Integration of Red Cell Genotyping into the Blood Supply Chain

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BloodCenter of Wisconsin
Conflict of interest statement

Inventor of patents on red cell genotyping owned by the Canadian Blood Services

Member of Grifols SA speaker bureau
Objectives

• Discuss the challenges of and benefits to implementing wide-spread, routine full RBC antigen typing of donor units

• Describe the implementation of a mass-scale process of red cell genotype screening and confirmatory phenotyping with licensed reagents

• Discuss the process and approach of (predicted) phenotype matching donor units with requests

• Understand the challenges with the use of historical phenotypes or genotypes to label a unit of blood
What problem are we trying to solve?

Mass-scale RBC characterization has the potential to change how blood centers provide antigen-negative blood

- To support alloimmunized patients:
  - multiple Abs, Antigen-pos with Ab (variants), rare
- To prevent alloimmunization:
  - SCD, AIHA, ‘DARA’ other chronically transfused patients
BloodCenter of Wisconsin provides blood to 64 hospitals serving a population of 3.7 million
High-level process of antigen typing

- **Donor Selection**
  - Optimize donor selection process

- **Donor Typing**
  - Obtain comprehensive results (low data loss)
  - Develop exception reports
  - Integrate interpretations (variants)

- **Data Management**
  - Maintain active database
  - Flexible targets (e.g. Vel 2013)

- **Donor Recruitment**
  - Develop a registry maintenance strategy
Mass-scale testing

Red Cell Typing

Outcomes

Evaluation

Targets

Requests

Alloimmunisation

Chemistry

- Mass-scale testing
- Red Cell Typing
- Alloimmunisation
- Mass-scale testing

- Requests
- Targets
- Alloimmunisation
- Chemistry

- Mass-scale testing
- Red Cell Typing
- Alloimmunisation
- Mass-scale testing

- Requests
- Targets
- Alloimmunisation
- Chemistry
Donor Selection – What targets to type?

Breakdown of 600 Phenotype Requests by Blood Group System

- Rh: 41%
- Kell: 20%
- Kidd: 13%
- Duffy: 15%
- MNS: 10%
- Misc: 1%

95% of requests covered by blood group antigen phenotyping
Goal of antigen-negative searches

Frequency of antigen-negative requests

- Common requests
- Multiple / Uncommon
- Rare

Database size

97%
Mass-scale testing

Red Cell Typing

Donors (3:3:1:1)

Process
- Import OpenArray files
- Apply call rules - genotypes to phenotypes
- Parse Data
- Confirm and Load Results to LIMS
- Comparative Analysis of Results

Database

% RBC Typed units

BloodCenter of Wisconsin
PART OF VERSITI
Wisconsin Tissue Bank
Donor Red Cell Genotyping (2010 - 2015)

- 24,332 donors on July 17, 2010
- 53,438 donors by 2015
- 307,182 units
- 2.1 units/donor/yr
Number of units with a genotype

Daily 7-day

Monthly 3-year
2013 = 30%
2014 = 33%
2015 = 35%
Blood donor phenotypes or genotypes

### Phenotyping
- 30 years
- 638,786 donors (1985 – 2013)
- 91% from 1991

### Genotyping
- 4 years
- 16% yr-over-yr

#### Tested by phenotype
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<th>Phenotypes</th>
<th>Tested by phenotype</th>
<th>Tested by genotype†</th>
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#### Tested by genotype†
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#### Historical Data
- Donors: 72,272
- Phenotypes: 322264
- Antigens: 1 - 28
- Years: 30

#### Genotyping Data
- Donors: 43,066
- Phenotypes: 1667026
- Antigens: 28 - 42
- Years: 4

**5×** indicates a 5-fold increase in the number of donors tested.
Antigen Query – supply chain information

- Portal transmits any blood group antigen information with a red cell unit by use of the ISBT 128 number without personal information
  - All common predicted phenotypes, and high-volume automated screening results of the Rh antigens included

- Antigens available to query: C, E, c, e, M, N, S, s, K, Fya, Fyb, Jka, Jkb (those antigen-negative types most likely encountered based on inventory and frequency)

- 14 hospital blood banks use antigen query, with most centers 30 – 200+ miles away from the blood center
Antigen Query: blood order portal

Patient-specific request
Antigen Query - workflow

The process closely mirrors Hospital’s current practice to phenotype units

Enter patient information and search criteria:
ABO, Antigens, Number of units

Scan a batch (any number) of units

Matching units, up to the number requested, will be displayed with oldest units identified first

If some or all of desired units are not found:

A new batch of units may be scanned and queried

An order may be sent to BloodCenter’s IRL for all or part of the remaining units
2009: selective low-volume, manual phenotyping
2015: genotyping + antigen query

Blood Center

53,000 donors
42 antigens

\[ \sum = 2.26 \times 10^6 \] (Genotypes)

Red Cell Genotyping

Rare/Screened Blood

Hospital Request

1:5000

<1:50

Hospital Transfusion Service

Antigen Query

DNA

BCW

Screening
Information in the supply chain

Historically Typed
Donor base
Molecular/Serology

Confirmed/labeled

Blood Center IRL

Confirmed/labeled

Hospital Transfusion Service

Confirmed/Labeled
Summary

- Comprehensive red cell typing has transformed the way antigen-negative blood is identified
  - Electronic handling of mass-scale genotype data (serologic confirmation); made accessible online
  - Delivery efficiencies to remote areas
  - RH, MNS, Kell, Duffy, Kidd are the ‘meat and potatoes’

- Additional licensed platforms (including phenotyping) are coming, and a test-of-record will accelerate the value of the information (labeled units)
  - Electronic ‘rules’ change A,C,G,T (nucleotide results) into a predicted phenotype
  - A phenotype plus a genotype may be more powerful than ether alone done twice
Summary

• Two historical (pheno/geno) types will further enhance the ability to provide labeled units
  – BECS handling of phenotypes and genotypes can be accomplished using different established nomenclatures
  – Electronic systems are needed to identify, correlate, and display phenotypes and genotypes; with a “comment box” used for information on variant antigens

• Historical and mass-scale labeling issues
  – Donor identification an important issue to address
  – Tests-of-record; LDT *versus* licensed test (validation)
  – How much information can be put on the label (42 Ags?)
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