

Bone Marrow Failure Research Program

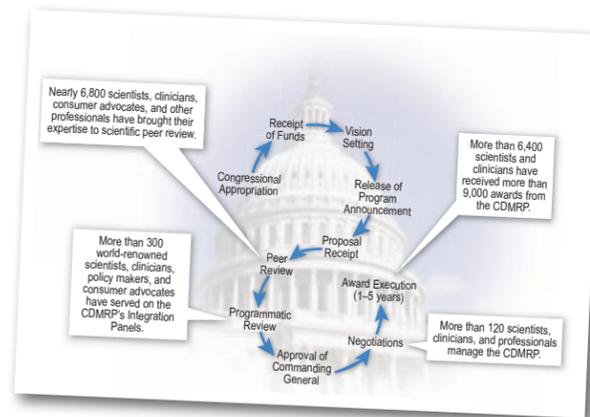


Congressionally Directed Medical Research Programs

HISTORY The Congressionally Directed Medical Research Programs (CDMRP) was born in 1992 from a powerful grassroots effort led by the breast cancer advocacy community that resulted in a congressional appropriation of funds for breast cancer research. This resulted in the initiation of a unique partnership among the public, Congress, and the military, which has persisted and grown to encompass multiple targeted programs. The CDMRP has received almost \$5.4 billion in appropriations from its inception in fiscal year 1993 (FY93) through FY09. Approximately 9,000 awards have been made across 19 different programs through FY08. Funds for the CDMRP are added by Congress to the Department of Defense budget annually to provide support for targeted research programs focused on a variety of cancers, genetic diseases, trauma-induced problems, childhood diseases, and other areas of health interest to military personnel and their families, the veteran population, and the general public. Under the auspices of the U.S. Army Medical Research and Materiel Command (USAMRMC), the CDMRP manages these programs from receipt of funds, through competitive selection of proposals and individual project performance, to award closeout.

PROPOSAL REVIEW

The CDMRP program management cycle includes a two-tier review process for proposal evaluation recommended by the National Academy of Sciences' Institute of Medicine. Each level of review is conducted by members of panels composed of scientists and clinicians, who are subject matter experts, and consumers. The first tier of evaluation is an external scientific peer review of applications against established criteria for determining scientific merit. The second tier is a programmatic review conducted by members of an Integration Panel who compare submissions and make funding recommendations based on programmatic priorities and mechanism-specific criteria. The Commanding General of USAMRMC issues the final approval for funding prior to award negotiations and execution of the proposed research project.



CONSUMER ADVOCATE PARTICIPATION

Consumer advocates (disease survivors, family members, or persons affected by bone marrow failure) actively participate throughout the annual cycle, including setting the program's vision, participating in the peer review of proposals, and contributing to the funding decision process. Their firsthand experiences with bone marrow failure provide a unique perspective that helps scientists understand the human side of how research will impact their community.

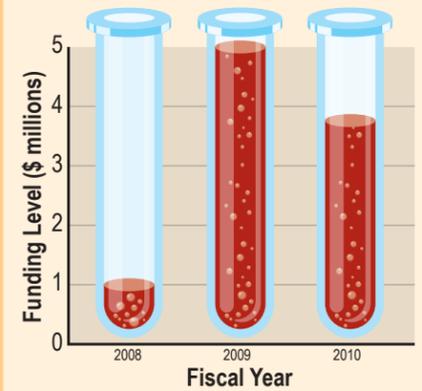
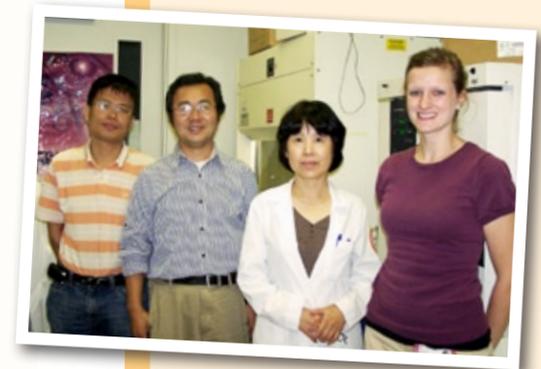
Bone Marrow Failure Research Program

Bone marrow failure is a general term covering many diseases of the sponge-like tissue found inside bones, which contains stem cells that usually have the ability to develop into red blood cells, white blood cells, and platelets. Disorders affecting the stem cell population may result in bone marrow failure—rare, potentially life-threatening diseases in which the bone marrow stops functioning or produces abnormal blood cells. These diseases are classified into two major categories: acquired bone marrow failure and inherited bone marrow failure. Acquired bone marrow failure may be caused by a variety of factors, including exposure to certain chemicals, environmental toxins, and viruses, or by autoimmune responses. Inherited forms of bone marrow failure arise from specific alterations or abnormalities of genes passed on from parent to child. Treatment options for bone marrow failure disorders include drug therapy and hematopoietic stem cell transplant; however, for some patients, the currently available treatment options may not be appropriate or feasible.

Through offering a variety of award mechanisms, the Bone Marrow Failure Research Program funds a broad research portfolio of innovative basic, translational, and preclinical studies.

The Role of TAK1 in the Pathogenesis of Bone Marrow Failure Syndromes

Jiwang Zhang, M.D., Ph.D., Loyola University, Chicago, Illinois Apoptosis is a series of events (morphological and biochemical) that a cell may undergo that result in cell death. A certain level of apoptosis, also called programmed cell death, is necessary for removing aged or abnormal cells thereby maintaining tissue homeostasis. In bone marrow blood stem cells (called hematopoietic stem cells [HSCs]), this life/death program is tightly controlled by a balance of chemical messages (signals) that result in cell survival or apoptosis. When apoptosis of HSCs is increased, there is a subsequent reduction in tissue cell production, ultimately resulting in tissue degenerative diseases. Bone marrow failure syndromes, such as aplastic anemia (AA) and myelodysplastic syndromes (MDS), are bone marrow degenerative disorders for which apoptotic loss of HSCs has been proposed as one of the important underlying developmental mechanisms of these diseases. Dr. Jiwang Zhang of Loyola University, recipient of a 2008 Bone Marrow Failure Research Program Investigator-Initiated Award, has found that TGFβ1-activated kinase 1 (TAK1), an enzyme involved in the processing of chemical signals, is highly expressed in normal HSCs. Mice in which the TAK1 gene has been deleted develop bone marrow failure due to an increased apoptotic loss of HSCs, indicating that TAK1 may mediate the survival signal. Dr. Zhang is studying whether TAK1-mediated survival signaling within these stem cells is adversely altered in AA and MDS and whether a lack of normal TAK1 functioning plays a role in the onset of these disorders. Dr. Zhang's research will provide greater insights into the basic pathogenesis of hematopoietic disorders, including bone marrow failure syndromes.



VISION

To understand and cure bone marrow failure disease

MISSION

To sponsor innovative research that will advance the understanding of inherited and acquired bone marrow failure diseases; to improve the health and life of individuals living with these diseases, with the ultimate goals of prevention and/or cure.



For more information, visit
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