



Blood transfusion Genomics Consortium Fringe Meeting

Multi-center validation study of the Universal Blood Donor Typing array

Barbera Veldhuisen
on behalf of the BGC

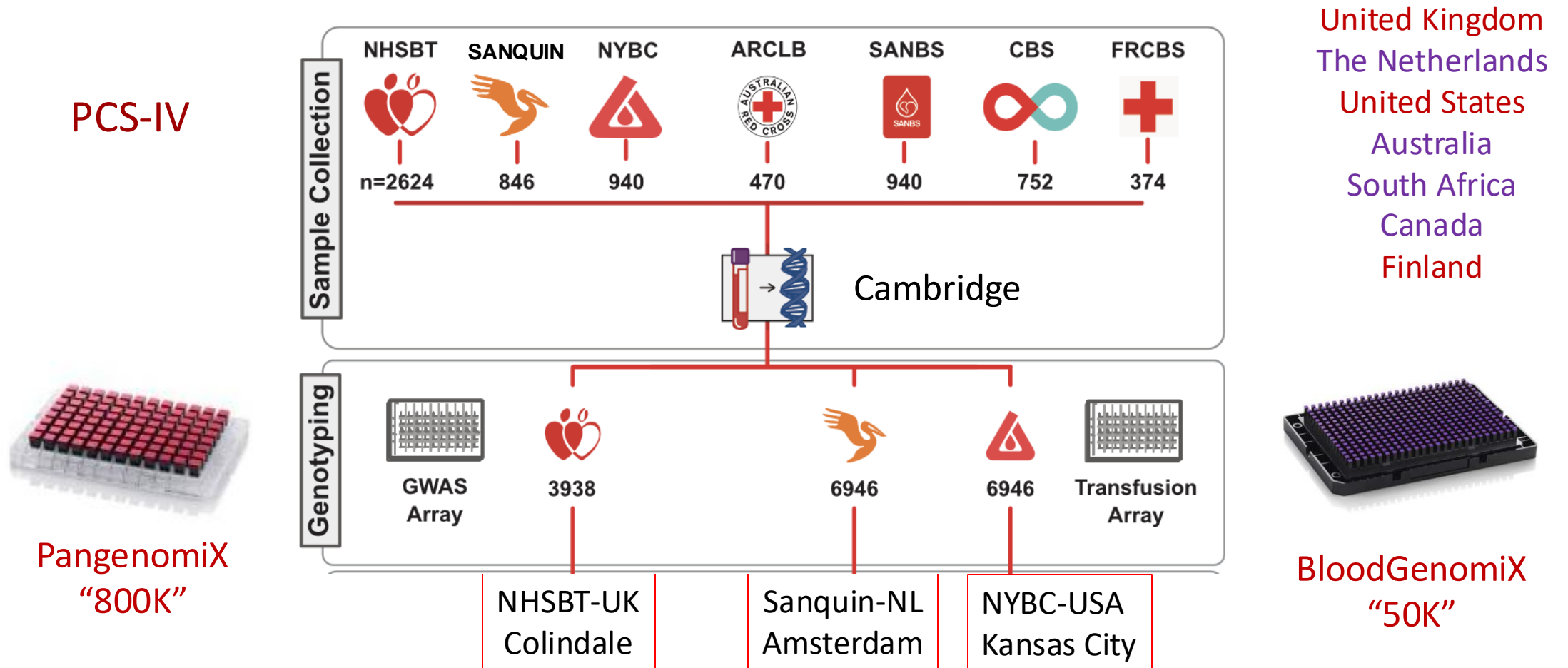
poster 558

Barcelona, Monday June 24, 2024



Validation of the BGC Universal Blood Donor typing array

- Multi-ethnic donor cohort of DNA samples collected by 7 BGC members
- Electronic donor record data (both genotype or serology)
- 17,716 samples: 6,952 samples (PCS-II) and **6,946** (PCS-IV)



Genotyping in the 3 accredited blood service laboratories



Furkhana Lydi Coli Aliyye Trevor

NHSBT Colindale, London

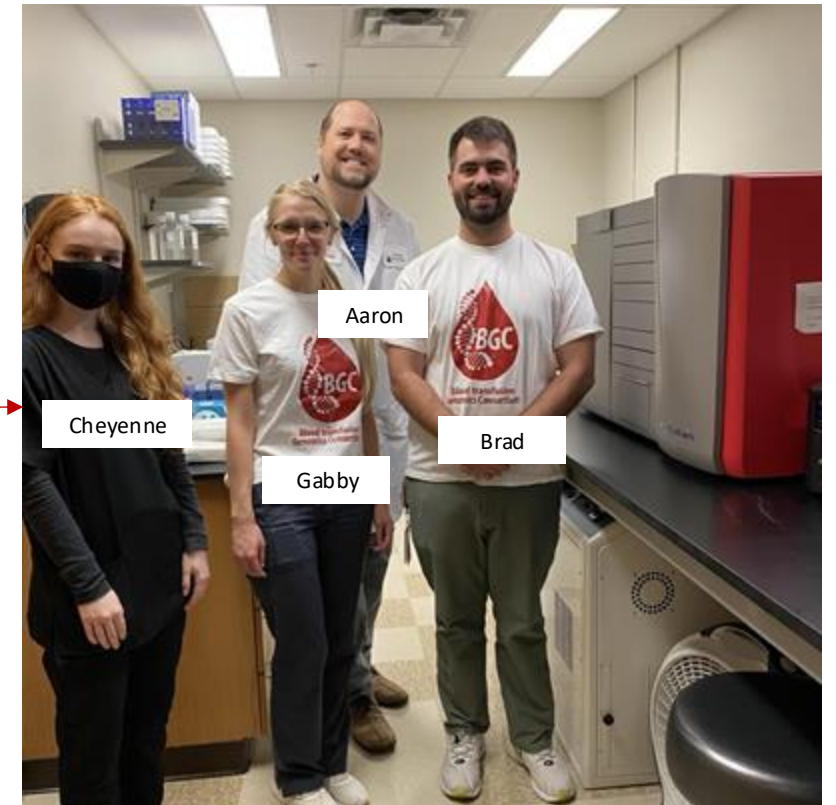


Barbera Marco Ellen Lianne

SANQUIN, Amsterdam



“Jonathan lab”
Cambridge



Cheyenne Aaron Gabby Brad

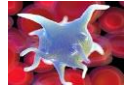
NYBC, Kansas City

BloodGenomiX array content

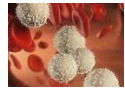
Transfusion module: 19,457 genomic variants



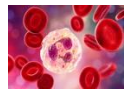
HEA: 4002 variants (44 blood group systems)



HPA: 657 variants



HLA: 7897 variants



HNA: 372 variants

Optional gender/ancestry: 5664 variants

Optional blood related traits: 865 variants

AIM PCS-IV study

- Determine *accuracy* and *reproducibility* of array
- In real-world setting of 3 blood service laboratories
- Using a multi-ethnic donor cohort

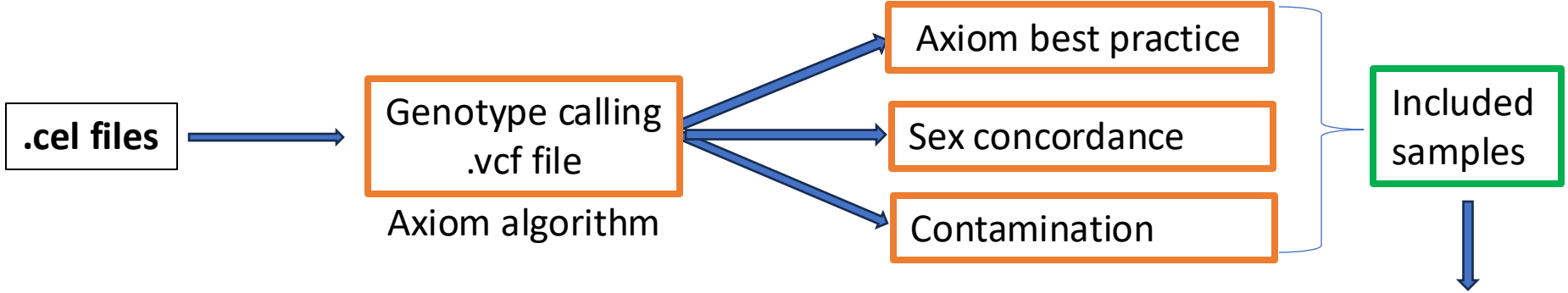
Validation

System	Antigens	Variants
RH	D, C, c, E, e, Cx, Cw, V, VS	15
MNS	M, N, S, s, U, He	11
LU	Lu(a), Lu(b)	1
KEL	K, k, Kp(a), Kp(b), Kp(c), Js(a), Js(b)	4
FY	Fy(a), Fy(b)	3
JK	Jk(a), Jk(b)	4
DI	Di(a), Di(b), Wr(a), Wr(b)	2
YT	Yt(a), Yt(b)	1
SC	Sc1, Sc2	1
DO	Do(a), Do(b), Hy, Jo(a)	3
CO	Co(a), Co(b)	1
LW	Lw(a), Lw(b)	1
CROM	Cr(a)	1
KN	Kn(a), Kn(b), McC(a), McC(b), Yk(a), KCAM, KDAS	4
VEL	Vel	1
Total	53	53

System	Antigens	Variants
HPA	HPA1, HPA2, HPA3, HPA4, HPA5, HPA6, HPA15	7
Total	14	7

System	Antigens	Variants
HLA	Class I: A, B and C	7897
HLA	Class II: DPB1, DQB1 and DRB1	
Total		7897

Data analysis (Integrated Analysis Package)



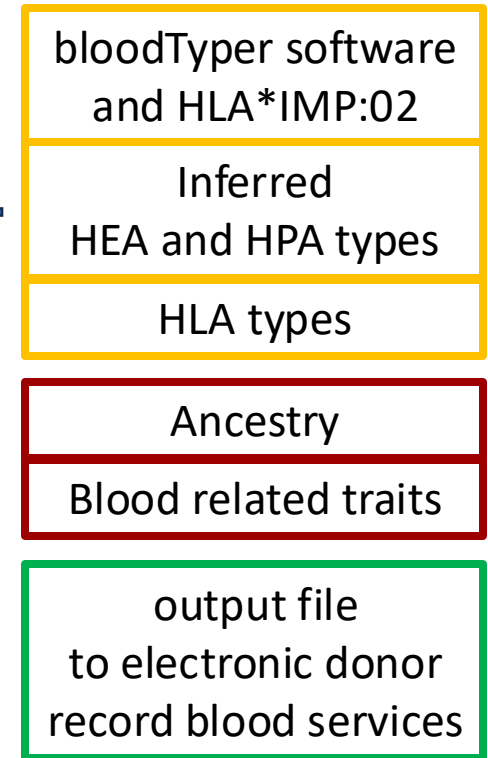
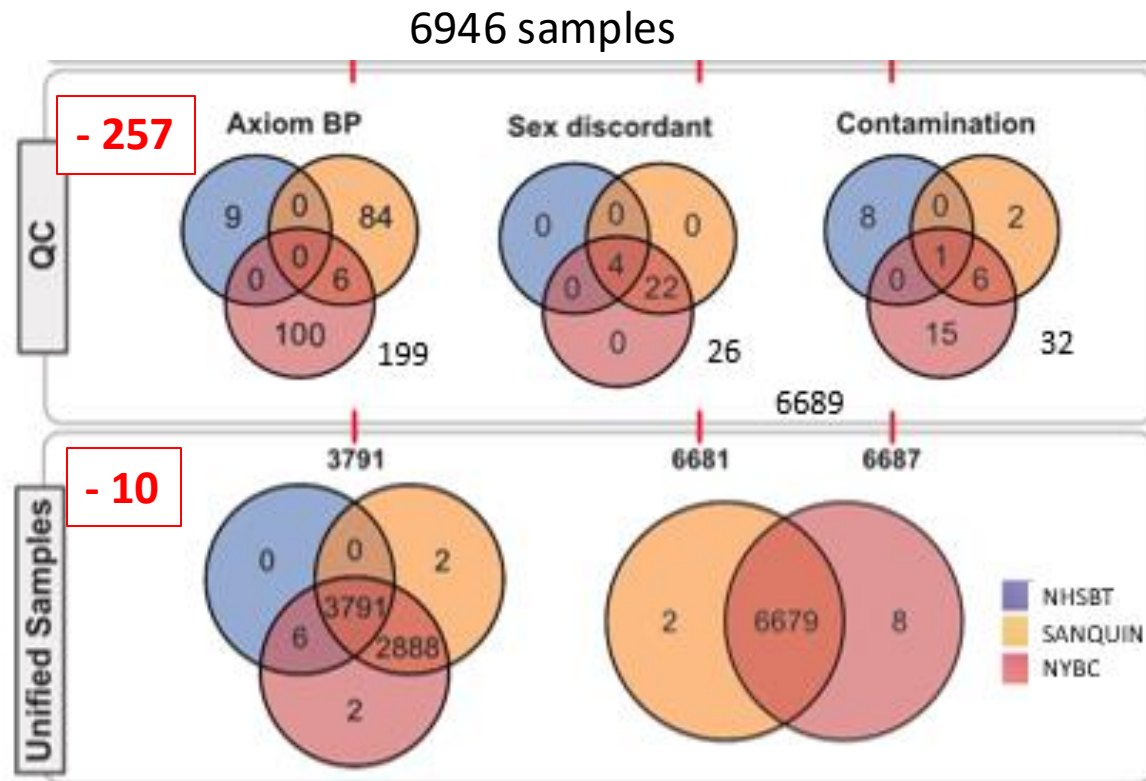
PCS-IV

- NHSBT: **3791** samples
- SANQUIN: **6681** samples
- NYBC: **6687** samples



unified set

6679 samples (96.2%)



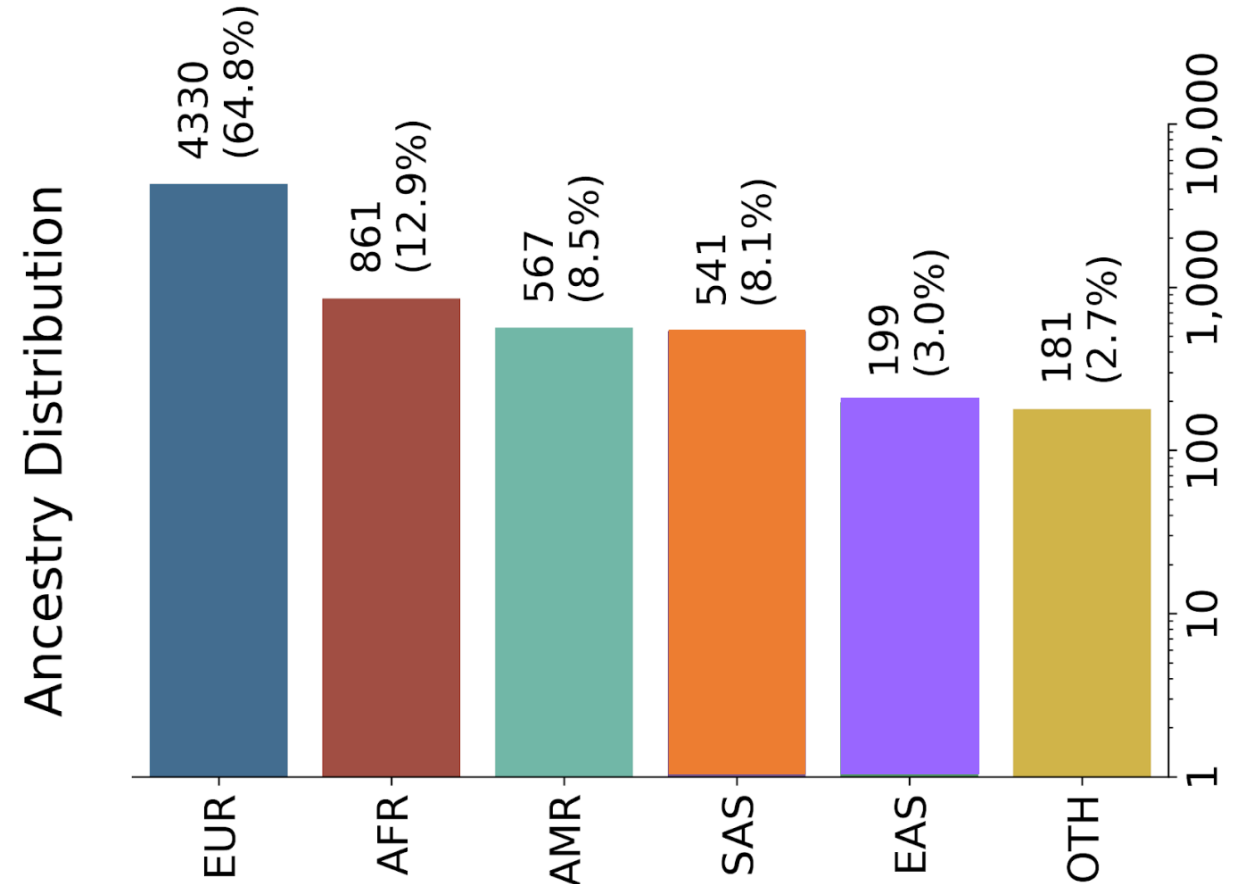
Genetic Ancestry of unified dataset (6679 samples)

Multi-ethnic donor cohort
35.2% of non-European ancestry

Results of Principal Component Analysis (PCA)



Numbers (%) of donors and their genetic ancestry



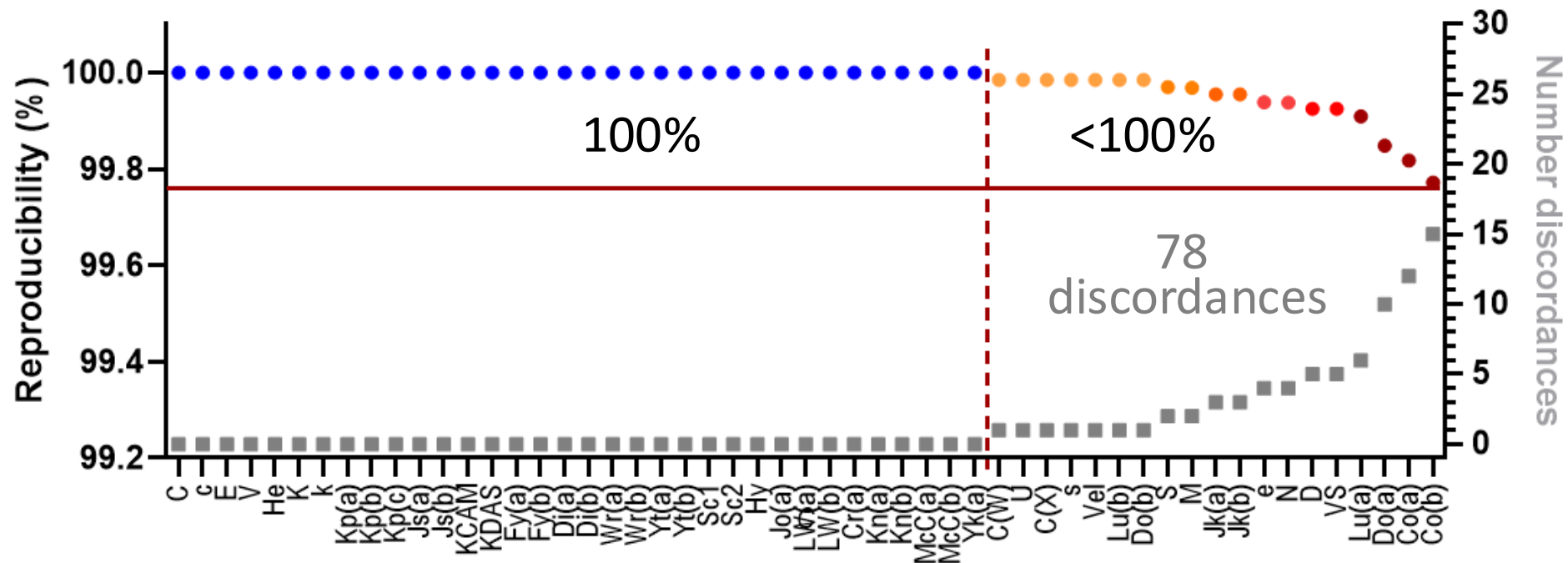
Reproducibility Human Erythrocytes Antigens: 99.98%

Comparison HEA inferred types between NYBC and Sanquin for 53 antigens

6679 * 53 = 353,987 possible comparisons

n = 2316 (0.65%) no comparison: no inferred phenotype in one or both labs

351,593 comparisons concordant: **99.98% reproducibility**



Accuracy HEA typing: 99.90%

Comparison HEA inferred types to donor test-of-record for 47 antigens

Unified set 6679 * 47 * 2 = 627,826 possible comparisons

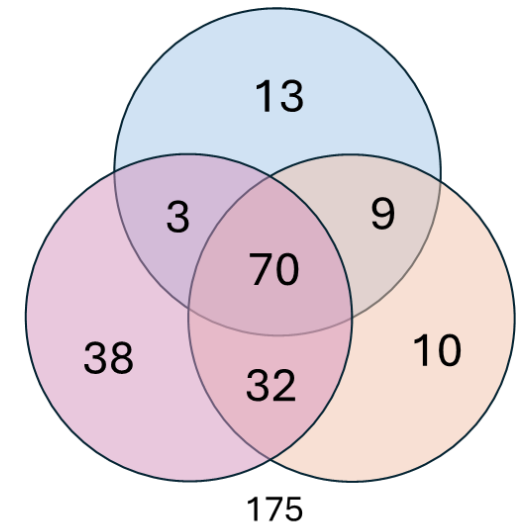
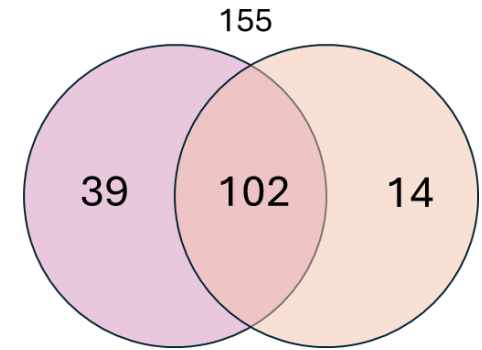
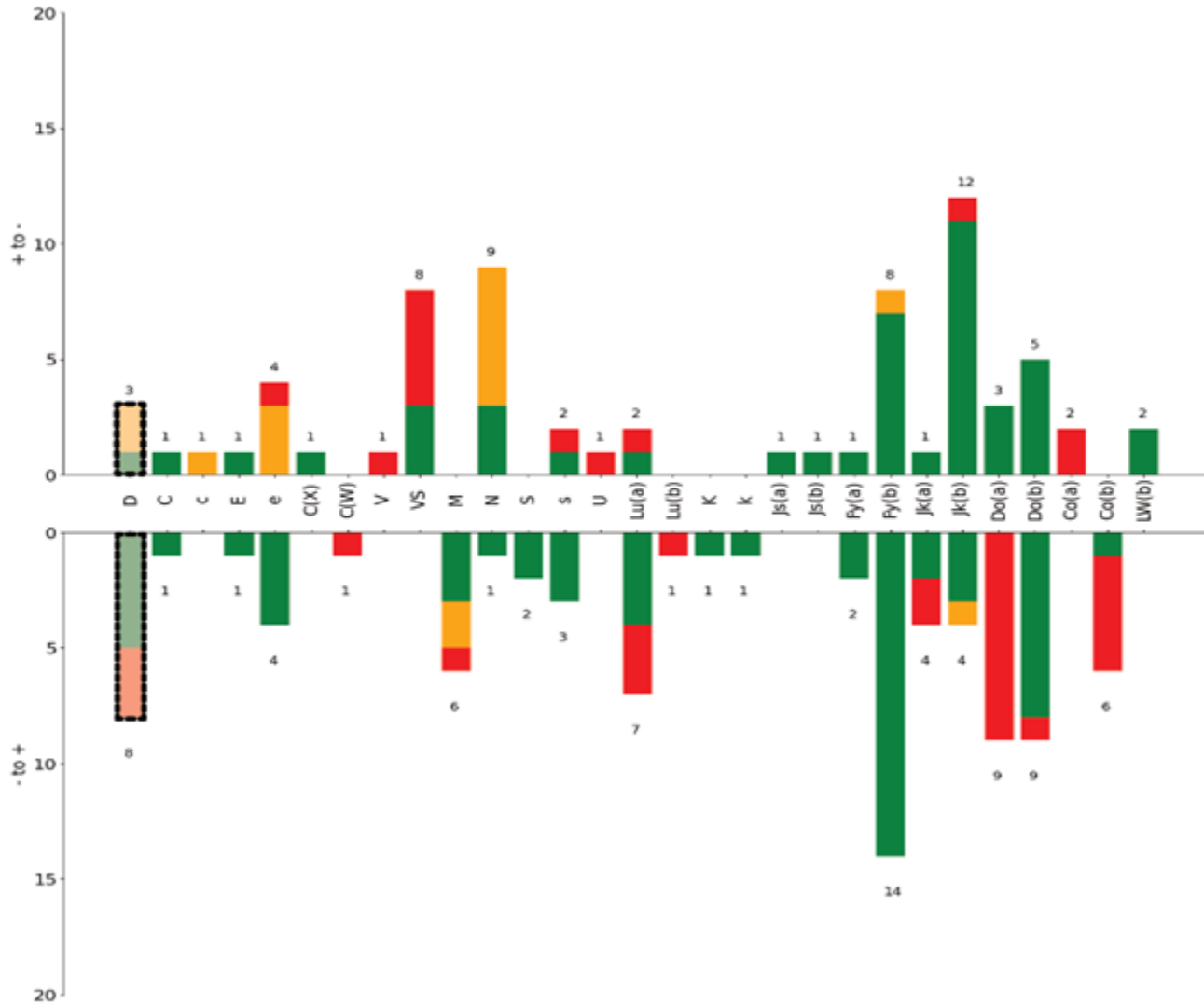
In total 245,717 (39.14%) comparisons

245,466 comparisons concordant: **99.90%**

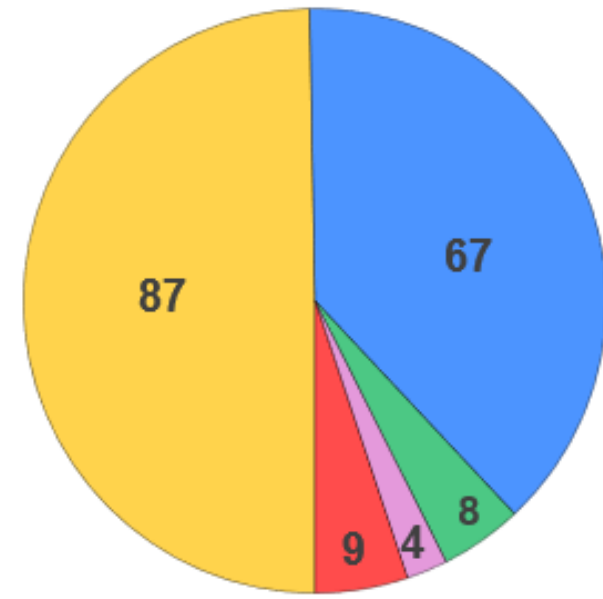
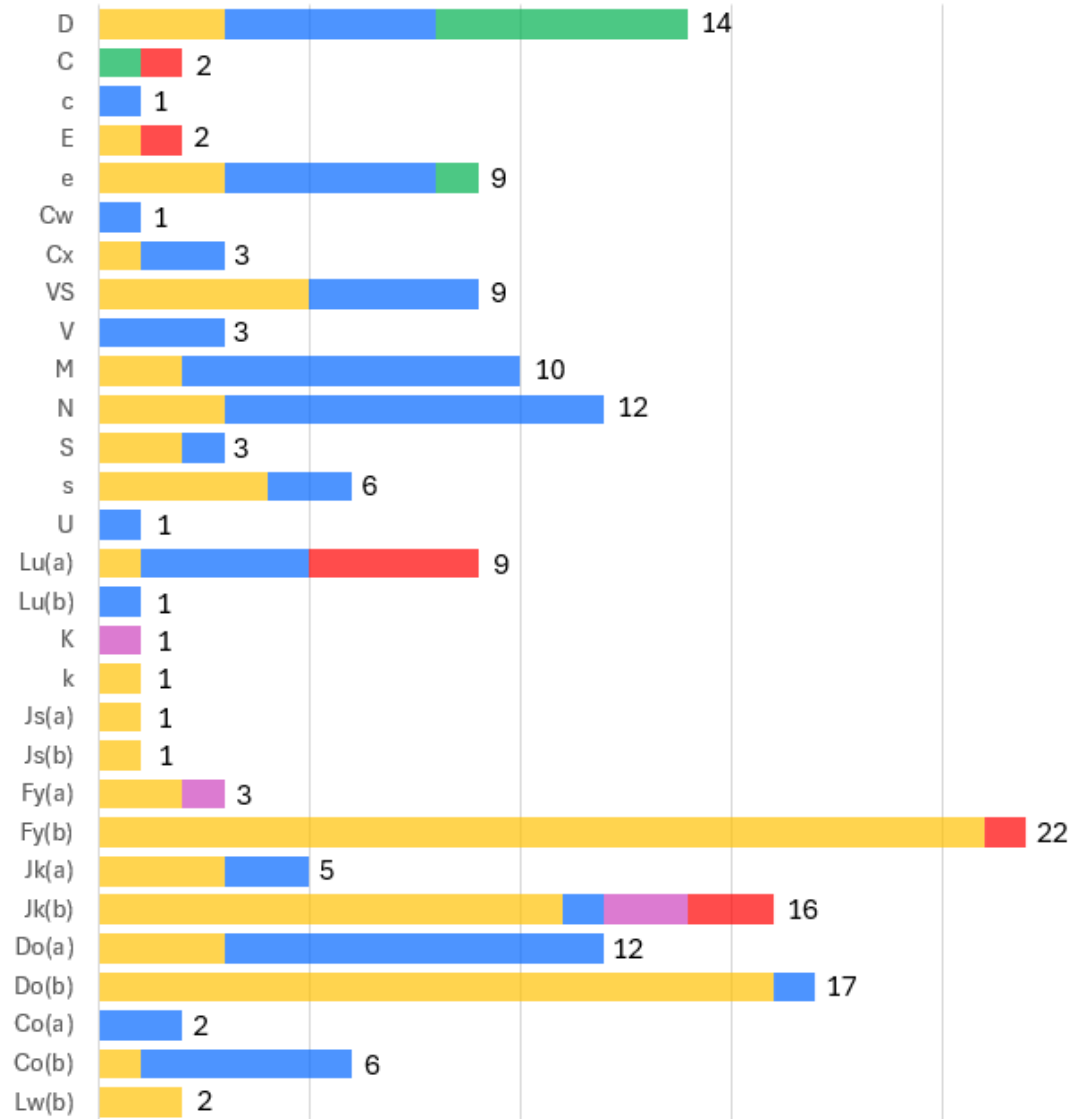
Unique sample-antigen discordances: **175**

Typing laboratory	Kansas City, NYBC	Amsterdam, Sanquin	Colindale, NHSBT	Unified NYBC/SANQUIN
Samples	6946	6946	3938	6946
Excluded samples (QC)	193 (2.78%)	175 (2.52%)	52 (1.32%)	267 (3.84%)
Passed samples	6753	6771	3886	6679
Possible comparisons	317,391	318,237	174,870	627,826
No. of comparisons	124,443 (39.21%)	125,312 (39.38%)	78,112 (44.67%)	245,717
Missing donor typing	191,361 (60.29%)	191,642 (60.22%)	96,299 (55.07%)	377,383
Missing genotype	947 (0.30%)	789 (0.25%)	359 (0.20%)	1664
Both missing	640 (0.20%)	494 (0.16%)	100 (0.06%)	3062
Concordant	124,302 (99.89%)	125,191 (99.90%)	78,017 (99.88%)	245,466
Discordant	141 (0.11%)	121 (0.10%)	95 (0.12%)	251 (155 unique)

HEA discordances unified data for SANQUIN and NYBC



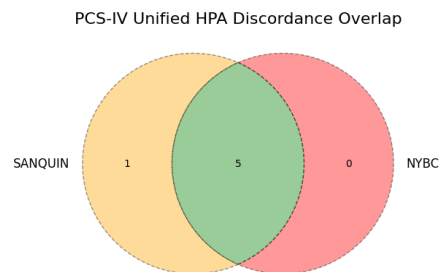
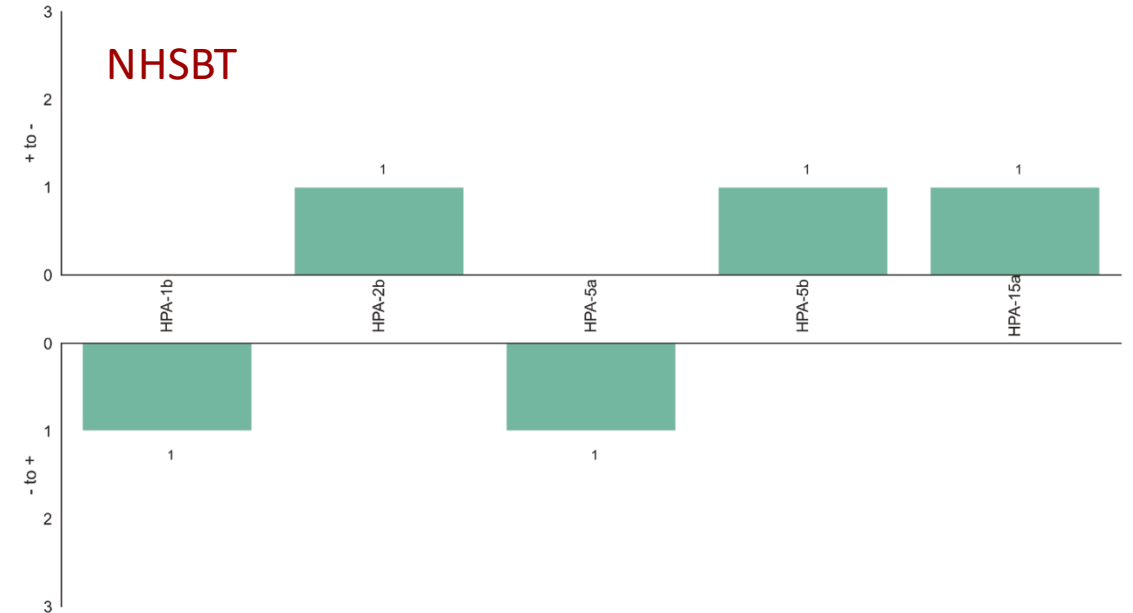
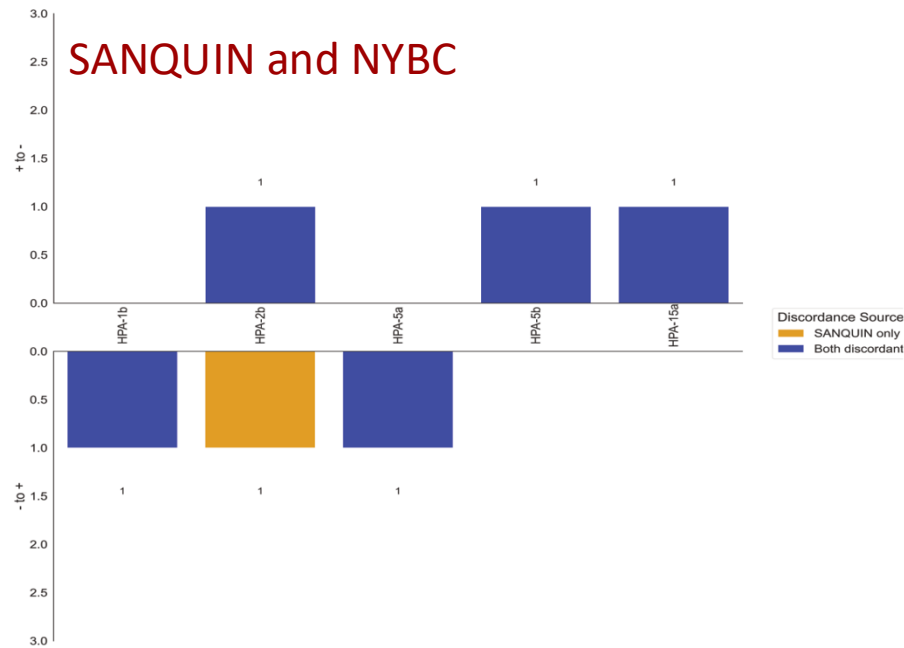
Resolution testing 175 discordances PCS-IV (all tree typing laboratories)



■ Clinical typing
 ■ Array
 ■ Algorithmic
 ■ Content
 ■ Miscellaneous

6 HPA discordances at SANQUIN, NYBC and NHSBT

NYBC:1389 , SQ:1417 and NHSBT:1433 comparisons



- For HPA-1,2,5 and 15: 6 discordances (5 samples)
- 5 overlapping, 1 only at Sanquin (batch effect)
- HPA-3 and HPA-6: did not perform to standards and are excluded
- HPA4: only one heterozygous HPA-4a/b sample

HLA concordance in PCS-IV

- 767 HLA typed samples from UK, Finland and Australia
- Class I (A,B, and C) and class II (DPB1,DQB1 and DRB1) determined by HLA*IMP:02 algorithm
- Concordance: 99.7%, 98.7% and 99.7% (class I: A,B and C)
- Concordance: **96.9%**, 99.9%, 98.9% (class II: DPB1,DQB1 and DRB1)

Lower concordance for DPB1 will be addressed with an updated HLA*IMP:02 reference table.

Summary

- The **BloodGenomiX** array for blood donor genotyping produces **highly accurate** red blood cell (**HEA**), platelet (**HPA**) and leukocyte (**HLA**) antigen genotypes, simultaneously and at scale.
- Inferred HEA phenotypes showed **99.9% concordance** compared to donor test-of-record.
- Testing between sites (NYBC/Sanquin) showed a **high level of reproducibility** (99.98% in 351,671 comparisons).
- Samples from non-European ancestry (35.2% of the donor cohort) performed at the same level (data not shown).



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bold: Principal Investigators; *italics*: Project Coordination; underlined: Analysis Team; **Blue**: Discordance Resolution; **Green**: Genotyping Lead

