



AUSTRIAN RED CROSS

Ethnische Diversivität und deren Folgen für die erythrozytäre Versorgung von Patienten

Christof Jungbauer, 36. Informationsgespräch der BSZ WNB
AKH, Kliniken am Südgarten, 26.11.2012



Content

- 1 Introduction
- 2 Antibody specificities to high frequency antigens:
incidence in Europe
- 3 Impact of migration
- 4 DNA based donor screening programs
- 5 Necessity, to screen for HFA-neg in ethnic minorities



Patients with red cell antibodies

Prevalence of the compatible blood type

Two situations may challenge an adequate blood supply:

- **Multiple antibody specificities**

e.g., anti-e, -Fy^a, -Jk^a (compatible blood: 1:670)

- **Specificity to a high frequency antigen (HFA)**

e.g., anti-k (compatible blood: 1:500)

e.g., anti-Kp^b (compatible blood: 1:10.000)



Patients with red cell antibodies

Prevalence of the compatible blood type

Two situations may challenge an adequate blood supply:

- Multiple antibody specificities

e.g., anti-e, -Fy^a, -Jk^a (compatible blood: 1:670)

- Specificity to a high frequency antigen (HFA)

e.g., **anti-U**

Blacks → 1: 50

Caucasians → 1: >10.000



Patients with red cell antibodies

Prevalence of the compatible blood type

Some (rare) blood types have an unequal prevalence in different ethnic populations

While blood establishments have some preparedness for the “local” specificities to HFA,

.... reagents and compatible donors for the supply of “exotic” rare blood types are missing

ISBT BLOOD GROUP SYSTEMS

modified from: [http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/](http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/Table_of_blood_group_antigens_within_systems_v2.0_110914.pdf)
[Table_of_blood_group_antigens_within_systems_v2.0_110914.pdf](http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/Table_of_blood_group_antigens_within_systems_v2.0_110914.pdf)

No.	System name	ISBT symbol	Number of antigens ²⁸⁷	Gene	Chromos. location	CD code
1	ABO	ABO	4	ABO	9q34.2	
2	MNS	MNS	46	GYP A, GYP B, GYP E	4q31.21	CD235
3	P1PK	P1PK	2	A4GALT	22q13.2	
4	Rh	RH	52	RHD, RHCE	1p36.11	CD240
5	Lutheran	LU	20	LU	19q13.32	CD239
6	Kell	KEL	32	KEL	7q34	CD238
7	Lewis	LE	6	FUT3	19p13.3	
8	Duffy	FY	5	DARC	1q23.2	CD234
9	Kidd	JK	3	SLC14A1	18q12.3	
10	Diego	DI	22	SLC4A1	17q21.31	CD233
11	Yt	YT	2	ACHE	7q22.1	
12	Xg	XG	2	XG, MIC2	Xp22.33	CD99
13	Scianna	SC	7	ERMAP	1p34.2	
14	Dombrock	DO	7	ART4	12p12.3	CD297
15	Colton	CO	4	AQP1	7p14.3	
16	Landsteiner-Wiener	LW	3	ICAM4	19p13.2	CD242
17	Chido/Rodgers	CH/RG	9	C4A, C4B	6p21.3	
18	H	H	1	FUT1	19q13.33	CD173
19	Kx	XK	1	XK	Xp21.1	
20	Gerbich	GE	11	GYP C, GYP D	2q14.3	CD236
21	Cromer	CROM	16	CD55	1q32.2	CD55
22	Knops	KN	9	CR1	1q32.2	CD35
23	Indian	IN	4	CD44	11p13	CD44
24	Ok	OK	3	BSG	19p13.3	CD147
25	Raph	RAPH	1	CD151	11p15.5	CD151
26	John Milton Hagen	JMH	6	SEMA7A	15q24.1	CD108
27	I	I	1	GCNT2	6p24.2	
28	Globoside	GLOB	1	B3GALT3	3q26.1	
29	Gill	GIL	1	AQP3	9p13.3	
30	Rh-associated gp	RHAG	4	RHAG	6p21-qter	CD241
31	Forssman	FORS	1	GBGT1	9q34.2	
32	Junior	JR	1	ABCG2	4q22	CD338
33	Langereis	LAN	1	ABCB6	2q36	

ISBT BLOOD GROUP SYSTEMS

modified from: [http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/](http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/Table_of_blood_group_antigens_within_systems_v2.0_110914.pdf)
[Table_of_blood_group_antigens_within_systems_v2.0_110914.pdf](http://www.isbtweb.org/fileadmin/user_upload/WP_on_Red_Cell_Immunogenetics_and/Table_of_blood_group_antigens_within_systems_v2.0_110914.pdf)

No.	System name	ISBT symbol	Number of hf-antigens	Gene	Chromos. location	CD code
1	ABO	ABO	4	ABO	9q34.2	
2	MNS	MNS	6/46	GYP A, GYP B, GYP E	4q31.21	CD235
3	P1PK	P1PK	1/2	A4GALT	22q13.2	
4	Rh	RH	11/52	RHD, RHCE	1p36.11	CD240
5	Lutheran	LU	14/20	LU	19q13.32	CD239
6	Kell	KEL	14/32	KEL	7q34	CD238
7	Lewis	LE	6	FUT3	19p13.3	
8	Duffy	FY	2/5	DARC	1q23.2	CD234
9	Kidd	JK	1/3	SLC14A1	18q12.3	
10	Diego	DI	2/22	SLC4A1	17q21.31	CD233
11	Yt	YT	1/2	ACHE	7q22.1	
12	Xg	XG	1/2	XG, MIC2	Xp22.33	CD99
13	Scianna	SC	2/7	ERMAP	1p34.2	
14	Dombrock	DO	3/7	ART4	12p12.3	CD297
15	Colton	CO	2/4	AQP1	7p14.3	
16	Landsteiner-Wiener	LW	2/3	ICAM4	19p13.2	CD242
17	Chido/Rodgers	CH/RG	7/9	C4A, C4B	6p21.3	
18	H	H	1/1	FUT1	19q13.33	CD173
19	Kx	XK	1/1	XK	Xp21.1	
20	Gerbich	GE	3/11	GYP C, GYP D	2q14.3	CD236
21	Cromer	CROM	8/16	CD55	1q32.2	CD55
22	Knops	KN	5/9	CR1	1q32.2	CD35
23	Indian	IN	1/4	CD44	11p13	CD44
24	Ok	OK	1/3	BSG	19p13.3	CD147
25	Raph	RAPH	1/1	CD151	11p15.5	CD151
26	John Milton Hagen	JMH	1/6	SEMA7A	15q24.1	CD108
27	I	I	1/1	GCNT2	6p24.2	
28	Globoside	GLOB	1/1	B3GALT3	3q26.1	
29	Gill	GIL	1/1	AQP3	9p13.3	
30	Rh-associated gp	RHAG	2/4	RHAG	6p21-qter	CD241
31	Forssman	FORS	1	GBGT1	9q34.2	
32	Junior	JR	1/1	ABCG2	4q22	CD338
33	Langereis	LAN	1/1	ABCB6	2q36	

Blood Group Antigen Gene Mutation Database

[Home](#) | [Systems](#) | [Resources](#) | [Administration](#) | [About](#)

The database currently has 1284 alleles of 41 genes.

Systems

ABO

Chido/Rodgers (CH/RG)

Colton (CO)

Cromer (CROM)

Diego (DI; band 3)

Dombrock (DO)

Duffy (FY)

Gerbich (GE)

Gill (GIL)

H

I

Indian (IN)

John Milton Hagen (JMH)

Kell (KEL)

Kidd (JK)

Knops (KN)

Kx (XK)

Landsteiner-Wiener (LW)

Lewis (LE)

Lutheran (LU)

MNS (glycophorin A/B/E)

Ok (OK)

P1PK and Globoside

Raph (RAPH)

Rh (RH)

Rh-associated glycoprotein (RhAG)

Scianna (SC)

T/Tn

Xa (XG)

Y



Which HFAs should be included in screening?

- **Incidence** of antibody specificities to HFAs in Europe
- **Clinical significance** of the ab specificities



Antibodies to high frequency antigens

Which specificities are relevant in Europe?

Germany, Switzerland, Austria (20 month), n=52

- 2 Kpb (19,6%), Vel (17,9%), Lub (14,3%), Yta (14,3%), Coa (5,4%),
Hoh (5,4%), AnWj (3,6%), Kx (3,6%), MAM (3,6%), Fy3 (1,8%),
Ku (1,8%), Lan (1,8%), Lu6 (1,8%), Rh17 (1,8%) and Tja (PP1Pk; 1,8%).

Seltsam A, Wagner FF, Salama A, Flegel WA. Antibodies to high-frequency antigens may decrease the quality of transfusion support: an observational study. *Transfusion* 2003;43:1563-6



Antibodies to high frequency antigens

Which specificities are relevant in Europe?

Germany, Switzerland, Austria (20 month), n=52

2

*“[...] 66% of the rare blood supply involved the four specificities anti-**Kpb**, **-Vel**, **-Lub** or **-Yta**.”*

Seltsam A, Wagner FF, Salama A, Flegel WA. Antibodies to high-frequency antigens may decrease the quality of transfusion support: an observational study. *Transfusion* 2003;43:1563-6

Antibodies to high frequency antigens

Incidence at the RCR, Swiss RC, Bern

2

Specificity anti-	Incidence count	Incidence %
Yta	92	26.4
Vel	51	14.7
Lub	48	13.8
k	39	11.2
Kpb	24	6.9
P	14	4.0
Jra	14	4.0
Gerbich	13	3.7
Lan	12	3.4
Coa	12	3.4
Ku	6	1.7
Rh17	5	1.4
K11	4	1.1
U	4	1.1
Jk3	3	0.9
Lu8	2	0.6
Wrb	2	0.6
Jsb	1	0.3
AnWj	1	0.3
Co3	1	0.3
	348	100.0

Courtesy of Hein Hustinx 2005



Antibodies to high frequency antigens

Which specificities are relevant in Europe?

France, 1994 to 2008 (n=2082)

Fy(a-b-) (26,1%), k- (19,4%), Yt(a-) (12,7%), r'r' (CCddee, 9,1%),
U- (7,0%), Vel- (5,6%), r''r'' (ccddEE, 3,5%), Lu(b-) (3,2%), D-- (1,1%),
Lu:-13 (0,9%), Js(b-) (0,9%), Kp(b-) (0,9%), RzRz (CCD.EE, 0,7%),
I- (0,5%), O_h (0,4%) and Ge:-2,3 (0,3%)

3

Peyrard T, Pham BN, Rouger P & Le Pennec PY in:

Reesink HW, et al. Donors with rare pheno (geno) type. Vox Sang 2008;95:236-53



Antibodies to high frequency antigens

Antibodies to FY-antigens made by **FY0^{ES}** people

~ 4.000.000 African inhabitants in France and its overseas territories

3

105 Anti-Fya

83 Anti-Fy3

24 Anti-Fy5



Antibodies to high frequency antigens

Which specificities are relevant in Europe?

“[...] Shortages in supply for the African-Caribbean population (U- D-, hrS-, HrB-, Js(b-) and RN/RN).”

3

Peyrard T, Pham BN, Rouger P & Le Pennec PY in:

Reesink HW, et al. Donors with rare pheno (geno) type. Vox Sang 2008;95:236-53



Antibodies to high frequency antigens

Which specificities are relevant in Europe?

*“[...] K0, McLeod, p, U-, Lan-, Vel- and Ge:-2,-3
are probably the most difficult phenotypes to find”*

3

Reesink HW, et al. Donors with rare pheno (geno) type. Vox Sang 2008;95:236-53



Antibodies to high frequency antigens

Calculated frequency of HFA-negatives in Austria

Austria: ~ 8.5 Mio inhabitants

3

k-, Yta-, Lub-, Coa-	4 x 17.000
r'r', Vel-, Kpb-	3 x 3.500
r''r''	1.750
<hr/>	
	80.000



Antibodies to high frequency antigens

Calculated frequency of HFA-negatives in Austria

Austria: ~ 8.5 Mio inhabitants

~40.000 people of African origin

3

k-, Yta-, Lub-, Coa-	4 x 17.000
r'r', Vel-, Kpb-	3 x 3.500
r''r''	1.750
<hr/>	
	80.000

FY0	26.000
U-	800
Jsb-	400
<hr/>	
	27.200

HFAs with unequal prevalence in different populations		Caucasians	East. Europ.	Blacks	Asians	Taiwanese	Japanese	Arabs	Indians	Melanesians	Mexicans	S.Am Indians	Jews
System	Antigen												
MNS	U			0,99									
RH	D												
	G												
	Hr			0,99									
	hrS			0,99*									
LU	LU6												*
KEL	Jsb			0,99									
FY	Fya												
	FY3			0,32				0,75					0,96
	FY5			0,32									
JK	JK3												
DI	Dib											0,96	
3 YT	Yta							0,97					.98
XG	CD99						*						
DO	Gya		0,99				0,99						
	Hy			0,99									
	Joa			0,99									
H	Oh; Para-Bombay					0,998			0,999				
GE	GE3									0,5			
CROM	Cra			0,99									
	Tca			0,99									
	Dra												*
	Esa			*							*	*	
	UMC						*						
IN	Inb								0,96				
OK	Oka						*						
RAPH	MER2												*

modifiziert nach: Reid ME. The Blood Group Antigen Facts Book. 2nd Ed 2004

HFAs with unequal prevalence in different populations		Caucasians	East. Europ.	Blacks	Asians	Taiwanese	Japanese	Arabs	Indians	Melanesians	Mexicans	S.Am Indians	Jews
System	Antigen												
MNS	U			0,99									
RH	D				0,99	0,99						0,99	
	G				0,999	0,999							
	Hr			0,99									
	hrS			0,99*									
LU	LU6												*
KEL	Jsb			0,99									
FY	Fya				0,99	0,99							
	FY3			0,32				0,75					0,96
	FY5			0,32									
JK	JK3												
DI	Dib											0,96	
3 YT	Yta							0,97					.98
XG	CD99						*						
DO	Gya		0,99				0,99						
	Hy			0,99									
	Joa			0,99									
H	Oh; Para-Bombay					0,998			0,999				
GE	GE3									0,5			
CROM	Cra			0,99									
	Tca			0,99									
	Dra												*
	Esa			*							*	*	
	UMC						*						
IN	Inb								0,96				
OK	Oka						*						
RAPH	MER2												*

modifiziert nach: Reid ME. The Blood Group Antigen Facts Book. 2nd Ed 2004



RHD genotyping

Variant D types in South East Asia

Shanghai population:

~ 0,4 % apparently RhD-negative

among them:

~ 17 % DEL - 1227 G>A

- 3 G>A

~ 4,35 % weak / partial D

Li Q. Vox Sang. 2009 Aug;97(2):139-46.

Fukumori Y. Transfus Med 1997;7:227-231

Mak KH. Transfusion 1993; 33:348-351

Shao CP. Vox Sang 2002;83:156-161



Antibodies specificities to high frequency antigens clinical significance

1

clinically significant	sometimes clinically significant	not significant if not reactive at 37°C	generally not significant
H bei O _h	Ata	AnWj	CH/RG
Diego	Colton	Lutheran	Cost
Duffy	Cromer	Sd ^a	JMH
Kell	Dombrock		HLA/Bg
Kidd	Gerbich		Knops
P	Indian		
P1PK2	Junior		
Rh	Lan		
S,s,U	LW		
Vel	Scianna		
	Yta		



Selection of publications

high-throughput RBC genotyping including HFAs

Table 1. Selection of recent publication on high-throughput RBC genotyping including HFAs

Number of RBC genotype/allels included	HFA included	Technique	Study size, n [§]	Concordance rate, %	Reference
18	LU2, KEL2, KEL4, DI2	microarray	372*	98–100	Denomme GA, Transfusion 2005
16	KEL2, KEL4	microarray	618	97–100	Montpetit A, Transfusion 2006
35	LU2, KEL1, FY0, LW5, DI2, CO1, DO4, DO5, SC1	microarray	188	100	Hashmi G, Transfusion 2005
#	MNS5, KEL2, KEL4, DO5	microarray	94	#	Beiboer SH, Transfusion 2005
33, 87, 9, 31 [§]	#	microarray	1,000 [¶]	99.8 [¶]	Avent ND, Transfusion 2007
16	LU2, KEL2, KEL4, KEL7, DI2, CO1	microarray	92	100	Karpasitou K, Transfusion 2008
17	LU2, KEL2, CO1	real-time PCR	200	100	Polin H, Vox Sang 2008

[§]Evaluation of defined samples.

*For most of the SNPs tested.

[§]ABO, RHD, RHCE, minor antigens

[#]Not specified for the tests on RBC polymorphisms.

[¶]Data from the Conformité Européenne (CE) submission www.progenika.com/eu/.



Donor typing:

In-house DNA typing programmes: antigens tested

Springe

M, N, S, s

Lu^a, Lu^b

Kp^a, Kp^b

Fy^a, Fy^b

Jk^a, Jk^b

Yt^a, Yt^b,

Co^a, Co^b

Bern

M, N, S, s

Lu^a, Lu^b

K, k, Kp^a, Kp^b, Js^a, Js^b

Fy^a, Fy^b, Fy⁰

Jk^a, Jk^b

Dp^a, Dp^b

Yt^a, Yt^b

Co^a, Co^b

Do^a, Do^b, Hy+

Sc1, Sc2

LW^a, LW^b

Vienna

M, N, S, s

Lu^a, Lu^b, Lu8, Lu14

K, k, Kp^a, Kp^b, Js^a, Js^b,

K11, KEL17, Kp^c

Fy^a, Fy^b, Fy^{BWK}, Fy⁰

Jk^a, Jk^b

Dp^a, Dp^b, Wr^a, Wr^b

Yt^a, Yt^b

Co^a, Co^b

In^a, In^b

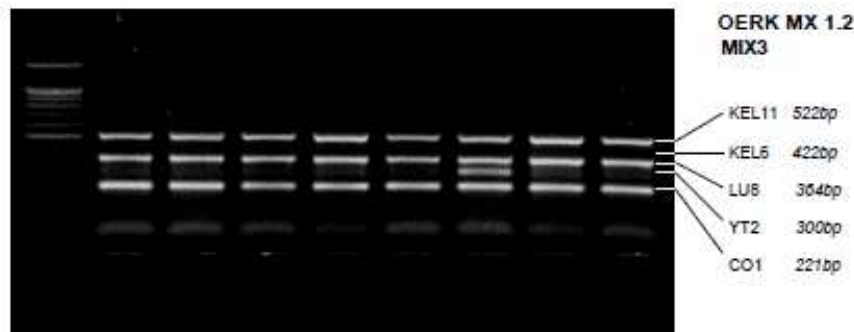
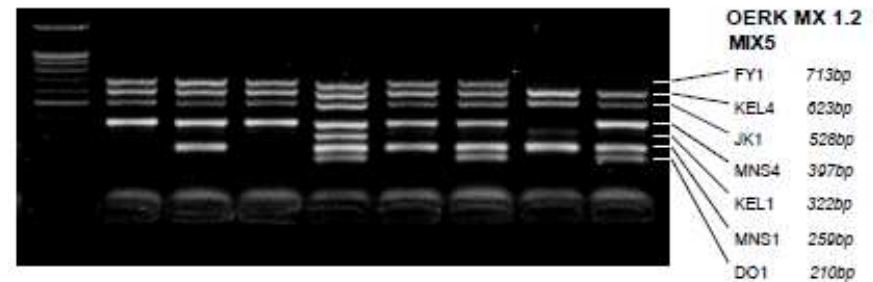
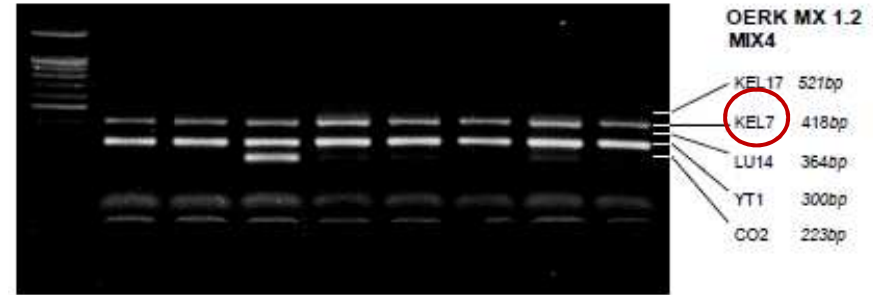
Do^a, Do^b



Multiplex PCR screening for 35 RBC antigens

Multiplex PCR genotyping for 36 red blood cell surface antigens (MX version 1.0 -1.2)

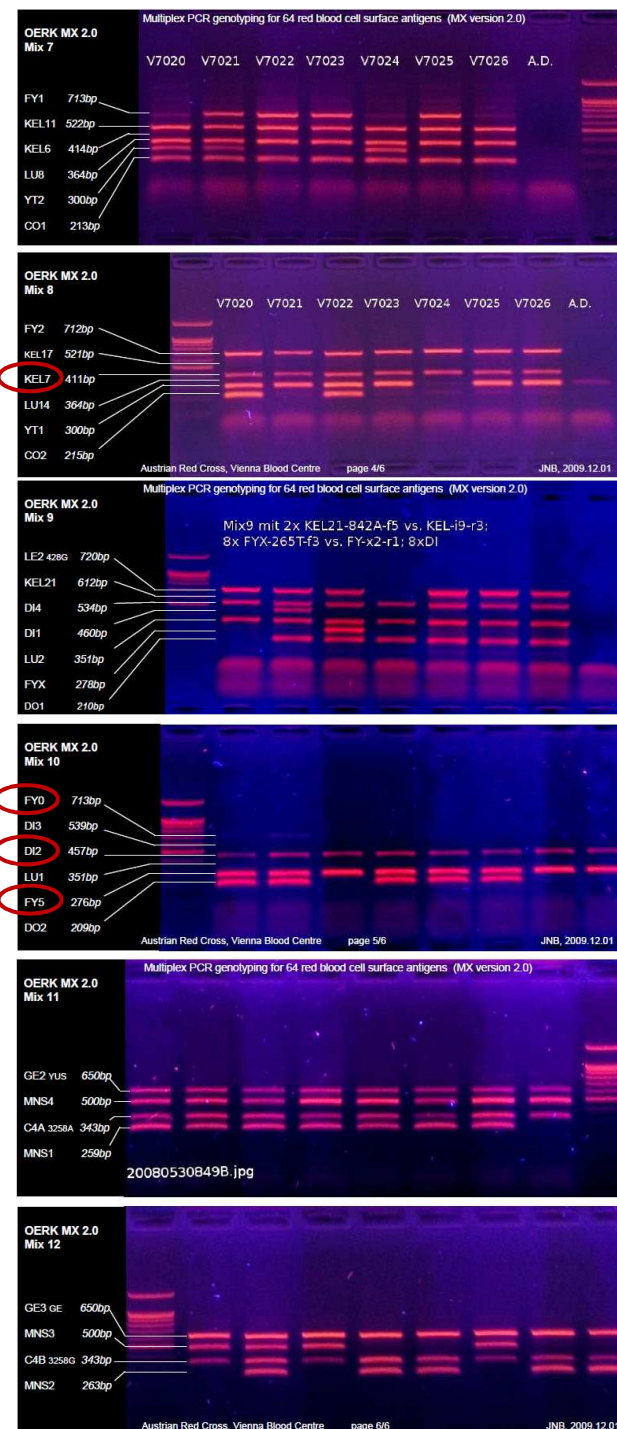
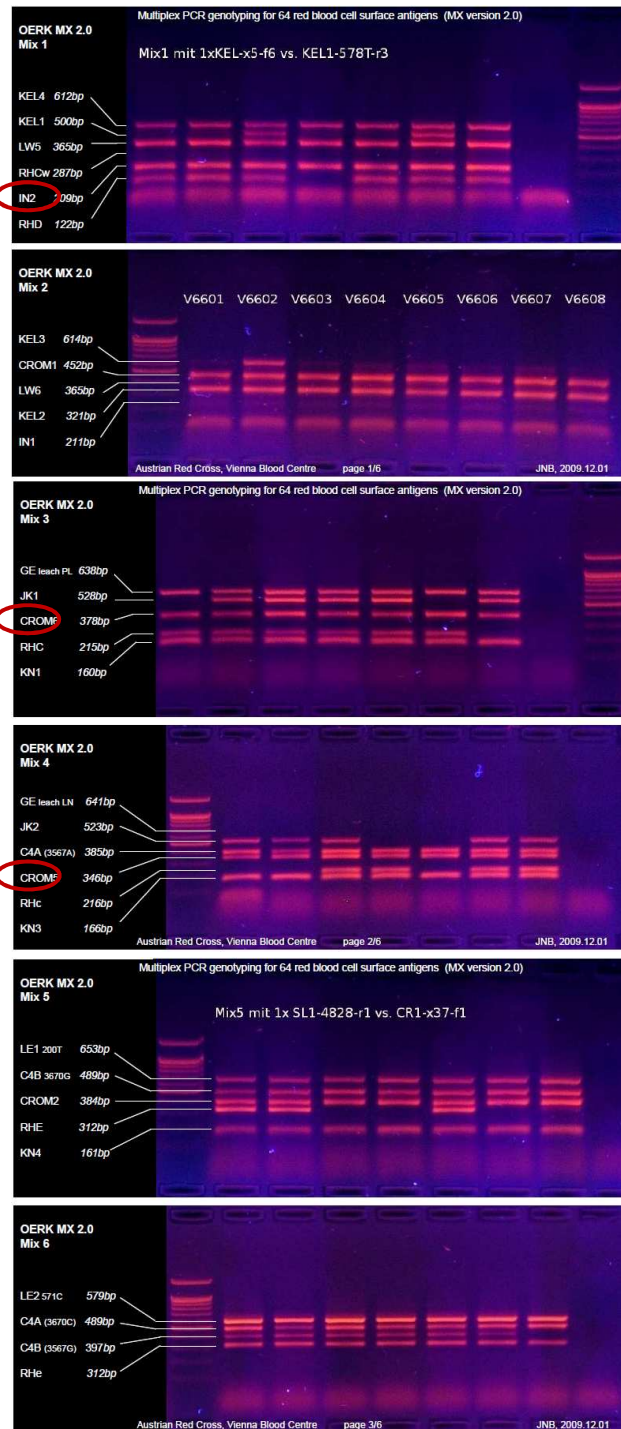
Multiplex PCR genotyping for 36 red blood cell surface antigens (MX version 1.0 -1.2)





AUSTRIAN RED CROSS

OERK MX 2.0 Multiplex PCR Screening for 64 RBC antigens





Observed genotype frequency of 6000 Eastern Austrian blood donors

	MNS1	MNS2	MNS3	MNS4	MNS5	LU1	LU2	LU8	LU14	KEL1	KEL2	KEL3	KEL4	KEL6	KEL7	KEL11	KEL17	KEL21
total tested	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000
homozygous positive	1794	1228	623	2752	6000	9	5578	5727	5	5	5470	1	5922	0	5999	5981	0	0
heterozygous	2978	2978	2625	2625	0	413	413	268	268	525	525	77	77	1	1	19	19	0
negative	1228	1794	2752	623	0	5578	9	5	5727	5470	5	5922	1	5999	0	0	5981	6000
obs. negative preval.	0,205	0,299	0,459	0,104	0,000	0,930	0,002	0,001	0,955	0,912	0,001	0,987	0,000	1,000	0,000	0,000	0,997	1,000
	FY1	FY2	FY	FYX	JK1	JK2	DI1	DI2	DI3	DI4	YT1	YT2	DO1	DO2	CO1	CO2	IN1	IN2
total tested	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000	6000
homozygous positive	1041	1831	5969	0	1591	1498	0	5978	0	6000	5308	24	878	2214	5526	11	0	6000
heterozygous	3127	3127	31	153	2911	2911	22	22	0	0	668	668	2908	2908	463	463	0	0
negative	1832	1042	0	5837	1498	1591	5978	0	6000	0	24	5308	2214	878	11	5526	6000	0
obs. negative preval.	0,305	0,174	0,000	0,973	0,250	0,265	0,996	0,000	1,000	0,000	0,004	0,885	0,369	0,146	0,002	0,921	1,000	0,000



AUSTRIAN RED CROSS

Conclusion I

Due to migration we have to expect more “exotic” HFA-specificities in future



AUSTRIAN RED CROSS

Conclusion II

DNA based typing methods provide independence from the availability of serological typing reagents



AUSTRIAN RED CROSS

Conclusion II

To find certain rarities, it will be necessary to screen potential donors from populations, which regularly would be deferred from donation (Malaria endemic areas)



2005 Vienna Blood Centre Mol Bio Team



Volker Witt

Dieter W. M. Schwartz

Peter Rabitsch[†] Claudia Hobel Christof Jungbauer

Elisabeth Schwartz-Jungl

Brigitte Redl

Eva Fuchs

Eva Mitterhauser

Wolfgang R. Mayr

Elisabeth Schistal

Andrea Neumahr



AUSTRIAN RED CROSS

Austrian Red Cross
Blood Service for Vienna, Lower Austria and Burgenland
Vienna Blood Centre

www.blut.at

www.roteskreuz.at