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14. ABSTRACT

1. Contingency Preparedness: 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.

2. Rapid Identification of Matched Donors: Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
				18	Jeffery Auletta, M.D. - Sr Vice President and Chief Scientific Director
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Grant Award N00014-24-1-2057

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® d/b/a NMDP

500 5th St N

Minneapolis, MN 55401

I. Heading

PI: Jeffrey Auletta, M.D.
National Marrow Donor Program
N00014-24-1-2057
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 World Headquarters 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. Specific Aim 1: Develop and Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event.

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. Specific Aim 2: 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. Specific Aim 3: Perform Immunogenetic and Genomic Studies in Transplantation and Cellular Therapy

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. Specific Aim 4: Conduct Observational and Prospective Clinical Trials in Transplantation and Cellular Therapy

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

Specific Aim 1: Develop and Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event

Activity 1-1: Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event

Radiation disaster and countermeasure research education

- Advanced HAZMAT Life Support (AHLS) for Radiological Incidents & Terrorism 4-hour course (1) Has a target audience of physicians, physician multipliers, nursing staff, administrators and coordinators from departments such as bone marrow transplant, hematology, oncology, radiation safety, nuclear medicine, and the emergency department, as well as emergency management, and first responders; and (2) Will include interactive lectures and tabletop exercises that trains healthcare professionals to evaluate and care for irradiated and radiologically contaminated patients.
    - Three RITN hospitals have been chosen to host two sessions.
        - Avera McKennan (Sioux Falls, SD)
        - Banner-University Medical Center (Tucson, AZ)
        - Cancelled due to low enrollment – Mount Sinai (New York, NY)
    - Dates yet to be determined.
- Radiation Emergency Assistance Center/Training Site (REAC/TS) Management of Radiation Illnesses and Injuries 2-day course is being piloted this fiscal year. This course was developed to integrate physicians, practitioners, nurses, and other healthcare providers, as well as other

disciplines in the healthcare field to the practical aspects of initial hospital management of irradiated and/or contaminated patients through lectures and hands-on practical exercises.

The course will focus on the fundamentals of radiobiology along with the medical care and management of patients involved with radiological and/or nuclear incidents. Topics include radiation physics; radiation detection/measurement/ identification; early evaluation and treatment of the acute radiation syndrome (ARS), and cutaneous injuries, contamination control; and mitigating risks to patients, providers, and facilities.

- Orlando Health has been chosen to host.
- The course will be held June 24-25, 2024

- FY2024 RITN Biennial Workshop
  - Planning Committee
    - Named in November 2023 and continues to plan for the July 9-10, 2024 Workshop.
    - Members representing RITN hospitals: Children's Mercy Hospital, Dana Farber Cancer Institute, Duke University, Emory University, Massachusetts General, Mayo Clinic Rochester, MD Anderson, Roswell Park Comprehensive Cancer Center, Rush University Medical Center, Stanford-Pleasanton, University Hospitals Seidman Cancer Center, University of Utah, University of Virginia, and West Virginia University Hospitals.
    - Members representing federal partners: the Administration for Strategic Preparedness and Response (ASPR), Armed Forces Radiobiology Research Institute (AFRRI), Association of State and Territorial Health Officials (ASTHO), Biomedical Advanced Research and Development Authority (BARDA), National Association of County and City Health Officials (NACCHO), and the National Institute of Allergy and Infectious Diseases (NIAID)/National Institutes of Health (NIH).
  - Abstracts for both the Operations Track and the Research Track were accepted January 22, 2024 through March 1, 2024.
    - The Operations and Research Tracks each received 12 abstracts, respectively.
  - Registration opened April 1, 2024.

Hospital radiation disaster preparedness

- Annual disaster readiness tabletop exercises (drills) will be scheduled for current RITN hospitals to participate for their annual task completion. Six sessions will be offered between June and August 2024.
- The Situation Manual (SitMan) will be released mid-April to allow hospitals time to determine which session they will participate in. Registration opens May 1, 2024.
- Additional disaster readiness exercises (drills) have yet to be scheduled: Saipan exercise and training, two Functional exercises, two Regional Tabletop exercises, one hospital coalition Tabletop exercise, and one exercise to be determined.

Hospital network growth

- Appropriate growth helps ensure support of the vision and needs of the Department of Defense-Office of Naval Research as well as the Department of Health and Human Services Administration for Strategic Preparedness and Response plans for response to a radiological/nuclear disaster with-in the continental U.S.
  - Targeted hospitals in the following cities:
    - Nashville, TN
    - Los Angeles, CA
    - San Antonio, TX

        - Memphis, TN
        - Phoenix, AZ
        - New Orleans, LA
        - Albuquerque, NM
    - Specific hospitals
        - Children's Hospital Los Angles (CHLA)
        - Corewell East Beaumont Children's Hospital (Royal Oak, MI)
        - St. David's Medical Center (Austin, TX)

Federal partnership development

- Association of Healthcare Preparedness Professionals (AHEPP)
    - AHEPP's mission is to provide healthcare and other preparedness professionals with opportunities for networking, resource sharing, continuing education, and scholarly exchange (ahepp.org).
    - RITN attended to network and further relationships with current hospital emergency managers as well as use the opportunity to recruit new hospitals for growth.
- National Association of County and City Health Officials (NACCHO) Preparedness Summit
    - The NACCHO Preparedness Summit's theme is "Public Health, Healthcare, and Emergency Management: Aligning to Address Cascading Challenges," and will provide an opportunity for sectors to come together, align missions, and discover better ways to work as true partners to meet the challenges of today and tomorrow.
    - RITN is a member of the Radiation Workshop Planning Committee which conducted a 1-day radiation-specific planning workshop Sunday, March 24, 2024, and over 100 people attended.

Specific Aim 2: Development of Science and Technology for Rapid Identification of Matched Donors

Activity 2-1: Expand the genetic diversity of the registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies

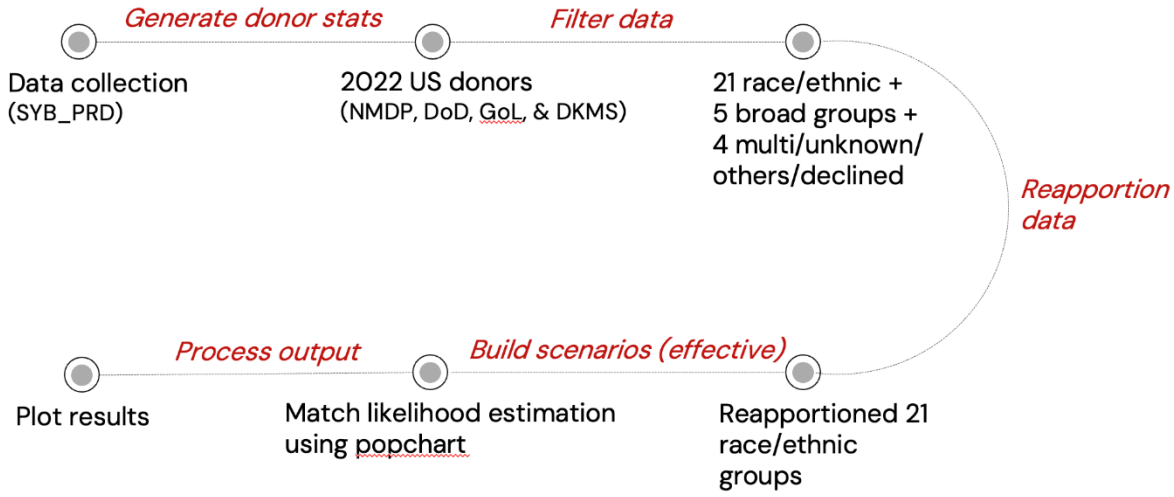
During the past quarter, a total of 45,002 newly registered volunteer donors were HLA typed and added to the NMDP Registry.

Activity 2-2: Modeling and analysis of registry coverage for the Warfighter

This quarter, efforts to increase the flexibility of the registry modeling codebase to handle more scenarios (number of matches or mismatches out of total HLA allele number) continued. Match rates down to the 5/8 level were calculated for all populations for the donor registry. Additional validation methods are being investigated. Donor availability statistics were refreshed from the last two years of data, and differences

were explored. An end-to-end pipeline for registry modeling was established with the following steps (Fig 1).

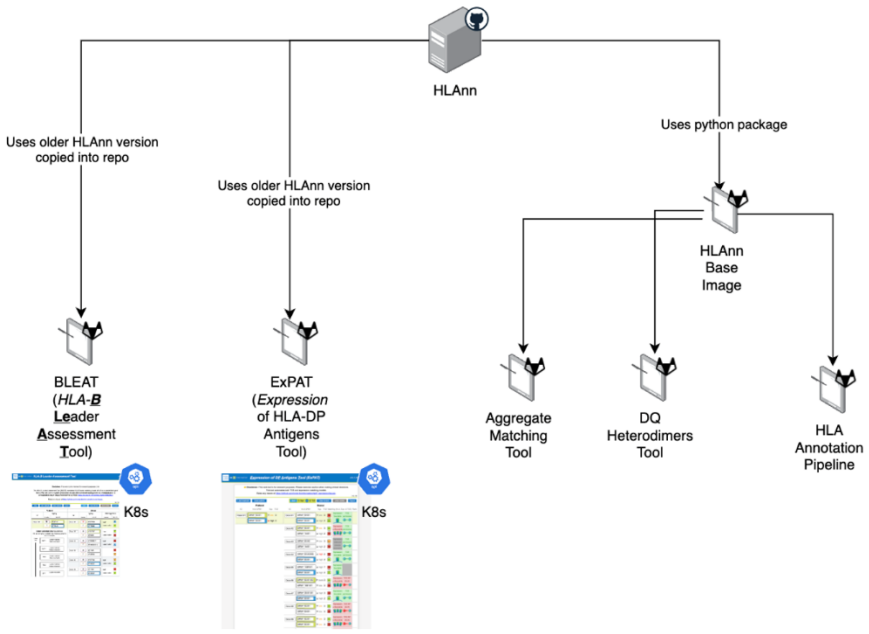
Fig 1: Registry modeling pipeline from generation of donor statistics to match rate model outputs with applied scenarios across diverse race and ethnic groups.



Activity 2-3: Development of science and technology for rapid communication of HLA data

A pilot for management and traceability of datasets was implemented using the Data Build Tool (DBT) platform. Improvements to py-ard services for HLA annotation and data handling were made to include capabilities for serology and x-s codes. Additional features added to the HLA Annotation Pipeline include annotation of non-classical genes and their sequences within the MHC, DQA1 imputation via DRB1, and detection of unsupported trans-dimers for DQ (Fig. 2, next page).

Fig. 2: HLA annotation pipeline



Activity 2-4: Use of population genetics and machine learning to automate the donor selection process

An abstract was accepted for presentation at the European Blood and Marrow Transplant (EBMT) conference on "An AI model to optimize donor selection using a contemporary dataset". This study applies a variety of machine learning methods to a large (> 30,000) patient cohort that spans both related and unrelated donors in a matched and mismatched setting. The main finding is that in most cases an unrelated donor is a better option than an HLA mismatched relative. This is demonstrated by evaluating the model and the full list of potential donors for patients transplanted during the interval 2016-2019. The abstract was accepted for an oral presentation and was scored among the top 100 abstracts.

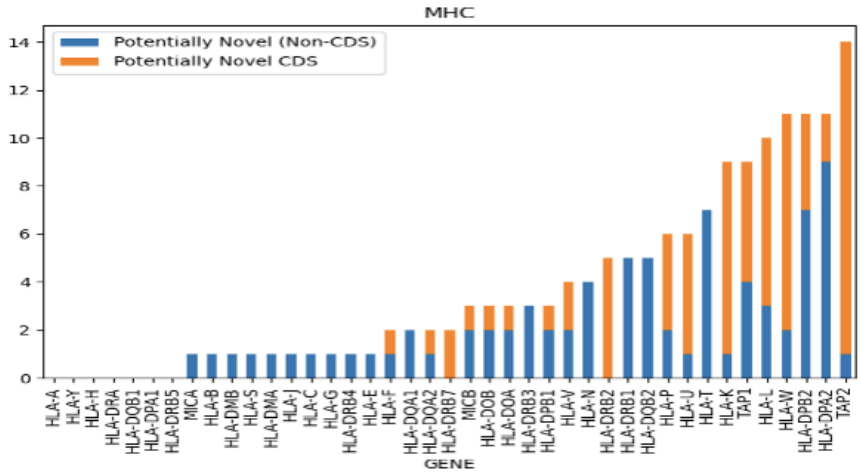
Specific Aim 3: Perform Immunogenetic and Genomic Studies in Transplantation and Cellular Therapy

Activity 3-1: 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

During the last quarter, a small pilot was conducted to evaluate the ability to generate and evaluate novel immunogenetic data on transplant donor and recipient pair samples. Eight samples were selected for full genomic sequence typing of the Major Histocompatibility Complex (MHC), Leukocyte Receptor Complex (LRC), and Killer Cell Immunoglobulin-like Receptors (KIR). Exploration of this data identifies potential novel alleles and areas of currently unknown impact on HCT. The number of potential novel alleles identified with this sequencing is shown in Figures 3 and 4 below.

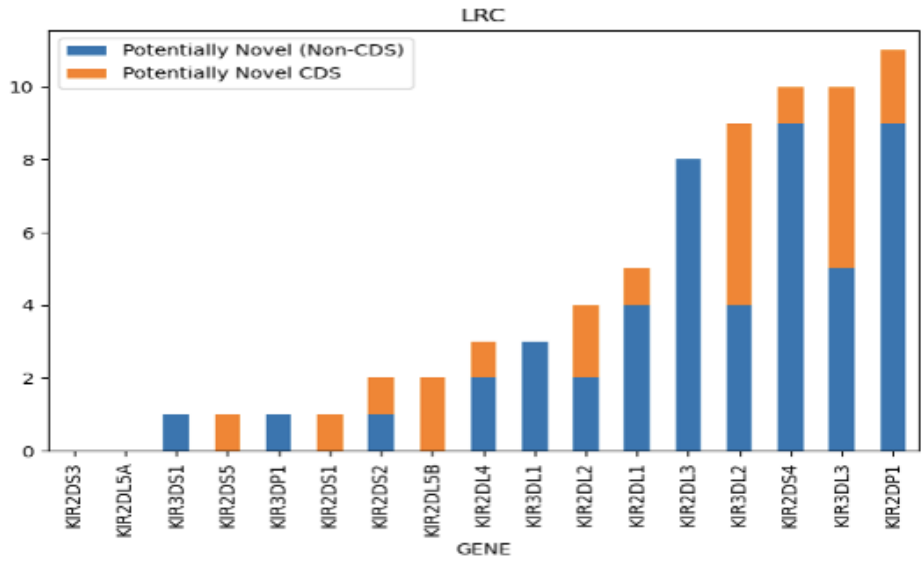
A set of 500 samples (200 Donor-Recipient pairs) will be selected next quarter for further detailed sequencing of novel regions in the MHC and LRC. Reference quality phased sequences of the MHC and LRC are expected from the selected vendor. Deliverables include fully phased sequences and highest resolution allele typing for all IPD-KIR genes (n=17) and all IPD/IMGT-HLA genes (n=45), including the non-HLA genes HFE, MICA/B, and TAP1/2; fully phased sequences for all LILR (n=13) and LAIR (n=2) genes in the LRC and the C4A/B genes in the MHC with variants called with respect to the reference gene sequences; for all of these genes the deliverables also include gene order without gene dropout and available phasing information. When appropriate, gene fusion and large structural variants (e.g. copy number variation) for the genes above will be highlighted and reported.

Fig. 3: Potential novel alleles in the MHC



Number of potentially novel alleles per gene

Fig. 4: Potential novel alleles in the LRC/KIR



Number of potentially novel alleles per gene

Meanwhile, ongoing audits continue to prepare HLA typing data from past sequencing efforts for use in further studies.

Activity 3-2: Development of a national framework to standardize measurable residual disease evaluation in the clinical care of patients receiving allogeneic transplant for acute myeloid leukemia

While allogeneic HCT is a curative therapy for many patients with acute myeloid leukemia (AML), the risk of relapse even after achieving a cytomorphological complete remission (CR) is the most common form of treatment failure and death. Transplant-related morbidity and mortality is a major obstacle for the effective use of alloHCT, resulting in the potential under- or over-utilization of conditioning regimen intensity to prevent AML relapse. The presence of residual leukemic burden, known as measurable residual disease (MRD), prior to transplant is associated with worse outcomes after transplantation. AML MRD testing is not standardized, and no clear path to translate findings from research laboratories to clinical transplant settings currently exists.

A multicenter prospective observational study was launched in 2022 to address this issue by developing a coordinated national framework to 1) allow collection of leftover initial AML diagnosis material from patients who have received alloHCT in US centers, 2) prospectively collect samples from AML patients after alloHCT to determine optimal timing and method for post-alloHCT MRD monitoring and 3) implement findings from phases 1 and 2, together with a central reference laboratory, to allow local centers to perform standardized MRD testing pre or post alloHCT. This would allow both selection of conditioning intensity, but also inform post-transplant maintenance and allow patient selection for novel clinical trials.

During the past quarter the protocol team continued to meet regularly to manage the IRB approved and ClinicalTrials.gov registered study protocol entitled, “MEASURE: Molecular Evaluation of AML patients after Stem cell transplant to Understand Relapse Events”. To date, 19 centers have committed to participate

in the study and combined plan to enroll >250 patients per year. All 19 sites have received local IRB approval for the protocol. Eighteen sites have fully opened the study and have enrolled a total of 151 patients through September March 2024.

Activity 3-3: Determine the impact of peripheral blood stem cell graft composition on the outcome of hematopoietic cell transplantation

While allogeneic HCT offers potentially curative therapy to patients with a variety of benign and malignant diseases, both acute and chronic GVHD continue to plague the field and often limit the longevity and quality of life for patients. The composition of PBSC grafts has been evaluated in multiple studies to attempt to discern associations between various cellular subsets and outcomes. The BMT CTN 0201 randomized trial of bone marrow versus PBSC found that PBSC grafts were associated with a higher risk of cGVHD and worse quality of life following unrelated donor HCT compared to BM. A correlative study of graft immunophenotype failed to identify any associations between PBSC graft composition and outcomes. However, the PBSC cohort included only 147 evaluable products limiting the power to evaluate various cellular subsets. The association between PBSC graft immunophenotype and outcomes remains unclear.

The primary aim of this study is to evaluate PBSC graft stem cell and associated immune cell composition and to determine at 12-months of follow-up how either the comprehensive graft cellular composition profile or specific graft composition elements influences the primary outcomes of time to neutrophil engraftment and overall survival. Secondary outcomes of interest include, but not limited to, incidence of acute and chronic GVHD, primary disease relapse, TRM, and DFS. The study will evaluate approximately 2,100 PBSC products over a 3-year accrual period with 1,100 collected in the U.S. through the NMDP and an additional 1,000 collected in Germany for U.S. based patients through the DKMS. The U.S. testing will be supported through the ONR (prior grant years and the current) and DKMS will support testing of German collected products. Data will be merged with CIBMTR collected clinical outcomes for analysis and correlation with clinical outcomes.

During the past quarter accrual continued for U.S. based donors. A total of 638 product samples were received and tested through March 31, 2024, with 71 tested in the last quarter. Preliminary analyses focused on graft composition correlation with donor characteristics and the impact of cryopreservation are underway. Initial results on the association of donor characteristics with graft composition will be presented as an oral abstract at the 2024 EBMT annual meeting and on the impact of cryopreservation will be presented at the 2024 European Federation of Immunogenetics (EFI) annual meeting.

- MAIT Cell Frequencies within PBSC Grafts Are Associated with Donor CMV Serostatus and Age: An Initial Analysis from the DKMS and NMDP Graft Composition Study (EBMT 2024)
- Cryopreservation Changes the Immune Effector Cell Composition of Peripheral Blood Stem Cell Grafts: An Analysis from the DKMS and NMDP Graft Composition Study (EFI 2024)

Activity 3-4: Determine the impact of non-HLA genes and gene expression on allogeneic cell transplantation

During the past quarter we completed an analysis of genomic sequencing of the KIR region using data from the human pangenome sequencing consortium and computational tools for comparing structural variation in genomes across populations (the pangenomics research toolkit). This work was submitted to the 2024 KIR Workshop as an abstract entitled “Pangenome Analysis of the KIR-Locus for 246 Haplotypes".

We completed a long reads-based MHC/LRC assembly/variant calling/phasing pipeline, and its performance has been tested with benchmark data from the Genome in a Bottle consortium project and KIR data from our laboratory partners.

This quarter, we also published the manuscript entitled "Donor germ-line variants associate with outcomes of allogeneic HSCT in patients with MDS" in American Journal of Hematology on 2024 Feb 9 https://pubmed.ncbi.nlm.nih.gov/38339773/.

Another manuscript entitled "Proteomics to predict relapse in patients with myelodysplastic syndromes undergoing allogeneic hematopoietic cell transplantation" was also published in *Biomarker Research* on 2024 Jan 25 https://pubmed.ncbi.nlm.nih.gov/38273355/

Specific Aim 4: Conduct Observational and Prospective Clinical Trials in Transplantation and Cellular Therapy

Activity 4-1: Conduct clinical outcomes research using the CIBMTR research database and repository.

Observational Research

- Published 8 manuscripts in peer-reviewed journals during the last quarter (see publications below).
- A total of 26 abstracts were submitted presented to at the 2024 Tandem annual meetings held in San Antonio, TX, February 21-24, 2024. Presentation title and type [oral (N=10) or poster (N=16) abstract] are listed in the table below. Abstracts were published in a supplement to the journal Transplant and Cellular Therapy in February 2024.

Table. Presentations at the 2024 Tandem Annual Meeting

Title	***Status***
Age, Gvhd Prophylaxis, and Timing Matter in Thrombotic Microangiopathy after Hematopoietic Cell Transplantation- a Secondary CIBMTR Analysis	**Oral**
Sars-Cov-2 Vaccination in the First Year after Hematopoietic Cell Transplant or Chimeric Antigen Receptor T Cell Therapy: A CIBMTR and BMT CTN Study	**Oral**
Predictive Modeling of Donor Mobilization for Hematopoietic Cell Transplantation	**Oral**
Post-Transplant Cyclophosphamide Eliminates Disparity in GvHD-Free, Relapse-Free Survival and Overall Survival between 8/8 Matched and 7/8 Mismatched Unrelated Donor Hematopoietic Cell Transplantation in Adults with Acute Leukemia or MDS	**Oral**

Donor Search and Selection Strategy to Facilitate Comparable Transplant Rates across Donor Search Prognosis Groups: A Report from the BMT CTN 1702 Trial	**Oral**
RGI-2001 with CNI-Based Prophylaxis Demonstrates Better Acute Gvhd-Free Survival Following Myeloablative Allohct without Increased Relapse: Comparison of a Multi-Center Phase 2b Study with a Contemporaneous CIBMTR Cohort	**Oral**
Graft Vs Host Disease (GVHD) in Pediatric Hematopoietic Stem Cell Transplant (HCT) Recipients and Impact on Overall Survival: A CIBMTR Analysis	**Oral**
Outcomes of Large B-Cell Lymphoma (LBCL) Patients with Secondary Central Nervous System Involvement Following Chimeric Antigen Receptor T-Cell Therapy: A CIBMTR Analysis	**Oral**
Calcineurin Inhibitor-Free Graft-Versus-Host Disease (GVHD) Prophylaxis in Hematopoietic Cell Transplantation (HCT) with Myeloablative Conditioning Regimens (MAC) and HLA-Matched Donors: Long Term Follow up of BMT CTN 1301 Progress II Trial	**Oral**
Monoallelic Germline Pathogenic Variants in DNA Damage Repair Genes and Their Impact on Post-Hematopoietic Cell Transplantation Outcomes in Severe Aplastic Anemia	**Oral**
What Do Pediatric Transplant Physicians Think about Palliative Care? Results from a National Survey	**Poster**
Real World Outcomes of Older Adults and Frail Patients with Relapse/Refractory Multiple Myeloma Receiving Idecabtagene Vicleucel	**Poster**
Discovery Proteomics for Analytes to Predict Outcomes after Hematopoietic Stem Cell Transplantation: A Real World Experience from BMT-CTN-1202	**Poster**
Assessment of HLA-DQ Genetic Variation with an HLA-DQ Heterodimers Tool and Implications in Clinical Transplantation	**Poster**
Housing, Finances and Employment Post-Allogeneic Hematopoietic Cell Transplant: Caregiver Perspectives	**Poster**
Development of a Continuous Dissemination and Implementation Process for Tct Research	**Poster**
Age-Related Differences in Utilization of Allogeneic HCT for Acute Myeloid Leukemia in California: Results of a Population-Based, Novel Linked Dataset	**Poster**
Social Determinants of Health, Disease, and Treatment Related Characteristics of Access Clinical Trial Participants	**Poster**
Factors Associated with Treatment Receipt in Medicare Beneficiaries Diagnosed with Acute Myeloid Leukemia	**Poster**

Patient Perspectives on Post-Allogeneic Hematopoietic Cell Transplant Caregiver Requirements	**Poster**
Exploring Access to Allogeneic Hematopoietic Cell Transplantation: Relationships between County-Level Social Vulnerability, Physician Density, and Transplant Unmet Need across the United States	**Poster**
Risk Factors for Solid Organ Graft Failure and Death in Solid Organ Transplant Recipients Undergoing Hematopoietic Cell Transplantation: A Center for International Blood and Marrow Transplant Research Study	**Poster**
CD19-Directed CART Therapy for T Cell/Histiocyte Rich Large B-Cell Lymphoma: A CIBMTR Analysis	**Poster**
Identification of Pre-Treatment Clinical Risk Factors Predictive of Inferior Survival and Increased Risk of Treatment Failure in CD19 Chimeric Antigen Receptor T Cell Recipients with Large B Cell Lymphoma	**Poster**
Real-World Treatment Patterns and Outcomes of Patients with Large B-Cell Lymphoma (LBCL) Who Received Loncastuximab Tesirine Prior to Chimeric Antigen Receptor T-Cell (CAR-T) Therapy	**Poster**
Novel Molecular Biomarkers Prognostic of Relapse after Allogeneic Hematopoietic Stem Cell Transplantation in Patients with Myelodysplastic Neoplasms (MDS)	**Poster**

Research data collection and systems enhancements
During the past quarter, CIBMTR continued support for electronic data submission initiatives, production FormsNet[SM] Recipient, FormsNet[SM] Donor, and AGNIS customers, as well as Data Warehouse users. Progress has been made on the following critical projects to upgrade our technology supporting the program:

Simplify Data Acquisition
To acquire timely, high quality, data with less administrative burden to current and new partners/patients.

FormsNet3[SM] (FN3)
Continued the quarterly releases of recipient form revisions to be current with existing treatment practices, as well as implemented revisions of forms to support the cellular therapies registry. Completed and in-process enhancements within Data Capture applications include:

- Functionality to disable diagnosis questions when a subsequent infusion for the same disease has been previously reported.
- Updates to support RITN forms, which will be released April 19, 2024. Enhanced mechanisms used during user's login to reduce multiple calls and improve login processing speed. Enhancement to cellular therapy database tables to better link multiple products
- Fixes to form 4003 to ensure that the correct number of forms are created from multiple instances on form 4000, and that the auto population on 4003 occurs correctly.

- Donor Center Forms Due performance improvements
- IDM test result automation
- Developed and tested the following forms that were released in January 2024:

Form	Form Name	Category
254R2	Mogamulizumab (Poteligeo) Supplemental Data Collection Form	Revised Recipient Form

Electronic data submission/AGNIS
CIBMTR continued support for electronic data submission initiatives and production AGNIS customers. Effort focused on support for CIBMTR form revision updates to existing forms.

- Recent AGNIS and other electronic data submission accomplishments:
    - Collaboration with the FormsNet team regarding ISCN submission via AGNIS to ensure functionality is the same as FormsNet
- The AGNIS team continues to release forms for centers to use in data submission to the CIBMTR as well as address questions or issues raised by centers and their vendors.
    - One AGNIS form was released to production:
        - 4003r5 Cellular Therapy Product
    - One AGNIS form was released to external test and is awaiting external partner testing before it will move to production:
        - 4001r1 Pre-Cellular Therapy Baseline Data

Automated data exchange using electronic data collection systems that interface directly with source health and laboratory records
CIBMTR has continued to update its reporting application to exchange additional discrete electronic data records. Using the data extracted directly from data collection systems at partner centers, CIBMTR further expanded capabilities to populate additional laboratory data points on 29 forms at both pre-infusion and post-infusion time points. These expanded capabilities provide partner transplant centers with improved time savings and eliminate the potential of manual data entry errors. The underlying structures for data exchange and storage were updated based on current standards – these updates are the foundation upon which we will be able to expand the types of data that can be exchanged electronically.

Simplify Data Analysis
Collect & analyze more data more frequently without increasing the burden on centers.

Integrated Data Warehouse (IDW)
CIBMTR continued to increase the capabilities of the IDW, which is the Operational Data Warehouse utilized for delivery of key data to stakeholders. Accomplishments include:

- Incorporated ongoing forms revisions into the warehouse
- Continued enhancing processes to support CIBMTR's Domestic and International CPI Processes.
- Completed the annual Center Volumes Data Reporting project for 2023
- Continued enhancing study information and visualizations to support our Clinical Research Outcomes team.
- Enhanced Sample Inventory data reporting dashboards with data from other CIBMTR systems
- Provided Cord Blood Banks a new patient level supplemental report in the Quarterly Cord Blood Quality Report
- Extended Survivorship Plan project to additional external centers

- Began planning to integrate the Veeva clinical data management system into NMDP systems.
- Completed development of additional Quality Control reports for internal partners.
- Provided variable-specific audit instructions for Japanese Data Center Hematopoietic Cell Transplantation.

Unified Domain Model (UDM)
Continuing the process of building this single source of truth of data that will contain high quality, validated data readily available to researchers for immunobiology, outcomes, and other types of analyses.

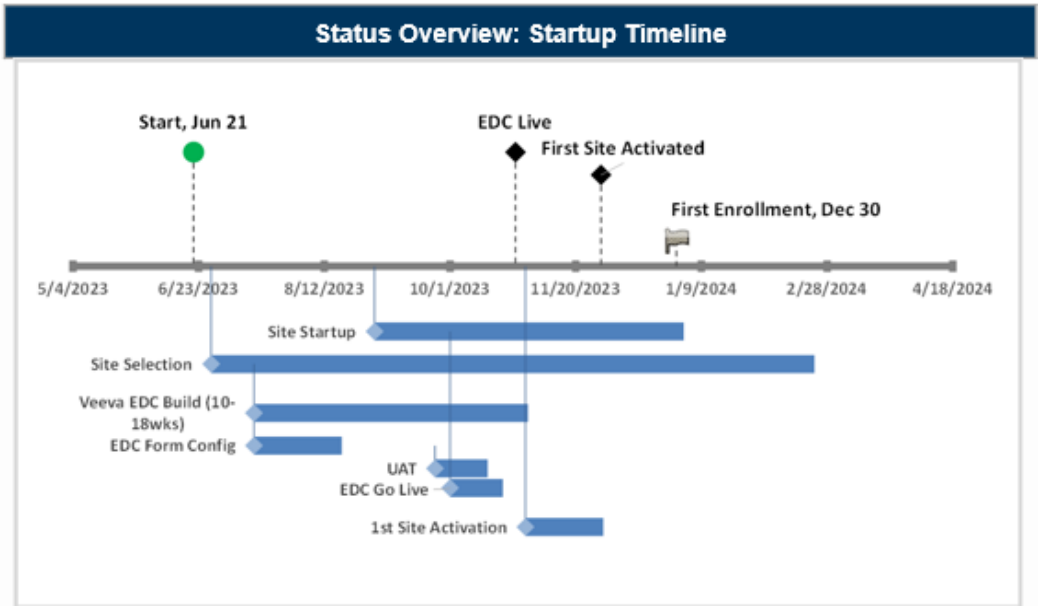
- Continued transitioning HCT data from the Research Database to the Unified Domain Model (UDM) including regular delivery of monthly data extracts directly from UDM comprised of thousands of patient outcome variables for statistical analysis.
- Continued development of discrete data domains focused on relapse, GVHD, infection, engraftment, lines of therapy, and numerous disease-specific data sets.
- Continued delivery of monthly and quarterly CAR T-cell data sets to our Japanese (JDCHCT) and pharmaceutical partners.
- Continued refinement and delivery of Periodic Safety Update Reports (PSUR) for CAR T-cell therapies.
- Provided quarterly Stem Cell Therapeutic Outcomes Data required for the HRSA SCTOD quarterly report.

Enhance Data Sharing and Visualization
Deliver data visualization and analytic tools that will enable stakeholders to more efficiently interact with data to identify relevant trends and patterns.

- The 1-year Survival Outcomes Calculator received an annual update and includes new variables
- The Center Performance Analytics (CPA) application received an annual update. The data focuses on first allogeneic transplants with at least 1 year of follow-up data for the years 2019 through 2021. In addition to new data, the update included new variables and charts
- The Data for RFI application received an annual update with data focusing on the years 2020 through 2023

Activity 4-2: Conduct clinical trials on the use of HLA mismatched graft sources to expand access to all patients in need of allogeneic cell transplantation

During the last quarter, work continued on the activation of a new prospective clinical trial protocol designed to build upon the successful MMUD post-transplant cyclophosphamide platform (timeline below). The study protocol entitled, "OPTIMIZE: A Phase II Study of Reduced Dose Post Transplantation Cyclophosphamide as GvHD Prophylaxis in Adult Patients with Hematologic Malignancies Receiving HLA-Mismatched Unrelated Donor Peripheral Blood Stem Cell Transplantation" was approved by the NMDP IRB in September 2023. The study will enroll up to 170 subjects at up to 50 participating sites with a goal of activating 20 sites by the end of September 2024. Ten sites were activated, and 11 subjects enrolled through the end of March 2024. Funds from this grant will support protocol defined correlative studies to evaluate immune reconstitution and explore mechanisms of relapse post-transplant.


Status Overview: Startup Timeline
Start, Jun 21
EDC Live
First Site Activated
First Enrollment, Dec 30
5/4/2023
6/23/2023
8/12/2023
10/1/2023
11/20/2023
1/9/2024
2/28/2024
4/18/2024
Site Startup
Site Selection
Veeva EDC Build (10-18wks)
EDC Form Config
UAT
EDC Go Live
1st Site Activation

Publications

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