## Review

## Rare donor programs in Switzerland, Germany, and Austria

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In 2009, the Working Party on Rare Donors of the German Society of Transfusion Medicine and Immunohematology (DGTI), which represents the German-speaking countries of Switzerland, Germany, and Austria (Fig. 1), started to develop a joint database for rare donors. The database was implemented in 2011 in Berne, Switzerland, and is maintained by the Swiss Red Cross Blood Service (public access: http:// www.iblutspende.ch/en/rare-donors/rare-donors.html).

Germany and Switzerland, which have mostly Caucasian populations, started rare donor programs in the 1990s (Table 1), focusing on donors negative for Kp<sup>b</sup>, Vel, Lu<sup>b</sup>, and Yt<sup>a</sup>. In 2003, Seltsam et al.<sup>1</sup> conducted a survey for patients



**Fig. 1.** Blood service centers in Austria, Germany, and Switzerland that reported rare donor screening programs. Centers (noted with squares) also store frozen red blood cell units.

with antibodies against high-prevalence antigens in the major reference laboratories and blood services in Germany, Switzerland, and Austria. During the 20-month observation period, 56 cases were reported. In 71 percent of these cases, antibodies against Kp<sup>b</sup>, Vel, Lu<sup>b</sup>, Yt<sup>a</sup>, or Co<sup>a</sup> were detected, confirming the direction of the early programs. In recent years, high-throughput molecular methods were developed and implemented. These methods have made it possible to test donors for high-frequency alleles independent of the availability of specific antisera, which often were not available in appropriate quantity and quality. At present, about 1100 donors with rare blood types are listed in the DGTI database (Table 2). Most of these donors are registered by the Swiss Blood Services. The listing of German and Austrian donors has not yet been completed.

In order to keep blood donation on a volunteer basis, no incentives are offered for rare donors.

In 2012, Switzerland imported four red blood cell (RBC) units with the Lu(b–) phenotype and exported two RBC units with the Jk(a–b–) phenotype. Seventeen rare blood units [1 Lu(b–), 3 K+k–, 5 Yt(a–), 8 Vel–] were shipped within the country. According to the German authorities no RBC units were imported in 2012. Germany exported 302 units to European countries, although the number of rare phenotypes included was not specified. From 2012 to 2014, 136 (37 cryopreserved) units were shipped domestically [44 Lu(b–), 71 Yt(a–), 3 Vel–, 9 AnWj–, 4 Co(a–), 1 Kp(b–), 2 PP1P<sup>k</sup>–, 1 R<sub>2</sub>R<sub>2</sub> (CCD.EE), 1 GE:–2]. Requests for rare phenotypes are not systematically documented by most blood services, thus no exact data are provided for unfilled requests.

Neither in Germany nor in Switzerland were intentionally incompatible transfusions reported in the case where a request for rare units could not be filled. It is likely that other measures, such as administration of erythropoietin or inclusion in an autologous blood program, were taken. This information, however, is scarce and laboratories normally cannot track these cases.

There is one known donor with the  $Rh_{null}$  phenotype in Switzerland. This donor carries the allele *RHAG\*01N.02*. In Germany, one donor with  $Rh_{null}$  and one with the  $Rh_{mod}$  
 Table 1. Historic and current testing methods and consequent donors identified in rare donor programs in Austria, Switzerland, and Germany

Program location/organizer	Years	Number of donors tested	Method of testing
Austrian Red Cross Blood Center, Vienna, Austria — C. Jungbauer et al.	2007-2015*	25,000	Molecular
Interregional Blood Transfusion SRC Ltd., Berne, Switzerland — H. Hustinx et al.	2010-2011	52,000	Serologic
	2011-2012	40,000	Serologic
	2013	35,000	Serologic
	2011-2015*	21,000	Molecular
Red Cross Blood Service, Institute, Zurich, Switzerland — B. Frey et al.	2012-2015 <sup>‡</sup>	40,000	Molecular
Red Cross Blood Service West Institute, Hagen, Germany — B. Just et al.	1996–1998	22,000	Serologic
	2004-2005	2000	Serologic
	2008-2009	5600	Serologic
	2009-today <sup>§</sup>	>250	Serologic
	2012-today <sup>1</sup>	>4000	Molecular
Bavarian Red Cross Blood Service Institute, Munich, Germany — J. Burkhart et al.	1999–2000	5500	Serologic
	1999–2000	5000	Serologic
	1999–2000	5000	Serologic
Red Cross Blood Service NSTOB Institute, Springe, Germany — F.F. Wagner et al.	2005-2007#	3400	Molecular
	2007-2013**	64,000	Molecular
	2013-today**	>22,000	Molecular
Red Cross Blood Service Baden-Württemberg, Hessen Institute, Baden-Baden, Germany —	1998–2012	15,000	Serologic
E.A. Scharberg et al.	2013-2014	35,000	Serologic
	2013-2014	150,000	Serologic
Red Cross Blood Service Baden-Württemberg, Hessen Institute Ulm, Ulm, Germany — I. von Zabern et al.	2009-2010#	2500	Molecular

\*Six multiplex polymerase chain reactions (5–7 primer pairs) for a single blood donor<sup>2</sup>; agarose gel electrophoresis.

<sup>+</sup>In-house method.

\*Matrix-assisted laser desorption/ionization, time-of-flight (MALDI-TOF).3

<sup>§</sup>Only donors of African or Asian origin are included.

"MALDI-TOF; testing for VEL\*01N/01N was added in 2014.

\*Manual testing using agarose gels.<sup>4</sup>

\*\*Semi-automated testing using pooled capillary electrophoresis; CO switched to VEL in August 2013.

	Rare donor screening/number of donors identified										
	Ko	Lan-	S-s- U-	Fy(a-b-)	MAR-	Vel-	LU:-14	Co(a-)	Yt(a-)	Kp(b-)	Lu(b-)
30 additional alleles are teste	_	-	-	-	-	_	Х	Х	Х	Х	Х
	-	-	-	-	-	-	8	31	68	2	20
Additional antigens were test	_	-	-	_	_	_	_	-	_	Х	-
	_	-	-	_	-	х	-	-	-	-	-
	_	-	-	_	Х	-	-	-	-	-	-
22 additional alleles are teste	_	-	-	_	-	х	-	Х	Х	Х	Х
	-	-	-	-	-	13	-	46	60	10	35
Additional alleles are tested	_	-	-	_	_	Х	Х	Х	Х	Х	Х
	-	-	-	-	-	3	7	28	86	6	44
	_	-	-	_	_	Х	_	-	_	_	-
	_	-	-	_	-		-	-	Х	-	-
	_	-	-	_	-	х		Х	Х	Х	Х
	_	_	Х	х	-	_	-	-	_	-	-
	-	-	3	62	-	17	-	11	19	3	8
Additional alleles are tested	_	-	-	-	-	Х	_	Х	Х	Х	Х
	_	_	-	_	-	0	_	12	9	0	5
	_	_	_	_	_	_	_	_	Х		Х
	_	Х	_	_	_	_	_	_	_	х	-
	х	_	_	_	-	х	_	_	_	-	_
	0	1	-	_	-	0	_	-	14	0	5
	_	_	_	_	-	_	_	Х	Х	Х	Х
	_	_	_	_	-	_	-	Х	х	х	Х
	_	_	_	_	_	х	_	_	х	х	х
	-	-	-	-	-	12	-	146	190	11	209
	_	_	_	-	_	_	-	_	_	Х	Х
	_	_	_	Х	_	х	-	_	_	х	Х
	_	_	_	_	х	_	-	_	_		
	-	-	-	3	8	5	-	-	-	1	12
	_	_	_	_	_	_	_	Х	х	х	х
	_	_	_	_	_	_	_	3	13	0	2

<b>Table 2.</b> Rare donors listed in the German Society for Transfusion
Medicine and Immunohematology (DGTI) database as of 2015

Phenotype	Number of donors
K+k-	316
Yt(a–)	214
Lu(b–)	145
Fy(a-b-)	105
Co(a–)	101
Vel-	39
r'r'	39
Kp(b–)	28
r″r″	26
Lu(a-b-)	10
MAR- (Rh:-51)	7
PP1P <sup>k</sup> -	3
R <sub>z</sub> R <sub>z</sub>	3
D	3
S-s-U-	2
S-s-U+ <sup>var</sup>	2
Jk(a-b-)	2
Kx- (McLeod)	2
Jr(a–)	2
Lan-	2
Di(b–)	1
Lw(a-b+)	1
O <sub>h</sub> (Bombay)	1
P <sup>k</sup> (P–; GLOB:–1)	1
Rh <sub>null</sub>	1

phenotype are known. The molecular background of the  $Rh_{null}$  donor is under investigation. The  $Rh_{mod}$  phenotype is caused by heterozygosity for the *RHAG\*01N.03* allele and a new allele with a single nucleotide polymorphism causing an amino acid substitution located at the transmembrane/intracellular border. This donor carries Rh antigens at a very low level that can be detected by absorption and elution methods only.

## References

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