HLA_SAVE: A wealth of transplant-associated immunogenetic data

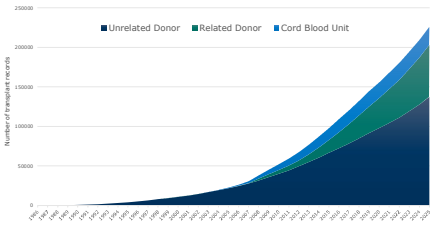
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CIBMTR is a research collaboration between the Medical College of Wisconsin and NMDP.

BACKGROUND

- HLA_SAVE is a cumulative dataset containing immunogenetic and demographic information of all allogeneic hematopoietic cell transplants (HCT) reported to the CIBMTR Outcomes Database.
- Supports the study of immunogenetic factors alone or as a variable in HCT outcomes when linked with CIBMTR data.
- Serves as the comprehensive source of data for CIBMTR studies.
- Includes over 300,000 related and unrelated donor and cord blood transplants from 1989 to present.
  - Over 308,000 observations
  - ~228 variables
- Used in seminal research toward establishment of HLA match guidelines (see 'Selected Key Research').

Figure 1: Size and composition of HLA_SAVE by year. Records for transplants with validated HLA match data of minimum n/6 are included.



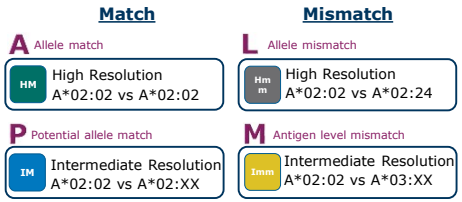
HLA_SAVE AND THE CIBMTR BIOREPOSITORY

- Samples from the CIBMTR Biorepository leverage HLA_SAVE for projects examining donor and recipient factors influencing transplant outcomes.
- The CIBMTR Biorepository contains paired samples from nearly 53,000 unrelated, 14,000 related, and 6,600 CBU transplants.
- There are currently over 4 million stored sample aliquots including:
  - **Non-viable samples (-80°C):** Granulocytes, peripheral blood mononuclear cells, Beta lymphoblastoid cell lines, whole blood, serum, plasma, and purified DNA
  - **Viable samples (-196°C):** Peripheral blood mononuclear cells, beta lymphoblastoid cell lines, and whole blood with DMSO

RESEARCH MATCH GRADE (MG)

- Research match grade (MG) describes the level of immunogenetic similarity between donor and recipient *at each allele*. Possibilities are:
  - High resolution match (HM) or mismatch (Hmm)
  - Intermediate resolution match (IM) or mismatch (Imm)
- MG at each locus are used to calculate the MG variable (MGV) (i.e. n/6, n/8, n/10, n/12).
- py-ard, developed by NMDP[SM] Bioinformatics, uses the most recent IMGT release to reconcile HLA nomenclature and reduce ambiguity to the antigen recognition domain (ARD) to assign MG and calculate MGV.
- This approach allows for consistent application of match criteria across studies.

Figure 2: Comparison of MG assigned by py-ard (squares) with Haplogic search algorithm predictions (purple).



COMPOSITION OF UNRELATED DONOR HIGH RESOLUTION MGV IN HLA_SAVE

Figure 3:Match grade variables of unrelated donor HCT in HLA_SAVE. Single-product HCT pairs with high resolution typing at A) HLA-ABCDRB1 (n=125,356), B) HLA-ABCDRB1DQB1 (n=122,616), and C) HLA-ABCDRB1DQB1DPB1 (n=97,556) are shown.

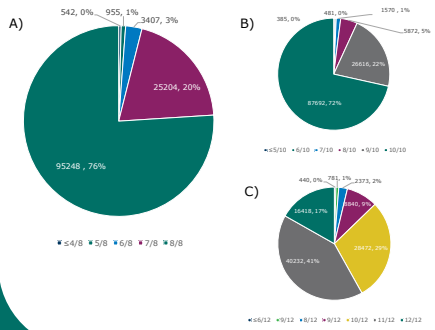
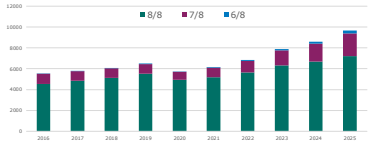


Figure 4: Transplant match grade by year



ENRICHMENT OF DATA THROUGH RETROSPECTIVE TYPING

- Donor-Recipient Pairs Project (DRPP) is a retrospective typing initiative to enrich the quality of transplant-associated immunogenetic data.
- Data are incorporated into HLA_SAVE for use in future studies surrounding impact of HLA and other immunogenetic factors in transplant outcomes.
- Currently includes >50,000 pairs typed including 24,000 ABO and CCR5 and 22,000 KIR presence/absence (P/A).

KIR_SAVE

- Like HLA_SAVE, KIR_SAVE is a cumulative dataset containing KIR typing that include P/A, high resolution, and copy number variation (CNV) for transplant pairs.
- KIR are receptors on NK cells and their ligands are particular groups of HLA Class I molecules, especially HLA-C and some HLA-A/B epitopes.
- KIR–HLA matching can be assessed by scoring the presence or absence of individual KIR ligands, determination of KIR haplotypes, or Bx content (B haplotype gene content).
- This data is scored for over 19,500 related and 3,000 unrelated donor and cord blood transplants from 1989 to 2018.

Table 1:HLA-KIR scoring of HCT transplants.

HLA-KIR Scoring
Presence of HLA epitopes
KIR Haplotypes
Bx Content
KIR Ligand Match Grades

SELECTED KEY RESEARCH USING HLA_SAVE

1. Flomenberg N et al. Impact of HLA class I and class II high-resolution matching on outcomes of unrelated donor bone marrow transplantation: HLA-C mismatching is associated with a strong adverse effect on transplantation outcome. Blood. 2004 Oct 1; 104(7):1923-30.
2. Lee SJ et al. High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. Blood. 2007 Dec 15; 110(13):4576-83.
3. Dehn J et al. Selection of unrelated donors and cord blood units for hematopoietic cell transplantation: guidelines from the NMDP/CIBMTR. Blood. 2019 Sep 19; 134(12):924-34.

DISCLOSURE

There are no relevant conflicts of interest to disclose.

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