awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

o A list of the new and/or additional Agent(s) that will be studied;
o A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Jason A. Lundgren
Email: lundgrenj@mail.nih.gov **Phone**: 301-594-6355 **Fax**: 301 493 0597

Program Official: Erik J. Stemmy
Email: erik.stemmy@nih.gov **Phone**: (301)-402-3947

SPREADSHEET SUMMARY
GRANT NUMBER: 3R01AI098775-03S1

INSTITUTION: BAYLOR COLLEGE OF MEDICINE

Budget	Year 3	Year 4	Year 5
Salaries and Wages	$2,320		
Fringe Benefits	$182		
TOTAL FEDERAL DC	$2,502		
TOTAL FEDERAL F&A	$1,434		
TOTAL COST	$3,936	$0	$0

Facilities and Administrative Costs	Year 3	Year 4	Year 5
F&A Cost Rate 1	57.3%		
F&A Cost Base 1	$2,502		
F&A Costs 1	$1,434		

Research Supplement to Promote Diversity in Health-Related Research

http://grants.nih.gov/grants/guide/pa-files/PA-12-149.html

Principal Investigator: Peter Hotez, MD, Ph.D.

Diversity Investigator: Ebe Ewere (High School Student)

Grant #: R01 AI 98775

Program Code: M51C B

Program Official: Erik Stemmy

Form Approved Through 8/31/2015 OMB No. 0925-0001

Department of Health and Human Services
Public Health Services

Grant Application

Do not exceed character length restrictions indicated.

LEAVE BLANK—FOR PHS USE ONLY.

Type	Activity	Number
Review Group		Formerly
Council/Board (Month, Year)		Date Received

1. TITLE OF PROJECT *(Do not exceed 81 characters, including spaces and punctuation.)*

RBD RECOMBINANT PROTEIN-BASED SARS VACCINE FOR BIODEFENSE - 5R01AI098775-03

2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION ☐ NO ☒ YES
(If "Yes," state number and title)

Number: PA-12-149 Title: Research Supplements to Promote Diversity in Health Related Research

3. PROGRAM DIRECTOR/PRINCIPAL INVESTIGATOR

3a. NAME (Last, first, middle)	3b. DEGREE(S)	3h. eRA Commons User Name
Hotez, Peter	MD, PhD	eRA Commons User Name

3c. POSITION TITLE
Professor

3d. MAILING ADDRESS *(Street, city, state, zip code)*
One Baylor Plaza, BCM 113
Houston, TX 77030-3411

3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT
Pediatrics, Tropical Medicine

3f. MAJOR SUBDIVISION
College of Medicine

3g. TELEPHONE AND FAX *(Area code, number and extension)*
TEL: 713-798-1199 FAX: 713-798-2299

E-MAIL ADDRESS:
hotez@bcm.edu

4. HUMAN SUBJECTS RESEARCH	4a. Research Exempt	If "Yes," Exemption No.
☒ No ☐ Yes	☐ No ☐ Yes	

4b. Federal-Wide Assurance No.	4c. Clinical Trial	4d. NIH-defined Phase III Clinical Trial
	☐ No ☐ Yes	☐ No ☐ Yes

5. VERTEBRATE ANIMALS ☒ No ☐ Yes — 5a. Animal Welfare Assurance No

6. DATES OF PROPOSED PERIOD OF SUPPORT *(month, day, year—MM/DD/YY)*		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT	
From	Through	7a. Direct Costs ($)	7b. Total Costs ($)	8a. Direct Costs ($)	8b. Total Costs ($)
06/09/14	08/01/14	$2,502	$3,936	$2,502	$3,936

9. APPLICANT ORGANIZATION
Name Baylor College of Medicine
Address
One Baylor Plaza
Houston, TX 77030-3411

10. TYPE OF ORGANIZATION
Public: → ☐ Federal ☐ State ☐ Local
Private: → ☒ Private Nonprofit
For-profit: → ☐ General ☐ Small Business
☐ Woman-owned ☐ Socially and Economically Disadvantaged

11. ENTITY IDENTIFICATION NUMBER
1741613878A1
DUNS NO.051113330 Cong. District TX-009

12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE
Name Leanne B. Scott, Ph.D.
Title Director, Sponsored Programs
Address Baylor College of Medicine
One Baylor Plaza, BCM 310
Houston, TX 77030-3411
Tel: 713-798-1297 FAX: 713-798-6990
E-Mail: spo@bcm.edu

13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION
Name Leanne B. Scott, Ph.D.
Title Director, Sponsored Programs
Address Baylor College of Medicine
One Baylor Plaza, BCM 310
Houston, TX 77030-3411
Tel: 713-798-1297 FAX: 713-798-6990
E-Mail: spo@bcm.edu

14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF OFFICIAL NAMED IN 13. *(In ink. "Per" signature not acceptable.)*
Leanne Scott

DATE
4-30-14

PROJECT SUMMARY (See instructions):

Funds are requested for a minority supplement to the parent grant AI-098775 on the development and manufacture of a recombinant receptor-binding domain (rRBD) protein to prevent severe acute respiratory syndrome (SARS) caused by the SARS coronavirus (SARS CoV). The project will serve as a basis for engaging an under-represented minority high school student in an eight-week long mentored program of molecular biology and biochemistry research. The program will be offered in association with the Office of Diversity and Community Outreach at Baylor College of Medicine.

Briefly, the parent grant seeks to develop a recombinant vaccine against SARS, now classified by NIAID as a Category C Priority Pathogen, by advancing the vaccine through early stage expression and preclinical characterization, process development, formulation, stability, technology transfer and cGMP manufacture.

The Actual Specific Aims of the parent grant are as folows:

Specific Aim 1: Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate.

Specific Aim 2: Process development, characterization, formulation and stability profiling. In parallel to Aim 1, a scalable and reproducible fermentation process for rRBD (10 liter scale) and a purification process using chromatographic technologies will be developed.

Specific Aim 3: Technology transfer, cGMP Manufacture, GLP toxicology and IND Preparation.

With the exception of the final cGMP manufacture and preclinical testing for efficacy using a mouse challenge model all of the work is conducted at the Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development of Baylor College of Medicine.

RELEVANCE (See instructions):

Under the guidance of an experienced researcher the minority student will learn fundamental techniques in molecular biology and biochemistry. These studies will be conducted in the larger context and environment of the steps needed to develop and test recombinant protein vaccines for important infectious agents and biodefense threats including SARS. Thus we hope to stimulate the imagination of the trainee about the role he/she could one day have in the important area of public health emergency preparedness.

PROJECT/PERFORMANCE SITE(S) (if additional space is needed, use Project/Performance Site Format Page)

Project/Performance Site Primary Location		
Organizational Name: Baylor College of Medicine		
DUNS: 051113330		
Street 1: One Baylor Plaza	Street 2:	
City: Houston	County: Harris	State: TX
Province:	Country: United States of America	Zip/Postal Code: 77030
Project/Performance Site Congressional Districts: TX-009		

Additional Project/Performance Site Location		
Organizational Name: Texas Childrens' Hospital		
DUNS: 074615394		
Street 1: 1102 Bates Ave	Street 2: Ste 550	
City: Houston	County: Harris	State: TX
Province:	Country: United States of America	Zip/Postal Code: 77030
Project/Performance Site Congressional Districts: TX-009		

SENIOR/KEY PERSONNEL. See instructions. *Use continuation pages as needed* to provide the required information in the format shown below. Start with Program Director(s)/Principal Investigator(s). List all other senior/key personnel in alphabetical order, last name first.

Name	eRA Commons User Name	Organization	Role on Project
Peter Hotez, MD, PhD	eRA Commons User Name	BCM	PI
Oluwatoyin Asojo, PhD		BCM	Co-I

OTHER SIGNIFICANT CONTRIBUTORS

Name	Organization	Role on Project
James L. Phillips, MD	BCM	Diversity&Community Outreach

Human Embryonic Stem Cells ☒ **No** ☐ **Yes**

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://stemcells.nih.gov/research/registry/eligibilityCriteria.asp. *Use continuation pages as needed.*

If a specific line cannot be referenced at this time, include a statement that one from the Registry will be used.

Cell Line

Program Director/Principal Investigator (Last, First, Middle): Hotez, Peter

DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY

FROM	THROUGH
06/09/2014	08/01/2014

List PERSONNEL *(Applicant organization only)*
Use Cal, Acad, or Summer to Enter Months Devoted to Project
Enter Dollar Amounts Requested *(omit cents)* for Salary Requested and Fringe Benefits

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Peter Hotez, MD, PhD	PD/PI	0						0
Ebe Ewere	Project Intern	EFFORT			Institutional Base Salary	2,320	182	2,502
Oluwatoyin Asojo, PhD	Co-I	0						
SUBTOTALS →						2,320	182	2502

CONSULTANT COSTS	0
EQUIPMENT *(Itemize)*	0
SUPPLIES *(Itemize by category)*	0
TRAVEL	0
INPATIENT CARE COSTS	0
OUTPATIENT CARE COSTS	0
ALTERATIONS AND RENOVATIONS *(Itemize by category)*	0
OTHER EXPENSES *(Itemize by category)*	0
CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS 0
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD *(Item 7a, Face Page)*	$ 2,502
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS 0
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD	$ 2,502

BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY

BUDGET CATEGORY TOTALS	INITIAL BUDGET PERIOD *(from Form Page 4)*	2nd ADDITIONAL YEAR OF SUPPORT REQUESTED	3rd ADDITIONAL YEAR OF SUPPORT REQUESTED	4th ADDITIONAL YEAR OF SUPPORT REQUESTED	5th ADDITIONAL YEAR OF SUPPORT REQUESTED
PERSONNEL: *Salary and fringe benefits. Applicant organization only.*	2,502				
CONSULTANT COSTS					
EQUIPMENT					
SUPPLIES					
TRAVEL					
INPATIENT CARE COSTS					
OUTPATIENT CARE COSTS					
ALTERATIONS AND RENOVATIONS					
OTHER EXPENSES					
DIRECT CONSORTIUM/ CONTRACTUAL COSTS					
SUBTOTAL DIRECT COSTS *(Sum = Item 8a, Face Page)*	2,502				
F&A CONSORTIUM/ CONTRACTUAL COSTS					
TOTAL DIRECT COSTS	2,502				

TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PROJECT PERIOD $ 2,502

JUSTIFICATION. Follow the budget justification instructions exactly. Use continuation pages as needed.

The only direct costs applicable to this request are for the salary of the Project Intern for the duration of the Initial Budget Period. The Project Intern will be paid at the minimum wage rate defined by the State of Texas which is $7.25/hour. The Project Intern will work a full 40 hours for the duration of the Initial Budget Period (8 weeks or 2 months).

Program Director/Principal Investigator (Last, First, Middle): Hotez, Peter

CHECKLIST

TYPE OF APPLICATION *(Check all that apply.)*

☐ NEW application. *(This application is being submitted to the PHS for the first time.)*

☐ RESUBMISSION of application number: _____
(This application replaces a prior unfunded version of a new, renewal, or revision application.)

☐ RENEWAL of grant number: _____
(This application is to extend a funded grant beyond its current project period.)

☒ REVISION to grant number: 5R01AI098775-03
(This application is for additional funds to supplement a currently funded grant.)

☐ CHANGE of program director/principal investigator.

Name of former program director/principal investigator: _____

☐ CHANGE of Grantee Institution. Name of former institution: _____

☐ FOREIGN application ☐ Domestic Grant with foreign involvement List Country(ies) Involved:

INVENTIONS AND PATENTS *(Renewal appl. only)* ☐ No ☐ Yes

If "Yes," ☐ Previously reported ☐ Not previously reported

1. PROGRAM INCOME ***(See instructions.)***
All applications must indicate whether program income is anticipated during the period(s) for which grant support is request. If program income is anticipated, use the format below to reflect the amount and source(s).

Budget Period	Anticipated Amount	Source(s)

2. ASSURANCES/CERTIFICATIONS ***(See instructions.)***
In signing the application Face Page, the authorized organizational representative agrees to comply with the policies, assurances and/or certifications listed in the application instructions when applicable. Descriptions of individual assurances/certifications are provided in Part III and listed in Part I, 4.1 under Item 14. If unable to certify compliance, where applicable, provide an explanation and place it after this page.

3. FACILITIES AND ADMINSTRATIVE COSTS (F&A)/ INDIRECT COSTS. See specific instructions.

☒ DHHS Agreement dated: 03/02/2010; 06/24/2010 ☐ No Facilities And Administrative Costs Requested.

☐ DHHS Agreement being negotiated with _____ Regional Office.

☐ No DHHS Agreement, but rate established with _____ Date _____

CALCULATION* *(The entire grant application, including the Checklist, will be reproduced and provided to peer reviewers as confidential information.)*

a. Initial budget period:	Amount of base $	2,502	x Rate applied	57.3	% = F&A costs	$	1,434
b. 02 year	Amount of base $		x Rate applied		% = F&A costs	$	
c. 03 year	Amount of base $		x Rate applied		% = F&A costs	$	
d. 04 year	Amount of base $		x Rate applied		% = F&A costs	$	
e. 05 year	Amount of base $		x Rate applied		% = F&A costs	$	
					TOTAL F&A Costs	$	1,434

*Check appropriate box(es):

☐ Salary and wages base ☒ Modified total direct cost base ☐ Other base *(Explain)*

☒ Off-site, other special rate, or more than one rate involved *(Explain)*

Explanation *(Attach separate sheet, if necessary.):*

Rate: 57.3% = BCM off campus rate 27.1% + TCH affiliate rate 30.2%

4. DISCLOSURE PERMISSION STATEMENT: If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)? ☐ Yes ☒ No

BIOGRAPHICAL SKETCH

NAME Peter Hotez MD PhD	POSITION TITLE Dean, National School of Tropical Medicine, Professor of Pediatrics, Molecular Virology & Microbiology, Baylor College of Medicine; President, Sabin Vaccine Institute
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 - 1986	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 vaccines for neglected tropical diseases (NTDs) and emerging infections. 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 (IND) application for a recombinant vaccine in 2004, with a second IND filed this year, both for hookworm infection. Today the Sabin PDP is also developing recombinant vaccines for major disease affecting developing countries, including hookworm, schistosomiasis, Chagas diseases and SARS. 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., Brazil, and Mexico, and then clinical testing in either the U.S. or developing countries. Thus, Sabin's PDP has acquired a track record of transitioning concepts and discoveries into actual vaccines for clinical testing. Sabin's PDP relocated to Baylor College of Medicine in, 2011 where it is known as Sabin Vaccine Institute and Texas Children's Center for Vaccine Development. He is also the founding Dean of the National School of Tropical Medicine at Baylor College of Medicine. Dr. Hotez is a recognized leader on vaccine development for tropical diseases and other infectious diseases.

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*
2010-11 President, American Society of Tropical Medicine and Hygiene
2011- Professor, Department of Pediatrics and Molecular Virology & Microbiology, and Head of Pediatric Tropical Medicine, Baylor College of Medicine
2011- Texas Children's Hospital Endowed Chair of Tropical Pediatrics
2011- Dean, National School of Tropical Medicine at Baylor College of Medicine

2013- Fellow in Disease and Poverty, James A. Baker III Institute, Rice University

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 Elected Member, Institute of Medicine of the U.S. National Academies
2009 Science and Technical Advisory Committee on Tropical Disease Research, WHO
2011 Member, National Institutes of Health (NIH) Council of Councils
2011 Elected Member, The Academy of Medicine, Engineering, and Science of Texas (TAMEST)
2011 Fellow of the American Society of Tropical Medicine and Hygiene (FASTMH)
2011 Abraham Horwitz Award for Excellence in Leadership in Inter-American Public Health, PAHO, WHO
2012 Elected Member, The Association of American Physicians (AAP)
2012 The Ralph D. Feigin, M.D. Award for Excellence, The Immunization Partnership
2013 Vaccine Nation, Top 50 most influential vaccine personalities
2013 David Pakcard Lecturer, Uniformed Services University of the Health Sciences
2013 Joseph F. Russo MD Lectureship, North American Society for Pediatric and Adolescent Gynecology
2013 JV Irons Keynote Lecture, The 63rd Annual James Steele Conference on Diseases in Nature
2013 Edward Kass Lectureship, IDWEEK - Infectious Diseases Societies in America Conference

C. Selected peer-reviewed publications (in chronological order). (Selected from 284 in PubMed)

1. Hotez PJ, Brooker S, Bethony JM, Bottazzi ME, Loukas A, Xiao S. Hookworm Infection. N Engl J Med 2004; 351:799-807.
2. Asojo OA, Goud G, Dhar K, Loukas A, Zhan B, Deumic V, Liu S, Borgstahl GE, Hotez PJ. X-ray structure of Na-ASP-2, a pathogenesis-related-1 protein from the nematode parasite, Necator americanus, and a vaccine antigen for human hookworm infection. J Mol Biol 2005; 346:801-14.
3. Hotez PJ. Neglected Infections of Poverty in the United States of America. PLoS Negl Trop Dis 2008; 2:e256. PMCID: PMC2430531.
4. 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.
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. 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.
7. Hotez PJ, Fenwick A, Savioli L, Molyneux DH. Rescuing the “bottom billion” through neglected tropical disease control. Lancet 2009; 373: 1570-4.
8. Hotez PJ. Peace through vaccine diplomacy. Science 2010; 327: 1301. www.sciencemag.org/content/327/5971/1301.full?sid=5be8053a-cc9c-4381-a6e9-815c955ba849
9. 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
10. 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.
11. Hotez PJ, Mistry N, Rubinstein J, Sachs JD. Integrating neglected tropical diseases into AIDS, tuberculosis, and malaria control. N Engl J Med 2011; 364: 2086-9.
12. Hotez PJ. A handful of ‘antipoverty’ vaccines exist for neglected diseases, but the world’s poorest billion people need more. Health Aff (Millwood) 2011; 30: 1080-7. PMID: 21653960.
13. Goud GN, Deumic V, Gupta R, et al. Expression, purification, and molecular analysis of the Necator americanus glutathione S-transferase 1 (Na-GST-1): a production process developed for a lead candidate recombinant hookworm vaccine antigen. Protein Expr Purif 2012; 83: 145-51.

14. Jiang S, Bottazzi ME, Du L, Lustigman S, Tseng CT, Curti E, Jones K, Zhan B, Hotez PJ. Roadmap to developing a recombinant coronavirus S protein receptor-binding domain vaccines for severe acute respiratory syndrome. Exp Rev Vaccines 2012; 11: 1405. PMID: 23252385
15. Hotez PJ, Diemert D, Bacon KM, Beaumier C, Bethony JM, Bottazzi ME, Brooker S, Couto AR, Freire Mda S, Homma A, Lee BY, Loukas A, Loblack M, Morel CM, Oliveira RC, Russell PK. The Human Hookworm Vaccine. Vaccine 2013; 31 Suppl 2:B227-32. PMID: 23598487

D. Research Support

Ongoing Research Support

23386 Hotez (PI) 01/01/2011-12/31/2014
Sponsor: Dutch Government
Title: 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.

1016395 Hotez (PI) 08/01/2011 – 09/30/2015
Sponsor: Private Source
Title: 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*.

Hotez (PI) 04/20/2012 – 04/19/2016
Private Source
Accelerating the development and testing of a therapeutic Chagas vaccine
The main goal of this project is to accelerate the early development of a vaccine for a major neglected tropical disease affecting the Amazon region and Latin America – Chagas disease.

NIH R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017
Sponsor: National Institutes of Health
Title: RBD Recombinant Protein-based SARS Vaccine for Biodefence
The main goal of this project is to develop, test and manufacture a novel recombinant SARS vaccine.

Bottazzi (Center Director) 10/01/2012 – 12/31/2017
Sponsor: Department of Health and Human Services / Texas A&M Univ.
Title: Centers for Innovation in Advanced Development and Manufacturing
The major goal of this project is to advance education and training for professionals in the area of vaccine biotechnology and product development
Role: Instructor

Hotez (PI) 09/01/2013 – 08/31/2017
Sponsor: Private Source
Title: Multivalent Anthelminthic Vaccine Discovery Program
The overarching goal of this four year project is to advance the development of a lead candidate *Ascaris* antigen and a *Trichuris* antigen, either or both of which ultimately could be formulated with the Human Hookworm Vaccine now under development by the Sabin PDP.

HOOKVAC Hotez (PI) 10/01/2013 – 09/30/2017
Sponsor: European Union via sub from Amsterdam Institute for Global Health and Development (AIGHD)
Title: Developing and Testing a novel, low-cost, effective HOOKworm VACcine to Control Human Hookworm Infection in endemic countries
Major goals of the project are to perform technology transfer of processes for fermentation purification and analytical testing of the human hookworm vaccine.

Hotez (PI) 01/01/2014 – 12/31/2016

Sponsor: University of Malaya
Title: Malaysian Neglected Tropical Disease Initiative
Major role of the project is to train and build capacity for Malaysian scientists in the area of vaccine biotechnology.

Hotez (PI) 01/01/2014 – 12/31/2017
Sponsor: (b)(4)
Title: West Nile Virus vaccine development
Main goal is to support West Nile Virus vaccine development.

Hotez/Bottazzi (MPI) 01/01/2014 – 12/31/2017
Sponsor: (b)(4)
Title: Hookworm Vaccine Discovery Program
The overarching goal of this four year project is to discover new candidate antigens for the development of a hookworm vaccine to complement the Human Hookworm Vaccine now under development by the Sabin PDP.

Bottazzi/Hotez (MPI) 07/01/2012 – 12/31/2013
Sponsor: Instituto Carlos Slim de la Salud
Title: 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.

Completed Research Support (selected support after 2010)

32472 Hotez (PI) 08/01/2006 – 12/31/2012
Sponsor: Sabin Vaccine Institute is conduit for The Bill and Melinda Gates Foundation
Title: Human Hookworm Vaccine Initiative 1
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

AI 90577 Hotez (PI) 01/01/2011 – 12/31/2012
Sponsor: 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)

RCA8608 Hotez (PI) 09/30/2009 - 09/30/2011
(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.

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

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Asojo, Oluwatoyin Ajibola	Associate 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
Trent University, Peterborough ON Canada	B.Sc.	05/92	Chemistry & Economics
Trent University, Peterborough ON Canada	B.Sc. Hons	05/93	Chemistry
University of Houston, TX	Ph.D.	12/99	Chemistry
NCI-SAIC Frederick, MD	Post doc	05/00	Crystallography

A. Personal Statement

I am currently Associate Professor at the National School of Tropical Medicine (NSTM) at Baylor College of medicine and collaborate with Dr. Hotez on the SARs grant. I will mentor the high school students placed at laboratories at NSTM. I am an URM female and over the course of my career I have mentored a diverse group of high school, pre-doctoral, and medical students. These students have played an integral part in my research and many of them have been co-authors on papers generated from my laboratoryI have served as a principal investigator or collaborator, on extramural contracts and grants, from the NIH, and DOD. I have unique skills and experiences that allow me to tackle innovative ideas and utilize diverse sources of information as evident from the diversity of projects I have worked on. I was initially trained as a chemist with my research area mainly in structural biology. As a structural biologist I have solved protein structures from bacteria, protozoa, viruses, human, (cancer) and nematodes. I have also carried out rational drug development studies on diverse targets. These experiences allowed me to develop an integrated view of science and see correlations in these complex biological systems that would not have been apparent if I had a more limited research portfolio. I look forward to mentoring the student.

B. Positions and Honors

Positions and Employment

1999-2000 Fellow, Structural Biology Program National Cancer Institute, Frederick, MD
2000-2001 Structural Biologist Tibotec-Virco, Rockville MD
2002-2003 Fellow, Macromolecular Crystallography Program National Cancer Institute Frederick MD
2002-2012 Scientific Collaborator Human Hookworm Vaccine Initiative GWU Washington DC
2003-2005 Research Assistant Prof. Eppley Institute University of Nebraska Medical Center, Omaha NE
2005- 2012 Assistant Prof. Pathology and Microbiology University of Nebraska Medical Center Omaha NE
2012- Associate Professor, National School of Tropical Medicine, Baylor College of Medicine, Houston

Other Experience and Professional Memberships

1999- American Chemical Society (Omaha Local section past chair/ chair / chair elect 2008 – 2011)
1999- American Crystallographic Association (Member)
2005- American Association for Cancer Research (Member)
2012- American Society of Tropical medicine and Hygiene (Member)
2005- Peer-Reviewer ACTA Cryst-D/F,
2005- Peer Reviewer Advanced Photon Source Macromolecular Crystallography proposals
2005-2007 Edna Ittner Research Grants UNMC
2011-2012 Biophysics Society (Member)
2009 Ad hoc Reviewer ARRA National Science Foundation
2011 Ad hoc Reviewer NIH study section
2013 Reviewer AACR Minority in Cancer Award
2013 NIH Bioinformatics to Mine Human Bio-specimens Data Workshop

2001, 2008- American Chemical Society Project SEED coordinator & mentor
2013- BCM Medical School Admissions Committee, BCM IMSD Committee,
2012- ABRCMS, SANCS Reviewer
2013 BCM Pediatrics Pilot Grants Reviewer
2013- ACS Chemistry Ambassador, Rice University Civic Scientist
2014- Ad hoc Reviewer NSF BIO

Honors

2013- CAPES-Fiocruz/CDTS Fellowship Program Visiting Professorship to Brazil
2013-2015 Master's Teacher's Fellowship Program
2012 AACR Minority in Cancer Research Award
2006 Univ. Nebraska Omaha Women of Color Award in Science and Technology
2005 Keystone Symposia scholarship
1994 -1999 Welch Pre-doctoral Fellowship University of Houston, Houston TX
1992 -1993 Dean's Honors List Graduating Class Trent University
1989 -1993 Trent International Program Full Scholarship Trent University Peterborough ON Canada
1987 -1989 United World College Scholarship Pearson United World College Vancouver BC Canada

C. Selected Peer-reviewed Publications (high school students are highlighted)

1. S. K. Nelson, A. Kelleher, **G. Robinson**, S. Reiling and O. A. Asojo, Crystal structure of 2-Keto-3-deoxy-D-manno-octulosonate-8-phosphate synthase from *Pseudomonas aeruginosa* Acta Cryst F Sept 2013 F.
2. O. A. Asojo*, G. N. Goud, B. Zhan, **K. Ordonez**, M. Sedlacek, K. Homma, V. Deumic, R. Gupta, J.Brelsford, M. K. Price, M. Ngamelue and P. J Hotez Crystallization and preliminary X-ray analysis of Na-SAA-2 from the human hookworm parasite Necator americanus. *Acta Crystallogr Sect F Struct Biol Cryst Commun* 66, 172-6, 2010.
3. Y. Lee, S. Mootien, C. Shoen, M. Destefano, P. Cirillo, O. A. Asojo, K. R. Yeung, M. Leidizet, P. A. Aristoff, R.A. Koski, P.A. Kaplan, K. Anthony, Inhibition of Mycobacterial Alanine Racemase Activity and Growth by Thiadiazolidinones Biochem Pharmacol. 2013 May 13. pii: S0006-2952(13)00288-8. doi: 10.1016/j.bcp.2013.05.004.
4. Bai, O.A. Asojo, P. Cirillo, M. Ciustea, M. Ledizet, P. A. Aristoff, L. Leng, R. A. Koski, T. J. Powell, R. Bucala, K. G. Anthony* A novel allosteric inhibitor of macrophage migration inhibitory factor (MIF). J. Biol Chem 2012 Jul 10. [Epub ahead of print]. PMCID: PMC3436310
5. O. A. Asojo* Structure of a two-CAP domain protein from the human hookworm parasite Necator americanus Acta D 2011 Vol 67(Pt 5), pages 455-62. PMCID: PMC3087624
6. O. A. Asojo*, R. A. Koski & N. Bonafé Structural studies of human glioma pathogenesis-related protein 1 Acta D 2011 Vol 67(Pt 10), p 847-855. PMCID: PMC3176621
7. S. A. Reiling, K.Homma, & O. A. Asojo*, Purification and crystallization of RNase HIII from *Staphylococcus aureus Acta Cryst.* (2011). F**67**, 79-82. PMCID: PMC3079978
8. N. Bonafé, B. Zhan, M. E. Bottazzi, O. A. Perez, R. A. Koski, O. A. Asojo*, Expression, purification, crystallization and preliminary X-ray analysis of a truncated soluble domain of human glioma pathogenesis-related protein 1. *Acta Crystallogr Sect F Struct Biol Cryst Commun*. 2010 Nov 1;66 (Pt 11):1487-9. Epub 2010 Oct 28 2010. PMCID: PMC3001655
9. M. Ngamelue, K. Homma, O. Lockridge, O. A. Asojo*, Crystal structure of recombinant full length human butyrylcholinesterase *Acta Cryst*. F**63**, 723–727, 2007. PMCID: PMC2376307
10. O. A. Asojo*, K. Homma, **M. Sedlacek**, M. Ngamelue, G. N. Goud, B. Zhan, V. Deumic, O. Asojo, P. J Hotez. X-ray structures of NaGST-1 and NaGST-2 two glutathione s-transferase from the human hookworm *Necator americanus*. *BMC Structural Biology*, 7:42, 2007. PMCID: PMC1924862
11. O. A. Asojo*, E. Schott, G. Vasta and A. M. Silva, X-ray structures of PmSOD1 and PmSOD2, Two Superoxide Dismutases from the Protozoan Parasite *Perkinsus marinus*. *Acta Cryst* F, Nov 1;62(Pt 11):1072-5, 2006. PMCID: PMC2225229
12. O. A. Asojo*, G. Goud, K. Dhar, A. Loukas, B. Zhan, V. Deumic, S. Liu, G.E. Borgstahl, P. J. Hotez, X-ray structure of *Na*-ASP-2, a Pathogenesis Related-1 protein from the nematode parasite *Necator americanus* and a vaccine antigen for human hookworm infection *J. Mol Biol.,* 346(3), 801-814, 2005.
13. Nachon*, O. A. Asojo, G.E. Borgstahl, P. Masson, and O. Lockridge, Role of Water in Aging of Human Butyrylcholinesterase Inhibited by Echothiophate: The Crystal Structure Suggests Two Alternative Mechanisms of Aging. Biochemistry 44, 1154-1162, 2005.

14. O. A. Asojo, C, Boulegue, D. M. Hoover, W. Lu, and J. Lubkowski*. High resolution structures of thymus and activation-regulated chemokine (TARC) *Acta Cryst.,* D59, 1165-1173, 2003.
15. O. A. Asojo*,* S. Gulnik, E. Afonina,T. S. Haque, J. A. Ellman,and A. M. Silva*. Novel uncomplexed and complexed structures of plasmepsin II, a protease from *Plasmodium falciparum. J. Mol Biol.*, 327:173-181, 2003.

D. Research Support

Ongoing Research Support

5U01AI082081-04 Anthony (PI) 05/01/12-04/30/14
NIH/NIAID sub-award from L2 Diagnostics
Broad-Spectrum Antimicrobials Targeting the D-Alanine Pathway
Project objectives: To identify small molecule inhibitors of the cell wall synthesis enzyme, alanine racemase for therapeutic development of a broad spectrum antibacterial against a variety of bacterial pathogens.
Role: Investigator

2R44AR056908-02A1 Anthony (PI) 10/01/12 – 09/30/15
NIH via subaward from L2 Diagnostics
Therapeutic inhibition of MIF in Rheumatoid Arthritis
The goal of this project is to characterize the precise mechanism of novel inhibitors of hMIF that are being developed as therapeutics for Rheumatoid Arthritis.
Role: Sub-PI

Hotez (Center Director, Consultant) 07/01/12 – 12/31/17
Sponsor: Department of Health and Human Services / Texas A&M Univ.
Title: Centers for Innovation in Advanced Development and Manufacturing
The major goal of this project is to advance education and training for professionals in the area of vaccine biotechnology and product development.
Role: Instructor

Past Research Support (last 3 years)

5K01CA113486 Asojo (PI) 06/03/2005 -05/31/2011
Structural Basis of Multidrug resistance in Cancer (No cost-extension 05/31/2010 -05/31/2011)
NCI Mentored Career Development Award for Underrepresented Minorities: the major goals of this project are to transition into an independent researcher and to characterize the structures and functions of the human multi-drug transporter ABCG2. Role: PI

Department of Defense Bayles (PI) 04/01/2009 – 03/30/2011
Fighting drug resistance infections
My role on this project is to carry out structural studies of CidA and LrgA, programmed cell death regulatory proteins. Role: Co-PI

SUMMARY OF THE PROJECT SPECIFIC AIMS AND APPROACH

Funds are requested for a minority supplement to the parent grant AI-098775 on the development and manufacture of a recombinant receptor-binding domain (rRBD) protein to prevent severe acute respiratory syndrome (SARS) caused by the SARS coronavirus (SARS CoV). The project will serve as a basis for engaging an under-represented minority high school student in an eight-week long mentored program of molecular biology and biochemistry research. The program will be offered in association with the Office of Diversity and Community Outreach at Baylor College of Medicine.

SPECIFIC AIMS. Briefly, the parent grant seeks to develop a recombinant vaccine against SARS, now classified by NIAID as a Category C Priority Pathogen, by advancing the vaccine through early stage expression and preclinical characterization, process development, formulation, stability, technology transfer and cGMP manufacture. The Actual Specific Aims of the parent grant are as folows:

Specific Aim 1*: *Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate. We will evaluate the expression of the recombinant RBD (rRBD) in bacteria and yeast expression systems and select one of them for expression of rRBD protein for subsequent studies based on yields, purity, stability, antigenicity, functionality, immunogenicity, and efficacy (for inducing neutralizing antibody responses and protection against SARS-CoV challenge) of the rRBD protein when formulated in alum. We will use the rRBD protein from the selected expression system for optimization of immunization regimens, and assess the ability of rRBD protein formulated with alum based adjuvants and/or GLA, a TLR4 antagonist adjuvant, to induce cross-neutralizing antibody response, cross-protection and long-term immune responses and protection in mouse models using the optimized immunization regimen. (Timeline Year 1-3)

Specific Aim 2: Process development, characterization, formulation and stability profiling. In parallel to Aim 1, a scalable and reproducible fermentation process for rRBD (10 liter scale) and a purification process using chromatographic technologies will be developed. Reproducibility will be confirmed and specific product quality assays will be developed and used to characterize the recombinant vaccine protein. Vaccine buffer formulations will be developed and characterized using an innovative approach, combining analytical/biochemical tools with biophysical assays to test different excipients and stabilizers and establish an optimal stability profile. The stabilized protein will be formulated with alum and/or GLA. The binding and effect on the structure stability will be examined. Immunogenicity and efficacy of the vaccine formulations will be evaluated in parallel as described in Aim 1. These assays and procedures will serve the basis for formal lot release and stability evaluation post-manufacturing. (Timeline Year 2-4)

Specific Aim 3: Technology transfer, cGMP Manufacture, GLP toxicology and IND Preparation. The cell bank production, production processes and formulation technology for the selected rRBD-based vaccine will be transferred to Walter Reed Army Institute of Research (WRAIR) pilot facility for 60-L scale GMP manufacture, formulation and fill and finish. The clinical lots will be released by BCM-Sabin and following a pre-IND meeting with the U.S. FDA, GLP toxicology will be initiated at Frontier Biosciences, a Maryland-based contractor. BCM-Sabin will prepare and submit an IND in preparation for the initiation of the clinical development plan. (Timeline Year 4-5)

With the exception of the final cGMP manufacture and preclinical testing for immunogenicity and efficacy using a mouse challenge model all of the work is conducted at the Sabin Vaccine Institute and Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine (BCM-Sabin).

APPROACH. The strengths of our approach rely on an extensive evidence base of preliminary data collected over the last seven years by our collaborators on the grant at the New York Blood Center (NYBC), which point to the RBD protein as a lead candidate vaccine antigen, together with an eleven-year track record of product development and testing for recombinant vaccines by the Sabin Vaccine Institute Product Development Partnership now based at Baylor College of Medicine (BCM-Sabin). Additionally, BCM-Sabin has had previous success in tech transferring processes for recombinant protein vaccines to Walter Reed Army Institute of Research, our cGMP contractor (CMO) of choice. Further, the group has demonstrated the feasibility of developing rRBD-based subunit vaccines. Specifically ,our collaborators at NYBC have shown that mammalian cell-expressed rRBD fused induces high titer of RBD-specific neutralizing antibodies in vaccinated animals and long-term (over a year) immune responses and protection against subsequent SARS-CoV challenge, while using the pseudotyped viruses expressing S protein originated from Tor2, GD03, or SZ3, the representative strains of human 2002–2003 & 2003–2004 SARS-CoV and palm civet SARS-CoV, respectively, we also found that mouse and rabbit antibodies raised against rRBD derived from either one of the aforementioned strains of SARS-CoV and the palm civet SARS-CoV cross-neutralize one another, suggesting their protective efficacy against challenge with heterogeneous viruses. Immunization of mice with rRBD derived from various expressing systems, including mammalian cells (293T and CHO), insect sf9 cells, and *E. coli* is capable of producing high-levels of RBD-specific neutralizing antibody and potent T cell responses against both pseudotyped and live SARS-CoV. Importantly, these rRBD proteins appear to maintain intact conformation and authentic antigenicity, reacting with the RBD-specific and conformation-dependent mAbs with neutralizing activity. These rRBD proteins elicited immunity that protected all vaccinated mice from SARS-CoV challenge. These preliminary data and expertise by NYBC is now being paired with the track record at BCM-Sabin/WRAIR for transitioning a recombinant protein-based vaccine through process development and formulation, technology transfer for cGMP manufacture, lot release and stability testing,and GLP toxicology testing. All steps needed in order to compile a regulatory file application (IND) in preparation for a submission to the FDA. .

The Major Deliverables
1. Development of a scalable, reproducible process for expression of the rRBD protein and formulation of the RBD-based vaccine with high quality and stability.
2. Establishment of an immunization regimen, including the optimized antigen dose, vaccination schedule and route and adjuvant formulation, for evaluation of the immunogenicity and efficacy of the vaccine.
3. Successful pilot cGMP manufacture of a subunit SARS vaccine comprised of rRBD protein and an adjuvant formulation.
4. Completion of the GLP toxicology testing with acceptable safety profile.
5. IND preparation and submission with U.S. FDA.

The parent grant was written and submitted in response to an RFA in biodefense - RFA-AI-11-014 Partnerships for Biodefense (R01) - BCM-Sabin is applying its proven product development partnership approach and strong peer-reviewed publication track record in research and development of parasitic recombinant protein vaccines to accelerate the development of a recombinant RBD-based vaccine to prevent SARS-CoV infection. To ensure success, BCM-Sabin provides program management throughout the project timeline and leverage the collaborations with the research and industry partners to augment the expertise for anti-SARS-CoV vaccine testing. The strengths of this proposal relay on the supporting proof of concept data that identifies the RBD protein as a lead candidate vaccine antigen selected for further process development, characterization and preclinical evaluation. Following feasibility of expression in both bacterial and yeast expression systems, the recombinant proteins are assessed at BCM-Sabin for scalability, yield, quality and stability. Antigenicity, functionality, immunogenicity and potency of the vaccine formulations will be developed and evaluated at NYBC and additional collaborators at University of Texas Medical Branch Galveston (UTMB). Furthermore, rRBD protein from the selected expression system will be compared at NYBC and UTMB for its ability to induce neutralizing antibodies and protection in laboratory animals against challenge infections with multiple strains of the SARS-CoV using different adjuvant platforms; alum (either Alhydrogel® or aluminum phosphate) and/or GLA, a TLR4 antagonist adjuvant. Once the most efficacious expression system is selected, BCM-Sabin will perform scale-up process development (PD) at the 10 liter fermentation scale followed by protein purification under detailed documentation. Reproducibility will be confirmed and specific product quality control assays will be developed in collaboration with NYBC and used to characterize rRBD. In

addition, vaccine buffer formulations will be developed and characterized, and excipients and stabilizers will be evaluated. The stabilized molecule will then be formulated with alum and/or GLA and their effect on the structure stability will also be examined. These assays and procedures will serve the basis for formal lot release and stability evaluation post-manufacturing. The developed process will then be transferred to WRAIR that successfully manufactured two hookworm vaccines with BCM-Sabin. After pilot lot material is produced and released and following a pre-IND meeting with the U.S. FDA, toxicology testing will commence and an IND application will be prepared. Thus a key strength is clear-cut project deliverables (see adjoining box).

The proposed project is ideal for mentoring a under-represented highschool student on fundamental techniques in molecular biology and biochemistry and providing a broad educational overview on the key steps in developing a vaccine to prevent a major public health threat.

PLAN/TIMELINE FOR RESEARCH AND CAREER DEVELOPMENT (INCLUDING MENTORSHIP ACTIVITIES)

We have planned for an 8 week period of research. During this period of research, the highschool student will meet with our research team regularly to observe research meetings, and also contribute to the meetings once they start collecting data. The student will be mentored through the entire research period and trained in various general aspects of research. Each week the student will have a one-on-one mentorship meeting where they can give feedback on their activities for the week and point out any areas that they may not understand, or may need additional training with.

The detailed RESEARCH AND MENTORSHIP PLAN is described below with a set of targets for each week:

Week 1:
- Laboratory orientation and rules
- Overview of Ethical guidelines in research – explanation of human subjects and animal protections
- Introduction to molecular biology and biochemistry, with emphasis on recombinant DNA technologies
- Overview of Professionalism
- Training in basic knowledge of nucleic acids, proteins, and respiratory viruses
- Attendance of laboratory meeting (group)
- Review of the research strategy and timelines (with Principal Investigator)

Weeks 2-6
Training and orientation on basic techniques in molecular biology and biochemistry
- How to prepare buffers and reagents
- How to prepare and run agarose gels and visualize and quantitate DNA
- How to use restriction endonucleases
- How to prepare plasmids and transfect yeast and bacteria
- How to induce protein expression and analyze recombinant proteins on SDS-PAGE

Week 2:
- Record manipulations and observations – Preparation of buffers and reagents; agarose gels and visualizing and quantitating DNA
- Attendance of laboratory meeting (group)
- Overview of the National Institutes of Health
- Mentorship meeting (one-on-one)

Week 3:
- Record manipulations and observations – use of restriction endonucleases and ligases
- Attendance of laboratory meeting (group)
- Mentorship meeting (one-on-one)
- Training on how to use empirical data in preparing a research project
- Training in how to find empirical data and how to organize it

Week 4:
- Record manipulations and observations –preparing plasmids and yeast and bacterial transfection
- Attendance of laboratory meeting (group)
- Mentorship meeting (one-on-one)
- Training in scientific writing and on how to write an abstract

Week 5:
- Record manipulations and observations –preparing plasmids and yeast and bacterial transfections
- Attendance of laboratory meeting (group)
- Mentorship meeting (one-on-one)
- Training in the history and function of the IRB

Week 6:
- Record manipulations and observations – protein expression and analysis of recombinant proteins on SDS PAGE
- Attendance of laboratory meeting (group)
- Mentorship meeting (one-on-one)
- Training in oral presentation skills

Week 7:
- Record manipulations and observations – protein expression and analysis of recombinant protein on SDS PAGE.
- Evaluation of experiments and data collection
- Introduction to creating a research poster
- Attendance of laboratory meeting (group)
- Produce a draft presentation of research findings with the assistance of mentor (one-on-one)

Week 8:
- Meetings with PI and laboratory staff to review results
- Finalize draft of research findings
- Presentation of findings at laboratory meeting
- Provide feedback on how to improve laboratory experiences
- Reflect on the summer research experience

Evidence of mentoring experience for the Principal Investigator:

Peter Hotez MD PhD - the Principal Investigator - is an elected member of the Institute of Medicine with more than 25 years of experience leading laboratory investigations on neglected and infectious diseases. Over the last decade he has led a non-profit product development partnership for the development, manufacture, and clinical testing of recombinant protein vaccines to combat neglected tropical diseases, and was recently named one of the fifty most influential people in vaccines. Dr. Hotez has supervised or co-supervised at least a dozen postdoctoral fellows and a dozen research faculty, in addition to three PhD candidates for their doctoral dissertations (including an MD PhD student now in training). He has also supervised the thesis work of numerous students for their master degree in public health (MPH) and related degrees. He is widely sought out by medical and graduate students, as well as undergraduates for career advice.

For this mentored program much of the direct training at the laboratory bench will be led by senior laboratory staff members and research-intensive faculty working in the larger laboratory group of Dr. Hotez. Similar arrangements have led to numerous successful mentoring experiences for other high school students and undergraduates. Last summer, two high school students received laboratory instruction and training in the Hotez laboratory.

Description of how the research and career development experiences will expand and foster the research capabilities of the candidate:

The described course of summer study will introduce the student to the basic principals of biomedical scientific research. The student will understand the planning process and the approaches that are used to develop a project, analyze the data, and in the preparation of data for presentation. The candidate/student will gain a basic understanding of molecular biology and biochemistry of macromoleces (nucleic acids and proteins) and how these approaches contribute to our understanding of the mechanisms that allow respiratory viruses to invade host tissues and how vaccines may be used to combat them. The student will gain experience in laboratory techniques, procedures, biosafety and ethics.

Under the guidance of experienced researcher the student will learn fundamental techniques in molecular biology and biochemistry including buffer and reagent preparation, agarose gels and DNA visualization and quantitation, use and application of restriction endonucleases, preparation of plasmids and transfection of yeast and bacteria, fusion protein induction and expression, and analysis of recombinant proteins on SDS-PAGE. These studies will be conducted in the larger context and environment of the steps needed to develop and test recombinant protein vaccines for important infectious agents and biodefense threats including SARS. Thus we hope to stimulate the imagination of the trainee about the role he/she could one day have in the important area of public health emergency preparedness.

Equally important, this student will observe the scientific process unfold in a laboratory setting. We anticipate that the student will become engaged in the practice and discipline of academic research and, since this is biomedical research, come to understand and appreciate the role of research in the practice of medicine. The overall goal is for this high school student is to see the challenges and opportunities that exist in arenas of higher education. One of the goals is to instill a sense of awe and excitement in the student as to all of the possibilities available to them in their future. It is our objective to provide this student with world-class training and experience in an 8 week defined course of study.

In conjunction with the Office of Diversity and Community Outreach at Baylor College of Medicine, the student will present a research poster at the annual student research symposium that this office sponsors each year in January.

Statement of Eligibility from the Investigator

Ebe Ewere [PII] is a sophomore at Hightower High School in Missouri City, Texas, and is a U.S. citizen [PII] We hope that the early exposure of this candidate to this area of scientific research and the experience he will gain by participating in a laboratory study will further influence his decision to pursue a career in the healthcare field, therefore impacting the national scientific workforce. This experience will also be beneficial to Ebe as he begins to make decisions about the pursuit of his undergraduate studies. Additionally, this experience will provide a better understanding of the relationship between research studies and the delivery of healthcare, as well as basic research methods. His presence here at Baylor in the capacity of project intern for the summer will further enhance our institution's goal of diversity, and its goal to have an impact in reducing the racial and ethnic disparity in the scientific and healthcare workforce. Ebe Ewere has not received any previous or current PHS support.

Peter Hotez, MD, PhD
Principal Investigator
Dean of School of Tropical Medicine
Baylor College of Medicine

James L. Phillips, MD
Senior Associate Dean
Office of Diversity and Community Outreach
Baylor College of Medicine

Leanna B. Scott, Ph.D.
Director, Sponsored Programs

BIOGRAPHICAL SKETCH

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Ewere, Ebe Aaron	POSITION TITLE
eRA COMMONS USER NAME (last four digits of social) PII	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Hightower High School's Medical Science Academy	N/A	06/16	N/A

NOTE: The Biographical Sketch may not exceed four pages. Follow the formats and instructions below.

A. Personal Statement

I first recognized my calling into a scientific career as a fifth grader when I was introduced into the wonderful sport of American football. I developed a newfound admiration for the human body and the way that it works. I realized that the teamwork between the muscles, bones and nerves within a successful athlete's body paralleled the teamwork between teammates on a successful football team. While in seventh grade, I had the opportunity to play on a team which further exposed me to the beauty of teamwork. Teamwork's importance and impact was everything I could have imagined and more, further engrossing me in the science behind the teamwork on the field as well as the teamwork occurring within my body. After one memorable season, I refrained from playing competitive football; however, my admiration for the human body continues to grow unceasingly.

My interest in the human body grew to include learning about the medical sciences. Anatomy, physiology, and psychology are some of my favorite subjects and I enjoy reading about them just for the sake of becoming more knowledgeable. However, as I got older, I found that I was not entirely satisfied with just being knowledgeable. The information that I obtained is relevant, but I wanted to be able to apply it. I heard about Fort Bend ISD's Medical Science Academy and knew that it was my golden opportunity to further my knowledge of medicine, apply it, and obtain a centralized academic focus in an area that I am so passionate for. I applied to the academy, received acceptance, and graciously took my first major step towards fulfilling my dreams of having a career in medicine.

Since enrolling in the Medical Science Academy, each day spent in my medical class has been a constant reconfirmation of where my passion lies. Being engrossed in the medical sciences has shown me many aspects of what the medical field really consists of and with that, I have grown to see that there are certain aspects that I like much more than others. Ever since I was on the football team in seventh grade, I told myself and others that I wanted to be an orthopaedic surgeon, but learning about the many different fields under medicine has led me to find many other topics of medicine, such as neurology, to be as interesting as orthopedics.

My interest in neurology has led me on a path of progressive research on a disease called cerebral palsy. The types of cerebral palsy that are most intriguing to me are hypertonic and ataxic cerebral palsy. My research has gotten me in contact with Dr. Iona Novak, a professor at University of Notre Dame in Australia who is also the head of the Cerebral Palsy Alliance. We discuss via email, and she has been a great asset to my research and understanding of the disease due to her structured guidance and various resources that she shares with me. Currently, there is no cure for cerebral palsy, but there are numerous methods of treatments and preventive measures that mothers can take to lower the risk of having a child with cerebral palsy such as

the administration of intravenous magnesium sulfate. Despite the current status of there being no known cure for cerebral palsy, I feel that with adequate research and experimentation, a cure could be discovered. If I choose to become a neurologist in the future, my greatest goal would be to discover the cure to such a debilitating disease. As much as I am attracted to neurology and orthopedics, I am still open to learning about other disciplines of medicine because I am aware that I need further exposure to truly know which area I am most passionate about.

Being a project intern in Baylor College of Medicine's Summer Research Program would give me access to various fields of medical science which will give me the needed exposure to help me discover in which field I should pursue a career. I also would hope to gain an understanding of what professional research is, engage in the application of my previously acquired medical knowledge through hands on training, and also expand and develop my knowledge base. I feel that participation in Baylor College of Medicine's Summer Research Program is a once in a lifetime experience. I truly believe that to be granted such an opportunity will benefit me in numerous ways and that it will place me in a position to help others as I apply my medical knowledge in making scientific discoveries.

B. Positions and Honors

Positions

2009 - 2010	Member of Quail Valley Middle School's Science Club
2009 - 2012	Student of Fort Bend ISD's Academy for the Gifted and Talented at Quail Valley
2010 - Present	Member of Grace International Church's Media and Technical Team
2010 - 2011	Member of the Quail Valley Middle School Football Team
2011 - 2012	Member of the Quail Valley Middle School Basketball Team
	Member of the i9 Sports Winter Basketball League Champion team
2012 - Present	Student of Hightower High School's Medical Science Academy
2012 - 2013	Class President of Medical Terminology Class at Hightower High School
2012 - Present	Chapter Historian for Health Occupations Students of America (HOSA)
	Recruiter for Grace International's Camera and Technical Team
Spring 2013	Freshman representative for Hightower High School at Fort Bend ISD's Annual Diversity Conference
2013 - Present	Class President of Anatomy and Physiology Class at Hightower High School
	Member of the Science UIL Club
	Registered Volunteer with City Wide Club
	Member of Bini Club of Houston, Inc.'s Youth Drama Team
	Member of Grace International Church's "Heavenly Steppers" Dance Team
2014 – Present	Sophomore representative for Hightower High School at Fort Bend ISD's Annual Diversity Conference
	Member of Baylor College of Medicine's Saturday Morning Science Program

Honors

2009 - 2010	Participant in the Mars Rover Competition
2010 – 2011	Participant in the Science Fair Competition – Chemistry Project
2011 - 2012	League leader in points per game and steals per game in i9 sports Winter Basketball League
	Participant in the Science Fair Competition – Physics Project
2012 - 2013	Recipient of the Academic Excellence Award
2012 - 2013	Recipient of the Most Improved Student of the Year Award – awarded by Pre-AP Spanish III Instructor

	Participant in the Science Fair Competition – Physics Project
2013 - 2014	Nominated for the Outstanding Sophomore Award
	Participant in the Science Fair Competition – Physics Project

Signature: Ebe Ewere

C. Selected Peer-reviewed Publications

N/A

D. Research Support

N/A

To whom it may concern:

Ebe Ewere (Name of Student), a student from Hightower High School (Insert name of school), located at 3333 Hurricane lane, missouri city TX 77459 (school address), would like to participate in the summer research experience offered to them through the Saturday Morning Science program at Baylor College of Medicine for the summer of 2014. I understand that said student will be working in a research lab under the direction of a Principal Investigator at Baylor College of Medicine who is operating under an active grant funded through the National Institutes of Health.

I approve of Ebe Ewere 's (name of student) participation in this research program, and I attest that their participation will not detract from or interfere with the student's course of studies.

Name of school official completing document: Lester Johnson

Role of school official: Associate Principal Phone #: 281 634 5279

Signature of school official: _____ Date: 2/27/14

Please affix school stamp or seal in the designated space below (if no stamp or seal please have school official sign with school name and address):

Ebe Ewere

Personal Info

Education

Hightower High School's Medical Science Academy

Cumulative GPA: Personal Info

Anticipated graduation date: June 2016

Experience

Research-Based

2009	Participant in the Mars Rover Competition
2010 - 2011	Participant in the Science Fair Competition – Chemistry Project
2011 – 2012	Participant in the Science Fair Competition – Physics Project
2012 – 2013	Participant in the Science Fair Competition – Physics Project
2014 – Present	Member of Baylor College of Medicine's Saturday Morning Science Program

Leadership-Based

2012 - Present	Chapter Historian for Health Occupations Students of America
2012-2013	Class President of Medical Terminology Class at Hightower High School
2013	Freshman representative for Hightower High School at Fort Bend ISD's Annual Diversity Conference
2013 - Present	Recruiter for Grace International's Media and Technical Team
2013 - Present	Class President of Anatomy and Physiology Class at Hightower High School
2014 - Present	Sophomore representative for Hightower High School at Fort Bend ISD's Annual Diversity Conference

Activities

2009 - 2010	Member of Quail Valley Middle School's Science Club
2010 - 2011	Member of i9 Sports Winter Basketball League
2010 - Present	Member of Grace International Church's Media and Technical Team
2013 – 2014	Member of the Science UIL Club
2010 - 2011	Member of the Quail Valley Middle School Basketball Team

2013 – Present Registered Volunteer with City Wide Club

2013 – Present Member of Bini Club of Houston, INC.'s youth drama team

2013 – Present Member of Grace International Church's "Heavenly Steppers" Dance Team

Honors

2011-2012 League leader in points per game and steals per game in i9 sports Winter Basketball League

2012-2013 Recipient of the Academic Excellence Award

2012-2013 Recipient of the Most Improved Student of the Year Award (from Spanish 3 Pre-AP class)

2013-2014 Nominated for the Outstanding Sophomore Award

Skills

Five years of Spanish education

Skilled with the Android and Microsoft operating systems

Adept with Microsoft Office Software

Experienced with still, digital and video cameras

Proficient in touch typing

RESEARCH
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 04/09/2016

NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 4R01AI098775-05
FAIN: R01AI098775

Principal Investigator(s):
Maria Elena Bottazzi, PHD
PETER J HOTEZ (contact), PHD
SHIBO JIANG, MD

Project Title: RBD recombinant protein-based SARS vaccine for biodefense

Leanne Brooks Scott
Business Official
One Baylor Plaza, BCM320A
Houston, TX 770303411

Award e-mailed to: bcmaward@bcm.edu

Period Of Performance:
Budget Period: 05/01/2016 – 04/30/2017
Project Period: 05/04/2012 – 04/30/2017

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $1,165,855 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to BAYLOR COLLEGE OF MEDICINE in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Allergy And Infectious Diseases of the National Institutes of Health under Award Number R01AI098775. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

Ann W. Devine
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 4R01AI098775-05

Award Calculation (U.S. Dollars)

Federal Direct Costs	$768,645
Federal F&A Costs	$397,210
Approved Budget	$1,165,855
Total Amount of Federal Funds Obligated (Federal Share)	$1,165,855
TOTAL FEDERAL AWARD AMOUNT	$1,165,855
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$1,165,855

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
5	$1,165,855	$1,165,855

Fiscal Information:

CFDA Name:	Allergy, Immunology and Transplantation Research
CFDA Number:	93.855
EIN:	1741613878A1
Document Number:	RAI098775B
PMS Account Type:	P (Subaccount)
Fiscal Year:	2016

IC	CAN	2016
AI	8472315	$1,165,855

NIH Administrative Data:
PCC: M51C B / **OC**: 414E / **Released**: PII 04/07/2016
Award Processed: 04/09/2016 12:00:53 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 4R01AI098775-05

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 4R01AI098775-05

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal

Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This award was issued as a non-competing continuation with a change in document number. This change was made solely to accommodate the HHS mandate to transition award payments to Payment Management System (PMS) subaccounts. Expenses for the project period should be treated as if this were a non-competing continuation award (e.g. Type 5). A Subaccount Transitional Federal Financial Report (FFR) is required for the previous budget periods to complete the transition. Recipients must use the SF-425 as they would for an interim or annual FFR and enter "Subaccount Transitional FFR" in box 12. This report covers grant funds in the pooled account and is used by NIH to end the grant's association with the pooled PMS payment account and transition award payments to the PMS subaccount established for the grant, including transferring any carryover funds and unliquidated obligations remaining in the pooled account. It is due within 90 days of the end of the calendar quarter in which the last budget period prior to this NoA ended. For more information, please refer to Notice NOT-OD-15-105

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is subject to Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) R01AI098775. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

Based on the project period start date of this project, this award is likely subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170. There are conditions that may exclude this award; see http://grants.nih.gov/grants/policy/awardconditions.htm for additional award applicability information.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

This award represents the final year of the competitive segment for this grant. See the NIH Grants Policy Statement Section 8.6 Closeout for complete closeout requirements at: http://grants.nih.gov/grants/policy/policy.htm#gps.

A final expenditure Federal Financial Report (FFR) (SF 425) must be submitted through the eRA Commons (Commons) within 120 days of the expiration date; see the NIH Grants Policy Statement Section 8.6.1 Financial Reports, http://grants.nih.gov/grants/policy/policy.htm#gps, for additional information on this submission requirement. The final FFR must indicate the exact balance of unobligated funds and may not reflect any unliquidated obligations. There must be no discrepancies between the final FFR expenditure data and the Payment Management System's (PMS) quarterly cash transaction data. A final quarterly federal cash transaction report is not

required for awards in PMS B subaccounts (i.e., awards to foreign entities and to Federal agencies). NIH will close the awards using the last recorded cash drawdown level in PMS for awards that do not require a final FFR on expenditures or quarterly federal cash transaction reporting. It is important to note that for financial closeout, if a grantee fails to submit a required final expenditure FFR, NIH will close the grant using the last recorded cash drawdown level. If the grantee submits a final expenditure FFR but does not reconcile any discrepancies between expenditures reported on the final expenditure FFR and the last cash report to PMS, NIH will close the award at the lower amount. This could be considered a debt or result in disallowed costs.

A Final Invention Statement and Certification form (HHS 568), (not applicable to training, construction, conference or cancer education grants) must be submitted within 120 days of the expiration date. The HHS 568 form may be downloaded at: http://grants.nih.gov/grants/forms.htm. This paragraph does not apply to Training grants, Fellowships, and certain other programs—i.e., activity codes C06, R13, R25, S10.

Unless an application for competitive renewal is submitted, a final progress report must also be submitted within 120 days of the expiration date. Instructions for preparing a Final Progress Report are at: http://grants.nih.gov/grants/funding/finalprogressreport.pdf. Any other specific requirements set forth in the terms and conditions of the award must also be addressed in the final progress report. Institute/Centers may accept the progress report contained in competitive renewal (type 2) in lieu of a separate final progress report. Contact the awarding IC for IC-specific policy regarding acceptance of a progress report contained in a competitive renewal application in lieu of a separate final progress report.

NIH strongly encourages electronic submission of the final progress report and the final invention statement through the Closeout feature in the Commons, but will accept an email or hard copy submission as indicated below.

Email: The final progress report and final invention statement may be e-mailed as PDF attachments to: NIHCloseoutCenter@mail.nih.gov.

Hard copy: Paper submissions of the final progress report and the final invention statement may be faxed to the NIH Division of Central Grants Processing, Grants Closeout Center, at 301-480-2304, or mailed to:

National Institutes of Health
Office of Extramural Research
Division of Central Grants Processing
Grants Closeout Center
6705 Rockledge Drive
Suite 5016, MSC 7986
Bethesda, MD 20892-7986 (for regular or U.S. Postal Service Express mail)
Bethesda, MD 20817 (for other courier/express deliveries only)

NOTE: If this is the final year of a competitive segment due to the transfer of the grant to another institution, then a Final Progress Report is not required. However, a final expenditure FFR is required and should be submitted electronically as noted above. If not already submitted, the Final Invention Statement is required and should be sent directly to the assigned Grants Management Specialist.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 4R01AI098775-05

This award includes funds awarded for consortium activity with NY Blood Center.
This award includes funds awarded for consortium activity with the University of Texas Medical Branch.

Consortiums are to be established and administered as described in the NIH Grants Policy Statement (NIH GPS). The referenced section of the NIH Grants Policy Statement is available at http://grants.nih.gov/grants/policy/nihgps/HTML5/section_15/15_consortium_agreements.htm.

****

Select Agents:
Awardee of a project that at any time involves a restricted experiment with a select agent, is responsible for notifying and receiving prior approval from the NIAID. Please be advised that changes in the use of a Select Agent will be considered a change in scope and require NIH awarding office prior approval. The approval is necessary for new select agent experiments as well as changes in on-going experiments that would require change in the biosafety plan and/or biosafety containment level. An approval to conduct a restricted experiment granted to an individual cannot be assumed an approval to other individuals who conduct the same restricted experiment as defined in the Select Agents Regulation 42 CFR Part 73, Section 13.b (http://www.selectagents.gov/Regulations.html).

Highly Pathogenic Agent:
NIAID defines a Highly Pathogenic Agent as an infectious Agent or Toxin that may warrant a biocontainment safety level of BSL3 or higher according to the current edition of the CDC/NIH Biosafety in Microbiological and Biomedical Laboratories (BMBL) (http://www.cdc.gov/OD/ohs/biosfty/bmbl5/bmbl5toc.htm). Research funded under this grant must adhere to the BMBL, including using the BMBL-recommended biocontainment level at a minimum. If your Institutional Biosafety Committee (or equivalent body) or designated institutional biosafety official recommend a higher biocontainment level, the highest recommended containment level must be used.
When submitting future Progress Reports indicate at the beginning of the report:

If no research with a Highly Pathogenic Agent or Select Agent has been performed or is planned to be performed under this grant.

If your IBC or equivalent body or official has determined, for example, by conducting a risk assessment, that the work being planned or performed under this grant may be conducted at a biocontainment safety level that is lower than BSL3.

If the work involves Select Agents and/or Highly Pathogenic Agents, also address the following points:

Any changes in the use of the Agent(s) or Toxin(s) including its restricted experiments that have resulted in a change in the required biocontainment level, and any resultant change in location, if applicable, as determined by your IBC or equivalent body or official.

If work with a new or additional Agent(s)/Toxin(s) is proposed in the upcoming project period, provide:

o A list of the new and/or additional Agent(s) that will be studied;
o A description of the work that will be done with the Agent(s), and whether or not the work is a restricted experiment;
o The title and location for each biocontainment resource/facility, including the name of the organization that operates the facility, and the biocontainment level at which the work will be conducted, with documentation of approval by your IBC or equivalent body or official. It is important to note if the work is being done in a new location.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Adam Graham
Email: adam.graham@nih.gov **Phone**: 301-761-5430 **Fax**: 301-493-0597

Program Official: Erik J. Stemmy
Email: erik.stemmy@nih.gov **Phone**: 240-627-3380

SPREADSHEET SUMMARY
GRANT NUMBER: 4R01AI098775-05

INSTITUTION: BAYLOR COLLEGE OF MEDICINE

Budget	Year 5
TOTAL FEDERAL DC	$768,645
TOTAL FEDERAL F&A	$397,210
TOTAL COST	$1,165,855

Facilities and Administrative Costs	Year 5
F&A Cost Rate 1	57.3%
F&A Cost Base 1	$693,211
F&A Costs 1	$397,210

A. COVER PAGE

Project Title: RBD recombinant protein-based SARS vaccine for biodefense	
Grant Number: 5R01AI098775-05	**Project/Grant Period:** 05/04/2012 - 04/30/2017
Reporting Period: 05/01/2015 - 04/30/2016	**Requested Budget Period:** 05/01/2016 - 04/30/2017
Report Term Frequency: Annual	**Date Submitted:** 03/15/2016
Program Director/Principal Investigator Information: PETER J HOTEZ , MD PHD BA **Phone number:** 832-824-0502 **Email:** hotez@bcm.edu	**Recipient Organization:** BAYLOR COLLEGE OF MEDICINE BAYLOR COLLEGE OF MEDICINE 1 BAYLOR PLAZA HOUSTON, TX 770303411 **DUNS:** 051113330 **EIN:** 1741613878A1 **RECIPIENT ID:** 35116-N4
Change of Contact PD/PI: N/A	
Administrative Official: LEANNE BROOKS SCOTT One Baylor Plaza Houston, TX 77030 **Phone number:** 713-798-6978 **Email:** spo@bcm.edu	**Signing Official:** LEANNE BROOKS SCOTT One Baylor Plaza Houston, TX 77030 **Phone number:** 713-798-6978 **Email:** spo@bcm.edu
Human Subjects: Yes HS Exempt: Yes Exemption Number: E4 Phase III Clinical Trial:	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** Yes If yes, previously reported: Yes

B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The major goals of the project are: Specific Aim 1: Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate (Timeline Year 1-3). Specific Aim 2: Process development, characterization, formulation and stability profiling (Timeline Year 2-4) and Specific Aim 3: Technology transfer, cGMP Manufacture, GLP toxicology and IND Preparation (Timeline Year 4-5).
As proposed, for this reporting period activities related to Specific Aim 1 (Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate) were initiated. Specifically, we have achieved 50% completion of the activities related to the sub-specific aims 1.A. Feasibility of scalable expression, 1.B. Antigenicity and functionality and 1.C. Immunogenicity. For sub-specific aim 1.D. Efficacy, 33.3% of this activity has been completed. The goals will not change for the next reporting period and no significant changes in approach or methods are envisioned.

B.1.a Have the major goals changed since the initial competing award or previous report?

Yes

Revised goals:

The major goals for the project are: Specific Aim 1: Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate (Timeline Year 1-3). Specific Aim 2: Process development, characterization, formulation and stability profiling (Timeline Year 2-4) and Specific Aim 3: Technology transfer, cGMP Manufacture, GLP toxicology and IND Preparation (Timeline Year 4-5).

Previously completed sub-specific aims: 1.A. (Feasibility of scalable expression), 1.B. (Antigenicity and functionality), 1.C. (Immunogenicity), 1.D. (Efficacy), 1.E. (Optimization of the immunization regimens), 2.A. (Development and optimization of a 10 L scale process (fermentation & purification)) and 2B. (Assay development).

For this reporting period, activities related to Specific Aim 1 (Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate) were advanced. Specifically, we have achieved 85% completion of activities related to the sub-aims 1.F. (Efficacy of rRBD-based vaccine to induce cross-protection in mice) and 1.G. (Efficacy of the rRBD-based vaccine to induce long-term immune responses and protection).

Activities related to Specific Aim 2 (Process development, characterization, formulation and stability profiling) were also advanced. Specifically, we have achieved 100% completion of sub- aim 2.C. (Execution of three successive process development runs at the 10 L scale). For sub- aim 2.D. (Formulation and stabilization), 85% of that activity has been completed.

As originally proposed for this reporting period, activities related to Specific Aim 3 (Technology transfer, cGMP Manufacture, GLP toxicology and IND Preparation) were initiated. Specifically, we have achieved 40% completion of the activities related to the sub-aim 3.A. (Strategy for Manufacture of Drug Substance and Drug Product). For sub-aims 3.B. (Lot release and start of a stability program) and 3.C. (IND Regulatory package preparation and submission), 30% of these activities have been completed.

A request of a Change of Scope was submitted to NIAID on January 15, 2016 and is awaiting approval to modify the specific aims to be completed during Year 5 of this application. The Consortium proposes to complete the 60-L scale GMP manufacture and testing currently ongoing for the SARS RBD vaccine. However, instead of performing the SARS RBD vaccine GLP toxicology and IND preparations, these activities would be replaced with MERS vaccine development activities including the expression, purification and feasibility-of-scale-up evaluation of the MERS-CoV rRBD protein vaccine and its preclinical characterization. In addition, we would evaluate the MERS vaccine antigenicity, immunogenicity and efficacy.

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: Year Four - SARS RPPR 2 page progress report.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: B4.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The Co-I was invited to present an update on the status of current work to the weekly meeting of the Division of Microbiology and Infectious Disease at the National Institutes of Health National Institute of Allergy and Infectious Diseases (NIH/NIAID) on December 17, 2015. The title of the presentation was "Vaccine Development against Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome."

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

As we move into year five, we plan to confirm the optimal adjuvant formulation of the selected yeast-expressed, rRBD protein-based SARS vaccine candidate RBD219-N1 combined with Alhydrogel®. Formulations of the RBD219-N1 protein combined in various ratios of Alhydrogel® will be compared. Alhydrogel® alone will be used as the control. We will assess augmentation of RBD-specific immunogenicity (IgG, IgG1, IgG2a antibody responses) and elicitation of effective neutralizing antibodies in the vaccinated mice using ELISA, as well as pseudo-type and live SARS-CoV-based neutralization assays. In addition, we will test the survival of immunized mice after virus challenge and for the possibility of the development of pathology in the lungs of vaccinated mice.

We will continue using product quality assays and formal stability evaluations to conduct lot release and post-manufacturing stability testing. Likewise, we will maintain our scheduled quality assurance activities with our associates at the Sabin Vaccine Institute as we prepare regulatory documents.

We will continue to closely coordinate with the consortium partners NYBC and UTMB.

The NYBC partners plan to further develop specific assays for evaluating the potency of the SARS-CoV RBD protein, RBD219-N1. The potency of the RBD protein will be evaluated by its ability to induce high titers of neutralizing antibodies in sera of mice immunized i.m. twice with 3 different doses (10, 5, 2.5 µg) of alum-formulated RBD protein at a fixed ratio of 1:8. In addition, the antigenic and functional potencies of the RBD protein, using the same amount used for mouse immunization, will also be determined quantitatively by its ability to bind to SARS-CoV RBD-specific mAb 33G4, and to SARS-CoV's receptor angiotensin converting enzyme 2 (ACE2) using ELISA platform assays. The correlation among the three RBD's potencies; the ability to induce neutralizing antibodies; and the ability to bind mAb 33G4 as well as the receptor ACE2, will be analyzed. If these parameters are significantly correlated, this particular lot of the RBD219N-1 protein will be used as the standard vaccine antigen, and the ELISA assays for measuring the binding of RBD protein to the mAb 33G4 will become the standard assay for evaluating the potency of newly produced RBD219N-1 proteins.

The UTMB partners will complete the preclinical evaluation of the optimal adjuvant formulation of the selected yeast-expressed, rRBD protein-based SARS vaccine candidate RBD219-N1 combined with Alhydrogel® as previously described.

A request of a Change of Scope was submitted to NIAID on January 15, 2016 and is awaiting approval to modify the specific aims to be completed during Year 5 of this application. The Consortium proposes to complete the 60-L scale GMP manufacture and testing currently ongoing for the SARS RBD vaccine. However, instead of performing the SARS RBD vaccine GLP toxicology and IND preparations, these activities would be replaced with MERS vaccine development activities including the expression, purification and feasibility-of-scale-up evaluation of the MERS-CoV rRBD protein vaccine and its preclinical characterization. In addition, we would evaluate vaccine antigenicity, immunogenicity and efficacy.

B.2 Year 4 Accomplishments

As described in last year's report, the immunization route for the selected SARS vaccine candidate RBD219-N1 was optimized (Aim 1) as were the 10 L scale process and assay development (Aim 2). For this reporting period, further progress was made toward completing Aim 1. Other major activities performed were in support of completing Aim 2 and advancing Aim 3.

Aim 1.F. Ability of the rRBD-based vaccine to induce cross-protection in mice.

The cross-neutralizing activity and long-term immunogenicity of the SARS-CoV RBD protein, RBD219-N1, were evaluated by testing the sera of mice immunized with alum-formulated RBD219-N1. We have shown that the RBD219-N1 vaccine induced highly potent anti-RBD neutralizing antibodies that also cross-neutralized divergent strains of SARS pseudovirus expressing SARS-CoV spike (S) proteins isolated at the early (Tor2 strain) and late stage (GD03 strain) of the 2003-4 SARS pandemic, as well as civet SARS-CoV (SZ3 strain). The RBD219-N1 vaccine further was able to induce long-term high levels of neutralizing antibodies against the SARS pseudovirus; high titers were maintained over a 7-months period. These data confirm the excellent potency of the SARS-CoV RBD vaccine against SARS-CoV infection.

Aim 1.G. Ability of the rRBD-based vaccine to induce long-term immune responses and protection, and Aim 2.D. Formulation and Stabilization.

To select the optimal adjuvant for the formulation of the RBD219-N1 vaccine, we compared several adjuvants (Alhydrogel® [aluminum hydroxide], Advax-2 [Inulin plus CpG], glucopyranosyl lipid adjuvant-stable emulsion [GLA-SE], glucopyranosyl lipid adjuvant-aqueous formulation [GLA-AF] plus Alhydrogel®, and MF59) with regard to their ability to improve the efficacy of RBD219-N1 vaccine in mice. Briefly, we immunized 6 groups of *Balb/c* mice (4 per group, 3 times, 3-weeks apart) via the intramuscular (i.m.) route. Mice were bled 10 days after the last immunization for testing the specific antibody responses before intranasal (i.n.) challenge with SARS-CoV. We sacrificed two mice in each group at days 3 and 6 post infection (p.i.) for determining the lung pathology and viral loads. As shown in Figure 1, mice immunized with RBD219-N1 or SARS-CoV S protein formulated with Alhydrogel® produced potent neutralizing antibody responses, resulting in complete protection against subsequent SARS-CoV infection. In contrast, we noted formulations with Advax-1, GLA-SE, MF59, or Tris buffer alone failed to elicit protective neutralizing antibody responses, resulting in incomplete protection against SARS-CoV infection, as evaluated by the isolation of infectious virus and quantitative PCR (qPCR) for viral RNA. We also noted that RBD219-N1 formulated with Alhydrogel® was the only vaccine formulation which did not cause eosinophilic infiltration within the lungs (data not shown). Taken together, these results suggest that RBD219-N1/Alhydrogel® is an effective and safe vaccine for SARS-CoV infection and disease.

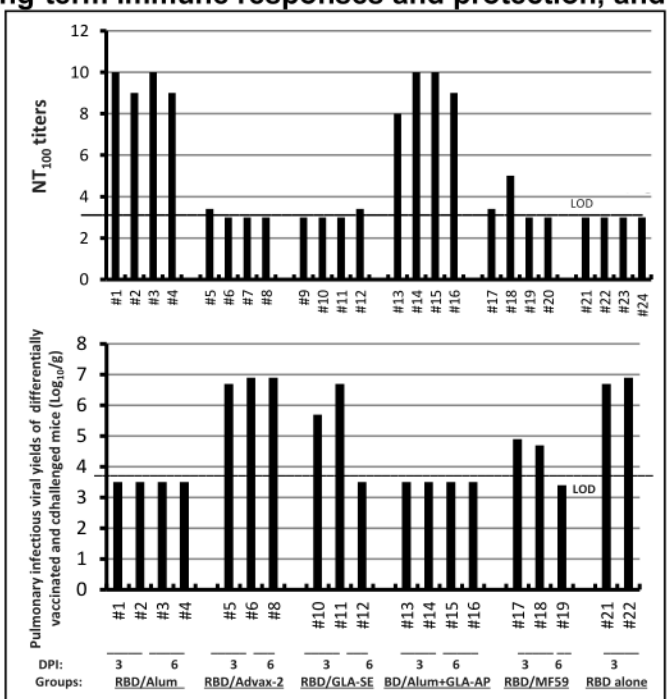

Figure 1. Protective neutralization antibody responses elicited by mice vaccinated with RBD219-N1 formulated in different adjuvants.

Although RBD219-N1 formulated on Alhydrogel® at a ratio of 1:25 has been proven effective in immunized animals against lethal SARS-CoV challenge without causing eosinophilic-type pulmonary immunopathology, such a high RBD219-N1-Alhydrogel® ratio is prohibitive in evaluating large dose ranges given the FDA's allowance of aluminum in vaccines. Therefore, we compared the efficacy of RBD219-N1 formulated on Alhydrogel® at either 1:25 or 1:8 ratios in mice using the same scheme described above. Five groups (N=6) were studied: Group 1) RBD219-N1/Alhydrogel® (RBD: 20, 10, 10 μg; Alhydrogel®: 500, 250, 250 μg, a ratio of 1:25), Group 2) RBD219-N1/Alhydrogel® (RBD: 20, 10, 10 μg; Alhydrogel®: 160, 80, 80 μg, a ratio of 1:8), Group 3) RBD219-N1/Alhydrogel® (RBD: 10, 10, 10 μg; Alhydrogel®: 80, 80, 80 μg, a ratio of 1:8), Group 4) Tris-Alhydrogel® as control (Alhydrogel®: 160, 160, 160 μg), and Group 5) SARS-CoV/Alhydrogel® (S: 3, 3, 3 μg; Alhydrogel®: pre-formulated). The sera were collected 10 days after the last vaccination to test RBD219-N1-specific IgG antibody responses by ELISA and neutralizing antibodies against live SARS-CoV infections. Results showed that mice immunized with RBD219-N1/Alhydrogel® at 1:25 produced significantly