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Department of Defense
Fiscal Year (FY) 2012 Budget Estimates

February 2011

Defense Advanced Research Projects Agency

Justification Book Volume 1

Research, Development, Test & Evaluation, Defense-Wide

Fiscal Year (FY) 2012 Budget Estimates

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Exhibit R-2, RDT&E Budget Item Justification: PB 2012 Defense Advanced Research Projects Agency	DATE: February 2011
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 1: *Basic Research*	**R-1 ITEM NOMENCLATURE** PE 0601117E: *BASIC OPERATIONAL MEDICAL SCIENCE*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
- Determine whether networks of neurons can be differentially activated through optogenetic stimulation. - Investigate how connectivity effects the rate at which information is transmitted between areas of the brain. - Evaluate the ability of functional Magnetic Resonance Imaging to accurately predict underlying behavior of groups of neurons through hemodynamic modeling. - Study the ability of primates to navigate virtual environments through the use of neural signals. - Determine if primates can evaluate and make use of information provided solely through a neural interface.			
Title: Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT)*	-	-	15.000
Description: *Previously funded in Synthetic Biology in PE 0601101E, Project TRS-01 The overarching goal of the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program is to create an ability to rapidly respond to a disease or threat and improve individual readiness and total force health protection. Service members in deployed settings have limited access to health care. The ability to perform continuous monitoring of physiological status to automatically and autonomously report a warning of a detrimental change and enable immediate diagnostic or therapeutic action would expand healthcare capabilities to these service members. Additionally, in vivo production of a vaccine would potentially eliminate the time to manufacture a vaccine ex vivo. This basic research effort will develop in vivo nucleic-acid circuits to control cellular machinery for diagnostic or vaccine applications and include research to: optimize orthogonality and modularity of genetic control elements; identify methods to increase sensitivity and specificity; and demonstrate methods to control cellular machinery in response to changes in physiological status. An additional strategic thrust is to develop methodologies for measuring health-specific biomarkers from a collected biospecimen to enable diagnostics at the point-of-need, in-garrison or deployed. This basic research effort will: develop new molecular methods for isolating and detecting health-associated biomarkers for application at the point-of-need or resource limited clinical facilities (point-of -care); develop new chemical and material methods for optimizing the analytical utility of minimal sample volumes; and, develop capabilities to archive and distribute biospecimens in a stable dried format without tubes, collection vials, or additional reagents. This program also has applied research efforts budgeted in PE 0602115E, Project BT-01. ***FY 2012 Plans:*** - Initiate development of modular and orthogonal nucleic acid-based elements for application within a detect-and-respond circuit. - Demonstrate controlled expression in mammalian cells of synthetic circuit in response to biomarkers associated with health status. - Develop oligonucleotide synthetic construct capable of utilizing cellular control elements to enhance potency, control dosing, and achieve effectiveness.			

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
- Develop novel materials and molecular approaches to enable deployable diagnostics. - Develop novel materials and approaches for stabilizing reagents and biospecimens at room temperature.			
Title: Dialysis-Like Therapeutics ***Description:*** Sepsis, a bacterial infection of the blood stream, is a significant cause of injury and death among combat-injured soldiers. The key goal of this program is to run the blood volume (approximately five liters) through an external machine (akin to a dialysis system) and literally scrub out harmful bacteria and their toxins. The proposed approach is low-shear/low-resistance fluidic structures to connect cellular and biomolecular purification techniques for blood purification. Initial basic research will develop novel low-shear, low-resistance fluidic structures that enable rapid, large volume blood filtration. Additional research will develop novel intrinsic separation techniques that selectively remove bacteria, toxins and host cells from complex fluids, as well as new methods for continuous sensing of these components. Finally, research into predictive control techniques for directing patient health will close the sense, scrub, and control loop. The applied research portion of the program is budgeted in PE 0602115E, Project BT-01. ***FY 2012 Plans:*** - Develop "label-free" intrinsic separation technologies that remove pathogens of different classes, toxins, and activated cells from complex fluids. - Design high flow, low shear microfluidics to transport wound fluid and blood without cellular activation. - Design pathogen sensors for continuous use in complex biological fluids. - Establish mathematical models to classify and predict patient state over relevant time scales.	-	-	5.000
Accomplishments/Planned Programs Subtotals	-	-	37.870

D. Other Program Funding Summary ($ in Millions)

N/A

E. Acquisition Strategy

N/A

F. Performance Metrics

Specific programmatic performance metrics are listed above in the program accomplishments and plans section.

Exhibit R-2, RDT&E Budget Item Justification: PB 2012 Defense Advanced Research Projects Agency	DATE: February 2011
APPROPRIATION/BUDGET ACTIVITY 0400: *Research, Development, Test & Evaluation, Defense-Wide* BA 2: *Applied Research*	**R-1 ITEM NOMENCLATURE** PE 0602115E: *BIOMEDICAL TECHNOLOGY*

C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
- Use optimized winner system and algorithm to investigate virus mitigation and frequency globally to predict the timing and geographic location of reassortment events. - Model processes to accurately predict the drift and shift of virus in pre-human animal reservoirs. - Create viral reservoir specific countermeasures that reduce probability that a novel viral pathogen could transfer from animals to humans. - Establish partners for transition of immune-hardening and pathogen anti-evolution technologies.			
Title: Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT)* ***Description:*** *Previously funded in Synthetic Biology in PE 0601101E, Project TRS-01 The overarching goal of the Autonomous Diagnostics to Enable Prevention and Therapeutics (ADEPT) program is to increase our ability to rapidly respond to a disease or threat and improve individual readiness and total force health protection. Service members in deployed settings have limited access to health care. New methods and devices are needed to address critical conditions on-site, to allow improved care at field hospital, fleet, and air transport settings, and to enable rapid response to emerging threats. This applied research effort will focus on development of devices for integrated diagnostics across multiple echelons of care: 1) Simple to operate diagnostic devices for critical biomarkers at the point of need; 2) highly multiplexed diagnostic devices for broad spectrum diagnostic and response to emerging threats in an automated format; and, 3) the ability to rapidly develop, integrate and distribute new assays for detection of new biomarkers and emerging threats. Research thrusts include: optimization of methodologies for extraction of targeted biomarkers from a biospecimen that has been room-temperature stabilized in a dried format; demonstration of novel molecular detection approaches towards specific biomarkers; optimization of integrated simple-to-operate diagnostic devices (sample in, results out); demonstration of novel molecular approaches for multiplexed analysis over the same or different classes of biomarkers; and, integration of sample preparation and analysis methods. A companion basic research effort is budgeted in PE 0601117E, Project MED-01. ***FY 2012 Plans:*** - Develop new materials and methods for low power diagnostics. - Develop new reagents and reagent storage methods for deployable diagnostics. - Develop processes for clinical sample collection and preparation for deployable diagnostics. - Develop methods and optimization criteria for extraction of targeted biomarker classes for the retrospective analysis of a dried and room-temperature stable biospecimen archive card. - Develop approach for biomarker research from archived biospecimen card, as the first step towards rapid synthesis of deployable diagnostic devices against new threats.	-	-	10.000
Title: Tactical Biomedical Technologies*	-	-	17.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
Description: *Previously funded in PE 0602715E, Project MBT-02 The Tactical Biomedical Technologies thrust will develop new approaches to deliver life-saving medical care on the battlefield. Uncontrolled blood loss is the leading cause of preventable death for soldiers on the battlefield. While immediate control of hemorrhage is the most effective strategy for treating combat casualties and saving lives, currently no method other than surgical intervention can effectively treat intracavitary bleeding. A focus in this thrust is the co-development of a materials-based agent(s) and delivery mechanism capable of damaged tissue-targeted hemostasis and wound control. This system will effectively treat compressible and non-compressible wounds regardless of geometry or location. Additionally, rapid response to emerging biological threats on the battlefield is impacted by logistical delays of delivering the necessary therapeutics. Creating a "pharmacy on demand" will enable far-forward medical providers to manufacture and produce small molecule drugs and biologics in order to ensure that the therapeutics are available when they need them. ***FY 2012 Plans:*** - Demonstrate hemostatic material compatibility with Food and Drug Administration (FDA)-approved agents that control pain, infection, and inflammation. - Achieve wound treatment system unit specs including coverage of at least 0.20 square meters of tissue area, mass of less than 200 grams, and a volume less than 150 ml. - Demonstrate scale-up for large volume hemostasis agent synthesis. - Demonstrate hemostasis agent stability consistent with operational requirements. - Test and validate the wound stasis system delivery device. - Develop a plan for wound stasis system FDA approval. - Fabricate devices capable of manufacturing six field relevant pharmaceuticals. - Investigate constructing a man-portable device capable of manufacturing four field relevant pharmaceuticals. - Demonstrate limited capability of manufacturing serum, antigen, and vaccine of DoD relevance through directed activity of microbial systems. - Show efficacy and safety of manufactured end products in in-vitro models.			
Title: Military Medical Imaging* ***Description:*** *Previously funded in PE 0602715E, Project MBT-02 The Military Medical Imaging thrust will develop medical imaging capabilities to support military missions and operations. The emergence of advanced medical imaging includes newly recognized physical properties of biological tissue, or metabolic pathway, or physiological function in order to map it into an image of diagnostic utility and performance. This need is ever increasing as	-	-	8.000

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C. Accomplishments/Planned Programs ($ in Millions)	FY 2010	FY 2011	FY 2012
- Initiate the development of physiologically accurate medical training simulations based on user expertise and provide detailed feedback to the user based on performance. - Explore viability of deploying versions on mobile platforms for maximum distribution.			
Title: Dialysis-Like Therapeutics ***Description:*** This thrust will develop and demonstrate dialysis-like structures that provide very high throughput (> 1.25 liters/hour) for continuous blood sensing and purification. Bench-level techniques for molecular and cellular "scrubbing" of targets such as bacteria, toxins, and select host cells from blood will be demonstrated. At the completion of the program, high throughput removal of circulating bacteria, toxins, and select host cells from blood without collateral activation of the coagulation and immunologic systems will be demonstrated. The basic research part of this program is budgeted in PE 0601117E, Project MED-01. ***FY 2012 Plans:*** - Develop integrated low-shear, high throughput (> 100 milliliters/hour) microfluidics components for complex fluid flow. - Demonstrate bench-level techniques for the sensing and removal of multiple blood targets including bacteria, toxins, and select host cells.	-	-	5.000
Accomplishments/Planned Programs Subtotals	-	-	110.000

D. Other Program Funding Summary ($ in Millions)

N/A

E. Acquisition Strategy

N/A

F. Performance Metrics

Specific programmatic performance metrics are listed above in the program accomplishments and plans section.