



Department of Defense Congressionally Directed Medical Research Programs



Annual Report September 30, 2003



U.S. Army Medical Research and Materiel Command



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September 30, 2003**

**U.S. Army Medical Research
and Materiel Command**

Congressionally Directed Medical Research Programs

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DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

September 30, 2003

Office of the Commanding General

Dear Colleagues:

The U.S. Army Medical Research and Materiel Command (USAMRMC) supports Army transformation by identifying, developing, procuring, and sustaining the medical technologies that will best support the rapidly deployable and responsive Army of the 21st century. The command sustains the health and fighting ability of soldiers, sailors, airmen, and Marines through programs in medical research, medical materiel development, medical logistics and facility planning, medical information systems, and development of new technologies to improve military health care on the battlefield.

The U.S. Congress has directed the Department of Defense to execute numerous targeted biomedical research programs. The U.S. Army subsequently established the Office of the Congressionally Directed Medical Research Programs (CDMRP) to administer these initiatives within the USAMRMC. The CDMRP manages peer reviewed research programs in breast, prostate, and ovarian cancers, neurofibromatosis, prion diseases, chronic myelogenous leukemia, tuberous sclerosis, military health, and other specified areas.

This 2003 Annual Report summarizes the history, management strategies, and achievements of the CDMRP. The success of the CDMRP can be attributed to the collective wisdom and dedication of a unique public/private partnership that includes the military, scientists, clinicians, consumer advocates, and policy makers. By funding highly meritorious and innovative research and identifying and filling gaps in scientific knowledge, this partnership is improving the health and quality of life of all individuals.

Sincerely,

A handwritten signature in black ink, appearing to read "Lester Martinez-Lopez", is positioned above the printed name.

Lester Martinez-Lopez, M.D.
Major General, Medical Corps
Commander



DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
1077 PATCHEL STREET
FORT DETRICK, MARYLAND 21702-5012

REPLY TO
ATTENTION OF:

September 30, 2003

Congressionally Directed Medical Research Programs

Dear Colleagues:

We are fortunate to be living in a scientifically rich era that has yielded significant improvements in the prevention, diagnosis, and treatment of human disease. However, there is still a critical need for disease-relevant medical research. The Department of Defense's (DOD's) Congressionally Directed Medical Research Programs (CDMRP) has become a leader in funding innovative, scientifically meritorious research in the fields of breast, prostate, and ovarian cancers, and neurofibromatosis. In fiscal year 2002, the CDMRP initiated programs in tuberous sclerosis, chronic myelogenous leukemia, and prion disease research. The CDMRP strives to complement other funding agencies by sponsoring research that fosters new directions for, addresses neglected issues in, and brings new investigators into targeted diseases. This Annual Report highlights the programs that are currently being managed by the CDMRP.

The CDMRP was created in response to the concerns of individuals living with breast cancer. Congress appropriated \$25 million (M) in fiscal year (FY92) for breast cancer research, and the efforts of grass-roots advocacy organizations resulted in a \$210M appropriation in FY93 for the establishment of a "peer reviewed breast cancer research program with the Department of the Army as executive agent." Based on recommendations from a 1993 Institute of Medicine (IOM) report, the CDMRP developed a unique proposal review model consisting of disease-specific scientific (peer) review and programmatic review. While peer reviewers primarily evaluate the scientific and technical merit of proposals, programmatic reviewers focus on factors such as innovation and relevance to the program's goals.

Since FY93, the CDMRP has acquired seven additional core research programs, which focus on prostate cancer, ovarian cancer, neurofibromatosis, tuberous sclerosis, chronic myelogenous leukemia, prion disease, and biomedical issues directly relevant to military health. Each of these programs is executed according to the two-tier model described in the 1993 IOM report. Consumer advocates are an integral part of the review process and program execution, serving as full voting members on both peer and programmatic review panels. I believe that the alliance of consumer advocates, basic and clinical research scientists, and the DOD is critical to the success of the programs managed by the CDMRP.

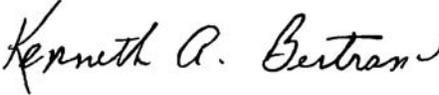
I would like to express my deepest gratitude to the following individuals for their participation in the CDMRP:

- Disease survivors, family members, and consumers whose courage and commitment led to the creation of these programs. They continue to infuse the CDMRP with passion, inspiration, and vision.
- The scientists and clinicians funded by the program who are facing the challenges of improving the lives and health of all people. They are our greatest hope for preventing, controlling, and curing these diseases.
- Members of the CDMRP's Integration Panels (i.e., advisory committees), past and present, who crafted comprehensive programs over the past 10 fiscal years of funding. The dedication and skill of these panel members are evidenced by their many accomplishments, which include setting investment strategies and conducting programmatic review of proposals on a yearly basis.

- Members of the CDMRP's peer review panels, who have met the daunting task of reviewing more than 21,000 proposals since FY93. Without their expertise and perseverance, the CDMRP goal of funding highly meritorious research could not have been accomplished.
- The many members of the DOD, the U.S. Army Medical Research and Materiel Command, the CDMRP Program Management Teams, and support staff whose constant enthusiasm and diligence sustain the research programs on a daily basis.

I am grateful for the integrity, vision, and devotion shown by these dedicated individuals. They have crafted innovative and vital programs that continue to forge new pathways in the management and execution of biomedical research.

Sincerely,

A handwritten signature in black ink that reads "Kenneth A. Bertram". The signature is written in a cursive style with a small flourish at the end.

Kenneth A. Bertram, M.D., Ph.D.
Colonel, US Army Medical Corps
Director

Table of Contents

Executive Summary	vii
I. Overview of the CDMRP	
History/Evolution.....	I-2
Programs Managed by the CDMRP	I-3
Program Execution and Management	I-5
Grants Management	I-7
Research Information Dissemination.....	I-9
II. CDMRP Accomplishments	
Background	II-2
Promoting Innovative Research.....	II-3
Recognizing Untapped Opportunities.....	II-4
Creating Partnerships	II-7
Guarding the Public Trust	II-9
III. Breast Cancer Research Program	
The Disease	III-2
Program Background	III-2
The Fiscal Year 2002 Program.....	III-3
The Vision for the Fiscal Year 2003 Program	III-4
Scientific Outcomes and Advances	III-5
Summary.....	III-11
Fiscal Year 2003 Integration Panel Members	III-12
IV. Prostate Cancer Research Program	
The Disease.....	IV-2
Program Background	IV-2
The Fiscal Year 2002 Program.....	IV-2
The Vision for the Fiscal Year 2003 Program	IV-4
Scientific Outcomes and Advances	IV-5
Summary.....	IV-11
Fiscal Year 2003 Integration Panel Members.....	IV-14
V. Neurofibromatosis Research Program	
The Disease	V-2
Program Background.....	V-2
The Fiscal Year 2002 Program	V-3
The Vision for the Fiscal Year 2003 Program.....	V-4
Scientific Outcomes and Advances.....	V-4
Summary.....	V-7
Fiscal Year 2003 Integration Panel Members.....	V-8
VI. Ovarian Cancer Research Program	
The Disease	VI-2
Program Background	VI-2
The Fiscal Year 2002 Program	VI-2
The Vision for the Fiscal Year 2003 Program.....	VI-3
Scientific Outcomes and Advances.....	VI-3
Summary.....	VI-7
Fiscal Year 2003 Integration Panel Members.....	VI-8
VII. Peer Reviewed Medical Research Program	
Military Relevance	VII-2
Program Background	VII-2
The Fiscal Year 2002 Program.....	VII-3
The Business Strategy for the Fiscal Year 2003 Program	VII-3
Scientific Outcomes and Advances	VII-3
Summary	VII-7
Fiscal Year 2003 Joint Programmatic Review Panel Members ..	VII-7
VIII. Chronic Myelogenous Leukemia Research Program	
The Disease	VIII-2
Program Background.....	VIII-2
The Fiscal Year 2002 Program	VIII-2
The Vision for the Fiscal Year 2003 Program	VIII-3
Summary	VIII-3
Fiscal Year 2003 Integration Panel Members.....	VIII-4
IX. Tuberos Sclerosis Complex Research Program	
The Disease	IX-2
Program Background.....	IX-2
The Fiscal Year 2002 Program	IX-2
The Vision for the Fiscal Year 2003 Program	IX-3
Summary	IX-3
Fiscal Year 2003 Ad Hoc Programmatic Reviewers	IX-4
X. National Prion Research Program	
The Disease.....	X-2
Program Background	X-2
The Fiscal Year 2002 Program.....	X-3
Summary	X-4
Fiscal Year 2002 Integration Panel Members	X-4
XI. Other Programs Managed by the CDMRP	
Background	XI-2
Alcoholism Research	XI-3
Arthropod-Borne Infectious Disease Control Research	XI-3
Breast Cancer Imaging Research	XI-4
Cancer Center of Excellence	XI-4
Center for Prostate Disease Research.....	XI-4
Children's Hospice Program.....	XI-6
Fragile X Research	XI-6
Gallo Cancer Center.....	XI-6
Hepatitis C Research	XI-7
Lung Cancer Research	XI-7
Monoclonal Antibodies, Massachusetts Biological Lab	XI-8
Muscular Dystrophy Research.....	XI-8
Appendix A - Fiscal Years 1992-2002.....	A-1
Appendix B - Fiscal Years 2002-2003	B-1
Appendix C - USAMRMC Office of the Congressionally Directed Medical Research Programs Staff.....	C-1
Appendix D - Acronyms	D-1



Executive Summary

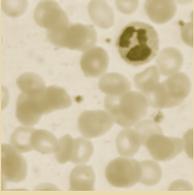


CDMRP Vision: To find and fund the best research to eradicate diseases and support the warfighter for the benefit of the American public.

CDMRP Mission: To provide hope by promoting innovative research, recognizing untapped opportunities, creating partnerships, and guarding the public trust.



...shaping the future of health care to prevent, control, and cure diseases.



Recent scientific breakthroughs and exciting new opportunities in research have increased anticipation and hope that a cure for cancer and other diseases is within our reach. Due to the work of highly motivated consumer advocacy groups, public awareness of scientific research continues to rise and shape this field. The Office of the Congressionally Directed Medical Research Programs (CDMRP) is one organization that is recognizing and mobilizing untapped opportunities to advance health care solutions identified by Congress and the Department of Defense (DOD). The CDMRP is a research area directorate within the U.S. Army Medical Research and Materiel Command (USAMRMC). The CDMRP manages congressional research appropriations that will improve the life of all Americans. As a manager for programs in targeted diseases, the CDMRP has interpreted congressional directives for each appropriation with rigor and integrity. As a result, the CDMRP has developed and implemented programs that are intended to bring sound scientific research forward in specific medical areas that is responsive to the needs of the American public.

Since its inception, the CDMRP has managed 29 research programs that total almost \$2.6 billion (B) in congressional appropriations. The appropriations set forth by Congress for fiscal year 2002 (FY02) total over \$390 million (M), with focus on breast, prostate, and ovarian cancers, military health, neurofibromatosis, tuberous sclerosis, transmissible spongiform encephalopathies, chronic myelogenous leukemia, and other diseases.

The Early Years

The origin of the CDMRP can be traced back to 1992 when a congressional appropriation of \$25M was made for "army breast cancer research." At the same time, the breast cancer consumer community, led by the National Breast Cancer Coalition (NBCC), was raising public and legislator awareness of gaps in breast cancer research and lobbied to increase the nation's investment in breast cancer research. In 1992, the NBCC presented President Clinton with a petition with 2.6 million

signatures for a comprehensive plan to put an end to breast cancer. This grassroots movement led to an FY93 congressional appropriation to the DOD for \$210M targeted toward breast cancer research. The USAMRMC was assigned responsibility for administering these dollars. Within the USAMRMC, a new research area directorate, the CDMRP, was established to administer the FY93 Breast Cancer Research Program (BCRP), as well as to manage awards that were supported by the FY92 DOD breast cancer research appropriation.

The USAMRMC is the medical research, development, logistics, and acquisition arm of the U.S. Army. The Command operates six medical research laboratories and institutes in the United States that are centers of excellence in specific areas of biomedical research. A large extramural research program and numerous cooperative research and development agreements with leading civilian organizations enhance the in-house capabilities of the USAMRMC. Part of the mission of the USAMRMC is to “invent global medical solutions for tomorrow.” Despite this history of research infrastructure and scientific rigor, in 1993, breast cancer was not considered part of the Army’s existing research and development expertise. As such, the USAMRMC sought the advice of the National Academy of Sciences Institute of Medicine (IOM) to identify gaps in breast cancer research and make recommendations as to how this new appropriation could best be used. The IOM made two important

Breast Cancer

The mission of the BCRP is to foster new directions, address neglected issues, and bring new investigators into the field of breast cancer research.

One out of every eight women will develop breast cancer in her lifetime. Approximately 39,800 women and 400 men were projected to die from this disease in 2003.¹

The BCRP is the second largest funder of extramural breast cancer research in the world, having been appropriated \$1.52B in FY92–03 to eradicating breast cancer. More than 3,600 grants have been awarded.



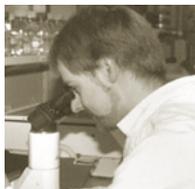
¹ American Cancer Society—Cancer Facts and Figures 2003.

recommendations: (1) to establish a defined strategy as to how the monies would be spend and (2) to institute a two-tiered review process in which both the scientific merit as well as the programmatic relevance would be addressed. These recommendations were applied to the FY93 BCRP and have been subsequently adapted for other programs managed by the CDMRP.

The CDMRP in Fiscal Year 2002

The CDMRP originated within an environment that necessitated and fostered novel approaches to its operation as a funding agency. The continued successes of the CDMRP and the work of consumer advocates have resulted in yearly appropriations for peer reviewed research. FY02 is the eleventh year that Congress has appropriated monies to be managed by the CDMRP, totaling almost \$2.6B. FY02 core programs within the CDMRP include the following:

- ◆ BCRP
- ◆ Prostate Cancer Research Program (PCRP)
- ◆ Neurofibromatosis Research Program (NFRP)
- ◆ Ovarian Cancer Research Program (OCRP)
- ◆ Peer Reviewed Medical Research Program (PRMRP)
- ◆ Chronic Myelogenous Leukemia Research Program (CMLRP)
- ◆ Tuberous Sclerosis Complex Research Program (TSCRCP)
- ◆ National Prion Research Program (NPRP)



Prostate Cancer

The vision of the PCRP is to conquer prostate cancer.

Prostate cancer is the second leading cause of cancer death in men, with almost 29,000 deaths expected to occur in 2003.²

Beginning in FY97, Congress appropriated money to fund peer reviewed prostate cancer research. To date, \$480M has been appropriated to the USAMRMC PCRP. Almost 800 awards have been made to support innovative ideas and technologies aimed at preventing, detecting, treating, and improving the quality of life of men with prostate cancer.

² American Cancer Society—Cancer Facts and Figures 2003.

Neurofibromatosis

Neurofibromatosis (NF) includes two distinct genetic disorders of the nervous system, NF1 and NF2. The mission of the NFRP is to promote research directed toward the understanding, diagnosis, and treatment of NF1 and NF2 and to enhance the quality of life for individuals with the disease.

NF1 occurs more commonly, affecting 1 out of 4,000, whereas NF2 occurs in 1 out of every 40,000 persons.³

Appropriations to the USAMRMC NFRP for FY96–03 total \$110.3M, representing the largest public research funding for NF.⁴ A total of 103 awards have been made to develop a multidisciplinary research portfolio that encompasses basic, clinical, and population-based research projects.

The Vision for the Fiscal Year 2003 Programs

The CDMRP continues to fulfill a unique niche in biomedical research. In FY03, Congress appropriated \$350M to continue investing in innovative research aimed at understanding and curing life-threatening diseases.

Scientific Outcomes and Advances

Noteworthy CDMRP accomplishments for the past year can be reported in four broad areas: promoting innovative research, recognizing untapped opportunities, creating partnerships, and guarding the public trust.

Promoting Innovative Research

Since its inception, the CDMRP has sought to “create an environment in which creative ideas and first-rate research can flourish and in which investigators are not afraid to gamble on risky but alluring ideas.” Although each award mechanism has different award requirements, an underlying goal of all the mechanisms offered by the CDMRP is to encourage investigators to seek out novel, creative ideas and solutions that will lead disease-specific research in new directions.

Examples of such innovative work are displayed by the following awards: Research from Dr. Skobe’s laboratory, for a BCRP Concept Award, has shown that lymphangiogenesis does in fact occur, in the tumor microenvironment and may lead to an a new therapeutic target. A PCRP Idea award granted to Drs. Asem and Kinch from Purdue University has

³ Report on Neurofibromatosis, Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Neurological Disorders and Stroke, 2003.

⁴ The National Neurofibromatosis Foundation, Inc.



Peer Reviewed Medical Research Program

The mission of the PRMRP is to support biomedical research with direct relevance to military health. To this end, congressional appropriations for the PRMRP from FY99–03 totaled nearly \$195M. As of 2002, 98 awards have been made to preserve the health of our military forces.



supported research to develop antibodies that will only target the cancerous prostate cell and not the normal cell. Dr. Andreas Kurtz, who was awarded an NFRP Idea award in 1999, discovered that mutations in mitochondrial DNA exist in normal tissues from NFI patients (a finding that may aid in the prediction of disease severity and eventually lead to new treatments). One of the projects that encompass an OCRP Program Project awarded to Dr. Daniel Meruleo has obtained preliminary data indicating that using a specific vector (specific DNA sequences that can be used to transport genetic material) in conjunction with a protein capable of producing an immune response to elicit cell death in ovarian cancer cells may be a viable treatment option for women with ovarian cancer.

Recognizing Untapped Opportunities

The CDMRP continues to devote itself to finding unique solutions that address underinvestigated areas of research and improve the management of its research programs. Each individual program decides which area(s) of research is of highest priority annually. Training and recruitment of new investigators, as well as the building of research resources in the form of centers of excellence, consortia, and imaging equipment, continue to be a major investment by the CDMRP. In addition to fostering these groundbreaking award mechanisms, the CDMRP continues to emphasize new and innovative practices to advance program management and execution by implementing electronic technology for proposal submission, review, and management. These processes have allowed the CDMRP to virtually eliminate paper processing, thus saving time and increase quality control of these documents.



Ovarian Cancer

The mission of the OCRP is to support innovative, integrated, multidisciplinary research efforts that will lead to a better understanding, detection, diagnosis, prevention, and control of ovarian cancer. In 2003, approximately 25,400 women will be diagnosed with ovarian cancer in the United States, and 14,300 will die from the disease.⁵

Nearly \$72M was appropriated for the USAMRMC OCRP in FY97–03. As of 2002, 63 awards have been made.

⁵ American Cancer Society—Cancer Facts and Figures 2003.

Chronic Myelogenous Leukemia

The vision of the CMLRP is to perfect the existing and develop new diagnostic and therapeutic approaches for chronic myelogenous leukemia (CML). CML is an overgrowth of granulocytes, a type of white blood cell; its cause is unknown. In 2003, approximately 1,700 people will die from the disease.⁶ The CMLRP was established in 2002, with congressional appropriations over the past 2 years totally over \$9M.

Creating Partnerships

Public, private, government, and military partnerships have been the key to the success of the CDMRP. Consumers are voting members on scientific peer-review panels and the Integration Panel, as well as active participants in executing some research projects. Therefore, the relationships developed between the research managers and scientists and those individuals affected by policies and research are critical for the success of the CDMRP. Military partnerships play an important role within the CDMRP; military personnel, civilian, and contractor staff are responsible for executing the congressional directives and work together to implement each program's vision. Additionally, several programs managed by the CDMRP have a direct military focus, particularly to improve the health of our military forces. The CDMRP's relationships with the scientific community, which serves on peer-review panels and the integration panel and assists in vision setting, are essential in fulfilling the program's vision of eradicating diseases. Without these partnerships the CDMRP's war against disease would be a losing one.



Tuberous Sclerosis

Tuberous sclerosis is a genetic disorder that can affect any or all systems of the body. The disorder is characterized by seizures, developmental delays, kidney disease, behavioral problems, and the growth of benign tumors (tubers) on vital organs such as the brain, kidneys, and heart. The mission of the TSCRP is to encourage innovative research aimed at understanding the role and function of proteins produced by the TSC1 and TSC2 tumor suppressor genes.

Nearly 1 million people worldwide have been diagnosed with tuberous sclerosis, with approximately 50,000 of those cases were reported in the United States.⁷

The TSCRP was established in FY02 with a \$1M appropriation; the TSCRP was continued in FY03 with an appropriation of \$2M.

⁶ American Cancer Society—Cancer Facts and Figures 2003.

⁷ Tuberous Sclerosis Alliance, 2003.



Guarding the Public Trust

As the CDMRP was created in response to the concerns of individuals affected by cancer and disease, guarding the public trust is of upmost importance. Over the past 11 years, the CDMRP has implemented efficient, cost-effective processes to administer its increasing number of programs and awards while compressing the time frame for funding. The Special Populations Program underscores the CDMRP's effort to bridge the gap that exists in the incidence, morbidity, and mortality among different ethnic groups for which the CDMRP provides support. The Common Scientific Outline reflects CDMRP's support for improved communication among funding agencies in the United States and abroad. Over the past year, a great amount of effort was put forth to increase public awareness of the CDMRP through advertising specific award mechanisms in national newspapers, distributing award information to consumer advocacy groups, and sponsoring funded investigators to attend scientific meetings.

Looking Ahead

Solving today's health crises remains a challenge. The CDMRP believes that by continuing to be responsive to the needs of consumers, researchers, and clinicians, the future of health care can be shaped to prevent, control, and cure diseases. In 2003, the CDMRP will move toward advancing health care solutions in areas identified by Congress and DOD by recognizing and mobilizing untapped opportunities, funding excellent research, creating partnerships, and guarding the public trust. Together we can succeed.

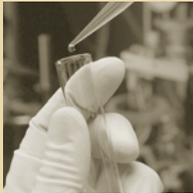
Prion Disease—Transmissible Spongiform Encephalopathies

"Transmissible spongiform encephalopathies" refers to several apparently related diseases that are relatively rare in humans but have been documented most extensively in hooved mammals. The current disease theory attributes transmissible spongiform encephalopathies to "prions," normal cell-membrane proteins with atypical three-dimensional configurations. The main goal of the NPRP is to eliminate the occurrence of this disease and to develop a diagnostic test to detect the presence of prion disease.

The USAMRMC NPRP was established in FY02 with a congressional appropriation of \$42.5M for research on prion disease; a total of 38 awards were made from the FY02 appropriation.



I. Overview of the CDMRP



*...shaping the future of health care
to prevent, control, and cure diseases.*



History/Evolution

In the past decade, heightened public awareness and increased interest in health issues have influenced scientific research. Cancer research has drawn particular attention, due in part to the rising impact of cancer and the work of highly visible consumer advocacy organizations. In response to these concerns, the U.S. Congress directed the Department of Defense (DOD) to manage intramural and extramural research programs that focus on specific diseases. The U.S. Army Medical Research and Materiel Command (USAMRMC)¹ has been responsible for managing targeted appropriations totaling over \$2.6 billion (B) for fiscal years 1992–2003 (FY92–03) for research on breast, prostate, and ovarian cancers; neurofibromatosis; peer reviewed medical research; chronic myelogenous leukemia; tuberous sclerosis complex; prions; and other health concerns. Together, these programs comprise the Office of the Congressionally Directed Medical Research Programs (CDMRP), a scientific research directorate within the USAMRMC.

In FY93, the Army sought the advice of the National Academy of Sciences (NAS) to effectively manage the \$210 million (M) appropriation for breast cancer research to be administered by the U.S. Army. In response, the NAS Institute of Medicine (IOM) issued a report entitled *Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command*. The IOM committee made several major recommendations in this report. First, the committee recommended an annual investment strategy to guide allocations of funds that best address the current needs in breast cancer research. Second, the committee recommended a two-tier review strategy consisting of scientific peer review and programmatic review. The first tier is conducted by external scientific, clinical, and consumer peer reviewers, while the second tier is conducted by an advisory committee of the nation's leading scientists, clinicians, and consumers. This two-tier review system was designed to ensure that the research portfolio reflects not only the most meritorious science but also the most programmatically relevant. Both of these recommendations have become cornerstones in the administration of most of the programs managed by the CDMRP. Further descriptions of the annual investment strategy and two-tier review process are in this section under Program Execution and Management.

¹ Known as the U.S. Army Medical Research and Development Command prior to 1995.

Programs Managed by the CDMRP

Since its inception, the CDMRP has managed 29 separate programs that total almost \$2.6B in congressional appropriations. Eight of these programs are considered core programs. Core programs have either received or have the potential to receive multiple appropriations and are characterized by standing Integration Panels (IPs). The other programs managed by the CDMRP are characterized by a one-time appropriation and/or are institutionally based programs. Although the programs within the CDMRP share many common features, each program is unique and emphasizes the specific needs of its research and advocacy communities. Highlights of each of the eight core programs follow. See Section XI for more information on the other programs.

Breast Cancer Research Program

The DOD Breast Cancer Research Program (BCRP) vision is to eradicate breast cancer. As the second largest funder of extramural breast cancer research in the world, the program has managed approximately \$1.52B in appropriations from FY92 to FY03. In addition, the BCRP is also a recognized leader in innovative program management. Over the past decade, a research portfolio has been supported that encompasses a wide spectrum of projects spanning prevention, detection, diagnosis, and treatment of breast cancer (Figure I-1). Research awards supported through this program are leading to the eradication of breast cancer by supporting innovative ideas, training future generations of scientists and clinicians, providing necessary research resources, and bringing bench research to the bedside. Through FY02, the BCRP has received over 19,840 proposals and has made 3,671 awards. More detailed information regarding the BCRP is included in Section III.

Prostate Cancer Research Program

The DOD Prostate Cancer Research Program's (PCRP's) vision is to conquer prostate cancer. The PCRP, established in FY97, marks its seventh year in FY03. As a major funder of prostate cancer research, the PCRP has been responsible for the management of \$480M in appropriations through FY03. The PCRP has supported innovative, multidisciplinary basic and clinical research relevant to prostate cancer (Figure I-2). In addition, the PCRP is committed to addressing the significant disparities in the incidence and mortality of prostate cancer that exist among different ethnic groups, and it has designed award mechanisms to stimulate research in these areas. For the first 6 years of this program, more than 3,400 proposals have been received, leading to 797 awards. The PCRP is described in greater detail in Section IV.



Figure I-1. FY92-02 BCRP Portfolio by Research Area



Figure I-2. FY97-02 PCRP Portfolio by Research Area

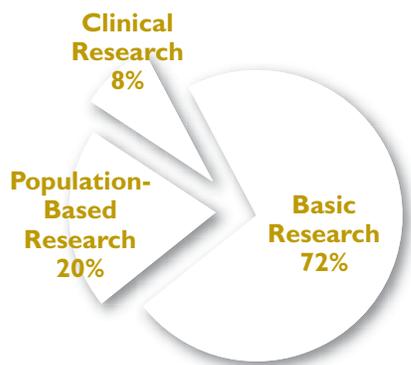


Figure I-3. FY96-02 NFRP Portfolio by Research Area



Figure I-4. FY97-02 OCRP Portfolio by Research Area



Figure I-5. Numbers of Funded Grants for FY99-02 PRMRP Portfolio by Research Area

Neurofibromatosis Research Program

The DOD Neurofibromatosis Research Program's (NFRP's) vision is to decrease the impact of neurofibromatosis (NF). As a leader in the support of NF research, the NFRP has managed \$110.3M in congressional appropriations for FY96-03. The NFRP has supported a multidisciplinary portfolio that encompasses basic, clinical, and population-based projects (Figure I-3) on both NF1 and NF2. In recent years, emphasis has been placed on bringing laboratory research to the clinic. Part of this clinical emphasis includes large natural history studies/consortium awards, awards to support the development and evaluation of preclinical model systems, and clinical trials. From FY96 to FY02, the NFRP received 299 proposals, leading to 103 awards. Further details on the NFRP appear in Section V.

Ovarian Cancer Research Program

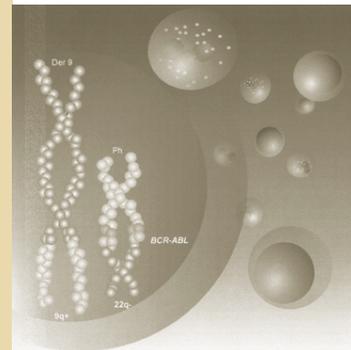
The DOD Ovarian Cancer Research Program's (OCRP's) vision is to prevent ovarian cancer. Appropriations for the FY97-03 OCRP total \$71.7M. The OCRP has built a multidisciplinary portfolio (Figure I-4) that emphasizes research resources and innovative research. Awards have been offered to promote collaborations across disciplines and institutions, groundbreaking research, and the training of new investigators in the ovarian cancer field. Since the Program's inception through September 2003, 575 proposals have been received and 63 awards have been made. More detailed information regarding the OCRP appears in Section VI.

Peer Reviewed Medical Research Program

The DOD Peer Reviewed Medical Research Program's (PRMRP's) mission is to support research on issues with direct relevance to military health. Appropriations for the FY99-02 PRMRP total \$194.5M. Since the Program was established in FY99, the PRMRP has built a portfolio of research that covers awards that span 32 topic areas relevant to military health (Figure I-5). An important feature in the execution of this program is the use of an advisory panel composed of representatives from the Army, Navy, Air Force, Marines, Department of Veterans Affairs, Office of the Assistant Secretary of Defense (Health Affairs), and U.S. Department of Health and Human Services to develop an investment strategy and conduct programmatic review. In the first 4 years of the Program, 558 proposals have been received and 98 awards have been made. The PRMRP is described in more detail in Section VII.

Chronic Myelogenous Leukemia Research Program

The DOD Chronic Myelogenous Leukemia Research Program's (CMLRP's) vision is to perfect the existing treatments and develop new diagnostic and therapeutic approaches for CML. The Program was established in FY02 with a \$5M appropriation for research on CML and was continued in FY03 with a congressional appropriation of \$4.25M. The CMLRP is supporting research that will lead to substantial improvement in the understanding, diagnosis, and treatment of CML and enhancement of the quality of life of persons with the disease. The CMLRP is described in more detail in Section VIII.



Tuberous Sclerosis Complex Research Program

The DOD Tuberous Sclerosis Complex Research Program's (TSCRPs) vision is to lessen the impact of tuberous sclerosis. The Program was established by a \$1M appropriation in FY02 for tuberous sclerosis research and was continued in FY03 with a congressional appropriation of \$2M. The TSCRPs is supporting innovative research directed toward a better understanding of the role and function of proteins produced by the TSC1 and TSC2 tumor suppressor genes. More detailed information regarding the TSCRPs can be found in Section IX.

National Prion Research Program

The DOD National Prion Research Program's (NPRP's) vision is to eliminate the occurrence of transmissible spongiform encephalopathies. The Program was established by a congressional appropriation of \$42.5M in FY02. The goal of the NPRP is to develop a rapid, sensitive, and reproducible test for the detection of prions suitable for use both as an ante-mortem diagnostic test and a screening assay. In support of this goal, additional topics of interest include the prevention, transmission, and pathogenesis of transmissible spongiform encephalopathies as well as a better understanding of chronic wasting disease. A total of 38 awards have been supported that span four award mechanisms, as depicted in Figure I-6. Further information on the NPRP appears in Section X.

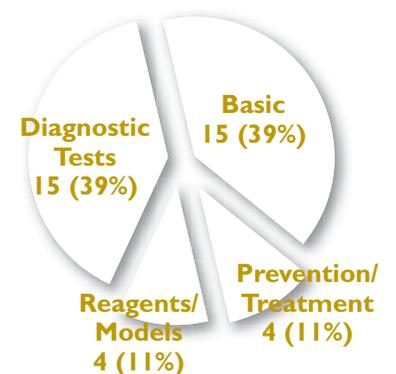


Figure I-6. FY02 NPRP Portfolio by Research Area



Figure I-7. CDMRP Flexible Execution and Management Cycle

Program Execution and Management

An important feature of the CDMRP is its ability to adapt to the current needs of the research, clinical, and consumer communities. The CDMRP can accomplish this because it utilizes, and has refined over the years, an effective program execution and management strategy.

The CDMRP uses a flexible 7-year execution and management cycle that spans all phases of program execution, from the development of a vision through the completion of research grants (Figure I-7). All programs within the CDMRP depend upon yearly, individual congressional appropriations. These funds are not in the President’s budget; Congress adds them annually to the DOD appropriation to fund new programs or to augment existing DOD or Army programs. The effectiveness of the programs, the work of consumer advocates, and the need for additional, focused biomedical research have led to continuing appropriations for programs managed by the CDMRP.

Early Program Planning

Early in each fiscal year, after the congressional appropriation has been signed into law and funds have been received by the USAMRMC, each program’s IP—an expert panel of scientists, clinicians, and consumer advocates—meets to deliberate issues and concerns unique to the individual program and establish a vision and investment strategy for the coming year. The development of an annual investment strategy stems from the 1993 IOM recommendations² and provides a high degree of flexibility. It allows each program to identify underfunded and underrepresented areas of research and to encourage research in those areas that are considered the most critical to patients, consumers, clinicians, and laboratory researchers. The investment strategy provides the framework and direction necessary to most effectively obligate each congressional appropriation, while avoiding unnecessary duplication with other funding agencies. (See Appendices A and B for summaries of congressional appropriations by program.)

² *Institute of Medicine, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, 1993.*

Program Development and Execution

A critical component of the investment strategy is developing specific award mechanisms that capture the current needs of both the research and advocacy communities. Separate announcements outlining the award mechanisms offered for each of the research programs managed by the CDMRP are released each fiscal year. The CDMRP has utilized over 40 different types of award mechanisms that fall into three categories: research, training and recruitment, and research resources.³

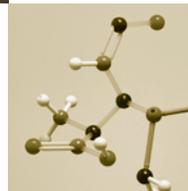
Proposals received in response to published announcements are subjected to a two-tier review. The CDMRP model for performing these reviews derives from the 1993 IOM recommendations.⁴ The two tiers are fundamentally different. The first tier is a scientific peer review of proposals against established criteria for determination of scientific merit. Panels organized by scientific discipline, specialty area, or award mechanism conduct scientific peer review. The primary responsibility of the scientific peer review panels is to provide unbiased, expert advice on the scientific and technical merit of proposals, based upon the review criteria published for each award mechanism. The second tier of the review process is programmatic review. Programmatic review is accomplished by the IP, the advisors that recommend the initial investment strategy. Programmatic review is a comparison-based process in which proposals from multiple research areas compete in a common pool against published review criteria. Scientifically sound proposals that most effectively address the unique focus and goals of the program are then recommended to the Commanding General, USAMRMC, for funding.

Grants Management

Awards are made in the form of grants, contracts, or cooperative agreements, and the research is executed over 1 to 5 years, depending on the type of award mechanism. With 4,910 awards made through FY03, the management of these grants, contracts, and/or cooperative agreements is a major focus of the CDMRP. As such, the CDMRP makes certain that the research supported by the American public is monitored thoroughly for technical progress and compliance with animal and human use regulations.

³ For a summary of many of the award mechanisms offered by the CDMRP between 1993 and 1999, see the DOD CDMRP Annual Report, September 1999 (Appendix A).

⁴ Institute of Medicine, Strategies for Managing the Breast Cancer Research Program: A Report to the U.S. Army Medical Research and Development Command, 1993.





Every CDMRP award is assigned to one Grants Manager for the life of that award, ensuring a broad knowledge of each grant, continuity among all parties involved in the award, and the most comprehensive assistance possible to the Principal Investigator (PI). In so doing, Grants Managers oversee all aspects of the funding process, both pre- and post-award distribution. This includes assessing overlap with other funding agencies, ensuring the completeness of the required regulatory documentation, and administering the overall grant. During the life of the award, Grants Managers review investigators' annual and final progress reports, conduct site visits to institutions, and maintain regular communication with each investigator. These efforts collectively enable the CDMRP to evaluate progress, publications, patents, and other products, as well as harvest and disseminate information on research accomplishments. Highlights of such accomplishments are included under the individual program sections.

Research Information Dissemination

Propagating the Word

The CDMRP recognizes the importance of disseminating program information to the public and has supported several efforts to foster program awareness.

<http://cdmrp.army.mil>

The CDMRP website disseminates up-to-date program information to the public and research community; more than 128,000 visits are made to the website annually. Features of the site include the following:

- ◆ *Research Programs* – individual programs managed by the CDMRP
- ◆ *Research Highlights* – scientific achievements obtained by CDMRP-funded investigators
- ◆ *Funding Opportunities* – calls to the scientific and clinical communities to submit proposals
- ◆ *CDMRP Annual Reports* – archived CDMRP Annual Reports
- ◆ *Search Awards* – search engines for posted awards that search by various criteria (including research program, FY, PI, institution, research topic, award mechanism, and clinical trial); award amounts, abstracts, and publications are provided for each award
- ◆ *Consumer Involvement* – information on consumer involvement in scientific peer review

- ◆ Publications – documents such as press releases, fact sheets, peer reviewed articles, and program award books
- ◆ Resources & Links – links to other sites

Advertisement of Funding Opportunities

Programs within the CDMRP prepare and issue Program Announcements that provide details on individual award mechanisms, the application process, and requirements for submitting proposals. The following publicity efforts are directed toward alerting the scientific research community when new Program Announcements are released:

- ◆ Posting the Program Announcements on the CDMRP website to enable immediate access
- ◆ Alerting over 400 institutional Sponsored Program Offices of upcoming award opportunities and encouraging them to link to the CDMRP website for up-to-date program information and funding opportunities
- ◆ Advertising in both broadly focused professional journals (e.g., *Science*) and business journals (e.g., *FedBizOpps*)
- ◆ Targeted advertising for some new mechanisms that are aimed toward recruiting new applicants or scientists in specific research areas (For example, the FY03 BCRP advertised the Clinical Research Nurse Award in the Oncology Nursing Forum and notified over 600 accredited nursing schools in the United States and Canada to recruit nurses in clinical breast cancer research. The FY03 PCRPT notified medical schools, urology departments, and National Cancer Institute-designated Comprehensive Cancer Centers about a new award mechanism, the Physician Research Training Award, to recruit physicians for careers in prostate cancer research.)
- ◆ Sending e-mails to prior applicants, scientific peer reviewers, and individuals who have requested that their names be placed on the CDMRP mailing list (For the FY03 programs, over 17,000 e-mails were sent to potential applicants.)
- ◆ Sending press releases to *The Cancer Letter*, *Washington FAX*, *UniSci Daily University Science News*, *Science Daily Magazine*, and *The Blue Sheet*
- ◆ Notifying websites that specialize in biomedical grant notification (e.g., Community of Science, *Science: The Next Wave*, and Texas Research Administrators Group database)



- ◆ Notifying over 50 professional associations (e.g., the American Association of Cancer Research [AACR] and the American Society of Clinical Oncology), the military press, military research laboratories, other federal agencies, federal websites maintaining funding information, and consumer advocacy organizations of upcoming funding opportunities
- ◆ Exhibiting the CDMRP display at national scientific meetings such as the Federation of American Societies for Experimental Biology American Urological Association and AACR.

Publications

Over 4,500 publications have resulted from investigators who received CDMRP awards through FY01. (These publications are provided to the CDMRP by award recipients.) In addition, the CDMRP staff has published articles and presented information at national scientific meetings. A list of the CDMRP recent peer reviewed articles, abstracts, and posters can be found on the website at <http://cdmrp.army.mil/pubs>.