# A new DNA based test for donor genotyping

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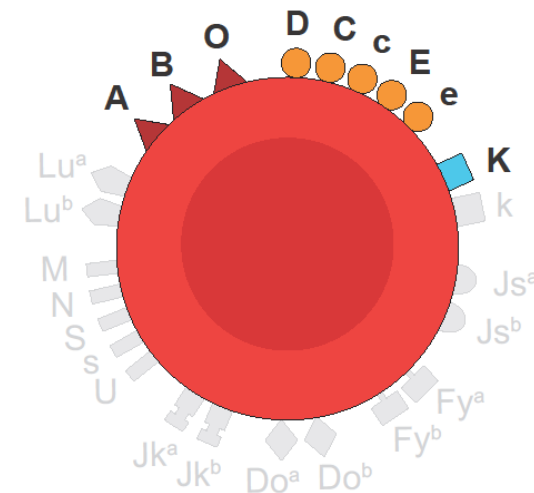
Background

Current Blood Matching

- We must ensure compatibility between donor and recipient to prevent formation of antibodies against non-self human blood group antigens

- Most patients are matched for **ABO and D**

- For those who are more at risk of developing antibodies we include **C/c, E/e and K**
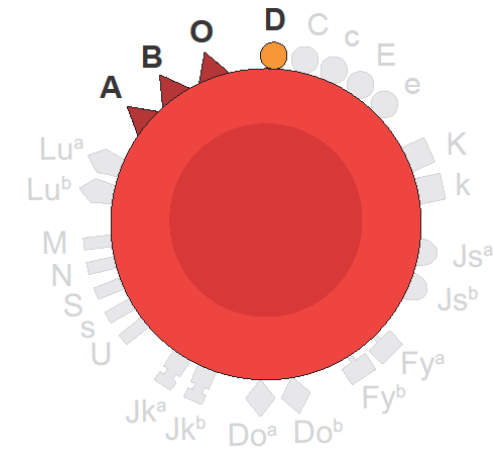
General Patient
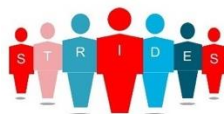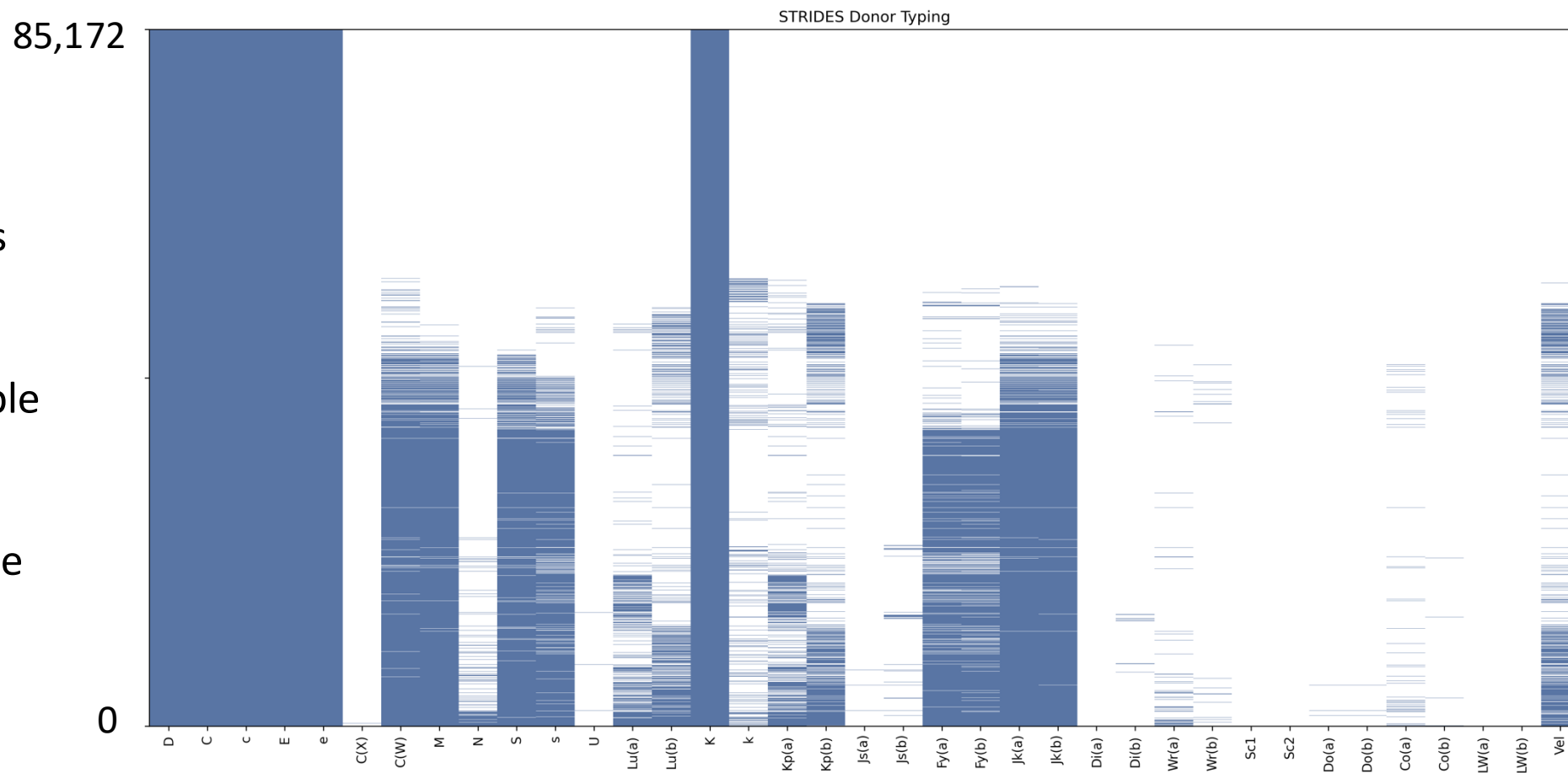

Regularly Transfused Patient

Many Important Antigens

- There are many other antigens which stimulate clinically significant antibodies

- These are only matched for in patients who have already formed antibodies

- Current blood matching practices cause harm to 18,000 patients in the UK each year
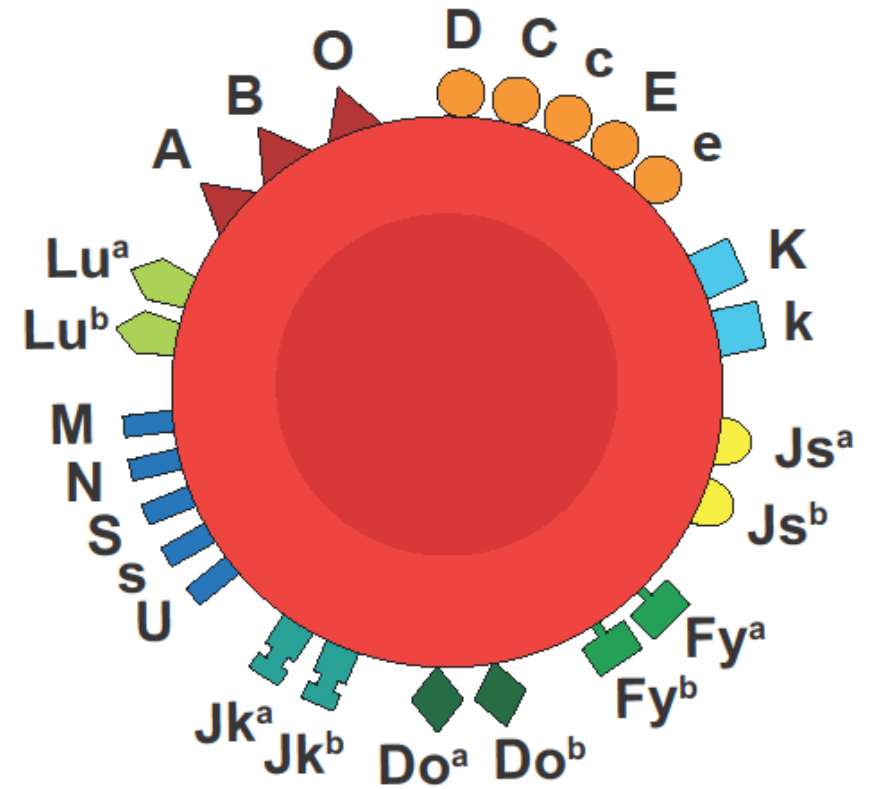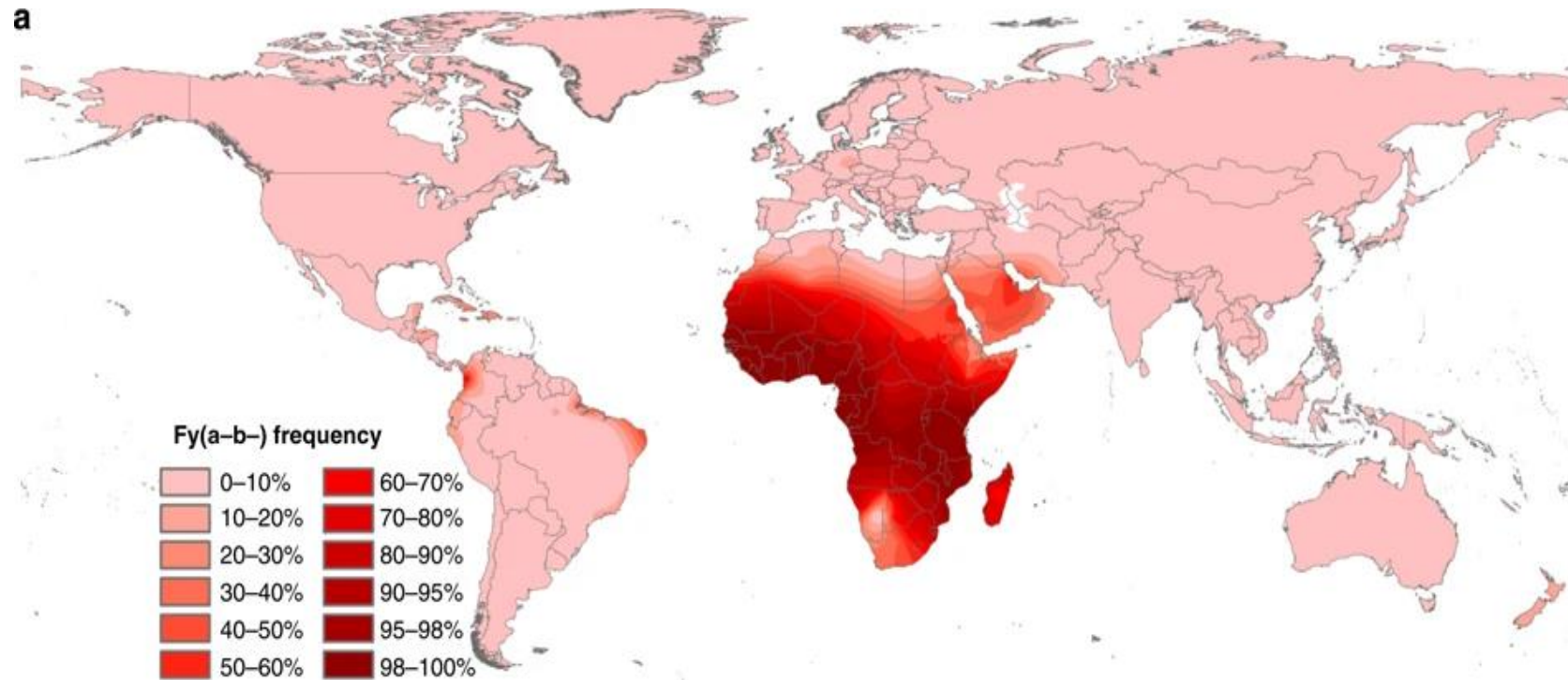
STRIDES antigen typing

- **85,172** NHSBT donors

- **764,570** types available

- **29.3%** typing coverage


STRIDES Donor Typing

NIHR | BioResource

NHS
Blood and Transplant

Ancestral differences in blood type

Fy(a–b–) frequency
- 0–10%
- 10–20%
- 20–30%
- 30–40%
- 40–50%
- 50–60%
- 60–70%
- 70–80%
- 80–90%
- 90–95%
- 95–98%
- 98–100%

African ancestry donor typing

- **1,461** African ancestry donors

- **23,309** types available

- **43%** typing coverage

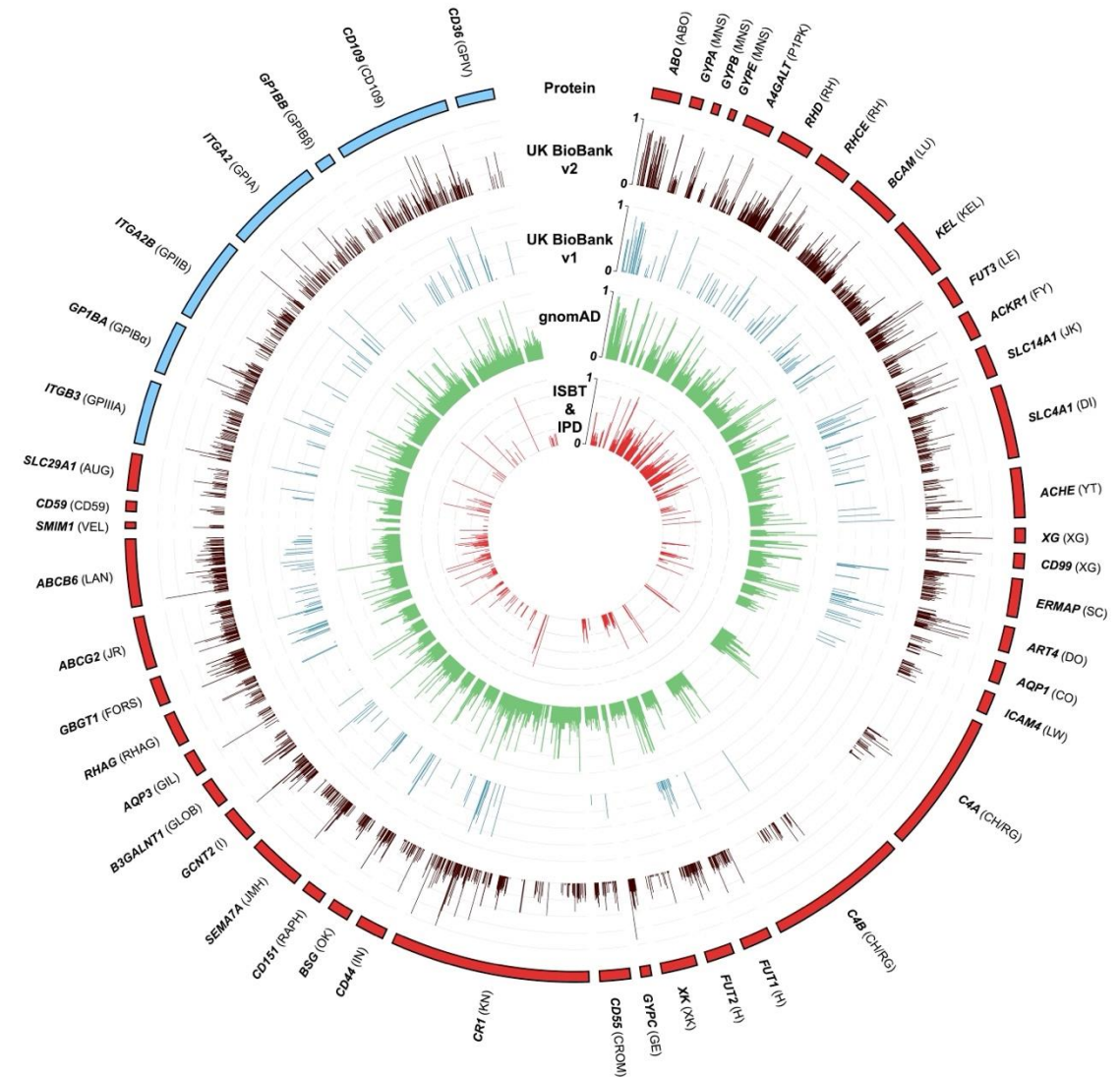| Phenotype	Count
African Donor	1461
Fy(a/b) typed	1313
Fy(a)-/Fy(b)-	744
Clinical U type	24
U-negative	7
Fy(a)-/Fy(b)-/U-	7

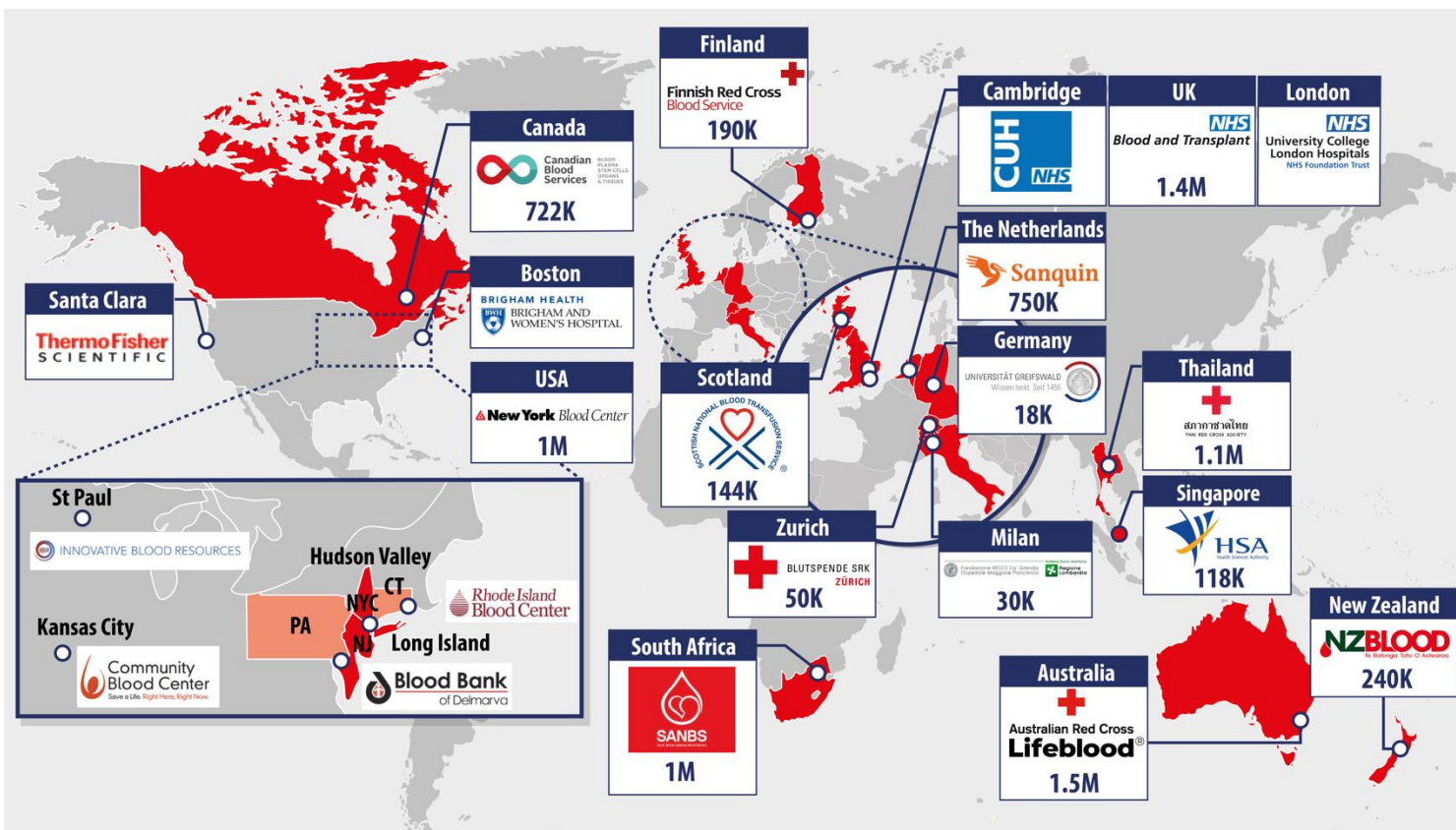STRIDES African Donor Typing
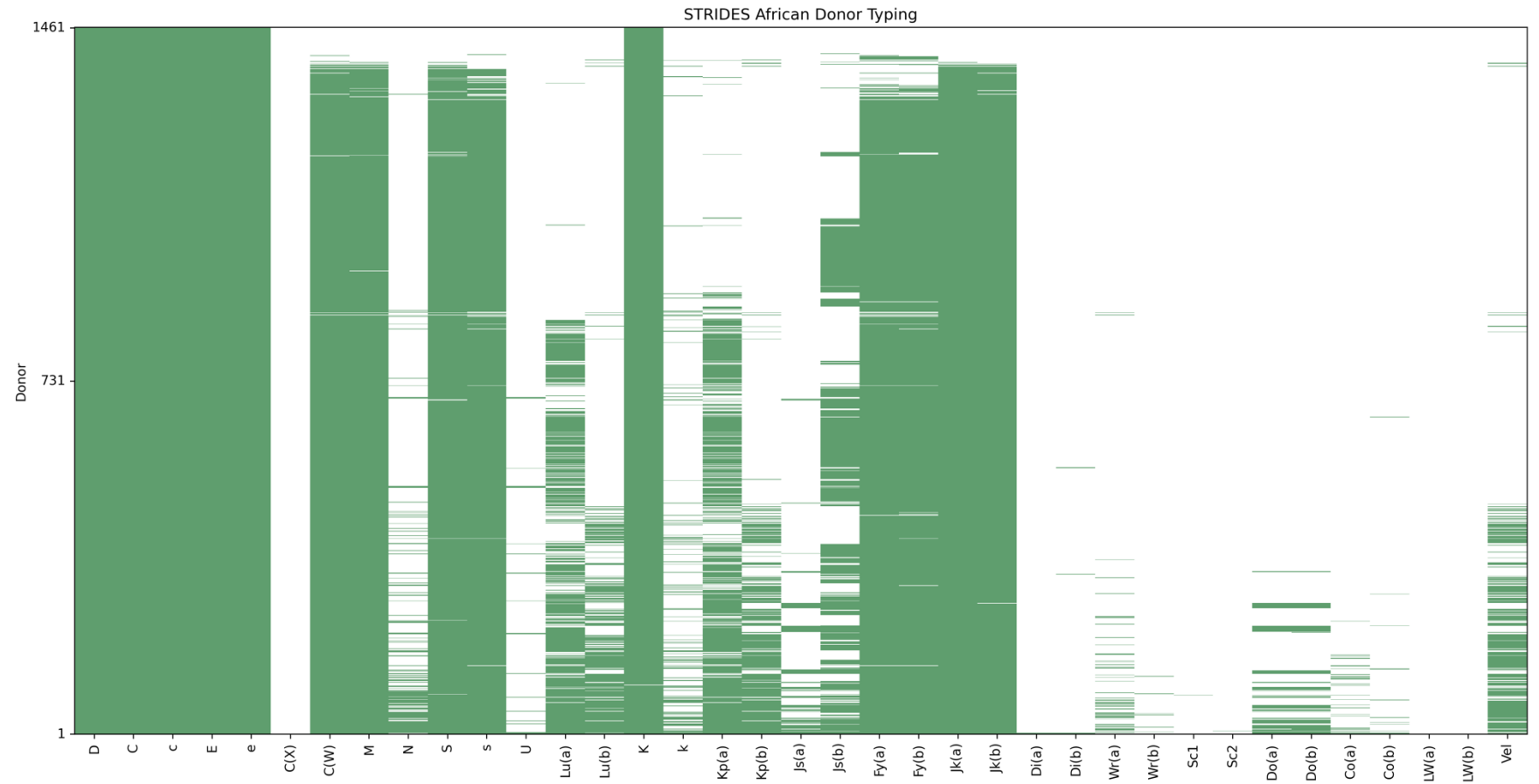
Blood Group Genomics

Blood Group Genomics

- Genetics underpinning blood groups is well known!

- It has been studied for the past 50 years

- We can infer a person's blood groups groups using their DNA sequence data!!

The Blood Transfusion Genomics Consortium

Principal Investigators	
Willem H Ouwehand	**Cambridge**
Andrea Harmer	**London**
Ellen v.d. Schoot	**Amsterdam**
Connie Westhoff	**New York**
William Lane	**Boston**
Shantanu Kaushikkar	**Santa Clara**
James Daly	Melbourne
Celina Montemayor	Toronto
Jukka Partanen	Helsinki
Ute Jentsch	Johannesburg
Maja Mattle-Greminger	Zurich
Sarah Morley	Auckland
Sara Trompeter	London
Andreas Greinacher	Greifswald
Pawinee Kupatawintu	Bangkok
Luca Valenti	Milan
Jennifer Laird	Scotland
Ai Leen Ang	Singapore
Founding members: bold; Chair/Dep. Chair: italics	

- **10 national** and **4 regional** blood services
- collect **8.3 million** units of blood per year
- require **885K new** donors to be engaged each year

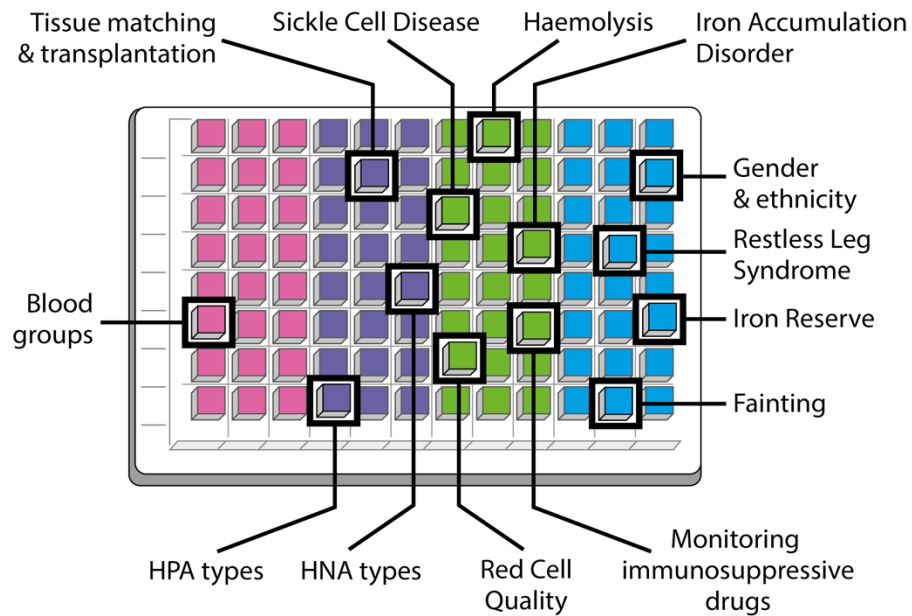Aim: Develop a simple DNA based test for donor and patient typing
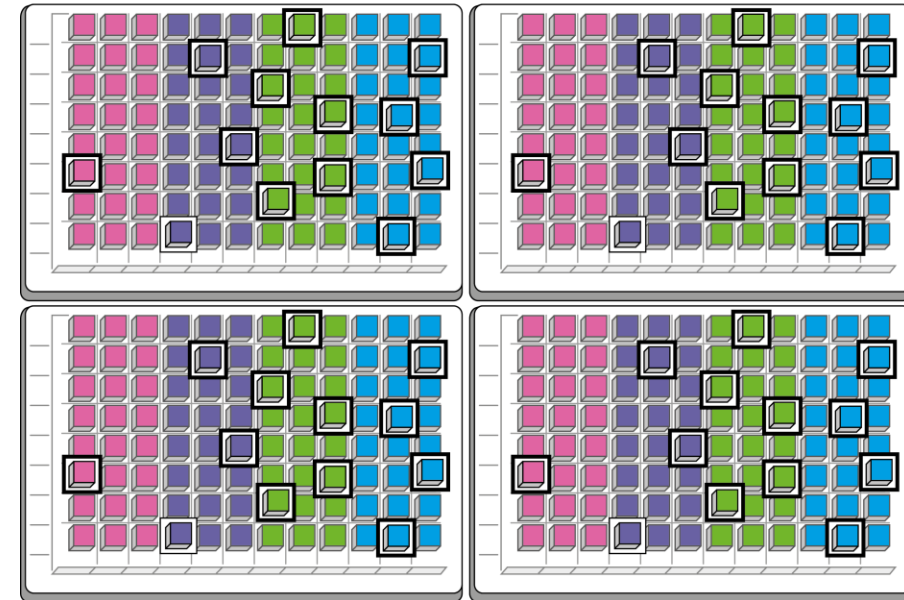
Two Arrays

UKBB v2.2

800,000 DNA variants - 96 samples

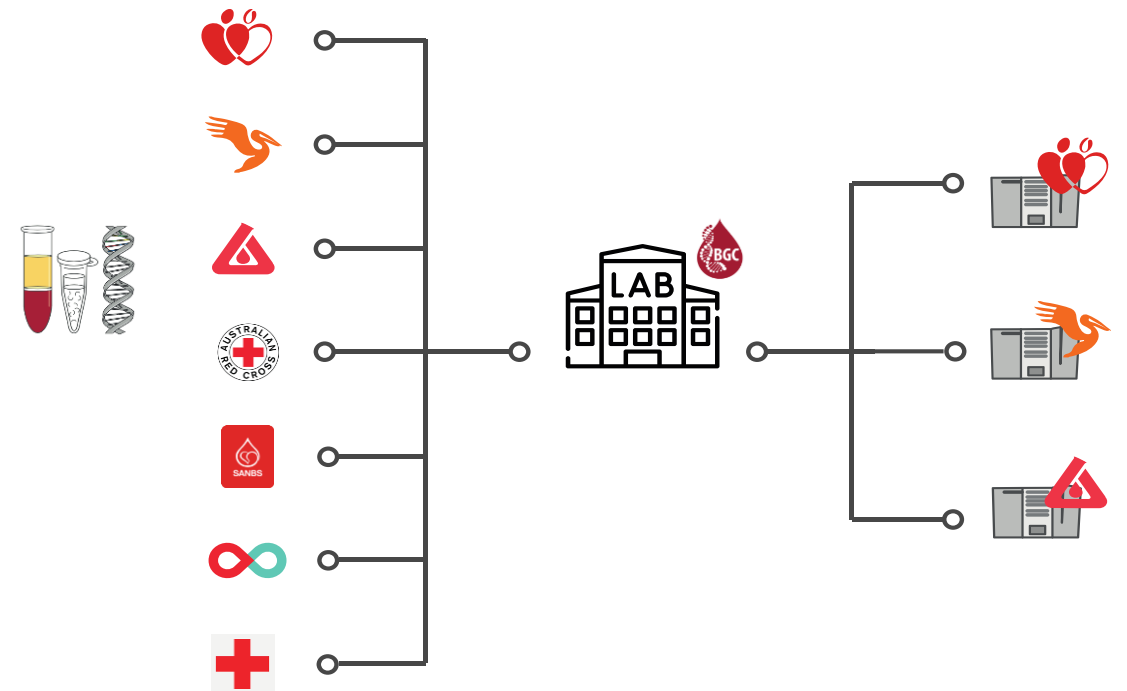**Content:** Donor & Patient Typing + GWAS grid

UBDT

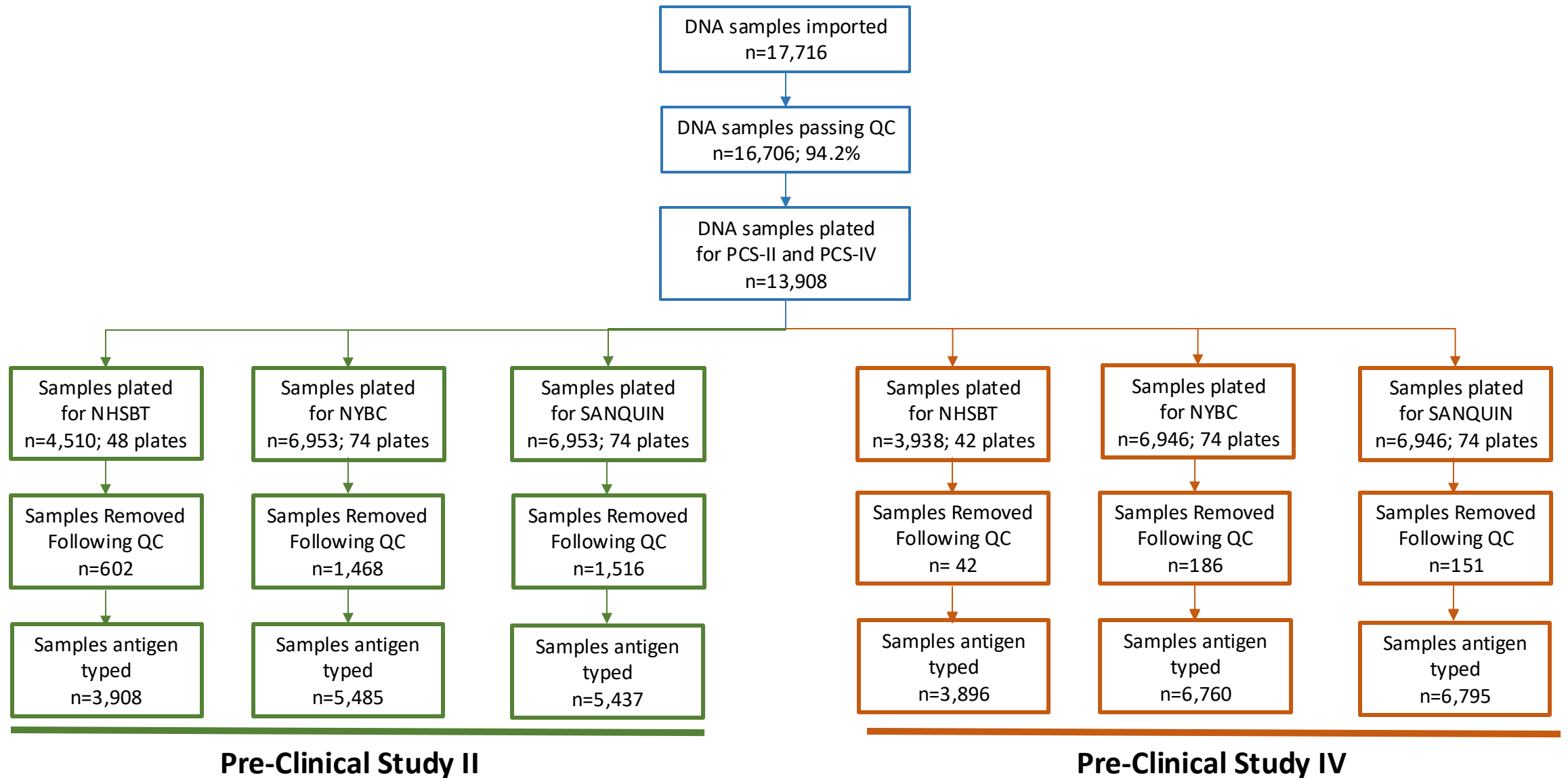**50,000 DNA variants - 384 samples**

Content: Donor & Patient Typing only
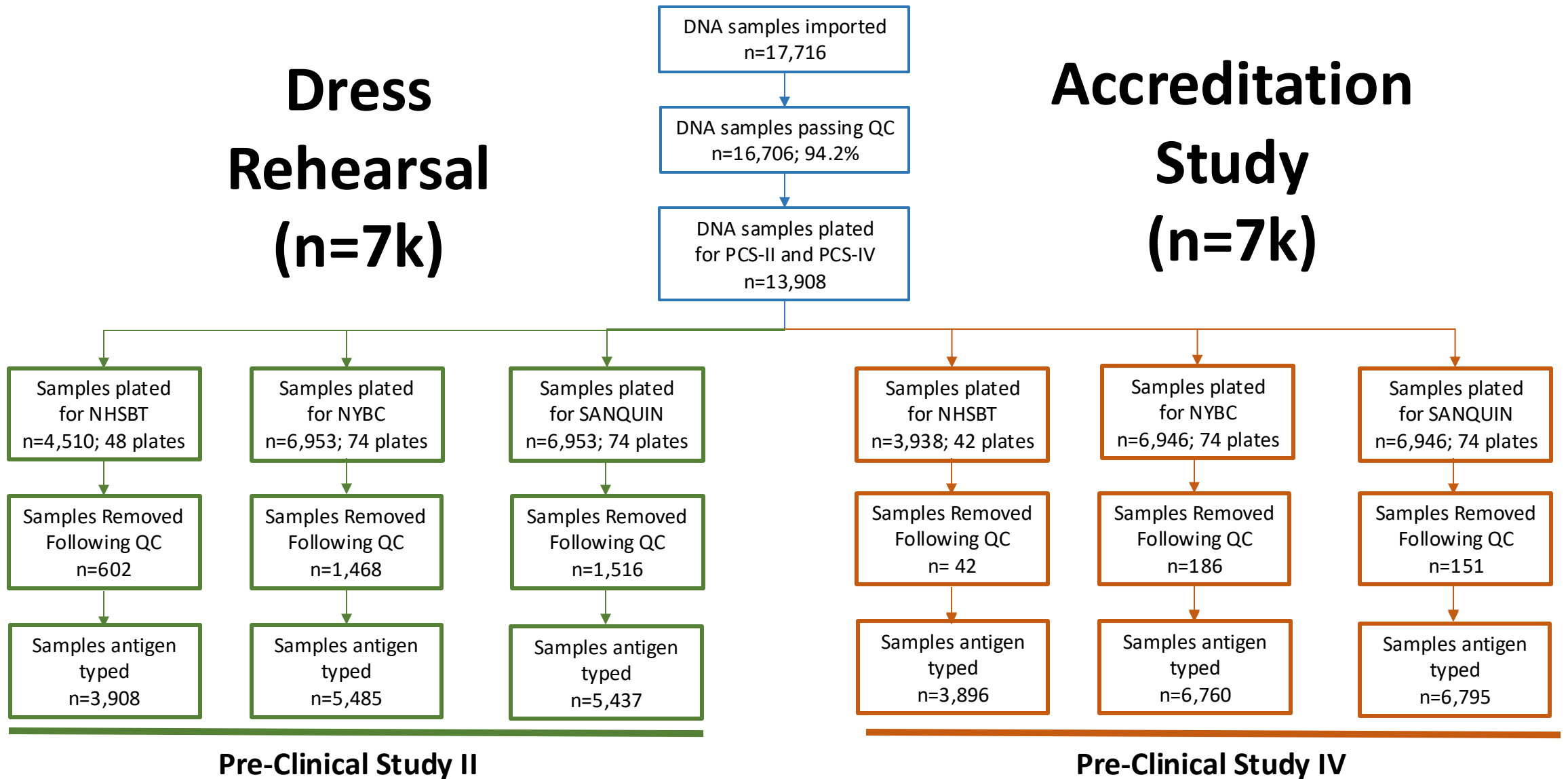
International Accreditation Study

- **17,716** DNA samples submitted by **7** blood services

- Electronic donor record data, including clinical antigen typing & sample tracking information, databased in **BGC Secure Research Computing Platform** (SRCP)

- **13,908** samples included following selection & DNA QC

Study Workflow

Study Workflow

Dress Rehearsal (n=7k)

Accreditation Study (n=7k)

```
DNA samples imported
n=17,716
        ↓
DNA samples passing QC
n=16,706; 94.2%
        ↓
DNA samples plated
for PCS-II and PCS-IV
n=13,908
```

Samples plated for NHSBT n=4,510; 48 plates	Samples plated for NYBC n=6,953; 74 plates	Samples plated for SANQUIN n=6,953; 74 plates	Samples plated for NHSBT n=3,938; 42 plates	Samples plated for NYBC n=6,946; 74 plates	Samples plated for SANQUIN n=6,946; 74 plates
Samples Removed Following QC n=602	Samples Removed Following QC n=1,468	Samples Removed Following QC n=1,516	Samples Removed Following QC n=42	Samples Removed Following QC n=186	Samples Removed Following QC n=151
Samples antigen typed n=3,908	Samples antigen typed n=5,485	Samples antigen typed n=5,437	Samples antigen typed n=3,896	Samples antigen typed n=6,760	Samples antigen typed n=6,795

Pre-Clinical Study II

Pre-Clinical Study IV

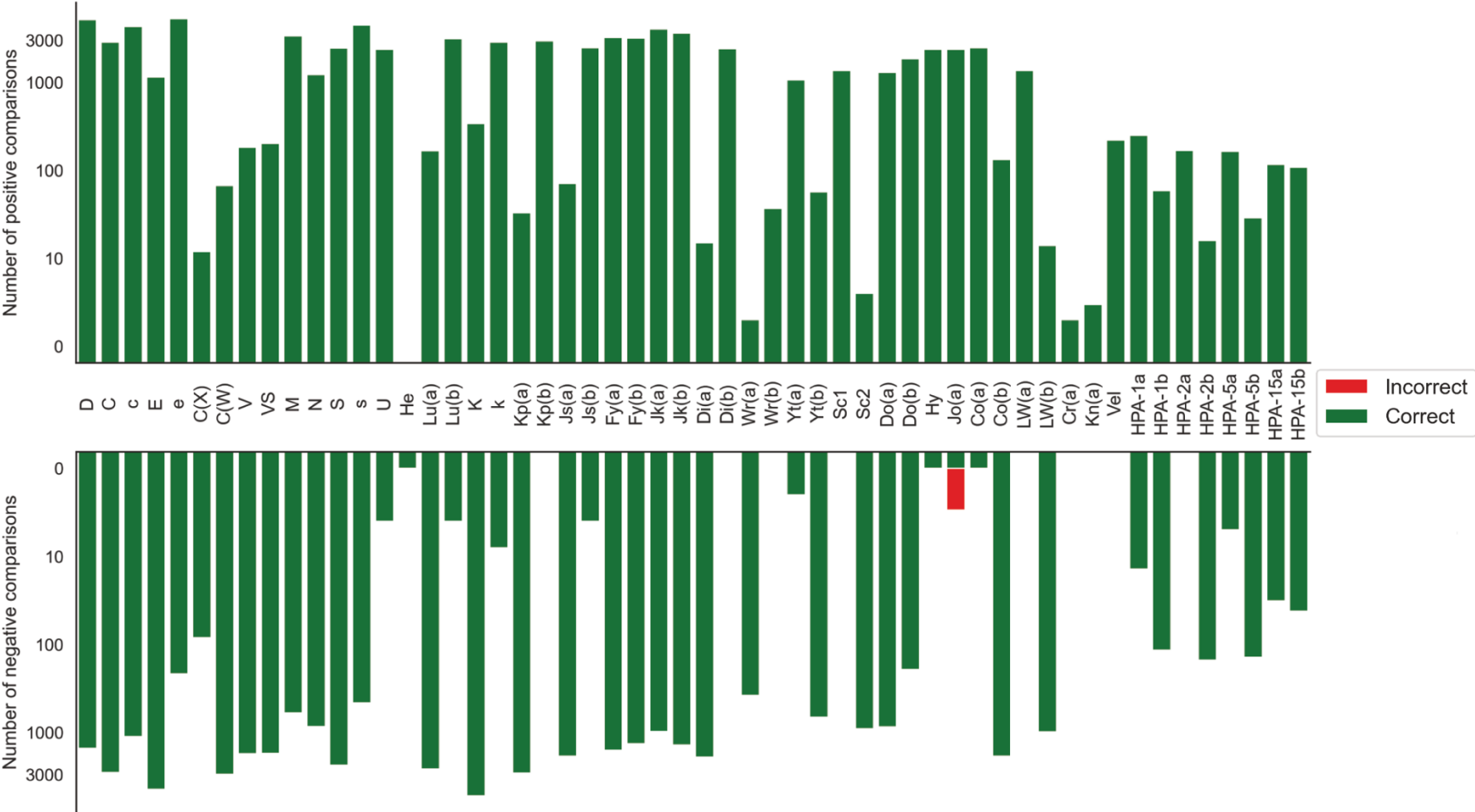# Ancestrally Diverse Panel

- Specific focus placed on ancestral diversity

- **35.2%** Non-European donors

- **1,428** African and Admixed American
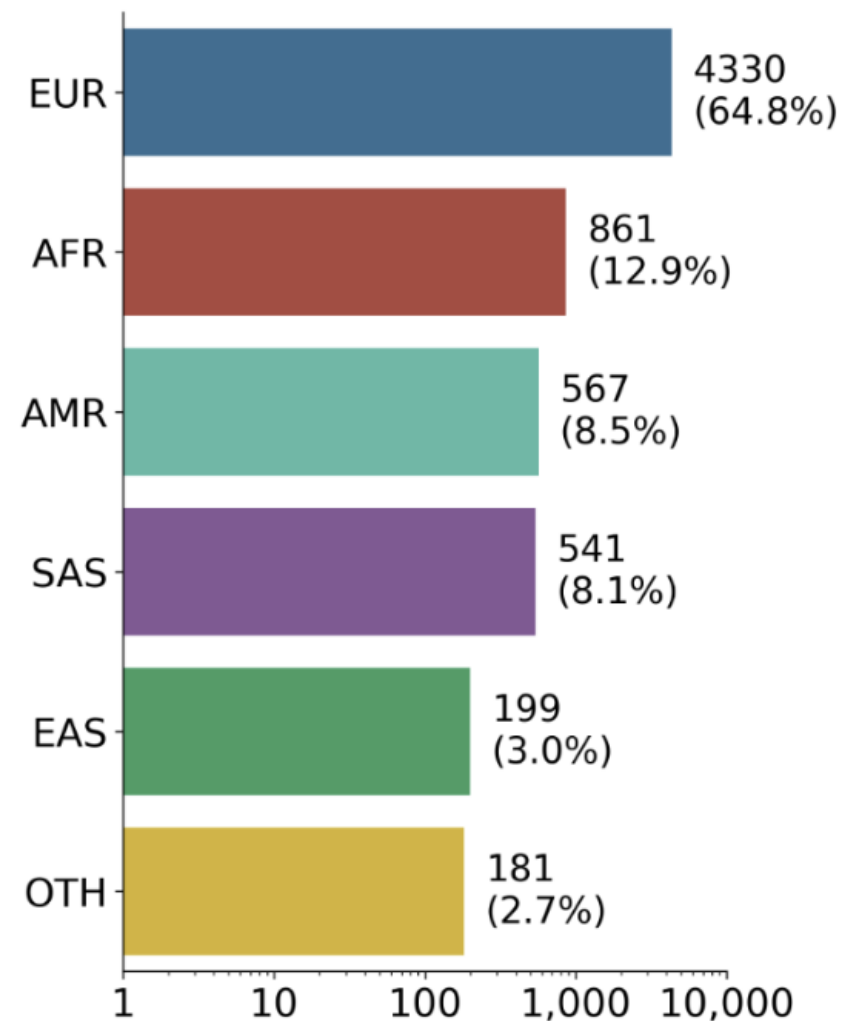
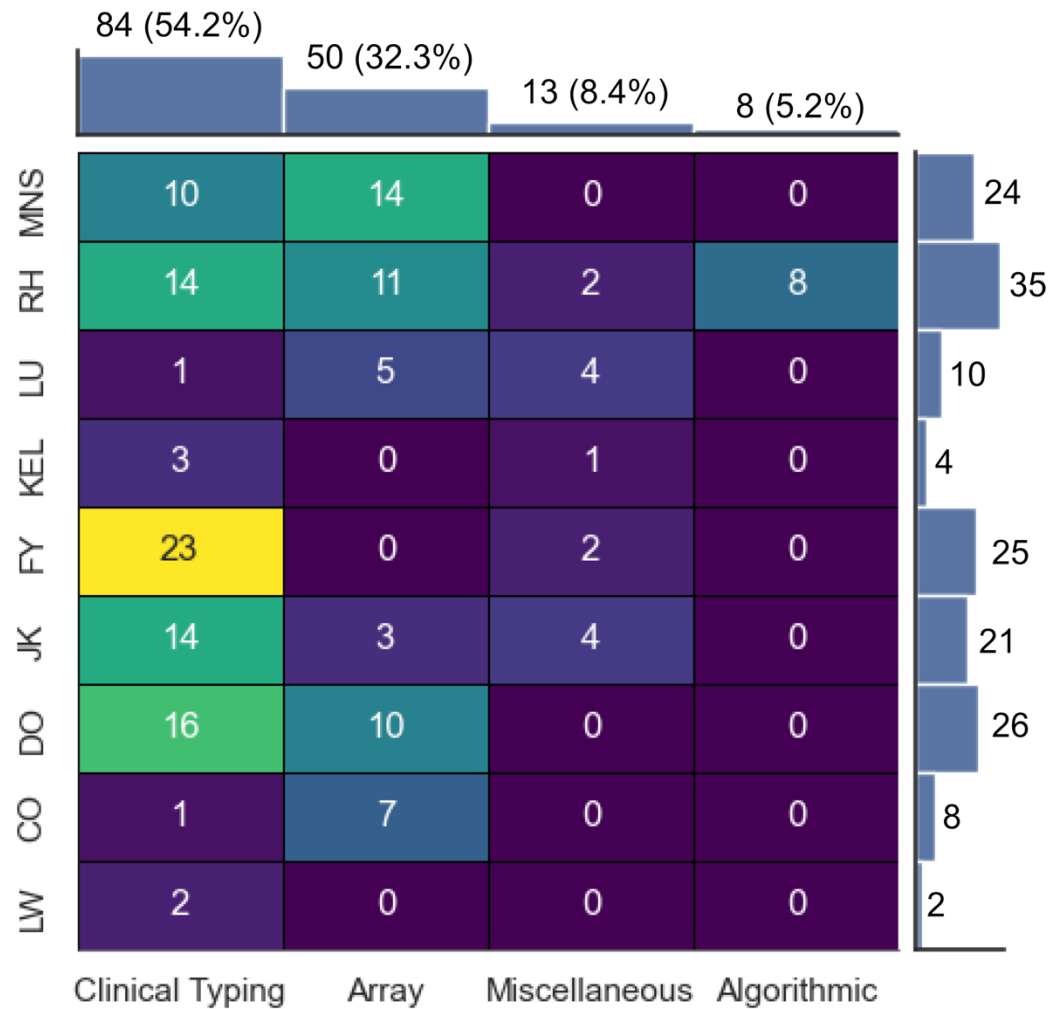# International accreditation data

- HEA
  - **123,124** comparisons
  - **99.9%** agreement

- HPA
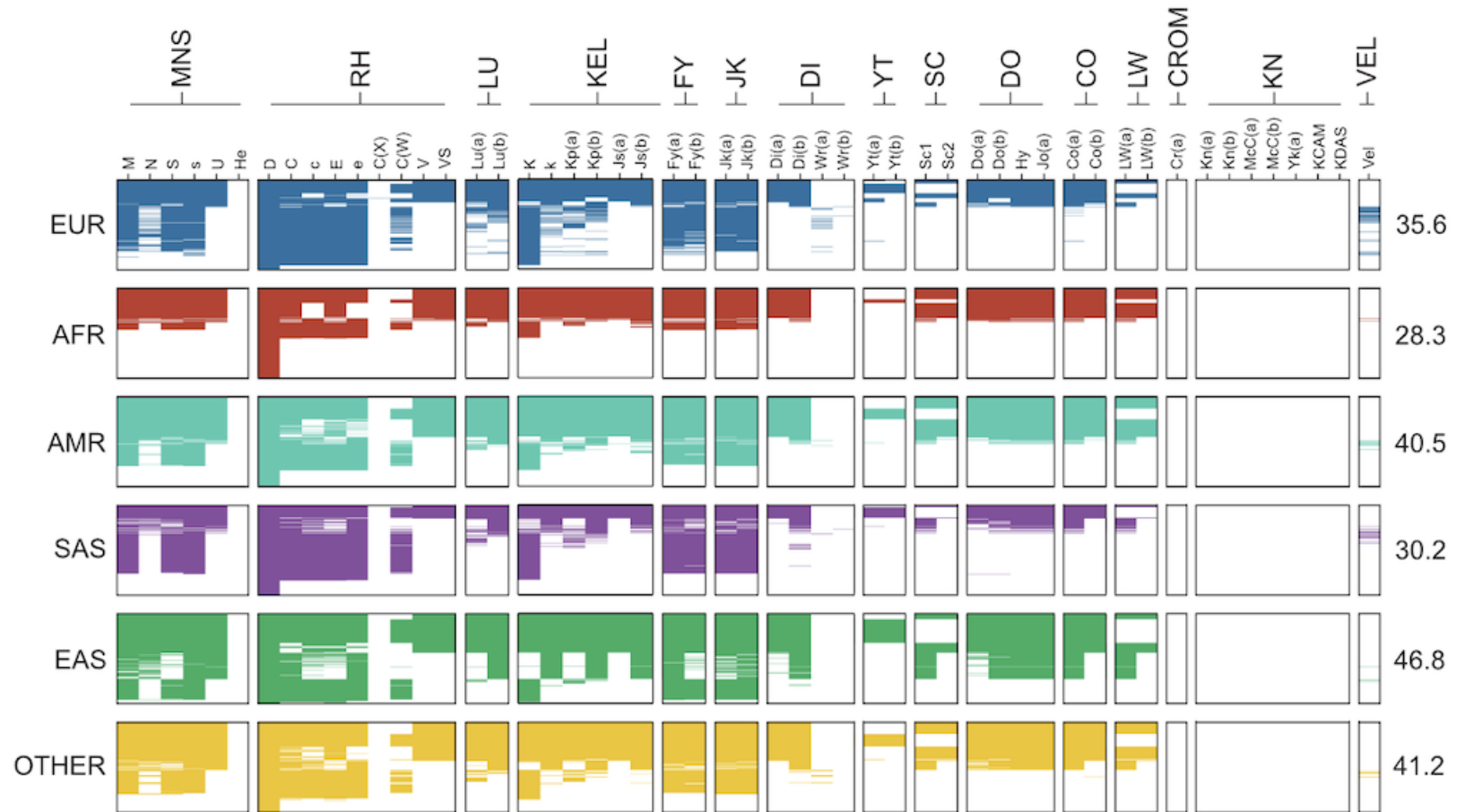 - **1421** comparisons
  - **99.6%** agreement

SANQUIN and NYBC replicate analysis

- **246,874** comparisons

- **99.9%** concordance

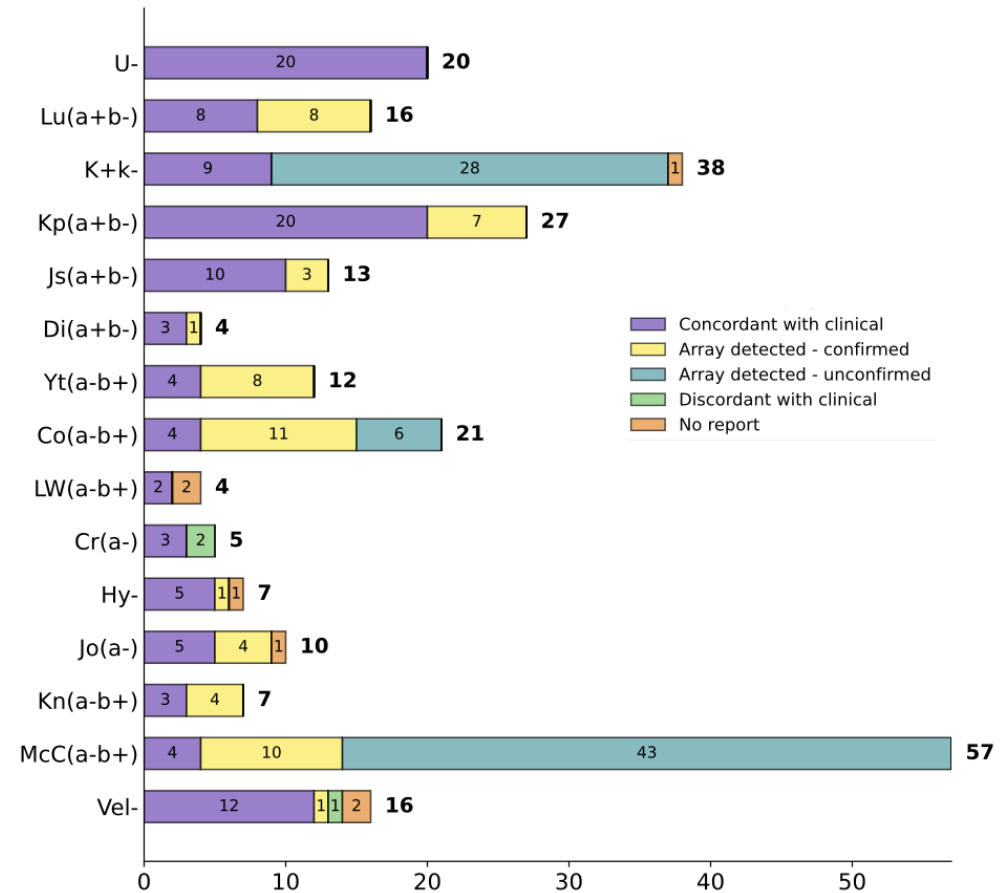- **255** total discordances (0.09%)
  (155 unique)

Clinical typing

- **124,364** types available

- **35.8 %** typing density

Array genotyping

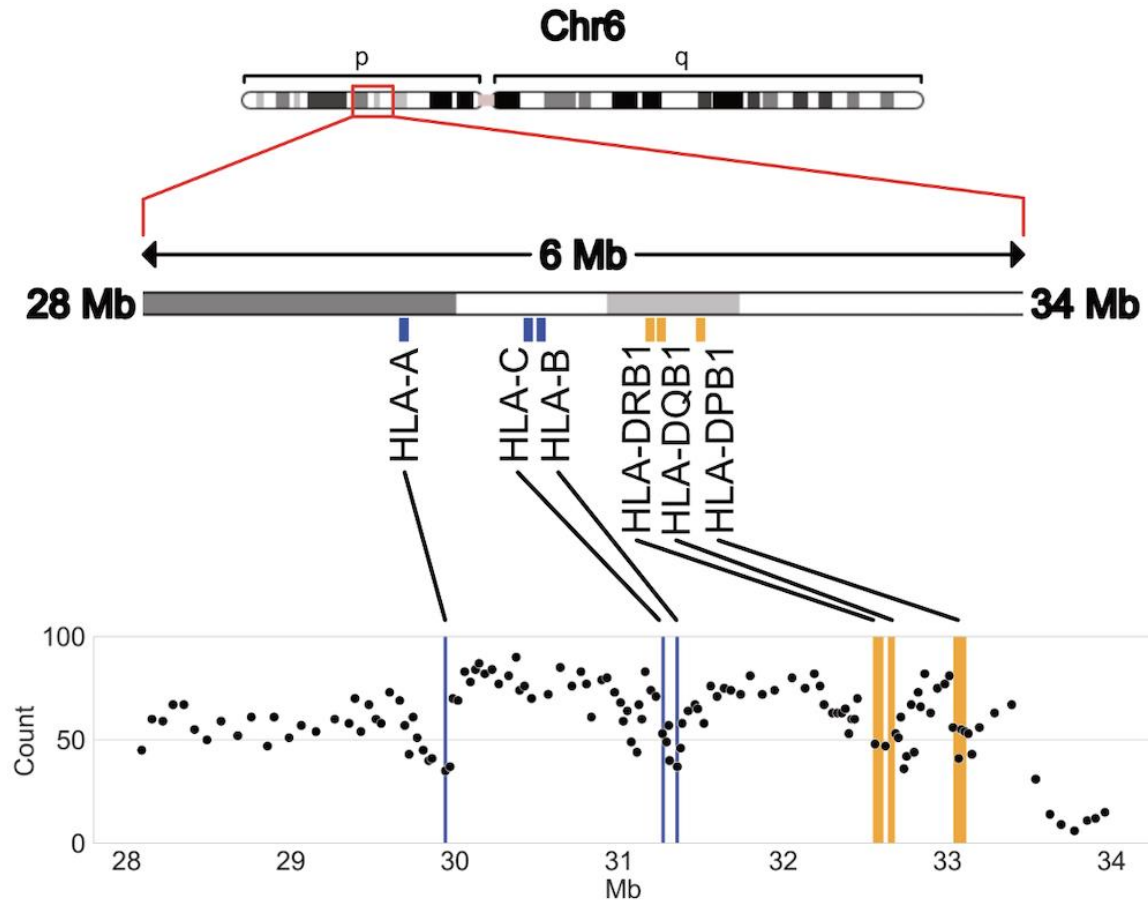- **345,848** types available

- **99.6%** typing density

HFA Negative Donors

- **256** HFA-negative donors

- **135** newly discovered
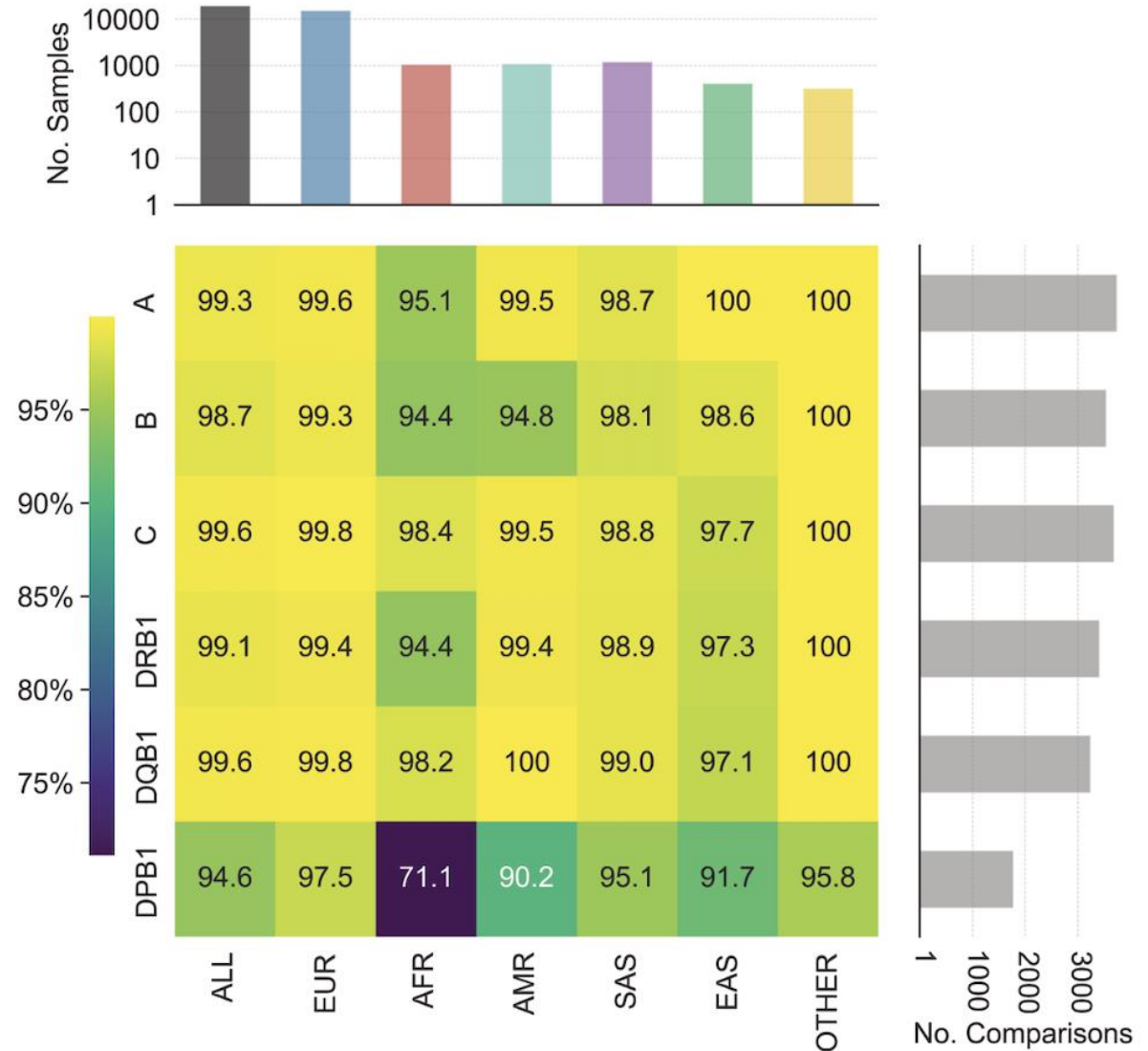
- These can now be confirmed

HLA typing

- **7896** variants for HLA typing

- 2-field HLA types (01:01)
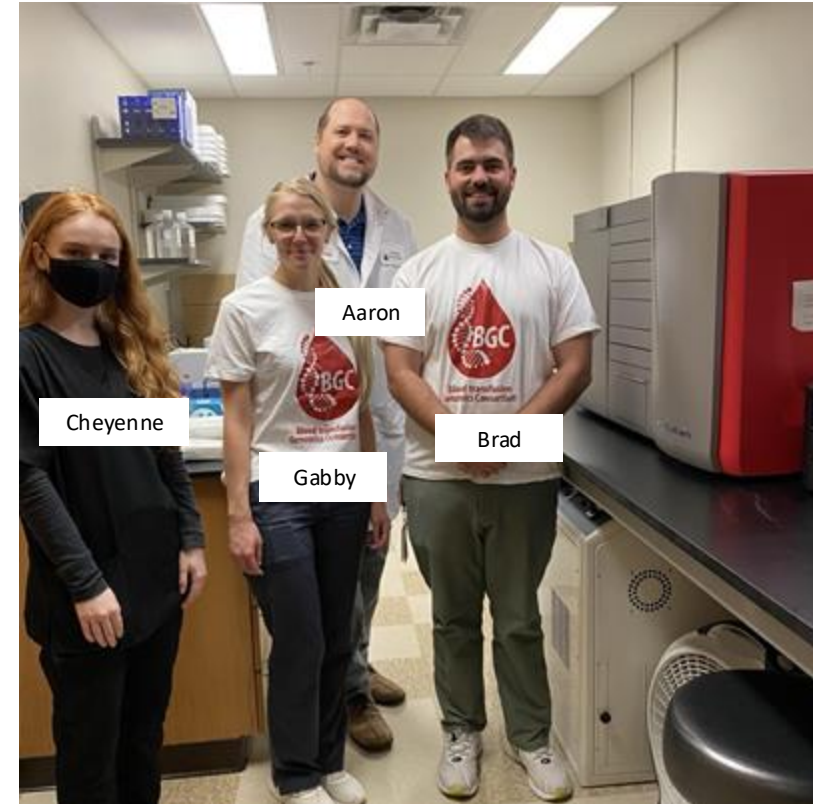
- Class I & II

HLA concordance

- 12,456 comparisons

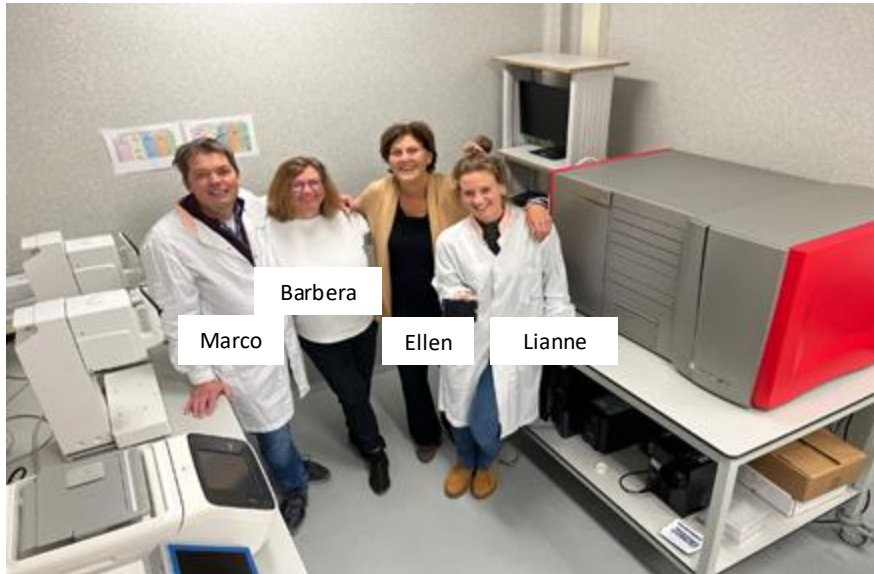- 97.9% concordance

- 265 discordances

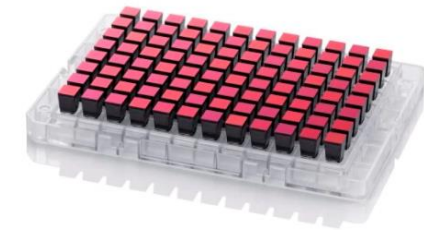# Future Direction

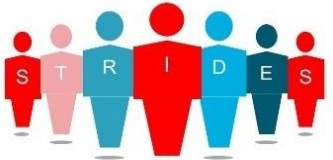# Genomics implemented in blood services

Summary

- Validated test for typing donors and patients

- At-scale genotyping in accredited NHSBT labs is underway.

  - **85,000** donors enrolled in NIHR STRIDES donor health study

  - **18,000** NHS England patients inherited anaemias

Precision Blood Matching in 2025

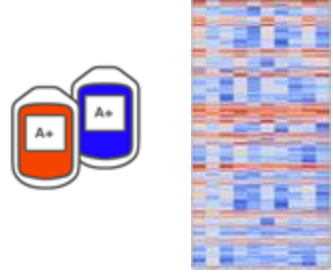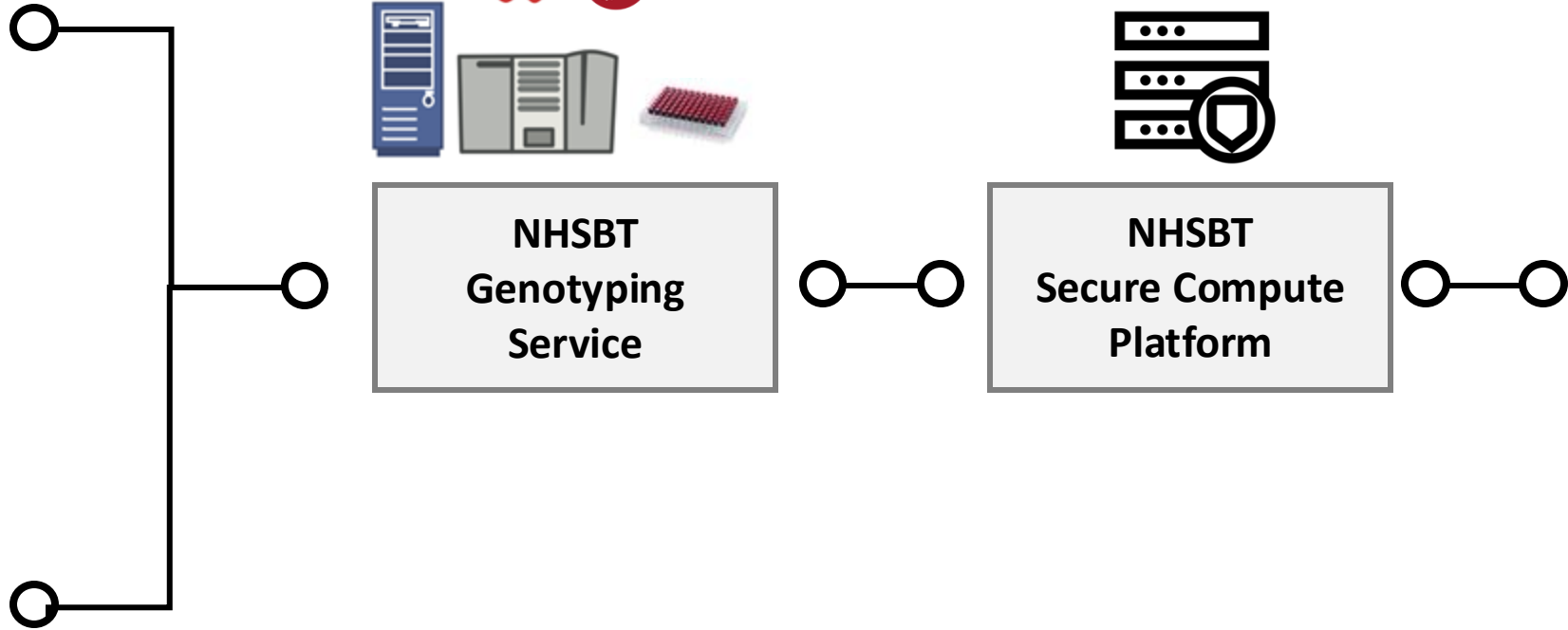|		
William Astle	Ute Jentsch	Lydia Quaye
Ai Leen Ang	Shantanu Kaushikkar	Orod Razeghi
Kirk Beard	Mary Kasanicki	David Roberts
John Bradley	Nathalie Kingston	Luisa Ronzine
Colin Brown	Lianne Koets	Kathleen Selling
Tom Bullock	Marco Koppelman	Melissa Schreiner
James Daly	Will Kruka	Marie Scully
John Danesh	Pawinee Kupatawintu	Ellen van der Schoot
Candice Davison	William Lane	Olga Shamardina
Emanuele Di Angelantonio	Jennifer Laird	Kathleen Stirrups
Alexander Dilthey	Maja Matååtle	Jonathan Stephens
Parita Ghia	Lorna McLintock	Matthew Thorpe
Jeremy Gollub	Stefan Meyer	Sara Trompeter
Aaron Gottschalk	Gail Miflin	Luca Valenti
Lavendri Govender	Celina Montemayor	Sumathi Venkatapathy
Andreas Greinacher	Ana-Maria Moreno	Sunitha Vege
Shane Grimsley	Sarah Morley	Barbera Veldhuisen
Andrea Harmer	Gorka Ochoa	Nico Vreeswijk
Matthew Hazell	John Ord	Lindsay Walker
Laura Hontoria del Hoyo	Willem H Ouwehand	Darleen Welford
Martin Howell	Folarin Oyebolu	Connie Westhoff
Kati Hyvärinen	Jukka Partanen	Mark Whelan