

MARCE

Middle Atlantic Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research

<http://marcebiodefense.org>

Request For Proposals (RFP)

Solicitation for Developmental Research Projects

Solicitation Release Date:	February 15, 2011
Letter of Intent Deadline (Required):	March 6, 2011 (<i>Sunday by 12:00 midnight</i>)
Electronic Submission Deadline:	March 20, 2011 (<i>Sunday by 12:00 midnight</i>)
Approximate Award Date:	May 1, 2011

The Middle Atlantic Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research (MARCE) fosters research that will enable rapid defense against bioterror agents and emerging infectious diseases. Multiple universities, government institutions, and corporate partners are currently working together to improve our nation's public health response system. The key objectives of the MARCE Developmental Research Program are to test innovative concepts, develop new technologies, and support "high-risk" opportunities that demonstrate potential for "high-yield" novel results in the area of biodefense and emerging infectious diseases research. With regard to product development, projects will be encouraged to address broad-spectrum activity, broad-spectrum technology, and broad-spectrum platforms. Applicants will be expected to relate their proposed project to the MARCE's over-arching theme of "**Emerging pathogen-host interactions**", and to select one Research Program to integrate their project within. More specific research topic requirements are outlined in this RFP under "Research Objectives". The P01-like Research Programs are as follows:

- Program I** – Interaction of Emerging Viruses with Host Cell Pathways.
- Program II** – Emerging Virus Entry into Host Cells: Strategies for Inhibition.
- Program III** – Bacteria & Protozoa that Invade or Cause Disease via the Mucosa.
- Program IV** – Interactions of Select Agent and Emerging Bacterial Pathogen Toxins with Host Cells.
- Program V** – Diagnostics: Development, Support and Discovery.

INSTRUCTIONS FOR APPLICANTS

ELIGIBILITY REQUIREMENTS

The Principal Investigator (PI) of the proposed Developmental Project must reside within the Middle Atlantic Region (MD, VA, WV, PA, DE, and D.C.). Collaborators to the PI may reside outside the Region. The PI must commit 10 to 20 percent effort (20 percent maximum) to the goals of this award. The PI may be a previous MARCE investigator, but an investigator cannot apply for a continuation of an existing Developmental Project. The PIs currently receiving RCE funds are ineligible to apply. Previous experience specifically in the field of biodefense or emerging infectious diseases is not required. Minorities, women and individuals with disabilities are encouraged to apply.

MECHANISM OF SUPPORT

This mechanism will provide support for **2 years** of research in the amount of **\$125,000 direct costs per year**. Indirect costs will be awarded at your currently approved institutional rate. **Four Grants will be awarded** in response to this solicitation.

RESEARCH OBJECTIVES

The **key objectives** of the MARCE Developmental Research Plan are to test innovative concepts, develop new technologies, and support “high-risk” opportunities that demonstrate potential for “high-yield” novel results in the area of biodefense and emerging infectious diseases research. Applications must be relevant to the NIAID Category A-C Priority Pathogens (<http://www3.niaid.nih.gov/topics/BiodefenseRelated/Biodefense/research/CatA.htm>) and emerging infectious diseases (EID) agents (<http://www3.niaid.nih.gov/research/topics/emerging/list.htm>) as defined here by the NIAID.

Furthermore, proposals will be expected to synergize with one of the five Research Programs. Each applicant must clearly note the Research Program to which they are applying. The MARCE website contains further details on current areas of study: <http://marcebiodefense.org>.

The over-arching theme for the overall MARCE Research Program is **“Emerging pathogen-host interactions”**. **The five Research Programs** centered on this theme are described below.

Program I – Interaction of Emerging Viruses with Host Cell Pathways. The central theme of this Research Program, which emphasizes under-studied NIAID Category A and emerging pathogens, is the analysis of virus-host interactions to detect therapeutic targets and identify and allow development of therapeutic agents. Many projects in this Research Program utilize innovative small molecule, proteomic and RNAi screening technologies to identify host pathways with which viral pathogens interact and to identify and characterize potential antiviral agents. The viral pathogens currently under investigation in this Research Program include phleboviruses (Rift Valley Fever virus), Hantaviruses (Sin Nombre virus, Andes virus, and Puumala virus), emerging paramyxoviruses (Nipah and Hendra viruses), and poxviruses.

Program II – Emerging Virus Entry into Host Cells: Strategies for Inhibition. The central theme of this Research Program is to focus on the attachment and entry of viruses into cells with the goal of teasing out and identifying the molecular details of both the viral and cellular factors involved in this process. By attaining a thorough understanding of the factors and events comprising the viral entry process, the potential of discovering and developing novel therapeutic modalities and prevention strategies are made possible. The viral pathogens currently under investigation include Filoviruses (Ebola and Marburg viruses), New World Arenaviruses (Junin and Machupo viruses), the rhabdovirus Australian bat lyssavirus, and the orthopoxviruses (variola and monkeypox viruses).

Program III – Bacteria & Protozoa that Invade or Cause Disease via the Mucosa. The central themes of this Research Program are: 1) how various pathogens interact with the gastrointestinal and respiratory mucosa; and 2) ways to stimulate different arms of the mucosal and systemic immune system. The objectives are to seek common features and virulence mechanisms among the different

pathogens that may be amenable to the design of broad spectrum prophylactic and therapeutic interventions to interrupt pathogenesis and synergistic immune responses to confer broad spectrum protection. The emerging bacterial pathogens currently under investigation in Program III include *Shigella*, enteric fever *Salmonella* (Typhi, Paratyphi A & B), non-typhoidal *Salmonella*, enteroaggregative *Escherichia coli* (EAEC), enterotoxigenic *E. coli* (ETEC), enterohemorrhagic *E. coli* and Shiga toxin-producing *E. coli* (EHEC & STEC), *Francisella tularensis*, and the protozoan *Cryptosporidium*.

Program IV – Interactions of Select Agent and Emerging Bacterial Pathogen Toxins with Host Cells. The central theme of Research Program IV is to study how toxins of various NIAID Category A-C microorganisms and certain emerging pathogens interact with host cells, the consequences of those interactions, and the development of methods to block or ameliorate the impact of these virulence factors on the target cells and the host. The toxins currently under investigation in this Research Program include Shiga toxin, ricin, *Clostridium perfringens* epsilon toxin, *Clostridium difficile* toxins A and B, Staphylococcal enterotoxin B, and other staphylococcal super antigens.

Program V – Diagnostics: Development, Support and Discovery. The central theme of Program V is to discover, develop, and support broad-based diagnostic methodologies with capacity for select target identification. Projects aim to incorporate state-of-the-art technologies and translational research capacity, and promote relationships with biotechnology companies that may lead to product development. Integration of Program V's existing Research Projects and new Developmental Projects is envisioned as follows: Research Program V is currently comprised of two 'Hubs' that house proven technologies well along the pathway toward commercialization and licensure. The Universal Nucleic Acid Amplification Technology Hub houses platforms that exploit broad-based PCR methods which, when combined with innovative, simple and rapid post amplification detection techniques, allow for specific target detection. This assay is being evaluated in multiple clinical matrices, human samples and animal models for common, biothreat and emerging pathogens. The second Hub leverages the already proven microwave-accelerated metal enhanced fluorescence platform by developing a multiplexed capacity for several agents in a high throughput screening format. The technology has the potential to detect a wide range of agents simultaneously in mixed complex media such as whole blood, with little pre-processing time. In response to this RFP, proposals centered on new, higher risk, innovative approaches or technologies complementary and synergistic with those represented in the Hubs will be selected for Developmental Awards. Furthermore, the proposal must be clearly linked to one of the existing Research Programs (I-IV, above), and/or a specific existing Research Project within these Programs (see MARCE website). In this way the new Diagnostics Developmental Project will promote synergy between a pathogen of interest and a method of detection.

APPLICATION PROCEDURES

Letter of Intent:

A Letter of Intent (LOI) is **required** and must include the following:

Name, institution, and contact information of Principal Investigator (PI)

Name and institution of any Co-PIs or collaborators receiving funds

Indicate the specific Research Program (Program I – Program V) to which you are applying

Proposed title of the application

Very brief description of the work being proposed (4-5 sentences will suffice)

Submission of a LOI is required to remain eligible for the award. The LOI will facilitate the coordination of appropriate reviewers for your full application.

LOIs are to be submitted electronically only. **Email to rcegrants@medicine.umaryland.edu by 11:59 PM EST on March 6, 2011.**

Full Application:

Developmental Research Proposals must include the following:

- ❑ Face page (Institutional signature is not required for the electronic submission)
- ❑ Abstract Page
- ❑ Table of Contents
- ❑ Detailed Budget for Initial Period (\$125,000 maximum direct costs; indirect costs will be awarded at the currently approved rate for your institution and should be included in the checklist page noted below; modular budgets are not allowed)
- ❑ Budget for Entire Proposed Period of Support (2 years of funding are allowed)
- ❑ Budgets Pertaining to Consortium/Contractual Arrangements
- ❑ Biographical Sketches of Principal Investigator and all Key Personnel (Biosketches must be current)
- ❑ Resources and Environment
- ❑ Research Plan (**A maximum of 8 pages of text will be allowed for Sections 1 and 2 listed below.** Clearly **state which Research Program (Programs I – V)** you are addressing in your proposal.)
 1. Specific Aims
 2. Research Strategy (Significance, Innovation and Approach)
 3. Bibliography and References Cited/Progress Report Publication ListAs appropriate, include:
 4. Protection of Human Subjects
 5. Inclusion of Women and Minorities
 6. Targeted/Planned Enrollment Table
 7. Inclusion of Children
 8. Vertebrate Animals
 9. Select Agent Research
 10. Multiple PD/PI Leadership Plan
 11. Consortium/Contractual Arrangements
 12. Letters of Support (e.g., Consultants)
 13. Resource Sharing Plan(s)
- ❑ Checklist

Full Applications are to be prepared using PHS398 forms and following the PHS398 instructions for formatting (<http://grants.nih.gov/grants/funding/phs398/phs398.html>). The application does NOT need to be signed by your institutional official. If your application is selected for the award, we will request formal institutional signatures at that time.

Submission of Application:

Completed applications are to be submitted electronically in a single word document and **emailed to rcegrants@medicine.umaryland.edu by 11:59 PM EST on March 20, 2011.** If you are unsure whether your proposed research would fit into the aims of this Request for Proposals, please contact Dr. Snyder as below.

MARCE contact for information on scientific scope/research:

Jennifer A. Snyder, Ph.D.
MARCE Associate Director
Center for Vaccine Development
University of Maryland School of Medicine
jsnyder@medicine.umaryland.edu

MARCE contact for information on budgets/forms:

Gloria Smedley, MBA
MARCE Research Administrator
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REVIEW CONSIDERATIONS

The submitted Developmental proposals will be scored by an array of external reviewers with significant experience and stature. Based on subject areas and number of applications, an external Ad Hoc Review Committee will be solidified. Each proposal will be assigned to 3-4 reviewers for scoring on each review parameter (listed below) and for provision of comments. To avoid conflicts of interest, reviewers will not be assigned any proposals where the PI or any collaborators are from his/her home institution. The internal MARCE Steering Committee will provide a second level of review and determination of consistency with the Developmental Plan's stated goals. Top-scoring proposals will be sent to the NIAID RCE Program Office for final review and approval. Four awards will be made in response to this solicitation.

The following review criteria will be applied:

Significance (15 points)

Approach and scientific merit (35 points)

Innovation (20 points)

Investigator (10 points)

Potential for continued funding of this project beyond the MARCE (10 points)

Consistency with the MARCE research priorities and goals (10 points)

Significance (15 points)

Does the study address an important problem within the overall area of Biodefense and Emerging Infections? If the aims of the application are achieved, how will they advance scientific knowledge? How will the results of these studies advance the goals of the MARCE? If the research goes as planned, are there opportunities for collaboration with other MARCE investigators at a later point? What will be the effect of these studies on the concepts or methods that drive this field?

Approach and scientific merit (35 points)

Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Does the investigator acknowledge potential problems and consider alternative tactics? (Note - the nature of these awards allows for applications with little preliminary data.)

Innovation (20 points)

Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

Investigator (10 points)

Is the investigator appropriately trained and well qualified to carry out the proposed work? Is the proposed research commensurate with his/her experience level? (Note the previous experience in the field of biodefense or emerging infections is not required.)

Potential for continued funding of this project beyond the MARCE (10 points)

If the goals of the project are met, is there potential for continued funding of this proposed project, for example a R01, R21 award, or "graduation" into full MARCE Research Project status?

Consistency with the MARCE research priorities and goals (10 points)

Is the proposal consistent with MARCE research priorities and goals? Does the proposal align with and complement one of the specific MARCE Research Programs I – V?