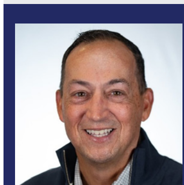
BONE MARROW FAILURE RESEARCH PROGRAM

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

MISSION: To encourage and support innovative research that is committed to advancing the understanding, prevention, and treatment of inherited and acquired bone marrow failure diseases, thereby improving the health of affected Service Members, Veterans and the general public, with the ultimate goal of cure

Congressional Appropriations FY08-FY24:

$71.6M total



"The research that gets funded through the program results in treatments, medicines or therapies that hopefully prevents the need for stem cell transplant. The benefit to the patient and family is returning to a quality of life as good or better than before their disease. But my strongest motivation for participating [on consumer peer review panels] is to pay tribute to those people I have met on this journey that were not as fortunate as me and did not survive their bone marrow failure."

Rob Minton, Be The Match, FY17 and FY22 Consumer Peer Reviewer

SCOPE OF THE PROBLEM

Many inherited bone marrow failure disorders increase risk of cancers.[2]

At least 20,000 Americans are diagnosed with a form of acquired bone marrow failure disease every year.[3]

Bone marrow failure disorders fall into one of two categories:[1]

INHERITED
Occurs from germline mutations passed down from parents

- Diamond-Blackfan anemia
- Dyskeratosis congenita/ telomere biology disorders
- Fanconi anemia
- Germline mutations
- Inherited neutropenia
- Schwachman-Diamond syndrome

ACQUIRED
Developed over time due to exposure to drugs, chemicals, radiation, viral infections, or other medical disorders

- Aplastic anemia
- Myelodysplastic syndromes
- Paroxysmal nocturnal hemoglobinuria
- Pearson's disease
- Radiation- or chemical-induced disease
- VEXAS syndrome

RELEVANCE TO MILITARY HEALTH

2010-2019 Military Health System Medical Encounters[4]

	Inherited*		Acquired	
	Service Members	DOD Beneficiaries	Service Members	DOD Beneficiaries
Patients	4,324	78,023	690	42,367
Outpatient Encounters	12,973	352,677	6,218	718,363
Hospital Bed Days	4,084	79,344	1,499	37,921

**Includes ICD codes for "Other neutropenia," which may include chemically and pharmacologically induced neutropenia more accurately represented as an acquired condition.*

PROGRAM PRIORITIES

Understanding the causes and progression of bone marrow failure diseases

Finding effective bone marrow failure **treatments** and **cures**

1 Moore CA and Krishnan K. *Bone Marrow Failure* (StatPearls Publishing, 2023).
2 Alter BP, et al. *Haematol* 103, no.1, 2018: 30-39.
3 https://www.govinfo.gov/content/pkg/BILLS-112hr640ih/html/BILLS-112hr640ih.htm.
4 Defense Medical Surveillance System, The Armed Forces Health Surveillance Branch, Defense Health Agency, Silver Spring, Maryland, 2010-2019; November 2020.

For more information, visit: **https://cdmrp.health.mil/bmfrp/**

PROGRAM IMPACT AND OUTCOMES

Supporting Research Capacity

BMFRP remains dedicated to growing the field of bone marrow failure research and providing opportunities for research training.

~**30% of awards** since FY08 supported:

- **New Investigators:** New to the field
- **Early-Career Investigators:** <10 years from first faculty appointment

Building Upon Success

The BMFRP invested in three separate Idea Development Awards over a six-year period advancing preclinical research in animal models of severe aplastic anemia. Each award built on prior findings and together support promising development of treatment options for individuals with severe disease.

ABOUT Severe Aplastic Anemia

- Difficult to treat
- Fatal if left untreated
- Excessive inflammation destroys blood stems cells

Katherine MacNamara, Ph.D., Albany Medical College

FY16

Dysfunctional Macrophages Drive Loss of Blood Stem Cells

- Macrophages are key cells of the immune system found in the blood
- Irregular cellular signaling of macrophages leads to loss of blood stem cells
- Targeting reduction of bone marrow macrophages to minimize the severity of disease

FY19

Macrophage Dysfunction Prolongs Inflammation

- Macrophages can promote and limit inflammation
- Continued inflammation blocks tissue repair and impairs blood stem cell production
- Correcting macrophage function improved production in models

FY22

Inflammatory Resolution as a Novel Treatment ***ONGOING RESEARCH***

- RvE1 is a cellular molecule known to reduce inflammation
- In models of disease, administering RvE1 may resolve inflammation
- Results of this research may offer new therapeutic options to protect from disease

IMPACTFUL RESULTS

BONE MARROW FAILURE SYNDROME

POIKILODERMA WITH NEUTROPENIA

- Caused by a genetic mutation in the USB1 gene
- Presents as a bumpy rash
- Persistent shortage of neutrophils, white blood cells involved in inflammation and fighting infection

HIGH-IMPACT RESEARCH

New Targets to Advance Treatment Options

- Blocking two proteins, PDPD5 and PAPD7, restored functions impaired by USB1 mutations
- PAPD5 and PAPD7 are new targets for developing inhibitors to restore neutrophil development

FANCONI ANEMIA

- Inherited disorder
- Affects DNA damage repair
- Genetic mutations impair bone marrow function and decrease production of all blood cells
- Affected individuals experience fatigue, frequent infections and blood clotting problems

Overcoming Blood Stem Cell Development Deficits

- Toll-like receptor 4 is a protein involved in the body's emergency response to quickly produce neutrophils
- Targeting toll-like receptor 4 may treat or prevent impaired blood stem cell maturation

A Safer Blood Stem Cell Transplant Regimen

- Targeting and inactivating the cell surface protein CD117 improves the safety of blood stem cell transplant

Point of Contact: CDMRP Public Affairs
dha.detrick.cdmrp.mbx.public-affairs@health.mil