ANZTCT ASM 2026

Integrating High-Resolution HLA Genotyping and HLA Antibody Data for Unrelated & Haploidentical Haematopoietic Stem Cell Therapy

ANZTCT Database Modernisation Proposal 2026

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Overview of Existing ANZTCT Registry Data Collection: HLA matching and donor source

11. Donor-recipient relation:

- ☐ syngeneic
- ☐ HLA-identical sibling (includes non-monozygotic twin)
- ☐ HLA-matched other relative*
- ☐ HLA-mismatched other relative*
  - ☐ 1 HLA mismatch
  - ☐ ≥2 HLA-mismatch
  - *Specify relation: _____
  - **Haploidentical?** ☐ Yes ☐ No
- ☐ Unrelated - Donor registry country _____

Complete HLA table for unrelated & mismatch related donors

A	B	C	DRB1	DQB1	DPB1	
						Antigenic
						Allelic

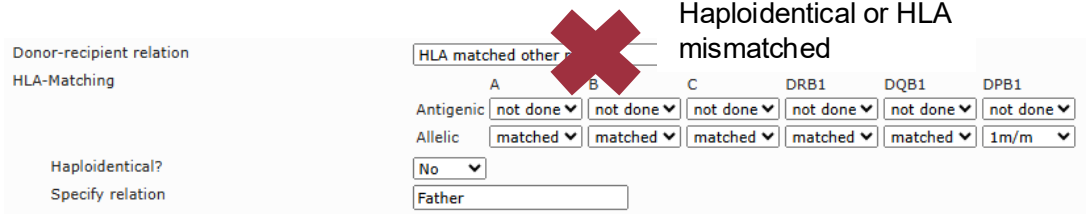
0=matched, 1=1m/m, 2=2m/m, ND=not done

Stem cell source	peripheral blood
Donor-recipient relation	2 or more HLA mismatched relative
HLA-Matching	

	A	B	C	DRB1	DQB1	DPB1
Antigenic	1m/m	matched	matched	1m/m	1m/m	1m/m
Allelic	1m/m	matched	matched	1m/m	1m/m	1m/m

Haploidentical?	Yes
Specify relation	Son

- HLA matching considered at HLA-A, -B, -C, DRB1 and DQB1, DPB1 excluded
- Inconsistencies with reporting haploidentical donor transplants
  - If not, all HLA loci are typed, an HLA matched relative may be haploidentical or mismatched
- No DSA data collected



Haploidentical or HLA mismatched

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Importance of Haploidentical Transplants for Identifying Haplotype-Level Genetic Differences

Haploidentical HCT provides a **natural experiment**:

- One shared haplotype, one mismatched
- Enables detection of haplotype-level genetic effects
- Reveals non-classical HLA and regulatory region influences
- Supports discovery of novel immunogenomic determinants
- Supports evaluation of new therapeutics (eg PT-Cy) in haploidentical settings

Gap: Australia currently does not capture high-resolution haploidentical HLA data nationally

Benefit: Australia can contribute unique, globally valuable haplotype-level insights.

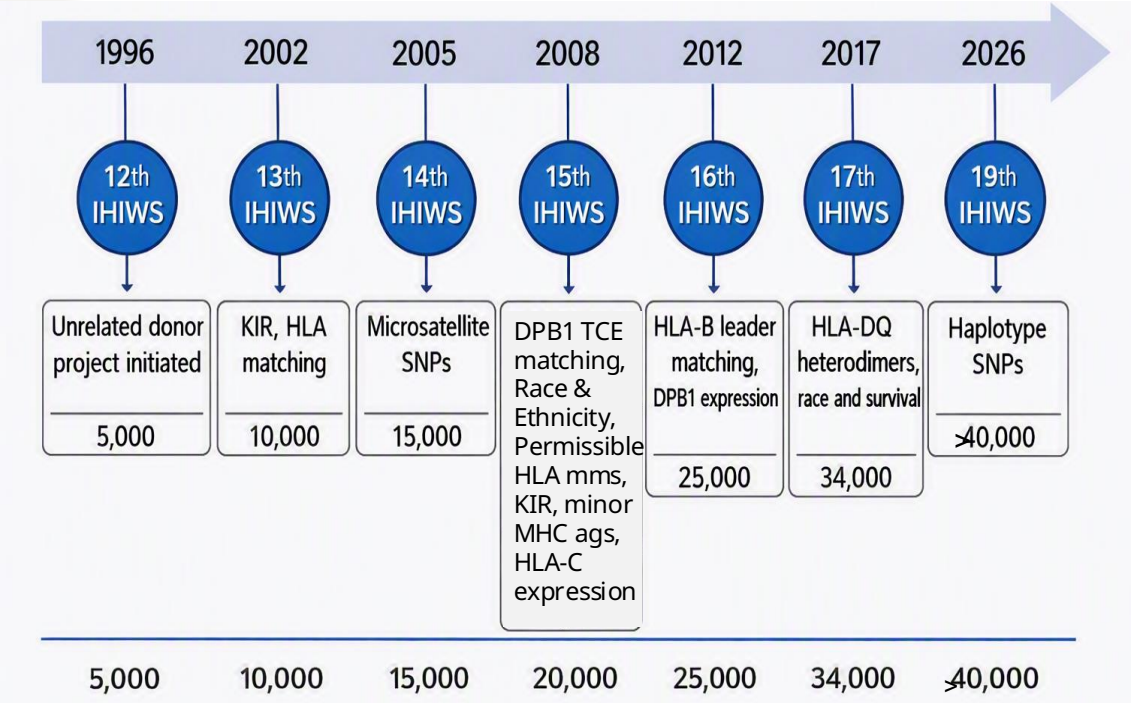
Why a single HLA and clinical outcome data registry database is critical

Clinical Practice and Research

- **Direct linkage of HLA, DSA, and clinical outcomes:** Enables real-time integration of immunogenetic and clinical data to correlate compatibility, antibodies, and post-transplant outcomes.
- **Accurate modelling of survival, relapse, GVHD, and graft failure:** Enables longitudinal and multivariate analysis across diverse cohorts to improve prognostic accuracy and evidence-based clinical decisions.
- **Machine-learning and AI predictive modelling:** Development of adaptive algorithms for donor selection, risk stratification, and personalized immunosuppression strategies.
- **Participation in international donor selection and transplant outcome studies:** Positions Australia within global collaborative networks such as IHIWS-HCT project and CIBMTR, enabling contribution to large-scale analyses and consensus standards.

International HLA & Immunogenetics Workshop-Haematopoietic Cell Transplant (IHIW-HCT) collaboration

- Clinical and HLA data from international transplant centres are used to evaluate the impact of HLA matching, non-HLA factors, permissible HLA mismatches, haplotype associated determinants, KIR genetics and novel transplant related factors.
- Australia has contributed 15 publications guiding clinical practice
- HLA data contributed on 4246 Australian unrelated donor transplants up until 2023 (~1000 for 2025/26 to collect and submit)
  - Represents ~10% of total international UD cohort



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Why a single HLA and clinical outcome data registry database is critical

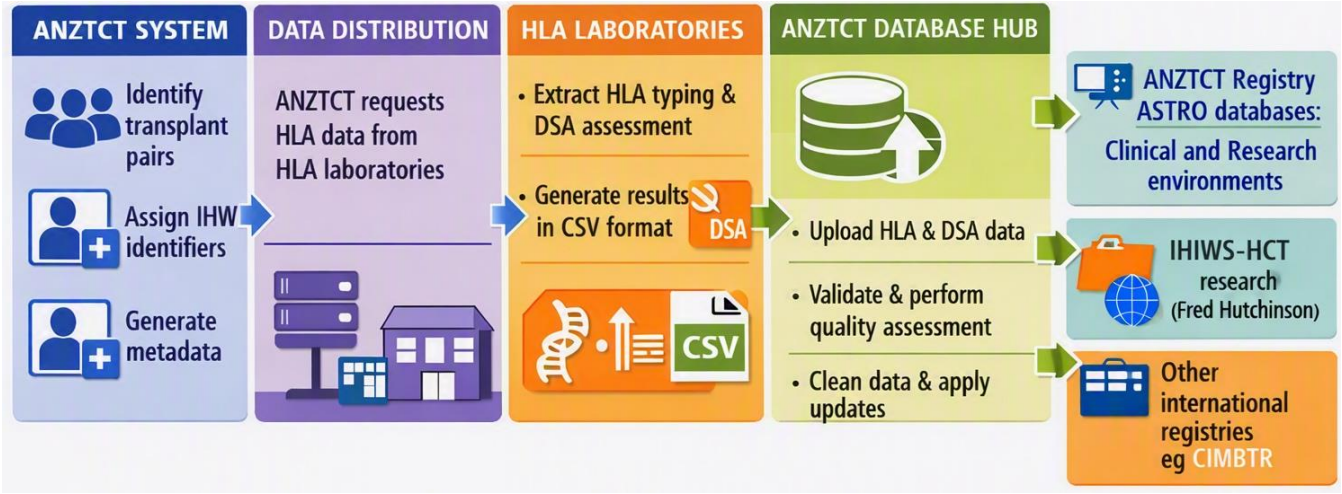
National benchmarking and auditing

- **National registry benchmarking and equity analysis:** Provides transparent, data-driven insights into access, outcomes, and resource allocation across institutions and demographic groups.
- **Compliance with accreditation authorities:** Maintains integrity, confidentiality, and auditability of sensitive health information.
- **Unified audit trails and nomenclature consistency:** Guarantees traceability of all data transactions and harmonization of HLA nomenclature, essential for reproducibility and cross-study comparability.

Project Aims and Methodology: Data integration

1. To establish a comprehensive, high-quality national registry database for Australia, integrating clinical outcomes and high-resolution HLA genotyping and HLA antibody data.

2. To replace all labour-intensive, manual data transfer process with an automated, accurate, and sustainable system aligned with international standards.



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Expected Data Outputs providing high resolution matching status from HLA laboratories

	Transplant Type	HLA-A	HLA-A	HLA-B	HLA-B	HLA-C	HLA-C	DRB1	DRB1	DRB3	DRB3	DQB1	DQB1	DQA1	DQA1	DPB1	DPB1	DPA1	DPA1
Patient 1	Haploidentical	01:01:01	24:02:01	15:01:01	39:01:01	03:03:01	07:02:01	01:01:01	13:01:01	01:01:02		05:01:01	06:03:01	01:01:01	01:03:01	04:01:01	04:01:01	01:03:01	01:03:01
Donor 1		01:01:01	01:01:01	08:01:01	08:01:01	07:01:01	07:01:01	03:01:01	11:01:01	01:01:02	02:02:01	02:01:01	03:01:01	05:01:01	05:05:01	02:01:02	04:02:01	01:03:01	01:03:01
Matching Grade		1	1	1	1	1	1	1	1			1	1	1	1	1	1	1	1
Patient 2	HLA Mismatched Relative	01:01:01	68:02:01	08:01:01	53:01:01	04:01:01	07:01:01	03:01:01	13:02:01	01:01:02	03:01:01	02:01:01	06:04:01	01:02:01	05:01:01	04:01:01	06:01:01	01:03:01	01:03:01
Donor 2		02:01:01	68:02:01	08:01:01	53:01:01	04:01:01	07:01:01	03:01:01	13:02:01	01:01:02	03:01:01	02:01:01	06:04:01	01:02:01	05:01:01	04:01:01	06:01:01	01:03:01	01:03:01
Matching Grade		1	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0
Patient 3	HLA Mismatched Relative	01:01:01	68:02:01	08:01:01	53:01:01	04:01:01	07:01:01	03:01:01	13:02:01	01:01:02	03:01:01	02:01:01	06:04:01	01:02:01	05:01:01	04:01:01	06:01:01	01:03:01	01:03:01
Donor 3		02:01:01	68:02:01	08:01:01	35:01:01	04:01:01	07:01:01	03:01:01	13:02:01	01:01:02	03:01:01	02:01:01	06:04:01	01:02:01	05:01:01	01:01:01	06:01:01	02:01:01	01:03:01
Matching Grade		1	0	0	0	0	0	0	0			0	0	0	0	1	0	1	0
Patient 4	HLA Matched	01:01:01	30:04:01	08:01:01	49:01:01	07:01:01	07:01:02	03:01:01	11:01:02	03:01:01	03:01:01	02:01:01	03:01:01	05:01:01	05:05:01	02:01:02	04:02:01	01:03:01	01:03:01
Donor 4		01:01:01	30:04:01	08:01:01	49:01:01	07:01:01	07:01:02	03:01:01	11:01:02	03:01:01	03:01:01	02:01:01	03:01:01	05:01:01	05:05:01	02:01:02	04:02:01	01:03:01	01:03:01
Matching Grade		0	0	0	0	0	0	0	0			0	0	0	0	0	0	0	0
Patient 5	HLA Matched	01:01:01	30:04:01	08:01:01	49:01:01	07:01:01	07:01:02	03:01:01	11:01:02	03:01:01	03:01:01	02:01:01	03:01:01	05:01:01	05:05:01	02:01:02	04:02:01	01:03:01	01:03:01
Donor 5		01:01:01	30:04:01	08:01:01	49:01:01	07:01:01	07:01:02	03:01:01	11:01:02	03:01:01	03:01:01	02:01:01	03:01:01	05:01:01	05:05:01	01:01:01	04:02:01	02:01:01	01:03:01
Matching Grade		0	0	0	0	0	0	0	0			0	0	0	0	1	0	1	0

	Transplant Type	Match Status 8/8	Match Status 10/10	Match Status 12/12	DPB1 TCE Model	DPB1 expression	HED Score	HLA-B Leader	DQ Dimer
Tx Pair 1	Haploidentical	4/8	5/10	6/12	?	?	?	?	?
Tx Pair 2	HLA Mismatched Relative	7/8	9/10	11/12	?	?	?	?	?
Tx Pair 3	HLA Mismatched Relative	7/8	9/10	9/12	?	?	?	?	?
Tx Pair 4	HLA Matched	8/8	10/10	12/12	?	?	?	?	?
Tx Pair 5	HLA Matched	8/8	10/10	11/12 (Perm TCE)	?	?	?	?	?

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Conclusions: Why This Proposal Must Be Supported

- **Australia's transplant data is fragmented** — limiting safety, equity, benchmarking, and national planning.
- **A unified HLA + DSA + outcomes registry is now critical infrastructure** for modern HCT.
- **Enables real-time national visibility** of trends, gaps, and resource needs for health-system planning.
- **Reduces manual reporting burden** for contributors and strengthens accreditation and compliance.
- **Transforms high-resolution HLA and outcome data into a national strategic asset** for precision donor selection and predictive modelling.
- **Positions Australia as a global leader** in immunogenomics and international transplant research.

Acknowledgments

- ANZTCT
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- Australian Transplant centres
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How Complete Registry Databases Enable Evidence-Driven Transplant Practice

High-quality registries such as CIBMTR demonstrate that when clinical, HLA, and outcome data are captured in a single, validated system, it becomes possible to:

- Identify factors that influence transplant outcomes
- Benchmark performance across centres and populations
- Develop evidence-based clinical practice guidelines
- Support precision medicine and predictive modelling
- Ensure equitable access and inform health-system planning

Australia needs a similarly complete, integrated registry to achieve these capabilities.

Overview of Existing ANZTCT Registry Data Collection: Current Constraints and consequence of gaps

Australia's current transplant data landscape is **fragmented**:

- Clinical outcomes stored separately from HLA genotyping
- No national system linking high-resolution HLA + HLA DSA + clinical outcomes
    - Incomplete donor selection evidence
    - Limited ability to analyse allele-level mismatches
    - No national visibility of DSA impact
- Missed opportunities for immunogenomic discovery
- Inability to meet international registry standards (CIBMTR, EBMT)
- Increasing transplant volumes + immunogenomic complexity
- Limits national reporting, donor selection optimisation, and global collaboration
- Australia risks falling behind global research capability

Gap: Australia cannot evaluate HLA mismatch impact, DSA significance, or haplotype-level effects with current infrastructure.

Importance of Integrating HLA and Clinical Data in a Single Database

High-resolution NGS typing enables:

- Accurate allele-level mismatch analysis
- DPB1 T-cell epitope modelling, DPB1 expression, HLA-B leader matching, HED Scores
- Identification of permissible mismatches
- Interpretation of donor-specific antibodies
- Discovery of non-HLA genetic contributors to outcomes
- Impact of HLA mismatching in PT-Cy era

Current uncertainty:

- Which antibodies matter most?
- What MFI thresholds are clinically significant?
- Class I vs Class II impact?
- DPB1-specific antibody relevance?

Gap: No robust, linked dataset to answer these questions.