OTHER SUPPORT – HOTEZ, PETER J.

CHANGES:
32472 – grant ended on 12/31/12
AI 90577 – grant ended on 12/31/12
1016395 – effort increased by EFFORT
Private Source grant – new grant was submitted and awarded on 4/20/12
DHHS/Texas A&M contract – was awarded on 11/1/12

CURRENT

23386 Hotez (PI) 01/01/2011-12/31/2014 EFFORT
Sponsor: Dutch Government €842,857
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 - 07/31/2013 EFFORT
Sponsor: Private Source
Title: Human Hookworm Vaccine Initiative 3 $1,491,311
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 – 03/19/2014 0 cal
Private Source $220,280
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.

R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $1,277,421
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, Consultant) 11/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $329,862
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

OVERLAP

None

OTHER SUPPORT - BOTTAZZI, MARIA ELENA

CHANGES:
32472 – grant ended on 12/31/12
1016395 – effort decreased by EFFORT
Private Source – new grant was submitted and awarded on 4/20/12
DHHS/Texas A&M contract – was awarded on 11/1/12
R01AI105431-01 - new grant submitted and awarded on 01/15/2013

ACTIVE

23386 Hotez (PI) 01/01/2011-12/31/2014 EFFORT
Sponsor: Dutch Government $285,715
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.
Role: Sub-PI

1016395 Hotez (PI) 08/01/2011 - 07/31/2013 EFFORT
Sponsor: Private Source
Title: Human Hookworm Vaccine Initiative 3 $1,491,311
Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.
Role: Co-Investigator

Hotez (PI) 04/20/2012 – 03/19/2014 0 cal
Private Source $220,280
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.
Role: Director of Product Development

R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $1,277,421
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, Consultant) 11/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $329,862
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.

1R01AI105431-01 Lustigman (PI) 01/15/2013 – 12/31/2017 EFFORT
Sponsor: NIH via New York Blood Center $270,000
Title: Development of a novel adjuvant for vaccine sparring
Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.
Role: Sub-PI

OVERLAP: None

OTHER SUPPORT - ZHAN, BIN

CHANGES:
32472 – grant ended on 12/31/12
R01A1078314-03 – effort increased by EFFORT
R01AI056189-07 – effort decreased by EFFORT
1016395 – effort decreased by EFFORT
Private Source – new grant was submitted and awarded on 4/20/12
DHHS/Texas A&M contract – was awarded on 11/1/12
R01AI105431-01 - new grant submitted and awarded on 01/15/2013

ACTIVE

1 R01A1078314-03 Lustigman (PI) 08/25/2009 – 07/31/2014 EFFORT
NIH/NIAID (Sub-award from New York Blood Center) $46,017
The development of a recombinant vaccine against human onchocerciasis
The major goal of this subcontract is clone, express, characterize and optimize the expression of the eight selected Onchocerca vaccine candidate antigens (r*Ov*Ags) using the yeast *Pichia* eukaryotic system.
Role: Co-PI

2R01AI056189-07 Aroian (PI) 08/01/2010 – 04/30/2014 EFFORT
NIH (sub-award from UCSD) $18,819
B. thuringiensis Crystal Proteins as Powerful Next-Generation Anthelmintics
The major goal of this subcontract is to test the effects of different formulated Cry5B against hookworm using *Ancylostoma ceylanicum*/hamster model
Role: Co-PI

23386 Hotez (PI) 01/01/2011-12/31/2014 EFFORT
Dutch Government $285,715
Product Development Support of the Human Hookworm Vaccine
The ultimate goal of the project is to conduct Phase 1 studies to assess the safety and immunogenicity of the *Na*-GST-1 and *Na*-APR-1 hookworm antigens in both adults and children.
Role: Director of Molecular Biology

1016395 Hotez (PI) 08/01/2011 – 07/31/2013 EFFORT
Human Hookworm Vaccine Initiative 3 $1,491,311
Sponsor: Private Source
Title: Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.
Role: Director of Molecular Biology

Hotez (PI) 04/20/2012 – 03/19/2014 EFFORT
Private Source $220,280
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.
Role: Director of Molecular Biology

R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/01/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $1,277,421
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.
Role: Director of Molecular Biology

Hotez (Center Director, Consultant) 07/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $329,862
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

1R01AI105431-01 Lustigman (PI) 04/01/2013 – 03/31/2018 EFFORT
Sponsor: NIH via New York Blood Center $270,000
Title: Development of a novel adjuvant for vaccine sparring
Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.
Role: Investigator

OVERLAP

None

OTHER SUPPORT

SARA LUSTIGMAN

See below for the change being made:
For OPP1017584 -- got three years continuation funding (from 11/1/2012 – 10/31/2015)
For R01AI105431-01 -- new grant submitted 06/2012 and awarded 01/15/2013

ACTIVE:

1. 1R01AI078314-01A2 (PI: S. Lustigman) 8/2009 – 7/2014 (b)(6)
NIH/NIAID $714,313

The development of a recombinant vaccine against human onchocerciasis

A collaborative research effort focused on the preclinical research and development process that will result, through a robust screening process, with the discovery of the best 2 recombinant *O. volvulus* vaccine antigens with the highest probability for success at inducing protective immunity in humans. The vaccine will target the *O. volvulus* larvae, known to be vulnerable to host immunological attack.

2. OPP1017584 (PI: J. McKerrow; Co-PI: S. Lustigman) 11/1/2012 – 10/31/2015 (b)(6)
Bill & Melinda Gates Foundation $304,347 (subcontract)

Developing a macrofilaricial drug for onchocerciasis using Anacor's novel oxaborole technology

A collaborative research effort between the University of California San Francisco Sandler Center, Anacor Pharmaceuticals and LFKRI of the NYBC to discover new drug therapies for the treatment of river blindness (onchocerciasis). The collaboration's goal is to identify a novel, potent macrofilaricidal drug candidate that is capable of killing adult worms.

Overlap: none

3. R01AI098775-01 MPI: Hotez/Bottazzi/Jiang; Co-PI S. Lustigman 05/01/2012 – 04/30/2017 (b)(6)
NIH/NIAID $300,000 (subcontract)

RBD Recombinant Protein-based SARS Vaccine for Biodefense

The main goal of this project is to develop, test and manufacture a novel recombinant SARS vaccine.

Overlap: none

4. 1R01AI105431-01 (PI: S. Lustigman) 1/2013 – 12/2017 (b)(6)
NIH/NIAID $1,052,327 (including three subcontracts)

Development of a novel adjuvant for vaccine sparring

Adjuvants are integrated into vaccines to insure their effectiveness and to support antigen sparing. Currently, alum is the only adjuvant licensed in the U.S., but it has had limited effectiveness when used with commercial flu vaccines. Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.

Overlap: none

E. IMPACT

E.1 Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARDS BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 Not Applicable for R01

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

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SARS-CoV became a select viral agent as of December 4, 2012. UTMB has been working diligently with various regulatory agents, both on and off the UTMB campus, to comply with all regulations concerning the usage of select agents. In short, we have made an inventory of the SARS-CoV that we have in the laboratory and moved our animal (A).BSL-3 laboratories from Mary Moody Northern (MMN) into the Galveston National Laboratory complex as of December 4th, 2012 with 24/7 security service. During this transition stage our group feels strongly that there will be no negative impact on the ongoing SARS program under this grant and if any, it will be minimal. The biocontainment level for SARS-CoV remains the same, level-3, however, the antigen became classified as a select agent.

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

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RPPR G1.pdf

G.2 Not Applicable

G.3 Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

Yes

Exemption number(s) E4

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: RBD recombinant protein-based SARS vaccine for biodefense-PROTOCOL-001

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional	Address

		District	
Primary: BAYLOR COLLEGE OF MEDICINE	051113330	TX-007	BAYLOR COLLEGE OF MEDICINE ONE BAYLOR PLAZA HOUSTON TX 770303411
New York Blood Center	073271827	NY-014	310 East 67 Street New York NY 100656275
The University of Texas Medical Branch	800771149	TX-014	301 University Boulevard Galveston TX 775550156
Texas Childrens Hospital	074615394	TX-007	1102 Bates Street Houston TX 770302399

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

utmb Health

Environmental Health & Safety
Biological & Chemical Safety Program
Materials Management Building, 2.112
301 University Blvd.
Galveston, Texas 77555-1111
O 409.772.1781 F 409.772.8921

February 11, 2013

To Whom It May Concern

The University of Texas Medical Branch at Galveston (UTMB) is a select agent registered entity with the U.S. Health and Human Services, Centers for Disease Control and Prevention Division of Select Agents and Toxins (CDC/DSAT) and U. S. Department of Agriculture, Animal and Plant Health Inspection Service, (USDA/APHIS) National Select Agent Program. The University has been inspected by the CDC/DSAT and USDA/APHIS National Select Agent Program for use of HHS Select Agents and Toxins, Overlap Select Agents and Toxins and USDA Select Agents and Toxins.

Per the requirements of 42 CFR 73 the original certificate of registration was issued October 19, 2004, renewal was granted on April 9, 2007 and again on April 1, 2010 for use of select agents at BioSafety Levels 2, 3, and 4 and Animal BioSafety Levels 3 and 4. Inspection by CDC/DSAT and USDA/APHIS occurred January 9th to 20th 2012, for the current renewal cycle and approval was granted on March 21, 2012 for three years. The University has been registered with Health and Human Services, Centers for Disease Control and Prevention as a select agent facility since 1997. The University has a Responsible Official and four Alternate Responsible Officials.

Attached please find a copy of the University Of Texas Medical Branch certificate of registration of the possession, use and transfer of select agents and toxins. The registration number has been redacted for security purposes. The registration number will be provided at the time of an official CDC/USDA Form 2 transfer of select agents.

Please feel free to contact me should you require additional information.

Sincerely,

Domenica Zimmerman

Domenica Zimmerman
BioSafety Officer
Alternate Responsible Official
UTMB Select Agent Program

Certificate of Registration

Entity Name: University of Texas Medical Branch
Address: 301 University Boulevard
Galveston, TX 77555-0633

Registration #:
Effective Date: March 21, 2012
Expiration Date: March 21, 2015

Responsible Official: Michael Shriner
Alternate Responsible Official(s): Carlos Escobar, Amy Goebel, Scott Weaver, Domenica Zimmerman

Based on information provided to the CDC Select Agent Program and the APHIS Agricultural Select Agent Programs, the above-named entity is authorized to possess, use, and transfer select agents and toxins under the conditions specified in the entity registration application, in accordance with 42 CFR part 73, 9 CFR part 121, and 7 CFR part 331.

Robbin S. Weyant, Director
Select Agent Program
Centers for Disease Control and Prevention

Freeda E. Isaac, DVM, Director
Select Agent Program
Veterinary Services

Charles L. Divan, Branch Chief
Select Agent Program
Plant Protection and Quarantine

At Baylor College of Medicine (BCM) and New York Blood Center (NYBC) no research is conducted or is planned to be performed under this grant with a Highly Pathogenic Agent or Select Agent. The institutional IBC officials have determined that the work being planned or performed under this grant at these institutions may be conducted at a biocontainment safety level that is lower than BSL3.

At University of Texas Medical Branch (UTMB) the work will involve Select Agents and/or Highly Pathogenic Agents. No changes have been done in the use of the Agent, the type of experiments or required biocontainment level. UTMB documentation of the registration status is included.

Inclusion Enrollment Report Table

This report format should NOT be used for data collection from study participants.

Study Title: RBD recombinant protein-based SARS vaccine for biodefense-PROTOCOL-001

Total Enrollment: 0 **Protocol Number:**

Grant Number: R01AI098775-02

PART A. TOTAL ENROLLMENT REPORT : Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race				
Ethnic Category	**Sex/Gender**			
	Females	**Males**	**Unknown or Not Reported**	**Total**
Hispanic or Latino	0	0	0	0
Not Hispanic or Latino	0	0	0	0
Unknown (Individuals not reporting ethnicity)	0	0	0	0
Ethnic Category:Total of All Subjects	0	0	0	0
Racial Categories				
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian Or Other Pacific Islander	0	0	0	0
Black Or African American	0	0	0	0
White	0	0	0	0
More than one race	0	0	0	0
Unknown or Not Reported	0	0	0	0
Racial Categories: Total of All Subjects	0	0	0	0

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)				
Racial Categories	**Sex/Gender**			
	Females	**Males**	**Unknown or Not Reported**	**Total**
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian Or Other Pacific Islander	0	0	0	0
Black Or African American	0	0	0	0
White	0	0	0	0
More than one race	0	0	0	0
Unknown or Not Reported	0	0	0	0
Racial Categories: Total of Hispanics Or Latinos	0	0	0	0

Inclusion Enrollment Comments: This project is not required to enroll subjects. The research has exemption approval and only involves the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens.

RESEARCH **Issue Date:** 04/14/2014

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 5R01AI098775-03
FAIN: R01AI098775

Principal Investigator(s):
Maria Elena Bottazzi
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

Budget Period: 05/01/2014 – 04/30/2015
Project Period: 05/04/2012 – 04/30/2017

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $1,134,359 (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 42 CFR Part 50 Subpart F. Subsequent to the compliance date of the 2011 revised FCOI regulation (i.e., on or before August 24, 2012), Awardees must be in compliance with all aspects of the 2011 revised regulation; until then, Awardees must comply with the 1995 regulation. 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,

Michael W. Fato
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 5R01AI098775-03

Award Calculation (U.S. Dollars)

Federal Direct Costs	$899,886
Federal F&A Costs	$234,473
Approved Budget	$1,134,359
Federal Share	$1,134,359
TOTAL FEDERAL AWARD AMOUNT	$1,134,359
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$1,134,359

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
3	$1,134,359	$1,134,359
4	$1,165,726	$1,165,726
5	$1,165,855	$1,165,855

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Number:	93.855
EIN:	1741613878A1
Document Number:	RAI098775A
PMS Account Type:	G (Pooled)
Fiscal Year:	2014

IC	CAN	2014	2015	2016
AI	8472315	$1,134,359	$1,165,726	$1,165,855

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 414E / **Released**: PII 04/11/2014
Award Processed: 12/26/2013 10:57:56 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01AI098775-03

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 – 5R01AI098775-03

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 74 or 45 CFR Part 92 as applicable.
d. The NIH Grants Policy Statement, including addenda in effect as of the beginning date of the budget period.
e. 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.)

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 Central Contractor Registration. 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/.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 5R01AI098775-03

THIS AWARD CONTAINS GRANT SPECIFIC RESTRICTIONS. THESE RESTRICTIONS MAY ONLY BE LIFTED BY A REVISED NOTICE OF AWARD.

RESTRICTION: Under governing PHS Policy, Federal funds administered by the Public Health Service (PHS) shall not be expended for research involving live vertebrate animals without prior approval by the Office of Laboratory Animal Welfare (OLAW) of an Assurance to comply with the PHS Policy on Humane Care and Use of Laboratory Animals and the project has been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). The present award is being made without currently valid verification of IACUC approval for the portion of this project being completed in CHINA with the following restriction: No activities that involve live vertebrate animals may be conducted at Frontier Biosciences located in CHINA pending acceptance by the NIH awarding component of verification of IACUC approval. The Program Officer has approved the funding of this application without the portion of Frontier Biosciences located in CHINA in year 05 as the project is viable without it. No funds may be expended for the foreign site pending the resolution of internal administrative issues. Once these issues have been resolved, this award may be revised to include the study originally planned for the foreign site. Failure to comply with this special condition can result in suspension and/or termination of this award, withholding of support, audit disallowances, and/or other appropriate action.

****

This award includes funds awarded for consortium activity with NY Blood Center and 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_2013/nihgps_ch15.htm#_Toc271265264.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

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: 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: 5R01AI098775-03

INSTITUTION: BAYLOR COLLEGE OF MEDICINE

Budget	Year 3	Year 4	Year 5
TOTAL FEDERAL DC	$899,886	$782,695	$768,645
TOTAL FEDERAL F&A	$234,473	$383,031	$397,210
TOTAL COST	$1,134,359	$1,165,726	$1,165,855

Facilities and Administrative Costs	Year 3	Year 4	Year 5
F&A Cost Rate 1	57.3%	57.3%	57.3%
F&A Cost Base 1	$409,202	$668,466	$693,211
F&A Costs 1	$234,473	$383,031	$397,210

A. COVER PAGE

Project Title: RBD recombinant protein-based SARS vaccine for biodefense	
Grant Number: 5R01AI098775-03	**Project/Grant Period:** 05/04/2012 - 04/30/2017
Reporting Period: 05/01/2013 - 04/30/2014	**Requested Budget Period:** 05/01/2014 - 04/30/2015
Report Term Frequency: Annual	**Date Submitted:** 03/14/2014
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 MS-310 HOUSTON, TX 770303411 **DUNS:** 051113330 **EIN:** 1741613878A1 **RECIPIENT ID:** 35116-N2
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?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: SARS NIH Annual report 2-page summary 03-13-14.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?

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
3R01AI098775-02S1	RBD recombinant protein-based SARS vaccine for biodefense	The project plan was to instruct the student on fundamental techniques in molecular biology and biochemistry and provide a broad educational overview on the key steps in developing a vaccine to prevent a major public health threat. The project plan included regular meetings with the research team; one-on-one mentorship meetings to provide feedback on weekly activities; answer questions and provide additional training if needed; and training in various general aspects of research. The student s work fell under Specific Aim 2 of the parent grant, specifically, Process development, characterization, formulation and stability profiling.	The student assisted with process development of a recombinant receptor-binding domain (rRBD) protein to prevent severe acute respiratory syndrome (SARS) caused by the SARS coronavirus (SARS CoV), a major part of the Specific Aim 2. The student assisted with the discovery of possible purification parameters as well as the identification of in-process samples over the chromatographic purification procedure thereby contributing to Milestone 1: A suitable expression is selected for expression of rRBD in small scale and Milestone 4: Established a reproducible 10L scale process for a stable rRBD-based vaccine in preparation for future technology transfer to a cGMP manufacturing facility.

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

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

ASM Biodefense and Emerging Diseases conference attended and presentation of a poster titled Process development of a SARS vaccine candidate: a yeast-expressed receptor-binding domain of the SARS-CoV spike protein by Wen-Hsiang Chen, Ph.D on 1/27-29, 2014.

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

For Year 3, activities will continue toward the completion of Specific Aim 1. Using the selected yeast-expressed, rRBD-based SARS candidate vaccine, additional detection of the antibody and cellular immune responses induced by rRBD proteins after vaccination in the presence or absence of GLA (Glycopyranosyl lipid A) and/or alum adjuvants will be explored followed by the evaluation of cross-neutralizing activity with a SARS-CoV pseudovirus neutralization assay.

Our initial studies will assist us in optimizing the immunization regimens for the selected SARS candidate vaccine, including immunization routes, adjuvant formulation, rRBD protein doses, as well as immunization dosages and intervals, in a hope to select the best immunization regimens for subsequent long-term immunogenicity evaluation and SARS-CoV challenge study.

To optimize immunization routes and adjuvant formulation, we will immunize mice via subcutaneous (s.c.) or intramuscular (i.m.) route, respectively, with the selected rRBD protein, in the presence or absence of alum and/or GLA adjuvant, followed by boosting of the mice twice at 3-week intervals. To optimize antigen doses, we will immunize mice with rRBD protein at 1, 5, 10, (or 20 µg if needed), respectively, using the optimized adjuvant and optimal route, and boost once or twice (with 1, 5, or 10 µg rRBD, respectively) at 3-week intervals. The optimization of immunization dosages and intervals will be tested in mice vaccinated with the selected rRBD protein and adjuvant using the optimized adjuvant formulation, optimized rRBD dose and optimal route, followed by boosting of the mice once at 2- or 8-week intervals or not boosted.

Vaccine-induced, RBD-specific immunogenicity, particularly IgG and neutralizing antibodies, will be assessed in vaccinated mouse sera, and T cellular immune responses will be detected using mouse spleens and lymph nodes collected 10 days after last boost. In addition, the ability of the SARS-CoV RBD vaccines to induce cross-neutralizing antibody responses will also be evaluated using SARS pseudovirus and live virus neutralization assays in collected sera of mice vaccinated with the rRBD candidate protein.

The rRBD-induced long-term immune responses will be tested in mice vaccinated with optimized vaccination regimen, and observed for a period of 6 or 12 month, respectively, followed by detection of antibody response, neutralizing activity against SARS pseudovirus and T cell responses as described above.

Once the best vaccination strategy has been established, we will conduct experiments to fully determine the protective efficacy of selected rBRD-based vaccine candidate(s) against lethal SARS-CoV infection. While the immunogenicity and the ability of tested vaccines to restrict viral replication and pathology in the lungs will be used as criteria for the assessment, whether vaccination would result in a Th2-type disease enhancement will be particularly emphasized.

For Year 3, activities we will continue for Specific Aim 2. We will continue optimizing the fermentation conditions and purification scheme for the yeast expressed RBD219-N1. In addition, we will further evaluate the assays which establish identity, yields, purity, conformation and integrity for our target protein after expression (e.g., HPLC-SEC, HPLC-RP, Mass Spectrometry etc.). Also, we will initiate the study for formulation and stabilization of RBD219-N1 in order to produce a formulation of a recombinant vaccine of maximal stability potentially suitable for emergency stockpiling.

We will continue to closely coordinate with the consortium partners NYBC and UTMB to fully execute the year 3 studies.

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

B.2 Year 2 Accomplishments. Year 2 was a breakout year for our SARS Vaccine development program. We determined that a specific receptor binding domain (RBD) construct known as RBD219-N1 could be expressed in the yeast Pichia pastoris at high yield and purity. Moreover, RBD219-N1 was shown to elicit high titers of neutralizing antibodies. Based on our results and following our Year 2 program review RBD219-N1 will be selected for process development and cGMP manufacture.

For this reporting period the major activities performed were linked to Aim 1 and Aim 2. **Aim 1.A. Feasibility of scalable expression.** 1.A.1. *E. coli* (bacteria) Expression. We completed the evaluation of alternative methods to address the solubility of bacterially expressed proteins. None of the strategies used led to suitable results as compared to the yeast expression strategy (see below) This sub aim has been completed and closed out. 1.A.2. *Pichia pastoris* (yeast) Expression. The yeast system was selected as the expression platform of choice. Four rRBDs (RBD193-N1, RBD193-N3, RBD219-WT and RBD219-N1) were evaluated for yield (>25mg/L), ease of purification and purity (>90%), antigenicity and immunogenicity. Table 1 ranks the rRBD candidates indicating that RBD219-N1 is the top candidate to advance into process development (Aim 2). To improve fermentation yield (~45mg/L clone OR), additional screening was performed to identify a final research seed stock. More than 80 clones were screened in the presenceof different concentrations of Zeocin identifying high copy transformants. Western blot results revealed Clone#27 as the highest expressor (compared to clone OR). Clone#27 was tested for expression yield in a 5L-scale fermentation with a yield of 70.5 mg/L.

Table 1. Comparison of the four yeast expressed RBD proteins. Note that RBD193-WT was the positive control expressed in mammalian cell 293T (Du et al., Viral Immunol. 2010).

Construct	Fermentation Yield (mg/L)	Antigenicity response (Fig. 3)	IgG Titers (Fig. 4A)	Neutralizing Antibody (Pseudovirus)	Neutralizing Antibody (Live virus)
RBD193-WT	N/A	Medium	3.5×10^5	4×10^4	2.3×10^3
RBD193-N1	~100	Medium	1.8×10^5	4.3×10^3	2.5×10^2
RBD193-N3	<16	Medium	1.9×10^5	1.4×10^4	1.6×10^3
RBD219-WT	~40	High	1.8×10^5	4×10^4	2.2×10^3
RBD219-N1	~45	High	1.4×10^6	4×10^4	4.5×10^3

1.A.3. RBD219-N1 Protein yield, purity and preliminary stability profile. *Protein yield.* Total fermentation supernatant of clone OR was purified using hydrophobic interaction chromatography and subsequent size exclusion column allowing us to obtain 95% of purified protein evidenced both by SDS-PAGE Coomassie stained gels and Western blot (Figure 1). *Preliminary stability profile.* The rRBD219-N1 soluble purified protein can be detected as a distinct and discrete band on a western blot probed with a conformational epitope-specific mAb 33G4 and with no evidence of degradation or aggregation (data not shown). **Aim 1.B. Antigenicity and functionality.** To validate the antigenicity of purified RBD proteins, we performed ELISA with five conformational anti-RBD mAbs (24H8, 19B2, 35B5, 33G4, and 31H12) and one linear anti-RBD mAb (17H9). We found that RBD219-WT and RBD219-N1 (1 µg/mL) exhibited the strongest binding to all conformational mAbs tested at concentration as low as 0.25 µg/mL, although their reactivity to the linear anti-RBD mAb 17H9 was significantly decreased (Figure 2), suggesting that deglycosylated RBD219-N1 protein, like RBD219-WT, was able to maintain conformation and antigenicity, despite the deletion of the N1 glycosylation site. The functionality was also evaluated by detecting the binding ability of these proteins to SARS-CoV's receptor ACE2. The results show that all purified RBD proteins react strongly with either cell-associated or soluble receptor when tested using the ACE2- or RBD-specific mAbs. (Figure not shown.) These results indicated that all RBD proteins with or without mutations maintain functionality. **Aim 1.C. Immunogenicity.** Immunogenicity was evaluated in an established mouse model by immunizing with purified RBD proteins adsorbed to Alum. Antibody responses and neutralizing antibodies were evaluated. Results show that RBD219-N1 induced significantly higher IgG titers against RBD219-WT as compared to all the other RBD proteins. The control RBD193-WT also induced significantly higher IgG titers against RBD219-WT (Figure 3A). For neutralizing antibodies, we tested sera from vaccinated mice 10 days post-last vaccination using both pseudovirus and live SARS-CoV-based neutralization assays. Immunization with RBD219-N1 resulted in significantly higher titers of neutralizing antibodies against live SARS-CoV infection compared to those elicited by the control RBD193-WT, RBD193-N1, RBD193-N3, or RBD219-WT (Figure 3B). In addition, immunization with the control RBD193-WT, RBD219-WT or

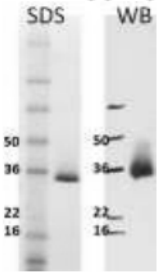

Figure 1. SDS-PAGE and Western blot analysis of yeast-expressed RBD proteins. SDS-PAGE (SDS, left panels) and Western blot (WB, right panels) analysis of 2 µg purified RBD219-N1.

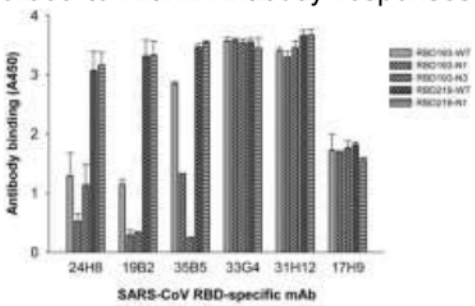

Figure 2. Antigenicity evaluation of SARS-CoVRBD proteins with 0.25 µg/mL anti-RBD mAbs

RBD219-N1 uniformly elicited potent neutralizing antibody responses against SARS pseudovirus infection, being significantly stronger than those induced by the other two RBD proteins (data not shown). As expected, the Alum PBS control did not elicit neutralizing antibody response against both pseudovirus and live SARS-CoV (Figure 3). These data confirm that RBD219-N1 possesses the strongest immunogenicity among RBD proteins tested. **Aim 1.D. Efficacy.** Pilot study comparing safety, immunogenicity, and efficacy of RBD- and S-based Alum vaccines (Tseng et al., 2010. PLoS One) in a lethal mouse model of SARS was done. Figure 4A shows mice immunized with RBD-219N1 elicited the highest titer of neutralizing antibody and were protected from clinical disease (i.e., weight loss) with no death (Figure 4B and 4C), when compared to those immunized with other vaccines. None of the mice given TBS/alum produced detectable neutralizing antibody whereas their geometric means of lung virus titers were $10^{9.9}$ and $10^{8.9}$ $TCID^{50}$/g on days 1 and 2 post infection (PI), respectively. In contrast, all vaccinated groups exhibited lower or even undetectable viral titers in the lungs at days 1 and 2 PI (Figure 4D and 4E). Whether mice vaccinated with RBD proteins might exhibit a T_H2-type immunopathology with prominent eosinophil infiltration as those vaccinated with SARS-CoV S protein is currently under investigation, they were more effective in reducing SARS-CoV infection and diseases. **Specific Aim 2.A. Development and optimization of a 10 L scale process.** 2.A.1 Upstream process optimization. Fermentation conditions including (temperatures, pHs, sorbitol co-feeds, medium salt concentrations, detergents and methanol feed rates) were optimized at 5L scale. The best induction condition was identified to be using a low salt buffer media, at 24°C, and pH 6.5 with a methanol flow rate increased from 11 to 15 mL/L/hr. This condition yield 70.5 mg/L of RBD219-N1 in the fermentation supernatant. 2.A.2 Downstream process. We purified the RBD219-N1 using a two-step purification process: Butyl Hydrophobic Interaction Chroma-tography (HIC) followed by Size Exclusion Chromatography (SEC) at small scale (up to 10mL scales). Alternative methods using cation exchange chromatography (Capto S) as the capture step, hydrophobic interaction chromatography (Butyl HP) as the intermediate purification step and gel filtration as a final buffer exchange step are under consideration. **2.B. Assay development.** SDS-PAGE (reduced and non-reduced) and Western Blot (Figure 1; non-reduced gel not shown) are the two main assays used to assess purity and identity of RBD219-N1. An ELISA technique and HPLC-SEC are under development as tools to verify identity and purity. Additional methods, e.g., host cell protein western blot, mass spectrometry, N-terminal sequencing, etc. are also under development. **2.C. Execution of 3 successive process development runs at the 10L scale.** The optimization of upstream and downstream processes is ongoing as mentioned above. The three successive process development runs are scheduled after the optimization of the process is complete.

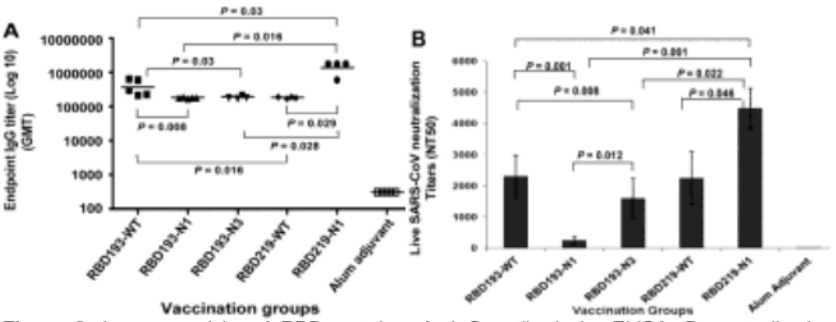

Figure 3. Immunogenicity of RBD proteins. A, IgG antibody by ELISA. B, neutralization antibody detection in mouse sera. The RBD proteins were used to immunize 6-8 week-old BALB/c mice for three times at 3-week intervals after adsorption to alhydrogel adjuvant.

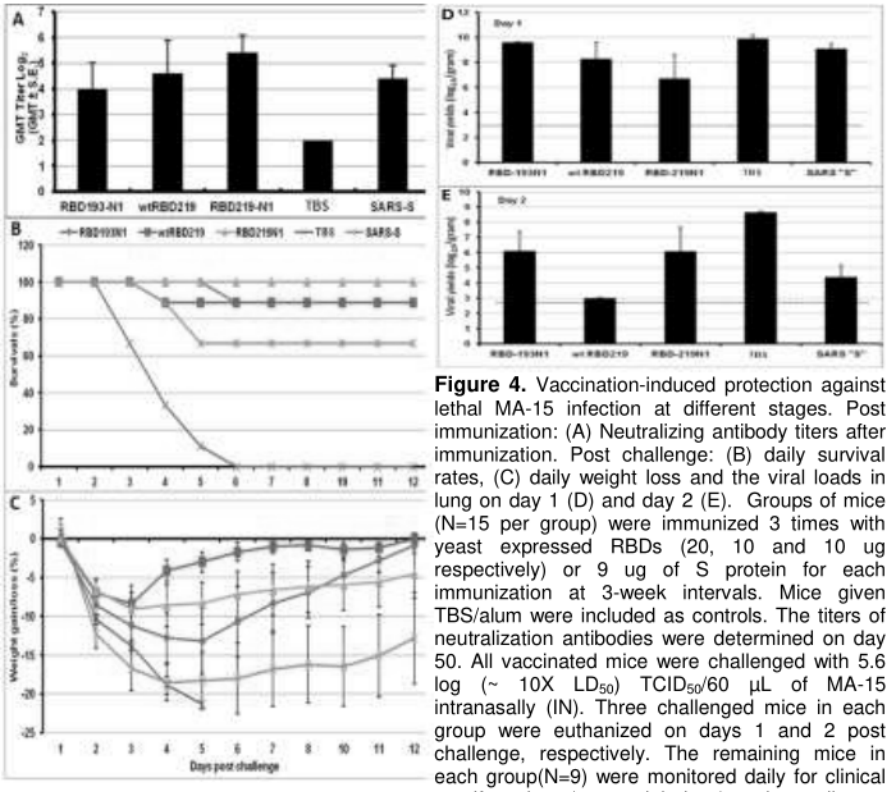

Figure 4. Vaccination-induced protection against lethal MA-15 infection at different stages. Post immunization: (A) Neutralizing antibody titers after immunization. Post challenge: (B) daily survival rates, (C) daily weight loss and the viral loads in lung on day 1 (D) and day 2 (E). Groups of mice (N=15 per group) were immunized 3 times with yeast expressed RBDs (20, 10 and 10 ug respectively) or 9 ug of S protein for each immunization at 3-week intervals. Mice given TBS/alum were included as controls. The titers of neutralization antibodies were determined on day 50. All vaccinated mice were challenged with 5.6 log (~ 10X LD_{50}) $TCID_{50}$/60 µL of MA-15 intranasally (IN). Three challenged mice in each group were euthanized on days 1 and 2 post challenge, respectively. The remaining mice in each group(N=9) were monitored daily for clinical manifestations (e.g., weight loss), and mortality

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

Funds were received for a minority supplement 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 served as a basis for engaging an under-represented minority high school student in an eight-week long mentored program of biotechnology and biochemistry research. The program was offered in association with the Office of Diversity and Community Outreach at Baylor College of Medicine.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

NIH Public Access Compliance	Citation
Complete	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 vaccine for severe acute respiratory syndrome. Expert Rev Vaccines. 2012 Dec;11(12):1405-13. PubMed PMID: 23252385; PubMed Central PMCID: PMC3586247.
PMC Journal - In process	Chen WH, Du L, Chag SM, Ma C, Tricoche N, Tao X, Seid CA, Hudspeth EM, Lustigman S, Tseng CT, Bottazzi ME, Hotez PJ, Zhan B, Jiang S. Yeast-expressed recombinant protein of the receptor-binding domain in SARS-CoV spike protein with deglycosylated forms as a SARS vaccine candidate. Hum Vaccin Immunother. 2013 Dec 30;10(3)PubMed PMID: 24355931.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period?

Yes

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization? Yes

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

NOTHING TO REPORT

C.5.b Resource sharing

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	SSN	DOB	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
eRA Commons User Name	Y	HOTEZ, PETER,	PII		BA,PHD, MD	PD/PI	EFFORT	0	0			NA
	Y	Bottazzi, Maria,				PD/PI		0	0			NA
	Y	JIANG, SHIBO,			PHD,MD	PD/PI		0	0	Fudan University	CHINA	NA
	Y	LUSTIGMAN, SARA,			PHD	Co-Investigator		0	0			NA
	N	Hudspeth, Elissa,			BS	Technician		0	0			NA
	N	Zhang, Naru,			Ph.D.	Research Fellow		0	0			NA
	N	Chan, Tehseng,			MD, PhD	Co-Investigator		0	0			NA
	N	Tricoche, Nancy,			BS	Non-Student Research Assistant		0	0			NA
	Y	Tseng, Chien-Te,			PHD,MS	Co-Investigator		0	0			NA
	N	Chag, Shivali,			MS	Non-Student Research Assistant		0	0			NA
	N	Seid, Chris,			Ph.D.	Staff scientist (Doctoral level)		0	0			NA
	N	Chen, Wen,			Ph.D.	Non-Student Research Assistant		0	0			NA
	N	Nino, Diane,			BSci	Project Manager		0	0			NA
	N	Nelson, Frederick,				High School Student		0	2			DS
	N	Pollet, Jeroen,			Ph.D.	Director, Formulation		0	0			NA
	Y	Du, Lanying,			PHD	Co-Investigator		0	0			NA
eRA Commons User Name	N	Tao, Xinrong,			Ph.D.	Postdoctoral Scholar, Fellow, or Other Postdoctoral Position		0	0			NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

NOTHING TO REPORT

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

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D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

NOTHING TO REPORT

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

No

NOTHING TO REPORT

OTHER SUPPORT – HOTEZ, PETER J.

CHANGES:
Private Source grant: received funding for another two years until 4/19/16

Newly awarded:
Two grants from Private Source subaward
University of Malaya
Private Source
Instituto Carlos Slim de la Salud

CURRENT

23386 Hotez (PI) 01/01/2011-12/31/202014 EFFORT
Sponsor: Dutch Government €842,857
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 - 04/30/2015 EFFORT
Sponsor: Private Source
Title: Human Hookworm Vaccine Initiative 3 $871,809
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 EFFORT
Private Source $225,928
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.

5R01AI098775-02 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $955,528
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, Consultant) 11/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $255,928
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/Bottazzi (MPI) 08/01/2013 – 07/31/2017 EFFORT
Sponsor: Private Source $328,435
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.

Hotez (PI) 01/01/2014 – 12/31/2016 EFFORT
Sponsor: University of Malaya $250,000
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 EFFORT
Sponsor: Private Source $160,000
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 EFFORT
Sponsor: Private Source $179,348
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 – 12/31/2014 EFFORT
Sponsor: Instituto Carlos Slim de la Salud $709,333
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.

OVERLAP

None. If funded, appropriate adjustments will be made to ensure that Dr. Hotez's time will total no than 100% on active projects at any given time

OTHER SUPPORT - BOTTAZZI, MARIA ELENA

CHANGES:
23386 – grant ended on 12/31/13
Private Source grant: received funding for another two years until 4/19/16

Newly awarded:
Two grants from Private Source
European Union via AIGHD subaward
University of Malaya
Private Source
Instituto Carlos Slim de la Salud

ACTIVE

1016395 Hotez (PI) 08/01/2011 – 04/30/15 EFFORT
Sponsor: Private Source
Title: Human Hookworm Vaccine Initiative 3 $871,809
Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.
Role: Co-Investigator

Hotez (PI) 04/20/2012 – 04/19/2016 EFFORT
Private Source $225,928
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.
Role: Director of Product Development

R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $955,528
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, Consultant) 11/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $255,928
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.

1R01AI105431-01 Lustigman (PI) 01/15/2013 – 12/31/2017 EFFORT
Sponsor: NIH via New York Blood Center $177,000
Title: Development of a novel adjuvant for vaccine sparring
Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.
Role: Sub-PI

Hotez/Bottazzi (MPI) 08/01/2013 – 07/31/2017 EFFORT
Sponsor: Private Source $328,435
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 Bottazzi (PI) 10/1/2013 – 9/30/2017 EFFORT

Sponsor: European Union via sub from (AIGHD) $91,121
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 EFFORT
Sponsor: University of Malaya $250,000
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.
Role: Co-I

Hotez (PI) 01/01/2014 – 12/31/2017 EFFORT
Sponsor: Private Source $160,000
Title: West Nile Virus vaccine development
Main goal is to support West Nile Virus vaccine development.
Role: Co-I

Hotez/Bottazzi (MPI) 01/01/2014 – 12/31/2017 EFFORT
Sponsor: Private Source $179,348
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 – 12/31/2014 EFFORT
Sponsor: Instituto Carlos Slim de la Salud $709,333
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.

OVERLAP

None. If funded, appropriate adjustments will be made to ensure that Dr. Bottazzi's time will total no than 100% on active projects at any given time

Other Support

Dr. Lanying Du received an R21 grant (R21 AI109094) for identification of critical neutralizing domain-based vaccines against new SARS-like virus MERS-CoV. She will put EFFORT of her effort for the R21 project (as shown below), but keep her originally approved EFFORT effort unchanged.

Dr. Sara Lustigman changed her Other Support for NIH/NIADI R01 grant (1R01AI078314-01A2) and a Private Source (OPP1017584) from EFFORT to EFFORT respectively. She also received several new grants from Private Source (OPP1086618, OPP1099849, OPP1083910, with effort of EFFORT and EFFORT respectively), and NIH/NIAID (1R56 1AI101372-01A1, with effort of EFFORT. She will keep her efforts on other grants unchanged.

LANYING DU

ACTIVE

1R21AI109094-01 (Du) 12/15/2013 – 11/30/2015 EFFORT
NIH/NIAID

Critical neutralizing domain-based vaccines against new SARS-like virus hCoV-EMC
The major goal of this project is develop a critical neutralizing domain (CND)-based subunit vaccine for the prevention of the newly identified MERS-CoV or other coronaviruses that may cause future outbreaks in humans.
Role: PI

OVERLAP: None

SHIBO JIANG

ACTIVE

1R21AI109094-01 (Du) 12/15/2013 – 11/30/2015 EFFORT
NIH/NIAID

Critical neutralizing domain-based vaccines against new SARS-like virus hCoV-EMC
The major goal of this project is develop a critical neutralizing domain (CND)-based subunit vaccine for the prevention of the newly identified MERS-CoV or other coronaviruses that may cause future outbreaks in humans.
Role: Co-Investigator

OVERLAP: None

SARA LUSTIGMAN
ACTIVE

1. 1R01AI078314-01A2 (PI: S. Lustigman) 8/2009 – 7/2014 (b)(6)

NIH/NIAID $603,776

The development of a recombinant vaccine against human onchocerciasis

A collaborative research effort focused on the preclinical research and development process that will result, through a robust screening process, with the discovery of the best 2 recombinant *O. volvulus* vaccine antigens with the highest probability for success at inducing protective immunity in humans. The vaccine will target the *O. volvulus* larvae, known to be vulnerable to host immunological attack.
Overlap: none

2. OPP1017584 (Bill & Melinda Gates Foundation) (PI: J. McKerrow; Co-PI: S. Lustigman)

$304,347 (subcontract) 11/1/2012 – 10/31/2015 (b)(6)

Developing a macrofilaricial drug for onchocerciasis using Anacor's novel oxaborole technology

A collaborative research effort between the University of California San Francisco Sandler Center, Anacor Pharmaceuticals and LFKRI of the NYBC to discover new drug therapies for the treatment of river blindness (onchocerciasis). The collaboration's goal is to identify a novel, potent macrofilaricidal drug candidate that is capable of killing adult worms.
Overlap: none

3. R01AI098775-01 MPI: Hotez/Bottazzi/Jiang; Co-PI S. Lustigman 05/01/2012 – 04/30/2017 (b)(6)

NIH/NIAID $273,860 (subcontract)

RBD Recombinant Protein-based SARS Vaccine for Biodefense
The main goal of this project is to develop, test and manufacture a novel recombinant SARS vaccine.
Overlap: none

4. 1R01AI105431-01 MPI: Lustigman (Contact PI)/Bottazzi/Shen 1/2013 – 12/2017 (b)(6)

NIH/NIAID $1,203,147 (including three subcontracts)

Development of a novel adjuvant for vaccine sparring

Adjuvants are integrated into vaccines to insure their effectiveness and to support antigen sparing. Currently, alum is the only adjuvant licensed in the U.S., but it has had limited effectiveness when used with commercial flu vaccines. Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.

5. OPP1086618 (Bill & Melinda Gates Foundation) (PI: S. Lustigman) 5//2013 – 10/2014 (b)(6)

$100,000

Innovative 3-D in vitro culturing system for filarial worms

To develop 3-Dimensional *in vitro* culturing systems that supports the development of *Onchocerca volvulus* and *Brugia malayi* infective larvae to the adult stages. This will provide greater numbers of adult worms for high

throughput screening for macrofilaricidal (that kill adult worms) drugs, which are needed to support the elimination of onchocerciasis in Africa.
Overlap: none

6. OPP1099849 (Bill & Melinda Gates Foundation) (PI: S. Lustigman) 8/2013 – 4/2015 (b)(6)
$299,364

Production of Onchocerca volvulus Larvae to Support Macrofilaricide Drug Discovery Projects

The goal is to produce at least 150,000 cryopreserved third-stage larvae of O. volvulus that will be used for research activities in line with the BMGF's macrofilaricidal drug discovery and development efforts.
Overlap: none

7. OPP1083910 (Bill & Melinda Gates Foundation) (PI: T. Nutman; Co-PI: S. Lustigman) 8/2013 – 8/2015
$232,495 (subcontract with NIH Foundation) (b)(6)

Rapid identification of individuals with viable adult female worms of Onchocerca volvulus: a means to the end

To identify host- and parasite-specific biomarker(s) present in human subjects with viable adult females of *Onchocerca volvulus* (Ov) and to develop and configure rapid point of care methods to detect (or sense) these biomarkers. This would be a final and necessary step in the progress towards elimination of onchocerciasis, an important neglected tropical disease.
Overlap: none

8. 1R56 1AI101372-01A1 MPI: Lustigman (Contact PI)/Ghedin/Unnasch 8/2013 – 7/2014 (b)(6)
NIH/NIAID

Molecular mechanisms of filarial endosymbiosis

Our goal for this project is to define the mechanisms that determine the interdependencies between the parasitic nematode *Brugia malayi* and its bacterial endosymbiont.
Overlap: none

PENDING

(b)(4)

If pending proposal is funded, appropriate adjustments will be made to ensure that Dr. Lustigman's time will total no than 100% on active projects at any given time.

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

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SARS-CoV became a select viral agent as of December 4, 2012. UTMB has been working diligently with various regulatory agents, both on and off the UTMB campus, to comply with all regulations concerning the usage of select agents. In short, we have made an inventory of the SARS-CoV that we have in the laboratory and moved our animal (A).BSL-3 laboratories from Mary Moody Northern (MMN) into the Galveston National Laboratory complex as of December 4th, 2012 with 24/7 security service. During this transition stage our group feels strongly that there will be no negative impact on the ongoing SARS program under this grant and if any, it

will be minimal. The biocontainment level for SARS-CoV remains the same, level-3, however, the antigen became classified as a select agent.

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

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G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

Yes

Exemption number(s) E4

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: RBD recombinant protein-based SARS vaccine for biodefense-PROTOCOL-001

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: BAYLOR COLLEGE OF MEDICINE	051113330	TX-009	BAYLOR COLLEGE OF MEDICINE ONE BAYLOR PLAZA HOUSTON TX 770303411
New York Blood Center	073271827	NY-014	310 East 67 Street New York NY 100656275
The University of Texas Medical Branch	800771149	TX-014	301 University Boulevard Galveston TX 775550156
Texas Childrens Hospital	074615394	TX-009	1102 Bates Street Houston TX 770302399

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

utmb Health

Environmental Health & Safety
Biological & Chemical Safety Program
Materials Management Building, 2.112
301 University Blvd.
Galveston, Texas 77555-1111
O 409.772.1781 F 409.772.8921

February 11, 2013

To Whom It May Concern

The University of Texas Medical Branch at Galveston (UTMB) is a select agent registered entity with the U.S. Health and Human Services, Centers for Disease Control and Prevention Division of Select Agents and Toxins (CDC/DSAT) and U. S. Department of Agriculture, Animal and Plant Health Inspection Service, (USDA/APHIS) National Select Agent Program. The University has been inspected by the CDC/DSAT and USDA/APHIS National Select Agent Program for use of HHS Select Agents and Toxins, Overlap Select Agents and Toxins and USDA Select Agents and Toxins.

Per the requirements of 42 CFR 73 the original certificate of registration was issued October 19, 2004, renewal was granted on April 9, 2007 and again on April 1, 2010 for use of select agents at BioSafety Levels 2, 3, and 4 and Animal BioSafety Levels 3 and 4. Inspection by CDC/DSAT and USDA/APHIS occurred January 9th to 20th 2012, for the current renewal cycle and approval was granted on March 21, 2012 for three years. The University has been registered with Health and Human Services, Centers for Disease Control and Prevention as a select agent facility since 1997. The University has a Responsible Official and four Alternate Responsible Officials.

Attached please find a copy of the University Of Texas Medical Branch certificate of registration of the possession, use and transfer of select agents and toxins. The registration number has been redacted for security purposes. The registration number will be provided at the time of an official CDC/USDA Form 2 transfer of select agents.

Please feel free to contact me should you require additional information.

Sincerely,

Domenica Zimmerman

Domenica Zimmerman
BioSafety Officer
Alternate Responsible Official
UTMB Select Agent Program

Certificate of Registration

Entity Name: University of Texas Medical Branch
Address: 301 University Boulevard
Galveston, TX 77555-0633

Registration #:
Effective Date: March 21, 2012
Expiration Date: March 21, 2015

Responsible Official: Michael Shriner
Alternate Responsible Official(s): Carlos Escobar, Amy Goebel, Scott Weaver, Domenica Zimmerman

Based on information provided to the CDC Select Agent Program and the APHIS Agriculture Select Agent Programs, the above-named entity is authorized to possess, use, and transfer select agents and toxins under the conditions specified in the entity registration application, in accordance with 42 CFR part 73, 9 CFR part 121, and 7 CFR part 331.

Robbin S. Weyant, Director
Select Agent Program
Centers for Disease Control and Prevention

Freeda E. Isaac, DVM, Director
Select Agent Program
Veterinary Services

Charles L. Divan, Branch Chief
Select Agent Program
Plant Protection and Quarantine

Inclusion Enrollment Report Table

This report format should NOT be used for data collection from study participants.

Study Title: RBD recombinant protein-based SARS vaccine for biodefense-PROTOCOL-001

Total Enrollment: 0 **Protocol Number:**

Grant Number: R01AI098775-03

PART A. TOTAL ENROLLMENT REPORT : Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race

Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	0	0	0	0
Not Hispanic or Latino	0	0	0	0
Unknown (Individuals not reporting ethnicity)	0	0	0	0
Ethnic Category:Total of All Subjects	0	0	0	0
Racial Categories				
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian Or Other Pacific Islander	0	0	0	0
Black Or African American	0	0	0	0
White	0	0	0	0
More than one race	0	0	0	0
Unknown or Not Reported	0	0	0	0
Racial Categories: Total of All Subjects	0	0	0	0

PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)

Racial Categories	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian Or Other Pacific Islander	0	0	0	0
Black Or African American	0	0	0	0
White	0	0	0	0
More than one race	0	0	0	0
Unknown or Not Reported	0	0	0	0
Racial Categories: Total of Hispanics Or Latinos	0	0	0	0

Inclusion Enrollment Comments: This project is not required to enroll subjects. The research has exemption approval and only involves the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens.

RESEARCH

Federal Award Date: 04/20/2015

Department of Health and Human Services
National Institutes of Health
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Grant Number: 5R01AI098775-04
FAIN: R01AI098775

Principal Investigator(s):
Maria Elena Bottazzi
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: 05/01/2015 – 04/30/2016
Project Period: 05/04/2012 – 04/30/2017

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $1,165,726 (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,

Vandhana Khurana
Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 5R01AI098775-04

Award Calculation (U.S. Dollars)

Federal Direct Costs	$782,695
Federal F&A Costs	$383,031
Approved Budget	$1,165,726
Total Amount of Federal Funds Obligated (Federal Share)	$1,165,726
TOTAL FEDERAL AWARD AMOUNT	$1,165,726
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$1,165,726

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
4	$1,165,726	$1,165,726
5	$1,165,855	$1,165,855

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Allergy, Immunology and Transplantation Research
CFDA Number:	93.855
EIN:	1741613878A1
Document Number:	RAI098775A
PMS Account Type:	G (Pooled)
Fiscal Year:	2015

IC	CAN	2015	2016
AI	8472315	$1,165,726	$1,165,855

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: M51C B / **OC**: 414E / **Released**: PII 04/17/2015
Award Processed: 03/23/2015 01:36:12 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5R01AI098775-04

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 – 5R01AI098775-04

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).

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 Central Contractor Registration. 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/.

Treatment of Program Income:
Additional Costs

SECTION IV – AI Special Terms and Conditions – 5R01AI098775-04

THIS AWARD CONTAINS GRANT SPECIFIC RESTRICTIONS. THESE RESTRICTIONS MAY ONLY BE LIFTED BY A REVISED NOTICE OF AWARD.

RESTRICTION: Under governing PHS Policy, Federal funds administered by the Public Health Service (PHS) shall not be expended for research involving live vertebrate animals without prior approval by the Office of Laboratory Animal Welfare (OLAW) of an Assurance to comply with the PHS Policy on Humane Care and Use of Laboratory Animals and the project has been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). The present award is being made without currently valid verification of IACUC approval for the portion of this project being completed in CHINA with the following restriction: No activities that involve live vertebrate animals may be conducted at Frontier Biosciences located in CHINA pending acceptance by the NIH awarding component of verification of IACUC approval. The Program Officer has approved the funding of this application without the portion of Frontier Biosciences located in CHINA in year 05 as the project is viable without it. No funds may be expended for the foreign site pending the resolution of internal administrative issues. Once these issues have been resolved, this award may be revised to include the study originally planned for the foreign site. Failure to comply with

this special condition can result in suspension and/or termination of this award, withholding of support, audit disallowances, and/or other appropriate action.

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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_2013/nihgps_ch15.htm#_Toc271265264.

No foreign performance activity may be added without prior approval of the NIAID Program and Grants Management Staff.

****

Awardees who conduct research involving Select Agents (see 42 CFR 73 for the Select Agent list; and 7 CFR 331 and 9 CFR 121 for the relevant animal and plant pathogens at http://www.selectagents.gov/Regulations.html) must complete registration with CDC (or APHIS, depending on the agent) before using NIH funds. No funds can be used for research involving Select Agents if the final registration certificate is denied.

Prior to conducting a restricted experiment with a Select Agent or Toxin, awardees must notify the NIAID and must request and receive approval from CDC or APHIS.

****

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: Jason A. Lundgren
Email: lundgrenj@mail.nih.gov **Phone**: 240-669-2973 **Fax**: 301-493-0597

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

SPREADSHEET SUMMARY
GRANT NUMBER: 5R01AI098775-04

INSTITUTION: BAYLOR COLLEGE OF MEDICINE

Budget	Year 4	Year 5
TOTAL FEDERAL DC	$782,695	$768,645
TOTAL FEDERAL F&A	$383,031	$397,210
TOTAL COST	$1,165,726	$1,165,855

Facilities and Administrative Costs	Year 4	Year 5
F&A Cost Rate 1	57.3%	57.3%
F&A Cost Base 1	$668,466	$693,211
F&A Costs 1	$383,031	$397,210

A. COVER PAGE

Project Title: RBD recombinant protein-based SARS vaccine for biodefense	
Grant Number: 5R01AI098775-04	**Project/Grant Period:** 05/04/2012 - 04/30/2017
Reporting Period: 05/01/2014 - 04/30/2015	**Requested Budget Period:** 05/01/2015 - 04/30/2016
Report Term Frequency: Annual	**Date Submitted:** 03/12/2015
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-N3
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:** No

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?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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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?

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
3R01AI098775-03S1	RBD recombinant protein-based SARS vaccine for biodefense	The project plan was to instruct the student on fundamental techniques in molecular biology and biochemistry and provide a broad educational overview on the key steps in developing a vaccine to prevent a major public health threat. The project plan included regular meetings with the research team; one-on-one mentorship meetings to provide feedback on weekly activities; answer questions and provide additional training if needed; and training in various general aspects of research. The student's work fell under Specific Aim 2 of the parent grant, specifically, Process development, characterization, formulation and stability profiling.	The student assisted with process development of a recombinant receptor-binding domain (rRBD) protein to prevent severe acute respiratory syndrome (SARS) caused by the SARS coronavirus (SARS CoV), a major part of the Specific Aim 2. The student assisted with the discovery of possible purification parameters as well as the identification of in-process samples over the chromatographic purification procedure thereby contributing to Milestone 1: A suitable expression is selected for expression of rRBD in small scale and Milestone 4: Established a reproducible 10L scale process for a stable rRBD-based vaccine in preparation for future technology transfer to a cGMP manufacturing facility.

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

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

The Contact PI was appointed as Member, Governor Rick Perry's Texas Task Force on Infectious Disease Preparedness and Response which allowed for the dissemination to communities about the project and enhance public understanding. In addition a presentation in the Civic Scientist Lecture Series, Baker Institute, Rice University (Houston, TX) was discussed the topic of "Influenza, SARS, Ebola and the

Next Pandemic: Perceptions in the Media and Public".

Co-I was asked to be a panelist for the Panel entitled "Working with International Non-Governmental Organizations (NGOs) and Not-for-Profit Organizations Against Emerging Infectious Disease and Biodefense Threats" at the 11th Annual Emerging Infectious Diseases & Biodefense Summit.

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

As we move into year four, we plan to complete the optimization of the adjuvant formulation using the selected yeast-expressed, rRBD protein-based SARS vaccine candidate RBD219-N1. Formulations of the RBD219-N1 protein with glucopyranosyl lipid A (GLA)-stable-emulsion (SE) and with GLA-AF (emulsion-free) in combination with Alhydrogel® are being compared. The protein alone is being 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 and pseudotyped and live SARS-CoV-based neutralization assays. The resulting adjuvanticity of the two GLA formulations on the immunogenicity of RBD219-N1 will be compared with that of Alhydrogel®, AddaVax and Advax-2 adjuvants. In addition, we plan to use any available residual funds to test for the survival of immunized mice after virus challenge and for the possibility of the development of pathology in the lungs of vaccinated mice. These experiments will enable us to select the best adjuvant/vaccine antigen formulations for cGMP manufacturing.

We are scheduling the execution of 3 successive process development runs at the 10L scale for year four. We plan to utilize the developed assays to characterize the purified protein. The technology transfer will be arranged after the three reproducible process development runs for cGMP Manufacture have been completed.

We will continue to closely coordinate with the consortium partners NYBC and UTMB. We will begin to engage in quality assurance activities with our associates at the Sabin Vaccine Institute and to coordinate efforts for technology transfer with WRAIR as we execute the year 4 activities.

B.2 Year 3 Accomplishments.

As described in last year's report, RBD219-N1 was chosen as the SARS vaccine candidate. The work related to Aims 1A to 1D has been completed and has been reported previously. For this reporting period, the major activities performed were in support of completing Aim 1 and advancing Aim 2.

Aim 1.E. Optimization of the immunization regimen.

We have optimized the immunization regimen for the candidate SARS-CoV RBD vaccine (RBD219-N1) in a mouse model. We vaccinated mice with RBD219-N1 adsorbed to Alhydrogel®, subcutaneously (s.c.) or intramuscularly (i.m.), three times, at 3-week intervals. Sera were collected 10 days after the last immunization and tested for IgG antibody responses and for neutralizing antibodies against SARS pseudovirus and live SARS-CoV infections.

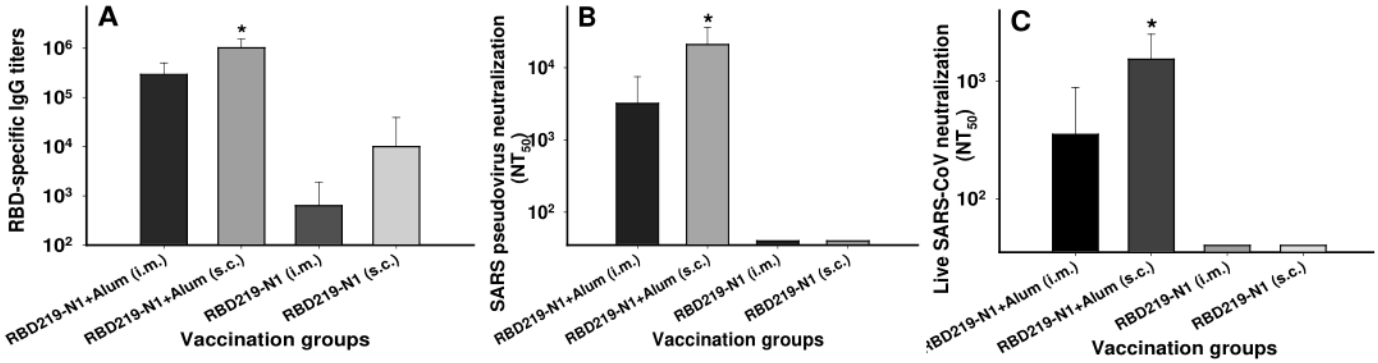

Figure 1. Optimization of immunization routes of SARS-CoV RBD protein. (A) Detection of IgG antibody response by ELISA in mouse sera. Neutralization antibody titers against SARS pseudovirus (B) and live SARS-CoV (C) in mouse sera. [Alhydrogel® abbreviated as Alum.]

The RBD219-N1/Alhydrogel® vaccine induced high titers of specific IgG (**Fig. 1A**) and neutralizing antibodies against infections of SARS pseudovirus in ACE2/293T cells (**Fig. 1B**) and live SARS-CoV in Vero cells (**Fig. 1C**) through both s.c. and i.m. routes. RBD219-N1 protein only induced low titer of IgG antibody without neutralizing activity (**Fig. 1A**). Although the antibody responses induced through s.c. route are significantly higher than that through i.m. route (**Fig. 1**), we still selected the i.m. route for subsequent adjuvant optimization because i.m. injection of the vaccines containing adjuvants has less chance to induce adverse local effects than s.c. injection (http://vaccine-safety-training.org/route-of-administration.html) and the majority of the clinically used vaccines are administered via i.m. route (http://www.immunize.org/catg.d/p3085.pdf).

To optimize additional adjuvant formulations, we first evaluated a glucopyranosyl lipid adjuvant-stable emulsion (GLA-SE), and compared its immunogenicity in mice to the RBD219-N1/Alhydrogel® vaccine using the same immunization scheme and analyses as described above.

Table 1. Immunogenicity of RBD219-N1 Vaccine Formulations (All vaccinations administered intramuscularly.)

	Antibody titers			Ratio	Neutralizing antibody titers (NT_{50})	
Groups	**IgG**	**IgG1**	**IgG2a**	**IgG1/IgG2a**	**SARS pseudovirus**	**Live SARS-CoV**
RBD219-N1 + Alhydrogel®	31,962	188,054	1,566	~120	9,192	676
RBD219-N1 + GLA-SE	33,262	26,047	75,713	~0.3	<20	20
RBD219-N1 protein only	1,049	<900	<900	NA	<20	<20

As shown in **Table 1**, RBD219-N1 vaccines elicited a similarly high RBD-specific antibody responses (IgG titers > 1:30,000) when formulated with either Alhydrogel® or the GLA-SE adjuvant. Notably, RBD219-N1 plus Alhydrogel® induced a higher IgG1 but lower IgG2a antibody response (IgG1/IgG2a ratio, 1:120), whereas the IgG1 and IgG2a antibodies elicited by RBD219-N1 plus GLA-SE were at a similar level (IgG1/IgG2a ratio, 3:1). RBD219-N1 protein alone only induced significantly lower antibody responses. Importantly, RBD219-N1 plus Alhydrogel® also elicited neutralizing antibodies against both pseudo-typed and live SARS-CoV. In contrast, immunization with RBD219-N1 plus GLA-SE, as well as the protein alone, did not. The reason why GLA-SE could not improve the ability of RBD219-N1 to induce neutralizing antibodies is currently being investigated in a repeat study.

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

The selected SARS-CoV RBD219-N1-Alhydrogel® vaccine candidate is immunogenic, inducing high neutralizing antibody titers. Importantly, mice vaccinated 3 times, 3-weeks apart, were fully protected against viral infection and mortality caused by SARS-CoV. Post-mortem examination of lungs from vaccinated and challenged mice revealed eosinophilic infiltration, which has prompted us to further explore the root cause and therefore continue evaluating alternate adjuvants for the vaccine formulation.

Specific Aim 2.A. Development and optimization of a 10 L scale process.

Aim 2.A.1. Upstream process optimization.

To improve the expression yield of RBD219-N1, several fermentation parameters were optimized at the 5 L scale, including temperature, pH, sorbitol co-feed, media salt concentration, detergents, methanol feed rate and clone copy number. For the final fermentation process, a low salt medium was inoculated with a high copy number clone, and the culture was induced at 24°C, pH 6.5 with a gradual increasing amount of the methanol flow rate from 11 to 15 mL/L/hr over 70±2 hours. This improved the yield of RBD219-N1 from, originally, 45 mg/L (**Figure 2a**) to 400 mg/L at the 10 L fermentation scale (**Figure 2b**).

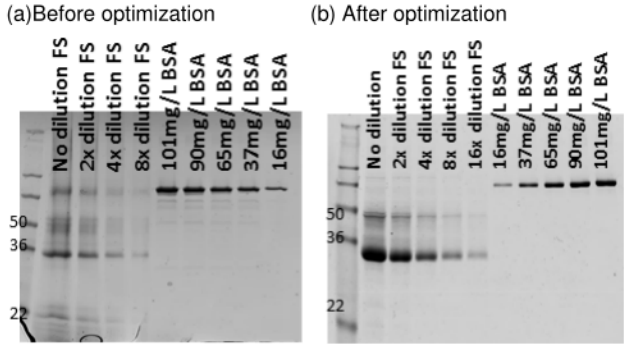

Figure 2. Quantitative gels for the fermentation supernatant (FS) before (a) and after (b) the upstream process was optimized.

Aim 2.A.2. Downstream process optimization.

We investigated three purification schemes: (1) Butyl Hydrophobic Interaction Chromatography (HIC) followed by Size Exclusion Chromatography (SEC); (2) Cation Exchange Chromatography (CEX) followed by HIC; and (3) CEX followed by SEC. Based on initial yield and purity, we discontinued schemes (2) and (3), and focused on the optimization of scheme (1). We investigated different buffer salts, binding capacity, step elution and injection volume for SEC and were able to lock down a purification scheme which met the goals of purity and yield. We were able to obtain a yield of 250 mg RBD219-N1 per L of fermentation supernatant (10 L fermentation, providing 6 L supernatant) with an overall recovery rate of approximately 45%.

Aim 2.B. Assay development.

We have developed four assays to assess the purity and identity of RBD219-N1: SDS-PAGE (reduced and non-reduced), Western Blot, HPLC-SEC and HPLC-RP. For the HPLC-RP, the column and buffer conditions were optimized. In the final assay, RBD219-N1 will be bound to a C4 column in 30% Acetonitrile/0.5% TFA and gradually eluted with Acetonitrile (2% increase/min). In addition, we also established endotoxin testing (Endosafe®-PTS™, Charles River Inc.) for the purified protein. In parallel, we are currently developing a quantitative Host-cell-protein slot blot assay to evaluate residual contaminants. Some other outsourced assays, e.g., mass spectrometry, N-terminal sequencing, etc., will also be used to characterize the protein and ensure its integrity.

Aim 2.C. Execution of three successive process development runs at the 10 L scale.

As described in Aim 2.A., we continued the optimization of our upstream and downstream processes in preparation of the three successive process development runs scheduled to be performed at the start of Project year 4.

Table 2. Formulations of RBD219-N1 vaccine for the pilot study. All vaccines were administered intramuscularly (100 µl/mouse).

No.	RBD219-N1 Dose	Adjuvant	Adjuvant Dose
1	**1st**: 20 µg; **2nd** and **3rd**: 10 µg	Alhydrogel®	500 µg/mouse
2	**1st**: 20 µg; **2nd** and **3rd**: 10 µg	Advax-2	1 mg/mouse
3	**1st**: 20 µg; **2nd** and **3rd**: 10 µg	GLA-SE	5 µg/mouse
4	**1st**: 20 µg; **2nd** and **3rd**: 10 µg	GLA-AF	5 µg/mouse
		Alhydrogel®	500 µg/mouse
5	**1st**: 20 µg; **2nd** and **3rd**: 10 µg	AddaVax	50 µl/mouse
6	**1st**: 20 µg; **2nd** and **3rd**: 10 µg	No adjuvant	--

Aim 2.D. Formulation and Stabilization.

Six different formulations (**Table 2**) were prepared for the pre-clinical study. All adjuvants will be mixed with RBD at the point-of-injection (POI) with the exception of Alhydrogel®, which is premixed. To determine the stability of the RBD formulations when GLA-AF is combined at the POI, variable amounts of GLA-AF were combined with fixed amounts of the formulated vaccines. These preparations were then analyzed at room temperature, 4 hours post mixing by Coomassie-stained reduced SDS-PAGE and BCA assay. Both the SDS-PAGE and BCA assay suggested that the RBD remains stable and that the amount of GLA-AF used would not displace RBD from the Alhydrogel®.

B.4. What opportunities for training and professional development has the project provided?

Funds were received for a minority supplement 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 served as a basis for engaging an under-represented minority high school student in an eight-week long mentored program of biotechnology and biochemistry research. The program was offered in association with the Office of Diversity and Community Outreach at Baylor College of Medicine.

C. PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Jiang S, Lu L, Du L, Debnath AK. Putative conformations of the receptor-binding domain in S protein of hCoV-EMC in complex with its receptor dipeptidyl peptidase-4. J Infect. 2013 Aug;67(2):156-8. PubMed PMID: 23603488; PubMed Central PMCID: PMC4355062.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

NOTHING TO REPORT

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period?

No

C.5 OTHER PRODUCTS AND RESOURCE SHARING

C.5.a Other products

NOTHING TO REPORT

C.5.b Resource sharing

NOTHING TO REPORT

D. PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID	S/K	Name	SSN	DOB	Degree(s)	Role	Cal	Aca	Sum	Foreign Org	Country	SS
eRA Commons User Name	Y	HOTEZ, PETER J	PII		BA,PHD, MD	PD/PI	EFFORT	0	0			NA
	Y	JIANG, SHIBO			PHD,MD	PD/PI		0	0	Fudan University	CHINA	NA
	Y	Bottazzi, Maria Elena				PD/PI		0	0			NA
	N	Du, Lanying			PHD	Co-Investigator		0	0			NA
	N	Ewere, Ebe				High School Student		0	2			NA
	N	Zhang, Naru			Ph.D.	Research Fellow		0	0			NA
	N	LUSTIGMAN, SARA			PHD	Co-Investigator		0	0			NA
	N	Seid, Chris			Ph.D.	Staff scientist (Doctoral level)		0	0			NA
	N	Tricoche, Nancy			BS	Non-Student Research Assistant		0	0			NA
	N	Tseng, Chien-Te K			PHD,MS	Co-Investigator		0	0			NA
	N	Nino, Diane			BSci	Project Manager		0	0			NA
	N	Pollet, Jeroen			Ph.D.	Director, Formulation		0	0			NA
	N	Tao, Xinrong			Ph.D.	Research Associate		0	0			NA
	N	Chen, Wen			Ph.D.	Non-Student Research Assistant		0	0			NA
	N	Chan, Tehseng			MD, PhD	Co-Investigator		0	0			NA
	N	Chag, Shivali			MS	Non-Student Research Assistant		0	0			NA
	N	Hudspeth, Elissa			BS	Technician		0	0			NA

Glossary of acronyms:
S/K - Senior/Key
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support

DOB - Date of Birth	RE - Reentry Supplement
Cal - Person Months (Calendar)	DI - Diversity Supplement
Aca - Person Months (Academic)	OT - Other
Sum - Person Months (Summer)	NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

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D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

OTHER SUPPORT
AT BAYLOR COLLEGE OF MEDICINE

HOTEZ, PETER J.

Newly awarded:
Adjuvant Technologies to Advance Chagas Disease Vaccine Development

CURRENT

23386 Hotez (PI) 01/01/2011-12/31/202014 EFFORT
Sponsor: Dutch Government €842,857
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 - 04/30/2015 EFFORT
Sponsor: Private Source
Title: Human Hookworm Vaccine Initiative 3 $871,809
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 EFFORT
Private Source $244,150
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.

5R01AI098775-02 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $899,886
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, Consultant) 11/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $255,928
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/Bottazzi (MPI) 08/01/2013 – 07/31/2017 EFFORT
Sponsor: Private Source $328,435
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.

Hotez (PI) 01/01/2014 – 12/31/2016 EFFORT
Sponsor: University of Malaya $250,000
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 EFFORT

Sponsor: Private Source $160,000
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
EFFORT
Sponsor: Private Source $179,348
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 – 12/31/2014
EFFORT
Sponsor: Instituto Carlos Slim de la Salud $709,333
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.

Hotez (PI) 11/1/2014 – 10/31/2016
EFFORT
Sponsor: Private Source
Title: Adjuvant Technologies to Advance Chagas Disease Vaccine Development $773,754
The overall goal of this project is to develop a new vaccine formulation for Chagas disease consisting of a promising protein-based antigen (Tc24) formulated with a novel TLR4 agonist adjuvant, E6020, which is designed to skew the immune response toward a T_H1 bias and the generation of cytotoxic T cells.

BOTTAZZI, MARIA ELENA

Newly awarded:
Adjuvant Technologies to Advance Chagas Disease Vaccine Development

ACTIVE

1016395 Hotez (PI) 08/01/2011 – 04/30/15 EFFORT
Sponsor: Private Source
Title: Human Hookworm Vaccine Initiative 3 $955,573
Clinical Development and Evaluation of the Na-GST-1 and Na-APR-1 Hookworm Vaccine Antigens
The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.
Role: Co-Investigator

Hotez (PI) 04/20/2012 – 12/31/2015 EFFORT
Private Source $244,150
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.
Role: Director of Product Development

R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017 EFFORT
Sponsor: National Institutes of Health $899,886
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, Consultant) 11/01/2012 – 12/31/2017 EFFORT
Sponsor: Department of Health and Human Services / Texas A&M Univ. $255,517
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.

1R01AI105431-01 Lustigman (PI) 01/15/2013 – 12/31/2017 EFFORT
Sponsor: NIH via New York Blood Center $177,000
Title: Development of a novel adjuvant for vaccine sparring
Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.
Role: Sub-PI

Hotez/Bottazzi (MPI) 08/01/2013 – 07/31/2017 EFFORT
Sponsor: Private Source $328,435
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 Bottazzi (PI) 10/1/2013 – 9/30/2017 EFFORT
Sponsor: European Union via sub from (AIGHD) $91,121
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 EFFORT
Sponsor: University of Malaya $250,000

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.
Role: Co-I

Hotez (PI) 01/01/2014 – 12/31/2017 EFFORT
Sponsor: Private Source $160,000
Title: West Nile Virus vaccine development
Main goal is to support West Nile Virus vaccine development.
Role: Co-I

Hotez/Bottazzi (MPI) 01/01/2014 – 12/31/2017 EFFORT
Sponsor: Private Source $179,348
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 – 12/31/2014 EFFORT
Sponsor: Instituto Carlos Slim de la Salud $709,333
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.

Bottazzi (Sub-PI) 11/1/2014 – 10/31/2016 EFFORT
Sponsor: Private Source ¥65,398,577
Title: Adjuvant Technologies to Advance Chagas Disease Vaccine Development
The overall goal of this project is to develop a new vaccine formulation for Chagas disease consisting of a promising protein-based antigen (Tc24) formulated with a novel TLR4 agonist adjuvant, E6020, which is designed to skew the immune response toward a T_H1 bias and the generation of cytotoxic T cells.

OTHER SUPPORT
AT NEW YORK BLOOD CENTER

Changes for Dr. Lustigman:
A pending grant from last year (b)(4) was not funded
NIH: One pending (b)(4) was submitted
No changes in all other eight previously funded projects

SARA LUSTIGMAN

ACTIVE

1. **1R01AI078314-01A2** (PI: S. Lustigman) 8/2009 – 7/2014 (+ one year no-cost extension) (b)(6)
   NIH/NIAID $603,776 (DC)

The development of a recombinant vaccine against human onchocerciasis

A collaborative research effort focused on the preclinical research and development process that will result, through a robust screening process, with the discovery of the best 2 recombinant *O. volvulus* vaccine antigens with the highest probability for success at inducing protective immunity in humans. The vaccine will target the *O. volvulus* larvae, known to be vulnerable to host immunological attack.
Overlap: none

2. **OPP1017584** (Bill & Melinda Gates Foundation) (PI: J. McKerrow; Co-PI: S. Lustigman)
   $320,000 (subcontract) 11/1/2012 – 10/31/2015 (b)(6)

Developing a macrofilaricial drug for onchocerciasis using Anacor's novel oxaborole technology

A collaborative research effort between the University of California San Francisco Sandler Center, Anacor Pharmaceuticals and LFKRI of the NYBC to discover new drug therapies for the treatment of river blindness (onchocerciasis). The collaboration's goal is to identify a novel, potent macrofilaricidal drug candidate that is capable of killing adult worms.
Overlap: none

3. **R01AI098775-01** MPI: Hotez/Bottazzi/Jiang; Co-PI S. Lustigman 05/01/2012 – 04/30/2017 (b)(6)
   NIH/NIAID $273,860 (subcontract)

RBD Recombinant Protein-based SARS Vaccine for Biodefense

The main goal of this project is to develop, test and manufacture a novel recombinant SARS vaccine.
Overlap: none

4. **1R01AI105431-01** MPI: Lustigman (Contact PI)/Bottazzi/Shen 1/2013 – 12/2017 (b)(6)
   NIH/NIAID $1,077,884

Development of a novel adjuvant for vaccine sparring

Adjuvants are integrated into vaccines to insure their effectiveness and to support antigen sparing. Currently, alum is the only adjuvant licensed in the U.S., but it has had limited effectiveness when used with commercial flu vaccines. Our objective is to produce a highly effective and safe rASP-1 adjuvanted flu vaccine in a simple aqueous formulation that requires a minimal antigen quantity per dose. By enhancing vaccine efficacy in this way, we can effectively increase the number of vaccine doses available.

5. **OPP1086618** (Bill & Melinda Gates Foundation) (PI: S. Lustigman) 5//2013 – 10/2014 (b)(6)
   $100,000

Innovative 3-D in vitro culturing system for filarial worms

To develop 3-Dimensional *in vitro* culturing systems that supports the development of *Onchocerca volvulus* and *Brugia malayi* infective larvae to the adult stages. This will provide greater numbers of adult worms for high throughput screening for macrofilaricidal (that kill adult worms) drugs, which are needed to support the elimination of onchocerciasis in Africa.
Overlap: none

6. 1R56 1AI101372-01A1 MPI: Lustigman (Contact PI)/Ghedin/Unnasch 8/2013 – 7/2014 (b)(6)
NIH/NIAID $613,492 (+ one year no-cost extension)

Molecular mechanisms of filarial endosymbiosis

Our goal for this project is to define the mechanisms that determine the interdependencies between the parasitic nematode *Brugia malayi* and its bacterial endosymbiont.

Overlap: none

7. OPP1099849 (Bill & Melinda Gates Foundation) (PI: S. Lustigman) 8/2013 – 4/2015 (b)(6)
$299,364

Production of Onchocerca volvulus Larvae to Support Macrofilaricide Drug Discovery Projects

The goal is to produce at least 150,000 cryopreserved third-stage larvae of O. volvulus that will be used for research activities in line with the BMGF's macrofilaricidal drug discovery and development efforts.
Overlap: none

8. OPP1083910 (Bill & Melinda Gates Foundation) (PI: T. Nutman; Co-PI: S. Lustigman) 8/2013 – 8/2015
$267,370 (subcontract with NIH Foundation) (b)(6)

Rapid identification of individuals with viable adult female worms of Onchocerca volvulus: a means to the end

To identify host- and parasite-specific biomarker(s) present in human subjects with viable adult females of *Onchocerca volvulus* (Ov) and to develop and configure rapid point of care methods to detect (or sense) these biomarkers. This would be a final and necessary step in the progress towards elimination of onchocerciasis, an important neglected tropical disease.
Overlap: none

PENDING

(b)(4)

If pending proposal is are funded, appropriate adjustments will be made to ensure that Dr. Lustigman's time will total no than 100% on active projects at any given time.

Changes for Drs. Shibo Jiang and Lanying Du:
Receive an R21 grant (R21 AI111152) for B. subtilis spore-delivered M2e-FP-based mucosal universal influenza vaccines (as shown above), but will keep the originally approved effort unchanged.

SHIBO JIANG

ACTIVE
1R21AI109094-01 (Du) 12/15/2013 – 11/30/2015 EFFORT
NIH/NIAID
Critical neutralizing domain-based vaccines against new SARS-like virus hCoV-EMC
Role: Co-Investigator
Overlap: None

ACTIVE
1R21 AI111152-01 (Du) 08/05/2014 – 07/31/2016 EFFORT
NIH/NIAID
B. subtilis spore-delivered M2e-FP-based mucosal universal influenza vaccines
Role: Co-Investigator
Overlap: None

LANYING DU
ACTIVE
1R21AI109094-01 (Du) 12/15/2013 – 11/30/2015 EFFORT
NIH/NIAID
Critical neutralizing domain-based vaccines against new SARS-like virus hCoV-EMC
Role: PI
Overlap: None

ACTIVE
1R21 AI111152-01 (Du) 08/05/2014 – 07/31/2016 EFFORT
NIH/NIAID
B. subtilis spore-delivered M2e-FP-based mucosal universal influenza vaccines
Role: PI
Overlap: None

E. IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

NOTHING TO REPORT

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

Not Applicable

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?

NOTHING TO REPORT

F. CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

File uploaded: F3d.pdf

F.3.d. Select Agents

SARS-CoV became a select viral agent as of December 4, 2012. UTMB has been working diligently with various regulatory agents, both on and off the UTMB campus, to comply with all regulations concerning the usage of select agents. In short, we have made an inventory of the SARS-CoV that we have in the laboratory and moved our animal (A).BSL-3 laboratories from Mary Moody Northern (MMN) into the Galveston National Laboratory complex as of December 4th, 2012 with 24/7 security service. During this transition stage our group feels strongly that there will be no negative impact on the ongoing SARS program under this grant and if any, it will be minimal. The biocontainment level for SARS-CoV remains the same, level-3, however, the antigen became classified as a select agent.

G. SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

File(s) uploaded:
utmb select agent.pdf

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

Yes

Exemption number(s) E4

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: RBD recombinant protein-based SARS vaccine for biodefense-PROTOCOL-001

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

No

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: BAYLOR COLLEGE OF MEDICINE	051113330	TX-009	BAYLOR COLLEGE OF MEDICINE ONE BAYLOR PLAZA HOUSTON TX 770303411
New York Blood Center	073271827	NY-014	310 East 67 Street New York NY 100656275
The University of Texas Medical Branch	800771149	TX-014	301 University Boulevard Galveston TX 775550156
Texas Childrens Hospital	074615394	TX-009	1102 Bates Street Houston TX 770302399

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

No

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Is there a change in performance sites that will affect F&A costs?

No

utmb Health

Environmental Health & Safety
Biological & Chemical Safety Program
Materials Management Building, 2.112
301 University Blvd.
Galveston, Texas 77555-1111
O 409.772.1781 F 409.772.8921

February 11, 2013

To Whom It May Concern

The University of Texas Medical Branch at Galveston (UTMB) is a select agent registered entity with the U.S. Health and Human Services, Centers for Disease Control and Prevention Division of Select Agents and Toxins (CDC/DSAT) and U. S. Department of Agriculture, Animal and Plant Health Inspection Service, (USDA/APHIS) National Select Agent Program. The University has been inspected by the CDC/DSAT and USDA/APHIS National Select Agent Program for use of HHS Select Agents and Toxins, Overlap Select Agents and Toxins and USDA Select Agents and Toxins.

Per the requirements of 42 CFR 73 the original certificate of registration was issued October 19, 2004, renewal was granted on April 9, 2007 and again on April 1, 2010 for use of select agents at BioSafety Levels 2, 3, and 4 and Animal BioSafety Levels 3 and 4. Inspection by CDC/DSAT and USDA/APHIS occurred January 9th to 20th 2012, for the current renewal cycle and approval was granted on March 21, 2012 for three years. The University has been registered with Health and Human Services, Centers for Disease Control and Prevention as a select agent facility since 1997. The University has a Responsible Official and four Alternate Responsible Officials.

Attached please find a copy of the University Of Texas Medical Branch certificate of registration of the possession, use and transfer of select agents and toxins. The registration number has been redacted for security purposes. The registration number will be provided at the time of an official CDC/USDA Form 2 transfer of select agents.

Please feel free to contact me should you require additional information.

Sincerely,

Domenica Zimmerman

Domenica Zimmerman
BioSafety Officer
Alternate Responsible Official
UTMB Select Agent Program

Certificate of Registration

Entity Name: University of Texas Medical Branch
Address: 301 University Boulevard
Galveston, TX 77555-0633

Registration #:
Effective Date: March 21, 2012
Expiration Date: March 21, 2015

Responsible Official: Michael Shriner
Alternate Responsible Official(s): Carlos Escobar, Amy Goebel, Scott Weaver, Domenica Zimmerman

Based on information provided to the CDC Select Agent Program and the APHIS Agriculture Select Agent Programs, the above-named entity is authorized to possess, use, and transfer select agents and toxins under the conditions specified in the entity registration application, in accordance with 42 CFR part 73, 9 CFR part 121, and 7 CFR part 331.

Robbin S. Weyant, Director
Select Agent Program
Centers for Disease Control and Prevention

Freeda E. Isaac, DVM, Director
Select Agent Program
Veterinary Services

Charles L. Divan, Branch Chief
Select Agent Program
Plant Protection and Quarantine

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 154039

Study Title: RBD recombinant protein-based SARS vaccine for biodefense-PROTOCOL-001

Foreign/Domestic: Domestic

Planned Enrollment Report

Comments: This project is not required to enroll subjects. The research has exemption approval and only involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens.

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/Alaska Native	0	0	0	0	**0**
Asian	0	0	0	0	**0**
Native Hawaiian or Other Pacific Islander	0	0	0	0	**0**
Black or African American	0	0	0	0	**0**
White	0	0	0	0	**0**
More than One Race	0	0	0	0	**0**
Total	**0**	**0**	**0**	**0**	**0**

Cumulative Enrollment Report

NOTE: No cumulative inclusion enrollment data exists in the previous inclusion format or modified format. Although prompted to do so, the PD/PI did not enter information in the modified format. No data can be provided.