



HLA & HPA typing with the BGC Array

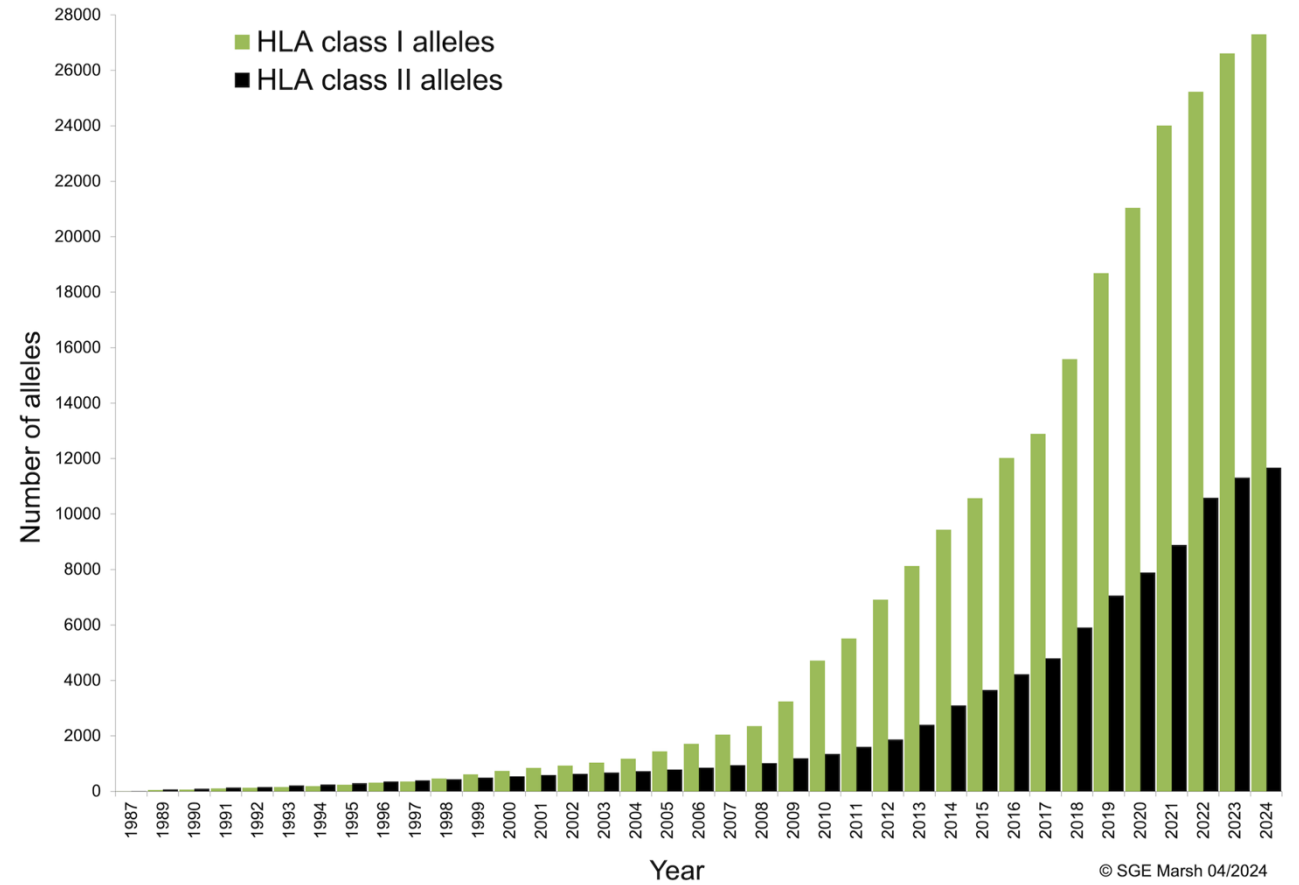
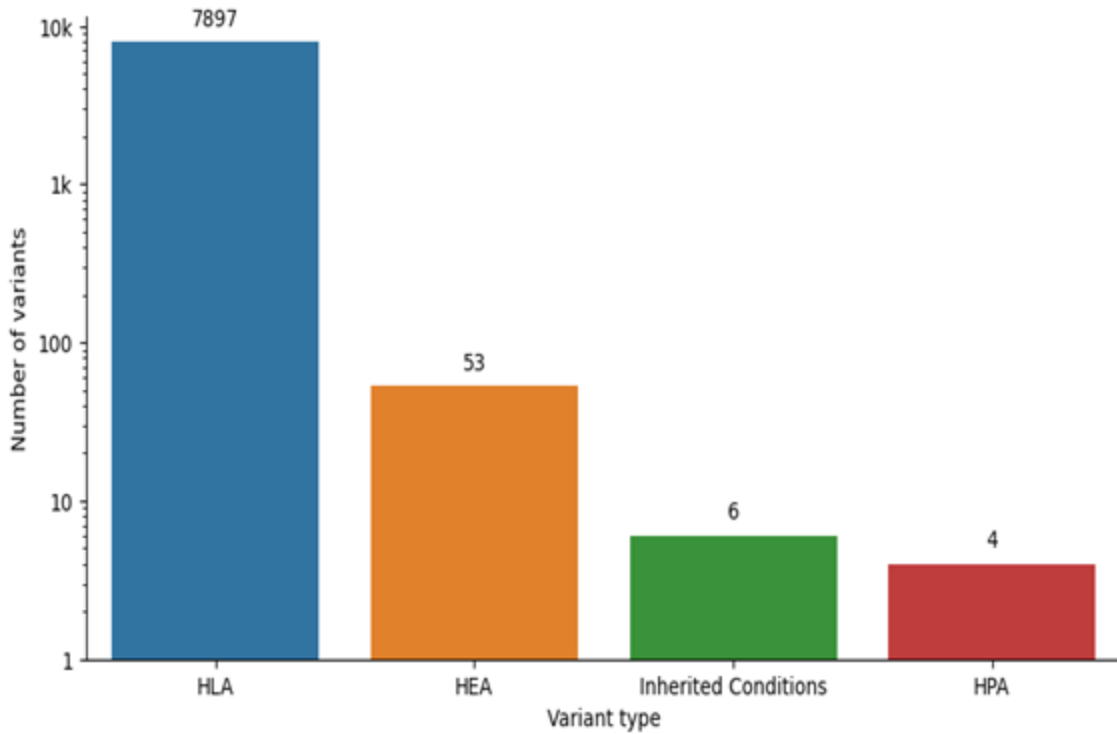
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on behalf of the Blood transfusion Genomics Consortium



HLA Imputation

Number of diagnostic variants on UBDT PC1 array by purpose



HLA samples

- Samples provided by
 - NHSBT (954)
 - ARCLB (554)
 - SANBS (261)
 - FRCBS (221)
 - SANQUIN (96)
- HLA typing methods
 - NGS, SBT, SSP, SSOP
 - Variable resolution

Ancestry	Total	
	Number of samples	%
EUR	1577	76.0%
SAS	133	6.4%
AMR	124	6.0%
AFR	139	6.7%
Other	57	2.7%
EAS	46	2.2%
Total	2076	

Genetically determined ancestry:

EUR, European

AMR, Admixed American

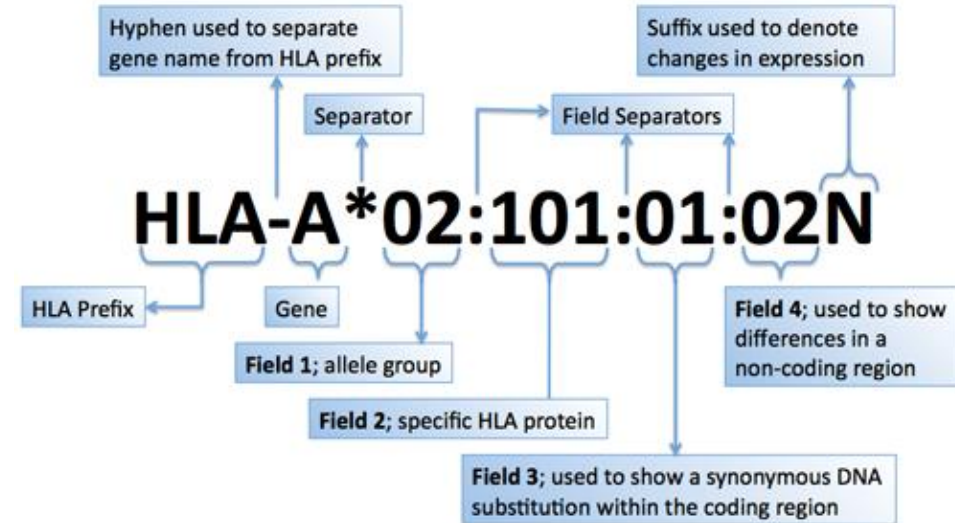
EAS, East Asian

SAS, South Asian

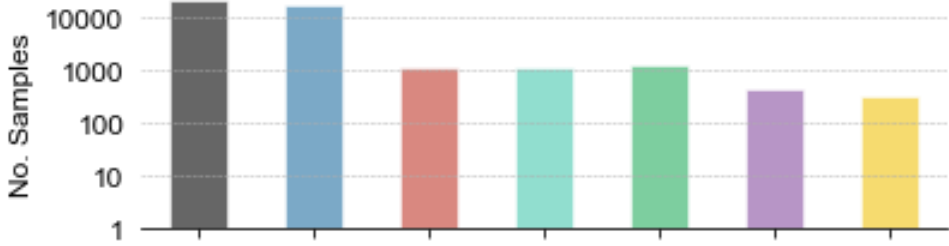
AFR, African

Resolution and concordance analysis

- Array results imputed to 2nd field
 - A*02:01
- Type of record varies
 - 1st field
 - Allele string
(A*02:01*,02:07,*02:09,*02:15N,*02:18,*02:20,*02:24.....)
 - Single allele (2nd, 3rd or 4th field)
- Concordance
 - Allele match
 - Potential allele match
 - Group match
 - Mismatch



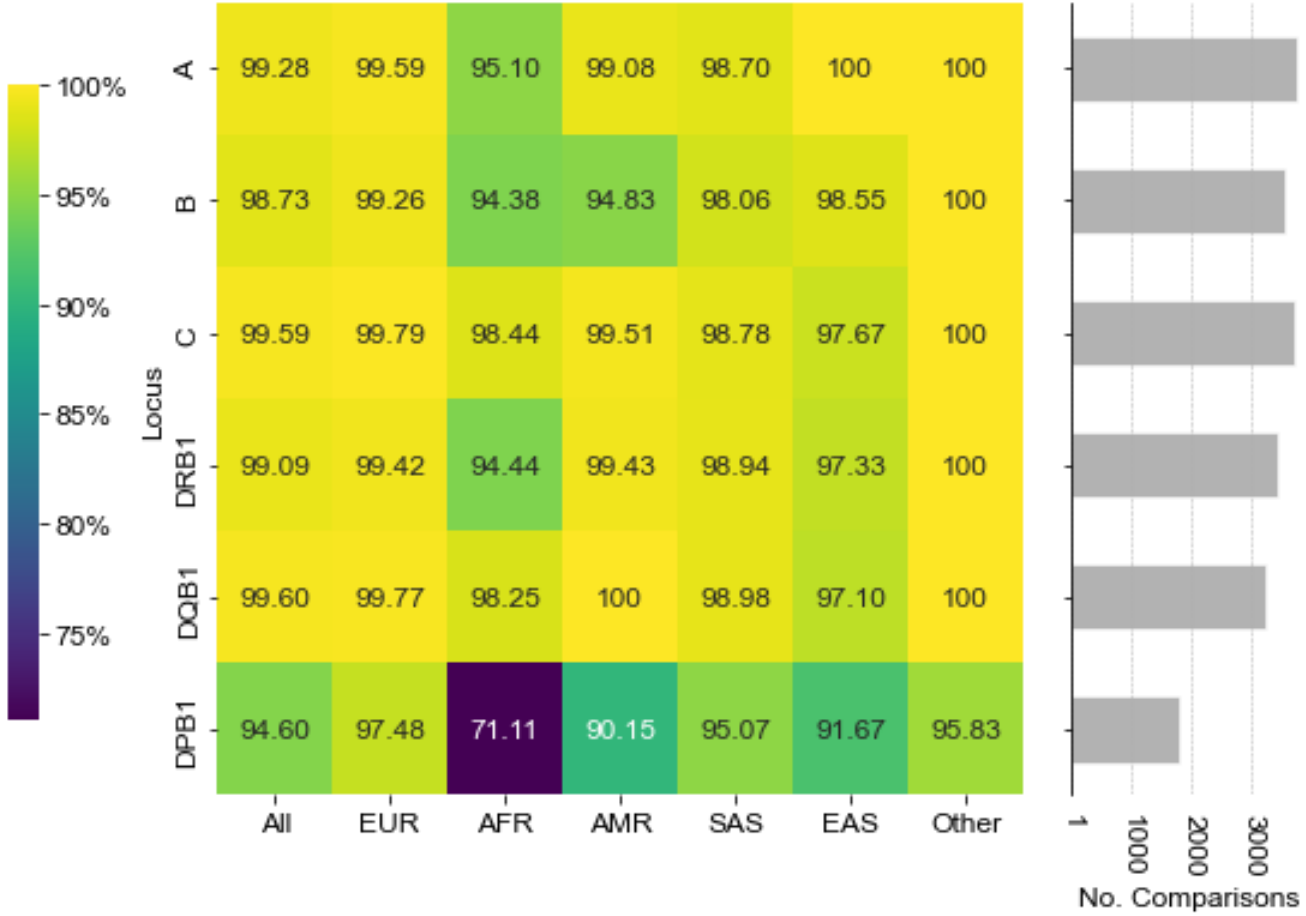
Overall Concordance



Concordance at 1st field

Greater than 98.5% at all loci except DPB1

Updating reference tables for imputation will improve DPB1 concordance

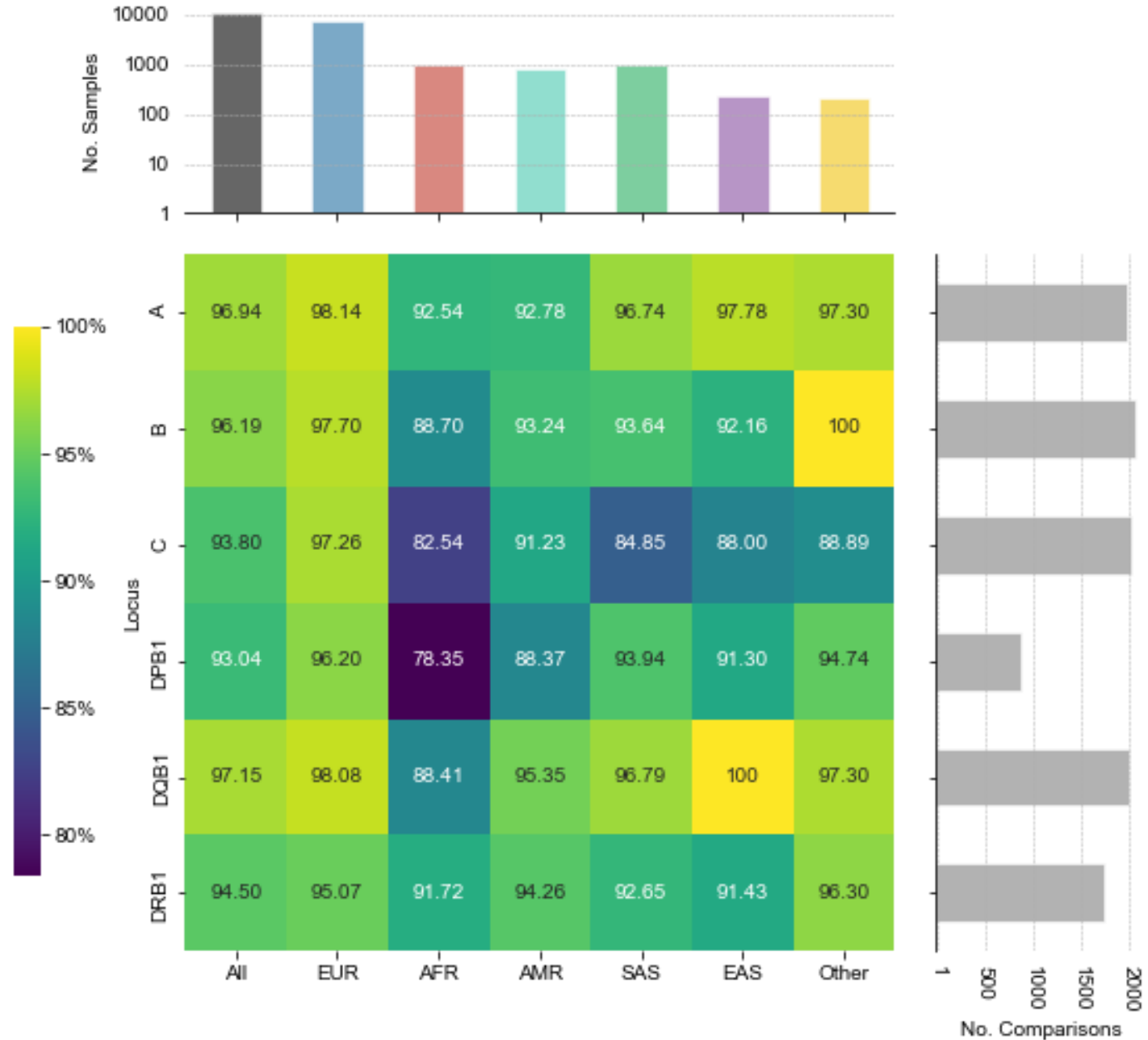


Allele Level Concordance

Concordance at 2nd field

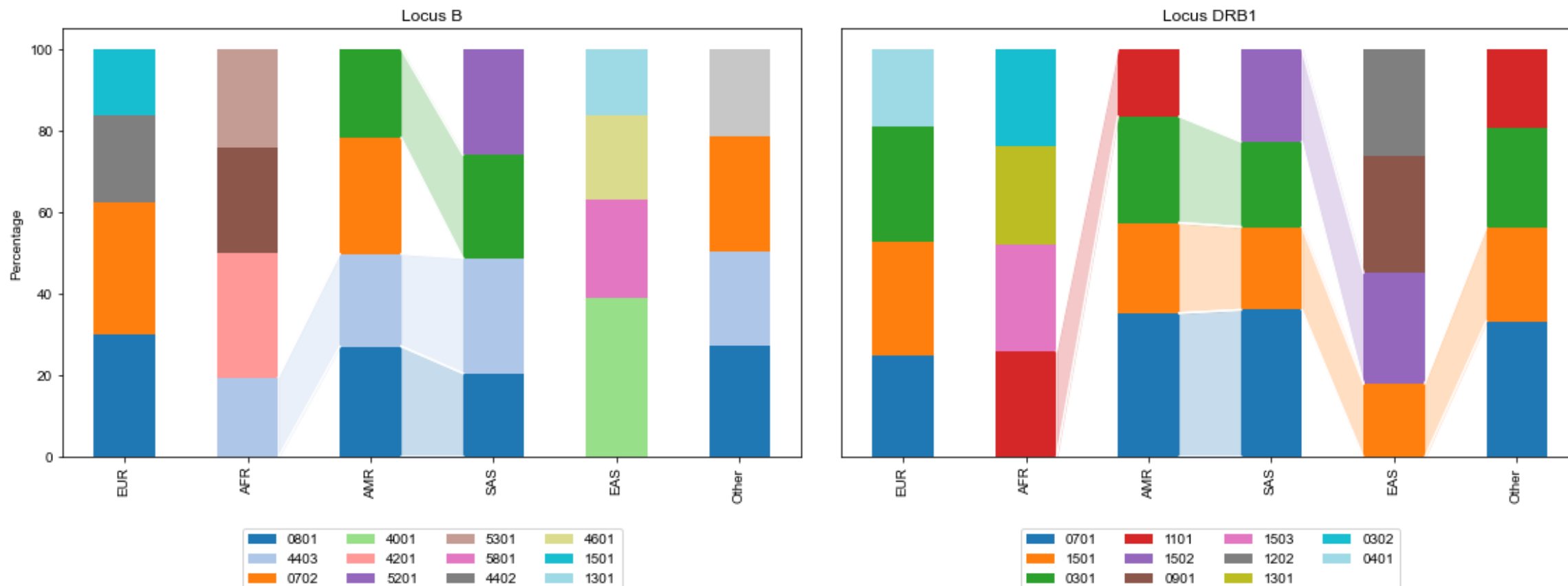
Compares favourably with other studies

Excludes samples not previously typed to allele level



HLA Diversity

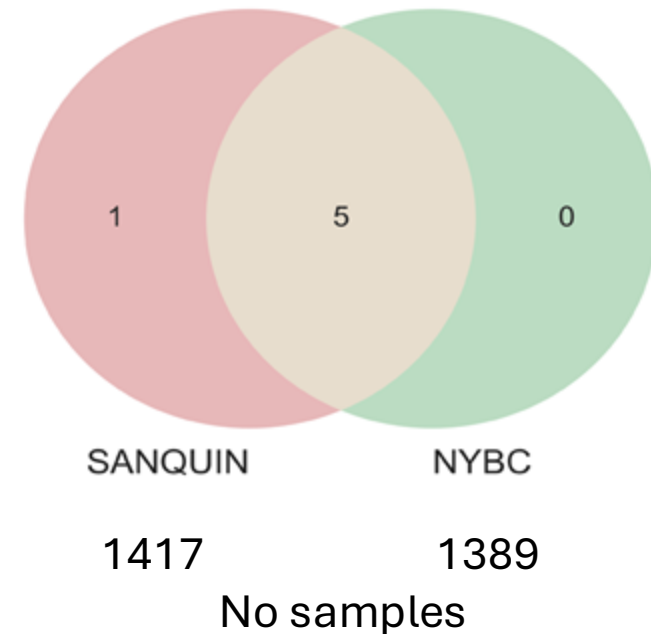
Top 4 alleles by ancestry group



HPA

- HPA-1,2,5,15 validated at diagnostic level
- Concordance with type of record >95.5%
- HPA-3,6 not working well in PCS-II or IV
- HPA-4 insufficient 4b samples to validate
- 8 known HPA-1a5b neg donors
- Array typing identified 106 HPA-1a5b neg donors

Overlap in discordant HPA antigen calls between SANQUIN and NYBC



Summary

- Excellent concordance
 - HLA - >98.5% at first field (excluding DPB1)
 - HPA - >95.5% for HPA-1,2,5,15
- Clinical application
 - Typing of platelet donors for HLA or HPA matched platelets
 - Replacing first or confirmatory types currently done by more expensive (high res) techniques
 - Typing red cell donors
 - HLA typing could support provision of matched red cells to prevent donor specific alloimmunisation in organ transplant recipients
 - HPA screening to identify HPA1a5b neg donors for confirmatory typing & recruitment
 - HLA screening to identify valuable types to target recruitment for platelet panels or stem cell registries



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