARS) caused by the SARS-associated coronavirus (SARS-CoV). The vaccine will be comprised of the receptor binding domain (RBD) of the SARS S protein, expressed as a recombinant protein (rRBD), and formulated with alum and/or an innate adjuvant, GLA. The Ultimate Goal of the proposed studies is to develop a highly effective and safe anti-SARS recombinant protein vaccine that can be used in humans. I have a broad background in molecular parasitology, immunology, vaccinology and functional genomics. In the last 20 years my studies, mostly funded by the NIH, were focused on identifying vaccine and drug targets against the filarial human parasitic nematodes. Over the years we identified more than 30 *O. volvulus* antigens of which 8 were proven to be protective in the mouse model, and they are presently being further developed for human use in collaboration with Dr. Peter Hotez and Dr. Bin Zhan (Director of the Molecular Biology Unit of the Human Hookworm Vaccine Initiative) and DR. Maria Elena Bottazzi (Program Director for Product Development), who are both Co-Investigators on my NIH 1R01AI078314-01A2 project. My collaboration with Drs. Peter Hotez, Bin Zhan and Maria Elena Bottazzi has started more than 10 years ago but since 2005 I have been also actively involved in their Hookworm Vaccine Initiative as a collaborator and advisor. Our collaboration resulted in multiple publications and collaborative work on moving forward filarial vaccine candidates through product development and pre-clinical studies. In addition, I am currently also collaborating with Drs. Hotez and Zhan on the product development of a novel parasite derived adjuvant (Ov-ASP-1). To further establish its adjuvanticity we have been using different vaccine models. In collaboration with Dr. Shibo Jiang (PI#2), Head of Viral Immunology we studied since 2005 two vaccine models of SARS, the Spike and the RBD vaccine antigens, as well as the influenza vaccines. Our collaboration is synergistic, complementary and productive because of Dr. Jiang's strong expertise in viral vaccine studies. So far, we have had six jointed publications. My lab has also established varied techniques for studying the adjuvanticity and immunogenicity of vaccine components in terms of antibody responses as well as cellular immune responses elicited against the by-stander vaccine antigens, particularly those against RBD. Most recently, we have been able to show that our adjuvant can support the production of anti-RBD responses in non-human primates. The current application builds logically on my prior work, and the productive collaboration with Drs. Hotez's and Jiang groups. My group will be responsible for testing the immunogenicity of rRBD protein to induce MHC-H-2d restricted SARS-CoV-specific cytotoxic T lymphocyte response by using ELISPOT and other alternative assays. In addition, I will be the NYBC liaison for all aspects involving the product development of recombinant RBD and adjuvant formulation for optimization.

B. Positions and Honors

Positions and Employment

3/88-9/94	Assistant Member, Laboratory of Virology and Parasitology, the Lindsley F. Kimball Research Institute (LFKRI), New York Blood Center (NYBC)
10/94-3/98	Associate Member, Laboratory of Virology and Parasitology, LFKRI, NYBC
4/98-12/00	Associate Member and Laboratory Head, Laboratory of Molecular Parasitology, LFKRI, NYBC
1/01-present	Member and Laboratory Head, Laboratory of Molecular Parasitology, LFKRI, NYBC

Other Experience and Professional Memberships

1991 - 1992	Committee Member, Immunodiagnosis of Onchocerca and Filariasis, World Health Organization
1995 - 2000	Scientific Advisory Group Member, Filarial Genome Project, World Health Organization
1998 - 2004	Scientific Advisory Board Member, Beijing Center for Molecular Parasitology, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China
2002	Scientific Advisory Member, Conference on the Eradicability of Onchocerciasis; the Carter Center, Atlanta, GA.
2003	October 15-17, member of a special panel on RNAi in *C. elegans* as a mean of identifying drug targets for filariasis; World Health Organization, Glion, Switzerland
2003	December 15-17, member of NIAID Special Emphasis Panel (ZAI1-AC-M(J3) & ZAI1-AC-M(J2))
2003 - 2006	ASTMH Scientific Program Committee – Filariasis
2006	February 16, member of NIAID Special Emphasis Panel (ZRG1 IDM-M02 M)
2006, 2007	Member, Scientific Working Group on Helminth Drug Initiative; World Health Organization
2006 -	A member of the Advisory Board of the Worm Institute for Research and Medicine (WIRM), The Scripps Research Institute.
2006 -	Deputy Editor, PLoS NTD (Neglected Tropical Diseases)
2006 -	A member of the Scientific Advisory Board of Filariasis Research Reagent Resource Center (FR3), sponsored by the NIH/NIAID.
2007 -	Editorial Board Member, Molecular and Biochemical Parasitology
2008	October 6-8, member of NIAID Special Emphasis Panel - ZAI1 DDS-M (J2)
9/2009 -	Chairperson of Disease Reference Group on Helminth infections (DRG4), UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR)
2010	January 25-28, Chairperson and member of the NIAID Special Emphasis Panel - ZAI1 AWA-M-M2

C. Selected Peer-reviewed Publications (Selected from 94 peer-reviewed publications)

Most relevant to the current application (in chronological order)

1) MacDonald AJ, Cao L, He Y, Zhao Q, **Jiang S** and **LUSTIGMAN S** (2005). r*Ov*-ASP-1, a recombinant secreted protein of the helminth *Onchocerca volvulus*, is a potent adjuvant for inducing antibodies to ovalbumin, HIV-1 polypeptide and SARS-CoV peptide antigens. Vaccine, **23**: 3446–3452. PMID: 15837368
2) He Y, Li J, Li W, **LUSTIGMAN S**, Farzan M and **Jiang S** (2006). Cross-Neutralization of Human and Palm Civet SARS Coronaviruses by Antibodies Targeting the Receptor-Binding Domain of Spike Protein. J. Immunology **176**: 6085–6092. PMID: 16670317
3) He Y, Li J, Heck S, **LUSTIGMAN S** and **Jiang S** (2006). Antigenic and Immunogenic Characterization of Recombinant Baculovirus-expressed Severe Acute Respiratory Syndrome Coronavirus Spike Protein: Implication for Vaccine Design. J. Virology **80**: 5757–5767. PMID: 16731915; PMCID: PMC1472569
4) He Y, Barker SJ, MacDonald AJ, Yu Y, Cao L, Li J, Parhar R, Heck S, Hartmann S, Golenbock DT, **Jiang S**, Libri NA, Semper AE, Rosenberg WM, **LUSTIGMAN S** (2009). Recombinant Ov-ASP-1, a Th1-biased protein adjuvant derived from the helminth *Onchocerca volvulus*, can directly bind and activate antigen-presenting cells. J Immunol. **182**:4005-16. PMID: 19299698

5) Zhao G, Du L, Xiao W, Sun S, Lin Y, Chen M, Kou Z, He Y, **LUSTIGMAN S**, **Jiang S**, Zheng BJ, Zhou Y (2010) Induction of protection against divergent H5N1 influenza viruses using a recombinant fusion protein linking influenza M2e to *Onchocerca volvulus* activation associated protein-1 (ASP-1) adjuvant. Vaccine **28**(44):7233-7240. PMID: 20732469

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

1) Abraham D, Leon O, Leon S and **LUSTIGMAN S** (2001). Development of a recombinant antigen vaccine against infection with the filarial worm *Onchocerca volvulus*. Infect. Immun., **69**:262-270. PMID: 16299326; PMID: PMC1307100
2) MacDonald AJM, Turaga PSD, Harmon-Brown C, Tierney TJ, Bennett KE, McCarthy MC, Simonek SC, Enyong PA, Moukatte DW and **LUSTIGMAN S** (2002). Differential cytokine and antibody responses to adult and larval stages of *Onchocerca volvulus* consistent with the development of concomitant immunity. Infect. Immun., **70**:2796-2804. PMID: 12010965; PMID: PMC127981
3) **LUSTIGMAN S**, MacDonald AJM and Abraham D (2003). $CD4^+$ dependent immunity to *Onchocerca volvulus* third-stage larvae in humans and the mouse vaccination model: common ground and distinctions. Int. J. Parasitol., **33**:1161-1171. PMID: 13678632
4) Bethony J, Loukas A, Smout M, Brooker S, Mendez S, Plieskatt J, Goud G, **Bottazzi ME**, Zhan B, Wang Y, Williamson A, **LUSTIGMAN S**, Correa-Oliveira R, Xiao S and **Hotez PJ**. (2005). Antibodies against a secreted protein from hookworm larvae reduce the intensity of hookworm infection in humans and vaccinated laboratory animals. FASEB J, **19**:1743-1745. PMID: 16037096
5) Tchakouté VL, Graham SP, Jensen SA, Makepeace BL, Nfon CK, Njongmeta LM, **LUSTIGMAN S**, Enyong PA, Tanya VN, Bianco AE and Trees AJ (2006). In a bovine model of onchocerciasis, protective immunity exists naturally, is absent in drug-cured hosts, and is induced by vaccination. Proceedings of the National Academy of Sciences of the USA **103**: 5971–5976. PMID: 16585501; PMCID: PMC1458682
6) Fujiwara RT, Zhan B, Mendez S, Loukas A, Bueno LL, Wang Y, Plieskatt J, Oksov Y, **LUSTIGMAN S**, **Bottazzi ME**, **Hotez P** and Bethony JM (2007). Reduction of worm fecundity and canine host blood loss mediates protection against hookworm infection elicited by vaccination with recombinant Ac-16. Clin Vaccine Immunol. **14**:281-287. PMID: 17267592; PMCID: PMC1828853
7) MacDonald AJ, Libri NA, **LUSTIGMAN S**, Barker SJ, Whelan MA, Semper AE and Rosenberg WM (2008). A novel, helminth-derived immunostimulant enhances human recall responses to hepatitis C virus and tetanus toxoid and is dependent on CD56+ cells for its action. Clin Exp Immunol. **152**:265-73. PMID: 18341617; PMCID: PMC2384101
8) Xiao W, Du L, Liang C, Guan J, **Jiang S**, **LUSTIGMAN S**, He Y and Zhou Y (2008). Evaluation of recombinant Onchocerca volvulus activation associated protein-1 (ASP-1) as a potent Th1-biased adjuvant with a panel of protein or peptide-based antigens and commercial inactivated vaccines. Vaccine, 26(39):5022-5029. PMID: 18675867; PMCID: PMC2597511
9) Bergquist R, **LUSTIGMAN S** (2010) Control of important helminthic infections: Vaccine development as part of the solution. Advances in Parasitology, **73**:297-326. PMID: 20627146
10) Zhan B, Perally S, Brophy PM, Xue J, Goud G, Liu S, Deumic V, de Oliveira LM, Bethony J, **Bottazzi ME**, Jiang D, Gillespie P, Xiao SH, Gupta R, Loukas A, Ranjit N, **LUSTIGMAN S**, Oksov Y, **Hotez P** (2010). Molecular Cloning, Biochemical Characterization and Partial Protective Immunity of the Heme-binding Glutathione S-Transferases from the Human Hookworm *Necator americanus*. Infection and Immunity, **78(4):**1552-63. PMID: 20145100; PMCID: PMC2849424

D. Research Support

Ongoing Research Support

1. 1R01AI078314-01A2 Lustigman (PI) 8/2009 – 7/2014

The development of a recombinant vaccine against human onchocerciasis

The proposal is focused on the preclinical research and development process that will result, through a robust screening process, with the discovery of the best 2 recombinant O. volvulus vaccine antigens with the highest

probability for success at inducing protective immunity in humans. The vaccine will target the O. volvulus larvae, known to be vulnerable to host immunological attack.

The product development aspect of the project is being done in collaboraiton with the Human Hookworm Vaccine Initiatve at the George Washington University and headed by Dr. Peter Hotez. My Co-investigators at the GWU are: Drs. Maria Elena Botazzi and Bin Zhan.
Role:PI

2. R01 AI072465-01A1 Unnasch T (PI) 5/08 – 4/12
Mapping Protein Interactions between Filaria and its Wolbachia Endosymbiont
The overall goal of this proposal will be to identify the proteins that are involved in this endosymbiotic relationship between *Wolbachia* and the filarial parasite *Brugia malayi* and then to establish the functional networks of the genes involved in the process.
Role: Co-Investigator

3. OPP1017584 (Bill & Melinda Gates Foundation) (PI: J. McKerrow) 10/31/2010 – 10/31/2012
Developing a macrofilaricial drug for onchocerciasis using Anacor's novel oxaborole technology
A collaborative research effort between the University of California San Francisco Sandler Center, Anacor Pharmaceuticals and LFKRI of the NYBC to discover new drug therapies for the treatment of river blindness (onchocerciasis). The collaboration's goal is to identify a novel, potent macro-filaricidal drug candidate that is capable of killing adult worms.
Role: Co-Investigator

4. (b)(4) Pilot Research Project Lustigman (PI) 11/09 – 6/11
Nonhuman primate pilot study of a novel protein adjuvant for vaccines against human pathogens
To maximize the possible therapeutic applications of rOv-ASP-1 as an immunopotentiating adjuvant for human use, we will test its adjuvanticity in a higher animal species and determine whether a reasonable dose can be safely and effectively used in non-human primates (6 animals).
Role: PI

Completed Research Support

1. 1R56AI069547-01A2 Lustigman S (PI) 9/1/2008- 2/28/2010
Malaria in Brazil: RBC variants & parasite invasion
To establish whether molecular variation in the *GYPB* gene, particularly the one that generates the *GYPB*S/s* alleles, influences host susceptibility to infection with *P. falciparum* in Brazilian Amazon endemic regions.

2. 3R56AI069547-01A2S1 Lustigman (PI) 9/1/2009 – 2/28/2010
Malaria in Brazil: RBC variants & parasite invasion
To study the association between P. falciparum ligand polymorphisms and the RBC invasion profiles used by the Amazonian field isolates and/or the ability of the variant ligand to bind to RBCs with defined phenotypes.

3. WHO/TDR: T24/181/103 A50594 Lustigman (PI) 10/15/07 – 2/28/09
Discovery of novel filaria drug targets using comparative genomics and RNA interference
To identify a high priority targets for macrofilaricide drug discovery using RNAi of target genes identified using bioinformatic filters to be essential for the development of the filarial nematode *Brugia malayi*.

4. R03 TW07349-01 Lustigman (PI) 7/1/2005 – 6/30/2009
Malaria Invasion via Glycophorin B in Brazilian Isolates
The establish the use of GPB mediated pathway of invasion in field parasite isolates from Porto Velho, Rondonia and then validate the importance of distinct GPB variant regions for invasion into RBCs**.**

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Chien-Te Kent Tseng	Associate Professor
eRA COMMONS USER NAME eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
National Chung-Hsing University, Taiwan	B.S.	1974-77	Plant Pathology
Mississippi State University, Starkville, MS	M.S.	1979-81	Immunobiology
University of Arkansas for Medical Sciences, Little Rock	Ph.D.	1994-97	Immunology

A. Personal Statement

The goal of this proposal is to evaluate the efficacy of a subunit of SARS-CoV S protein, termed Receptor Binding Domain (RBD) protein, as a lead candidate vaccine against SARS-CoV infection both in *vitro* and in two well-established mouse models for lethal SARS-CoV infection. Specifically, we plan to establish the best strategy to 1) express the recombinant (r) RBD protein, 2) optimize the vaccination regimens, 3) evaluate the duration of the immunogenicity, 4) protect against diseases and mortality associated with SARS-CoV infection and, finally, 5) minimize or even eliminate the concern of vaccination-induced enhancement of diseases. I have the expertise, leadership, and hands-on experience to successfully carry out the proposed studies with my team members at UTMB in testing the efficacy in mouse models. These two lethal mouse models for SARS-CoV infection are wild-type (*wt*) *Balb/c* mice challenged with mouse-adapted (MA) SARS-CoV (MA-15) and transgenic mice expressing human angiotensin-converting enzyme 2 and challenged with clinical isolates of SARS-CoV, designated "*wt* mice/MA-15" and "ACE2 Tg^+ mice/SARS-CoV," respectively. Specifically, we will initially employ the *wt* mice/MA-15 model to evaluate the protective efficacy of the recombinant (r) RBD-based vaccine following an optimized vaccination regimen with regard to antigen dose/s, vaccination frequency and intervals, as well as adjuvant formulation. Once we have achieved a positive outcome in the "*wt* mice/MA-15" model, we will validate, by using the other mouse model (i.e., ACE2 Tg^+ mice/SARS-CoV), the protective efficacy of the candidate vaccine against both homologous and heterologous clinical isolate/s of SARS-CoV. To assess the efficacy of this rRBD-based vaccine in mice, we will determine 1) titers of RBD-specific, non-neutralizing antibodies, 2) magnitudes of specific T cell responses in vaccinated mice prior to viral challenge, 3) yields of infectious progeny viruses within the lungs, 4) lung pathology emphasizing an assessment of eosinophilic infiltration (if any), 5) clinical manifestations (e.g., weight loss), and, finally, 6) the accumulated mortality-rate in vaccinated versus unvaccinated mice. All of the methodologies required for the proposed studies have been well-established in our laboratories. The UTMB team is comprised of highly experienced scientists (and their staff) from the Departments of Microbiology and Immunology and Pathology, the Center for Biodefense and Emerging Diseases, and the Sealy Center for Vaccine Development (SCVD). This multidisciplinary team has the required experience and complementary expertise to undertake this important task. Furthermore, the team has a well-established, collaborative track-record specifically on the mouse models for SARS since 2003. The Galveston National Laboratory at UTMB, where the proposed work will be conducted, has the necessary infrastructure in terms of state-of-the- art animal and bio-containment facilities required to effectively accomplish the proposed studies within the time-frame proposed. With the support of various funding sources (NIH/NIAID and private sectors), I have been working on vaccine and antiviral evaluation over the past few years and have gained substantial experience. With my experience, dedication, and enthusiasm on SARS research, I feel confident to lead this UTMB SARS research team to complete the experiments proposed for this RO1 application in a timely, thorough, and professional manner.

B. Positions and Honors

1981-1985	Research Assistant	Poultry Disease Research Center, Athens, Georgia
1985-1988	Research Associate	Alton Ochesner Medical Foundation, New Orleans, LA
1988-1993	Senior Research Associate	University of Texas Health Science Center at Houston, TX
1993-1994	Research Scientist	University of Arkansas for Medical Sciences, Little Rock, AR
1994-1997	Ph.D. student	University of Arkansas for Medical Sciences, Little Rock, AR
1997-2001	Postdoctoral Fellow	University of Texas Medical Branch, Galveston, TX
2001-2003	Instructor	University of Texas Medical Branch, Galveston, TX
2003-2007	Assistant Professor	University of Texas Medical Branch, Galveston, TX
2007-Present	Associate Professor	University of Texas Medical Branch, Galveston, TX

C. Selected Peer-reviewed Publications (From a total of 36)

1. Wack, A., E. Soldaini, **C. K. Tseng**, S. Nuti, G.R. Klimpel, and S. Abrignani. 2001. Binding of the hepatitis C envelope protein E2 to CD81 provides a costimulatory signal for human T cells. Eur. J. Immunol.31:166-175. [http://www.ncbi.nlm.nih.gov/pubmed/11169450]

2. **Tseng, C.K**., E. Miskovsky, M. Houghton, and G.R. Klimpel. 2001. Characterization of liver TCR$\gamma\delta$+ T cells obtained from individuals chronically infected with hepatitis C virus (HCV). Evidence for these T cells playing a role in the liver pathology associated with HCV infections. Hepatology 33: 1312-1320. [http://www.ncbi.nlm.nih.gov/pubmed/1134326]

3. **Tseng, C.K.**, and G.R. Klimpel. 2002. Binding of the hepatitis C virus envelope protein E2 to CD81 inhibits natural killer (NK) cell functions. J. Exp. Med. 195: 43-50. [PMCID: 2196015]

4. **Tseng, C.K.**, L. Perrone, H. Zhu, S. Makino, and C.J. Peters. 2005. Severe acute respiratory syndrome and the innate immune responses: Modulation of effector cell function without productive infection. J. Immunol. 174: 7977-7985. [http://www.ncbi.nlm.nih.gov/pubmed/15944304]

5**. Tseng, C.K.**, J. Tseng, L. Perrone, M. Worthy, V. Popov, and C.J. Peters. 2005. Apical entry and release of severe acute respiratory syndrome-associated coronavirus (SARS-CoV) in polarized calu-3 lung epithelial cells. J. Virology 79: 9470-9479. [PMCID: 1181546]

6. Yang, S., S-J. Chen, M-F. Hsu, J-D. Wu, **C.K. Tseng**, Y-F Liu, H-C Chen, C-W Kuo, C-S Wu, L-W. Chang, W.-C Chen, S-Y. Liao, T-Y. Chang, H-H. Hung, H-L. Shr, C-Y. Liu, Y-A Huang, L-Y. Chang, J-H. Hsu, C.J. Peters, A. H-J. Wang, and M-C. Hsu. 2006. Synthesis, crystal structure, structure-activity relationships, and antiviral activity of a potent SARS coronavirus 3CL protease inhibitor. J. Med. Chemistry 49:4971-80. [http://www.ncbi.nlm.nih.gov/pubmed/16884309]

7. Huang, C., N. Ito, **C.K. Tseng**, and S. Makino. 2006. Severe Acute Respiratory Syndrome Coronavirus 7a Accessory Protein Is a Viral Structural Protein. J. Virology 80: 7287-7294. [PMCID: 1563709]

8. **Tseng, C.T.**, Huang, C. Newman, P., Wang, N., Narayanan, K., Watts, D.M., Makino, S., Packard, M.M., Zaki, S.R., Chan, T.S. and Peters, C.J. 2007. Severe acute respiratory syndrome coronavirus infection of mice transgenic for the human angiotensin-converting enzyme 2 virus receptor. J. Virology 81: 1162-73. [PMCID: 1797529]

9. Santhana G. Devaraj, N. Wang, Z. Chen, Z. Chen, M. Tseng, N. Barretto, R. Lin, C.J. Peters, **C. K. Tseng**, S. Baker, and K. Li 2007. Regulation of IRF-3-dependent Innate Immunity by the Papain-like Protease Domain of the Severe Acute Respiratory Syndrome Coronavirus. J. Biol. Chem. 282: 32208-32221. [PMCID: 2756044, NIHMSID129989]

10. Narayanan, K., C. Huang, K.G. Lokugamage, W. Kamitani, T. Ikegami, **C.K. Tseng**, and S. Makino. 2008. Severe Acute Respiratory Syndrome Coronavirus Nsp1 Suppresses Host Gene Expression, Including Type I Interferon, in Infected Cells. Journal of Virology 82:4471-9. [PMCID: 2293030]

11. Guangyu Li', Nan Wang, Hilda Guzman, Elena Sbrana, Tomoki Yoshikawa, Chien**-Te Kent Tseng**, Robert B. Tesh, and Shu-Yuan Xiao. 2008. Dhori Virus (*Orthomyxoviridae: Thogotovirus*) Infection of Mice Produces a Disease and Cytokine Response Pattern Similar That of Highly Virulent Influenza A (H5N1). American Journal of Tropical Medicine & Hygiene 78:675-80. [http://www.ncbi.nlm.nih.gov/pubmed/18385368]

12. Lokugamage, Kumari, N. Yosikawa, N. Ito, D. Watts, N. Wang, P. Newman, **C.K. Tseng**, C.J. Peters, and S. Makino. 2008. Chimeric coronavirus-like particles carrying severe acute respiratory syndrome coronavirus

(SCoV) S protein protects mice against challenge with SCoV Vaccine 26:797-808. [PMCID: 2267761, NIHMSID39182]
13. Yoshikawa, T., T. Hill, C.J. Peters, and **C.K. Tseng** 2009. Severe acute respiratory syndrome (SARS) coronavirus-induced lung epithelial cytokines exacerbate SARS pathogenesis by modulating intrinsic functions of monocyte-derived macrophages and dendritic cells. Journal of Virology 83:3039-48. [PMCID: 2655569]
14. Yoshikawa N, T. Yoshikawa, T. Hill T, C. Huang, D.M. Watts, S. Makino, G. Milligan, T. Chan , C.J. Peters, and **C.K. Tseng**. 2009. Differential virological and immunological outcome of severe acute respiratory syndrome coronavirus infection in susceptible and resistant transgenic mice expressing human angiotensin-converting enzyme 2. Journal of Virology 83:5451-65. [PMCID: 2681954]
15. Yoshikawa T, Hill TE, Yoshikawa N, Popov VL, Galindo CL, et al. (2010) Dynamic Innate Immune Responses of Human Bronchial Epithelial Cells to Severe Acute Respiratory Syndrome-Associated Coronavirus Infection. PLoS ONE 5(1): e8729. doi:10.1371/journal.pone.0008729 [PMCID: 2806919]

D. Research Support

Ongoing Research Support:

1. Private Source (PIs: Womack, J.E. and Peters, C.J.) 07/01/10-06/30/11
Project title: Finding a novel mammalian gene for resistant to Rift Valley fever virus
Role: Co-Investigator EFFORT

2. NIH/NIAID (1R21 AI072201-01A1): NCE- 09/01/10-08/31/11
Project title: Inflammatory Responses and SARS Pathogenesis: An *In Vitro* Model.
Role: PI EFFORT

Completed Research Support:

1. NIH/NIAID (NO1- AI-30039: Couch, Robert) 07/01/05-12/31/10
Subcontract- Viral Respiratory Pathogens Research Unit (VRPRU-SARS)
The purpose is to conduct collaborative research on SARS and SARS coronavirus in an established in vitro model and in small animals for evaluating the protective efficacy of candidate vaccines.
Role: Co-investigator EFFORT

2. NIH/NIAID (NO1- AI25489: Bob Tesh):09/01/09-12/31/10 (Extension with fund)
US Based collaboration in emerging viral and prior diseases
Role: Co-investigator EFFORT of Project 3: Pathogenesis of SARS-CoV and Dhori virus (PI: CJ Peters)

3. NIH/NIAID-WRCE/Career development grant: funding extended to 2/28/10
Project title: Antiviral agents as Therapy for SARS.
Role: P.I. EFFORT

4. NIH/NIAID (NO1- AI25489: Bob Tesh):09/30/02-08/31/10
US Based collaboration in emerging viral and prior diseases
Role: Co-investigator EFFORT of Project 3: Pathogenesis of SARS-CoV and Dhori virus (PI: CJ Peters).

5. Contract/Private Source (10/01/09-9/30/10)
Project title: Genome-wide RNA interference analysis of viral-host interactions"
Role: P.I. EFFORT

6. Contract/Private Source (10/01/09-04/30/10)
Project title: Evaluation of the protective efficacy of neutralizing antibodies raised against hydrophobic heptad repeat (HR) of the Spike protein of coronaviruses against SARS-CoV infection in transgenic mice.
Role: P.I. EFFORT

7. Contract/Private Source 07/01/07-12/31/09
Project title: Micro-neutralization test for the samples obtained from vaccinated animals.

8. Contract/AlphaVax (07/01/08-8/31/09)
Project title: Evaluation of the efficacy of recombinant VEE-based vaccines against SARS- CoV infection in transgenic mice
Role: P.I. EFFORT

9. NIH/NIAID (R21 AI-063118-01: Chan, Tehsheng): 09/01/05-08/31/07
Project title: SARS: A transgenic mouse model for pathogenesis, treatment, and vaccine studies. Role: Co-investigator EFFORT

10. NIH/NIAID (NO1-AI-15435: Chan, Tehsheng): 09/14/06 – 03/31/08
Project title: SARS Lung Mouse Model
Role: Co-investigator EFFORT
11. Private Source Tseng, Chien-Te Kent): 09/01/05-06/30/07
Project title: Evaluation of anti-SARS compounds in animal models
The contractor will evaluate the efficacy of selected compounds developed by TaiGen Biotechnology against SARS-CoV replication and/or associated pathogenesis in newly established mouse models and hamsters.
Role: PI EFFORT
12. Private Source (C.J. Peters) 01/06/05-09/29/06
Preparation of inactivated SARS antigen
This is a subcontract for the manufacture of bulk samples of inactivated SARS-CoV strain Urbani.
Role: Co-investigator EFFORT

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Du, Lanying	Assistant Member
eRA COMMONS USER NAME (credential, e.g., agency login) eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Peking Union Medical College, Beijing, China	B.S.	1995	Basic Medicine
Peking University, Beijing, China	M.S.	2003	Pathogenic Biology
The University of Hong Kong, Hong Kong, China	Ph.D.	2007	Microbiology & Immunology
Lindsley F. Kimball Research Institute New York Blood Center, New York	Postdoctoral	2010	Immunology & Virology

A. Personal Statement

The goal of the proposed study is to develop a highly promising lead candidate vaccine against severe acute respiratory syndrome (SARS), the first new human infectious disease of this century classified by NIAID as a Category C biodefense. The vaccine will be designed based on the receptor binding domain (RBD) of SARS-coronavirus (SARS-CoV) spike (S) protein, a region that induced highly potent neutralizing antibodies and protection against virus infection. The vaccine candidate will be further scaled up, characterized, and tested for stability, then goes to technology transfer, cGMP manufacture, GLP toxicology and investigational new drug (IND) preparation and filing. I have strong scientific background in microbiology, molecular biology, cell biology, immunology and other related fields. As the Co-Investigator and an Assistant Member in the laboratory of Dr. Shibo Jiang, the PI#2 of this project, I currently focus my research on the development of recombinant protein vaccines against emerging infectious diseases, particularly SARS and influenza, and evaluated the immune efficacy of these vaccines in different animal models. With extensive experience in protein expression and purification, detection of pseudovirus-based neutralizing activity as well as cross-protection against virus infection, I have developed several important SARS subunit vaccines based on the recombinant RBD protein of SARS-CoV in different expression systems and demonstrated their high potency in inducing strong neutralizing antibodies and complete protection against virus challenge. My research findings related to SARS have been published in around 20 peer-reviewed journals and presented in a number of national and international conferences. My strong background and extensive experience in SARS study have demonstrated my ability to serve as the key researcher in the proposed project.

B. Positions and Honors

Positions and Employment

1995-96 Research Assistant, Beijing BioTinge-Tech Center for Biotechnology, Chinese Academy of Medical Sciences, Beijing, China
1996-99 Senior Researcher, Dept. of Biochemistry and Clinical Diagnosis, Beijing Company of Modern Bio-Technology LTD, Beijing, China
1999-03 Pre-doctoral researcher, School of Basic Medical Sciences, Peking University Health Science Center, Peking University, Beijing, China
2002-03 Research Assistant, Vascular Bioengineering Laboratory, Dept. of Surgery and Bioengineering, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

2003-07 Postgraduate, Dept. of Microbiology, Li Ka Shing Faculty of Medicine, University of Hong Kong, Hong Kong
2007-10 Postdoctoral Research Fellow, Viral Immunology Laboratory, Lindsley F. Kimball Research Institute, New York Blood Center, NY, USA
2010-11 Senior Research Fellow, Viral Immunology Laboratory, Lindsley F. Kimball Research Institute, New York Blood Center, NY, USA
2011- Assistant Member, Viral Immunology Laboratory, Lindsley F. Kimball Research Institute, New York Blood Center, NY, USA

Other Experience and Professional Memberships

2001- The Chinese Society of Medical Sciences, Member
2001- The Chinese Microbiology Society, Member
2005- American Society for Virology, Associate Member
2008- American Society for Microbiology, Postdoctoral Member
2008- Canadian Journal of Microbiology, Invited Reviewer
2008- Viral Immunology, Invited Reviewer
2010- American Association of Immunologists, Regular Member
2010- New York Academy of Sciences, Member

Honors

2003-07 Postgraduate Scholarship Award, the University of Hong Kong
2006 Conference Grant Award, the University of Hong Kong, the Committee on Research and Conference Grants (CRCG) for Research Students
2006 Travel Grant Award, the 16th European Congress of Clinical Microbiology and Infectious Diseases (16th ECCMID)
2006 Student Travel Grant Award, the 2006 American Society for Virology 25th Annual Meeting (25th ASV)
2008 Postdoctoral Fellow Travel Grant Award, the 2008 American Society for Virology 27th Annual Meeting (27th ASV)
2009 Financial Aid for attending 2009 Cold Spring Harbor Laboratory meeting on harnessing immunity to prevent and treat disease.
2010 New York Blood Center 2010 Quarterly Employee Recognition Award

C. Selected Peer-reviewed Publications (Selected from 35 peer-reviewed publications)

Most relevant to the current application (in chronological order)

1. **Du L**, Zhao G, He Y, Guo Y, Zheng BJ, **Jiang S**, Zhou Y. Receptor-binding domain of SARS-CoV spike protein induces long-term protective immunity in an animal model. *Vaccine.* 2007;25(15):2832-2838. http://www.ncbi.nlm.nih.gov/pubmed/17092615
2. **Du L**, Zhao G, Lin Y, Sui H, Chan C, Ma S, He Y, **Jiang S**, Wu CY, Yuen KY, Jin DY, Zhou Y, Zheng BJ. Intranasal vaccination of recombinant adeno-associated virus encoding receptor-binding domain of severe acute respiratory syndrome coronavirus (SARS-CoV) spike protein induces strong mucosal immune responses and provides long-term protection against SARS-CoV infection. *J Immunol.* 2008;180(2):948-956. PMC2603051
3. **Du L**, He Y, Zhou Y, Liu S, Zheng BJ, **Jiang S**. The spike protein of SARS-CoV – a target for vaccine and therapeutic development. *Nature Rev Microbiol.* 2009;7(3):226-236. PMC2750777

4. **Du L**, Zhao G, Li L, He Y, Zhou Y, Zheng BJ, **Jiang S**. Antigenicity and immunogenicity of SARS-CoV S protein receptor-binding domain stably expressed in CHO cells. *Biochem Biophys Res Commun*. 2009;384(4):486-490. PMC2750803

5. **Du L**, Zhao G, Chan CC, Sun S, Chen M, Liu Z, Guo H, He Y, Zhou Y, Zheng BJ, **Jiang S**. Recombinant receptor-binding domain of SARS-CoV spike protein expressed in mammalian, insect and E. coli cells elicits potent neutralizing antibody and protective immunity. *Virology*. 2009;393(1):144-150. PMC2753736

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

1. **Du L**, He Y, Wang Y, Zhang H, Ma S, Wong CK, Wu SH, Ng F, Huang JD, Yuen KY, **Jiang S**, Zhou Y, Zheng BJ. Recombinant adeno-associated virus expressing the receptor-binding domain of severe acute respiratory syndrome coronavirus S protein elicits neutralizing antibodies: implication for developing SARS vaccines. *Virology.* 2006;353(1):6-16. http://www.ncbi.nlm.nih.gov/pubmed/16793110

2. **Du L**, Kao RY, Zhou Y, He Y, Zhao G, Wong C, **Jiang S**, Yuen KY, Jin DY, Zheng BJ. Cleavage of spike protein of SARS coronavirus by protease Factor Xa is associated with viral infectivity. *Biochem Biophys Res Commun.* 2007;359(1):174-179. PMC2323977

3. **Du L**, Zhao G, Lin Y, Chan C, He Y, **Jiang S**, Wu C, Jin DY, Yuen KY, Zhou Y, Zheng BJ. Priming with rAAV encoding RBD of SARS-CoV S protein and boosting with RBD-specific peptides for T cell epitopes elevated humoral and cellular immune responses against SARS-CoV infection. *Vaccine.* 2008;26(13):1644-1651. PMC2600875

4. Xiao W*, **Du L***, Liang C, Guan J, **Jiang S**, **Lustigman S**, He Y, Zhou Y. Evaluation of recombinant onchocerca volvulus activation associated protein-1 (*Ov*-ASP-1) as a potent Th1-biased adjuvant with a panel of protein or peptide-based antigens and commercial inactivated vaccines. *Vaccine.* 2008;26(39):5022-5029. (*Equal first-authors). PMC2597511

5. **Du L**, He Y, **Jiang S**, Zheng BJ. Development of subunit vaccines against severe acute respiratory syndrome. *Drugs Today* (Barc). 2008;44(1):63-73. http://www.ncbi.nlm.nih.gov/pubmed/18301805

6. **Du L**, Zhao G, Chan C, He Y, Zhou Y, Zheng BJ, **Jiang S**. A 219-mer recombinant receptor-binding domain of SARS-CoV spike protein induces highly potent immune responses and protection. *Viral. Immunol.* 2010;23(2):211-219. PMC2883479

7. **Du L**, Zhou Y, **Jiang S**. Research and development of universal influenza vaccines. *Microbes Infect.* 2010;12(4):280-286. http://www.ncbi.nlm.nih.gov/pubmed/20079871

8. **Du L**, Zhao G, Zhang X, Liu Z, Yu H, Zheng BJ, Zhou Y, **Jiang S**. Development of a safe and convenient neutralization assay for rapid screening of influenza HA-specific neutralizing monoclonal antibodies. *Biochem Biophys Res Commun*. 2010;397(3):580-585. http://www.ncbi.nlm.nih.gov/pubmed/20617558

9. Zhao G, **Du L**, Xiao W, Sun S, Lin Y, Chen M, Kou Z, He Y, **Lustigman S**, **Jiang S**, Zheng BJ, Zhou Y. Induction of protection against divergent H5N1 influenza viruses using a recombinant fusion protein linking influenza M2e to Onchocerca volvulus activation associated protein-1 (ASP-1) adjuvant. *Vaccine* 2010;28(44):7233-7240. http://www.ncbi.nlm.nih.gov/pubmed/20732469

10. **Du L**, Leung VH, Zhang X, Zhou J, Chen M, He W, Zhang HY, Chan CC, Poon, VK, Zhao G, Sun S, Cai Li, Zhou Y, Zheng BJ, **Jiang S**. A recombinant vaccine of H5N1 HA1 fused with foldon and human IgG Fc induced complete cross-clade protection against divergent H5N1 viruses. *PLoS One* 2011;6(1):e16555. PMC3029370

Relative patent to the current application

1. **Jiang S**, **Du L**. Immunopotentiator-linked oligomeric influenza immunogenic compositions. Filed October 05, 2010. *US Serial No*. 61/106,101.
2. **Jiang S**, **Du L**, Zhou Y. Influenza hemagglutinin-specific monoclonal antibodies for preventing and treating influenza virus infection. Filed October 20, 2010. *US Serial No*. 61/405,100.

D. Research Support

Ongoing Research Support

1R03 AI088449-01A1 Du (PI) 2011 – 2012 NIH/NIAID
Rational design of M2e-FP conserved epitope-based universal influenza A vaccines
The goal of this project is to develop recombinant protein-based universal influenza vaccines using conserved sequences of M2e and HA fusion peptide of H5N1 virus.
Role: PI
Overlap: None

Completed Research Support

1R01 AI68002-04 Jiang (PI) 2007 – 2011 NIH/NIAID
SARS-CoV S protein receptor-binding domain-based vaccines
The goal of this project is to express RBD of SARS-CoV S protein in E. coli or yeast systems as subunit vaccines for prevention of SARS.
Role: Research Fellow
Overlap: None

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Bin Zhan	POSITION TITLE Research Professor
eRA COMMONS USER NAME	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing,*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Fujian Medical College, Fuzhou, China	M.D.	1983	Medicine
Chinese Academy of Preventive Medicine, Shanghai, China	M.S.	1989	Parasitology
University of Texas Medical Branch at Galveston, Galveston, Texas	Postdoctoral	1994	Molecularbiology

A. Personal Statement

I decided to dedicate myself to the infectious diseases and parasitological research when I realized so many people in my country and other developing countries suffer from the infectious and parasitic diseases during my study in medical college. Soon after I received my MD degree I joined the fight against infectious diseases and parasites with multidisciplinary studies of epidemiology, immunology, and molecular biology of malaria, leishmania and hookworm. Particularly, I have focused my research on developing human hookworm vaccines since 2000 when the Human Hookworm Vaccine Initiative (HHVI) was funded by Private Source Private Source My research includes the discovery and cloning of novel hookworm antigens by immunological and molecular biological methods, characterizing their biological functions in the survival of hookworm in the host as well as evaluating their potential as protective antigens and/or hookworm vaccines. From my work, more than 40 new hookworm antigens as well as their DNA have been identified and cloned from different species and stages of hookworm. Many of them have been characterized and tested for their vaccine potential. Some of these vaccine candidates are in process development and pilot manufacture for clinic trials. Except for vaccine development for hookworm I also devote myself into the vaccine research against other parasitic infection such as malaria, leishmania, chagas disease and Onchocerchiasis. I have more than 60 publications in peer-reviewed journals. Due to my successful and productive research work in molecular biology, immunology and infectious diseases, I am confident that I can co-lead the proposed project with my expertise and experience.

B. Positions and Honors.

Position and Employment

1983 - 1986 Assistant lecturer, Fujian Medical College, Fuzhou, China
1989 - 1984 Assistant professor, Chinese Academy of Preventive Medicine, Institute of Parasitic Diseases, Shanghai, China.
1994 - 1994 Research Associate, New York Medical College, Valhalla, NY
1994 - 1996 Post Doctoral Fellow, University of Texas Medical Branch, Galveston, TX
1996 - 1997 Visiting scientist, Yale University Medical School, New Haven, CT.
1997 - 2000 Associate Professor, Chinese Academy of Preventive Medicine, Institute of Parasitic Diseases, Shanghai, China.
2000 - 2003 Assistant Research Professor, The George Washington University Medical Center, DC
2004 - 2008 Associate Research Professor, The George Washington University Medical Center, DC
2009 - present Research Professor , The George Washington University Medical Center, DC

Other Experience and Professional Memberships

1998 – 2000 Acting Chief, Department of Pharmacology, Chinese Academy of Preventive Medicine, Institute of Parasitic Diseases, Shanghai, China

2001 - Members, American Society of Parasitologist, American Society of Tropical Medicine and Hygiene Sigma XI, The Scientific Research Society

C. Selected peer-reviewed publications (in chronological order).

1. Bin Zhan, Mahnaz Badamchian, Bo Meihua, James Ashcom, Jianjun Feng, John Hawdon, Xiao Shuhua, and Peter J. Hotez. Molecular cloning and purification of Ac-TMP, a developmentally regulated putative tissue inhibitor of metalloprotease released in relative abundance by adult *Ancylostoma* hookworms. *Am. J. Trop. Med. Hyg*. 2002; 66(3):238-244.
2. Bin Zhan, Peter J Hotez, Yan Wang and John M Hawdon. A developmentally regulated metalloprotease secreted by host-stimulated *Ancylostoma caninum* third-stage infective larvae is a member of the astacin family of protease. *Mol. Biochem. Parasitol*. 2002; 120:291-296.
3. Sridhar Basavaraju, Bin Zhan, Malcolm W. Kennedy, Yueyuan Liu, John Hawdon and Peter J. Hotez . Ac-FAR-1, a 20 kDa Fatty Acid- and Retinol-Binding Protein Secreted by Adult *Ancylostoma caninum* Hookworms: gene transcription pattern, ligand binding properties and structural characterisation. *Molecular and Biochemical Parasitology*. 2003; 126:63-71.
4. Bin Zhan, Yueyuan Liu, Mahnaz Badamchian, Angela Williamson, Jianjun Feng, Alex Loukas, John M. Hawdon and Peter J. Hotez. Molecular characterization of the *Ancylostoma*-secreted Protein (ASP) family from the adult stage of *Ancylostoma caninum*. *Int. J. Parasitol*. 2003; 33:897-907.
5. Gaddam Narsa Goud, Bin Zhan, Kashinath Ghosh, Alex Loukas, John Hawdon, Azra Dobardzic, Vehid Deumic, Sen Liu, Reshad Dobardzic, Bernard C. Zook, Qun Jin, Yueyuan Liu, Laura Hoffman, Sophia Chung-Debose, Rachna Patel, Susana Mendez, and Peter J. Hotez. Cloning, yeast expression, isolation, and vaccine testing of recombinant Ancylostoma-secreted protein (ASP)-1 and ASP-2 from Ancylostoma ceylanicum. *J Infect Dis*. 2004; 189(5):919-29.
6. Bin Zhan, Yan Wang, Yueyuan Liu, Angela Williamson, Alex Loukas, John M. Hawdon, Xue Hae-chou, Xiao Shu-hua, and Peter J. Hotez. *Ac*-SAA-1, an immunodominant 16 kDa surface-associated antigen of infective larvae and adults of *Ancylostoma caninum*. *Int. J Parasitol.* 2004; 34:1037-45.
7. Bin Zhan, Sen Liu, Samirah Perally, Jian Xue, Ricardo Fujiwara, Peter Brophy, Shuhua Xiao, Yueyuan Liu, Jianjun Feng, Angela Williamson, Yan Wang, Lilian L. Bueno, Susana Mendez, Gaddam Goud, Jeffrey M. Bethony, John M. Hawdon, Alex Loukas, Karen Jones and Peter J. Hotez.Biochemical characterization and vaccine potential of a heme binding glutathione transferase (GST) from the adult hookworm *Ancylostoma caninum*. *Infection and Immunity* 2005; 73(10):6903-11.
8. Susana Mendez, Bin Zhan, Gaddam Goud, Kashinath Ghosh, Azra Dobardzic, Wenhui Wu, Sen Liu, Vehid Deumic, Reshad Dobardzic, Yueyuan Liu, Jeff Bethony and Peter J. Hotez. Effect of combining the larval antigens *Ancylostoma* Secreted Protein 2 (ASP-2) and metalloprotease 1 (MTP-1) in protecting hamsters against hookworm infection and disease caused by *Ancylostoma ceylanicum*. *Vaccine*. 2005; 23:3123-30.
9. Jianjun Feng, Bin Zhan, Yueyuan Liu, Sen Liu, Angela Williamson, Gaddam Goud, Alex Loukas, Peter Hotez. Molecular cloning and characterization of *Ac*-MTP-2, an astacin-like metalloprotease released by adult *Ancylostoma caninum*. *Mol. and Biochem. Parasitol.* 2007; 152(2):132-8.
10. Ricardo Fujiwara, Bin Zhan, Susana Mendez, Alex Loukas, Lilian L. Bueno, Yan Wang, Jordan Plieskatt, Yelena Oksov, Sara Lustigman, Maria Elena Bottazzi, Peter Hotez and Jeffrey M. Bethony. Reduction of worm fecundity and canine host blood loss mediates protection against hookworm infection elicited by vaccination with recombinant Ac-16. *Clin Vaccine Immunol*. 2007;14(3):281-7.
11. Shuhua Xiao, Bin Zhan, Jian Xue, Gaddam Narsa Goud, Alex Loukas Yueyuan Liu, Angela Williamson, Sen Liu, Vehid Deumic, Peter Hotez. The evaluation of recombinant hookworm antigens as vaccines in hamsters (*Mesocricetus auratus*) challenged with human hookworm, *Necator americanus*. *Experimental Parasitology*, 2008;118(1):32-40.
12. Ranjit N, Zhan B, Stenzel DJ, Mulvenna J, Fujiwara R, Hotez PJ, Loukas A. A family of cathepsin B cysteine proteases expressed in the gut of the human hookworm, *Necator americanus.* Mol Biochem Parasitol. 2008;160(2):90-9.
13. Zhan B, Gupta R, Wong SP, Bier S, Jiang D, Goud G, Hotez P._Molecular cloning and characterization of

Ac-TMP-2, a tissue inhibitor of metalloproteinase secreted by adult *Ancylostoma caninum*. Mol Biochem Parasitol. 2008 Dec;162(2):142-8

14. Ranjit N, Zhan B, Hamilton B, Stenzel D, Lowther J, Pearson M, Gorman J, Hotez P, Loukas A. Proteolytic Degradation of Hemoglobin in the Intestine of the Human Hookworm *Necator americanus*. J Infect Dis. 2009;199(6):904-12.
15. Bin Zhan, Samirah Perally, Peter M Brophy, Jian Xue, Gaddam Goud, Sen Liu, Vehid Deumic, Luciana M de Oliveira. Jeffrey Bethony. Desheng Jiang, Portia Gillespie, Shu-hua Xiao, Richi Gupta, Alex Loukas, Najju Ranjit, Sara Lustigman, Yelena Oksov, Peter Hotez. Molecular Cloning, Biochemical Characterization, and Vaccine Potential of the Heme-binding Glutathione Transferases from the Human Hookworm *Necator americanus*. Infection and Immunity, 2010, 78(4):1552-63

C. Research Support

Ongoing Research Support

32472 Hotez (PI) 08/01/2000 – 07/31/2011
Human Hookworm Vaccine Initiative 1
The Bill and Melinda Gates Foundation via Albert B. Sabin Vaccine Institute
Human Hookworm Vaccine Initiative (HHVI): Clinical Development & Evaluation of the *Na*-ASP-2 Hookworm Vaccine
The goal of this study is to continue product development, including the manufacture of a second pilot lot, and to conduct a global health impact analysis of the human hookworm vaccine with the Sabin Vaccine institute.
Role: Unit Director - Hookworm Antigen Discovery

38988 Hotez (PI) 08/01/2006 – 07/31/2011
Human Hookworm Vaccine Initiative 2
Human Hookworm Vaccine Initiative (HHVI): To develop and test the Na-APR-1 Hookworm Vaccine
The goal of this study is to conduct the process development, cGMP manufacture and testing, and clinical evaluation of APR-1 in order to develop a bivalent human hookworm vaccine with the Sabin Vaccine Institute
Role: Unit Director - Hookworm Antigen Discovery

1 R01A1078314-01 Lustigman (PI) 08/25/2009 – 7/31//2014
NIH/NIAID
The development of a recombinant vaccine against human onchocerciasis
The major goal of this subcontract is clone, express, characterize and optimize the expression of the eight selected Onchocerca vaccine candidate antigens (r*Ov*Ags) using the yeast *Pichia* eukaryotic system.
Role: Co-PI

2R01AI056189 - 06A1 Aroian (PI) 08/01/2010 – 07/31/2012
NIH
B. thuringiensis Crystal Proteins as Powerful Next-Generation Anthelmintics
The major goal of this subcontract is to test the effects of different formulated Cry5B against hookworm using *Ancylostoma ceylanicum*/hamster model
Role: Co-PI

Bottazzi/Bethony (MPI) 01/01/2011-12/31/2014
Sponsor Ministry of Foreign Affairs, The Netherlands
Product Development Support of the Human Hookworm Vaccine

The ultimate goal of the project is to conduct Phase 1 studies to assess the safety and immunogenicity of the *Na*-GST-1 and *Na*-APR-1 hookworm antigens in both adults and children.
Role: Director of Molecular Biology

Hotez (PI) 09/01/2011 – 07/31/2016
Sponsor: Private Source
Human Hookworm Vaccine Initiative 3
Title: Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.
Role: Director of Molecular Biology

1 R01A1078314-01A2 Lustigman (PI) 08/25/2009 – 07/31/2014
NIH/NIAID (Subcontract from New York Blood Center)
The development of a recombinant vaccine against human onchocerciasis
The major goal of this subcontract is clone, express, characterize and optimize the expression of the eight selected Onchocerca vaccine candidate antigens (r*Ov*Ags) using the yeast *Pichia* eukaryotic system.
Role: Co-PI

Completed Research Support

1 R43 CA123991-01A2 Bonafe 06/01/2008 – 05/31/2009
NIH/NCI Phase I SBIR
Glioma therapeutics targeting glioma pathogenesis-related protein
The major goal is to produce recombinant proteins using the yeast *Pichia* eukaryotic system in order to express and purify the glioma pathogenesis-related protein.

Chinese National Natural Science Foundation Zhan (PI) 1992 - 1994
Application of Polymerase Chain Reaction on the diagnosis of malaria. A novel PCR method was developed to diagnose malaria (*Plasmodium falciparum*) with high sensitivity and specificity

P50 AI039461 Feng (PI) 1997 - 2000
NIH/NIAID TMRC in China
Emerging Infectious Diseases in China.
My study part is to perform a epidemiological investigation of hookworm infection in China and identify the genetic variation of hookworm from different parts of China.
Role: Co-PI

Private Source Bottazzi (PI) 11/01/2006 - 10/31/2008 on NCE to 10/31/2009
Ancylostoma Caninum derived antigens as potential veterinary diagnostic tools.
The major goal is to explore the possibility of identifying relevant new tools and develop them for the diagnosis of hookworm disease in dogs.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Teh-sheng Chan	Professor
eRA COMMONS USER NAME eRA Commons User Name	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Natl. Taiwan Univ., College of Medicine	M.D.	1963	Medicine and Surgery
Yale University	Ph.D.	1969	Molecular Biophysics
Rockefeller University	Postdoc	1969-71	Microbial Genetics
Massachusetts Institute of Technology	Postdoc	1971-73	Somatic Cell Genetics

A. Personal Statement

As a co-investigator of this grant application, I will be responsible for breeding, genotyping, and characterizing transgenic mice expressing the human ACE2 gene. Publications 12 and 13 listed below describe the properties of two of the transgenic lineages, and their use as lethal and nonlethal models for SARS infection. Either or both lineages will be suitable for vaccine studies, with various end-points for assessing vaccine efficacies. I am the originator of these lines and have been collaborating with Dr. C.-T. K. Tseng and his group on different SARS research projects since the outbreak of SARS in 2002. The most recent research interest has focused on the role of cytokines in the pathogenesis of SARS by using several lines of mouse knock-out mutants. Thus, our group and that of Dr. Tseng have formed a productive team tackling several aspects of SARS infection.

My other ongoing research project is to develop a new, improved mouse model for SARS, by using knock-in technology.

B. Positions and Honors

Positions and Employment

1962-1963 Intern, National Taiwan University Hospital, Taipei
1969-1971 Postdoctoral Fellow, Rockefeller University (Dr. Norton Zinder), New York
1971-1973 Research Associate, Massachusetts Institute of Technology (Dr. Howard Green), Cambridge
1973-1978 Assistant Professor, Dept. of Physiology, University of Connecticut Health Center, Farmington
1978-1993 Associate Professor, Dept. of Microbiology, University of Texas Medical Branch, Galveston
1993-Present Professor, Dept. of Microbiology and Immunology, University of Texas Medical Branch

Awards and Honors:

1963 *Summa cum laude*, Natl. Taiwan Univ. College of Medicine
1963 Formosan Medical Association Award
1969-1972 Helen Hay Whitney Fellowship Award
1992 The Best Original Research Article Award. *J. Genet. Mol. Biol.*
1993 The Distinguished Teaching Award, University of Texas Medical Branch

C. Selected Peer-Reviewed Publications (selected from 57 peer-reviewed publications)

1. **Chan, T.-s.** and A. Garen. Amino acid substitution resulting from suppression of nonsense mutations, V. Tryptophan insertion by Su9+ suppressor gene. *J. Mol. Biol.* 49:231-234; 1970. [http://www.ncbi.nlm.nih.gov/pubmed/4317908]
2. **Chan, T.-s.**, R. W. Webster, and N. D Zinder. Suppression of UGA codon by a tryptophan tRNA. *J. Mol. Biol.* 56:101-116; 1971. [http://www.ncbi.nlm.nih.gov/pubmed/4929882]

3. Green, H. and **T.-s. Chan**. Pyrimidine starvation induced by adenosine in fibroblasts and cells of lymphoid origin: the role of adenosine deaminase. *Science* 182:836-837; 1973. [http://www.ncbi.nlm.nih.gov/pubmed/ 4795749]
4. **Chan, T.-s**. Deoxyguanosine toxicity on lymphoid cells as a cause for immunosuppression in purine nucleoside phosphorylase deficiency. *Cell* 14:523-530; 1978. http://www.ncbi.nlm.nih.gov/pubmed/ 99242
5. **Chan, T.-s**. Purine excretion by macrophages lacking adenosine deaminase activity. *Proc. Natl. Acad. Sci.* USA 76:925-929; 1979. [http://www.ncbi.nlm.nih.gov/pubmed/311477]
6. Sun, J., F. Bodola, X. Fan, H. Irshad, L. Soong, S. M. Lemon and **T.-s. Chan**. Hepatitis C virus core and envelope proteins do not suppress the host ability to clear a hepatic viral infection. *J. Virol.*, 25:11992-11998; 2001. [http://www.ncbi.nlm.nih.gov/pubmed/11711589]
7. Young, H. W., J. G. Molina, D. Dimina, H. Zhong, M. Jacobson, L. N. Chan, **T.-s. Chan**, J. J. Lee, M. R. Blackburn. A3 adenosine receptor signaling contributes to airway inflammation and mucus production in adenosine deaminase-deficient mice. *J. Immunol*. 173: 1380-1389; 2004. [http://www.ncbi.nlm.nih.gov/pubmed/15240734]
8. Sun, J, B. Tumurbaatar, J. Jia, H. Diao, F. Bodola, S. M. Lemon, W. Tang, D. G. Bowen, G. W. McCaughan, P. Bertolino and **T.-s. Chan**. Parenchymal expression of CD86/B7.2 contributes to hepatitis C virus-related liver injury. *J. Virol*. 79:10730-10739, 2005. [http://www.ncbi.nlm.nih.gov/pubmed/16057865]
9. Korenaga, M., **T.-s. Chan**, J. Sun, S. Weinman. Hepatitis C virus core protein inhibits mitochondrial electron transport and increases ROS production. *J. Biol. Chem*. 280:37481-37488, 2005 [http://www.ncbi.nlm.nih.gov/pubmed/16150732]
10. Tumurbataar, B., Y. Sun, **T. Chan**, J. Sun. Cre-estrogen receptor-mediated hepatitis C virus structural protein expression in mice. *J. Virol. Methods*. 146: 5-13, 2007. [PMCID: 2104783]
11. Tseng, K. C.-T., C. Huang, P. Newman, N. Wang, K. Narayanan, D. Watts, S. Makino, M. Packard, S. R. Zaki, **T.-s. Chan**, C. J. Peters. Severe acute respiratory syndrome coronavirus infection of mice transgenic for the human angiotensin-converting enzyme 2 virus receptor. *J. Virol*. 81: 1162-1173, 2007. [PMCID: 1797529]
12. Yoshikawa, N., T. Yoshikawa, T. Hill, C. Huang, D. M. Watts, S. Makino**, T.-s. Chan**, C. J. Peters, and C.-T. K. Tseng. Differential virological and immunological outcome of severe acute respiratory syndrome-coronavirus (SARS-CoV) infection of susceptible and resistant transgenic mice expressing human angiotensin-converting enzyme 2. *J. Virol.* 83:5451-5465, 2009. [PMC2681954]
13. Desai, M. M., B. Tumurbataar, Y. Zhang, L.-N. L. Chan, J. Sun, **T.-s. Chan**. Aberrant Transcription and post-transcriptional processing of hepatitis C virus non-structural genes in transgenic mice. *Transgenic Res*. Online first™ 24 February 2011. [http://www.ncbi.nlm.nih.gov/pubmed/21347690]
14. Desai, M. M., B. Gong, **T.-s. Chan**, R. A. Davey, L. Soong. , A. A. Kolokoltsov, J. Sun. Differential Type I Interferon-Mediated Autophagic Trafficking of Hepatitis C Virus Proteins in Mouse Liver. *Gastroenterology*. In press.

C**. Research Support for Past Three Years**

Active:

1RO1 AI069142 (PI: J. Sun, Co-I: T. Chan) 12/1/2006-11/31/2011
Immune mechanism of HCV persistence and pathogenesis
The aim is to delineate the immunopathogenesis of hepatitis C using transgenic mouse models

Completed:

1 R21AI063118-01A1 (PI: Chan) 07/01/2005-06/30/2008
NIH/NIAID
Transgenic Mouse Models for Pathogenesis and Therapy
We propose to develop transgenic mouse lines to develop a SARS –murine model.

A transgenic mouse strain deficient in adenosine deaminase, which develops asthma-like disease, has been derived. The goal of this grant is to elucidate the mechanism of the asthma-like disease in this mouse model.

014029001 – NIH (PI: T. Chan) 09/14/2006 – 03/31/2008
Subaward from Utah State University (N01AI15435).
SARS lung mouse model
This contract is to develop transgenic mice expressing human ACE2 specifically in the lung for use in SARS research.

OMB Number: 4040-0001
Expiration Date: 06/30/2011

*** ORGANIZATIONAL DUNS:** 0511133300000

*** Budget Type:** ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry *** Start Date:** 05/01/2012 *** End Date:** 04/30/2013 **Budget Period** 1

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.		Peter	J	Hotez	M.D.	PD/PI	Institutional Base Salary	EFFORT			19,970.00	4,593.00	24,563.00
2.		Maria	Elena	Bottazzi	PhD	PD/PI					39,940.00	9,186.00	49,126.00
3.		Bin		Zhan	MD	Co-I					12,531.00	2,882.00	15,413.00
4.													
5.													
6.													
7.													
8.													
9.	**Total Funds requested for all Senior Key Persons in the attached file**												

Total Senior/Key Person 89,102.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Scientist for Molecular Biology	EFFORT			58,066.00	17,420.00	75,486.00
1	Associate Director for Product Development				30,750.00	9,225.00	39,975.00
1	Director, Process Development				4,870.00	1,461.00	6,331.00
1	Research Assistant				29,904.00	8,971.00	38,875.00
4	**Total Number Other Personnel**					**Total Other Personnel**	160,667.00

Total Salary, Wages and Fringe Benefits (A+B) 249,769.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 1

* ORGANIZATIONAL DUNS: 0511133300000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry * Start Date: 05/01/2012 * End Date: 04/30/2013 Budget Period 1

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.	Floor model refrigerated incubated shaker	9,600.00
2.	Sample application pump, Air Sensor and Buffer Selection kit fo	13,025.00
3.	Circular Dichroism Chiral Dector w/software	31,158.00
4.	Mobius with DLS (Zeta potential instrument with dynamic light s	62,475.00
5.	Acquitiy Fluorescence Detector	14,832.00
6.	Parallel Bioreactor System	140,000.00
7.	Biochemistry Analyzers	13,818.00
8.	Spectrophotometer	8,513.00
9.	Akta Explorer High Flow Kit	5,082.00
10.		
11.	**Total funds requested for all equipment listed in the attached file**	
	Total Equipment	298,503.00

Additional Equipment: Add Attachment | Delete Attachment | View Attachment

D. Travel

		Funds Requested ($)
1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	20,000.00
2.	Foreign Travel Costs	
	Total Travel Cost	20,000.00

E. Participant/Trainee Support Costs

		Funds Requested ($)
1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees	**Total Participant/Trainee Support Costs**

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 1

Next Period

* ORGANIZATIONAL DUNS: 0511133300000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry * Start Date: 05/01/2012 * End Date: 04/30/2013 Budget Period

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	65,231.00
2. Publication Costs	1,000.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	642,800.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping	5,000.00
9. Equipment Maintenance	9,000.00
10.	
Total Other Direct Costs	723,031.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	1,291,303.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	BCM MTDC	56.50	50,000.00	28,250.00
2.	BCM-off campus affiliate (TCH) MTDC	57.30	350,000.00	200,550.00
3.				
4.				
	Total Indirect Costs			228,800.00

Cognizant Federal Agency DHHS, ARIF KARIM, 214-767-3261

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	1,520,103.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1240-FINAL_Budg_Just.pdf Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 2

*** ORGANIZATIONAL DUNS:** 0511133300000

*** Budget Type:** ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry *** Start Date:** 05/01/2013 *** End Date:** 04/30/2014 **Budget Period** 2

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.		Peter	J	Hotez	M.D.	PD/PI	Institutional Base Salary	EFFORT			19,970.00	4,593.00	24,563.00
2.		Maria	Elena	Bottazzi	PhD	PD/PI					39,940.00	9,186.00	49,126.00
3.													
4.													
5.													
6.													
7.													
8.													

9. **Total Funds requested for all Senior Key Persons in the attached file**

Total Senior/Key Person 73,689.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Associate Director for Product Development	EFFORT			19,004.00	5,701.00	24,705.00
1	Director, Process Development				10,031.00	3,009.00	13,040.00
1	Research Scientist for upstream development				4,751.00	1,425.00	6,176.00
1	Research Scientist for downstream development				5,279.00	1,584.00	6,863.00
1	Research Assistant				30,801.00	9,240.00	40,041.00
5	**Total Number Other Personnel**					**Total Other Personnel**	90,825.00

Total Salary, Wages and Fringe Benefits (A+B) 164,514.00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 2

* ORGANIZATIONAL DUNS: 0511133300000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry * Start Date: 05/01/2013 * End Date: 04/30/2014 Budget Period 2

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
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8.		
9.		
10.		
11.	Total funds requested for all equipment listed in the attached file	
	Total Equipment	

Additional Equipment: Add Attachment Delete Attachment View Attachment

D. Travel **Funds Requested ($)**

1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	10,000.00
2.	Foreign Travel Costs	
	Total Travel Cost	10,000.00

E. Participant/Trainee Support Costs **Funds Requested ($)**

1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees	Total Participant/Trainee Support Costs

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 2

Next Period

* ORGANIZATIONAL DUNS: 0511133300000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry * Start Date: 05/01/2013 * End Date: 04/30/2014 Budget Period 2

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	60,485.00
2. Publication Costs	1,000.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	798,600.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping	5,000.00
9. Equipment Maintenance	9,000.00
10.	
Total Other Direct Costs	874,085.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	1,048,599.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	BCM-off campus affiliate (TCH) MTDC	57.30	249,999.00	143,249.00
2.				
3.				
4.				
	Total Indirect Costs			143,249.00

Cognizant Federal Agency DHHS, Arif Karim, 214-767-3261

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	1,191,848.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1240-FINAL_Budg_Just.pdf Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 3

*** ORGANIZATIONAL DUNS:** 0511133300000

*** Budget Type:** ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry *** Start Date:** 05/01/2014 *** End Date:** 04/30/2015 **Budget Period** 3

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.		Peter		Hotez		PD/PI	Institutional Base Salary	EFFORT			19,970.00	4,593.00	24,563.00
2.		Maria	Elena	Bottazzi	PhD	PD/PI					29,955.00	6,890.00	36,845.00
3.													
4.													
5.													
6.													
7.													
8.													
9.	**Total Funds requested for all Senior Key Persons in the attached file**												

Total Senior/Key Person 61,408.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Associate Director for Product Development	EFFORT			26,098.00	7,829.00	33,927.00
1	Director, Process Development				20,665.00	6,200.00	26,865.00
1	Research Scientist for Molecular Biology				6,160.00	1,848.00	8,008.00
1	Research Scientist for Upstream Development				24,467.00	7,340.00	31,807.00
1	Research Scientist for Downstream Development				27,186.00	8,156.00	35,342.00
1	Research Assistant				31,725.00	9,518.00	41,243.00
6	**Total Number Other Personnel**					**Total Other Personnel**	177,192.00

Total Salary, Wages and Fringe Benefits (A+B) 238,600.00

Close Form

RESEARCH & RELATED BUDGET - SECTION C, D, & E, BUDGET PERIOD 3

* ORGANIZATIONAL DUNS: 0511133300000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry * Start Date: 05/01/2014 * End Date: 04/30/2015 Budget Period 3

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

	Equipment item	* Funds Requested ($)
1.		
2.		
3.		
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8.		
9.		
10.		
11.	Total funds requested for all equipment listed in the attached file	
	Total Equipment	

Additional Equipment: Add Attachment Delete Attachment View Attachment

D. Travel **Funds Requested ($)**

1.	Domestic Travel Costs (Incl. Canada, Mexico and U.S. Possessions)	20,000.00
2.	Foreign Travel Costs	
	Total Travel Cost	20,000.00

E. Participant/Trainee Support Costs **Funds Requested ($)**

1.	Tuition/Fees/Health Insurance	
2.	Stipends	
3.	Travel	
4.	Subsistence	
5.	Other	
	Number of Participants/Trainees	Total Participant/Trainee Support Costs

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Close Form

RESEARCH & RELATED BUDGET - SECTION F-K, BUDGET PERIOD 3

Next Period

* ORGANIZATIONAL DUNS: 0511133300000

* Budget Type: ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry * Start Date: 05/01/2014 * End Date: 04/30/2015 Budget Period 3

F. Other Direct Costs	Funds Requested ($)
1. Materials and Supplies	71,400.00
2. Publication Costs	5,000.00
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	516,850.00
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Shipping	5,000.00
9. Equipment Maintenance	10,000.00
10. Fee-for-service: Sabin	75,000.00
Total Other Direct Costs	683,250.00

G. Direct Costs	Funds Requested ($)
Total Direct Costs (A thru F)	941,850.00

H. Indirect Costs

	Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	* Funds Requested ($)
1.	BCM-off campus affiliate (TCH) MTDC	57.30	425,000.00	243,525.00
2.				
3.				
4.				
	Total Indirect Costs			243,525.00

Cognizant Federal Agency DHHS, Arif Karim, 214-767-3261

(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)
Total Direct and Indirect Institutional Costs (G + H)	1,185,375.00

J. Fee	Funds Requested ($)

K. * Budget Justification 1240-FINAL_Budg_Just.pdf Add Attachment Delete Attachment View Attachment

(Only attach one file.)

OMB Number: 4040-0001
Expiration Date: 06/30/2011

Previous Period

RESEARCH & RELATED BUDGET - SECTION A & B, BUDGET PERIOD 4

*** ORGANIZATIONAL DUNS:** 0511133300000

*** Budget Type:** ☒ Project ☐ Subaward/Consortium

Enter name of Organization: Baylor College of Medicine

Delete Entry *** Start Date:** 05/01/2015 *** End Date:** 04/30/2016 **Budget Period** 4

A. Senior/Key Person

	Prefix	* First Name	Middle Name	* Last Name	Suffix	* Project Role	Base Salary ($)	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
1.		Peter	J	Hotez	M.D.	PD/PI	Institutional Base Salary	EFFORT			19,970.00	4,593.00	24,563.00
2.		Maria	Elena	Bottazzi	PhD	PD/PI					19,970.00	4,593.00	24,563.00
3.													
4.													
5.													
6.													
7.													
8.													
9.	**Total Funds requested for all Senior Key Persons in the attached file**												

Total Senior/Key Person 49,126.00

Additional Senior Key Persons: Add Attachment Delete Attachment View Attachment

B. Other Personnel

* Number of Personnel	* Project Role	Cal. Months	Acad. Months	Sum. Months	* Requested Salary ($)	* Fringe Benefits ($)	* Funds Requested ($)
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Associate Director for Product Development	EFFORT			6,720.00	2,016.00	8,736.00
1	Director, Process Development				10,642.00	3,193.00	13,835.00
1	Research Assistant				6,535.00	1,961.00	8,496.00
3	**Total Number Other Personnel**					**Total Other Personnel**	31,067.00

Total Salary, Wages and Fringe Benefits (A+B) 80,193.00