

# REPORT DOCUMENTATION PAGE

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14. ABSTRACT <p><u>1. Contingency Preparedness:</u> Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.</p> <p><u>2. Rapid Identification of Matched Donors:</u> Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.</p> <p><u>3. Immunogenic Studies:</u> Increase understanding of the immunologic factors important in HSC transplantation.</p> <p><u>4. Clinical Research in Transplantation:</u> Create a platform that facilitates multicenter collaboration and data management.</p>					
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Grant Award N00014-23-1-2057

DEVELOPMENT OF MEDICAL TECHNOLOGY  
FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS  
QUARTERLY RESEARCH PERFORMANCE REPORT  
SUBMITTED April 12, 2024

Office of Naval Research

And

The National Marrow Donor Program<sup>®</sup> d/b/a NMDP

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## **I. Heading**

PI: Jeffrey Auletta, M.D.

National Marrow Donor Program

N00014-23-1-2057

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

## **II. Scientific and Technical Objectives**

The main goal of all activities funded through this grant is to develop, test and mature the ability of the NMDP Coordinating Center and NMDP contracted network sites to address contingency events wherein civilian or military personnel are exposed to marrow toxic agents, primarily ionizing radiation or chemical weapons containing nitrogen mustard. As a result of prior efforts in this regard a solid foundation has been established. The proposed new activities will continue to enhance and expand our capabilities in each of the four focus areas. Contingency preparedness activities will continue to integrate NMDP's role with federal, state, and local agencies.

An accident, a military incident, or a terrorist act in which a number of individuals are exposed to marrow toxic agents will result in injuries from mild to lethal. But the extent of individual injuries and the likelihood of recovery in many cases will not be apparent until days or weeks after the event. Casualties will be triaged by first responders, and those with major marrow injuries who will need aggressive medical support and may be ultimately candidates for hematopoietic cell transplantation (HCT) will need to be identified. While these patients are being supported, HCT donor identification activities will be initiated because it will not be initially clear which ones may ultimately require HCT. NMDP-approved transplant centers will provide a uniform and consistent clinical foundation for receiving, evaluating, and caring for casualties. NMDP Coordinating Center will orchestrate the selection and testing necessary to rapidly identify the best available donor or cord blood unit for each patient utilizing its state-of-the-art communication infrastructure, sample repository, laboratory network, and human leukocyte antigen (HLA) expertise. NMDP's on-going immunobiology bioinformatics and clinical research activities promote studies to advance the science and technology of HCT transplantation and directly translate research results to improve outcomes and quality of life for the patients.

Importantly, most individuals with near-lethal marrow toxic injuries will recover their own marrow function provided they receive intensive supportive care from the medical professionals that are part of the contingency response community. These professionals can save the lives of persons with severe marrow suppression using the knowledge and skills practiced every day to treat patients undergoing HCT coordinated through the NMDP.

## **III. Approach**

### **A. Contingency Preparedness**

HCT teams are uniquely positioned to care for the casualties with marrow toxic injuries, such as Acute Radiation Syndrome (ARS), from exposure to ionizing radiation or chemicals. The NMDP manages a network of hospitals that work in concert to facilitate unrelated HCT. The Radiation Injury Treatment Network (RITN), comprised of a subset of NMDP's network centers as well as non-NMDP network centers, is a national network of medical centers with expertise in the management of bone marrow failure and works with partners from other medical specialties to assist with managing ARS and its health-related consequences in response to marrow toxic mass casualty incidents.

B. Development of Science and Technology for Rapid Identification of Matched Donors  
Rapid progression to successful transplantation following a marrow toxic exposure or disease diagnosis affects survival. Decreasing the time to identify the optimal donor is critical. Methods are under development to rapidly identify and provide the optimal donor for HCT.

C. Immunogenetic Studies in Transplantation  
Improving strategies to avoid and manage complications due to graft alloreactivity is essential to improve the outcomes of HCT. Research efforts focus on strategies to maximize success of HCT while minimizing the toxicity related to alloreactivity between the donor graft and the recipient.

D. Clinical Research in Transplantation  
Clinical research creates a platform that facilitates multi-center collaboration and data management to address issues important for managing radiation exposure casualties. Advancing the already robust research capabilities of the NMDP network will facilitate a coordinated and effective contingency response.

**IV. Updates**

**A. Contingency Preparedness**

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*Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event*

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Activity under this grant is complete and will continue under a subsequent award.

**B. Development of Science and Technology for Rapid Identification of Matched Donors**

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*Expand the genetic diversity of the registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies*

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No activity to report. Activity under this grant will be completed in the next quarter.

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*Modeling and analysis of registry coverage for the Warfighter*

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Activity under this grant is complete and will continue under a subsequent award.

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*Development of science and technology for rapid communication of HLA data*

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Activity under this grant is complete and will continue under a subsequent award.

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*Use of population genetics and machine learning to automate the donor selection process*

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Activity under this grant is complete and will continue under a subsequent award.

### **C. Immunogenetic Studies in Transplantation**

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*Evaluate HLA disparity and impact on HCT by adding selected pairs to the Donor/Recipient Pair project utilizing sample selection criteria that optimize the new data generated by the typing project*

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Activity under this grant is complete and will continue under a subsequent award.

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*Development of a national framework to standardize measurable residual disease evaluation in the clinical care of patients receiving allogeneic transplant for acute myeloid leukemia*

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Activity under this grant is complete and will continue under a subsequent award.

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*Determine the impact of peripheral blood stem cell graft composition on the outcome of hematopoietic cell transplantation*

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Activity under this grant is complete and will continue under a subsequent award.

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*Determine the impact of non-HLA genes and gene expression on allogeneic cell transplantation*

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Activity under this grant is complete and will continue under a subsequent award.

## **D. Clinical Research in Transplantation**

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*Conduct clinical outcomes research using the CIBMTR research database and repository.*

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Activity under this grant is complete and will continue under a subsequent award.

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*Conduct clinical trials on the use of HLA mismatched graft sources to expand access to all patients in need of allogeneic cell transplantation*

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Activity under this grant is complete and will continue under a subsequent award.

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