



DEPARTMENT OF THE ARMY
WALTER REED ARMY INSTITUTE OF RESEARCH
503 ROBERT GRANT ROAD
SILVER SPRING, MD 20910-7500

28 Apr 11

Mr. Michael W. Marine
Chief Executive Officer
Sabin Vaccine Institute
2000 Pennsylvania Avenue NW
Suite 7100
Washington, DC 20006

Re: Letter of Support for the WRAIR Pilot Bioproduction Facility to act as cGMP manufacturer for a recombinant protein-based SARS vaccine identified in NIH RFA-AI-11-014: Partnerships for Biodefense

Dear Mr. Marine:

Walter Reed Army Institute of Research (WRAIR), Pilot Bioproduction Facility (PBF), is pleased to provide this Letter of Support for inclusion in the Sabin Vaccine Institute proposal to develop and test a recombinant protein-based SARS vaccine. As part of the development and testing regimen described in the proposal, WRAIR-PBF is willing and able to perform cGMP manufacturing services for the preparation of the vaccine. Attached is a scope of work proposed for the vaccine including an itemized cost estimate based on current (CY11) costs. These services will be provided as part of a Cooperative Research and Development Agreement between WRAIR and Sabin Vaccine Institute post award of the grant. The CRADA specifies patent and publication rights for the client and the government. This preliminary Letter of Commitment is non-binding and preliminary to the negotiation of a final agreement with the Sabin Vaccine Institute. Also attached is background information on the mission of the PBF.

Best Regards,

(b)(6)

Kenneth H. Eckels, PhD
Chief, Pilot Bioproduction Facility
WRAIR

With the concurrence of the Sabin Vaccine Institute:

(b)(6)

Brian R. Davis
Chief Operating Officer

Vaccine Production and Costs

Production Item	Cost K\$*
Master and Working Cell Banking	80
Fermentation	180
Purification	220
Fill	44
TOTAL	524

*CY 11 costs

Scope of Work

1. Prepare under GMP conditions Master and Working cell banks for SARS recombinant (yeast, bacteria); 100 vials of each.
2. Ferment under GMP condition up to 300 L of SARS recombinant (yeast or bacteria); process concentrated bacterial paste or supernatant fluids from yeast.
3. Purify under GMP conditions an aliquot of SARS recombinant gene product to prepare bulk vaccine.
4. Fill under GMP conditions bulk vaccine into vaccine vials, up to 2,000 vials.
5. Lab-scale processes for all of the above will be provided to the PBF.
6. A research-grade construct seed will be provided to the PBF for cell banking.

Pilot Bioproduction Facility, WRAIR

Established in 1958 as the Department of Biologics Research, the Pilot Bioproduction Facility (PBF) has specialized in developing vaccines for DOD mission-related disease threats. More recently, projects for public and private partners have been accomplished through inter-agency and cooperative agreements. The PBF's mission is research, development, production, and testing of vaccines for human use. The PBF at Forest Glen, MD is a multi-use facility designed and operated for production of vaccines following current Good Manufacturing Practices (cGMP) regulations. Compliance with cGMP ensures that products prepared in the facility will be safe, potent, and reproducible.

PBF Successes

In the facility's distinguished history, the PBF has received awards and accolades for its role in developing vaccines for deadly diseases like hepatitis A, Japanese encephalitis, and meningitis. More recently, the facility has played a key role in the development of vaccines for dengue fever, malaria, HIV, cholera, and shigellosis. Many of these experimental vaccines have progressed to advanced clinical testing.



May 9, 2011

Mr. Michael W. Marine
Chief Executive Officer
Sabin Vaccine Institute
2000 Pennsylvania Avenue NW, Suite 7100
Washington, DC 20006

RE: Letter of Support in response to NIH/NIAID Partnerships for Biodefense (R01)
RFA-AI-11-014 Regarding Subcontract with Frontier BioSciences, Inc. ("Frontier
BioSciences")

Project Title: RBD Recombinant Protein-based SARS Vaccine for Biodefense Preparedness

Dear Mr. Marine:

Frontier BioSciences would be happy to participate in the above-referenced project. We look forward to working closely with you and your staff. We will ensure high quality deliverables and flexibility to your program requirements, and will work effectively with your team to meet your proposed timeline for your program. We are fully prepared to establish the necessary agreements and contracts if this proposal is funded.

The attached proposal estimates the cost necessary to implement the project.

Please feel free to contact me if you require other information or have any questions regarding Frontier Bioscience's participation. Please notify us if the project is funded, so that we may implement a subcontract without delay.

Thank you for the opportunity to be involved in this important project.

(b)(6)

05/09/11

Elizabeth C. Wong
Vice President, Business Development

Date

Contact Information:

Phone (b)(6)
Cell (b)(6)
Ema (b)(6)

With the concurrence of The Sabin Vaccine Institute:

(b)(6)

Brian R. Davis
Chief Operating Officer



May 9, 2011

Mr. Michael W. Marine
Chief Executive Officer
Sabin Vaccine Institute
2000 Pennsylvania Avenue NW, Suite 7100
Washington, DC 20006

Re: RBD Recombinant Protein-based SARS Vaccine for Biodefense Preparedness

Dear Mr. Marine:

Thank you for the opportunity to provide a proposal for your **RBD Recombinant Protein-based SARS Vaccine for Biodefense Preparedness**.

Included in this proposal is the study outline provided by Sabin. Our cost estimate was based upon the details included in this outline.

The final pricing may vary upon the finalization of the protocol, as well as consideration of other components not included in this proposal.

RBD Recombinant Protein-based SARS Vaccine for Biodefense Preparedness

Species	Rat
GLP Status	GLP
Acclimation Period	1 week
In Life Period	9 weeks, not including 1-week acclimation period
Recovery Period	2 weeks
No. Animals/Sex/Dose Group	Main – 10/sex/group Satellite – 5/sex/group
No. of Dose Groups (including control)	7 dose groups, including control
Total number of animals on study	210
Dose Formulation Analysis	Performed by Sabin
Formulations	Dose prep prior to dosing (4 dose timepoints)
Dose Frequency	Once on SD0, 21, 42 and 63
Route	Intramuscular
Cage side observations	At least 2 times/day
Clinical Observations	During quarantine, and prior to dosing on SD 0, 21, 42 and 63 and 1 – 3 hours post dose; Once daily on Study Days 1 through 7 and weekly thereafter throughout the remainder of the in-life study.
Body Weights	Prior to randomization, and prior to dosing on days SD0, 21, 42 and 63 and on Study Days 2, 4, 6, 8, 15, 29, 36, 50, 57, 66, 71



RBD Recombinant Protein-based SARS Vaccine for Biodefense Preparedness

	and 77. Fasted body weights will also be collected from all surviving main study animals prior to their scheduled sacrifice on Study Day 67 or 78.
Body Temperature	Body temperature will be determined prior to each dose, 6 hours (± 10 minutes) and 24 hours (± 20 minutes) post dosing. If any temperature is $> 40^{\circ}$ C, additional measurements will be taken every 24 hours until the values return to normal.
Food Consumption	Food consumption will be measured individually for each surviving main study animal weekly throughout the treatment and observation periods.
Draize Scoring	Inoculation sites from all main study animals will be evaluated prior to dosing on Study Day 0, 21, 42, and 63 and on SD 1-7; SD22-28; SD43-49 and SD64-70 and prior to termination on SD 67 or 78.
Clinical Chemistry	During pre-test period and on Study Day 4 and prior to dosing on Study Days 22, 43 and 64, and prior to termination on Study Day 67 or 78. (5 rats/sex/group/time point).
Hematology	During pre-test period and on Study Day 4 and prior to dosing on Study Days 22, 43 and 64, and prior to termination on Study Day 67 or 78. (5 rats/sex/group/time point).
Coagulation Parameters	During pre-test period and on Study Day 4 and prior to dosing on Study Days 22, 43 and 64, and prior to termination on Study Day 67 or 78. (5 rats/sex/group/time point).
Urinalysis	N/A
Antibody Sample Collection	From Satellite animals, up to 5 animals/sex/group, on Study Day 1, 22, 43, and 64 prior to dosing, and from Main Study animals, SD 67 (terminal deaths) and from Main Study and Satellite animals up to 10 animals/sex/group, on day 78.
Necropsy/Tissue preservation	Tissues from all Main Study animals will be collected at necropsy and fixed in 10% neutral buffered formalin, with the exception of the eyes (with optic nerves) which will be fixed in Davidson's solution, and the testes and epididymides which will be fixed in Bouin's fixative.
Bone Marrow	Collected and fixed in methanol. Evaluated upon request at additional charge.
Histopathology	Main study animals in Groups 2, 4 and 6 only. Additional groups evaluated at additional charge.
Report	Standard GLP Report

Cost: \$186,450

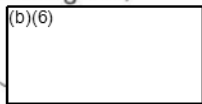


We understand that this project is scheduled for 2016/2017. Please let us know when the project is funded so we can get the appropriate paperwork in place and assign the resources.

We look forward to working closely with you and your staff. We will ensure high quality deliverables and flexibility to your program requirements, and will work effectively with your team to meet your proposed timeline for your program.

Should you have any questions regarding this proposal, please do not hesitate to call me.

Best regards,

(b)(6)


Beth Wong, VP Business Development



May 12, 2011

Mr. Michael Marine
Chief Executive Office
Sabin Vaccine Institute
2000 Pennsylvania Ave NE
Washington DC 20006

RE: "Grant RBD recombinant protein-based SARS vaccine for biodefense preparedness' in response to NIH's RFA for Partnerships for Biodefense".

Dear Mr. Marine:

The purpose of this letter is to convey Immune Design Corp.'s (IDC) support for your grant application entitled, "RBD recombinant protein-based SARS vaccine for biodefense preparedness' in response to NIH's RFA for Partnerships for Biodefense."

If the grant is funded, and pending execution of an MTA between IDC and the Sabin Vaccine Institute, we will supply you with our Glycopyranosyl Lipid Adjuvant (GLA, aqueous and stable emulsion formulations), a TLR4 agonist, for use in feasibility studies and the GLP toxicology study as detailed in your grant application. The current cost the formulated GLA well be approximately \$175,000.

We look forward to working with you on this important project.

Sincerely,

(b)(6)

Steven G. Reed, Ph.D.
President

With the concurrence of The Sabin Vaccine Institute:

(b)(6)

Brian R. Davis
Chief Operating Officer

1124 COLUMBIA STREET, SUITE 700
SEATTLE, WA 98104
P: 206.682.0645 F: 206.682.0648
INFO@IMMUNEDESIGN.COM

Resource Sharing Plan

We will adhere to the NIH Grant Policy regarding the sharing of unique research resources developed through NIH-sponsored research, including research data and reagents. Data files will be made available to outside researchers in a timely fashion - no later than the acceptance for publication of the main findings reported in individual manuscripts. Requests for reagents that are generated as part of this project will be distributed in a timely manner. Distribution to academic and other non-profit researchers will occur under agreements no more restrictive than the Materials Transfer Agreement of the Baylor College of Medicine and the New York Blood Center or the Simple Letter Agreement for the Transfer of Materials as described in the Guidelines for Disseminating Research Resources Arising Out of NIH-Funded Research (Federal Register, Vol 64, No 246, p.72094). Distribution of resources to for-profit institutions will be determined based on the resource itself, the ability of the Baylor College of Medicine and the New York Blood Center to efficiently meet demand, and the necessity for further development of the resource. Distribution to for-profit entities may occur under Material Transfer agreements or non-exclusive license arrangements. Only under extreme circumstances would exclusive licensing be considered; The offices of Patents & Licensing of the Baylor College of Medicine and the New York Blood Center will contact NIH's technology transfer office to discuss the need for exclusive licensing of research resources, should the Baylor College of Medicine and the New York Blood Center believe this is required for adequate distribution of the resource to both for-profit and non-profits.

PHS 398 Checklist

OMB Number: 0925-0001

1. Application Type:

From SF 424 (R&R) Cover Page. The responses provided on the R&R cover page are repeated here for your reference, as you answer the questions that are specific to the PHS398.

* Type of Application:

New Resubmission Renewal Continuation Revision

Federal Identifier:

2. Change of Investigator / Change of Institution Questions

Change of principal investigator / program director

Name of former principal investigator / program director:

Prefix:

* First Name:

Middle Name:

* Last Name:

Suffix:

Change of Grantee Institution

* Name of former institution:

3. Inventions and Patents (For renewal applications only)

* Inventions and Patents: Yes No

If the answer is "Yes" then please answer the following:

* Previously Reported: Yes No

4. * Program Income

Is program income anticipated during the periods for which the grant support is requested?

Yes No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount (\$)	*Source(s)
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>
<input type="text"/>	<input type="text"/>	<input type="text"/>

5. * Disclosure Permission Statement

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

Yes No



Grant Number: 3R01AI098775-02S1

Principal Investigator(s):

Maria Elena Bottazzi
PETER J HOTEZ (contact)
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: 06/24/2013 – 08/02/2013

Project Period: 05/04/2012 – 04/30/2017

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of \$3,936 (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,

Shellie M. Wilburn

Grants Management Officer
NATIONAL INSTITUTE OF ALLERGY AND INFECTIOUS DISEASES

Additional information follows

SECTION I – AWARD DATA – 3R01AI098775-02S1**Award Calculation (U.S. Dollars)**

Salaries and Wages	\$2,320
Fringe Benefits	\$182
Federal Direct Costs	\$2,502
Federal F&A Costs	\$1,434
Approved Budget	\$3,936
Federal Share	\$3,936
TOTAL FEDERAL AWARD AMOUNT	\$3,936
AMOUNT OF THIS ACTION (FEDERAL SHARE)	\$3,936

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (2)	
GRANT NUMBER	TOTAL FEDERAL AWARD AMOUNT
3R01AI098775-02S1	\$3,936
5R01AI098775-02	\$1,085,321
TOTAL	\$1,089,257

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
2	\$3,936	\$1,089,257
3	\$0	\$1,134,359
4	\$0	\$1,165,726
5	\$0	\$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
 Fiscal Year: 2013

	IC	CAN	2013
AI	8012165		\$3,936

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: 414C / Released: 06/21/2013
 Award Processed: 06/24/2013 12:04:45 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 3R01AI098775-02S1

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 – 3R01AI098775-02S1

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:

- The grant program legislation and program regulation cited in this Notice of Award.
- Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
- 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.

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 – 3R01AI098775-02S1

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

This award provides support under the Research Supplements to Promote Diversity in Health-Related Research Program for Frederick Nelson /BAYLOR COLLEGE OF MEDICINE beginning 06/10/2013. These funds (\$2,502 Direct Costs and \$1,434 Facilities and Administrative Costs) are restricted for the above purpose only and may not be transferred to any other individual. Funds awarded are available for carryover for awards given carryover authority as reflected in section III of this award notice. However, the funds remain restricted for the individual and the purpose for which the supplement is awarded.

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: Vandhana Khurana
Email: khuranav@mail.nih.gov **Phone:** 301-496-7075 **Fax:** 301-493-0597

Program Official: Rachelle Salomon
Email: salomonra@mail.nih.gov **Phone:** 301-402-2202 **Fax:** 301-496-8030


SPREADSHEET SUMMARY

GRANT NUMBER: 3R01AI098775-02S1

INSTITUTION: BAYLOR COLLEGE OF MEDICINE

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

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

Department of Health and Human Services Public Health Services Grant Application <i>Do not exceed character length restrictions indicated.</i>		LEAVE BLANK—FOR PHS USE ONLY.			
		Type	Activity	Number	
		Review Group		Formerly	
		Council/Board (Month, Year)		Date Received	
1. TITLE OF PROJECT (<i>Do not exceed 81 characters, including spaces and punctuation.</i>) RBD RECOMBINANT PROTEIN-BASED SARS VACCINE FOR BIODEFENSE -1R01AI098775-01					
2. RESPONSE TO SPECIFIC REQUEST FOR APPLICATIONS OR PROGRAM ANNOUNCEMENT OR SOLICITATION <input type="checkbox"/> NO <input checked="" type="checkbox"/> YES <i>(If "Yes," state number and title)</i> Number: PA-12-149 Title: Research Supplements to Promote Diversity in Health Related Research					
3. PROGRAM DIRECTOR/PRINCIPAL INVESTIGATOR					
3a. NAME (Last, first, middle) Peter Hotez		3b. DEGREE(S) MD PhD		3h. eRA Commons User Name eRA Commons User Name	
3c. POSITION TITLE Professor		3d. MAILING ADDRESS (<i>Street, city, state, zip code</i>) One Baylor Plaza BCM 113 Houston, TX 77030-3411			
3e. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT Pediatrics, Tropical Medicine					
3f. MAJOR SUBDIVISION College of Medicine					
3g. TELEPHONE AND FAX (<i>Area code, number and extension</i>) TEL: 713-798-1199 FAX: 713-798-2299		E-MAIL ADDRESS: hotez@bcm.edu			
4. HUMAN SUBJECTS RESEARCH <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes		4a. Research Exempt <input type="checkbox"/> No <input type="checkbox"/> Yes		If "Yes," Exemption No.	
4b. Federal-Wide Assurance No.		4c. Clinical Trial <input type="checkbox"/> No <input type="checkbox"/> Yes		4d. NIH-defined Phase III Clinical Trial <input type="checkbox"/> No <input type="checkbox"/> Yes	
5. VERTEBRATE ANIMALS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes			5a. Animal Welfare Assurance No.		
6. DATES OF PROPOSED PERIOD OF SUPPORT (<i>month, day, year—MM/DD/YY</i>) From Through 06/10/13 08/02/13		7. COSTS REQUESTED FOR INITIAL BUDGET PERIOD 7a. Direct Costs (\$) 7b. Total Costs (\$) \$2,502 \$3,936		8. COSTS REQUESTED FOR PROPOSED PERIOD OF SUPPORT 8a. Direct Costs (\$) 8b. Total Costs (\$) \$2,502 \$3,936	
9. APPLICANT ORGANIZATION Name Baylor College Of Medicine Address One Baylor Plaza Houston, TX. 77030-3411		10. TYPE OF ORGANIZATION Public: → <input type="checkbox"/> Federal <input type="checkbox"/> State <input type="checkbox"/> Local Private: → <input checked="" type="checkbox"/> Private Nonprofit For-profit: → <input type="checkbox"/> General <input type="checkbox"/> Small Business <input type="checkbox"/> Woman-owned <input type="checkbox"/> Socially and Economically Disadvantaged			
		11. ENTITY IDENTIFICATION NUMBER 1741613878A1 DUNS NO. 051113330 Cong. District TX-009			
12. ADMINISTRATIVE OFFICIAL TO BE NOTIFIED IF AWARD IS MADE Name Leanne B. Scott, Ph.D. Title Director, Sponsored Programs Address One Baylor Plaza BCM 310 Houston, Texas 77030-3411 Tel: 713.798.1297 FAX: 713.798.6990 E-Mail: spo@bcm.edu		13. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION Name Leanne B. Scott, Ph.D. Title Director, Sponsored Programs Address One Baylor Plaza BCM 310 Houston, Texas 77030-3411 Tel: 713.798.1297 FAX: 713.798.6990 E-Mail: spo@bcm.edu			
14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.		SIGNATURE OF OFFICIAL NAMED IN 13. <i>(In ink. "Per" signature not acceptable.)</i> 		DATE 4-15-13	

PROJECT SUMMARY (See instructions):

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

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

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

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

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

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

RELEVANCE (See instructions):

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

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

Project/Performance Site Primary Location			
Organizational Name: Baylor College of Medicine			
DUNS: 051113330			
Street 1: One Baylor Plaza		Street 2:	
City: Houston	County: Harris	State: TX	
Province:	Country: United States of America	Zip/Postal Code: 77030	
Project/Performance Site Congressional Districts: TX-009			
Additional Project/Performance Site Location			
Organizational Name: Texas Children's Hospital			
DUNS: 074615394			
Street 1: 1102 Bates Ave. Ste 550		Street 2:	
City: Houston	County: Harris	State: TX	
Province:	Country: United States of America	Zip/Postal Code: 77030	
Project/Performance Site Congressional Districts: TX-009			

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

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

Name	eRA Commons User Name	Organization	Role on Project
Peter Hotez, MD, PhD	<input type="text" value="eRA Commons User Name"/>	BCM	PI

OTHER SIGNIFICANT CONTRIBUTORS

Name	Organization	Role on Project
James L. Phillips, MD	BCM	Other Significant Contributor

Human Embryonic Stem Cells No Yes

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

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

Cell Line

**DETAILED BUDGET FOR INITIAL BUDGET PERIOD
DIRECT COSTS ONLY**

FROM
06/10/2013

THROUGH
08/02/2013

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

NAME	ROLE ON PROJECT	Cal. Mnths	Acad. Mnths	Summer Mnths	INST.BASE SALARY	SALARY REQUESTED	FRINGE BENEFITS	TOTAL
Peter Hotez, MD, PhD	PD/PI	0				0	0	0
Frederick Nelson	Project Intern	EFFORT			Institutional Base Salary	2,320	182	2,502
SUBTOTALS →						2,320	182	2,502

CONSULTANT COSTS	
EQUIPMENT (<i>Itemize</i>)	
SUPPLIES (<i>Itemize by category</i>)	
TRAVEL	
INPATIENT CARE COSTS	
OUTPATIENT CARE COSTS	
ALTERATIONS AND RENOVATIONS (<i>Itemize by category</i>)	
OTHER EXPENSES (<i>Itemize by category</i>)	

CONSORTIUM/CONTRACTUAL COSTS	DIRECT COSTS	
SUBTOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD (<i>Item 7a, Face Page</i>)		\$ 2,502
CONSORTIUM/CONTRACTUAL COSTS	FACILITIES AND ADMINISTRATIVE COSTS	
TOTAL DIRECT COSTS FOR INITIAL BUDGET PERIOD		\$ 2,502

**BUDGET FOR ENTIRE PROPOSED PROJECT PERIOD
DIRECT COSTS ONLY**

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

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

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

CHECKLIST

TYPE OF APPLICATION (Check all that apply.)

- NEW application. (This application is being submitted to the PHS for the first time.)
- RESUBMISSION of application number: _____
(This application replaces a prior unfunded version of a new, renewal, or revision application.)
- RENEWAL of grant number: _____
(This application is to extend a funded grant beyond its current project period.)
- REVISION to grant number: 1R01AI098775-01
(This application is for additional funds to supplement a currently funded grant.)
- CHANGE of program director/principal investigator.
Name of former program director/principal investigator: _____
- CHANGE of Grantee Institution. Name of former institution: _____
- FOREIGN application Domestic Grant with foreign involvement List Country(ies) Involved: _____

INVENTIONS AND PATENTS (Renewal appl. only) No Yes
 If "Yes," Previously reported Not previously reported

1. PROGRAM INCOME (See instructions.)

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

Budget Period	Anticipated Amount	Source(s)
N/A		

2. ASSURANCES/CERTIFICATIONS (See instructions.)

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

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

- DHHS Agreement dated: 03/02/2010; 06/24/2010 No Facilities And Administrative Costs Requested.
- DHHS Agreement being negotiated with _____ Regional Office.
- No DHHS Agreement, but rate established with _____ Date _____

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

a. Initial budget period:	Amount of base \$	<u>2,502</u>	x Rate applied <input checked="" type="checkbox"/>	<u>57.3</u>	% = F&A costs	\$	<u>1,434</u>	
b. 02 year	Amount of base \$		x Rate applied		% = F&A costs	\$		
c. 03 year	Amount of base \$		x Rate applied		% = F&A costs	\$		
d. 04 year	Amount of base \$		x Rate applied		% = F&A costs	\$		
e. 05 year	Amount of base \$		x Rate applied		% = F&A costs	\$		
TOTAL F&A Costs							\$	1,434

*Check appropriate box(es):

- Salary and wages base Modified total direct cost base Other base (Explain)
- Off-site, other special rate, or more than one rate involved (Explain)

Explanation (Attach separate sheet, if necessary.):

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

BIOGRAPHICAL SKETCH

NAME Peter Hotez MD PhD		POSITION TITLE Dean, National School of Tropical Medicine, Professor of Pediatrics, Molecular Virology & Microbiology, Baylor College of Medicine; President, Sabin Vaccine Institute	
eRA COMMONS USER NAME eRA Commons User Name			
EDUCATION/TRAINING			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Yale University (magna cum laude)	BA	1976 - 1980	Molec. Biophysics
Rockefeller University	PhD	1980 - 1986	Biochemistry (Parasitol.)
Cornell University Medical College	MD	1980 - 1987	Medical Science
Harvard Medical School (Mass. Gen. Hosp)	Residency	1987 - 1989	Pediatrics
Yale University School of Medicine	Fellowship	1989 - 1991	Molecular Parasitology

A. Personal Statement.

Professor Peter Hotez is a laboratory and clinician investigator with a major interest in vaccines for neglected tropical diseases (NTDs) and emerging infections. He is an elected member of the Institute of Medicine and founding director of one of the first non-profit public private partnerships (PDP) for developing vaccines to combat NTDs. PDPs use industrial practices but develop products in the non-profit sector because they target diseases of the world's poorest people. Launched in 2000, the PDP of the Sabin Vaccine Institute filed its first Investigational New Drug (IND) application for a recombinant vaccine in 2004, with a second IND filed this year, both for hookworm infection. Today the Sabin PDP is also developing recombinant vaccines for major disease affecting developing countries, including hookworm, schistosomiasis, Chagas diseases and SARS. These vaccines are engineered in yeast and bacteria. Process development at the 10 liter fermentation scale, followed by protein purification and formulation studies are conducted at Sabin followed by technology transfer to a pilot scale manufacturer either in the U.S., Brazil, and Mexico, and then clinical testing in either the U.S. or developing countries. Thus, Sabin's PDP has acquired a track record of transitioning concepts and discoveries into actual vaccines for clinical testing. Sabin's PDP relocated to Baylor College of Medicine in, 2011 where it is known as Sabin Vaccine Institute and Texas Children's Center for Vaccine Development. He is also the founding Dean of the National School of Tropical Medicine at Baylor College of Medicine. Dr. Hotez is a recognized leader on vaccine development for tropical diseases and other infectious diseases.

B. Positions and Honors.

Positions and Employment

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

- 2011- Texas Children's Hospital Endowed Chair of Tropical Pediatrics
- 2011- Dean, National School of Tropical Medicine at Baylor College of Medicine
- 2013- Fellow in Disease and Poverty, James A. Baker III Institute, Rice University

Honors (after 2005)

- 2006 Leverhulme Medal, Liverpool School of Tropical Medicine
- 2006 Ambassador, Paul G. Rogers Society for Global Health Research, ResearchAmerica!
- 2007 Member of Advisory Board (Council), Fogarty International Center, National Institutes of Health
- 2008 Science and Technical Advisory Group on Neglected Tropical Diseases, WHO
- 2008 Elected Member, Institute of Medicine of the U.S. National Academies
- 2009 Science and Technical Advisory Committee on Tropical Disease Research, WHO
- 2011 Member, National Institutes of Health (NIH) Council of Councils
- 2011 Elected Member, The Academy of Medicine, Engineering, and Science of Texas (TAMEST)
- 2011 Fellow of the American Society of Tropical Medicine and Hygiene (FASTMH)
- 2011 Abraham Horwitz Award for Excellence in Leadership in Inter-American Public Health, PAHO, WHO
- 2012 Elected Member, The Association of American Physicians (AAP)
- 2012 The Ralph D. Feigin, M.D. Award for Excellence, The Immunization Partnership
- 2013 Vaccine Nation, Top 50 most influential vaccine personalities

C. Selected peer-reviewed publications (in chronological order). (Selected from 275)

1. Hotez PJ, Brooker S, Bethony JM, Bottazzi ME, Loukas A, Xiao S. Hookworm Infection. *N Engl J Med* 2004; 351:799-807.
2. Asojo OA, Goud G, Dhar K, Loukas A, Zhan B, Deumic V, Liu S, Borgstahl GE, Hotez PJ. X-ray structure of Na-ASP-2, a pathogenesis-related-1 protein from the nematode parasite, *Necator americanus*, and a vaccine antigen for human hookworm infection. *J Mol Biol* 2005; 346:801-14.
3. Hotez PJ. Neglected Infections of Poverty in the United States of America. *PLoS Negl Trop Dis* 2008; 2:e256. PMID: PMC2430531.
4. Bethony JM, Simon G, Diemert DJ, Parenti D, Desrosiers A, Schuck S, Fujiwara R, Santiago H, Hotez PJ. Randomized, placebo-controlled, double-blind trial of the Na-ASP-2 hookworm vaccine in unexposed adults. *Vaccine* 2008; 26: 2408-17.
5. Hotez PJ, Fenwick A, Savioli L, Molyneux DH. Rescuing the "bottom billion" through neglected tropical disease control. *Lancet* 2009; 373: 1570-4.
6. Hotez PJ. Peace through vaccine diplomacy. *Science* 2010; 327: 1301. www.sciencemag.org/content/327/5971/1301.full?sid=5be8053a-cc9c-4381-a6e9-815c955ba849
7. Pearson MS, Pickering DA, Tribolet L, Cooper L, Mulvenna J, Oliveira LM, Bethony JM, Hotez PJ, Loukas A. Neutralizing antibodies to the hookworm hemoglobinase *Na-APR-1*: implications for a multivalent vaccine against hookworm infection and schistosomiasis. *J Infect Dis* 2010; 201:1561-9. jid.oxfordjournals.org/content/201/10/1561.full
8. Zhan B, Perally S, Brophy PM, Xue J, Goud G, Liu S, Deumic V, de Oliveira LM, Bethony J, Bottazzi ME, Jiang D, Gillespie P, Xiao SH, Gupta R, Loukas A, Ranjit N, Lustigman S, Oksov Y, Hotez P. Molecular Cloning, Biochemical Characterization and Partial Protective Immunity of the Heme-binding Glutathione S-Transferases from the Human Hookworm *Necator americanus*. *Infect Immun* 2010; 78:1552-63. PMID: PMC2849424
9. Hotez PJ, Bethony JM, Diemert DJ, Pearson M, Loukas A. Developing vaccines to combat hookworm infection and intestinal schistosomiasis. *Nat Rev Microbiol* 2010; 8: 814-26.
10. Hotez PJ, Mistry N, Rubinstein J, Sachs JD. Integrating neglected tropical diseases into AIDS, tuberculosis, and malaria control. *N Engl J Med* 2011; 364: 2086-9.
11. Hotez PJ. A handful of 'antipoverty' vaccines exist for neglected diseases, but the world's poorest billion people need more. *Health Aff (Millwood)* 2011; 30: 1080-7. PMID: 21653960.
12. Goud GN, Deumic V, Gupta R, et al. Expression, purification, and molecular analysis of the *Necator americanus* glutathione S-transferase 1 (Na-GST-1): a production process developed for a lead candidate recombinant hookworm vaccine antigen. *Protein Expr Purif* 2012; 83: 145-51.

13. Jiang S, Bottazzi ME, Du L, Lustigman S, Tseng CT, Curti E, Jones K, Zhan B, Hotez PJ. Roadmap to developing a recombinant coronavirus S protein receptor-binding domain vaccines for severe acute respiratory syndrome. *Exp Rev Vaccines* 2012; 11: 1405. PMID: 23252385
14. Lee BY, Bacon KM, Bottazzi ME, Hotez PJ. The global economic burden of Chagas disease: a computational simulation model. *LANCET INFECTIOUS DISEASES* 2013; [Epub ahead of print].

D. Research Support

Ongoing Research Support

23386 Hotez (PI) 01/01/2011-12/31/2014

Sponsor: Dutch Government

Title: Product Development Support of the Human Hookworm Vaccine

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

1016395 Hotez (PI) 08/01/2011 - 07/31/2013

Sponsor: (b)(4)

Title: Human Hookworm Vaccine Initiative 3

Clinical Development and Evaluation of the *Na*-GST-1 and *Na*-APR-1 Hookworm Vaccine Antigens

The project purpose is to provide proof-of-principle that vaccination with two adult-stage hookworm antigens will reduce the burden of infection caused by *Necator americanus*.

Hotez (PI) 04/20/2012 - 03/19/2014

(b)(4)

Accelerating the development and testing of a therapeutic Chagas vaccine

The main goal of this project is to accelerate the early development of a vaccine for a major neglected tropical disease affecting the Amazon region and Latin America – Chagas disease.

NIH R01AI098775-01 Hotez/Bottazzi/Jiang (MPI) 05/04/2012 – 04/30/2017

Sponsor: National Institutes of Health

Title: RBD Recombinant Protein-based SARS Vaccine for Biodefence

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

Bottazzi Center Director 07/01/2012 - 12/31/2017

Sponsor: Department of Health and Human Services / Texas A&M Univ.

Title: Centers for Innovation in Advanced Development and Manufacturing

The major goal of this project is to advance education and training for professionals in the area of vaccine biotechnology and product development

Role: Instructor

Completed Research Support (selected support after 2009)

32472 Hotez (PI) 08/01/2006 - 12/31/2012

Sponsor: Sabin Vaccine Institute is conduit for The Bill and Melinda Gates Foundation

Title: Human Hookworm Vaccine Initiative 1

Human Hookworm Vaccine Initiative (HHVI): Clinical Development & Evaluation of the *Na*-ASP-2 Hookworm Vaccine

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

AI/90577 Hotez (PI) 01/01/2011 - 12/31/2012

Sponsor: National Institutes of Health

Title: Product development of a membrane tetraspanin vaccine against schistosomiasis

The goal of this project is the development of a high-yield, low-cost process for producing and formulating a

recombinant Sm-TSP-2 schistosomiasis vaccine (10-liter scale)

RCA8608 Hotez (PI)

09/30/2009 - 09/30/2011

(b)(4) -PATH-MVI

Development of a Malaria transmission blocking Vaccine

To develop a feasibility of expression study for the expression and scale-up of the Anopheles-APN-1 target candidate antigen as a malaria transmission blocking vaccine. The goal of this study is to conduct the early feasibility of expression using both yeast and bacterial expression systems.

38988 Hotez (PI)

08/01/2006 - 07/31/2011

Human Hookworm Vaccine Initiative 2

Sabin Vaccine Institute-Human Hookworm Vaccine Initiative (HHVI): To develop and test the Na-APR-1 Hookworm Vaccine

The goal of this study is to conduct the process development, cGMP manufacture and testing, and clinical evaluation of APR-1 in order to develop a bivalent human hookworm vaccine with the Sabin Vaccine Institute

SUMMARY OF THE PROJECT SPECIFIC AIMS AND APPROACH

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

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

Specific Aim 1: Expression, purification and pre-clinical characterization of the rRBD protein as a vaccine candidate. We will evaluate the expression of the recombinant RBD (rRBD) in bacteria and yeast expression systems and select one of them for expression of rRBD protein for subsequent studies based on yields, purity, stability, antigenicity, functionality, immunogenicity, and efficacy (for inducing neutralizing antibody responses and protection against SARS-CoV challenge) of the rRBD protein when formulated in alum. We will use the rRBD protein from the selected expression system for optimization of immunization regimens, and assess the ability of rRBD protein formulated with alum based adjuvants and/or GLA, a TL R4 antagonist adjuvant, to induce cross-neutralizing antibody response, cross-protection and long-term immune responses and protection in mouse models using the optimized immunization regimen. (Timeline Year 1-3)

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

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

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

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

The Major Deliverables
<ol style="list-style-type: none"> 1. Development of a scalable, reproducible process for expression of the rRBD protein and formulation of the RBD-based vaccine with high quality and stability. 2. Establishment of an immunization regimen, including the optimized antigen dose, vaccination schedule and route and adjuvant formulation, for evaluation of the immunogenicity and efficacy of the vaccine. 3. Successful pilot cGMP manufacture of a subunit SARS vaccine comprised of rRBD protein and an adjuvant formulation. 4. Completion of the GLP toxicology testing with acceptable safety profile. 5. IND preparation and submission with U.S. FDA.

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

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

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

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

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

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

Week 1:

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

Weeks 2-6

Training and orientation on basic techniques in molecular biology and biochemistry

- How to prepare buffers and reagents
- How to prepare and run agarose gels and visualize and quantitate DNA
- How to use restriction endonucleases
- How to prepare plasmids and transfect yeast and bacteria
- How to induce protein expression and analyze recombinant proteins on SDS-PAGE

Week 2:

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

Week 3:

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

Week 4:

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

Week 5:

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

Week 6:

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

Week 7:

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

Week 8:

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

Evidence of mentoring experience for the Principal Investigator:

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

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

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

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

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

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

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

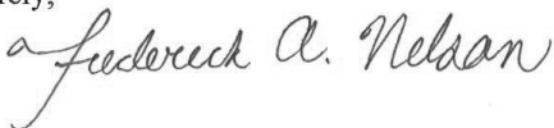
When I was young, I had always wanted to become a doctor. From watching the Discovery Health channel to playing with the instruments at the doctor's office, I was just fascinated with the profession. I loved the idea of becoming a doctor, but I loved working with science even more. My mother is a middle school life science teacher and I would always help her set up for laboratory experiments and even perform a couple with my mother. Honestly, it just seemed fun at the time. That innocent fun soon transformed into a passion to gain understanding of our natural world. The fact that science is ever-changing and never static is what excites my curiosity. Every day, new things are being discovered, theories being tested, and cures are being found, and I want to someday be a part of that amazing process.

Currently, I am involved in the Science National Honor Society and S.T.E.M Club at my high school, and participated in science fair completions at the district and regional levels. One of my experiments, titled "CSI: Daphnia," explored how the contamination of aquatic environments from ordinary pollutants (common runoff pollutants) of varying concentrations can harm aquatic life. I used the *Daphnia pulex* in my research because of their transparency and visible heart beatings and palpitations, if present. Conducting this experiment gave me a small dose of what biomedical research is like, and I absolutely loved it. I remember telling my science teacher Dr. Dilmaliwat that I felt like a scientist as I preformed the experiment. She smiled and told me that it was because I *was* a scientist. I was mind blown. It did not occur to me that what I was doing was exactly what researchers in universities and professionals are doing. Confucius once said "choose a job you love, and you will never have to work a day in your life." His words hit me hard, because I have done tedious and exhausting tasks at Sears but only simply exercised my passion with conducting experiments and research in the great name of science.

I had the honor and privilege of meeting Lisa Jackson, administrator of the Environmental Protection Agency, during a seminar in the summer of 2012. Mrs. Jackson described her journey through college and graduate school at the Princeton University as a winnable challenge despite not only being a person on ethnic minority but also as a woman in a male dominated field. I was in awe throughout the entire presentation. I can honestly say that that day I was (and still am) inspired to keep pushing forward in the face of adversity. As the first person on African American descent to serve as Administrator of EPA, Lisa Jackson made a name for all of her hard work and dedication – something I longed for myself one day.

Participating in SMS Summer Intern Program would be an invaluable experience for me, considering my academic interests and career goals. Not only that, participation in this internship will help me grow as a young college bound researcher on the path to practice medicine as a profession. If given the opportunity of this internship, I will not disappoint. I will go above and beyond and make great strides to becoming the best that I can be, for my mother, my community, my country, and for the sake of science.

Sincerely,



Frederick Nelson

Personal Info

WORK EXPERIENCE:

Alief Early College School Newspaper: *Knightly News*, Chief Editor

- Manage and supervise staff
- Publish and distribute final copies of the newspaper

Sears Outlet: Sales Associate (8/25- Present)

- Sell new, used, discontinued, scratch and dent appliances

HONORS AND AWARDS:

Science Fair (District) 1ST Place: 10th grade

Science Fair (District) 4th Place: 11th grade

Microsoft Office 2007 Word Certified

AP Scholar Award (College Board)

Houston Community College Dean's List: 11th grade

Honor Roll: 10th, 11th, 12th grade

ACTIVITIES:

School Newspaper: 11th grade

Student Council: 9th, 10th, 11th, 12th grades

National Science Honor Society: 11th, 12th grades

National Honor Society: 11th, 12th grade

Texas Governor's School of Leadership in the Humanities: 10th, 11th grades

National Society of Collegiate Scholars: 12th grade

Class Officers: 10th, 12th grades

Saturday Morning Science at the Baylor College of Medicine: 12th grade

COMMUNITY SERVICE:

PAIR (Partnership for the Advancement & Immersion of Refugees): 11th grade

- Mentored and tutored refugee youth at Fondren Middle School (Fall 2011, Spring 2012)

Community Service Club: 10th, 11th grades

- Participated in various events and service projects in the Alief community
 - Served as a vendor with Chinese New Year Festival, 1/27/12, 9 Hours
 - Helped to clean ACC Park, 2/26/11, 4 Hours
 - Assisted with clean up at Boone park, 2/12/11, 6 Hours
 - Assisted in tree planting at Hackberry Park, 1/29/11, 8 Hours
- Ushered at the Hobby Center, 12/15/12, 6 Hours



To whom it may concern:

(b)(6)

(Name of Student), a student from Alief Early College High School

(Insert name of school), located at 2811 Hayes Rd. (school address), would like to participate in the summer research experience offered to them through the Saturday Morning Science program at Baylor College of Medicine for the summer of 2013. I understand that said student will be working in a research lab under the direction of a Principal Investigator at Baylor College of Medicine who is operating under an active grant funded through the National Institutes of Health.

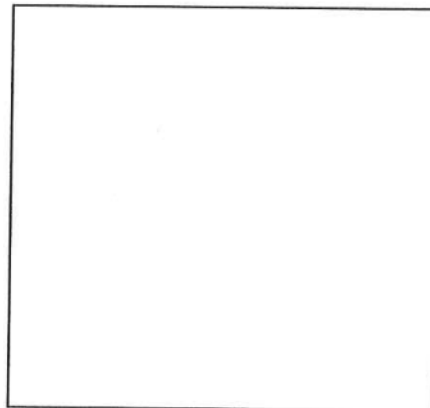
I approve of (b)(6)'s (name of student) participation in this research program, and I attest that their participation will not detract from or interfere with the student's course of studies.

Name of school official completing document: Terri Guidry

Role of school official: Counselor Phone #: 281-988-3010

Signature of school official: (b)(6) Date: 2/28/13

Please affix school stamp or seal in the designated space below:



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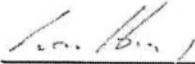
Withheld pursuant to exemption

Personal Info

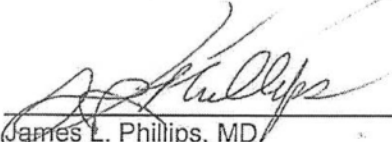
of the Freedom of Information and Privacy Act

Statement of Eligibility from the Investigator

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



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



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



Leanne B. Scott, PhD
Director, Sponsored Programs
Baylor College of Medicine



Grant Number: 3R01AI098775-03S1
FAIN: R01AI098775

Principal Investigator(s):
Maria Elena Bottazzi
PETER J HOTEZ (contact)
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: 06/16/2014 – 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 \$3,936 (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,

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

Additional information follows

SECTION I – AWARD DATA – 3R01AI098775-03S1**Award Calculation (U.S. Dollars)**

Salaries and Wages	\$2,320
Fringe Benefits	\$182
Federal Direct Costs	\$2,502
Federal F&A Costs	\$1,434
Approved Budget	\$3,936
Federal Share	\$3,936
TOTAL FEDERAL AWARD AMOUNT	\$3,936
AMOUNT OF THIS ACTION (FEDERAL SHARE)	\$3,936

SUMMARY TOTAL FEDERAL AWARD AMOUNT YEAR (3)	
GRANT NUMBER	TOTAL FEDERAL AWARD AMOUNT
3R01AI098775-03S1	\$3,936
5R01AI098775-03	\$1,134,359
TOTAL	\$1,138,295

SUMMARY TOTALS FOR ALL YEARS		
YR	THIS AWARD	CUMULATIVE TOTALS
3	\$3,936	\$1,138,295
4	\$0	\$1,165,726
5	\$0	\$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
AI	8012165	\$3,936

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:** 414C / **Released:** 06/10/2014
Award Processed: 05/08/2014 01:52:21 PM

SECTION II – PAYMENT/HOTLINE INFORMATION – 3R01AI098775-03S1

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 – 3R01AI098775-03S1

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 – 3R01AI098775-03S1

This award provides support under the Research Supplements to Promote Diversity in Health-Related Research Program for Ebe Ewere at the Baylor College of Medicine beginning 06/09/2014. These funds (\$2,502 Direct Costs and \$1,434 Facilities and Administrative Costs) are restricted for the above purpose only and may not be transferred to any other individual. Funds awarded are available for carryover for awards given carryover authority as reflected in section III of this award notice. However, the funds remain restricted for the individual and the purpose for which the supplement is awarded.

In future years a separate progress report for the Research Supplement to Promote Diversity in Health-Related Research is required as part of the progress report of the parent grant.

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