

45°

**Convegno Nazionale
di Studi di Medicina Trasfusionale**

Rimini | 29-31 maggio 2024



**Rare blood groups and blood donors:
which organization?**

Nicoletta Revelli

*Reference Immunohematology Laboratory
SC Medicina Trasfusionale - Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico di Milano*

as a speaker, I declare that:

I DO NOT HAVE any personal or third-party commercial interests; I have not had any relationship in the last two years with subjects with commercial interests such as to influence my function in order to draw any advantage.

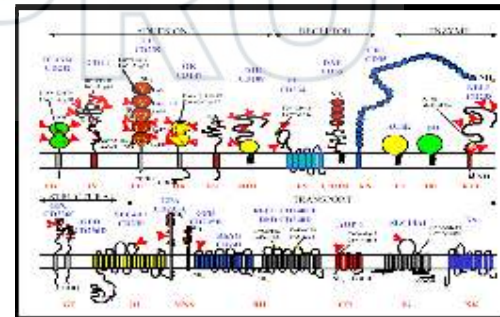
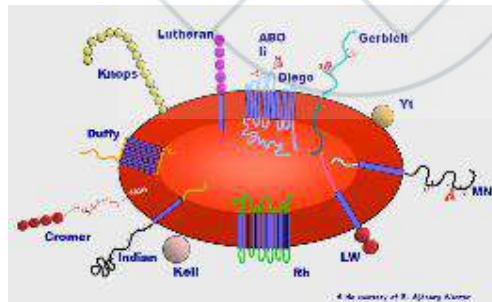
Alloimmunization

- Individuals exposed to red blood cell (RBCs) antigens may produce antibodies against the antigens expressed by RBCs
- The incidence of alloimmunization ranges between 1%–6% in the general population and up to 30% in chronically transfused patients



Blood group systems and RBC antigens

- > **380** minor blood groups
- **45** Systems (genetically determined by 50 genes)
- **1** Collection
- **2** Series:
 - 700 (low frequency antigen)
 - 901 (high frequency antigen)



ISBT (International Society of Blood Transfusion) Working Party on Terminology for Red Cell Surface Antigens

<http://ibgrr.blood.co.uk/isbt>

Provision of compatible blood

The provision of compatible blood is challenging for:

- Patients negative for a high-frequency antigen (HFA) who have made the corresponding alloantibody
- Patients who have made a combination of alloantibodies



Patients with RBCs complex immunization

- In most cases identification of HFAs or combination of alloantibodies is time consuming, complex and it might delay transfusions
- Although 3-5% of patients with complex immunization may need **rare blood**, no clinical guidelines address their blood management
- In particular according to some authors transfusion support is unsatisfactory in **about one-third** of hospitalized patients with alloantibodies to HFAs

Seltsam A, et al. Antibodies to high-frequency antigens may decrease the quality of transfusion support: An observational study. *Transfusion* 2003;43:1563-6

Definition of Rare Blood Donor

A donor is defined as '*rare blood donor*' when:

➤ **Negative for high-frequency antigens**

- frequency is less than 1:1000 (0.1%)
- variable: 1:250 in France
1:100 to 1:1000 in Japan

Country	Definition of Rare	Country	Definition of Rare
China	1/1000	New Zealand	1/1000
Finland	Not given	Singapore	1/1000
France	1/250	South Africa	<1/100
Germany	1/1000	Spain	1/1000
India	O ^h	Switzerland	Not given
Iran	1/1000, highs and lows	Taiwan	<1/1000
Israel	1/1000	The Netherlands	<1/1000
Italy	<1/1000	UK	IRDP cat +
Japan	1/100 to <1/1000	USA	<1/1000

➤ **Negative for multiple common antigens**

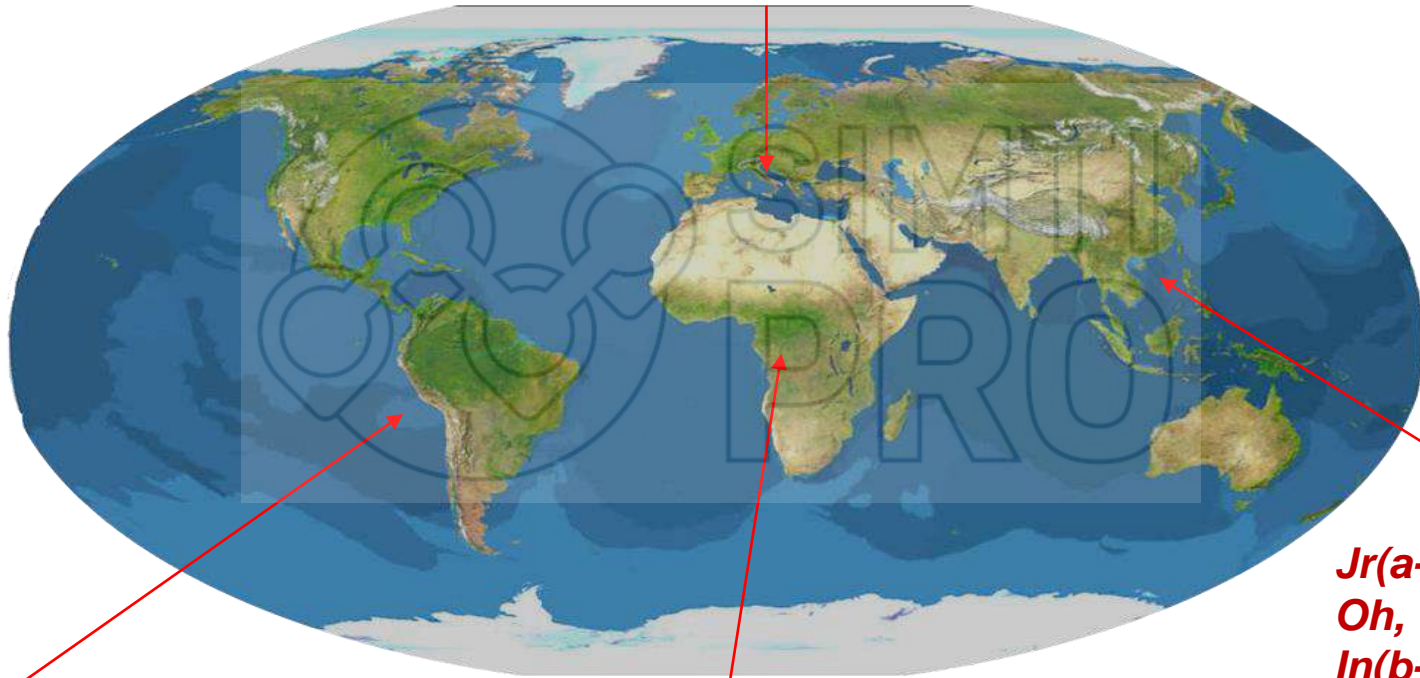
2012 ISBT Working Party on Rare Donors Meeting



Standards: American Rare Donor Program (ARDP)

Rare blood phenotypes in different countries

K-, Yt(a-), Vel-, Kp(b-), LW(a-), Lan-, Kn(a-), En(a-), Gy(a-), PP₁P^k-



*Di(b-), Ge:-2,3,
Es(a-), GUTI-*

Fy(a-b-), Js(b-), U-, At(a-), hr^S-, hr^B-, Hy-, Jo(a-), Cr(a-), Tc(a-), Sl(a-)

*Jr(a-), Jk(a-b-),
Oh, Ge:-2,-3,
In(b-), Ok(a-), P-*

Rare blood donors most difficult to find

Country	Most Difficult Types to Obtain
China	Rh _{null} ; D - -
Finland	Vel neg; O _h ; hr ^S -
France	U- ; Fy(a-b-); Vel-; Rh _{null} ; D - - ; Hr-; Hr ^B -
Germany	Fy(a-b-); U-; Gy(a-); Hy-; Jo(a-); Js(b-); O _h ; D- -; Rh _{null} ; K ₀ ; Kx-; Jk(a-b-); Ge-; PP1Pk-; Di(b-)
India	In(a+b-); D-; Rh _{null} ; Co(a-b-)
Iran	D - -; E- c- K- Jk(b-); E-c- K- Jk(b-) Fy(b-); C- E- Jk(b-) S- M-; E- C- c- e- ; I-
Israel	Rh _{null} ; Jr(a-); Vel-
Italy	SC:-1; LW(a-b-); K ₀ ; Jk(a-b-); Lan-; I-; P-; P ^k -; Jr(a-); S-s-U-; hr ^B -; Di(a+b-); Hy-; Jo(a-); Kp(b-); Js(b-)
Japan	D-; PP1P ^k -; I-; En(a-); Ge-
New Zealand	K ₀
Singapore	Di(b-)
South Africa	Ge-; Lan-; Jk(a-b-), Lu:-5; PP1P ^k -
Spain	K ₀ ; McLeod; Co(a-b-); GE:-2,-3; Rh _{null} ; RH:-17; GE:-2; Cr(a-); LW(a-); In(b-); SC:-1; At(a-); Lan-; RH:-46; Jk(a-b-); P-; I-; U-
Switzerland	Lan-; Jr(a-); U-; Rh _{null} ; K ₀ ; O _h
Taiwan	Di(b-); Rh _{null}
The Netherlands	D- U-; K ₀ ; Rh _{null} ; Di(b-); Multiple antibodies & rare phenotype{(e.g. Fy(a-b-))}
USA	E- hr ^S -; SC:-1,-2; At(a-); Lan-; I-; Jr(a-); PP1P ^k -; E- hr ^B -

2012 ISBT Working Party on Rare Donors Meeting



Rare phenotypes difficult to find



- Some rare phenotypes are very difficult to find compared to others such as:
Rh_{null}, Ko, McLeod, U-, Di(b-), Jk(a-b-), Sc:-1, I-, Lw(a-b-), hr^{B-}
- Maintain a quickly accessible stock of rare blood units for ***Kp(b-), Vel-, Lu(b-) and Yt(a-)*** would guarantee adequate transfusion support for the majority of patients with complex immunization
- For this reason in Italy, as in France, both donors and patients enter the register, with the idea that patients can become donors and vice versa

Impact prevalence of single antigens

A simple calculation can be used to estimate the number of units that must be tested to satisfy the transfusion requirement of a patient immunized by combination of antigens:

Patient with anti-K, anti-Jkb and anti-s alloantibodies:

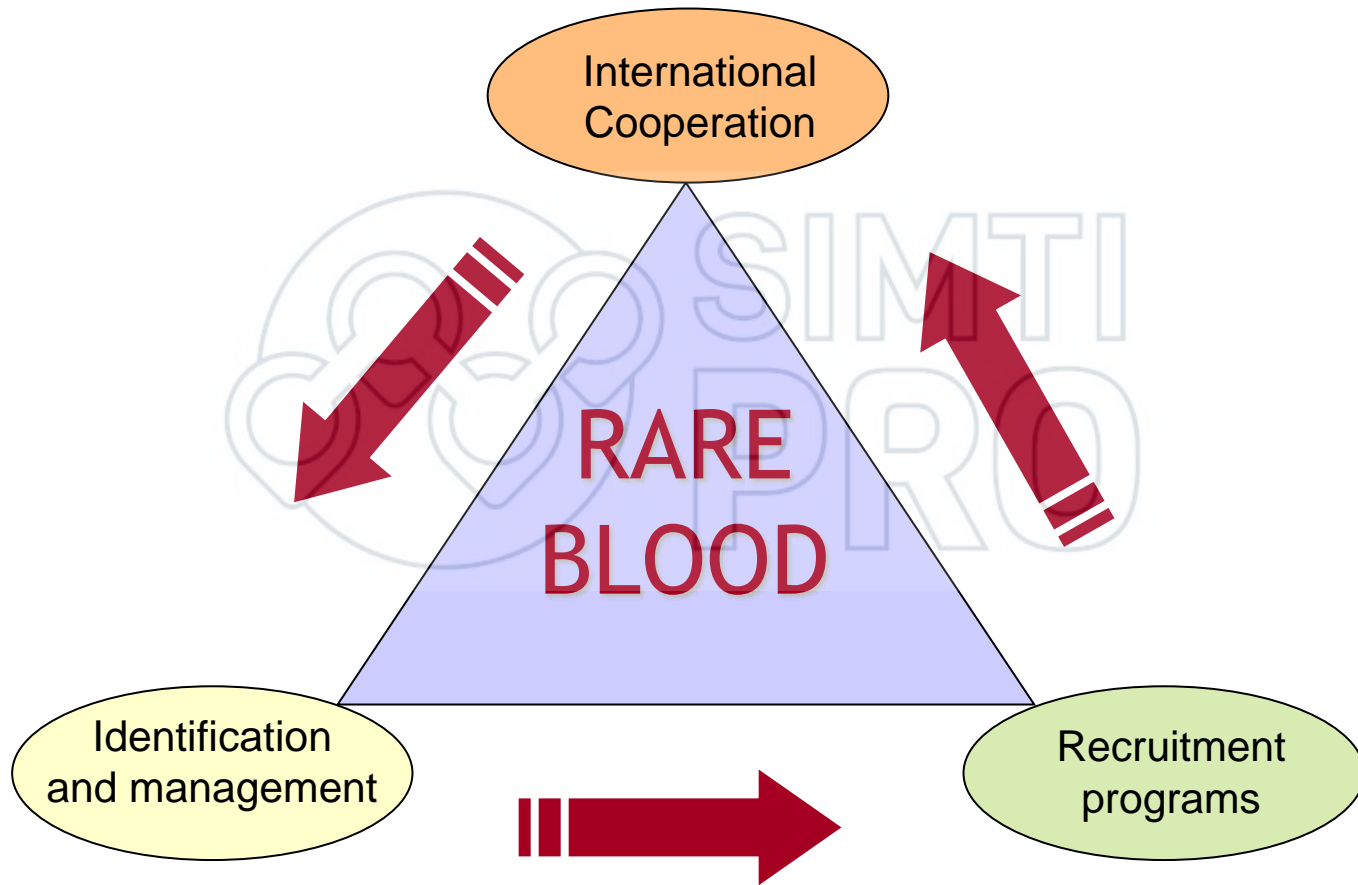
K- donors: 91%; Jk(b-): 26%; s-:10%

The percentage of negative donors for each antigen will be:
 $0.91 \times 0.26 \times 0.10 = 0.023$

Approximately **2 out of 100 donors** will be negative for K, Jkb and s

Without considering ABO group, RH type and phenotype!

Key factors for rare blood donor provision



Identification of rare blood donors

Identification of rare blood donors is a critical factor in establishing a rare blood donor registry

- Screen **70-150** samples of blood donors at the same time or routinely
- Presence of unusual antibodies:
 - **in donors**
 - **in patients**
- Type family members, especially siblings
- Freeze and store blood from rare donors



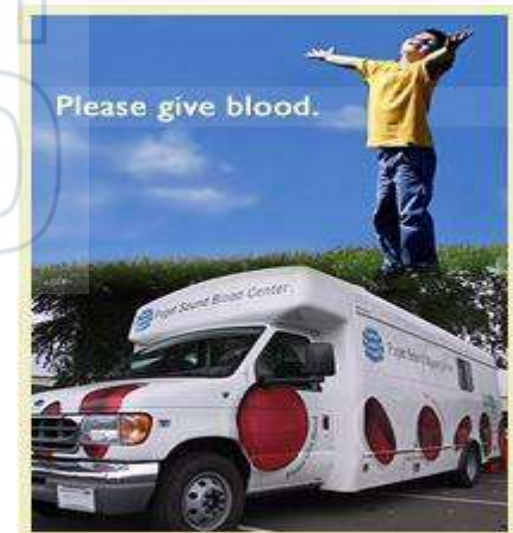
How do we detect a “rare blood donor”?

CRITERIA TYPING	PRO	CONS
All blood donors	<ol style="list-style-type: none">1. Highly typed inventory2. Rare donors found by chance	<ol style="list-style-type: none">1. Costs2. Scarcity reagents
Blood donors with pre-defined characteristics	<ol style="list-style-type: none">1. Focus on donors that fulfill local needs (ABO, Rh, ethnicity)2. Maybe cheaper	<ol style="list-style-type: none">1. Risk of missing rare donors negative for high frequency antigens

Recruitment programs

Recruitment and retention are critical for maintaining an adequate supply of rare blood donors

- Focusing on rare type found in the own geographic area or on ethnic population
- Typing program based on antigens frequency within the different population groups



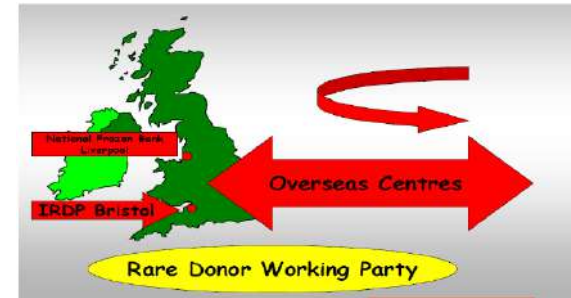
Getting the rare phenotype donor



FOR RARE BLOOD TYPES,
RARE BLOOD DONOR REGISTRIES
HAVE BEEN ESTABLISHED...

- In **1959**, the American Association of Blood Banks (AABB) set up a rare donor file to meet the transfusion needs of patients with unusual blood group antibodies
- In **1964**, the ISBT and World Health Organization (WHO) launched the collaborative program called International Rare Donor Panel (IRDPP) to generate data from various sources (UK, USA and Japan)
- In **1998** there is a well-established American Rare Donor Program (ARDP) jointly managed by the American Red Cross and AABB

International Rare Donor Panel (IRDP)



- IRDP was established to facilitate the rapid location and exchange of rare blood between countries
- The compilation and maintenance of the IRDP was assigned to the International Blood Group Reference Laboratory (IBGRL) in Bristol UK
- The panel currently contains details of rare donors from **27 contributing countries** and also frozen units inventories from frozen blood banks around the world

ISBT Working Party (WP) on Rare Donors

The ISBT WP on Rare Donors was formed in 1984 to promote international collaboration with regard to the provision of donor blood with rare phenotypes

The main goals of the Working Party are:



- to develop guidelines to for standardize listing, labelling, shipping, testing and reimbursement for rare donors blood
- to increase the number of donors in the IRDP by promoting the growth of rare donor programs
- to communicate to ISBT members so that they have access to information related to rare blood

The availability of rare blood in Italy



- National data regarding the need and provision for rare blood units are lacking
- In 1990, Law n. 107 on: *'Regulation of transfusion activities concerning human blood and its components and the production of plasma derivatives'* stated:
 - ***“.. that every Region should have a bank of frozen blood components, collected from donors of rare or uncommon blood groups, in connection with the National Institute of Health”***

Rare Donors Registries/Banks in Italy

The **Rare Blood Components Registry/Bank of Lombardy Region** was established in 2005 at the *Policlinico Hospital* in Milan by an official agreement with the Lombardy Region Government


In 2010 another **Regional Rare Blood Donor Registry/Bank of Sicily** was established at the Hospital of Ragusa



Goals of the Rare Blood Components Registry/Bank of Lombardy Region

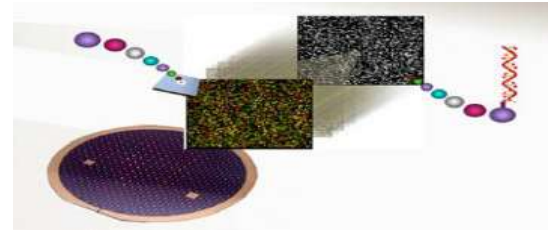
Selection criteria

- Identify rare blood donors
- Create a regional donors Registry
- Organize a Bank of frozen rare blood units

	
Age	≤ 55 years
ABO group	O or A
Rh phenotype and K antigen	CCDee, ccdee, ccDee, ccDDEE, K-
Number of donations	≥ 2

All donors from ethnic minorities are extensively typed





Step 1 - typing:

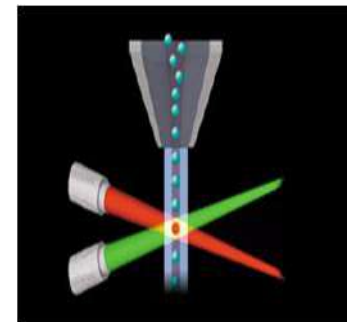
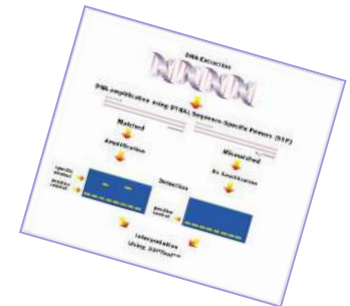
Blood donors' samples are typed with the microarray platform for 38 erythrocyte antigens (RHCE, KEL, JK, FY, MNS, DO, LW, CO, SC, LU, DI) and by serology with fully automated instrument for:

Ge:-2, PP₁P^k, Yt^a, Lu^b, Lan and Vel erythrocyte antigens

Step 2 - confirmation:

The typings of rare donors are confirmed by:

- Automated serological method
or
- Molecular methods (PCR-SSP/other microarray method)





“Emonet”: local informatic system

EmoNet

File Tools Presentazioni Laboratorio Emoteca Emoderivati/Materiali Uso clinico I.E. Operazioni Funzioni di finestra Window Help

Tipizzazione[Dati tipizzazione]

Dati anagrafici
CAI 0620240 C [redacted] Fe [redacted] 979 0 NEG(D)ccdee (C)

Gruppo
ABO 0 Tipo Rh NEG Livello D Data det. 13-08-2015 FtRh ccdee Livello C

Tipizzazione eritrocitaria
RARO GR Congelare **SEMPRE**

Sistema	Antigene	Risultato	Livello	Data
DI	Wra	-	1	23-03-2015 11:29
	Wrb	+	1	23-03-2015 11:29
DO	Doa	-	2	13-08-2015 17:56
	DoB	+	2	13-08-2015 17:56
	Hy	+	2	13-08-2015 17:56
	Joa	+	2	13-08-2015 17:56
CO	Coa	-	2	13-08-2015 17:56
	Cob	+	2	13-08-2015 17:56
YT	Yta	+	1	23-03-2015 11:29
	Ytb	-	1	23-03-2015 11:29
Sc	Sc1	+	2	13-08-2015 17:56

Tipizzazione piastrinica

Sistema	Antigene	Risultato	Livello	Data
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HLA-A [] [] HLA-B [] [] HLA-C [] []
HLA-DR [] [] HLA-DP [] [] HLA-DQ [] []

“Cryoteca” housed database

“Cryoteca” report

Ricerca Avanzata / Stampa

Antigene selezionato: Fyb

CAI	COGNOME	NOME	OTNASCOITA	RES	PROV	T_SOSP	T_DATE	UNIT
229190	20/07/191	0	POS	cdDec	04/12/197, 1			
509661	31/03/191	0	POS	cdDec	04/08/197, 1			
513855	16/11/191	0	POS	cdDec	04/08/197, 1			
145894	28/11/190	0	POS	cdDec	04/11/197, 0			
182784	08/10/189	0	POS	cdDec	04/08/197, 1			
223559	03/11/190	0	POS	cdDec	0			
372257	11/01/192	0	NEG	ccccc	0			
226642	23/02/2002	0	NEG	ccccc	04/20/197, 0			
453311	13/07/187	0	POS	cdDec	D-11,05/1910 0.13.00.			
467548	01/01/192	0	POS	cdDec	04/04/197, 0			
474073	24/09/194	0	POS	cdDec	0			
577206	11/08/195	0	POS	cdDec	04/08/197, 1			
677625	02/09/192	0	POS	cdDec	04/08/197, 0			
529635	11/09/191	0	POS	cdDec	D-05,05/2011 10.04.00.			
311485	11/09/190	0	POS	cdDec	04/03/197, 0			
226641	13/09/191	0	POS	cdDec	04/08/197, 1			


Consuntivi Alfa Inidennati 10/06/2013
Antigene selezionato: Fyb-Fyb

CAI	COGNOME	NOME	OTNASCOITA	RES	PROV	T_SOSP	T_DATE	UNIT
229190	20/07/191	0	POS	cdDec	04/12/197, 1			
509661	31/03/191	0	POS	cdDec	04/08/197, 1			
513855	16/11/191	0	POS	cdDec	04/08/197, 1			
145894	28/11/190	0	POS	cdDec	04/11/197, 0			
182784	08/10/189	0	POS	cdDec	04/08/197, 1			
223559	03/11/190	0	POS	cdDec	0			
372257	11/01/192	0	NEG	ccccc	0			
226642	23/02/2002	0	NEG	ccccc	04/20/197, 0			
453311	13/07/187	0	POS	cdDec	D-11,05/1910 0.13.00.			
467548	01/01/192	0	POS	cdDec	04/04/197, 0			
474073	24/09/194	0	POS	cdDec	0			
577206	11/08/195	0	POS	cdDec	04/08/197, 1			
677625	02/09/192	0	POS	cdDec	04/08/197, 0			
529635	11/09/191	0	POS	cdDec	D-05,05/2011 10.04.00.			
311485	11/09/190	0	POS	cdDec	04/03/197, 0			
226641	13/09/191	0	POS	cdDec	04/08/197, 1			

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Recruitment leaflet for rare blood donors



FONDAZIONE IRCCS CA' GRANDA
OSPEDALE MAGGIORE POLICLINICO
I.C.D. CENTRO TRASFUSIONALE


Isaac Jr Acquah
Piazza Cuoco, 7
20137 Milano MI

Gentile donatore/donatrice


La ringraziamo per la donazione di sangue che ha effettuato presso il Centro TrASFusionale e di Immunematologia dell'IRCCS Fondazione IRCCS CA' GRANDA Ospedale Maggiore Policlinico. Oltre ad esprimere il nostro apprezzamento per la donazione, desideriamo informarLa che Lei è una persona speciale perché i suoi globuli rossi hanno un assetto antigenico raro. Desideriamo inoltre ricordarLe che altri membri della Sua famiglia possono presentare le stesse caratteristiche. La invitiamo pertanto a parlare di questo programma con i Suoi familiari e, se non sono donatori di sangue, di invitarli a donare. Nel ringraziarLa per essere stata di grande aiuto ai pazienti che vivono grazie alla Sua generosità, La preghiamo di contattarci qualora volesse avere ulteriori delucidazioni su questo programma o Le porgiamo i nostri più cordiali saluti.

Laboratorio di Immunematologia

Tel: 02 5503.4048
e-mail: labioimm@policlinico.mi.it



REGIONE LOMBARDIA
DIRETTORE GENERALE REGIONALE E UFFICIO A CURA DELL'INTERVENTO REGIONALE PER LA DONAZIONE DI SANGUE
Via Francesco Morosini, 20 - 20122 Milano - Telefono: 02 5812.1 - Fax: 02 5812.1000
Codice Fiscale: 01601000961



REGIONE EMILIA-ROMAGNA



FONDAZIONE IRCCS CA' GRANDA
OSPEDALE MAGGIORE POLICLINICO
I.C.D. CENTRO TRASFUSIONALE

Il programma dei donatori di gruppo raro



I gruppi sanguigni. Il sangue contiene diversi tipi di cellule, fra cui i globuli rossi, che svolgono la funzione di trasportare ossigeno ai tessuti. Sulla superficie dei globuli rossi si trovano alcune sostanze (denominate antigeni), che vengono trasmesse geneticamente e di cui sono state identificate sino ad ora più di 300 varietà diverse. I gruppi sanguigni sono determinati dalla presenza di questi antigeni, tra i quali i più noti sono quelli del sistema ABO. Ad esempio, se una persona è di gruppo A, ciò significa che i suoi globuli rossi hanno sulla loro superficie l'antigene A, analogamente una persona di gruppo B possiede l'antigene B, mentre una persona che non ha né l'antigene A né l'antigene B sono di gruppo O, mentre persone che possiedono sia l'antigene A che l'antigene B sono di gruppo AB. In alcuni sistemi solo poche persone non hanno un determinato antigene (ovvero il loro sangue viene indicato come "negativo" per l'antigeno stesso).



Plasmina. Il sangue contiene alcuni globuli rossi anche le plasmine, che svolgono la funzione di emolizzare. Sulla superficie delle plasmine si trovano degli antigeni plasmatici specifici che sono immunogeni e possono stimolare la produzione di anticorpi clinicamente rilevanti in individui esposti all'antigene che non possiedono in seguito a trasfusione o durante la gravidanza ed il parto. Questi anticorpi sono responsabili di alcune parafisi, tra cui la trombocitopenia neonatale alloimmunata causata dal passaggio di anticorpi di classe IgG dalla madre al feto attraverso la placenta. Questi anticorpi, prodotti dalla madre durante la gravidanza e diretti contro gli antigeni plasmatici specifici che lei non possiede e che il feto ha ereditato dal padre, possono determinare piastrinopenia nel feto e nel neonato. In questi casi è indispensabile utilizzare per la trasfusione da donatore che non esprimono l'antigene plasmatico implicato.



Il sangue di gruppo raro. Una persona viene definita di "gruppo raro" quando la negatività per un determinato antigene eritrocitario o plasmatico viene riscontrata in meno di 1 soggetto ogni 1.000 esaminati. Questa caratteristica non comporta problemi di salute ma un'incerta disponibilità quando deve essere affrontata una tra le problematiche più impegnative in campo trasfusionale, ovvero il reperimento di unità di globuli rossi o di plasmine per soggetti che hanno creato anticorpi contro antigeni dei globuli rossi o delle plasmine. La ricerca di unità compatibili per questi soggetti può comportare la spiccata di un elevato numero di donatori, procedura che se viene eseguita al momento del bisogno non assicura in alcuni casi il reperimento delle unità stesse.



Come vengono identificati i donatori di gruppo raro. Il Laboratorio di Immunematologia del Centro effettua regolarmente la determinazione degli antigeni eritrocitari e plasmatici dei donatori di sangue ed invia i risultati ai registri informatici, che consentono in ogni momento di identificare donatori con particolari caratteristiche, di convocarli per la donazione e di gestire le unità di sangue prelevate. Come per ogni altra informazione raccolta al Centro TrASFusionale, anche i dati relativi allo stato di donatore di gruppo raro sono gestiti in conformità con le attuali disposizioni di legge sul trattamento dei dati personali.



Il registro dei donatori di gruppo raro. Con il lavoro precedentemente descritto, nel corso degli anni si è costituito un "registro di donatori di gruppo raro" che ha consentito di soddisfare numerose richieste di trasfusione per pazienti immunizzati. Nel 2009 la Regione Lombardia ha istituito presso questo Centro la Banca di Autoconfezioni di Gruppo Raro (Banca), Centro di riferimento della Regione Lombardia per la ricerca di unità di gruppo raro per soggetti immunizzati afferenti a tutte le strutture ospedaliere della Regione. Inoltre, in seguito all'istituzione del Laboratorio di Immunematologia ai registri internazionali dei donatori di gruppo raro "American Rare Donor Program" (ARDD) e "International Rare Donor Panel" (IRD), potranno pervenire a questo Centro anche richieste trasfusionali da altri Paesi.



La convocazione per la donazione. La convocazione per la donazione viene gestita da un gruppo selezionato di volontari telefonisti. La donazione avviene su appuntamento e spesso con modalità d'urgenza. In alcuni casi, le unità di globuli rossi verranno conservate allo stato congelato al fine di poterne disporre per casi urgenti non programmabili.



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DIRETTORE GENERALE REGIONALE E UFFICIO A CURA DELL'INTERVENTO REGIONALE PER LA DONAZIONE DI SANGUE
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Codice Fiscale: 01601000961



REGIONE EMILIA-ROMAGNA



You are one in a million. Maybe your blood is too!



Rare Blood Registry/Bank Activity Report (2005 - 2023)

125,064 blood donors have been typed identifying:

- 18,141 donors with rare combinations of antigens
- 1,295 donors negative for high-frequency antigens
- 70 donors with rare Rh phenotypes



Rare Blood Registry/Bank Activity Report 2023

Tabella III – Donatori rari identificati nel 2023

Fattore significativo	A+	A-	O+	O-	AB+	AB-	B+	B-	Anno 2023
Fy(a-); Jk(a-); S-	68	24	68	35			2		197
Fy(a-); Jk(b-); S-	69	26	73	40					208
Fy(b-); Jk(b-); S-	50	11	48	19	4		10		142
Fy(b-); Jk(a-); S-	37	10	50	19	3		6		125
Fy(a-); Jk(a-); s-	19	12	19	14					64
Fy(a-); Jk(b-); s-	23	10	19	5					57
Fy(b-); Jk(b-); s-	6	2	7	6			1		22
Fy(b-); Jk(a-); s-	7	4	5	4			1		21
Totale combinazione antigeni	279	99	289	142	7		20		836
Co(a-b+)	2	1	1						4
Fy(a-b-)	5	1	16				4		28
k-	2	4	7	2					15
Lu(b-)	4		3	2					9
Yt(a-)	1		2	1					4
Totale alta frequenza	14	6	29	5			4		60
CCdee						1			1
Totale per fenotipo raro						1			1
TOTALE	293	105	318	147	7	1	24		897

Frozen Rare Units Inventory

- Rare units are frozen using the high concentration glycerol method and cryopreserved in mechanical freezers at -80 C
- To date there are **1,835** units of cryopreserved red blood cells
- From 2005-2023, **1,041** units were thawed, 539 for high frequency antigens and 449 for combination antigens



Frozen Rare Unit Expiration

- Frozen rare blood units are stored for 10 years (*Ministerial Decree 02/11/2015*)
- Units frozen after 2005 are valid for 7 days (*closed circuit*) while those before have an expiration of 24 hours from the moment of thawing
- In the presence of very rare phenotypes it is possible to postpone the expiry date and the units can be transfused in emergency situations in agreement with the clinician





Frozen Rare Unit Inventory (2023)

Total Phenotype RH **263**

Total High frequency **1.127**

Total Combinations of alloantibodies **267**

Total Autologous and dedicated **178**

Tabella Unità di Sangue Rare criopreservate presso la Sede della Banca										
Fattore Significativo	A+	A-	O+	O-	Oh	AB+	AB-	B+	B-	Totale
CCDEE	29	8						8		45
ccdEE		14		64						78
CCdee		65		40					5	110
--D--	6		24							30
Totale Unità Rare per fenotipo Rh	35	79	32	104				8	5	263
Co(a-)	45	38	63	14						160
Fy(a-b-)	93		52	28		3		7	6	189
Fy(a-b-)/Js(b-)			7							7
Fy(a-b-)/U-			13							13
Ge:-2			5	7				37		49
Jr(a-)			18							18
Js(b-)			3							3
k-	45	22	33	29				1	3	133
Ko/Js(b-)	5									5
Kp(b-)	36	1	5	7						49
Lu(a+b-)	67	25	105	40						237
Lu(a-b-)	16		10	3					6	35
LW(a-b+)			2							2
Oh(Bombay)					23					23
PP1Pk-	12		3	1						16
Sc:-1				1						1
Vel-	3		1	2						6
Yt(a-)	30	47	70	34						181
Totale per Antigeni ad alta frequenza	352	133	390	166	23	3		45	16	1.127
Totale per Combinazione di Antigeni	51	21	147	38		1		9		267
Totale Unità autologhe	53		90	9	3	4				159
Totale Unità medicate	9	5	5							19
TOTALE Unità Rare	500	238	664	317	26	8		62	21	1.835

Rare Units Inventory Management



- Rare units are identified with a '*rare*' label
- They are separated from the rest of the inventory and placed in a dedicated refrigerator of blood bank
- The inventory of rare units is checked daily in order to decide whether:
 - to freeze or maintain the units in liquid phase for specific patients
 - to keep units in liquid phase for urgent requests
- At least two donations per year are frozen for each specificity

Rare blood units released

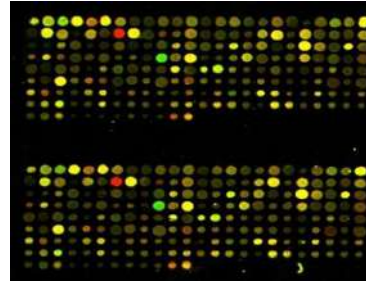
Rare blood units released from 2005 to 2023				
Year	Combinations of alloantibodies	Alloantibodies at high frequency	Total	AAF %
2005	437	14	458	3%
2006	509	11	520	2%
2007	480	11	491	2%
2008	471	26	498	5%
2009	473	31	504	6%
2010	456	33	482	7%
2011	418	40	458	9%
2012	427	77	504	15%
2013	470	96	566	17%
2014	442	119	561	21%
2015	593	107	701	15%
2016	570	84	654	13%
2017	613	64	677	9%
2018	571	80	651	12%
2019	508	99	607	16%
2020	544	29	573	5%
2021	490	39	529	7%
2022	476	81	557	14%
2023	384	52	436	11%
TOTAL	9.822	1.093	10.495	10%

Main problems

- Some phenotypes are very difficult to find even at international level
- Selection criteria for donors are different in the countries
- Cost of rare blood units
- Shipping of units

A screenshot of an American Red Cross activity report. The report is titled "American Red Cross" and "INVOICE SUMMARY ACTIVITY". It contains a table with columns for "SUMMARY OF ACTIVITY BY STATE" and "ACTIVITY". The table lists various states and their corresponding activity levels.

Working in progress



Serological typing and DNA-based genotyping with targeted microarrays are the gold-standard for blood group analysis

There are two approaches that can be followed to expand and improve erythrocyte typing:

1. **Next-generation sequencing (NGS):** proposed as an alternative approach providing accurate and high throughput sequencing for large numbers of samples and allowing to detect rare and novel blood group variants
2. **SNP microarray:** high-throughput, cost-effective methods, only for known alleles

Preliminary validation of a targeted next-generation sequencing approach for red blood groups typing

Aim

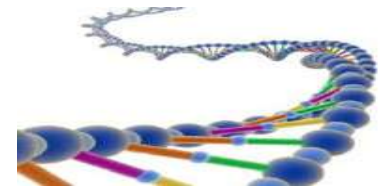
To evaluate the accuracy of an NGS-based customized target panel approach for red blood (RBC) groups characterization and to compare the diagnostic yield of NGS analysis to that of standard serological and molecular biology tools

Methods

Blood samples from 16 healthy donors, representative of the majority of RBC variants, were characterized by conventional RBC serological typing and molecular biology tools, and using a customized NGS panel tools

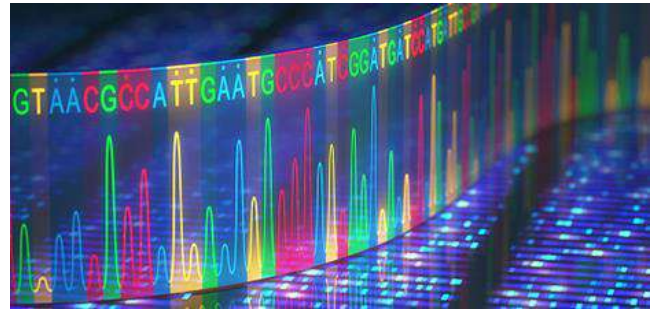
Results

- 16 SYSTEMS were analyzed with both conventional serological/SNP arrays and NGS typing
- Complete concordance for 12 systems (75%):
AB0, LU, KEL, DI, YT, SC, DO, CO, LW, GE, LAN, VEL
- Discrepancies for 4 systems (25%): FY, JK, MNS, RHD/RHCE



Ronzoni et al. ePoster

NGS for RBC Typing



PRO

- NGS-based approach provided a wider and accurate RBC typing, also including RBC systems not usually analyzed with conventional techniques, and allowing to evaluate more samples simultaneously in one-step solution
- Allow to define novel and rare RBC variants

CONS

- Bionformatic expertise
- Structural variants could not be identified
- Low accuracy for MNS and Rh systems

Comprehensive SNP Microarrays

A new customized comprehensive SNP microarray, including 53 HEA in 15 blood group systems, HPA1,2,5,15 and HLA, is being validated by **Blood Transfusion Genomic Consortium (BGC)**



Milan



and the future.....?

The National Blood Center has an ongoing project to develop a national network for the management of rare group donors operating with procedures recognized at national level for donor typing activities and for the management of ***rare blood units by high frequency phenotype***



Because a National Rare Blood Network

To guarantee the transfusion of blood components, which constitutes an essential level of care, to patients with rare phenotypes and/or complex alloimmunizations

Project proposal for a National Rare Blood Network

Transfusion facilities



Regional Compensation Structures (SRC)

National Blood Center (CNS)

Level I, II and III
Immunohematology Laboratories

Establish a working group composed of SRC, CNS and technical experts

Analyze the feasibility of the project and define the operational steps necessary to achieve shared objectives

Design the National Network proposal and strengthen its implementation through a specific agreement between the Regions

Expected outcomes

Create a section of Sistra, appropriately constructed, for the management of rare blood donors:

- Record the typing results
- List the rare blood units, in the liquid phase and in the frozen phase
- Manage requests for rare blood coming from individual ST
- Monitor stocks at national level and report activities



Design a regional/interregional network of LIRS for:

- Large-scale typing and /or carrying out complex immunization investigations
- Maintain typing programs over time
- Consolidate the adherence to standardized operational and laboratory procedures
- Optimize available resources
- Disseminate training and knowledge

Take message a home



- The existence of a national registry of rare donors would allow a better follow up of patients with complex immunization
- The active participation of all members and teamwork throughout the process is required
- The challenge is to get the **right blood** to the right patient at the **right time**

***Thanks for
your attention!***

