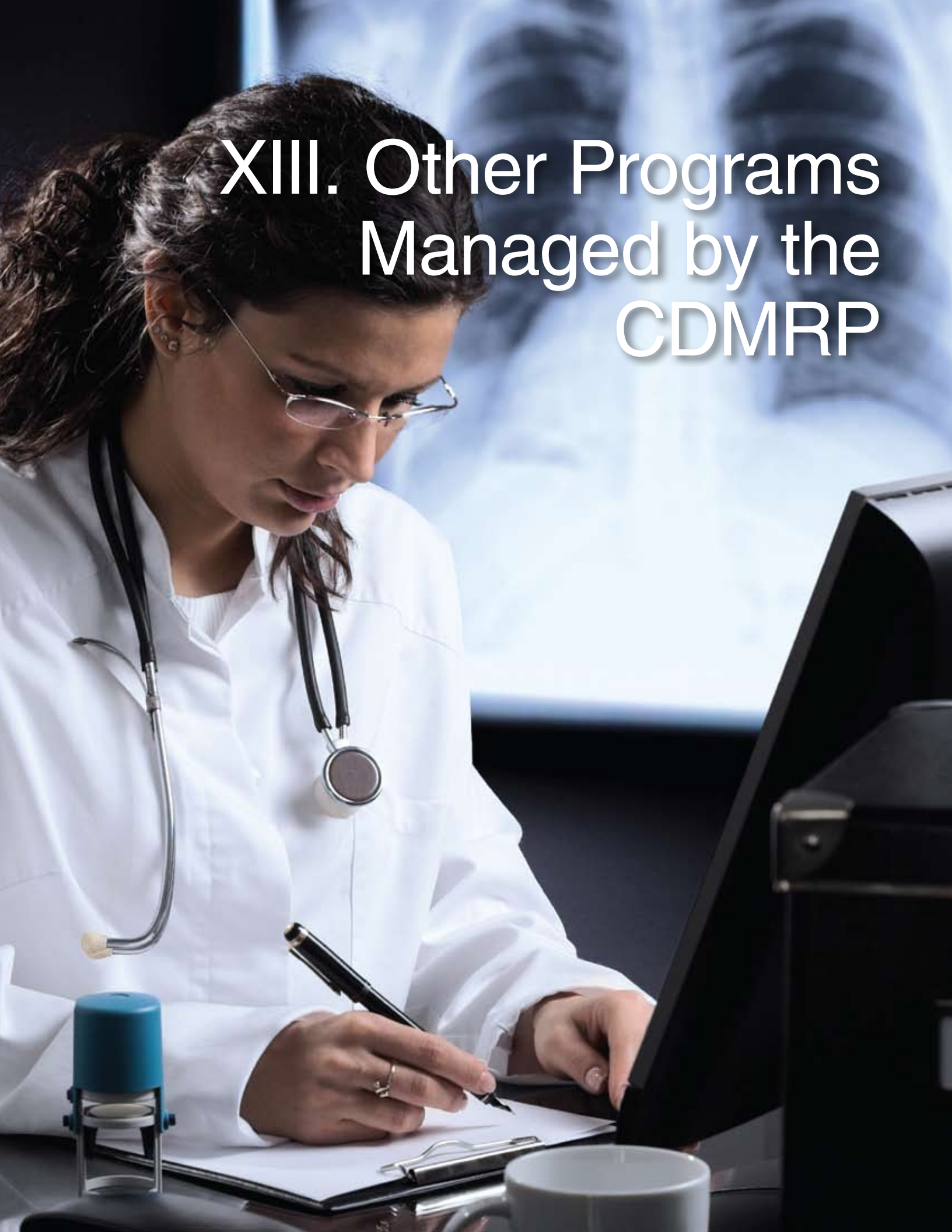


XIII. Other Programs Managed by the CDMRP


Enabling
Success

Over recent decades, the public health communities have been working hard to influence the funding of scientific research. From fiscal year 1995 (FY95) to FY08, Congress has directed the Department of Defense (DOD) to manage numerous targeted research initiatives that fill gaps in research funding. Each of these programs managed by the U.S. Army Medical Research and Materiel Command's Office of the Congressionally Directed Medical Research Programs (CDMRP) seeks to fill unmet needs in medical research.

The goal of the CDMRP in managing these programs is to fund scientifically meritorious research that addresses topic areas specified by Congress. The CDMRP works individually with funded investigators to enable success in terms of impacting the health and well-being of our country and the world.

Since 1992, the CDMRP has executed 84 research programs, of which 108 are characterized by a one-time appropriation, are institutionally based research programs, or are no longer active. A total of 19 programs are being managed by the CDMRP in FY08. Lists of the other programs managed by the CDMRP in FY07 and FY08 can be found at the end of this section.

Included in this section are the Bone Marrow Failure Research Program, which was initiated in FY08 with an appropriation of $1M, and the Chronic Myelogenous Leukemia (CML) Research Program, which was funded by Congress from FY02 to FY06. Research results from active CML grants are highlighted here.

Also included in this section are highlights of the Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs. The CDMRP has worked with these programs since FY00 and FY04, respectively, to fill gaps and leverage research and product development not supported elsewhere in the CDMRP portfolio.

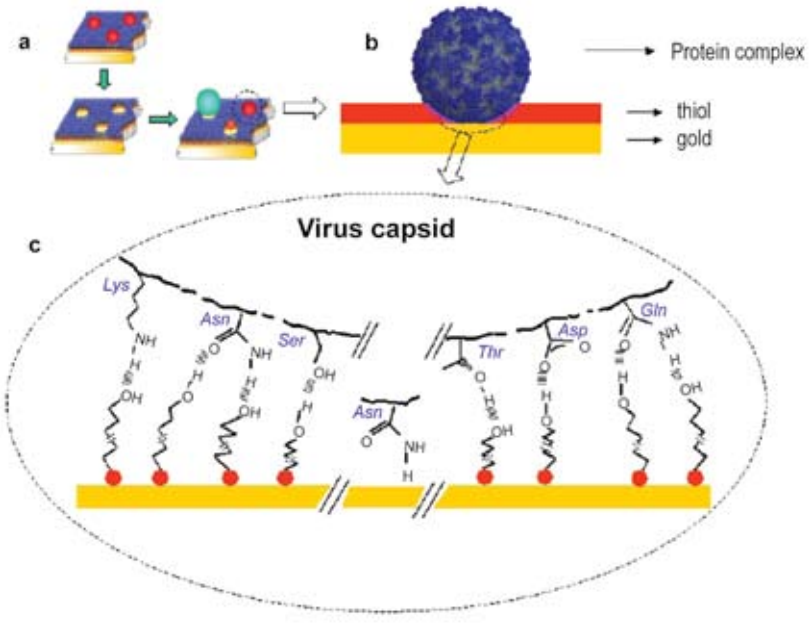
Program Accomplishments

The CDMRP has worked with other programs to enable success across the disease spectrum. Highlights of some of the accomplishments of other programs managed by the CDMRP follow.

Enabling Success Through Advanced Technologies

Cancer Prevention

Diagnosing and treating cancer at its earliest stages lead to the best prognosis. Dr. Basil Rigas and colleagues at the State University of New York at Stony Brook are focused on the prevention of cancer development through the innovative use of remote biological sensing and detection of cancer biomarkers. The system under development uses surface molecular imprinting of cancer-related proteins onto a substrate to act as an electrochemical sensor to detect cancer biomarkers. Separate work includes developing a drug delivery system that will deliver therapeutic agents to kill cancer cells locally. Using the electrochemical sensors, the researchers have demonstrated the ability to detect nanogram quantities of a marker associated with colorectal cancer. Additionally, studies of colon and breast cancer biomarkers are under way. By merging the detection of biomarkers with localized delivery of therapeutic agents through nanoshell technology, the research team hopes to show that the in situ detection and treatment of cancer is possible.



Diagnostic and Therapeutic Cancer Care Equipment

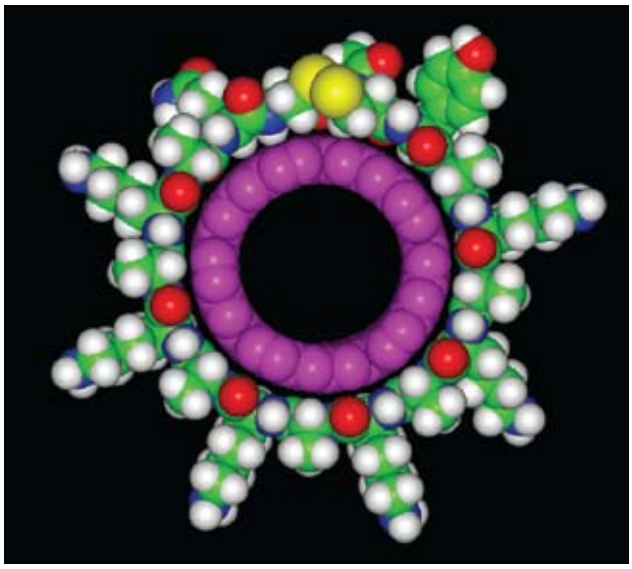
The development of stereotactic radiosurgery techniques allows for higher targeted radiation doses to be administered in fewer fractions than conventional radiation therapies while sparing surrounding normal tissue structures. The CyberKnife™ system, used by investigators at the Boston Medical Center (Boston, Massachusetts) employs robotics to treat malignant or benign tumors anywhere in the body with submillimeter accuracy by delivering multiple beams of highly conformal radiation that converge upon a tumor. Image guidance and computer-controlled robotics combine to continuously track, detect, and correct for tumor and patient movement throughout the treatment. Boston Medical Center is implementing a research plan designed to determine the therapeutic impact of CyberKnife radiosurgery for the treatment of metastatic tumors of the spine, medically inoperable lung cancer, and locally advanced or recurrent head and neck cancer.

Genetic Cancer

Cancer cells can accumulate changes in their DNA that cause them to rapidly proliferate, resulting in the spread of the disease. Understanding the DNA changes inside cancer cells and the genes that are affected by these changes may lead to the genetic causes for each form of cancer and gene-targeted therapies. The goal of the Genetic Cancer Research Program at Cold Spring Harbor Laboratory is to determine the molecular changes that have occurred in breast and ovarian tumors and interpret the significance of these changes. The Principal Investigators, Drs. Michael Wigler and Robert Lucito, use two microarray-based methods they have developed to facilitate these tasks: ROMA (representational oligonucleotide microarray analysis) to detect genomic deletions and amplifications and MOMA (methylation detection representational oligonucleotide microarray analysis) to identify changes in genomic CpG island methylation. The investigators have identified more than 1,000 CpG islands in the genome that undergo methylation alterations during carcinogenesis, including a number of genes that are hypermethylated, leading to loss of gene function.

Biomedical Sciences and Technology

The potential of biomedical technology has created a new paradigm in which teams of scientists from multiple fields come together to perform cutting-edge interdisciplinary research. To respond to this opportunity, the Institute of Biomedical Sciences and Technology (IBMST) was created at the University of Texas at Dallas. Headed by Dr. Steven Goodman, the IBMST is a consortium of 115 investigators from 24 universities and medical schools located in 11 states. The IBMST faculty combines expertise in the biological, physical, and engineering sciences to conduct interdisciplinary research in four focus areas: (1) diseases of the aging brain, (2) blood disorders, (3) molecular diagnostics and biomolecular technology, and (4) bioengineering, security, and defense. The Biomedical Sciences and Technology Research Program utilizes these four focus areas of the IBMST in studies to improve the health and combat readiness of military forces. One of the projects in this program focuses on the use of nanotechnology, in particular the use of carbon nanotubes (CNTs) as vehicles to target cancer cells and kill them with a combination of thermal ablation and drug delivery. IBMST investigators have demonstrated that CNTs with antibodies against breast or lymphoma cells can target these cancer cells and kill them by thermal ablation upon exposure to near infrared light. In another project, a new DNA microarray-based platform has been developed based on homologous strand exchange and magnetic nanomanipulation to improve sensitivity of detection of DNA rearrangements. Detection of the desired sequence occurs through a shift in the surface plasmon-resonance angle of the duplex and is quantitated by the amount of positive magnetic torque required to dissociate the duplex. This technology can complement cytogenic and other hybridization-based methods for the clinical diagnosis and staging of cancer and other diseases involving DNA rearrangements.



Model of a cyclic peptide encircling a carbon nanotube

Enabling Success Through Promotion of Public Health

National Prion Research Program

The National Prion Research Program (NPRP) was established in 2002 with $42.5 million (M) from Congress. The goal of the NPRP was to create a coordinated effort with other federal agencies to rapidly develop a diagnostic test to detect the presence of prion diseases, including Creutzfeldt-Jakob disease in humans, bovine spongiform encephalopathy in cows, scrapie in sheep, and chronic wasting disease (CWD) in deer and other deer-like animals. Funds were awarded for 38 extramural projects related to prion detection and prion diseases. Two meetings were held in December 2005 and October 2007 with the NPRP investigators and international prion investigators to discuss the critical issues in prion-related public health. Presentations at these meetings highlighted the progress that has been made by NPRP-funded investigators in the basic biology, detection and diagnostics, prevention, and therapeutics and surveillance of prion diseases. However, many challenges and roadblocks remain to discoveries that confront this science and its community of researchers. Support is particularly important in the advancement of young researchers and scientists who do not have access to the materials or who lack the required infrastructure to support their scientific work. Support is also needed for ongoing basic and applied research because many diagnostic and detection technologies for antemortem prion diagnostic tests have only reached the initial stages of development. Without additional resources, many of these efforts will languish because their development is too premature to be picked up by a commercialization enterprise.

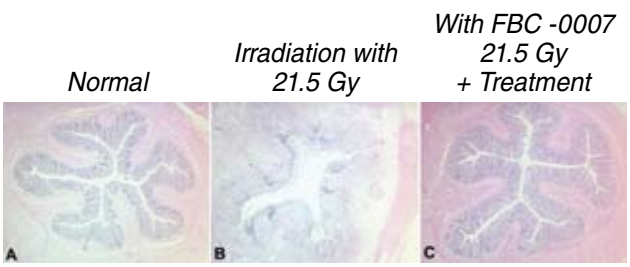
Smoking Cessation (Lung Cancer Research Program)

Project TALK (Teens and Young Adults Acquiring Lung Cancer Knowledge) is a smoking education and prevention program developed through the Lung Cancer Research Program. An educational video game, "Escape with Your Life," was developed for high-risk youth. The game is set in a "scary hospital animation, and the user's mission is to escape from the hospital while exploring various rooms (patient records, the nursery, radiology, surgery, waste disposal, accounting, etc.). Each room introduces the participant to various hazards, health issues, and other consequences associated with tobacco use. While playing the game, the user acquires helpful skills aimed at adopting tobacco-free lifestyles and collects points allowing him/her to escape from the hospital. The video game is offered to schools and other institutions in an attractive and age-appropriate kiosk design and is also provided to the users as a CD for use on their computers. The educational video game is being tested in two Houston-area alternative schools. In preliminary studies, the participants found the game easy to use and enjoyable. Nearly all participants said the game had increased their knowledge about the harmful effects of smoking, and more than 75 percent said they were inspired

to quit or never start smoking. Two-thirds planned to share the game with family or friends. Based on feedback from participants, Project TALK will be modified to appeal to a wider segment of the young-adult population in Houston, Texas.

Respiratory Biodefense

The Respiratory Biodefense Research Program, directed by Dr. Robert Mason (National Jewish Medical and Research Center, Denver, Colorado) includes research programs on (1) development of an effective radioprotectorant, (2) production of improved vaccines for influenza and mycobacterium tuberculosis, (3) development of post-exposure therapies to control anthrax infection, and (4) modulation of the immune system to control pandemic influenza. The lead product being developed by this program, with DOD support, is a new radioprotective drug, FBC-0007. At the present time, no treatment is available for individuals exposed to high levels of radiation such as what could be released by a "dirty bomb" or a small nuclear weapon. FBC-0007 has now been through extensive preclinical testing and has been shown to be highly effective against radiation injury. It protects the brain, lungs, gastrointestinal tract, and immune system against radiation injury. With the support of the DOD, FBC-0007 is now being prepared for human testing. Large-scale synthesis and preclinical safety testing of the compound are under way. Rapid development of this new drug is essential to prepare for a nuclear accident or terrorist use of a dirty bomb.



Histology of rectum of rats 10 days following 21.5 Gy irradiation. A. Control rat rectum – not irradiated. B. Extensive destruction of rectal mucosa following irradiation. C. No significant injury to rectal mucosa from irradiation when treated with FBC-0007.

Alcoholism Research

Funding provided through the Alcoholism Research Program to the Ernest Gallo Clinic and Research Center (EGCRC) generated some of the preliminary data that allowed EGCRC investigators to successfully compete for several new research awards. Preliminary data from Dr. Ulrike Heberlein's projects showing the feasibility of translating alcoholism research in *Drosophila* to rodent models helped obtain a 5-year Specialized Alcohol Research Center grant from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). This center, which will be directed by Dr. Robert O. Messing, is one of seven specialized alcohol research centers in the United States and the only center located at an independent research institute. Projects within the center will examine novel proteins to determine whether they or the signaling pathways in which they participate contain potential drug targets for treating alcohol use disorders, and whether the genes that encode these proteins are associated with the risk of alcoholism in humans.

Drugs of abuse, including alcohol, increase dopamine levels in the nucleus accumbens (NAcb), which may represent a positive signal that facilitates learning about the drug experience and can thus increase an individual's future tendency to seek the drug. Data developed through funding of work in Dr. Antonello Bonci's laboratory examining how activation of dopamine-sensing receptors alters the excitability of neurons in the NAcb helped Dr. F. Woodward Hopf, co-investigator in this work, obtain an NIAAA R01 award. Dr. Hopf's study will examine how NAcb dopamine receptor signaling may be altered after long-term ethanol drinking and abstinence, and whether NAcb dopamine activity plays a significant role in alcohol relapse.

Preventive Medicine Research Institute

A pilot study by Dr. Dean Ornish and colleagues at the Preventive Medicine Research Institute showed that men with low-risk prostate cancer who made improvements in fitness, stress management, and nutrition altered the expression of genes that have a role in tumor progression and other illnesses. The researchers sampled gene expression in normal prostate tissue from 30 men diagnosed with low-risk prostate cancer who had decided not to undergo conventional treatment for reasons unrelated to the study. Comparison of the samples at baseline with the samples after 3 months of comprehensive lifestyle changes revealed that gene expression was beneficially affected in more than 500 genes. Certain disease-preventing genes were upregulated, or turned on, and certain disease-promoting genes, including oncogenes involved in prostate cancer and breast cancer, were downregulated, or turned off. The implications of this study are not limited to men with prostate cancer. Results suggest that comprehensive lifestyle changes may cause changes in gene expression that could be beneficial to the general population as well as those with prostate cancer. These findings were published in the June 16, 2008, issue of the *Proceedings of the National Academy of Sciences*.

A second study by Dr. Ornish showed that people with depression who could be motivated to change their health behaviors by exercising, eating well, and managing stress, and who received emotional support from peers, not only felt better, but also reduced their clinical risk factors for heart disease.

Although depressed patients were medically and psychologically worse off at the beginning of the study (e.g., higher body mass, diastolic blood pressure, dietary fat intake, hostility, and stress) than patients who were in better mental health, they were still able to change their health behaviors over 3 months. By 3 months, 73 percent of the initially depressed patients became nondepressed, and this improvement was similar in both men and women. In addition, initially depressed patients who became nondepressed had improved mental health, mitigated coronary risk factors, and reduced feelings of hostility and stress. In patients with angina pectoris, those who became angina free by 3 months showed the greatest improvements in exercise capacity, depression, and health-related quality of life, which could drastically reduce their need for revascularization procedures and the associated costs. These findings were published in 2008 in *The American Journal of Cardiology*.

Bone Marrow Failure Research Program

The Bone Marrow Failure Research Program (BMFRP) was established in 2008 with a $1M appropriation. Bone marrow is soft tissue located within bones responsible for blood cell formation. A bone marrow failure disease is the outcome of bone marrow dysfunction or abnormal blood cell production. Bone marrow failure diseases include, but are not limited to, aplastic anemia, myelodysplastic syndromes, myelofibrosis, and other genetic defects. Causes are largely unknown but may include genetic and environmental factors such as exposure to radiation, drugs, toxins, or infection. The goal of the FY08 program is to support research of clear scientific merit that will improve knowledge of disease processes and intervention potential. The FY08 BMFRP received a total of 21 proposals through the Investigator Initiated Research Award; 1 award is anticipated. The congressional appropriations and investment strategy executed by the BMFRP for FY08 are summarized in Appendix B, Table B-12.

Enabling Success Through Therapeutics

Chronic Myelogenous Leukemia

CML, also known as chronic myeloid leukemia or chronic granulocytic leukemia, is an overgrowth of granulocytes, a type of white blood cell. Its cause is unknown. The disease accounts for about 20 percent of adult leukemias in Western countries. In 2007, approximately 4,570 individuals were diagnosed with CML, and an estimated 490 died from the disease. The goal of the CML Research Program (CMLRP) is to support research leading to substantial improvement in the understanding, diagnosis, and treatment of CML and enhance the quality of life of persons with the disease. CMLRP-funded research accomplishments fall into three broad areas:

- **Basic science:** A better understanding of disease processes will facilitate the development of the next generation of therapeutic agents. The CMLRP has funded basic science research that has increased our knowledge of the pathobiology of CML. Work being done by Dr. Danilo Perrotti (The Ohio State University) has shown that activity of the protein BCR/ABL, expressed in most CML cells and associated with disease development, inhibits activity of a tumor suppressor protein, phosphatase 2A (PP2A), and therefore allows CML cells to continue proliferating. Treating cells with a compound that increases the activity level of PP2A decreases tumor growth, suggesting that this compound has the potential to be a new CML treatment option.
- **Therapeutic development:** Genetic mutations occur that confer resistance to currently available CML treatment agents. In addition, few therapies exist to treat individuals whose disease accelerates from chronic to blast crisis (the acute stage of disease). New therapeutics are needed that can be used in conjunction with the existing agents or as options when resistance to standard treatments or blast crisis develops. As examples, Dr. Joel Gottesfeld (Scripps Research Institute) identified a set of molecules that inhibit proliferation of CML cells in a BCR/ABL-independent manner. Dr. Craig Jordan (University of Rochester) has found a naturally occurring antiproliferative compound, parthenolide, that specifically kills the malignant stem cells found in CML patients who are in blast crisis while sparing normal hematopoietic stem cells. This compound may hold significant promise for treating blast crisis. Dr. E. Premkumar Reddy (Temple University) is developing an agent that will target CML cells that are resistant to the drug Gleevec. Dr. Kapil Bhalla (Medical College of Georgia Cancer Center) has discovered a new agent that inhibits that activity of BCR/ABL.
- **Model organism development:** Model organisms are utilized by the scientific community as surrogates for the study of pathways, processes, and therapeutics before they are studied in humans. Researchers are examining the genetics, molecular mechanisms, cellular functions, and therapeutic efficacy of compounds for CML in systems that include (but are not limited to) *Caenorhabditis elegans*

(a small roundworm); *Drosophila melanogaster* (fruit flies); *Danio rerio* (zebrafish); *Gallus gallus* (chickens); and *Mus musculus* (mice). Using a variety of model organisms to study a disease also allows for important comparisons and validations. Many CMLRP-funded researchers have been involved in developing and validating new mouse and zebra fish models of CML for understanding the genetic, molecular, and cellular changes that accompany the development and progression of CML, and for use in preclinical testing of potential new therapeutic agents. In particular, Dr. Craig Jordan and his team have developed and validated a new mouse model applicable to chronic and blast crisis CML. This model provides new ways to compare the properties of normal versus malignant stem cells and to evaluate the relative effects of therapeutic regimens in vivo.

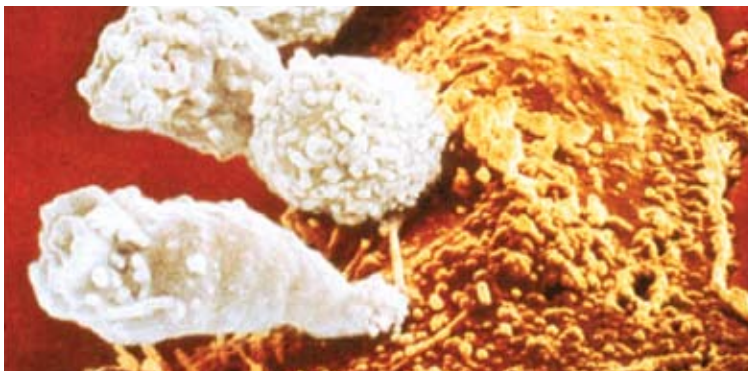
Lung Cancer Research Program

The Lung Cancer Research Program is dedicated to the development of new therapeutics for lung cancer. A major goal of this program is to not only develop more effective therapies but to rationally select the patients that are most likely to benefit from these new agents. Dr. Waun Ki Hong's group at M.D. Anderson Cancer Center is using a novel adaptive clinical trial design in DOD-sponsored clinical trials. In the course of patient accrual for a clinical trial, clinical factors and molecular markers are analyzed and patients are guided to a particular treatment arm using a statistical approach termed "Bayesian adaptive randomization." Taking this approach, information such as biomarker expression in individuals can be used to inform the statistical model over the course of the study to identify improved outcomes on particular treatments and can also be used to predict treatment benefits (or lack of benefit) with desirable statistical properties. Applying this novel adaptive randomization design, more efficient clinical trials can be conducted that require fewer patients than the traditional randomization schemes and may lead to the identification of patients that can be treated more effectively with the agents studied. The identification of biomarker profiles that can predict the effectiveness of particular drugs or therapeutic regimens in selected patient populations will be key to the development of personalized therapies for lung cancer.

Biological and Immunological Infectious Agent and Cancer Vaccine Research

Ellis Reinherz, M.D.
Dana-Farber Cancer Institute

Researchers led by Dr. Ellis Reinherz at the Cancer Vaccine Center (CVC) at the Dana-Farber Cancer Institute are creating, developing, and evaluating the safety and efficacy of new immunologic therapies in patients with cancer. Of importance to this work is the prediction of human tumor antigens, a process that is made faster and more efficient through advanced bioinformatics approaches. Through funding provided by the CDMRP, the CVC has recently developed a new means of anticipating antigenic peptides that eliminates the costly experimental assays of traditional T-cell epitope identification. TANTIGEN (http://bio.dfci.harvard.edu/research/bioinformatics-tools.php) is a biological sequence data source and analysis platform for cancer

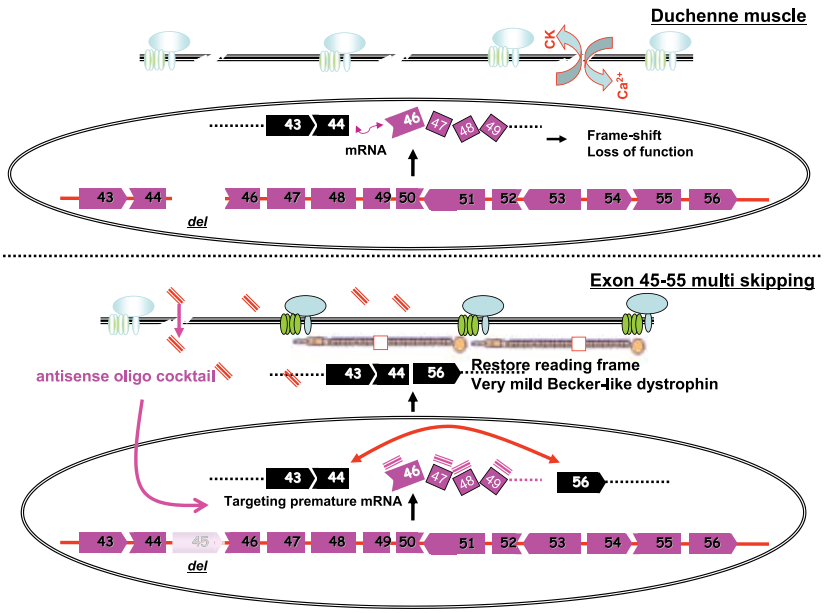


Cytotoxic T cells attacking a tumor target.

vaccine target discovery focusing on human tumor T-cell-related antigens. Currently, the database contains information on 2,169 antigen entries from 251 defined protein antigens, 835 T-cell epitopes, and 121 human leukocyte antigen (HLA) ligands. These represent targets for vaccine research and development against a variety of cancers, including lung, breast, prostate, colon, brain, pancreatic, and liver cancer; melanoma; and chronic and acute myeloid leukemias. Each antigen entry includes basic information on the antigen, links to other databases (Uniprot, NCBI Gene, and GeneCard), and gene expression profiles. Advanced bioinformatics tools contained within TANTIGEN enable analysis of antigenic diversity and prediction of HLA ligands and T-cell epitopes. Embedded visualization tools delineate the profiles of individual tumor antigens. Other tools within TANTIGEN include search by keyword or T-cell epitope/HLA ligand sequence, sequence comparison by BLAST (the Basic Local Alignment Search Tool), multiple sequence alignment, and classification of tumor antigens. These analyses are integrated within TANTIGEN, allowing researchers to omit exhaustive literature searches and enabling the use of multiple prediction servers, the integration of results, and statistical analysis. TANTIGEN represents a new generation of tumor antigen databases that enable scientists and clinicians to conduct complex analyses ultimately resulting in successful new immunotherapies.

Cooperative International Neuromuscular Research Group (CINRG)

Duchenne muscular dystrophy is the most prevalent of muscular dystropies and is the result of mutations on the enormous dystrophin gene on the X chromosome (2.3 million base pairs). While it is clearly a genetic disorder, most cases in the United States are not inherited; rather, they are the result of spontaneous mutations in 1 of the 79 exons and introns comprising the gene. The majority of genetic lesions are deletion mutations, with the loss of one or more exons. Funds provided through the CDMRP to Dr. Eric Hoffman (Children's National Medical Center, Washington, DC) have funded an interdisciplinary U.S./Japan research program in molecular therapeutics for Duchenne muscular dystrophy. The therapy is based on "exon-skipping," where antisense oligonucleotides are used to force a cell's transcriptional machinery to skip over the added exons in an out-of-frame, nonfunctioning Duchenne deletion and bring the remaining exons back into frame and restore partial cellular function. As a result of the extensive research carried out by the international CDMRP- and Japan-sponsored consortium, public and private partnerships are being formed to complete the toxicity studies required for a U.S. Food and Drug Administration Investigational New Drug application. Clinical trials are being planned for the United States in 2009.



Enabling Success Through Small Businesses

The SBIR and STTR programs are congressionally mandated, government-wide programs funding competitive research and development contracts with small businesses. The DOD SBIR/STTR programs are designed to harness the innovative talents of U.S. small businesses for our country's military and economic strength. These are technology- and product-driven programs intended to develop goods and services that are of potential use to the government and that a small business can continue to commercialize outside the SBIR/STTR programs.

The objectives of the DOD SBIR/STTR Programs include stimulating technological innovation in DOD Critical Technology Areas, increasing the role of small businesses in meeting DOD research and development needs, encouraging participation by minority and disadvantaged persons in technological innovation, and increasing the commercial application of DOD-supported research or research and development results.[1] The programs are organized in three phases of development: Phase I establishes proof of principle, Phase II involves prototype development and testing, and Phase III centers on commercialization. SBIR/STTR funding is available for Phase I and Phase II projects while Phase III support must come from private and non-SBIR government sources.

The CDMRP has been working with the SBIR and STTR programs since FY00 and FY04, respectively, to fill gaps and leverage research and product development not supported elsewhere in the CDMRP portfolio. Through September 2008, the SBIR/STTR programs have supported more than $20.8M in technology development for CDMRP priority areas including breast, prostate, ovarian, and lung cancers; angiogenesis; wound healing; prion-related diseases; and detection of biological and chemical agents.

[1] The Department of Defense Small Business Innovation Research (SBIR) Program, Program Solicitation FY08.

Enabling Success Through Small Businesses

Small Business Highlights

Rapid and Early Detection of Prions

Principal Investigator Brandt Cassidy, Ph.D.
Co-Principal Investigator Ken Clinkenbeard, Ph.D.

DNA Solutions, Inc., a small business based in Oklahoma City, Oklahoma, received a Phase II SBIR award in December 2007 to continue development of a system for live detection of CWD in collaboration with Oklahoma State University. This infectious disease affects several species of deer, moose, and elk and is closely related to bovine spongiform encephalopathy (mad cow disease), Creutzfeldt-Jakob's disease, and Alzheimer's disease. The investigators will create a cell culture model system by selecting for cells that display rapid and sustained prion propagation after exposure to CWD-positive brain homogenate. After optimizing culturing conditions and an Elispot detection method, the project should result in a test sensitive enough to detect CWD from easily obtainable antemortem samples, such as blood, saliva, urine, feces, or biopsy samples.

Enhanced DCE-MRI Imaging of Ovarian Cancer

Principal Investigator David Kynor, M.S.

A Phase II SBIR contract was awarded to Creare, Inc., a New Hampshire-based company, to develop a noninvasive method for enhanced ovarian cancer screening and treatment monitoring. The project is developing automated motion correction algorithms that permit use of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) for detection of primary tumors of the ovaries and abdominal metastases. Localized angiogenic "hot spots" can be identified for early cancer detection. Collaborators at North Carolina State University will assist the investigators in evaluating the DCE-MRI-based strategy for screening in a hen model of ovarian cancer. The technology will also be applied to the development of a new functional approach to analysis of tumor perfusion during treatment. The method will distinguish between regions of normal tissue, well-perfused tumor tissue, and necrotic tissue by detecting localized changes in perfusion, allowing analysis and detection of very early signs of positive response to drug therapy. The algorithms developed by Creare will be applied to serial DCE-MRI data sets from ovarian cancer patients in collaboration with Memorial Sloan-Kettering Cancer Center.

Other Programs Managed by the CDMRP, FY07

Alcoholism Research, $5.5M, Ernest Gallo Clinic and Research Center (Emeryville, California), PI: Dr. Ray White

ALS Therapy Development for Gulf War Research, $1M, ALS Therapy Development Institute (Cambridge, Massachusetts), PI: Dr. Gerard DeZutter

DOD Biological and Immunological Infectious Agent and Cancer Vaccine Research, $1.9M, Dana-Farber Cancer Institute (Boston, Massachusetts), PI: Dr. Ellis Reinherz

Cancer Biomolecular Markers Research, $1M, Sbarro Health Research Organization (Philadelphia, Pennsylvania), PI: Dr. Antonio Giordano

Center for Targeted Cancer Therapy, $1M, University of Texas Health Science Center at San Antonio (San Antonio, Texas), PI: Dr. John Cole

Diagnostic and Therapeutic Cancer Care Equipment, $3M, Boston Medical Center for the Joe Moakley Hospital (Boston, Massachusetts), PI: Dr. Lisa Kachnic

Duchenne Muscular Dystrophy (DMD) Repair and Regeneration Clinical Trials, $1.5M, Children's Hospital of Pittsburgh (Pittsburgh, Pennsylvania), PI: Dr. Johnny Huard

Early and Rapid Analyzer for Heart Attack Diagnosis, $1M, Sensera, Inc. (Chelmsford, Massachusetts), PI: Dr. Fred Apple

CIC Interdisciplinary Research for Prevention, Diagnosis, and Treatment of Cancer, $2.25M, University of Rochester (Rochester, New York), PI: Dr. Richard Fisher

Cancer Genomics Center for Women in the Military,$1.8M, Cold Spring Harbor Laboratory (Cold Spring Harbor, New York), PIs: Dr. Robert Lucito and Dr. Michael Wigler

Cooperative International Neuromuscular Research, $1.9M, Children's Hospital (Washington, DC), PI: Dr. Eric Hoffman

Genomic Medicine and Gene Therapy, $1.8M, Moses Cone Health System (Durham, North Carolina), PI: Dr. Margaret Pericak-Vance

Life Sciences Research Initiative, $1M, Pioneer Valley Life Sciences Institute (Springfield, Massachusetts), PI: Dr. Lawrence Schwartz

Military Dependent Childhood Cancer Research (USOC/COG), $3M, National Childhood Cancer Foundation (Arcadia, California), PI: Dr. Gregory Reaman

Military Dependent Pediatric Brain Tumor and Neurological Disease Research, $1.2M, Miami Children's Hospital (Miami, Florida), PI: Dr. Prasanna Jayakar

National Center for Cancer Prevention Through Remote Biological Sensing, $1.1M, State University of New York, Stony Brook (Stony Brook, New York), PI: Dr. Basil Rigas

Neutron/Hadron Particle Therapy, $3.3M, Northern Illinois University (Dekalb, Illinois), PI: Dr. John Lewis

NVCI New Radiation Therapy Systems, $1M, Nevada Cancer Institute (Las Vegas, Nevada), PI: Dr. Nicholas Vogelzang

Prader-Willi Syndrome (PWS) Research, $1M, California State University at Fullerton (Fullerton, California), PI: Dr. Daniela Rubin

Preventive Medicine Research Institute, $1.8M, Preventive Medicine Research Institute (Sausalito, California), PI: Dr. Dean Ornish

Prostate Cancer DNA Detection Initiative, $1.2M, Gen-Probe, Inc. (The Woodlands, Texas), PI: Dr. Harry Rittenhouse

Center for Respiratory Biodefense (also funded with an appropriation entitled "Respiratory Biodefense"), $2.65M, National Jewish Medical and Research Center (Denver, Colorado), PI: Dr. Robert Mason

Spinal Muscular Atrophy Research, $3.3M, Lexicon Genetics, Inc. (The Woodlands, Texas), PI: Dr. Brian Zambrowicz, Columbia University (New York, New York), and PI: Dr. Christopher Henderson

Targeted Nanotherapy for Advanced Breast and Prostate Cancers, $1M, Triton Biosystems, Inc. (Chelmsford, Massachusetts), PI: Dr. Robert Ivkov

Targeted Radiation Therapy for Cancer Initiative, $2M, The Geneva Foundation (Lakewood, Washington), PI: Dr. John Halligan

Veterinary Manpower Development for Defense, $0.5M, Tufts University (Boston, Massachusetts), PI: Dr. M. Sawkat Anwer

Warfighter Cancer Care Engineering, $1.2M, Indiana University Cancer Center (Indianapolis, Indiana), PI: Dr. Stephen Williams

Other Programs Managed by the CDMRP, FY08

ALS Therapy Development for Gulf War Illness Research, $1.2M, Identification of disease risk factors, development of diagnostic tools, elucidation of mechanisms that regulate disease progression, and identification and development of definitive therapeutic interventions for ALS.

Bone Marrow Failure Research Program, $1M, Support research of clear scientific merit that will improve knowledge of disease processes and intervention potential.

Cancer Prevention Through Remote Biological Sensing, $1.6M, Development of wireless sensor technology for implantation in the body to identify biomarkers associated with cancer for the delivery of medication in situ to eliminate neoplastic cells.

Childhood Cancer Research (listed in FY08 with an appropriation entitled "COG/USOC [Childhood Oncology Group/Uniformed Services Oncology Consortium] Pediatric Cancer Center"), $1.6M, Advance the application of genome-wide mapping of pediatric cancers to identify functional pathways that involve tumor cell survival and drug sensitivity.

Christian Sarkine Autism Treatment Center, $2M, Promote innovative research on the genetic, epigenetic, and environmental factors that may predispose an individual to the development of autism spectrum disorders, and to better diagnose and treat the disorder.

Duchenne Muscular Dystrophy, $4M, Investigate regeneration and repair of dystrophic and injured skeletal muscle by using adult-derived stem cells.

Gallo Cancer Center (listed in FY08 with an appropriation entitled "UMDNJ [University of Medicine and Dentistry of New Jersey] Cancer Initiative [Note, includes continuation of the Gallo Prostate Cancer Center]"), $2.4M, Understand prostate cancer with the goal of eradicating prostate cancer and improving the lives of men at risk for the disease through research, treatment, education, and prevention.

Genetic Cancer Research (listed in FY08 with an appropriation entitled "Cold Spring Harbor Laboratory Women's Cancer Genomics Center"), $3.2M, Identification and characterization of causative genetic defects in human cancers and in particular for ovarian and breast cancers.

Molecular Switch Vaccines for Biodefense and Cancer, $1.6M, Develop vaccines that will prevent primary or secondary occurrences of some cancers and infectious diseases, and also have use in biodefense using genetically modified *Listeria* bacteria.

Muscle Research Consortium (listed in FY08 with an appropriation entitled "Cooperative International Neuromuscular Research Group [CINRG]"), $5.2M, Increase the number and quality of clinical trials in muscle-related disease patients with the goal of improving muscle structure and function.

Neutron Therapy Research (listed in FY08 with appropriations entitled "Neutron/Hadron Particle Therapy" and "Proton Therapy"), $4M, Develop applications of neutron therapy beyond its current uses through additional basic and clinical research.

NVCI New Radiation Therapy Systems (listed in FY08 with an appropriation entitled "Prevention of Radiation Injury by Use of Statins"), $1.6M, Develop new practices that advance current radiation therapy modalities into more tumor-targeted, healthy tissue-sparing procedures.

Pediatric Brain Tumor and Neurological Disease Research, $1.6M, Develop novel diagnostics and therapeutics for brain tumors and neurological diseases specific to children.

Prader-Willi Syndrome (PWS) Research, $1.5M, Improve understanding of the molecular and cellular mechanisms underlying PWS with the ultimate aim of developing new interventions to improve the quality of life of individuals with PWS and their families.

Preventive Medicine Research Institute (listed in FY08 with an appropriation entitled "Impact of Intensive Lifestyle Modification on Chronic Medical Conditions"), $2M, Develop, implement, and evaluate dietary and lifestyle changes that will serve as a means to prevent cardiovascular disease.

Respiratory Biodefense (listed in FY08 with an appropriation entitled "Respiratory Biodefense Initiative"), $1.6M, Develop and test new drugs, vaccines, and immunomodulatory approaches to protect civilians and military personnel against the adverse health effects of radiation, toxic chemicals, and biological agents.

Spinal Muscular Atrophy (SMA) Research Program, $3.2M, Identify the protein defects causing SMA that will lead to potential therapeutics.

Targeted Radiation Therapy for Cancer Initiative, $1M, Enhance targeted radiation therapy modalities to improve target localization, spare normal tissue, and increase tumor control in cancer patients.

Veterinary Manpower Development for Defense (listed in FY08 with an appropriation entitled "Veterinary Research Manpower Development for Defense"), $0.5M, Develop training for veterinarians in public health and biomedical research so that they may plan and implement responses to bioterror outbreaks.

Warfighter Cancer Care Engineering, $1.2M, Use a systems engineering approach to provide more successful prevention strategies, more effective treatments, and more efficient care delivery.

The Other Programs Team

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