



EXECUTIVE SUMMARY

CDMRP Vision: To be the preferred and responsive source for accessible research funding, shaping the future of health care to prevent, control, and cure diseases.

CDMRP Mission: To advance health care solutions in areas identified by Congress and the Department of Defense by funding excellent research, recognizing and mobilizing untapped opportunities, creating partnerships, and guarding the public trust.

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. More than ever, there is a heightened urgency to seize these opportunities in an effort to lead us to a clearer understanding of, and cure for, disease. 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).¹ 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 invigorate research in specific medical areas and are scientifically sound and responsive to the needs of the scientific and advocacy communities.

The CDMRP currently manages 18 research programs that total nearly \$2.3 billion (B) in congressional appropriations and focus on breast, prostate, and ovarian cancers, neurofibromatosis, tuberous sclerosis, transmissible spongiform encephalopathies, and chronic myelogenous leukemia, among 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 2.6 million-signature petition for a comprehensive plan to put an end to breast cancer. This grassroots movement led to a fiscal year 1993 (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)



Breast Cancer

Approximately 40,000 deaths are expected in 2002 as a result of breast cancer.¹ Due to the ongoing efforts of advocacy groups and increased public awareness of health issues, Congress has continued to appropriate money for the USAMRMC BCRP. From FY92–02, Congress has appropriated almost \$1.4B to the BCRP for a multidisciplinary effort aimed at eradicating breast cancer. More than 3,200 grants have been awarded. ♦

¹ *Cancer Facts and Figures, American Cancer Society, 2002.*

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

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 recommendations that were applied to the FY93 BCRP and have been subsequently adapted for other programs managed by the CDMRP.

The first recommendation defined a strategy for how the FY93 appropriation should be spent. To carry out this recommendation, the CDMRP sought the advice of a council of leaders in breast cancer research, clinical practice, and advocacy to develop an investment strategy. Today, investment strategies are designed annually by a similar council of leaders for each program, named the Integration Panel, to address the most relevant needs of the research, consumer, and clinical communities. The second IOM recommendation outlined a two-tier review process – scientific merit review followed by a programmatic review. The review process was designed to ensure that the research portfolio reflected not only the most meritorious science, but also the most programmatically relevant. The concept of two-tier review has been applied to all programs managed by the CDMRP.

THE CDMRP IN FY01

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

Prostate Cancer

Prostate cancer is the second leading cause of cancer death in men, with over 30,000 deaths expected to occur in 2002.¹

Beginning in FY97, Congress appropriated money to fund peer-reviewed prostate cancer research. To date, \$395M has been appropriated to the USAMRMC PCRPP. More than 650 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. ♦

¹ *Cancer Facts and Figures, American Cancer Society, 2002.*

and the work of consumer advocates have resulted in yearly appropriations for peer-reviewed research. FY01 is the 10th year that Congress has appropriated monies to be managed by the CDMRP, totaling almost \$2.0B. FY01 core programs within the CDMRP include the:

- ▶ BCRP
- ▶ Prostate Cancer Research Program (PCRPP)
- ▶ Neurofibromatosis Research Program (NFRP)
- ▶ Ovarian Cancer Research Program (OCRPP)
- ▶ Peer Reviewed Medical Research Program (PRMRP)

THE VISION FOR THE FY02 PROGRAMS

The CDMRP continues to define a unique niche in biomedical research. In FY02, Congress appropriated \$390M for targeted biomedical research, expanding the core operation of the CDMRP to include three new programs: National Prion Research Program (NPRP); Chronic Myelogenous Leukemia Research Program (CMLRP); and Tuberos



Sclerosis Complex Research Program (TSCRPP). Together with the BCRP, PCRPP, NFRP, OCRPP, and PRMRP, these eight programs comprise the heart of the CDMRP.

SCIENTIFIC OUTCOMES AND ADVANCES

Noteworthy CDMRP accomplishments for the past year can be reported in four broad areas: advances in management execution strategies, award opportunities, outreach and communication, and scientific achievements.

Neurofibromatosis

Neurofibromatosis (NF) includes two distinct genetic disorders of the nervous system, NF1 and NF2. Together, these two genetic disorders affect more than 100,000 Americans of both genders and all ethnic groups.¹

Appropriations to the USAMRMC NFRP for FY96–02 total \$90.3M, representing the largest public research funding for NF.² A total of 85 awards have been made to develop a multidisciplinary research portfolio that encompasses basic, clinical, and population-based research projects. The NFRP emphasizes the establishment of innovative, multidisciplinary research groups and the translation of basic research into clinical treatments for individuals with NF. ♦

¹ Report on Neurofibromatosis, Department of Health and Human Services, Public Health Service, National Institutes of Health, National Institute of Neurological Disorders and Stroke, 1993.

² The National Neurofibromatosis Foundation, Inc.



Award Opportunities – Thinking Outside of the Box

In the second area of accomplishment, the CDMRP has uniquely provided support for areas of highest priority and greatest need among individual programs.

Award mechanisms are offered to sponsor research that may not be funded by other agencies, create foundations on which future research can be built, and encourage the next generation of researchers.

For example, the Biotechnology Clinical Partnership Award was designed in the BCRP to support prospective clinical trials in the areas of breast cancer therapeutics and chemoprevention through the establishment of partnerships between the biotechnology industry and academic institutions. The BCRP also created the Physician-Scientist Training Award to address the critical shortage of physicians performing clinical breast cancer research and the Innovator Award to encourage the most talented individuals in any area of endeavor to pursue their own

creative approaches that may significantly contribute to the conquest of breast cancer. The NFRP recently filled a scientific niche by creating the Therapeutic Development Award, which supports the development and evaluation of preclinical model systems for neurofibromatosis.

Advances in Management Execution Strategies

One of the past year's accomplishments has been the expansion of electronic proposal submission. In 2001, the CDMRP requested and received all proposals for the NFRP via a web-based system. In 2002, the CDMRP expanded its electronic proposal submission to include almost all of the core programs. Peer and programmatic review, post-award registrations, and grant management processes were also conducted using electronic processes. The new practices emphasize the CDMRP's commitment to streamlining program execution, proposal submission, review, registration, and funding. Thus, processes are made simpler and faster for applicants, reviewers, and administrators.

Ovarian Cancer

In 2002, approximately 23,300 women will be diagnosed with ovarian cancer in the United States, and 13,900 will die from the disease.¹

Nearly \$62M was appropriated for the USAMRMC OCRP in FY97–02. The OCRP focuses on building the foundation for a broad, multidisciplinary ovarian cancer research enterprise. The program is dedicated to supporting innovative meritorious research, building infrastructure, and training new researchers. Toward this end, 45 awards have been made. ♦

¹ Cancer Facts and Figures, American Cancer Society, 2002.

Outreach and Communication

Reaching out and communicating with all people who are ultimately affected by disease is an important goal of the CDMRP. Over the past year, the CDMRP's commitment to foster program awareness and share knowledge and information is reflected in two important arenas – the Special Populations Program and the Common Scientific Outline. The Special Populations Program underscores the CDMRP's effort to implement strategies that promote cultural competency throughout all deliberations and products of the CDMRP, while the Common Scientific Outline reflects CDMRP's support for improved communication among funding agencies.

Scientific Achievements

The last area of accomplishment, the program's scientific achievements, is a culmination or outgrowth of the first three. Through sound management practices and commitment to



Chronic Myelogenous Leukemia

Chronic myelogenous leukemia (CML) is an overgrowth of granulocytes, a type of white blood cell; its cause is unknown. In 2002, approximately 4,400 individuals will be diagnosed with CML, and approximately 2,000 will die from the disease.¹ Congress appropriated \$5M in FY02 for research on CML, marking the establishment of the CMLRP. The CMLRP will be conducted according to the two-tier review model recommended by the National Academy of Sciences IOM; this model is currently used for all core programs managed by the CDMRP. The CMLRP will support research that will lead to the substantial improvement in the understanding, diagnosis, and treatment of CML, and enhance the quality of life of persons with the disease. ♦

¹ National Cancer Institute Physician Data Query and American Cancer Society - Facts and Figures 2002.

flexibility, the science funded by the CDMRP is coming to fruition. The CDMRP has funded a broad array of science in research, training and recruitment, and infrastructure. Examples of several notable scientific achievements in each of these categories follow.

Research Awards: Research awards represent an extensive portfolio of diverse mechanisms that encompass most aspects of scientific investigations ranging from basic laboratory questions to clinical applications. For example, researchers funded by the BCRP at the University of Western Ontario demonstrated that citrus limonoids, a class of chemically related compounds present in citrus fruit, slowed the growth of tumors and reduced the incidence of lung metastases in a mouse model of breast cancer. Meanwhile, researchers funded by the PCRP at the New York University School of Medicine have isolated a mutated form of herpes simplex virus-1, the virus that causes cold sores, and shown it to be an effective antitumor agent in an animal model of prostate

cancer. In addition, researchers funded by the NFRP at the University of Florida, Gainesville, are linking the learning deficits that are often observed in individuals with NF1 to the disruption of the functioning of the protein that is produced by the NF1 gene. More details on these exciting findings can be found in the individual program chapters in this report.

Training and Recruitment Awards: Training and Recruitment Award mechanisms are offered to encourage the nation's finest scientists to join the CDMRP in its mission. The programs of the CDMRP promote the training and mentoring of the next generation of scientists toward independent careers in which creative thinking will produce treatments for human diseases. Other mechanisms assist established investigators with changing career directions into specific areas of research, such as breast, prostate, and ovarian cancers and neurofibromatosis. Dr. Karen Chichowski, who completed a nested postdoctoral fellowship as part of Dr. Tyler Jack's FY96 NFRP award,

Tuberous Sclerosis

Tuberous sclerosis is a genetic disorder that can affect any or all systems of the body. The disorder is characterized by seizures, development delays, kidney disease, behavioral problems, and the growth of benign tumors (tumors) on vital organs such as the brain, kidneys, and heart. These tumors typically calcify with age, becoming hard (sclerotic).

Tuberous sclerosis affects as many as 25,000 to 40,000 individuals in the United States and about 1 to 2 million individuals worldwide.¹

The TSCRCP was established in FY02 with a \$1M appropriation for research directed toward a better understanding of the role and function of proteins produced by the tuberous sclerosis complex 1 (TSC1) and TSC2 tumor suppressor genes. The TSCRCP will promote innovative research toward this end. ♦

¹ National Cancer Institute Physician Data Query and American Cancer Society - Facts and Figures 2002

exemplifies the success of trainees supported by the CDMRP. After publishing a first-authored manuscript in *Science* during her fellowship, she obtained a faculty position in the Division of Genetics at Brigham and Women's Hospital and has become a key player in the field of NF1 research.

Infrastructure Awards: The Infrastructure Awards offered by the CDMRP have two primary goals: (1) to create or make available resources, such as tissue repositories, animal models, and cell lines; and (2) to establish and support research centers of excellence or consortia. The BCRP, PCRCP, OCRCP, and NFRP have each supported awards to establish infrastructure that focuses on program-specific needs and targeted issues. For example, researchers funded by the OCRCP at the Peter MacCallum Cancer Institute are collecting epidemiological and molecular biological data with the goal of identifying potentially modifiable risk factors for ovarian cancer. A major focus of their Program Project is to create a new

classification of ovarian cancer based in part on molecular subtypes. Meanwhile, researchers funded by the NFRP at Harvard Partners Center for Genetics and Genomics are conducting a natural history study of NF1. They have been screening NF1 patients for mutations in the NF1 gene and found to date that no specific type of NF1 mutation leads to the development of plexiform neurofibromas, which are commonly observed in NF1 patients. More details on these important projects can be found in the individual program sections in this report.

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 USAMRMC NPRP was established in FY02 with a congressional appropriation of \$42.5M for research on prion disease. Because the health threats posed by transmissible spongiform encephalopathies currently appear to involve food and possibly blood supplies, input on the major issues in this field were garnered from the military, scientific, regulatory, industry, and public health sectors. The goal of the NPRP is to develop a rapid, sensitive, and reproducible test for the detection of prions. ♦

**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.