Rh Blood Group System

Number of antigens 52

Polymorphic	D, C, E, c, e, f, Ce, G, hr^S, C^G, Rh26 (c-like), cE, hr^B, Rh41
Low prevalence	C^W, C^X, V^, E^W, VS^, CE, D^W, hr^H, Go^a, Rh32, Rh33, Rh35, Be^a, Evans, Tar, Rh42, Crawford, Riv, JAL, STEM, FPTT, BARC, JAHK, DAK^, LOCR, CENR
High prevalence	Hr_0, Hr, Rh29, Hr^B, Rh39, Nou, Sec, Dav, MAR, CEST, CELO, CEAG

^ = polymorphic in populations with African ancestry.

Terminology

ISBT symbol (number)	RH (004)
CD number	CD240D (RhD); CD240CE (RhCcEe)
Obsolete name	*Rhesus*, which is obsolete because it is a genus of monkey
History	Antibodies, made in 1940 by Landsteiner and Wiener, in rabbits or guinea pigs in response to injected rhesus monkey (*Macacus rhesus*) RBCs, were thought to be the same specificity as the human antibody reported in 1939 and the antigen detected by them was named Rh.

Expression

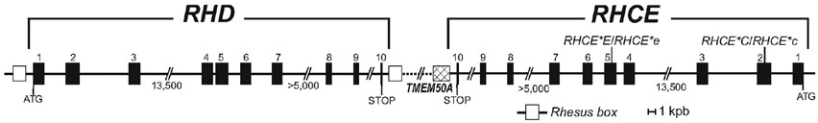
Cord RBCs	Expressed
Tissues	Erythroid specific

Gene[1,2]

Chromosome	1p36.11
Name	*RHD*, *RHCE*

The Blood Group Antigen (3/e). DOI: http://dx.doi.org/ 10.1016/B978-0-12-415849-8.00006-5

Organization	*RHD* and *RHCE*, each with 10 exons, are distributed over 69 kbp of DNA in opposite orientation with their 3′ ends facing each other. The genes are separated by a region of about 30 kbp of DNA that contains the TMEM50A gene (previously called *SMP1* for Small Membrane Protein 1). The 3′ and 5′ ends of *RHD* are flanked by two 9 kbp homologous regions of DNA named the *Rhesus boxes*[3].
Product	RhD polypeptide (obsolete names: Rh30; Rh30B; Rh30D; D_{30}) RhCE polypeptide (obsolete names: Rh30; Rh30A; Rh30C)



In diagrams representing *RH* exons, the information for *RHCE* is presented in the order of exon 1 to exon 10. The opposite orientation of *RHD* and *RHCE* and a putative "hairpin" formation allows homologous DNA segments to come into close proximity, and most gene recombination occurs through gene conversion rather than unequal crossover.

A third ancestral homologous gene (*RHAG*), located on chromosome 6, encodes the Rh-associated glycoprotein [RHAG **(030)**] and is essential for the expression of Rh antigens.

Database accession numbers

Gene	*RHD*	*RHCE*
GenBank	NG_007494 (gene) NM_016124 (mRNA)	NM_138618 (mRNA) NM_020485 (mRNA)
Accession number	L08429	DQ322275 (RHCE*01)
Entrez Gene ID	6007	6006
Allele names	*RHD*01*	*RHCE*01* or *RHCE*ce* *RHCE*02* or *RHCE*Ce* *RHCE*03* or *RHCE*cE* *RHCE*04* or *RHCE*CE*

Differences in nucleotides between *RHD* and *RHCE* and amino acids encoded

Differences between *RHD* and *RHCE*Ce* and *RHCE*cE* are not given.

Exon	Nucleotide #*RHD* > *RHCE*ce*	Amino acid RhD > Rhce
1	48G>C	Trp16Cys
2	150T>C 178A>C 201G>A 203G>A 307T>C	Silent Ile60Leu Silent Ser68Asn Ser103Pro
3	361T>A 380T>C 383A>G 455A>C	Leu121Met Val127Ala Asp128Gly Asn152Thr
4	505A>C 509T>G 514A>T 544T>A 577G>A 594A>T 602C>G	Met169Leu Met170Arg Ile172Phe Ser182Thr Glu193Lys Lys198Asn Thr201Arg
5	667T>G 697G>C 712G>A 733G>C 744C>T 787G>A 800A>T	Phe223Val Glu233Gln Val238Met Val245Leu Silent Gly263Arg Lys267Met
6	916G>A 932A>G	Val306Ile Tyr311Cys
7	941G>T 968C>A 974G>T 979A>G 985 G>C 986 G>A 989 A>C 992 A>T 1025T>C 1048G>C 1053C>T 1057G>T 1059A>G 1060G>A 1061C>A 1063G>T	Gly314Val Pro323His Ser325Ile Ile327Val Gly329His Gly329His Tyr330Ser Asn331Ile Ile342Thr Asp350His Silent Gly353Trp Gly353Trp Ala354Asn Ala354Asn Silent

(*Continued*)

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Exon	Nucleotide #*RHD* > *RHCE**ce	Amino acid RhD > Rhce
8	No differences	No differences
9	1170T>C 1193A>T	Silent Glu398Val
10	No differences	No differences

Molecular bases of partial and weak partial D phenotypes

People with a partial D phenotype can make anti-D even though their RBCs are D+. Reference allele *RHD*01* (L08429) encodes D (RH1). Nucleotide differences from the reference allele, and amino acids affected, are given. In the following tables, when an exon(s) of *RHD* is substituted with the equivalent exon(s) of *RHCE*, the number of the substituted exon is given in parentheses. The nucleotide and amino acid changes between all *RHD* and *RHCE* exons are given in the previous table "Differences in nucleotides between *RHD* and *RHCE* and amino acids encoded."

Some of the variant D phenotypes in this table have not (yet) been associated with production of alloanti-D. They are included because of similarities to established partial D phenotypes, which may include the epitope profile and antigen site density when tested with monoclonal anti-D.

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
DII	*RHD*02* or *RHD*DII*	7	1061C>A	Ala354Asp	(Few)
DIIIa DAK+ or RH:54 (Previously DIIIa type 5)	*RHD*03.01*or *RHD*DIIIa*	2 3 4 4 5	186G>T 410C>T 455A>C 602C>G 667T>G	Leu62Phe Ala137Val Asn152Thr Thr201Arg Phe223Val	Africans (Many)
DIIIb− Caucasian G– or RH:–12	*RHD*03.02* or *RHD*DIIIb*	2	D-CE(2)-D	See table for CE exon 2	Caucasians (Rare)
DIIIc	*RHD*03.03* or *RHD*DIIIc*	3	D-CE(3)-D	See table for CE exon 3	Caucasians (Many)
DIII type 4	*RHD*03.04* or *RHD*DIII.04*	2 3 3	186G>T 410C>T 455A>C	Leu62Phe Ala137Val Asn152Thr	(Few)
DIII type 6	*RHD*03.06* or *RHD*DIII.06*	3 3 4 5	410C>T 455A>C 602C>G 667T>G	Ala137Val Asn152Thr Thr201Arg Phe223Val	Africans (Many)
DIII type 7^ (likely the serologically defined (historic) DIIIb of Tippett and Sanger) G− or RH:−12	*RHD*03.07* or *RHD*DIII.07*	2 3 3 4 5	Exon 2 410C>T 455A>C 602C>G 667T>G	See table Ala137Val Asn152Thr Thr201Arg Phe223Val	Africans (Few)

(*Continued*)

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Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
DIVa (previously DIVa.2) Go(a+) or RH:30	*RHD*04.01* or *RHD*DIVa.01*	2 3 3 7	186G>T 410C>T 455A>C 1048G>C	Leu62Phe Alla137Val Asn152Thr Asp350His	Africans (Many)
DIVa type 2 (obsolete – same as original DIVa)					
DIVb Evans+ or RH:37	*RHD*04.02* or *RHD*DIVb*	7 7 7 7 7 8–9	D-CE (part 7–9) -D 1048G>C 1057G>T 1059A>G 1060G>A 1061C>A See table	See table Asp350His Gly353Trp Gly353Trp Ala354Asn Ala354Asn See table	Europeans, Japanese (Many)
DIV type 3	*RHD*04.03* or *RHD* DIV.03*	6, 7, 8, 9	D-CE(6–9)-D	See table	(Few)
DIV type 4	*RHD*04.04* or *RHD*DIV.04*	7 7 7 7 7	1048G>C 1057G>T 1059A>G 1060G>A 1061C>A	Asp350His Gly353Trp Gly353Trp Ala354Asn Ala354Asn	(Few)
DIV type 5	*RHD*04.05* or *RHD*DIV.05*	7, 8, 9	*D–CE(7–9)–D*	See table	(Few)
DV type 1 (KOU, FK) D^W+ or RH:23	*RHD*05.01* or *RHD*DV.01*	5 5	667T>G 697G>C	Phe223Val Glu233Gln	Europeans, Japanese, (Many) Africans (Several)

DV type 2 (Hus) D^W+ or RH:23	*RHD*05.02* or *RHD*DV.02*	5	D-CE(5)-D	See table	Europeans, Japanese, (Many), Africans (Several)
DV type 3 (DBS0) E±	*RHD*05.03* or *RHD*DV.03*	5 5 5 5	667T>G 676G>C 697G>C 712 G>A	Phe223Val Ala226Pro Glu233Gln Val238Met	(Few)
DV type 4 (SM) D^W+ or RH:23	*RHD*05.04* or *RHD*DV.04*	5	697G>C	Glu233Gln	(Few)
DV type 5 (DHK, DYO) D^W+ or RH:23	*RHD*05.05* or *RHD*DV.05*	5	697G>A	Glu233Lys	Japanese (Many), Austrians
DV type 6	*RHD*05.06* or *RHD*DV.06*	5 5 5	667T>G 697G>C 712G>A	Phe223Val Glu233Gln Val238Met	Japanese
DV type 7 (DAL) D^W– or RH:–23	*RHD*05.07* or *RHD*DV.07*	5 5 5 5 5	667T>G 697G>C 712G>A 733G>C 787G>A	Phe223Val Glu233Gln Val238Met Val245Leu Gly263Arg	European (Several)

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Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
DV type 8 (TT)	*RHD*05.08* or *RHD*DV.08*	5 5 5 5	667T>G 697G>C 712G>A 733G>C	Phe223Val Glu233Gln Val238Met Val245Leu	Japanese (Several)
DV type 9 (TO)	*RHD*05.09* or *RHD*DV.09*	5 5	697G>C 712G>A	Glu233Gln Val238Met	Japanese (Few)
DVI type 1 G±/– BARC– or RH:±/–12, –52	*RHD*06.01* or *RHD*DVI.01*	4,5	D-CE(4–5)-D	See table	Europeans (Many)
DVI type 2 BARC+ or RH:52	*RHD*06.02* or *RHD*DVI.02*	4,5,6	D-CE(4–6)-D	See table	Europeans (Many)
DVI type 3 BARC+ or RH:52	*RHD*06.03* or *RHD*DVI.03*	3,4,5,6	D-CE(3–6)-D	See table	Germans, Chinese (Few)
DVI type 4 BARC+ or RH:52	*RHD*06.04* or *RHD*DVI.04*	3, 4, 5	D-CE(3–5)-D	See table	Spanish (Many)
DVII Tar+ or RH:40	*RHD*07.01* or *RHD*DVII.01*	2	329T>C	Leu110Pro	Europeans, Israelis (Many)
DVII type 2 Tar+ or RH:40	*RHD*07.02* or *RHD*DVII.02*	2 2	307T>C 329 T>C	Ser103Pro Leu110Pro	(Few)
DFV	*RHD*08.01* or *RHD*DFV*	5	667T>G	Phe223Val	Africans, Indians (Few)

DAR1	*RHD*09.01* or *RHD*DAR1*	4 5 7	602C>G 667T>G 1025T>C	Thr201Arg Phe223Val Ile342Thr	Africans (Many), Europeans (Few)
DAR1.1 Weak D 4.2.1 (silent change distinguish from DAR1)	*RHD*09.01.01* or *RHD*DAR1.01*	4 5 7 7	602C>G 667T>G 957G>C 1025T>C	Thr201Arg Phe223Val Silent Ile342Thr	Africans (Many)
DAR1.2 Weak D 4.2.2 (silent changes distinguish from DAR1)	*RHD*09.01.02* or *RHD*DAR1.02*	4 5 5 7 7	602C>G 667T>G 744C>T 957G>C 1025T>C	Thr201Arg Phe223Val Silent Silent Ile342Thr	
DAR1.3 Weak D 4.2.3 (silent change distinguishes from DAR1)	*RHD*09.01.02* or *RHD*DAR1.02*	4 5 5 7	602C>G 667T>G 744C>T 1025T>C	Thr201Arg Phe223Val Silent Ile342Thr	
DAR2 (DARE)	*RHD*09.02* or *RHD*DAR2*	4 5 5 7	602C>G 667T>G 697G>C 1025T>C	Thr201Arg Phe223Val Glu233Gln Ile342Thr	Ethiopians (Many)
DAR3 Weak partial D 4.0.1	*RHD*09.03* or *RHD*DAR3*	4 5	602C>G 667T>G	Thr201Arg Phe223Val	Europeans (Many)
DAR3.1 Weak partial D 4.0 (silent change distinguishes from DAR3)	*RHD*09.03.01* or *RHD*DAR3.01*	4 5 6	602C>G 667T>G 819G>A	Thr201Arg Phe223Val Silent	Africans (Many)

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Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
DAR4 Weak partial D 4.1	*RHD*09.04* or *RHD*DAR4*	1 4 5 6	48G>C 602C>G 667T>G 819G>A	Trp16Cys Thr201Arg Phe223Val Silent	Africans (Many), Europeans (Few)
DAR5 Weak partial D 4.3 or DEL[†]	*RHD*09.05* or *RHD*DAR5*	4 5 6 6	602C>G 667T>G 819G>A 872C>G	Thr201Arg Phe223Val silent Pro291Arg	Austrians
DAU0	*RHD*10.00* or *RHD*DAU0*	8	1136C>T	Thr379Met	Africans (Many), Eurasians (Few)
DAU1	*RHD*10.01* or *RHD*DAU1*	5 8	689G>T 1136C>T	Ser230Ile Thr379Met	Africans
DAU2	*RHD*10.02* or *RHD*DAU2*	2 7 8	209G>A 998G>A 1136C>T	Arg70Gln Ser333Asn Thr379Met	Africans
DAU3	*RHD*10.03* or *RHD*DAU3*	6 8	835G>A 1136C>T	Val279Met Thr379Met	Africans
DAU4	*RHD*10.04* or *RHD*DAU4*	5 8	697G>A 1136C>T	Glu233Lys Thr379Met	Africans
DAU5	*RHD*10.05* or *RHD*DAU5*	5 5 8	667T>G 697G>C 1136C>T	Phe223Val Glu233Gln Thr379Met	Africans, Canadians, Germans (Several)

DAU6	*RHD*10.06* or *RHD*DAU6*	7 8	998G>A 1136C>T	Ser333Asn Thr379Met	Africans
DAU7	*RHD*10.07* or *RHD*DAU7*	6 7 8	835G>A 998G>A 1136C>T	Val279Met Ser333Asn Thr379Met	Africans (Rare)
Weak Partial D 11 (or Del)[†]	*RHD*11* or *RHD*Weak partial 11*	6	885G>T	Met295Ile	European (Many)
DOL1 DAK+ or RH:54	*RHD*12.01* or *RHD*DOL1*	4 5	509T>C 667T>G	Met170Thr Phe223Val	(Many)
DOL2 DAK+ or RH:54	*RHD*12.02* or *RHD*DOL2*	4 5 8	509T>C 667T>G 1132C>G	Met170Thr Phe223Val Leu378Val	(Few)
DOL3	*RHD*12.03* or *RHD*DOL3*	3 4 5	410C>T 509T>C 667T>G	Ala137Val Met170Thr Phe223Val	(Few)
DBS1	*RHD*13.01* or *RHD*DBS1*	5 5	D-CE(5)-D 676G>C	See table Ala226Pro	(Few)
DBS2	*RHD*13.02* or *RHD*DBS2*	5 5 5	667T>G 676G>C 697G>C	Phe223Val Ala226Pro Glu233Gln	Germans, Japanese (Few)
DBT1 Rh32+ or RH:32	*RHD*14.01* or *RHD*DBT1*	5, 6, 7	D-CE(5–7)-D	See table	Caucasians, Japanese, Blacks, Moroccans (Several)

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Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
DBT2 Rh32+ or RH:32	*RHD*14.02* or *RHD*DBT2*	5, 6, 7, 8, 9	D-CE(5–9)-D	See table	Japanese (Few)
Weak partial D 15	*RHD*15* or *RHD*Weak partial 15*	6	845G>A	Gly282Asp	Asians (Many), Europeans (Many)
DCS1	*RHD*16.01* or *RHD*DCS1*	5 5	667G>T 676G>C	Phe223Val Ala226Pro	Austrians (Several)
DCS2	*RHD*16.02* or *RHD*DCS2*	5	676G>C	Ala226Pro	Germans, Chinese (Several)
DFR1 FPTT+ or RH:50	*RHD*17.01* or *RHD*DFR1*	4 4 4	505A>C 509T>G 514A>T	Met169Leu Met170Arg Ile172Phe	Caucasians (Many)
DFR2	*RHD*17.02* or *RHD*DFR2*	4	D-CE(4)-D	See table	(Few)
DFR3	*RHD*17.03* or *RHD*DFR3*	4 4 4 4	505A>C 509T>G 514A>T 539G>C	Met169Leu Met170Arg Ile172Phe Gly180Ala	(Few)
DFR4	*RHD*17.04* or *RHD*DFR4*	4 4	505A>C 509T>G	Met169Leu Met170Arg	(Few)
DFW	*RHD*18* or *RHD*DFW*	4	497A>C	His166Pro	(Few)
DHMi	*RHD*19* or *RHD*DHMi*	6	848C>T	Thr283Ile	Caucasians (Many)

DHO	*RHD*20* or *RHD*DHO*	5	704A>C	Lys235Thr	Germans (Few)
Weak partial D 21	*RHD*21* or *RHD*weak partial 21*	6	938C>T	Pro313Leu	Austrians, Germans (Few)
DHR	*RHD*22* or *RHD*DHR*	5	686G>A	Arg229Lys	(Few)
DMH	*RHD*23* or *RHD*DMH*	2	161T>C	Leu54Pro	Portuguese (Few)
DNAK	*RHD*24* or *RHD*DNAK*	7	1070G>A	Gly357Asp	(Few)
DNB	*RHD*25* or *RHD*DNB*	7	1063G>A	Gly355Ser	Swiss, Germans, Danish (Many)
DNU	*RHD*26* or *RHD*DNU*	7	1057G>A	Gly353Arg	(Few)
DDE	*RHD*27* or *RHD*DDE*	1	120T>A	Asp40Glu	(Few)
DFL	*RHD*28* or *RHD*DFL*	4	494A>G	Tyr165Cys	Austrians, French (Few)
DYU (DQC)	*RHD*29* or *RHD*DYU*	5	700A>T	Arg234Trp	(Few)
DTO	*RHD*30* or *RHD*DTO*	5 5	667T>G 674C>T	Phe223Val Ser225Phe	(Few)
DVL1	*RHD*31* or *RHD*DVL1*	5	deletion 684 to 686 GAG	Arg229del	(Few)
DVL2	*RHD*32* or *RHD*DVL2*	5	deletion 705 to 707 GAA	Lys235del	Swiss (Many)
DWI (DWLLE)	*RHD*33* or *RHD*DWI*	7	1073T>C	Met358Thr	(Few)

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Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
DIM(DIleM)	*RHD*34* or *RHD*DIM*	6	854G>A	Cys285Tyr	(Few)
DMA	*RHD*35* or *RHD*DMA*	5	621G>C	Leu207Phe	(Few)
DLO	*RHD*36* or *RHD*DLO*	6	851C>T	Ser284Leu	(Few)
DUC2	*RHD*37* or *RHD*DUC2*	5	733G>C	Val245Leu	(Few)

[†]Weak D phenotype when *in cis* to *RHCE*ce* and Del phenotype when *in cis* to *RHCE*Ce*.
[^]The published molecular basis for DIIIb was determined using DNA from Caucasian probands who are G– and probably have a weak D phenotype, and thus are not DIIIb as defined by Tippett. It is likely that the DIII type 7 phenotype is the same as the originally serologically defined DIIIb phenotype of Tippett and Sanger.

Molecular bases of weak D phenotypes[4–6]

The weak D phenotype is a quantitative, and not a qualitative, polymorphism, and in most cases all immunogenic D epitopes are present. However, some rare individuals who were considered to have a weak D phenotype were later found to have made anti-D. There is debate about the clinical significance of the anti-D, and the possibility that they are autoanti-D may be difficult to rule out[7]. The D antigen with reduced expression is usually detected by the indirect antiglobulin test. If a person with a D+ phenotype that was previously reported as a weak D has made alloanti-D, the allele is now listed in the "Molecular bases of partial and weak partial RhD phenotypes" table.
Nucleotide differences from reference allele *RHD*01* (L08429), and amino acids affected, are given.

Allele encodes weak D	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
Type 1	*RHD*01W.01* or *RHD*weak D type 1*	6	809T>G	Val270Gly	European (Many)
Type 1.1	*RHD*01W.01.01* or *RHD*weak D type 1.1*	1 6	52C>G 809G>A	Leu18Val Val270Gly	Northern Germans (Many)
Type 2	*RHD*01W.02* or *RHD*weak D type 2*	9	1154G>C	Gly385Ala	European (Many)
Type 2.1	*RHD*01W.02.01* or *RHD*Weak D type 2.1*	2 9	301T>A 1154G>C	Phe101Ile Gly385Ala	(Few)
Type 3	*RHD*01W.03* or *RHD*weak D type 3*	1	8C>G	Ser3Cys	European (Many)
Types 4.0, 4.1, 4.2, 4.2.2, 4.3	*See partial DAR* or *RHD*09.03*				
Type 5	*RHD*01W.05* or *RHD*weak D type 5*[†]	3	446C>A	Ala149Asp	European (Several)
Type 6	*RHD*01W.06*	1	29G>A	Arg10Gln	Taiwanese, Germans (Few)
Type 7	*RHD*01W.07*	7	1016G>A	Gly339Glu	Germans (Few)
Type 8	*RHD*01W.08*	6	919G>A	Gly307Arg	Germans (Few)
Type 9	*RHD*01W.09*	6	880G>C	Ala294Pro	Germans (Few)
Type 10	*RHD*01W.10*	9	1177T>C	Trp393Arg	Germans (Few)
Type 11	See partial D *RHD*11*				
Type 12	*RHD*01W.12*	6	830G>A	Gly277Glu	(Few)

Type 13	*RHD*01W.13*	6	826G>C	Ala276Pro	Austrians (Few)
Type 14	*RHD*01W.14*	4 4 4	544T>A 594A>T 602C>G	Ser182Thr Lys198Asn Thr201Arg	Austrians (Few)
Type 15	See partial *RHD*15*				
Type 16	*RHD*01W.16*	5	658T>C	Trp220Arg	(Few)
Type 17	*RHD*01W.17*	3	340C>T	Arg114Trp	(Few)
Type 18	*RHD*01W.18*	1	19C>T	Arg7Trp	(Few)
Type 19	*RHD*01W.19*	4	611T>C	Ile204Thr	(Few)
Type 20	*RHD*01W.20*	10	1250T>C	Phe417Ser	(Several)
Type 21	See partial *RHD*21*				
Type 22	*RHD*01W.22*	9	1224G>C	Trp408Cys	(Few)
Type 23	*RHD*01W.23*	4	634G>T	Gly212Cys	Japanese
Type 24	*RHD*01W.24*	7	1013T>C	Leu338Pro	Japanese
Type 25	*RHD*01W.25*	3	341G>A	Arg114Gln	(Several)
Type 26	*RHD*01W.26*	1	26T>A	Val9Asp	(Few)
Type 27	*RHD*01W.27*	5	661C>T	Pro221Ser	(Few)
Type 28	*RHD*01W.28*	8	(1152 A>C)	Thr384Thr splice site change	(Few)

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Allele encodes weak D	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
Type 29	*RHD*01W.29*	2 2 4 5 7	178A>C 201G>A 203G>A 594A>T 1025T>C	Ile60Leu Ser68Asn Lys198Asn Phe223Val Ile342Thr	(Few)
Type 30	*RHD*01W.30*	7	1018G>A 1019A>T	Glu340Met	(Few)
Type 31	*RHD*01W.31*	1	17C>T	Leu6Pro	(Few)
Type 32	*RHD*01W.32*	8	1121A>T	Ile374Asn	(Few)
Type 33 Probably a partial D; as alloanti-D has been made	*RHD*01W.33*	4	520G>A	Val174Met	Taiwanese, Europeans (Several)
Type 34	*RHD*01W.34*	6	809T>A	Val270Glu	Taiwanese (Few)
Type 35	*RHD*01W.35*	2	260G>A	Gly87Asp	(Few)
Type 36	*RHD*01W.36*	6	842T>G	Val281Gly	(Few)
Type 37	*RHD*01W.37*	3	399G>T	Lys133Asn	(Few)
Type 38	*RHD*01W.38*	6	833G>A	Gly278Asp	(Few)
Type 39	*RHD*01W.39*	7	1015G>A	Gly339Arg	(Few)

Type 40	*RHD*01W.40*	4	602C>G	Thr201Arg	(Few)
Type 41	*RHD*01W.41*	9	1193A>T	Glu398Val	(Few)
Type 42	*RHD*01W.42*	9	1226A>T	Lys409Met	(Few)
Type 43	*RHD*01W.43*	4	605T>C	Ala202Val	Koreans (Few)
Type 44	*RHD*01W.44*	5	728A>G	Tyr243Cys	(Few)
Type 45	*RHD*01W.45*	9	1195G>A	Ala399Thr	Austrians (Few)
Type 46	*RHD*01W.46*	9	1221C>A	Phe407Leu	(Few)
Type 47	*RHD*01W.47*	3	340C>G	Arg114Gly	(Few)
Type 48	*RHD*01W.48*	2	182G>T	Gly61Val	(Few)
Type 49	*RHD*01W.49*	5	770C>T	Ser257Phe	(Few)
Type 50	*RHD*01W.50*	5	727T>A	Tyr243Asn	Germans (Few)
Type 51	*RHD*01W.51*	4	594A>T 602C>G	Lys198Asn Thr201Arg	Chinese (Few)
Type 52	*RHD*01W.52*	1	92T>C	Phe31Ser	Chinese (Few)
Type 53	*RHD*01W.53*	5	740T>G	Val247Gly	Chinese (Few)
Type 54	*RHD*01W.54*	3	365C>T	Ser122Leu	(Few)
Type 55	*RHD*01W.55*	6	895C>G	Leu299Val	(Few)
Type 56	*RHD*01W.56*	1	65C>A	Ala22Glu	French (Few)

(*Continued*)

(Continued)

Allele encodes weak D	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
Type 57	*RHD*01W.57*	5	640C>T	Leu214Phe	French (Few)
Type 58	*RHD*01W.58*	7	1006G>C	Gly336Arg	French (Few)
Type 59	*RHD*01W.59*	8	1148T>C	Leu383Pro	French (Few)
Type 60	*RHD*01W.60*	9	1219-1224 del TTCTGG	Phe407 Trp408del	French (Few)
Type 61	*RHD*01W.61*	1	28C>T	Arg10Trp	Chinese, Germans (Few)
Type 62	*RHD*01W.62*	5	661C>A	Pro221Thr	Germans (Few)
Type 63	*RHD*01W.63*	5	758T>A	Ile253Asn	Germans (Few)

Type 64	*RHD*01W.64*	6	881C>T	Ala294Val	Germans (Few)
Type 65	*RHD*01W.65*	1	68C>A	Ala23Asp	Germans (Few)
Type 66	*RHD*01W.66*	6	916G>A	Val306Ile	Austrians (Few)
Type 67	*RHD*01W.67*	5	722C>T	Thr241Ile	Germans (Few)
Type 68	*RHD*01W.68*	9	1213C>G	Gln405Glu	Germans (Few)
Type 69	*RHD*01W.69*	7	953G>A	Arg318Gln	Austrians (Few)
Type 70	*RHD*01W.70*	7	1012C>G	Leu338Val	Austrians (Few)
Type 71	*RHD*01W.71*	1	29G>C	Arg10Pro	Chinese
Type 72	*RHD*01W.72*	9	1212C>A	Asp404Glu	Chinese
Type 73	*RHD*01W.73*	10	1241C>T	Ala414Val	Chinese

† = This and subsequent weak *RHD* can also use the *RHD*weak D type #* designation (following the obvious pattern above); in the interest of space, this is not included.

Molecular bases of Del phenotype[8]

Very weakly expressed D antigen is detectable only by adsorption and elution of anti-D.

Nucleotide differences from *RHD*01* reference allele (L08429), and amino acids affected, are given for some of the reported Del.

Allele encodes	Allele name	Exon (intron)	Nucleotide	Amino acid	Ethnicity (prevalence)
Del	*RHD*01EL.01* or *RHD*DEL1*	9	1227G>A	Lys409Lys Splice site change	Chinese, Koreans, Europeans (Several)
Del	*RHD*01EL.02* or *RHD*DEL2*	1	3G>A Start codon lost	Met1Ile	Chinese
Del	*RHD*01EL.03* or *RHD*DEL3*	1	53T>C	Leu18Pro	Chinese
Del	*RHD*01EL.04* or *RHD*DEL4*	1	147delA, fs	fs, Stop	Germans (Few)
Del	*RHD*01EL.05* or *RHD*DEL5*	(1)	+1g>a	Splice site change	Japanese (Few)
Del or weak D	*RHD*01EL.06* or *RHD*DEL6*	2	251T>C	Leu84Pro	Chinese
Del or weak D	*RHD*01EL.07* or *RHD*DEL7*	3	410C>A	Ala137Glu	Chinese
Del	*RHD*01EL.08* or *RHD*DEL8*	(3)	+1g>a	Splice site change	Germans, Austrians, Slovenians (Few)
Del or D–	*RHD*01EL.09* or *RHD*DEL9*	(3)	+2t>a	Splice site change	Germans (Few)
Del	*RHD*01EL.10* or *RHD*DEL10*	9	1222T>C	Trp408Arg	Koreans (Few)
Del	*RHD*01EL.11* or *RHD*DEL11*	10	1252 ins T	Stop418Leu (488 amino acids)	Austrians (Few)
Del	*RHD*01EL.12* or *RHD*DEL12*	3	458T>C	Leu153Pro	Germans (Few)
Del or D–	*RHD*01EL.13* or *RHD*DEL13*	5	785delA	fs, Stop	(Few)

Del phenotype also is associated with *RHD*11* and *RHD*09.05* (*RHD*DAR5*).

Molecular bases of D-negative phenotype[8–10]

Several molecular backgrounds result in the D-negative phenotype: deletion of *RHD* predominates in people of European descent; in Asian populations an intact but silenced *RHD* is common; in black African populations two-thirds of D-negative people have an inactive *RHD*, (the *RHD* pseudogene or *RHD**Ψ) with a 37 bp internal duplication resulting in a premature stop codon. Alleles encoding D-negative phenotypes are designated with N (to represent the null of the *RHD*), and numbered according to the background allele on which the change has occurred.

*RHD*01* is used when the changes are on the consensus sequence or if the derivation of the RHD allele is not known. The partial allele number is used when the changes are on a partial *RHD* background. Nucleotide differences from *RHD*01* reference allele (L08429), and amino acids affected, are given for some of the reported D−.

Allele encodes	Allele name	Exon (intron)	Nucleotide	Amino acid	Ethnicity (prevalence)
D–	*RHD*01N.01*	1–10	*RHD* deletion	No protein	Caucasians (Many)
D–	*RHD*01N.01* or *RHD*Pseudogene* *RHD*Ψ*	(3) 4 5 5 5 6	37bp insert 609G>A 654G>C 667T>G 674C>T 807T>G	No protein	Africans (Many)
D–	*RHD*01N.02*	1–9	CE(1–9)-D	Hybrid	Germans (Few)
D–	*RHD*01N.03*	2–9	D-CE(2–9)-D	Hybrid	
D–	*RHD*01N.04*	3–9	D-CE(3–9)-D	Hybrid	Germans, Chinese, Koreans (Several)
D–	*RHD*01N.05*	2–7	D-CE(2–7)-D	Hybrid	(Few)
D–C+^{VW} or RH:−1, +^{VW}2	*RHD*01N.06*	3–7	D-CE(3–7)-D Type 2 hybrid (Part of r′^{S})	Hybrid	Africans (Several)
D–C+^{W} or RH:−1, +^{W}2	*RHD*03N.01*	4–7	DIIIa-CE(4–7)-D Type 1 hybrid (Part of r′^{S})	Hybrid	Africans (Many)
r″^{G} D– G+	*RHD*01N.07*	4–7	D-CE(4–7)-D	Hybrid	(Few)
D–	*RHD*01N.08*	1	48G>A	Trp16Stop	Germans (Few)

D–	*RHD*01N.09*	1 5 5 7	121C>T 643T>C 646 T>C 988T>C	Gln41Stop	(Few)
D–	*RHD*01N.10*	2	270G>A	Trp90Stop	Chinese
D–	*RHD*01N.11*	2	325delA, fs	109fs>Stop	Chinese
D–	*RHD*01N.12*	3	449delT, fs	150fs>Stop	Austrians (Few)
D–	*RHD*01N.13*	4	487delACAG, fs	Met167Stop	Caucasians (Few)
D–	*RHD*01N.14*	4	554G>A	Trp185Stop	Koreans (Few)
D–	*RHD*01N.15*	5	635G>T, splice site change	Gly212Val	Germans (Few)
D–	*RHD*01N.16*	5	711delC, fs	238fs> 245Stop	Chinese (Few)
D–	*RHD*01N.17*	5	652delA, 653T>G, fs	228Stop	Chinese
D–	*RHD*01N.18*	6	807T>G	Tyr269Stop	Germans (Few)
D–	*RHD*01N.19*	6	933C>A	Tyr311Stop	Chinese (Few)
D–	*RHD*01N.20*	7	941G>T	Gly314Val	Japanese (Few)
D–	*RHD*01N.21*	7	990C>G	Tyr330Stop	Germans (Few)
D–	*RHD*01N.22*	9	1203T>A	Tyr401Stop	Russians (Few)

(*Continued*)

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Allele encodes	Allele name	Exon (intron)	Nucleotide	Amino acid	Ethnicity (prevalence)
D–	*RHD*01N.23*	3	343delC, fs	115fs>Stop	Germans (Few)
D–	*RHD*01N.24*	(2)	+1g>a	splice site change	Chinese (Few)
D–	*RHD*01N.25*	(2)	–1g>a	splice site change	Koreans (Few)
D–	*RHD*01N.26*	(8)	+1g>a	splice site change	Germans (Few)
D–	*RHD*01N.27*	(6)	ins tggct+2del taag	fs and splice site change	Chinese (Few)
D–	*RHD*01N.28*	7 7	970del CAC, 976del TCCATCATGGGC TACA), fs	His324del, fs>352Stop	Chinese (Few)

Log on to the ISBT, dbRBC, and Rhesus Base, websites for more information, hyperlinks to original reports, and updates.

Molecular bases of phenotypes associated with RhCE

The RHCE common alleles are designated *RHCE*01* for ce, *RHCE*02* for Ce, *RHCE*03* for cE, and *RHCE*04* for CE. Serologically similar phenotypes can have different allelic backgrounds. Reported alterations in antigen expression are noted. As an alternative terminology, the nucleotides that differ from the reference allele (*RHCE*01* or *RHCE*ce*) may be listed, e.g., *RHCE*01.02* (*RHCE*ceTI*) can be written *RHCE*ce48C*, *1025T*.

In the following tables, when an exon(s) of *RHCE* is substituted with the equivalent exon(s) of *RHD*, the number of the substituted exon is given in parentheses. The nucleotide and amino acid changes between all *RHD* and *RHCE* exons are given in the table "Differences in nucleotides between *RHD* and *RHCE* and amino acids encoded" (above).

Molecular bases of Rhce phenotypes

People who express a partial D on their RBCs can be immunized to make anti-D; however, the availability of D-negative blood precludes the need to name the specific anti-D made by each type of partial D phenotype. As a parallel scenario, people who are homozygous or hemizygous for alleles encoding partial c and/or partial e can produce alloantibody that is directed at conventional Rhce and appears as anti-Rh17 in that only RBCs with the D−− phenotype (or those expressing the same Rhce variant) do not react. These antibodies are not necessarily mutually compatible. In contrast to the availability of D-negative blood donors for transfusion, Rh17-negative blood donors are rare. Thus, some antibodies, especially those made by people with partial e antigens, have been given names to aid in communication and finding compatible blood.

Reference allele *RHCE*01* or *RHCE*ce* (Accession number DQ322275) encodes c (RH4), e (RH5), f (RH6), RH17, RH18, RH19, RH31, RH34, etc. Differences from *RHCE*01* reference allele are given in rows 2 and 3. These differences are also present in all other alleles in this table. Nucleotide differences from the reference allele, and amino acids affected, are given for some of the reported Rhce variants.

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
c+e+f+RH:4,5,6	*RHCE*01* or *RHCE*ce*				
c+ or RH:4	*RHCE*^*	2	307C	Pro103	
e+ or RH:5	*RHCE*^^*	5	676G	Ala226	
e+ (weak with some monoclonal anti-e)	*RHCE*01.01* or *RHCE*ce.01*	1	48G>C	Trp16Cys	Africans (Many) Europeans (Several)
Partial c, partial e	*RHCE*01.02* or *RHCE*ceTI*	1 7	48G>C 1025C>T	Trp16Cys Thr342Ile	Africans (Several)
Partial e	*RHCE*01.03* or *RHCE*ceTI type 2*	7	1025C>T	Thr342Ile	(Few)
Partial c, partial e V+^{W} VS– Hr– hr^{S}– or RH:+^{w}10,–18,–19,–20	*RHCE*01.04* or *RHCE*ceAR*	1 5 5 5 5 6	48G>C 712A>G 733C>G 787A>G 800T>A 916A>G	Trp16Cys Met238Val Leu245Val Arg263Gly Met267Lys Ile306Val	Africans (Many)
Partial c, partial e Hr– hr^{S}– or RH:–18,–19	*RHCE*01.05* or *RHCE*ceEK*	1 5 5 5	48G>C 712A>G 787A>G 800T>A	Trp16Cys Met238Val Arg263Gly Met267Lys	Africans (Several)
Partial e hr^{B}– CEAG– or RH:–31,–59	*RHCE*01.06* or *RHCE*ceAG*	2	254C>G	Ala85Gly	Africans (Many)
Partial c, partial e hr^{S}– hr^{B}– or RH:–19,–31	*RHCE*01.07* or *RHCE*ceMO*	1 5	48G>C 667G>T	Trp16Cys Val223Phe	Africans (Many)

c+e± Hr– hr^S– STEM+ or RH:–18,–19,49	*RHCE*01.08* or *RHCE*ceBI*	1 5 6 8	48G>C 712A>G 818C>T 1132C>G	Trp16Cys Met238Val Ala273Val Leu378Val	Africans (Many)
c+e± Hr– hr^S– STEM+^{W} or RH:–18,–19,49	*RHCE*01.09* or *RHCE*ceSM*	1 5 6	48G>C 712A>G 818C>T	Trp16Cys Met238Val Ala273Val	Blacks (Many)
c+e+^{W} weakly reactive with some MAb anti-D	*RHCE*01.10.01* or *RHCE*ceSL*	1 3	48G>C 365TC>T	Trp16Cys Ser122Leu	European (Few)
c+e+^{W}	*RHCE*01.10.02*	3	365TC>T	Ser122Leu	European (Rare)
c+e+^{w} weakly reactive with some MAb anti-D	*RHCE*01.11* or *RHCE*ceRT*	3	461G>C	Arg154Thr	Japanese, Germans (Few)
c+e+^{W} (very weak)	*RHCE*01.12* or *RHCE*ceRA*	1 4	48G>C 538G>C	Trp16Cys Gly180Arg	Indians (Few)
c+e+^{VW} CELO+^{W} or RH:+^{W}58	*RHCE*01.13* or *RHCE*ceBP*	5	685-687 delAGA	Arg229del	Caucasians (Few)
c+^{W}, e+^{W} Be(a+) or RH:36	*RHCE*01.14* or *RHCE*ceBE*	5	662C>G	Pro221Arg	Caucasians (Germans, Poles) (Several)
c+^{W} or e+^{W} Rh26– LOCR+ or RH:–26,55	*RHCE*01.15* or *RHCE*ceLOCR*	2	286G>A	Gly96Ser	Dutch, Germans (Few)

(*Continued*)

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Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
Partial c, partial e V+VS+hr^{B}+^{VW}/– or RH:10,20,+^{VW}31	*RHCE*01.20.01* or *RHCE*ceVS.01*	5	733C>G	Leu245Val	Africans (Many)
Partial c, partial e V+VS+hr^{B}– or RH:10,20,–31	*RHCE*01.20.02* or *RHCE* ceVS.02*	1 5	48G>C 733C>G	Trp16Cys Leu245Val	Africans (Many)
Partial c, partial e V–VS+hr^{B}– or RH:–10,20,–31	*RHCE*01.20.03* or *RHCE* ceVS.03*	1 5 7	48G>C 733C>G 1006G>T	Trp16Cys Leu245Val Gly336Cys	Africans (Many)
Partial e V+VS+or RH:10,20 Probably hr^{B}– or RH:–31	*RHCE*01.20.04* or *RHCE*ceVS.04*	1 5 7	48G>C 733C>G 1025C>T	Trp16Cys Leu245Val Thr342Ile	Africans (Some)
Partial e V–VS+hr^{B}– or RH:–10,20,–31	*RHCE*01.20.05* or *RHCE*ceVS.05*	5 7	733C>G 1006G>T	Leu245Val Gly336Cys	Africans (Several)

Partial c, partial e hr^S+/–VS+hr^B–Crawford+ CELO– RH:+/–19,20,–31,43,–58 Strongly reactive with some MAb anti-D	*RHCE*01.20.06* or *RHCE*ceCF* *RHCE*ceVS.06*	1 5 5	48G>C 697C>G 733C>G	Trp16Cys Gln233Glu Leu245Val	Africans (Many)
Partial c, partial e RHVS+/^{W},hr^B+^{W},JAL+, CEST–:+^{W}/–19, +^{W}20,+^{W}/–31,48,–57	*RHCE*01.20.07* or *RHCE*ceJAL* *RHCE*ceVS.07*	3 5 5	340C>T 733C>G	Arg114Trp Leu245Val	Africans (Many)
e+^{W} V+VS+or RH:10,20 Probably hr^B– (RH:–31)	*RHCE*01.20.08* or *RHCE*ceVS.08*	1 5 5	48G>C 733C>G 748G>A	Trp16Cys Leu245Val Val250Met	Africans (Few)
e+^{W} V+VS+hr^B+^{W} or RH:10,20,+^{W}31	*RHCE*01.20.09* or *RHCE*ceVS.09*	1 5 7 8	48G>C 733C>G 941T>C 1006G>T	Trp16Cys Leu245Val Val314Ala Gly336Cys	African (Several)
e+^{W} JAL+ or RH:48	*RHCE*01.21*	3	341G>A	Arg114Gln	Asian, Caucasians (Few)

(*Continued*)

(Continued)

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
e+^{W} partial D (D^{HAR}) Rh33+FPTT+ or RH:33,50 D+ with some anti-D	*RHCE*01.22* or *RHCE*ceHAR*	5	ce-D(5)-ce	See table	Caucasians (Germans) (Many)
e+^{W}	*RHCE*01.23*	5	649T>C	Trp217Arg	Caucasians (Germans) (Few)
e+^{W}	*RHCE*01.24*	4	512G>A	His171Arg	Caucasians (Germans) (Few)
e+^{W}	*RHCE*01.25*	5	730G>A	Ala244Thr	Caucasians (Germans) (Few)
e+^{W}	*RHCE*01.26*	6	872C>T	Pro291Leu	Caucasians (Germans) (Rare)
e+^{W}	*RHCE*01.27*	9	1154G>C	Gly385Ala	Caucasians (Germans) (Few)
c+^{W}	*RHCE*01.28*	10	1254A>C	Stop418Tyr	Caucasians (Germans) (Few)
C–E–c+e– (Dc−haplotype)	*RHCE*01.29* *RHCE*ceBOL*	4 to 9	ce-D(4–9)-ce	See table	(Few)
e+^{W}	*RHCE*01.30*	4	526G>A	Ala176Thr	African (Few)

^ = Can be used if testing is focused on only c.
^^ = Can be used if testing is focused on only e.

Molecular bases of RhCe phenotypes

People who are homozygous for alleles encoding partial C and/or partial e can produce alloanti-C and/or anti-e or an alloantibody that is directed at conventional RhCe and appears as anti-Rh17 in that only RBCs with the D−− phenotype (or those expressing the same RhCe variant) do not react. These antibodies are not necessarily mutually compatible. Donors who are Rh17-negative are rare. Thus, antibodies with broad RhCe specificity have been given names to aid in communication and finding compatible blood.
Differences between *RHCE*01* reference allele (Accession number DQ322275) and the *RHCE*02* (*RHCE*Ce*) are given in rows 2 and 3. These differences are also present in all other alleles in this table. Nucleotide differences and amino acids affected are given.

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
C+e+ Ce+ or RH:2,5,7	*RHCE*02* or *RHCE*Ce*	1 2			
C+ or RH:2	*RHCE*C^*	1 2	48G>C *RHC exon 2*	Trp16Cys See table	
e+ or RH:5	*RHCE*e^*	5	676G	Ala226	
$C+^{W}$/–, $e+^{W}$ JAL+ or RH:48	*RHCE*02.01* or *RHCE*CeMA or RHCE*CeJAL* or or *RHCE*Ce.01*	3	340C>T	Arg114Trp	Caucasians (Many)
C+e+	*RHCE*02.02* or *RHCE*CeFV* or *RHCE*Ce.02*†	5 5 5	667G>T 697C>G 712A>G	Val223Phe Gln233Glu Met238Val	Caucasians (Few)
r^{G} $C+^{W}e+^{W}$ JAHK+ or RH:53	*RHCE*02.03* or *RHCE*CeJAHK*	3	365C>T	Ser122Leu	Europeans (Several)
Partial C	*RHCE*02.04* or *RHE*CeVA*	5 5	CE-D(5)-CE	See table	Caucasians (Few)
Partial C C^{W}+ MAR– or RH:8,–51	*RHCE*02.08.01* or *RHCE*CeCW*	1	122A>G	Gln41Arg	Scandinavians (Many)
C^{W}+, CENR– or RH:8,–56	*RHCE*02.08.02* or *RHCE*CeNR*	1 6 to 10	122A>G Ce-D(6–10)	Gln41Arg See table	Blacks (Few)

(*Continued*)

(Continued)

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
Partial C C^X+ MAR– or RH:9,−51	*RHCE*02.09* or *RHCE*CeCX*	1	106G>A	Ala36Thr	Scandinavians (Many)
R^N $C+^W$/–$e+^W$ Rh32+ Sec– DAK+ or RH:32,–46,54	*RHCE*02.10.01* or *RHCE*CeRN.01*	4	Ce-D(4)-ce	See table	Africans (Many)
R^N $C+^W$/–$e+^W$ Rh32+ Sec– DAK+ or RH:32,–46,54	*RHCE*02.10.02* or *RHCE*CeRN.02*	3 4	455C>A Ce-D(4)-Ce	Thr152Asn See table above	? exists
$C+^W$	*RHCE*02.11*	2	286G>A	Gly96Ser	Caucasians (Rare)
$C+^W$	*RHCE*02.12*	3	344T>G	Leu115Arg	Caucasians (Rare)
$e+^W$	*RHCE*02.13*	3	364T>C	Ser122Pro	Caucasians (Rare)
$C+^W$	*RHCE*02.14*	4	497A>T	His166Leu	Caucasians (Rare)
$e+^W$	*RHCE*02.15*	5	689G>C	Ser230Thr	Caucasians (Rare)
$C+^W$ $e+^W$	*RHCE*02.16*	5	728A>G	Tyr243Cys	Caucasians (Rare)
$e+^W$	*RHCE*02.17*	5	800T>A	Met267Lys	Caucasians (Rare)
$C+^W$ $e+^W$	*RHCE*02.18*	6	890T>C	Leu297Pro	Caucasians (Rare)
$e+^W$	*RHCE*02.19*	3 8	464T>G 1118C>T	Met155Arg Ala373Val	Caucasians (Rare)
$C+^W$ $e+^W$	*RHCE*02.20*	1	79–81delCTC	Leu27del	Caucasians (Rare)
$C+^W$	*RHCE*02.21*	4	527C>T	Ala176Val	Caucasians (Rare)
$C+^W$ $e+^W$/–	*RHCE*02.22*	5	667G>T	Val223Phe	Caucasians (Rare)

(*Continued*)

(Continued)

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
C+^{W}	*RHCE*02.23*	7	941T>C	Val314Ala	Caucasians (Rare)
C+^{W} e+^{W}	*RHCE*02.24*	7	1007G>A	Gly336Asp	Caucasians (Rare)
C+^{W}	*RHCE*02.25*	7	1007G>T	Gly336Val	Caucasians (Rare)

† = This and subsequent RHCE*Ce alleles can also be referred to by the *RHCE*Ce.01*, *RHCE*Ce.02*, etc., designation (following the pattern above); in the interest of space, this is not included.
^ = Can be used if testing is focussed on only C or e.

RBCs from people with the r′^{S} haplotypes (types 1 and 2) type C+ express a partial C, and when immunized by "normal" C frequently make alloanti-C. As the r′^{S} haplotypes (types 1 and 2) arise from altered *RHD* they are not included in this table.

Molecular bases of RhcE phenotypes[11,12]

Differences between *RHCE*01* reference allele (Accession number DQ322275) and the *RHCE*03* (*RHCE*cE*) are given in rows 2 and 3. These differences are also present in all other alleles in this table. Nucleotide differences and amino acids affected are given.

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
c+E+cE+ RH:3,4,27	*RHCE*03* or *RHCE*cE*				
c+ or RH:4	*RHCE*c^*	2	307C	Pro103	
E+ or RH:3	*RHCE*E^*	5	676C	226Pro	
Partial E E type I c+E+^{W}/– E^{W}+ or RH:11	*RHCE*03.01* or *RHCE*cEEW* or *RHCE*cE.01*†	4	500T>A	Met167Lys	Caucasians, Asians (Many)

(*Continued*)

(Continued)

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
E type II Partial E c+^{W}/–	*RHCE*03.02* or *RHCE*cEKK*	1-3	D(1-3)-cE	See table	Caucasians, Japanese (Few)
E type III Partial E	*RHCE*03.03* or *RHCE*cEFM*	5 5	697C>G 712A>G	Gln233Glu Met238Val	Japanese, Caucasians (Few)
E type IV E c+^{W}	*RHCE*03.04*	4	602G>C	Arg201Thr	Caucasians (Few)
Partial E, E type V Partial E c+^{W}	*RHCE*03.05* or *RHCE*cEKH*	3	461G>C	Arg154Thr	Japanese (Few)
c+^{W}, E+/+^{W}	*RHCE*03.06*	1	28C>T	Arg10Trp	Caucasians (Rare)
E+^{W}	*RHCE*03.07*	3	344T>C	Leu115Pro	Caucasians (Rare)
E+^{W}	*RHCE*03.08*	3	356G>A	Ser119Asn	Caucasians (Rare)
c+^{W}, E+^{W}	*RHCE*03.09*	3	374T>A	Ile125Asn	Caucasians (Rare)
E+^{W}	*RHCE*03.10*	4	506T>A	Ile169Gln	Caucasians (Rare)
c+^{W}, E+^{W}	*RHCE*03.11*	6	908T>A	Leu303Gln	Caucasians (Rare)
E+^{W}	*RHCE*03.12*	33	464T>G 477T>G	Met155Arg Asn159Lys	Caucasians (Rare)
c+^{W}, E+^{W}	*RHCE*03.13*	5	728A>G	Try243Cys	Caucasians (Rare)
c+^{W}, E+^{VW}/–	*RHCE*03.14*	5	734T>C	Leu245Pro	Caucasians (Rare)
E+^{W}	*RHCE*03.15.0* or *RHCE*cEBA*	3 3	380C>T 383G>A	Ala127Val Gly128Asp	Caucasians (Rare)
E+^{W}	*RHCE*03.15.02* or *RHCE*ceJU*	3 3 3	361A>T 380C>T 383G>A	Met121Glu Ala127Val Gly128Asp	Caucasians (Rare)

† = This and subsequent RHCE*cE alleles can also be referred to by the *RHCE*cE.01*, *RHCE*cE.02*, etc., designation (following the pattern above); in the interest of space, this is not included.
^ = Can be used if testing is focussed on only c or E.

Molecular bases of RhCE phenotypes

Differences between *RHCE*01* reference allele (Accession number DQ322275) and the *RHCE*04* (*RHCE*CE*) are given in rows 2 and 3. These differences are also present in the other allele in this table. The nucleotide difference and amino acid affected are given.

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
C+E+CE+ or RH:2,3,22	*RHCE*04 or RHCE*CE*	1 2 5			South American Indians, Native Americans, (Many) Caucasians (Several)
C+ or RH:2	*RHCE*C^*	1 2	48G>C *RHC exon 2*	Trp16Cys See table	
E+ or RH:3	*RHCE*E^*	5	676C	226Pro	
C+^{W} E±	*RHCE*04.01*	5	722C>T	Thr241Ile	Caucasians (Few)

^ = Can be used if testing is focussed on only C or E.

Molecular bases of silencing of *RHCE*; on any background

Heterozygosity for a silenced allele is usually revealed by discrepancy between molecular and serologic testing. Homozygosity or compound heterozygosity leads to an $RhCE_{null}$ phenotype; if *in cis* to a deleted or silenced *RHD*, the outcome is an amorph type of Rh_{null}. If *in cis* to *RHD*, the outcome is a D−− haplotype without an exalted D antigen. The nucleotide differences from the *RHCE* parent *(RHCE*01*, *RHCE*02*, *RHCE*03*, or *RHCE*04*) reference allele, and amino acids affected, are given.

Phenotype	Allele name	Exon (intron)	Nucleotide	Amino acid	Ethnicity (prevalence)
c– e–	*RHCE*01N.01* or *RHCE*ceN.01*	1	80–84 del	Lys31Stop	Caucasians (Few)
c– e–	*RHCE*01N.02* or *RHCE*ceN.02*	7	960–963 del G	Gly321fs	Caucasians (Few)
c– e–	*RHCE*01N.03* or *RHCE*ceN.03*	(4)	+1g>t	Disrupts slice site	Caucasians (Few)
C– e–	*RHCE*02N.01* or *RHCE*CeN.01*	7	966–969del or nt change +del	Ile322, His323fs; Gly398Stop	Caucasians (Few)
c– E–	*RHCE*03N.01* or *RHCE*cEMI*	3	350–358del	Arg120del, Met121del, Ser122del	Caucasians (Few)
c– E–	*RHCE*03N.02* or *RHCE*cE907del*	6	907del C	fs, Leu303Stop	Hispanics (Several)

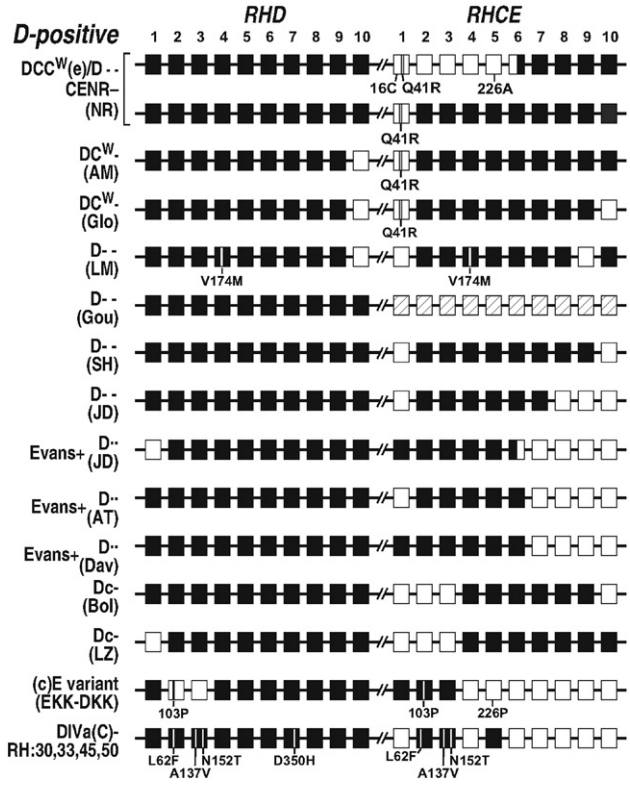
Molecular bases of hybrid haplotypes resulting in an altered or silenced RH alleles

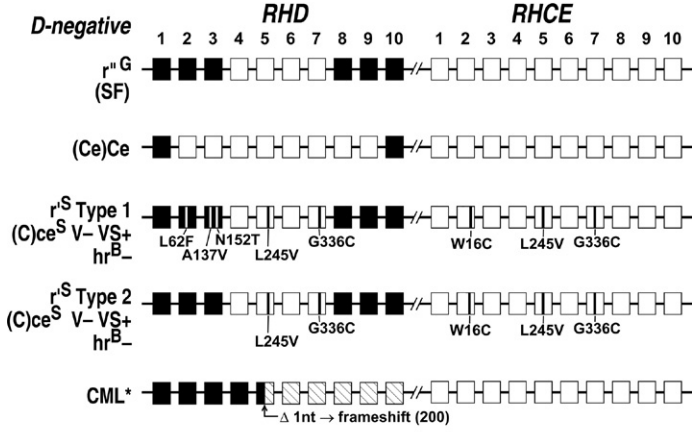
RBCs with these phenotypes have an exalted expression of D.

Phenotype	Haplotype name	RHD allele	RHCE allele	Ethnicity (prevalence)
D+^{S} C– C^{W}+^{W} E– c– e–; DC^{W}–	DC^{W}– (AM)	*RHD*D–CE(10)*	*RHCE*CeCW-D(2–10)*	(Rare)
D+^{S} C– C^{W}+^{W} E– c– e–; DC^{W}–	DC^{W}– (GLO)	*RHD*D–CE(10)*	*RHCE*CeCW-D(2–9)–CE*	(Rare)
D+^{S} C– E– c– e– D– –	D– – (LM)	*RHD*01W.033–CE(10)*	*RHCE*CE-DW33(2–8)–CE-D(10)*	(Rare)
D+^{S} C– E– c– e– D– –	D– – (SH)	*RHD*01*	*RHCE*CE-D(2–9)-CE*	(Rare)
C+^{VW} Go(a+) Rh33+ Riv+ FPTT+ or RH:30,33,45,50	DIVa(C)–	*RHD*DIVa*	*RHCE*CE-DIVa(2,3)-CE-D(5)-CE*	Africans (Few)
D– C+^{W} V– VS+ hr^{B}– Hr^{B}–Rh42+ or RH:–1, +^{w}2,–10,20, –31,–34,42	r$'^{S}$ type 1	*RHD*DIIIa-ceVS.03(4–7)-D*	*RHCE*ceVS.03 RHCE*01.20.03*	Africans (Many)
D–, C+^{VW} V– VS+ hr^{B}– Hr^{B}– Rh42– or RH:–1, +^{vw}2,–10, 20,–31,–34,–42	r$'^{S}$ type 2	*RHD*D-ceVS.03 (3–7)-D*	*RHCE*ceVS.03 RHCE*01.20.03*	Africans (Several)

Rearranged *RHD* and *RHCE*[1,9,11,13]

White boxes show exons encoded by *RHCE*; black boxes show exons encoded by *RHD*; hatched boxes depict exons that are not expressed. Amino acid substitutions, rather than nucleotide substitutions are shown under the exons.



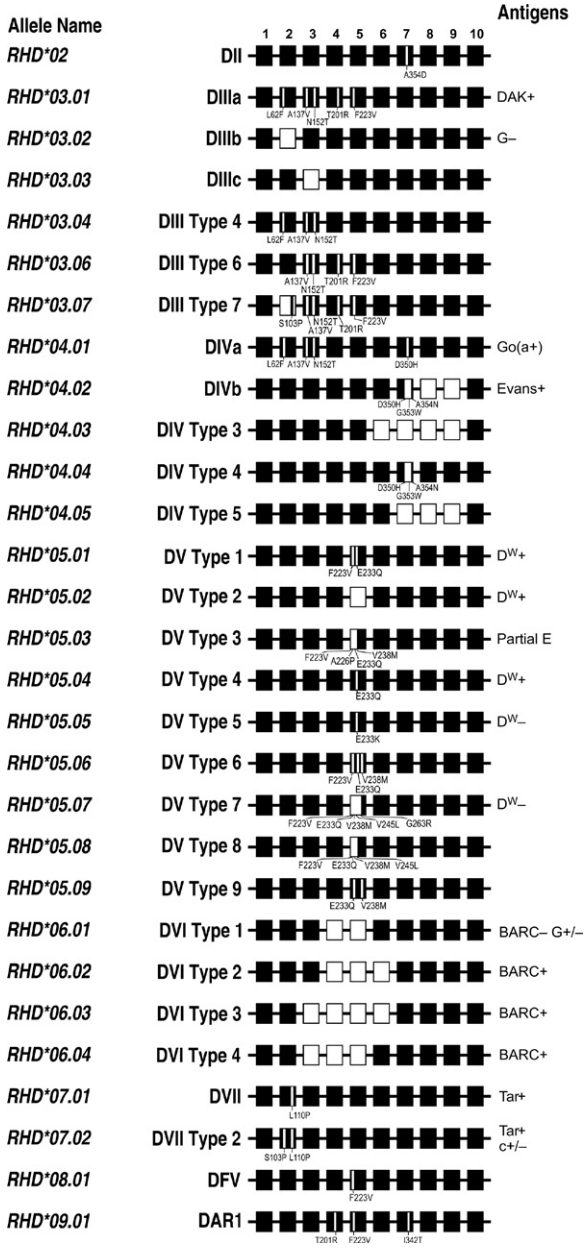


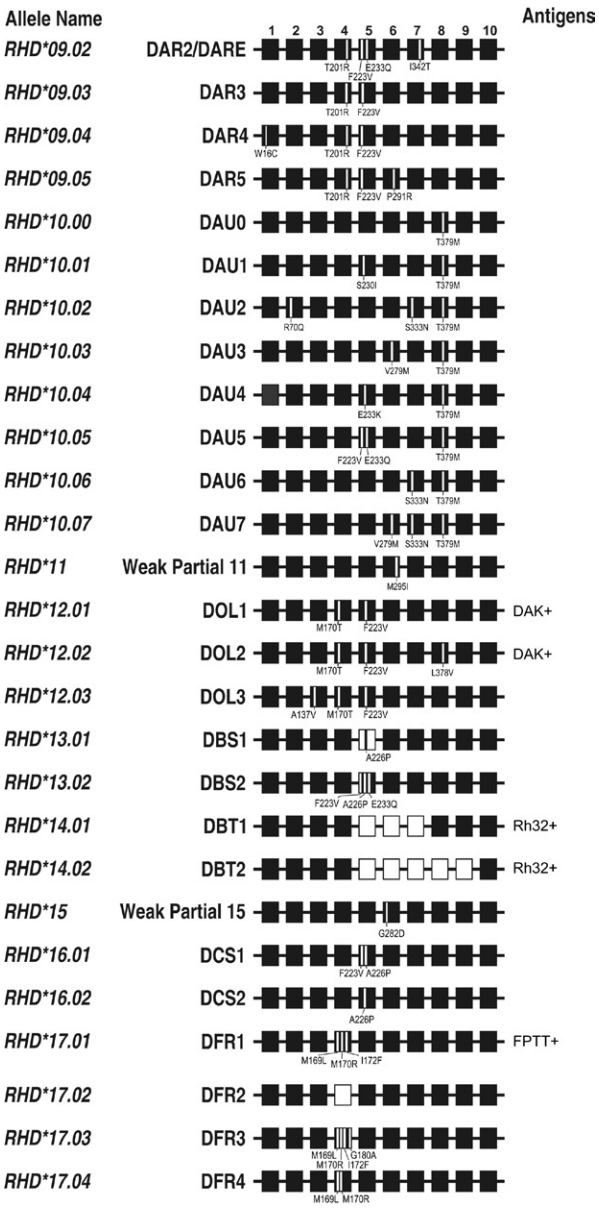
* *RHD* and *RHCE* identified in a D-positive patient, with chronic myeloid leukemia, who became D-negative

RHD alleles and associated information

Black boxes show exons encoded by *RHD*, white boxes show exons encoded by *RHCE*. Amino acid substitutions, rather than nucleotide substitutions, are shown under the exons.

Partial RhD and weak partial RhD phenotypes





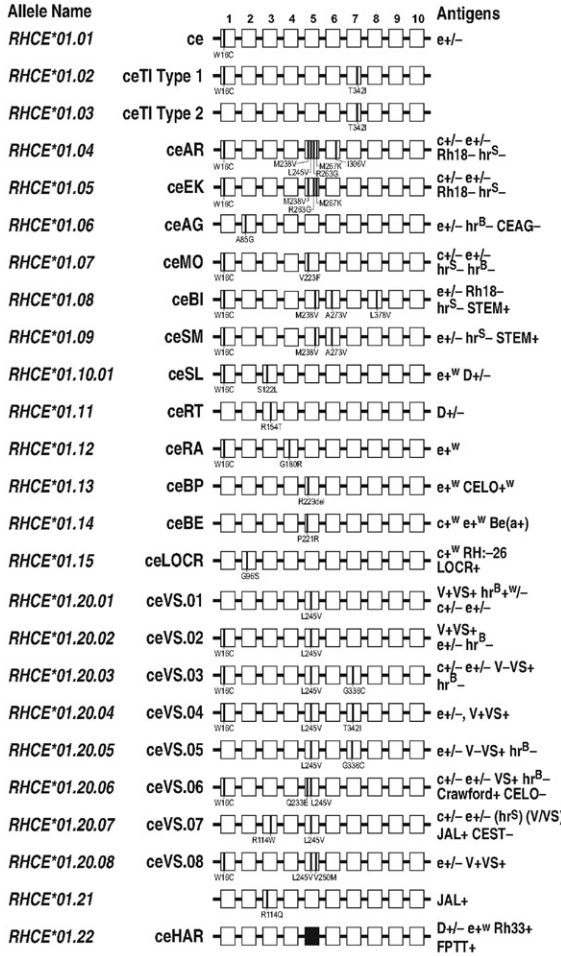
For additional alleles and more information, see table "Molecular bases of partial and weak partial D phenotypes."

RHCE alleles and associated information[14–16]

White boxes show exons encoded by *RHCE*; black boxes show exons encoded by *RHD*. Amino acid substitutions, rather than nucleotide substitutions, are shown under the exons. Associated low prevalence antigens and other relevant serological findings are given next to the exon diagram.

Partial and weak Rhce phenotypes

Differences from Rhce encoded by *RHCE*01* are given.

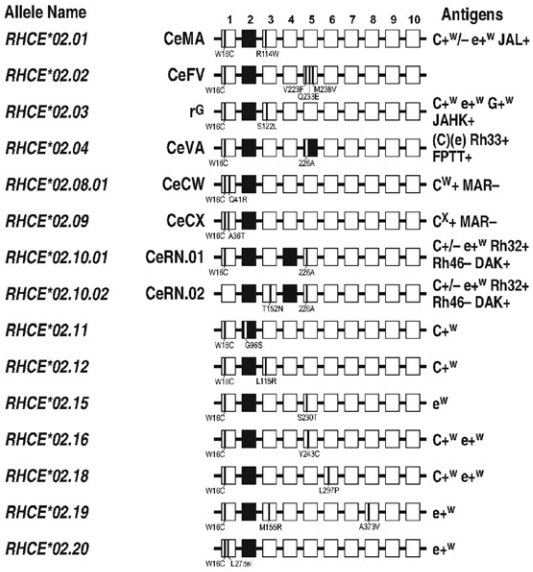


( ) denotes reduced antigen expression

+/– positive with some antibodies (could be weak) negative with other antibodies

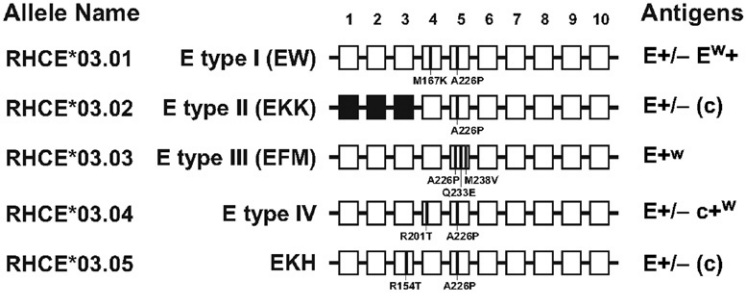
For additional alleles and more information, see table "Molecular bases of Rhce phenotypes"

Partial and weak RhCe phenotypes



( ) denotes reduced antigen expression
+/– positive with some antibodies (could be weak) negative with other antibodies
For additional alleles and more information, see table "Molecular bases of RhCe phenotypes."

Partial and weak RhcE Phenotypes



( ) denotes reduced antigen expression
+/– positive with some antibodies (could be weak) negative with other antibodies.
For additional alleles and more information see table "Molecular bases of RhcE phenotypes."

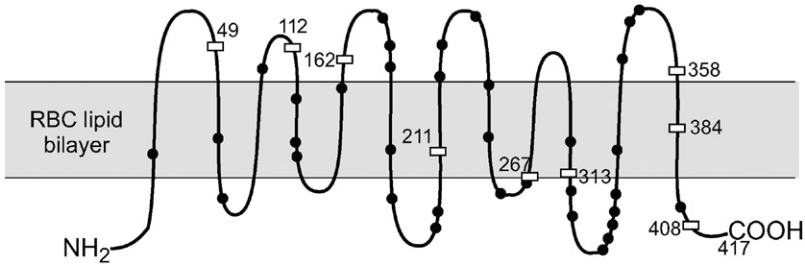
Amino acid sequence of RhCE and RhD[17,18]

The full sequence is the RhCE (C and E) protein. Differences in the sequence for c, e and D proteins are shown.

```
RhC:    MSSKYPRSVR    RCLPLCALTL    EAALILLFYF    FTHYDASLED    QKGLVASYQV   50
Rhc:                      W
RhD:                      W

RhC:    GQDLTVMAAI    GLGFLTSSFR    RHSWSSVAFN    LFMLALGVQW    AILLDGFLSQ  100
Rhc:            L             N
RhD:            I             S

RhC:    FPSGKVVITL    FSIRLATMSA    MSVLISAGAV    LGKVNLAQLV    VMVLVEVTAL  150
Rhc:      P
RhD:      S                         L     VD

RhC:    GTLRMVISNI    FNTDYHMNLR    HFYVFAAYFG    LTVAWCLPKP    LPKGTEDNDQ  200
RhD:     N                  MM     I              S              E    K

RhE:    RATIPSLSAM    LGALFLWMFW    PSVNSPLLRS    PIQRKNAMFN    TYYALAVSVV  250
Rhe:                                    A
RhD:    T                           F  A            E    V          V

RhC:    TAISGSSLAH    PQRKISMTYV    HSAVLAGGVA    VGTSCHLIPS    PWLAMVLGLV  300
RhD:                    G    K

RhC:    AGLISIGGAK    CLPVCCNRVL    GIHHISVMHS    IFSLLGLLGE    ITYIVLLVLH  350
RhD:         V        Y    G       P S I GY      N              I        D

RhC:    TVWNGNGMIG    FQVLLSIGEL    SLAIVIALTS    GLLTGLLLNL    KIWKAPHVAK  400
RhD:      GA                                                          E

RhC:    YFDDQVFWKF    PHLAVGF                                         417
```

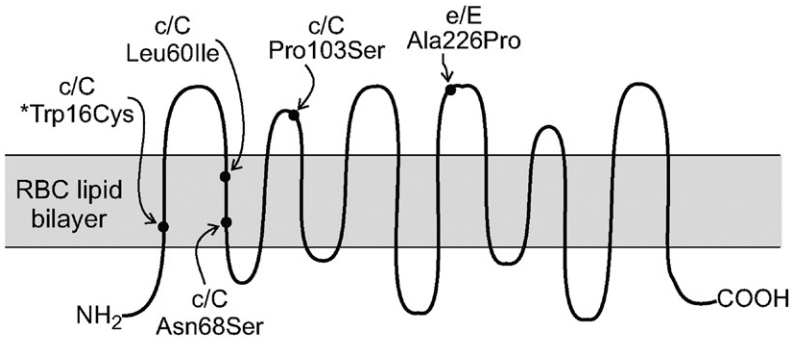
Carrier molecule

The assembly of the Rh proteins (RhD, RhCE) and the Rh-associated glycoprotein (RhAG) as a core complex in the RBC membrane appears to be essential for Rh-antigen expression. RhD and RhCE are multipass, acylated, palmitoylated, non-glycosylated proteins.



Circles indicate the amino acid positions that differ between RhD and RhCE. Depending on the RhCE haplotype, RhD differs from RhCE by 32 to 35 amino acids. The D antigen is unusual in that it is not derived from an amino acid polymorphism, but from the presence of the entire RhD protein. Expression of D antigen can vary qualitatively and quantitatively. Segments of

RhD and RhCE encoded by a particular exon are defined by numbered boxes, representing the start and finish of each exon.



*Trp usually but not exclusively associated with c antigen
Cys usually but not exclusively associated with C antigen.

74% of C–c+black Americans with normal c have Cys16.

M_r (SDS-PAGE)	30,000–32,000	
Cysteine residues	4 in RhD; 6 in RhCE	
Palmitoylation sites	2 in RhD:	Cys12, Cys186
	3 in RhCE:	Cys12, Cys186, Cys311
Copies per RBC	100,000–200,000 for RhD and RhCE combined	

Function

The Rh membrane core complex interacts with band 3, GPA, GPB, LW, and CD47, and is associated with the RBC membrane skeleton via ankyrin and protein 4.2. This complex maintains erythrocyte membrane integrity, as demonstrated by the abnormal morphology and functioning of stomatocytic Rh_{null} RBCs[9]. The Rh core proteins in the membrane may transport ammonia[19] and CO_2[20]. RhAG homologs are expressed in other tissues[1,21].

Disease association

Rh incompatibility is still the main cause of HDFN.
Compensated hemolytic anemia occurs in some individuals with Rh_{null} or Rh_{mod} RBCs. Reduced expression of Rh antigens and Rh mosaicism can occur in leukemia, myeloid metaplasia, myelofibrosis, and polycythemia. Rh and one form of hereditary spherocytosis are linked because both genes are on chromosome 1. Some Rh antigens are expressed weakly on South East Asian ovalocytes.

Phenotypes (% occurrence)

Haplotype	Caucasians	Blacks	Native Americans	Asians
DCe (R_1)	42	17	44	70
Ce (r′)	2	2	2	2
DcE (R_2)	14	11	34	21
cE (r″)	1	0	6	0
Dce (R_0)	4	44	2	3
ce (r)	37	26	6	3
DCE (R_z)	0	0	6	1
CE (r^y)	0	0	0	0

Phenotype (alternative)	Caucasians	Blacks	Asians	D-antigen copy number
D-positive				
R_1R_1 (R_1r')	18.5	2.0	51.8	14,500–19,300
R_2R_2 (R_2r'')	2.3	0.2	4.4	15,800–33,300
R_1r (R_1R_0; R_0r')	34.9	21.0	8.5	9,900–14,600
R_2r (R_2R_0; R_0r'')	11.8	18.6	2.5	14,000–16,000
R_0r (R_0R_0)	2.1	45.8	0.3	12,000–20,000
R_zR_z (R_zr^y)	0.01	Rare	Rare	
R_1R_z (R_zr'; R_1r^y)	0.2	Rare	1.4	
R_2R_z (R_zr''; R_2r^y)	0.1	Rare	0.4	
R_1R_2 (R_1r''; R_2r'; R_zr; R_0R_z; R_0r^y)	13.3	4.0	30.0	23,000–36,000
D-negative				
r′r	0.8	Rare	0.1	
r′r′	Rare	Rare	0.1	
r″r	0.9	Rare	Rare	
r″r″	Rare	Rare	Rare	

(*Continued*)

(Continued)

Phenotype (alternative)	Caucasians	Blacks	Asians	D-antigen copy number
rr	15.1	6.8	0.1	
r′r″ (r^yr)	0.05	Rare	Rare	
r′r^y; r″r^y; r^yr^y	Rare	Rare	Rare	
r′^{S}r	0	1–2	0	

Null: Rh_{null}
Unusual: Rh_{mod}; many variants.

Comparison of Rh_{null} and Rh_{mod} RBCs

Phenotype	Rh proteins/ antigens	RhAG	LW	CD47	GPB: S, s, and U antigens	Altered gene
Amorph Rh_{null}	Absent	Reduced (20%)	Absent	Reduced by 90%	Reduced by 50% S/s normal; U weak	*RHCE* (*RHD* deleted)
Regulator Rh_{null}	Absent	Absent	Absent	Reduced	Reduced by 70% S/s weak; U absent	*RHAG*
Rh_{mod}	Reduced (variable)	Absent or reduced (variable)	Absent or reduced	Reduced (variable)	Reduced (variable) S/s normal; U normal/ weak	*RHAG*

Comments

Useful websites are dbRBC (for *RHD*, *RHCE*, *RHAG*), Rhesus Base (for *RHD*), and NYBC (for *RHCE*) to obtain further details see hyperlinks to original papers, and updates.

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D Antigen

Terminology

ISBT symbol (number)	RH1 (004001 or 4.1)
Obsolete names	Rh_0
History	The original "Rh" antigen stimulated a transfusion reaction, which was investigated by Levine and Stetson in 1939. The reactions of this antibody paralleled those of the anti-"Rh" reported by Landsteiner and Wiener in 1940, but stimulated in animals. Some years later, upon recognition that the human and the animal anti-"Rh" did not react with the same antigen, the accumulation of publications about the clinically important human anti-"Rh" made a name change undesirable. Ultimately however, the antigen name switched to D and the system took the Rh name.

Occurrence

Caucasians	85%
Blacks	92%
Asians	99%
Native Americans	99%

Expression

Cord RBCs	Expressed
Altered	Partial and weak D phenotypes; exalted on D deletion phenotypes; appears exalted on GPA-deficient RBCs because of reduction of sialic acid

Number of D antigen sites per RBC

Common D phenotypes	10,000–33,000
Weak D phenotypes	<100–10,000
Exalted D phenotypes	75,000–200,000

Molecular basis of D antigen

See System pages.

Effect of enzymes and chemicals on D antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)

α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

***In vitro* characteristics of alloanti-D**

Immunoglobulin class	Most IgG, some IgM (IgA rare)
Optimal technique	IAT; enzymes
Complement binding	Extremely rarely

Clinical significance of alloanti-D

Transfusion reaction	Mild to severe/immediate or delayed
HDFN	Mild to severe

Autoanti-D

Yes	May appear as mimicking alloantibody

Partial D phenotypes: Qualitative variation of D

Tippett and Sanger studied the interactions of RBCs and serum from D+ people who had made anti-D. They observed a limited number of reaction patterns, and initially divided samples with partial D antigens into six categories (D^{I} to D^{VI}, which are now written without a superscript). The D antigen is a mosaic of different epitopes. People with RBCs lacking one or more of these epitopes (referred to as expressing a partial D antigen) can make alloanti-D directed at the missing D epitopes. Partial D phenotypes initially were classified into seven D categories (DI to DVII; DI later became obsolete) based on the interaction of the RBCs and sera of the D category members, and also by the reaction patterns with selected polyclonal anti-D. Low-prevalence marker antigens aided in their identification. Many other partial D were added later (e.g., DFR, DBT, DOL and DAU; see tables and figures in the Rh system pages). Monoclonal anti-D revealed different reaction patterns, and each reaction pattern recognizes a different epitope (epD) of the D mosaic. Seven reaction patterns were initially recognized and these were expanded to nine patterns with awareness that more epitopes would be identified.

Reactions with anti-D have shown that some partial D phenotypes have consistently strongly expressed D epitopes (e.g., DIII, DIVa), others have variable expression of the relevant epitopes, thereby demonstrating qualitative and quantitative alteration (e.g., DVa, DVII). Yet others have very weakly expressed epitopes (e.g., DVI Type 1, DAR) and these are referred to as "weak partial D phenotypes."

Epitope profiles of partial D antigens: The nine epitope model[1]

	Reactions with monoclonal anti-D							
	epD1	epD2	epD3	epD4	epD5	epD6/7	epD8	epD9
DII	+	+/0	+	0	+	+	+	0
DIIIa	+	+	+	+	+	+	+	+
DIIIb	+	+	+	+	+	+	+	+
DIIIc	+	+	+	+	+	+	+	+
DIVa	0	0	0	+	+	+	+	0
DIVb	0	0	0	0	+	+	+	0
DVa	0	+	+	+	0	+	+	+
DVI	0	0	+	+	0	0	0	+
DVII	+	+	+	+	+	+	0	+
DFR	+/0	+/0	+	+	+/0	+/0	0	+
DBT	0	0	0	0	0	+/0	+	0
DHAR	0	0	0	0	+/0	+/0	0	0

+= Positive; +/0 = Positive with some anti-D, negative with other anti-D; 0 = Negative.

Recognition of new partial D phenotypes and use of hundreds of monoclonal anti-D has sub-split the nine epitopes. The nine epitope model, which was directly related to the original D categories, was expanded to accommodate the new reaction patterns. Sub-splits of the patterns by reactions observed with new unique partial D are being denoted by a dot followed by a second Arabic number, e.g., the sub-split of epD1 was defined by reactions with DFR cells: anti-epD1.1 are positive and anti-epD1.2 are negative with DFR cells. New reaction patterns defined with monoclonal anti-D have been assigned numbers above 9 (see table). These patterns were defined through multi-center ISBT workshops for a standardized and logical approach.

Epitope profiles of partial D antigens: the expanded 30 epitope model[2]

Anti-epD	Partial D phenotype																	
	DII	DIII	DIVa	DIVb	DV1	DV2	DV3/4	DV5	DVI	DVII	DFR	DBT	DHAR	DHMi	DNB	DAR	DNU	DOL
1.1	+	+	0	0	0	0	0	0	0	+	+	0	0	+	+	V	V	V
1.2	+	+	0	0	0				0	+	0	0	0	+				
2.1	+	+	0	0	+	+	+	0	0	+	+	0	0	+	+	+	+	+
2.2	+	+	0	0	+	+	+	0	0	+	0	0	0	0	+	0	+	+
3.1	+	+	0	0	+	+	+	+	+	+	+	0	0	+	V	+	+	+
4.1	0	+	+	0	+	+	+	+	+	+	+	0	0	+	+	+	+	+
5.1	+	+	+	+	0	0	0	0	0	+	+	0	+	+	+	+	+	+
5.2	+	+	+	+	+	+	0	0	0	+	+	0	0	+	+	+	0	+
5.3	+	+	+	+	0	0	0	0	0	+	0	0	+	+	+	0	+	0
5.4	+	+	+	+	+	0	0	0	0	+	0	0	0	+	+	+	+	V
5.5	+	+	+	+	0				0	+	0	0	0	0				
6.1	+	+	+	+	+	+	+	+	0	+	+	+	+	+	+	+	+	+
6.2	+	+	+	+	+	+	+	+	0	+	+	+	0	+	+	+	+	+
6.3	+	+	+	+	+	+	+	+	0	+	+	0	0	+	+	+	+	+

(*Continued*)

6.4	+	+	+	+	+	+	+	+	0	+	0	+	+	+	+	+	+	+
6.5	+	+	+	+	+	+	+	+	0	+	0	+	0	+	+	+	+	+
6.6	+	+	+	+	+	+	+	+	0	+	0	0	+	+	+	+	+	V
6.7	+	+	+	+	+	+	0	0	0	+	0	0	0	V	+	+	+	+
6.8	+	+	+	+	+	+	+	+	0	+	0	0	0		+	+	+	+
8.1	+	+	+	+	+	+	+	+	0	0	0	0	0	V	+	0	0	+
8.2	+	+	+	+	+	+	+	+	0	0	0	+	0	V	+	+	+	+
8.3	+	+	+	+	+	+	0	0	0	0	0	+	0		0			
9.1	0	+	0	0	+	+	+	+	+	+	+	0	0	+	+	+	0	+
10.1	+	+	0	0	0				0	0	0	0	0	0				
11.1	+	+	+	+	0				0	0	0	0	0	0				
12.1	+	+	+	+	+				0	+	0	+	0	0				
13.1	+	+	+	0	+	+	+	+	0	+	+	0	0	0	+	+	+	+
14.1	+	+	+	0	+				0	+	+	0	0	+				
15.1	+	+	+	0	+	+	+	+	+	+	+	0	0	+	+	+	+	+
16.1	+	+	+	+	+				+	+	+	+	0	+				

Nomenclature of partial D recommended by International Society of Blood Transfusion Working Party on Red Cell Immunogenetics and Blood Group Terminology[2,3]

D category phenotypes retain the original numbering system, but the historical superscript Roman numeral is now on the line, e.g., D^{VI} is written DVI. Subtypes of D categories are denoted by Arabic numerals, e.g., DVI type 1, DVI type 2, etc. Other (and new) partial D will be denoted by up to four upper case letters, e.g., DBT, DAR, DNU, DOL. Overall weak expression of D will be referred to as weak D (see later)[2].

Selected Partial D Phenotypes[1,4–7]

Partial D phenotype	Associated haplotype	Approximate number of D antigen sites	Number of probands	Ethnic origin	Made anti-D
DII	Ce	3,200	One	Caucasians	Yes
DIIIa	ce G+	12,300	Many	Blacks	Yes
DIIIb	ce G–		Few	Blacks	Yes
DIIIc	Ce G+	26,900	Many	Caucasians	Yes
DIII type 4		33,250	Few	Caucasians	Yes
DIVa	ce, [(C)–]	9,300	Many	Blacks	Yes
DIVb	Ce, cE	4,000	Many	Caucasians, Japanese	Yes
DIV type 3	Ce	600	One	Caucasians	
DIV type 4	Ce		Several		
DVa	ce, Ce, cE	9,400	Many	Caucasians, Japanese, Blacks	Yes
DVI type 1	cE	300–1,000	Many	Caucasians	Yes
DVI type 2	Ce	1,600–2,900	Many	Caucasians, Japanese	Yes
DVI type 3	Ce	14,500	Few	Caucasians	Yes
DVI type 4	Ce		One	Caucasians	
DVII	Ce	3,600–8,400	Many	Caucasians	Yes
DFR	Ce>cE	5,300	Many	Caucasians	Yes

(*Continued*)

(Continued)

Partial D phenotype	Associated haplotype	Approximate number of D antigen sites	Number of probands	Ethnic origin	Made anti-D
DBT type 1	Ce>(C)(e) and ce	4,300	Several	Caucasians, Japanese, Blacks	Yes
DBT type 2	Ce		Several	Japanese	
DHAR (ceHAR)	c(e) G–		Many	Caucasians	Yes
DHMi	cE	2,400	Several	Caucasians	Yes
DNB	Ce	6,000	Many	European (1 in 292 in Swiss)	Yes
DNU	Ce	10,000	Few	Caucasians	
DOL	ce	4,700	Several	Blacks	Yes
DAR	ce		Many	Blacks	Yes
Weak D type 4.2.2	ce	1,650	Few	Caucasians	Yes
DCS1	cE	3,000	One	Caucasians	
DCS-2	cE	800	Several	Caucasians	
DTI	cE		One	Japanese	
DBS	cE or ce		One	Asians	
DAL			Several	Caucasians	
DFW	Ce		One	Caucasians	
DHO	Ce	1,300		Caucasians	
DHR	cE	3,800		Caucasians	
DMH	ce			Caucasians	Yes
DIM	cE	200	One	Caucasians	
Weak D type 15	cE	300	Few	Caucasians	Yes
DAU0	ce	15,000	Many	Blacks (Caucasians)	
DAU1	ce	2,100	Several	Blacks	
DAU2	ce	370	Several	Blacks	Yes
DAU3	ce	10,880	Many	Blacks	Yes

Some partial D phenotypes in this table are not yet associated with production of alloanti-D; such phenotypes are included here because of their similarity to known partial D phenotypes as determined by molecular analysis or by the D epitope profile.
For additional partial D phenotypes see the system pages.

Weak D phenotypes: Quantitative variation of D

The weak D phenotype is a quantitative, not a qualitative, polymorphism and therefore all D epitopes are present. This reduced D antigen expression is usually detected by the indirect antiglobulin test, although some weak D phenotypes are directly agglutinated by MAb anti-D. For the molecular bases of weak D phenotypes see tables and figures in the system pages.

The different types of weak D defined at the molecular level, in accordance with ISBT nomenclature, are referred to as "type" with Arabic numerals, e.g., weak D type 1.

For molecular bases on weak D phenotypes, see system pages.

The weak D phenotypes shown in the table were those initially defined[7], but their number has greatly increased, as may be seen from the tables in the system pages.

Weak D phenotype	Associated haplotype	Approximate number of D antigen sites
Type 1	Ce	1,300
Type 2	cE	500
Type 3	Ce	1,900
Type 4.0	ce	2,300
Type 4.1		3,800
Type 5	cE	300
Type 6	Ce	1,000
Type 7	Ce	2,400
Type 8	Ce	1,000
Type 9	cE	250
Type 10	cE, Ce (majority)	1,200
Type 11	ce	200
Type 12	Ce	100
Type 13	Ce	1,000
Type 14	cE	
Type 16	cE	250
Type 17		60
Type 21	Ce	5,200

In European populations weak D types 1, 2, and 3 predominate[8].

Clinically relevant information about the D antigen

D phenotype	Amino acid changes in RhD	D Expression	Tests used to detect D	In patient			In donor
				Can make anti-D through transfusion or pregnancy	RBC suitable for transfusion	RhIgG prophylaxis recommended	Can immunize D– recipient
D+	None	Normal	Direct agglutination	No	D+[†]	No	Yes
Partial D	Usually extracellular	Altered (some D epitopes present, some absent)	Direct agglutination or IAT[^]	Yes	D– or matched partial D phenotype	Yes	Yes
Weak partial D	Usually extracellular	Altered (some D epitopes present, some absent) weak or variable	Direct agglutination or IAT[^]	Yes	D– or matched weak partial D phenotype	Yes	Possible
Weak D	Usually transmembrane or intracellular	Normal but weak	IAT (Direct agglutination for some)	No	D+ (or D–)	No	Possible
D–	RhD absent	Absent	IAT	Yes	D–[^^]	Yes	No

[†]Although cross-match compatible D– RBCs can be safely transfused, these RBCs/components should be reserved for use to D– patients.
[^]Depending on reagent used.
[^^]When suitable D– RBC components are not available, e.g., when the patient has made multiple additional alloantibodies or in times of blood shortage, D+RBC components may be transfused until anti-D is made. The most suitable candidates for such a strategy are males or women unable to have children.

Rh

Comments

Expression of D may be weakened by a Ce, CE or (C)ce^{S} complex *in trans*. A Rhesus Similarity Index[6] was devised to characterize the extent of qualitative changes in aberrant D antigens. Based on D epitope density profiles ascertained by using FACS analysis with a panel of monoclonal anti-D, this quantitative method may aid in the discrimination of normal D from partial D and weak D.

References

[1] Tippett, P., et al., 1996. The Rh antigen D: partial D antigens and associated low incidence antigens. Vox Sang 70, 123–131.

[2] Scott, M., 2002. Section 1A: Rh serology. Coordinator's report. Transfus Clin Biol 9, 23–29.

[3] Storry, J.R., et al., 2011. International Society of Blood Transfusion Working Party on red cell immunogenetics and blood group terminology: Berlin report. Vox Sang 101, 77–82.

[4] Avent, N.D., Reid, M.E., 2000. The Rh blood group system: a review. Blood 95, 375–387.

[5] Müller, T.H., et al., 2001. PCR screening for common weak D types shows different distributions in three Central European populations. Transfusion 41, 45–52.

[6] Wagner, F.F., et al., 2000. Weak D alleles express distinct phenotypes. Blood 95, 2699–2708.

[7] Wagner, F.F., et al., 2002. The *DAU* allele cluster of the *RHD* gene. Blood 100, 306–311.

[8] Flegel, W.A., Wagner, F.F., 2002. Molecular biology of partial D and weak D: implications for blood bank practice. Clin Lab 48, 53–59.

C Antigen

Terminology

ISBT symbol (number)	RH2 (004002 or 4.2)
Obsolete name	rh′
History	Reported in 1941 when it was recognized that, in addition to D, the Rh system had four other common antigens. Named because "C" was the next available letter in the alphabet.

Occurrence

Caucasians	68%
Blacks	27%
Asians	93%

Antithetical antigen

c (**RH4**)

Expression

Cord RBCs	Expressed
Altered	See System pages for unusual Rh complexes

Molecular basis associated with C antigen

Amino acid	Ser103; requirements for expression of C antigen are not fully understood
Nucleotide	T at bp 307 in exon 2 of *RHCE*C*

See System pages for weak and partial C antigens.

Effect of enzymes and chemicals on C antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-C

Immunoglobulin class	IgG; IgM
Optimal technique	IAT; enzymes

Clinical significance of alloanti-C

Transfusion reaction	Mild to severe/immediate or delayed/hemoglobinuria
HDFN	Mild

Autoanti-C

Yes, may be mimicking alloantibody.

Comments

Anti-C is often found in antibody mixtures, especially with anti-G (see **RH12**) or anti-D (see **RH1**).
Apparent anti-C in Blacks may be anti-hr^B (see **RH31**).
Alloanti-C can be made by C+ individuals who express one of many partial C phenotypes such as (C)ce^S (r'^S), C^W+, C^X+, and D(C)(e)/ce phenotypes (see table "Molecular bases of RhCe phenotypes" in System pages).
C+RBCs express the G antigen (see **RH12**).
D(C)e RBCs carrying the low-prevalence antigen HOFM (**700050**) express C weakly.

E Antigen

Terminology

ISBT symbol (number)	RH3 (004003 or 4.3)
Obsolete name	rh″

History	Reported in 1943 and named after the next letter in the alphabet when it was realized that the antigen was part the Rh system.

Occurrence

Caucasians	29%
Blacks	22%
Asians	39%

Antithetical antigen

e (**RH5**)

Expression

Cord RBCs	Expressed
Altered	See System pages for unusual Rh complexes

Molecular basis associated with E antigen

Amino acid	Pro226; requirements for expression of E antigen are not fully understood
Nucleotide	C at bp 676 in exon 5 of *RHCE*E*

See System pages for weak and partial E antigens.

Effect of enzymes and chemicals on E antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-E

Immunoglobulin class	IgG and IgM
Optimal technique	RT; IAT; enzymes

Clinical significance of alloanti-E

Transfusion reaction	Mild to moderate/immediate or delayed/ hemoglobinuria
HDFN	Mild

Autoanti-E

Yes, may be mimicking alloantibody.

Comments

The E antigen is comprised of several epitopes as defined by monoclonal anti-E[1].
Anti-E is often present in sera containing anti-c.
Some examples of anti-E appear to be naturally-occurring.

Reference

[1] Noizat-Pirenne, F., et al., 1998. Heterogeneity of blood group RhE variants revealed by serological analysis and molecular alteration of the *RHCE* gene and transcript. Br J Haematol 103, 429–436.

c Antigen

Terminology

ISBT symbol (number)	RH4 (004004 or 4.4)
Obsolete names	hr′
History	Briefly reported in 1941 when it was recognized that, in addition to D, the Rh system had four other common antigens; named when the antithetical relationship to C was recognized.

Occurrence

Caucasians	80%
Blacks	98%
Asians	47%

Antithetical antigen

C (**RH2**)

Expression

Cord RBCs	Expressed
Altered	See System pages for unusual Rh complexes

Molecular basis associated with c antigen[1]

Amino acid	Pro103 (and Pro102[2]) requirements for expression of c antigen are not fully understood.

	RhD with a substitution of Ser103Pro expresses a weak c antigen.
Nucleotide	C at bp 307 in exon 2 of *RHCE*c*

See System pages for weak and partial c antigens.

Effect of enzymes and chemicals on c antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-c

Immunoglobulin class	Most IgG; some IgM
Optimal technique	IAT; enzymes

Clinical significance of alloanti-c

Transfusion reaction	Mild to severe/immediate or delayed/ hemoglobulinuria
HDFN	Mild to severe

Autoanti-c

Yes, may be mimicking alloantibody.

References

[1] Faas, B.H.W., et al., 2001. Partial expression of RHc on the RHD polypeptide. Transfusion 41, 1136–1142.

[2] Westhoff, C.M., et al., 2000. Evidence supporting the requirement for two proline residues for expression of the "c" antigen. Transfusion 40, 321–324.

e Antigen

Terminology

ISBT symbol (number)	RH5 (004005 or 4.5)
Obsolete name	hr″
History	Named in 1945 when its antithetical relationship to E was recognized.

Occurrence

Caucasians	98%
Blacks	98%
Asians	96%

Antithetical antigen

E (**RH3**)

Expression

Cord RBCs	Expressed
Altered	See System pages for unusual Rh complexes

See table for reactions of monoclonal anti-e with unusual Rh complexes.

Molecular basis associated with e antigen

Amino acid	Ala226; requirements for expression of e antigen are not fully understood
Nucleotide	G at bp 676 in exon 5 of *RHCE*e*

See System pages for weak and partial e antigens.

Effect of enzymes and chemicals on e antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-e

Immunoglobulin class	Most IgG; some IgM
Optimal technique	IAT; enzymes

Clinical significance of alloanti-e

Transfusion reaction	Mild to moderate/delayed/hemoglobinuria
HDFN	Rare, usually mild

Autoanti-e

Common

Comments

Alloanti-e-like antibodies may be made by people with e+ RBCs lacking some e epitopes. This occurs more frequently in Blacks than in Caucasians[1,2].
Many e variants, in people at risk of immunization against lacking Rhe epitopes, have been defined with monoclonal anti-e and molecular studies[3,4].
The e antigen *in cis* with C and C^W (e.g., DCC^We and CC^We) is also a partial antigen. This also applies in the presence of C and C^X.

Reaction of monoclonal anti-e with RBCs expressing e-variant phenotypes[4]

Phenotype	MS16	MS21	MS62/MS63	MS69	MS70
hr^S–, hr^B–, (ceMO)	W	W	0	0	0
hr^S– (ceAR)	+	+	0	W	+
hr^S– (ceEK)	+	+	+	+	+
hr^B– (ce^S) (ceVS, etc)	+	+	+	+	0
ce Cys16 (ce48C)	0	+	W	0	NT
CeRN^	W	0	0	W	0
RHCE*ceJAL	0	0	2+ to 3+	0	NT
ceCF	0	NT	3+	0	NT
ceSL	0	0	3+	NT	NT

^Previously referred to as $\overset{=N}{R}$.

References

[1] Chou, S.T., Westhoff, C.A., 2011. The role of molecular immunohematology in sickle cell disease. Transfus Apher Sci 44, 73–79.

[2] Issitt, P.D., 1991. An invited review: the Rh antigen e, its variants, and some closely related serological observations. Immunohematology 7, 29–36.

[3] Chou, S.T., Westhoff, C.M., 2010. The Rh and RhAG blood group systems. Immunohematology 26, 178–186.

[4] Noizat-Pirenne, F., et al., 2002. Rare RHCE phenotypes in black individuals of Afro-Caribbean origin: identification and transfusion safety. Blood 100, 4223–4231.

f Antigen

Terminology

ISBT symbol (number)	RH6 (004006 or 4.6)
Obsolete names	ce; hr
History	Reported in 1953 and named with the next letter of the alphabet when it was observed that c and e *in cis* were required for its expression.

Occurrence

Caucasians	65%
Blacks	92%
Asians	12%

Expression

Cord RBCs	Expressed
Altered	In some unusual Rh complexes, particularly in those with altered c and/or e expression

Molecular basis associated with f antigen

The f antigen is expressed on the Rhce protein, but the requirements for expression of the antigen are not understood.

Effect of enzymes and chemicals on f antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-f

Immunoglobulin class	Most IgG; some IgM
Optimal technique	RT; IAT; enzymes

Clinical significance of alloanti-f

Transfusion reaction	Mild/delayed/hemoglobinuria
HDFN	Mild

Autoanti-f

Yes

Comments

The f antigen is a compound antigen expressed on RBCs with c (**RH4**) and e (**RH5**) on the same protein (Rhce), e.g., on R_1r (DCe/ce), R_0R_0 (Dce/Dce) RBCs. The antigen is not expressed when c and e are on separate Rh proteins, e.g., on R_1R_2 (DCe/DcE) RBCs. The f antigen is expressed on RBCs of some people with the Dc− haplotype.

Anti-f is frequently a component of sera containing anti-c or anti-e, and can be made by people with partial c and e antigens. Anti-f is useful in distinguishing DCE/ce from DCe/cDE. Apparent anti-f in Blacks may be anti-hr^S (see **RH19**). Anti-f frequently fades *in vitro* and *in vivo*.

Ce Antigen

Terminology

ISBT symbol (number)	RH7 (004007 or 4.7)
Obsolete name	rh_i
History	Reported in 1958 when it was observed that C and e *in cis* were required for its expression.

Occurrence

Caucasians	68%
Blacks	27%
Asians	92%

Expression

Cord RBCs	Expressed

Molecular basis associated with Ce antigen

The Ce antigen is expressed on the RhCe protein, but the requirements for expression of the antigen are not understood.

Effect of enzymes and chemicals on Ce antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Ce

Immunoglobulin class	IgG more common than IgM
Optimal technique	IAT; enzymes

Clinical significance of alloanti-Ce

Transfusion reaction	Mild/delayed
HDFN	Mild

Comments

Ce is a compound antigen expressed on RBCs with C **(RH2)** and e **(RH5)** on the same protein (RhCe), e.g., on DCe/ce (R_1r) RBCs but not on DCE/ce (R_zr) RBCs.
Anti-Ce is usually found in sera containing anti-C. Apparent anti-Ce in a C+ Black may be anti-hr^B (see **RH31**).

C^W Antigen

Terminology

ISBT symbol (number)	RH8 (004008 or 4.8)
Obsolete names	Willis, rh^w
History	Reported in 1946 and named because of the association with C and "W" from "Willis," the first proband whose RBCs carried the antigen. For years C^W was thought to be antithetical to C. The weak C antigen on C^W+ RBCs is due to an altered expression of C rather than to "cross-reactivity" of anti-C^W.

Occurrence

Caucasians	2%
Blacks	1%
Finns	4%
Latvians	9%

Expression

Cord RBCs	Expressed
Altered	Weaker on DC^W–

See System pages for DC^W– phenotypes and unusual Rh complexes.

Molecular basis associated with C^W antigen[1]

Amino acid	Arg41
Nucleotide	G at bp 122 in exon 1 of *RHCE*
C^W– (wild type)	Gln41 and A at bp 122

Effect of enzymes and chemicals on C^W antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-C^W

Immunoglobulin class	IgG and IgM
Optimal technique	RT; IAT; enzymes

Clinical significance of alloanti-C^W

Transfusion reaction	Mild to severe; immediate/delayed
HDFN	Mild to moderate

Comments

Anti-C^W are often naturally-occurring and found in multispecific sera.
Most C^W+ are C+; rare examples are C–. C^W has been associated with D(C)C^We, D(C)C^WE, (C)C^We, (C)C^WE, DC^W– and C^{W}ce haplotypes.
Alloanti-C can be made by individuals with the C+C^W+ phenotypes.
The e antigen *in cis* with C and C^W (e.g. DCC^{W}e and CC^{W}e) is also a partial antigen.
There is an association between C^W (RH9) and MAR (RH51) antigens.

Reference

[1] Mouro, I., et al., 1995. Molecular basis of the RhC^W (Rh8) and RhC^X (Rh9) blood group specificities. Blood 86, 1196–1201.

C^X Antigen

Terminology

ISBT symbol (number)	RH9 (004009 or 4.9)
Obsolete name	rh^X
History	Reported in 1954 and named because of the association with C and "X," because X was the next letter in the alphabet after W and the antigen had characteristics similar to C^W. C^X was thought to be antithetical to C. The weak C antigen on C^X+ RBCs is due to an altered expression of C rather than to "cross-reactivity" of anti-C^X.

Occurrence

Less than 0.01%; more common in Finns.

Expression

Cord RBCs	Expressed

Molecular basis associated with C^X antigen[1]

Amino acid	Thr36 on RhCe and rarely Rhce
Nucleotide	A at bp 106 in exon 1 of *RHCE*
C^X– (wild type)	Ala36 and G at bp 106

Effect of enzymes and chemicals on C^X antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-C^X

Immunoglobulin class	IgG and IgM
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-C^X

Transfusion reaction	No to moderate; immediate/delayed
HDFN	Mild to moderate

Comments

Anti-C^X are often naturally-occurring and found in multispecific sera.
C^X+ are C+ except in the rare haplotype C^Xce^S V–VS+ found in Somalia.
C^X has been associated with D(C)C^Xe, (C)C^Xe, and C^Xce^S haplotypes.
Alloanti-C (and potentially alloanti-e) can be made by individuals with the C+C^X+ phenotypes.
There is an association between C^X (RH8) and MAR (RH51) antigens.

Reference

[1] Mouro, I., et al., 1995. Molecular basis of the RhC^W (Rh8) and RhC^X (Rh9) blood group specificities. Blood 86, 1196–1201.

V Antigen

Terminology

ISBT symbol (number)	RH10 (004010 or 4.10)
Obsolete names	ce^{s}; hr^{V}
History	Reported in 1955 and named after the first letter of the last name of the proband to make anti-V.

Occurrence

Caucasians	1%
Blacks	30%

Expression

Cord RBCs	Expressed

Molecular basis associated with V antigen[1]

The V antigen is associated with expression of VS antigen. For alleles encoding V see System pages.

Effect of enzymes and chemicals on V antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-V

Immunoglobulin class	IgG
Optimal technique	IAT; enzyme

Clinical significance of alloanti-V

Transfusion reaction	Mild/delayed
HDFN	No

Comments

Anti-V frequently occurs in multispecific sera, particularly in sera containing anti-D.
Most V+ RBCs are also VS+ (**RH20**).

Reference

[1] Daniels, G.L., et al., 1998. The VS and V blood group polymorphisms in Africans: a serological and molecular analysis. Transfusion 38, 951–958.

E^W Antigen

Terminology

ISBT symbol (number)	RH11 (004011 or 4.11)
Obsolete name	rh^{W2}
History	Reported in 1955 as the cause of HDFN, and named after the affected family.

Occurrence

Less than 0.01%; more common in people of German ancestry.

Expression

Cord RBCs	Expressed

Molecular basis associated with E^W antigen

Amino acid	Lys167
Nucleotide	A at bp 500 in exon 4 of *RHCE*CE*
E^W– (wild type)	Met167 and T at bp 500

Effect of enzymes and chemicals on E^W antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-E^W

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-E^W

HDFN	Yes

Comments

E^W has only been found associated with the DcE^W haplotype. The E associated with expression of E^W is a partial antigen (category EI) that is detected by some, but not all anti-E.
Anti-E^W is a rare specificity.

G Antigen

Terminology

ISBT symbol (number)	RH12 (004012 or 4.12)
Obsolete name	rh^G
History	Reported in 1958 when a donor's D–C– RBCs were agglutinated by most anti-CD; given the next available letter in the alphabet.

Occurrence

Caucasians	84%
Blacks	92%
Asians	100%

Expression

Cord RBCs	Expressed
Altered	Weak on r^G and r''^G RBCs

See System pages for unusual Rh complexes

Molecular basis associated with G antigen[1]

Amino acid	Ser103 on Rh proteins expressing C or D
G–	Pro103 usually associated with D– phenotype and rarely with D+ phenotype[2].
Nucleotide	T at bp 307 in exon 2 of *RHD* or *RHCE*C*

See System pages.

Effect of enzymes and chemicals on G antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-G

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-G

Transfusion reaction	No to severe/delayed
HDFN	No to severe

Comments

Anti-G is found as a component in sera from rr (ce/ce) people with anti-D (and/or anti-C), D+G– people with anti-C, and some DIIIb people with anti-D.

References

[1] Faas, B.H.W., et al., 1996. Involvement of Ser103 of the Rh polypeptides in G epitope formation. Transfusion 36, 506–511.

[2] Faas, B.H.W., et al., 2001. Partial expression of RHc on the RHD polypeptide. Transfusion 41, 1136–1142.

Hr_0 Antigen

Terminology

ISBT symbol (number)	RH17 (004017 or 4.17)
History	Anti-Hr_0 reported in 1958 and allocated Rh17 in 1962; defined by absorption/elution studies using sera from D−− probands. Hr_0 was considered to be a high-prevalence antigen expressed by all common Rh haplotypes.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed

Molecular basis of Hr_0 (Rh17)

See System pages.

Effect of enzymes and chemicals on Hr_0 (Rh17) antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (markedly enhanced)

α-Chymotrypsin	Resistant (markedly enhanced)
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-Hr_0 (Rh17)

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-Hr_0 (-Rh17)

Transfusion reaction	No to severe
HDFN	No to severe

Autoanti-Hr_0 (Rh17)

Antibody with broad Rh specificity in patients with AIHA previously also known as anti-pdl.

Comments

Selected anti-Rh17 may be used to distinguish Rh_{mod} from Rh_{null} phenotypes. Anti-Rh17 is made by individuals with the following phenotypes: D−−, D··, Dc−, DC^W-.

Hr_0 (Rh17) appears to be composed of several epitopes, some of which may be lacking on RBCs with unusual Rh haplotypes, including those with partial C or c and/or e expression. People with phenotypes that have altered C or c and/or e can make an alloantibody that is directed at the conventional RhCE protein and initially appears to be anti-Rh17. Such antibodies, upon further testing, can be shown to have a precise specificity [see CEST (**RH57**), CELO (**RH58**), CEAG (**RH59**)].

Hr Antigen

Terminology

ISBT symbol (number)	RH18 (004018 or 4.18)
Obsolete names	Hr^S; Shabalala
History	Reported in 1960; two antibodies were distinguished in the serum of Mrs. Shabalala, the Bantu proband. One of the antibodies, anti-Hr, was removed by absorption with R_2R_2 (DcE/DcE) RBCs leaving anti-hr^S.

Occurrence

Most populations	100%

Hr– only found in Blacks.

Molecular basis associated with Hr antigen[1]

See Rh System pages.

Clinical significance of alloanti-Hr

Transfusion reaction	No to fatal
HDFN	Moderate[2]

Comments

Hr antigen is present on all RBCs except hr^{S}–, Rh_{null}, and RhCE-depleted phenotypes.
Anti-Hr is made by hr^{S}– people, and may be part of the immune response of people whose RBCs have Rh-depleted phenotypes. Several alleles encode the Hr– phenotype; see System pages.

References

[1] Noizat-Pirenne, F., et al., 2002. Rare RHCE phenotypes in black individuals of Afro-Caribbean origin: identification and transfusion safety. Blood 100, 4223–4231.
[2] Moores, P., 1994. Rh18 and hrS blood groups and antibodies. Vox Sang 66, 225–230.

hr^{S} Antigen

Terminology

ISBT symbol (number)	RH19 (004019 or 4.19)
Obsolete name	Shabalala
History	Reported in 1960. The name "hr" was from Wiener's terminology for e, and superscript "S" was from Shabalala, the e+ proband who made an apparent alloanti-e. See Rh18 (Hr).

Occurrence

All populations	98% (R_2R_2 RBCs lack hr^{S})

RBCs of approximately 1% of Blacks are hr^{S}– as 1% of e+ Bantu people are hr^{S}–.

Expression

Cord RBCs	Expressed
Altered	Reduced on $DC^{X}e$ and phenotypes with altered e antigens

Molecular basis associated with hr^{S} antigen[1]

See Rh System pages.

Effect of enzymes and chemicals on hr^S antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-hr^S

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-hr^S

Transfusion reaction	No to fatal if with anti-Rh18
HDFN	Little evidence to indicate that anti-hr^S in the absence of anti-Hr has caused HDFN

Comments

Anti-hr^S reacts preferentially with haplotypes containing ce, and on initial testing may be mistaken for anti-f (see **RH6**). Antibodies made by hr^S– people are not necessarily anti-hr^S and, unless tested with appropriate rare e variant cells, are more correctly called anti-e-like.
cE haplotypes do not express hr^S[2,3].

References

[1] Noizat-Pirenne, F., et al., 2002. Rare RHCE phenotypes in black individuals of Afro-Caribbean origin: identification and transfusion safety. Blood 100, 4223–4231.
[2] Issitt, P.D., 1991. An invited review: the Rh antigen e, its variants, and some closely related serological observations. Immunohematology 7, 29–36.
[3] Moores, P., 1994. Rh18 and hrS blood groups and antibodies. Vox Sang 66, 225–230.

VS Antigen

Terminology

ISBT symbol (number)	RH20 (004020 or 4.20)
Obsolete name	e^s
History	Reported in 1960 and named after the initials of the first lady to make the antibody; the initial of her first name was used because of the association with the V antigen.

Occurrence

Blacks	26% to 40%
Other populations	<0.01%

Expression

Cord RBCs	Expressed
Altered	D(C)(e^S) FPTT+[1]; DC^We/Dce^S (1 example, Inkelberger); Dce^S/DCe (1 example, Manday), and see System pages

Molecular basis associated with VS antigen[2]

Amino acid	Val245 in Rhce (several different alleles)
Nucleotide	G at bp 733 in exon 5 of *RHCE*
VS– (wild type)	Leu245 and C at bp 733

For RHCE*ceVS alleles expressing VS with or without V, see System pages.

Effect of enzymes and chemicals on VS antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-VS

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-VS

Transfusion reaction	Mild/delayed
HDFN	Positive DAT; no clinical HDFN

Comments

Anti-VS is often a component of sera with other specificities. Anti-VS are heterogeneous and may be naturally-occurring.

The majority of V+ RBCs are VS+ (**RH:20**). The majority of apparent hr^B– (**RH:–31**) RBCs are VS+[3].

References

[1] Bizot, M., et al., 1988. An antiserum identifying a red cell determinant expressed by Rh:33 and by some "new" depressed Rh phenotypes. Transfusion 28, 342–345.

[2] Daniels, G.L., et al., 1998. The VS and V blood group polymorphisms in Africans: a serological and molecular analysis. Transfusion 38, 951–958.

[3] Pham, B.N., et al., 2009. Heterogeneous molecular background of the weak C, VS+, hr B−, Hr B− phenotype in black persons. Transfusion 49, 495–504.

C^G Antigen

Terminology

ISBT symbol (number)	RH21 (004021 or 4.21)
History	Reported in 1961; considered to be the weak C antigen found on r^Gr^G and r^Gr RBCs. C^G is also made by all cells expressing C.

Occurrence

Caucasians	68%

Comments

There is no monospecific anti-C^G, but a minority of anti-C are anti-CC^G. Some consider that the C made by r'^S is actually C^{G1}.

Reference

[1] Issitt, P.D., Anstee, D.J., 1998. Applied Blood Group Serology, fourth ed. Montgomery Scientific Publications, Durham, N.C.

CE Antigen

Terminology

ISBT symbol (number)	RH22 (004022 or 4.22)
Obsolete names	Jarvis
History	Reported in 1962 and named when it was observed that C and E *in cis* were required for its expression.

Occurrence

Less than 1% in most populations; 2% in Asians.

Expression

Cord RBCs	Expressed

Molecular basis associated with CE antigen

The CE antigen is expressed on the RhCE protein but the requirements for expression of CE are not understood.

Effect of enzymes and chemicals on CE antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-CE

Optimal technique	RT [Original anti-CE (Jarvis)]; 37°C

Clinical significance of alloanti-CE

No data are available because only two examples have been reported.

Comments

The two reported anti-CE appeared to be naturally-occurring, and were in sera that also contained anti-C.
This compound antigen is expressed on RBCs with C and E on the same protein (RhCE), e.g., on DCE (R_z) and CE (r^y) haplotypes.

D^W Antigen

Terminology

ISBT symbol (number)	RH23 (004023 or 4.23)
Obsolete name	Weil
History	Reported in 1962, and named after the first proband whose RBCs had this low prevalence antigen; shown to be an Rh antigen in 1965 and was associated with DVa.

Occurrence

All populations	<0.01%

Expression

Cord RBCs	Expressed

Molecular basis associated with D^W antigen

Associated with the partial D antigen encoded by several types of *RHD*DV*, in which all or part of exon 5 of *RHD* is replaced by the same exon from *RHCE*[1]. See System pages.

Effect of enzymes and chemicals on D^W antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-D^W

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-D^W

HDFN	Moderate

Comments

Sera containing anti-D^W often contain anti-E.
Anti-D^W (anti-Rh23) is a rare specificity and has been found in multispecific sera. Some examples contain anti-Rh32, and these specificities are not separable. The molecular basis of the Rh haplotype in a person (NR) with D^W–, Rh32– RBCs that were agglutinated by one example of anti-Rh23/Rh32 is given in the system pages.

Reference

[1] Rouillac, C., et al., 1995. Transcript analysis of D category phenotypes predicts hybrid Rh D-CE-D proteins associated with alteration of D epitopes. Blood 85, 2937–2944.

Rh26 (c-like) Antigen

Terminology

ISBT symbol (number)	RH26 (004026 or 4.26)
Obsolete name	Deal
History	This variant of c was identified in 1964 when the serum of Mrs. Deal, considered to contain a potent anti-c, did not react with some c+ RBCs.

Occurrence

Expressed on the majority of c-positive RBCs.
The c+Rh26– phenotype has been found in Italians and Dutch.

Antithetical antigen

LOCR (**RH55**)

Molecular basis associated with Rh26 antigen[1]

Amino acid	Gly96 on Rhce
Nucleotide	G at bp 286 in exon 2 of *RHCE*ce*

Effect of enzymes and chemicals on Rh26 antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Rh26

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Rh26

No data are available.

Comments

One c– Rh26+ sample has been described. Rh26– RBCs have weak expression of f antigen.

Reference

[1] Faas, B.H.W., et al., 1997. Involvement of Gly96 in the formation of the Rh26 epitope. Transfusion 37, 1123–1130.

cE Antigen

Terminology

ISBT symbol (number)	RH27 (004027 or 4.27)
History	Reported in 1965 and named when it was observed that c and E *in cis* were required for its expression.

Occurrence

Caucasians	28%
Blacks	22%
Asians	38%

Molecular basis associated with cE antigen

The cE antigen is expressed on the RhcE protein, but the requirements for expression of cE are not understood.

Effect of enzymes and chemicals on cE antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-cE

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes
Complement binding	Yes (one example)

Comments

Few examples of anti-cE have been reported. Expressed on RBCs having c [**RH4**] and E [**RH3**] antigens on the same protein (RhcE) e.g., R_2r (DcE/ce), r″r (cE/ce). The antigen is not expressed when c and E occur on separate haplotypes (in *trans*), e.g., R_zr (DCE/ce).

hr^H Antigen

Terminology

ISBT symbol (number)	RH28 (004028 or 4.28)
History	Reported in 1964. The antigen hr^H, primarily studied among South African Blacks, may be present on some RBCs that type V–VS+. hr^H has a complex relationship with VS (**RH20**).

Occurrence

All populations	<0.01%.

Rh29 Antigen

Terminology

ISBT symbol (number)	RH29 (004029 or 4.29)
Obsolete name	Total Rh
History	Reported in 1961 and given the next available number. The only Rh29– RBCs are Rh_{null}, which were originally called −−−/−−− when the first proband, an Australian Aboriginal woman, was identified.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed

Molecular basis of Rh29 antigen

For molecular basis of Rh29– (Rh_{null}), see RH and RHAG System pages.

Effect of enzymes and chemicals on Rh29 antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant (markedly enhanced)
α-Chymotrypsin	Resistant (enhanced)
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-Rh29

Immunoglobulin class	IgG and IgM
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Rh29

Transfusion reaction	No data available but potentially capable
HDFN	No to severe

Autoanti-Rh29

Antibody in AIHA with broad Rh specificity may be anti-Rh29 (previously also known as anti-dl).

Comments

Anti-Rh29 is the immune response of some Rh_{null} individuals (both amorph and regulator type). Some anti-Rh29 react with Rh_{mod} cells.

Go^a Antigen

Terminology

ISBT symbol (number)	RH30 (004030 or 4.30)
Obsolete names	Gonzales; D^{Cor}
History	Named after Mrs. Gonzales, the first maker of anti-Go^a. Reported briefly in 1962, and more extensively in 1967 when Go^a was shown to be an Rh antigen. In 1968, Go^a was confirmed to be a marker for D category IV (DIVa). Before partial D phenotypes were categorized, DIVa was called D^{Cor}.

Occurrence

Blacks	2%

Expression

Cord RBCs	Expressed

Molecular basis associated with Go^a antigen

Go^a is associated with the partial D antigen of category DIVa. See System pages.

Effect of enzymes and chemicals on Go^a antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-Go^a

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Go^a

Transfusion reaction	Moderate/delayed
HDFN	Mild to severe

Comments

Go^a is also expressed on RBCs with the rare DIVa(C)− Rh33+Riv+FPTT+ complex.
Anti-Go^a may be immune, but are often in multispecific sera, frequently with anti-Rh32 (see **RH32**) and/or anti-Evans (**RH37**); these Rh specificities are not separable by absorption/elution.

hr^B Antigen

Terminology

ISBT symbol (number)	RH31 (004031 or 4.31)
Obsolete name	Bastiaan
History	Reported in 1972. Named "hr" from Wiener's terminology for e and "B" from Bastiaan, the first antibody producer. See Hr^B (**RH34**).

Occurrence

All populations	98% [R_2R_2 (DcE/DcE) RBCs lack hr^B]
Blacks	97%, which includes numerous partial e

Expression

Cord RBCs	Expressed
Altered	Reduced on phenotypes with weak e antigens. See System pages

Molecular basis associated with hr^B antigen[1]

See System pages.

Effect of enzymes and chemicals on hr^B antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-hr^B

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-hr^B

Transfusion reaction	Generally not clinically significant, but precise information is limited because anti-e-like antibodies are often incorrectly called anti-hr^B. However, the immune response of some hr^B– people may broaden to the clinically significant anti-Hr^B (**RH34**).
HDFN	Positive DAT; no clinical HDFN

Autoanti-hr^B

Yes, rare (often with transient suppression of antigen). Investigation of DNA from patients with apparent autoanti-hr^B has revealed the presence of partial e phenotypes, and suggests that some autoantibodies are alloantibodies.

Comments

cE haplotypes do not express hr^B. The majority of apparent e+ hr^B– RBCs are VS+[2].
Anti-hr^B can be mistaken for anti-Ce (see **RH7**).
The molecular basis of the hr^B– phenotype is heterogeneous, as are the anti-hr^B and e-like antibodies made by people with the hr^B– phenoytype[1,3]. The fine specificity can often be determined by RH DNA typing of the patient, and testing the patient's plasma against RBCs characterized at the DNA level. Due to

limited availability of correctly characterized antibodies and RBC samples, prior to the use of RH DNA analysis many samples could only be partially characterized, and were (appropriately) labeled as anti-e-like.

References

[1] Pham, B.N., et al., 2009a. Heterogeneous molecular background of the weak C, VS+, hr B−, Hr B− phenotype in black persons. Transfusion 49, 495–504.

[2] Beal, C.L., et al., 1996. The *r′* gene is overrepresented in hr^B-negative individuals. Immunohematology 11, 74–77.

[3] Pham, B.N., et al., 2009b. Anti-Hr^B and anti-hr^b revisited. Transfusion 49, 2400–2405.

Rh32 Antigen

Terminology

ISBT symbol (number)	RH32 (004032 or 4.32)
Obsolete names	$\overset{=N}{R}$
History	Reported in 1971 after several years of investigation and was assigned the next Rh number in 1972. Incorrectly called $\overset{=N}{R}$, which is the name of the original (1960) haplotype with weak C and e antigens later shown to express Rh32. $\overset{=N}{R}$ is now referred to as R^N.

Occurrence

Blacks	1% ($\overset{=N}{R}$ phenotype)
Caucasians and Japanese	Rare (associated with the DBT partial D phenotype)

Antithetical antigen

Sec (**RH46**)

Expression

Cord RBCs	Expressed
Altered	May be slightly weaker on DBT phenotype RBCs and other rare variants

Molecular basis associated with Rh32 antigen[1,2]

R^N (formerly $\overset{=N}{R}$) phenotype: *RHCE*ceRN* hybrid in which exon 4 of *RHCE* is replaced by the corresponding exon of *RHD* [with or without nt 445C>A in exon 3 (Thr152Asn)].

Partial D phenotype *RHD*DBT* hybrid in which either exons 5 to 7 or exons 5 to 9 of *RHD* are replaced by the corresponding exons of *RHCE*.
See System pages.

Effect of enzymes and chemicals on Rh32 antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-Rh32

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Rh32

Transfusion reaction	None reported
HDFN	Mild to severe

Comments

*RHCE*ceRN* encodes Rh32 in combination with weakened expression of C (**RH2**) and e (**RH5**) antigens, and may be associated with normal or elevated expression of D antigen (**RH1**). It may be necessary to use sensitive techniques to detect the C antigen on some RBCs.
The RBCs of one proband with the DBT phenotype had weakened expression of C and e; another proband had weakened expression of C only.
Anti-Rh32 may be immune, but are often naturally-occurring in multispecific sera. Anti-Rh32 cannot be separated from anti-Go^{a} (see **RH30**) or anti-Evans (see **RH37**) by absorption/elution of sera containing these antibodies.

References

[1] Beckers, E.A.M., et al., 1996. The genetic basis of a new partial D antigen: D^{DBT}. Br J Haematol 93, 720–727.
[2] Rouillac, C., et al., 1996. Molecular basis of the altered antigenic expression of RhD in weak D (D^{u}) and RhC/e in R^{N} phenotypes. Blood 87, 4853–4861.

Rh33 Antigen

Terminology

ISBT symbol (number)	RH33 (004033 or 4.33)
Obsolete names	Har; R_0^{Har}; D^{Har}

History	Reported in 1971 and given the next Rh number. Although the complex expressing Rh33 was first detected on RBCs from a German donor, the complex was named R_0^{Har} after the name of an English donor with an informative family.

Occurrence

Less than 0.01%; Rh33 is more common in people of German ancestry.

Expression

Cord RBCs	Presumed expressed
Altered	R_1^{Lisa1}

Molecular basis associated with Rh33 antigen

Encoded by *RHCE*ceHAR*, an RHCE*ce allele in which exon 5 is replaced by exon 5 of *RHD*[2]. *RHCE*CeVA*, also a hybrid gene with exon 5 originating from *RHD*, encodes Rh33 and weak C and e antigens. *RHCE*CeVA* may be the allele encoding R_1^{Lisa}[3].
See System pages.

Effect of enzymes and chemicals on Rh33 antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Rh33

Immunoglobulin class	IgM
Optimal technique	RT; enzymes

Clinical significance of alloanti-Rh33

No data are available.

Comments

*RHCE*ceHAR* encodes a partial D antigen, normal c (**RH4**), weak e (**RH5**), weak f (**RH6**), and weak Hr_0 (**RH17**) antigens; it does not encode C (**RH2**), E (**RH3**), G (**RH12**), hr^S (**RH19**) or Hr (**RH18**) antigens.
Rh33 is also expressed by the rare complexes DIVa(C)−, R_0^{JOH} and R_1^{Lisa}. All Rh33+ RBCs also express the low prevalence antigen FPTT (**RH50**).

Anti-Rh33 is a rare specificity. Two examples were in serum also containing anti-D.

References

[1] Moores, P., et al., 1991. Rh33 in two of three German siblings with D+ C+ c+ E− e+red cells. Transfusion 31, 759–761.
[2] Beckers, E.A.M., et al., 1996. The R_0^{Har}Rh:33 phenotype results from substitution of exon 5 of the *RHCE* gene by the corresponding exon of the *RHD* gene. Br J Haematol 92, 751–757.
[3] Noizat-Pirenne, F., et al., 2002. Molecular background of *D*(*C*)(*e*) haplotypes within the white population. Transfusion 42, 627–633.

Hr^B Antigen

Terminology

ISBT symbol (number)	RH34 (004034 or 4.34)
Obsolete names	Bas; Baas; Bastiaan; Rh34
History	Reported in 1972. Anti-Hr^B initially described the total immune response of Mrs. Bastiaan (hence "B" in the name), a South African. Later, absorptions showed her serum contained two specificities: anti-hr^B (see **RH31**) and an antibody reacting with RBCs of all common phenotypes that was called anti-Hr^{B1}.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed

Molecular basis associated with Hr^B antigen

See Rh System pages for molecular basis of Hr^B– phenotypes.

Effect of enzymes and chemicals on Hr^B antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Hr^B

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-Hr^B

Transfusion reaction	No data available, presumed to be significant because of similarity to anti-RH18
HDFN	Positive DAT but no clinical HDFN[1]

Comments

Weak examples of anti-Hr^B resemble anti-C (see **RH3**) in that C+ RBCs give the strongest reactions; c+ RBCs give intermediate strength reactions; and DcE/DcE (R_2R_2) cells give the weakest reactions. Several alleles encode the Hr^B– phenotype; see System pages.

There was debate as to whether anti-Hr^B and anti-hr^B were separate specificities or two aspects of a single specificity. Anti-Hr^B and anti-hr^B are indeed separate specificities[2,3].

References

[1] Moores, P., Smart, E., 1991. Serology and genetics of the red blood cell factor Rh34. Vox Sang 61, 122–129.

[2] Pham, B.N., et al., 2009a. Anti-Hr^B and anti-hr^b revisited. Transfusion 49, 2400–2405.

[3] Pham, B.N., et al., 2009b. Heterogeneous molecular background of the weak C, VS+, hr B−, Hr B- phenotype in black persons. Transfusion 49, 495–504.

Rh35 Antigen

Terminology

ISBT symbol (number)	RH35 (004035 or 4.35)
Obsolete name	1114
History	Reported in 1971. Rh35 is produced by an Rh complex that produces weak C and e antigens and normal D antigen.

Occurrence

Less than 0.01%; Rh35 was originally found in people of Danish ancestry.

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with Rh35 antigen

For the molecular basis of a phenotype with weak C and e expression (CeMA), which may be Rh35+, see System pages.

Effect of enzymes and chemicals on Rh35 antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Rh35

Immunoglobulin class	IgG
Optimal technique	Enzymes

Clinical significance of alloanti-Rh35

No data available because only one example of the antibody has been reported.

Be^a Antigen

Terminology

ISBT symbol (number)	RH36 (004036 or 4.36)
Obsolete name	Berrens
History	Reported in 1953, and named after the family in which HDFN occurred. Be^a is produced by a complex that produces weak c, e, and f antigens, and no D antigen. Family studies in 1974 confirmed it as an Rh antigen.

Occurrence

All populations	<0.1%.

Propositi were of German/Polish extraction from the Baltic region.

Expression

Cord RBCs	Expressed

Molecular basis associated with Be^a antigen[1]

Amino acid	Arg221 in Rhce
Nucleotide	G at bp 662 in exon 5 of *RHCE*ce*
Be(a–) (wild type)	Pro221 and C at bp 662

Effect of enzymes and chemicals on Be^a antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-Be^a

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Be^a

Transfusion reaction	None reported
HDFN	Moderate to severe

Comments

Anti-Be^a is immune. Be^a appears to be highly immunogenic: the primary stimulus for production of anti-Be^a in 2 non-transfused women occurred during their first pregnancy and in each case the child of the second pregnancy had severe HDFN[1].

Reference

[1] Hue-Roye, K., et al., 2010. The low prevalence Rh antigen Be^a (Rh36) is associated with *RHCE*ce* 662C>G in exon 5, which is predicted to encode Rhce 221Arg. Vox Sang 98, e263–e268.

Evans Antigen

Terminology

ISBT symbol (number)	RH37 (004037 or 4.37)
History	Evans, identified in 1968, was named after the family in which HDFN occurred. Evans segregated with a D−− like complex (D··) in the family of the second Evans+ proband. Family studies, reported in 1978, confirmed Evans as an Rh antigen.

Occurrence

Less than 0.01%; may be more common in Welsh and Scots.

Expression

Cord RBCs	Expressed
Altered	Weak on DIVb RBCs

Molecular basis associated with Evans antigen[1,2]

Dav	*RHD*(*1–6*)-*RHCE*(*7–10*)//*RHD*
JD	*RHD*(*1–5 and part 6*)-*RHCE*(*part 6 and 6–10*)// *RHCE*(*1*)-*RHD*(*2–10*)
AT	*RHCE*(*1*)-*RHD*(*2–6*)-*RHCE*(*7–10*)//*RHD*
DIVb	*RHCE*//*RHD*(*1–6 and part of 7*)-*RHCE*(*part of 7–9*)-*RHD10*

RhD-CE-D hybrids with different proportions of RhCE into RhD. See System pages.

Effect of enzymes and chemicals on Evans antigen on intact RBCs

Ficin/Papain	Resistant (markedly enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant
Acid	Presumed resistant

In vitro characteristics of alloanti-Evans

Immunoglobulin class	IgM less common than IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Evans

Transfusion reaction	None reported
HDFN	Mild and moderate

Comments

The Rh complex D·· produces Evans antigen, elevated expression of D, normal expression of G, the high prevalence antigens Rh29 and Dav; C, c, E, and e antigens are not produced. However, a preliminary study suggested that RBCs from JD express a minute amount of e[3].

Anti-Evans may be naturally-occurring, and is often found in multispecific sera. Anti-Evans cannot be separated from anti-Go^a (see **RH30**) or anti-Rh32 (see **RH32**) by absorption/elution of sera containing these antibodies.

References

[1] Avent, N.D., Reid, M.E., 2000. The Rh blood group system: a review. Blood 95, 375–387.

[2] Huang, C.-H., et al., 2000. Molecular biology and genetics of the Rh blood group system. Semin Hematol 37, 150–165.

[3] Lomas-Francis, C., et al., 2011. Surprising findings with RBCs expressing the low prevalence RH antigen Evans [abstract]. Transfusion 51 (Suppl.), 35A–36A.

Rh39 Antigen

Terminology

ISBT symbol (number)	RH39 (004039 or 4.39)
Obsolete name	C-like
History	Reported in 1979. Anti-Rh39 reacts more strongly with C+ than C– RBCs, and can be absorbed to exhaustion by all C+ and C– RBCs with common and uncommon Rh phenotypes except Rh_{null}.

Occurrence

All populations	100%

Autoanti-Rh39

Yes, always; made by some C– people.

Comments

One patient with this "mimicking" anti-C antibody proceeded to make alloanti-C.

Tar Antigen

Terminology

ISBT symbol (number)	RH40 (004040 or 4.40)
Obsolete name	Targett
History	Reported in 1975, and named after the proband whose RBCs expressed the antigen. When family studies in 1979 showed Tar to be an Rh antigen, it was awarded an Rh number. In 1986, Tar was established as a marker for the DVII partial D antigen.

Occurrence

All populations	<0.01%.

Expression

Cord RBCs	Expressed

Molecular basis associated with Tar antigen[1]

Amino acid	Pro110
Nucleotide	C at bp 329 in exon 2 of *RHD*
Tar– (wild type RhD)	Leu110 and T at bp 329

Effect of enzymes and chemicals on Tar antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Resistant

In vitro characteristics of alloanti-Tar

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Tar

HDFN	Moderate

Comments

In addition to the association with DVII *in cis* to Ce, Tar is expressed on a variant RhD protein that also expresses weak c[2]. Tar also was found on a D− − like complex, which produced weaker than usual D antigen.
Anti-Tar is a rare specificity; the antibody has been produced through pregnancy and has been found without known stimulus.

References

[1] Rouillac, C., et al., 1995. Leu110Pro substitution in the RhD polypeptide is responsible for the D^{VII} category blood group phenotype. Am J Hematol 49, 87–88.
[2] Faas, B.H.W., et al., 2001. Partial expression of RHc on the RHD polypeptide. Transfusion 41, 1136–1142.

Rh41 Antigen

Terminology

ISBT symbol (number)	RH41 (004041 or 4.41)
Obsolete name	Ce-like

History	Reported in 1981 and given the next Rh number in 1990. The only example of anti-Rh41 reacted with RBCs that have C and e in the same haplotype. However, unlike anti-Ce, anti-Rh41 reacts with r'^{S} (C)ce^{S} RBCs, and does not react with C^{W} and e *in cis*[1].

Occurrence

Caucasians	70%

Expression

Cord RBCs	Presumed expressed

Reference

[1] Svoboda, R.K., et al., 1981. Anti-Rh41, a new Rh antibody found in association with an abnormal expression of chromosome 1 genetic markers. Transfusion 21, 150–156.

Rh42 Antigen

Terminology

ISBT symbol (number)	RH42 (004042 or 4.42)
Obsolete names	Ce^{S}; Cce^{S}; rh^{S}; Thornton
History	Reported in 1980. It is a marker for the Cce^{S} V– VS+ haplotype.

Occurrence

Caucasians	<0.1%
Blacks	2%

Expression

Cord RBCs	Expressed

Molecular basis associated with Rh42 antigen

Encoded by the RHD*DIIIa-CE(4–7)-D hybrid allele that encodes the type 1 but not the type 2 (C)ce^{S} (r'^{S}) haplotype[1]. See System pages.

Effect of enzymes and chemicals on Rh42 antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)

In vitro characteristics of alloanti-Rh42

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Rh42

Transfusion reaction	None reported
HDFN	Moderate

Comments

At least two examples of anti-Rh42 have been reported.

Reference

[1] Pham, B.N., et al., 2009. Heterogeneous molecular background of the weak C, VS+, hr B−, Hr B− phenotype in black persons. Transfusion 49, 495–504.

Crawford Antigen

Terminology

ISBT symbol (number)	RH43 (004043 or 4.43)
History	Reported in 1980, the only example of anti-Crawford was found in a reagent anti-D.

Occurrence

Blacks	0.1%

Expression

Cord RBCs	Expressed

Antithetical antigen

CELO (**RH58**)

Molecular basis associated with Crawford antigen[1]

Amino acids	16Cys, 233Glu, 245Val in Rhce
Nucleotides	C at bp 48, G at bp 697, and G at bp 733 in *RHCE*ce*

See System pages.

Effect of enzymes and chemicals on Crawford antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)

In vitro characteristics of alloanti-Crawford

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Comment

Crawford is encoded by an RHCE allele (*RHCE*ceCF*) that also encodes some D-specific amino acids. These D-specific amino acids are recognized by several potent MAb anti-D and (D−) Crawford+ RBCs have been erroneously typed as D+.

Reference

[1] Flegel, W.A., et al., 2006. The RHCE allele ceCF: the molecular basis of Crawford (RH43). Transfusion 46, 1334–1342.

Nou Antigen

Terminology

ISBT symbol (number)	RH44 (004044 or 4.44)
History	The antigen was reported in 1969 and named after Mme Nou, from the Ivory Coast, who was homozygous for *DIVa*(*C*)−. Anti-Nou, reported in 1981, is a component of some anti-Hr_0 (see **RH17**) sera and can be separated by adsorption/elution with DIVa(C)−/DIVa(C)− cells; the antibody does not react with Rh_{null}, D−−, D··, DC^W− or Dc− cells.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed

Effect of enzymes and chemicals on Nou antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)

Riv Antigen

Terminology

ISBT symbol (number)	RH45 (004045 or 4.45)
History	Reported in 1983 and named for the Puerto Rican family in which the antigen and antibody were identified.

Occurrence

Six Riv+ probands are known.

Expression

Cord RBCs	Expressed

Molecular basis of Riv antigen[1]

Associated with a *RHCE*CE–DIVa(2–3)–CE–D(5)–CE* hybrid allele encoding a complex hybrid RhD-RhCE protein. See System pages "Rearranged *RHD* and *RHCE*."

Effect of enzymes and chemicals on Riv antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Riv

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Riv

HDFN	Mild; caused by the only example of anti-Riv in a serum which also contained anti-Go^a (see **RH30**)[2]

Comments

The Riv antigen is expressed by the rare Rh complex DIVa(C)–; this complex (which also expresses Go^a (**RH30**), Rh33 (**RH33**), FPTT (**RH50**), the D antigen (**RH1**) characteristic of category DIVa, G (**RH12**), Nou (**RH44**), and

very weak C (**RH2**), but no c (**RH4**), E (**RH3**), e (**RH5**) or f (**RH6**) antigen), was shown to be encoded by *RHD*DIVa in cis* to an *RHCE*CE–DIVa(2–3)–CE–D(5)–CE* hybrid allele.

References

[1] Halter Hipsky, C., et al., 2011. Molecular basis of the rare gene complex, *DIV(C)–*, which encodes four low prevalence antigens in the Rh blood group system. Vox Sang (epub.).

[2] Delehanty, C.L., et al., 1983. Riv: a new low incidence Rh antigen [abstract]. Transfusion 23, 410.

Sec Antigen

Terminology

ISBT symbol (number)	RH46 (004046 or 4.46)
History	Described in 1989, given an Rh number in 1990, named after the first antibody producer.

Occurrence

All populations	100%

Antithetical antigen

Rh32 (**RH32**)

Expression

Cord RBCs	Expressed

Molecular basis associated with the Sec (RH46) antigen

See System pages.

Effect of enzymes and chemicals on Sec (RH46) antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-Sec (-RH46)

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-Sec (-RH46)

HDFN	No to severe

Comments

Immunized D(C)(e)/D(C)(e) people, homozygous for Rh32 and RH:−46, make anti-Sec.
Sec is expressed by RBCs of common Rh phenotype but is absent from Rh_{null} RBCs and not expressed by the following haplotypes: R^N, D−−, Dc−, DC^W-, and D··.

Dav Antigen

Terminology

ISBT symbol (number)	RH47 (004047 or 4.47)
History	Reported in 1982 and named after the first donor with D·· RBCs. Anti-Dav is a component of some anti-Hr_0 (see **RH17**) sera, and can be separated by adsorption/elution with D··/D·· cells.

Occurrence

All populations	100%

Expression

Cord RBCs	Expressed

Effect of enzymes and chemicals on Dav antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)

Comments

Anti-Dav reacts with cells of all common Rh phenotypes and with D·· cells, but not with Rh_{null}, DIVa(C)−, D−−, DC^W- and Dc− cells.

JAL Antigen

Terminology

ISBT symbol (number)	RH48 (004048 or 4.48)
Obsolete names	S.Allen; J.Allen
History	Reported and numbered in 1990 after more than a decade of using the Allen serum; named after J. Allen, whose RBCs possessed the antigen.

Occurrence

Less than 0.01%; found in English, French-speaking Swiss, Brazilians, and Blacks.

Antithetical antigen

CEST (**RH57**)

Expression

Cord RBCs	Expressed

Molecular basis of JAL antigen[1,2]

Amino acids	Trp114 and Val245 or Gln114 in Rhce in Blacks Trp114 in RhCe in Caucasians
Nucleotides	T at bp 340 and G at bp 733 or A at bp 341 in *RHCE*ce* in Blacks T at bp 340 in *RHCE*Ce* in Caucasians

Effect of enzymes and chemicals on JAL antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-JAL

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-JAL

HDFN	Positive DAT, no clinical HDFN

Comments

The JAL antigen is encoded by two different RH alleles: in Blacks JAL is associated with weak expression of c antigen (**RH4**) on Rhce while in Caucasians JAL is associated with a weak C antigen (**RH2**) on RhCe. JAL is variably associated with weak e (**RH5**) expression. Expression of JAL on RhCe appears to be stronger than JAL expressed on Rhce[1]. Three examples of anti-JAL are reported: only one is monospecific[3,4].

References

[1] Hustinx, H., et al., 2009. Molecular basis of the Rh antigen RH48 (JAL). Vox Sang 96, 234–239.
[2] Westhoff, C., et al., 2009. The JAL Antigen (RH48) is the result of a change in RHCE that encodes Arg114Trp. Transfusion 49, 725–732.
[3] Lomas, C., et al., 1990. A low-incidence red cell antigen JAL associated with two unusual Rh gene complexes. Vox Sang 59, 39–43.
[4] Poole, J., et al., 1990. The red cell antigen JAL in the Swiss population: family studies showing that JAL is an Rh antigen (RH48). Vox Sang 59, 44–47.

STEM Antigen

Terminology

ISBT symbol (number)	RH49 (004049 or 4.49)
Obsolete name	Stemper
History	Reported in 1993 (Rh number was assigned at the 1992 ISBT meeting), and named after the Black family in which the antibody/antigen was first identified.

Occurrence

Indians (in South Africa)	0.4%
Blacks	6%

Expression

Cord RBCs	Expressed
Altered	Variable expression among STEM+[1]

Molecular basis of STEM antigen[2]

Amino acid	Cys16, Val238, Val273, Val378 in Rhce (RhceBI) Cys16, Val238, Val273 in Rhce (RhceSM)
Nucleotide	C at bp 48, G at 712, T at 818, G at 1132 in *RHCE*ce* (*RHCE*ceBI*) C at bp 48, G at 712, T at 818 in *RHCE*ce* (*RHCE*ceSM*)
STEM– (wild type)	Trp16, Met238, Val273, (with Leu 378 for ceBI) and G at bp 48, A at 712, C at 818 (with C at 1132 for ceBI)

Effect of enzymes and chemicals on STEM antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)

Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-STEM

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-STEM

HDFN	Mild

Comments

STEM may be associated with Dce haplotypes that do not produce hr^S (**RH19**)[1]. Approximately 65% of hr^S–Hr– RBCs and 30% of hr^B–Hr^B– RBCs are STEM+.

References

[1] Marais, I., et al., 1993. STEM, a new low-frequency Rh antigen associated with the e− variant phenotypes hr^S-(Rh: −18, −19) and hr^B-(Rh: −31, −34). Transf Med 3, 35–41.

[2] Halter-Hipsky, C., et al., 2009. Two alleles with RHCE*nt818C>T change encode the low prevalence Rh antigen STEM [abstract]. Blood 114 (Suppl.), 1226–1227.

FPTT Antigen

Terminology

ISBT symbol (number)	RH50 (004050 or 4.50)
Obsolete names	700048; Mol
History	Reported in 1988 and named after the "French Post Telegraph and Telecommunication" because several of the original probands worked and donated blood there. Achieved Rh antigen status in 1994.

Occurrence

All populations	<0.01%

Expression

Cord RBCs	Expressed
Altered	Strength varies with type of FPTT+ Rh complex

Molecular basis associated with FPTT antigen[1–3]

In the partial D phenotype DFR, FPTT is associated with a hybrid *RH*(*D–CE–D*) gene in which part of exon 4 of *RHD* is replaced by the same part of exon 4 of *RHCE*.
FPTT is also associated with a hybrid *RHCE*ce*, in which exon 5 of *RHCE* is replaced by exon 5 of *RHD*. See System pages.

Effect of enzymes and chemicals on FPTT antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-FPTT

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-FPTT

No data are available.

Comments

FPTT antigen is also associated with rare "depressed" Rh phenotypes that have depressed C (**RH2**) and/or e (**RH5**) antigens (one family had weakened expression of VS antigen [**RH20**])[4].
The rare haplotype DIVa(C)− is FPTT+. All Rh33+ RBCs are FPTT+, but not all FPTT+ are Rh33+.
The only reported example of anti-FPTT was in a multispecific serum (Mol.) from a woman who had not been transfused or pregnant.

References

[1] Beckers, E.A.M., et al., 1996. The R_0^{Har}Rh:33 phenotype results from substitution of exon 5 of the *RHCE* gene by the corresponding exon of the *RHD* gene. Br J Haematol 92, 751–757.
[2] Noizat-Pirenne, F., et al., 2002. Molecular background of *D*(*C*)(*e*) haplotypes within the white population. Transfusion 42, 627–633.
[3] Rouillac, C., et al., 1995. Transcript analysis of D category phenotypes predicts hybrid Rh D–CE–D proteins associated with alteration of D epitopes. Blood 85, 2937–2944.
[4] Bizot, M., et al., 1988. An antiserum identifying a red cell determinant expressed by Rh:33 and by some "new" depressed Rh phenotypes. Transfusion 28, 342–345.

MAR Antigen

Terminology

ISBT symbol (number)	RH51 (004051 or 4.51)
History	Reported in 1994 and named after the first antibody producer, a Finnish woman with C^W+, C^X+ RBCs.

Occurrence

All populations	100%

Occurrence of MAR– phenotype in Finns is 0.2%.

Expression

Cord RBCs	Expressed
Altered	Weak on $hr^B–$; RH:32; DC^We/DC^We; DC^Xe/DC^Xe RBCs

Molecular basis associated with MAR antigen

MAR is likely to be expressed in the vicinity of amino acid residues 36–41 of the RhCe protein[1,2]. MAR– RBCs have the DC^We/DC^Xe phenotype and thus express both C^W (**RH8**) and C^X (**RH9**) antigens.
See System pages.

Effect of enzymes and chemicals on MAR antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant

In vitro characteristics of alloanti-MAR

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-MAR

The only reported example of anti-MAR was found in the serum of a non-transfused DC^We/DC^Xe woman upon delivery of her second child[3,4].

Comments

Antibodies made by people with C^W+C^X+ RBCs detect a high-prevalence antigen (MAR) and are weakly reactive with C^W+/C^W+ or C^X+/C^X+ RBCs. Antibodies made by people with C^W+/C^W+, or C^X+/C^X+ RBCs are non-reactive with C^W+/C^X+ RBCs[3,4]. There is an association between MAR (**RH51**), C^W (**RH8**) and C^X (**RH9**) antigens.

References

[1] Mouro, I., et al., 1995. Molecular basis of the RhC^W (Rh8) and RhC^X (Rh9) blood group specificities. Blood 86, 1196–1201.

[2] Sistonen, P., et al., 1994. A novel high-incidence Rh antigen revealing the existence of an allelic sub-system including C^w (Rh8) and C^x (Rh9) with exceptional distribution in the Finnish population. Vox Sang 66, 287–292.

[3] O'Shea, K.P., et al., 2001. An anti-MAR-like antibody in a DC^We/DC^We person. Transfusion 41, 53–55.

[4] Poole, J., et al., 2001. Anti-Rh51-like in a rare C^WDe/C^WDe individual [abstract]. Transfus Med 11 (Suppl. 1), 32.

BARC Antigen

Terminology

ISBT symbol (number)	RH52 (004052 or 4.52)
History	Reported in 1989 as a low-prevalence antigen associated with some DVI RBCs. Named after the Badger American Red Cross, where the antibody was first found. Confirmed as an Rh antigen in 1996 and awarded the next number.

Occurrence

All populations	<0.01%

Expression

Cord RBCs	Presumed expressed
Altered	Correlation between strength of BARC antigen and partial D antigen See Comments.

Molecular basis associated with BARC antigen[1–3]

BARC is associated with partial D category VI in a DVICe haplotype. There are three types of DVICe and each is encoded by a hybrid *RHD*D–CE–D*. See System pages.

Effect of enzymes and chemicals on BARC antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Presumed resistant
α-Chymotrypsin	Presumed resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-BARC

Immunoglobulin class	IgG
Optimal technique	IAT; enzymes

Clinical significance of alloanti-BARC

No data are available.

Comments

BARC subdivides category DVI[4]. Almost all DVI *in cis* to Ce express BARC; DVI *in cis* to cE does not express BARC. DVI RBCs with a weak expression of D have a weak expression of BARC. RBCs with a stronger expression of D have a strong expression of BARC. Anti-BARC is separated from a multispecific serum (Horowitz) by absorption and elution.

References

[1] Mouro, I., et al., 1994. Rearrangements of the blood group RhD gene associated with the D^{VI} category phenotype. Blood 83, 1129–1135.

[2] Wagner, F.F., et al., 2001. A D^{V}-like phenotype is obliterated by A226P in the partial D DBS. Transfusion 41, 1052–1058.

[3] Wagner, F.F., et al., 1998. Three molecular structures cause rhesus D category VI phenotypes with distinct immunohematological features. Blood 91, 2157–2168.

[4] Tippett, P., et al., 1996. The Rh antigen D: partial D antigens and associated low incidence antigens. Vox Sang 70, 123–131.

JAHK Antigen

Terminology

ISBT symbol (number)	RH53 (004053 or 4.53)
History	First described in 1995 as a low-prevalence antigen associated with the r^G haplotype. Family studies reported in 2002 confirmed Rh antigen status, and an Rh number was allocated. Name extracted from the family name of the original antibody producer.

Occurrence

All populations	<0.01%

Expression

Cord RBCs	Presumed expressed

Molecular basis associated with JAHK antigen[1]

Amino acid	Leu122 in RhCe
Nucleotide	T at bp 365 in exon 3 of *RHCE*Ce*
JAHK−(wild type)	Ser122 and C at bp 365

See System pages.

Effect of enzymes and chemicals on JAHK antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-JAHK

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-JAHK

Not known.

Comments

Present on RBCs with r^G phenotype but not with the r''^G phenotype[2]. Anti-JAHK is found in multispecific sera[2,3].

References

[1] Scharberg, E.A., et al., 2005. Molecular basis of the JAHK (RH53) antigen. Transfusion 45, 1314–1318.

[2] Green, C., et al., 2002. JAHK: a low frequency antigen associated with the r^G complex of the Rh blood group system. Transfus Med 12, 55–61.

[3] Kosanke, J., et al., 2002. Confirmation that the JAHK antigen is associated with the r^G haplotype. Immunohematology 18, 46–47.

DAK Antigen

Terminology

ISBT symbol (number)	RH54 (004054 or 4.54)
History	Described in 1999; named "D" for the D antigen, and "AK" from the initials of the original antibody producer. Confirmed as an Rh antigen in 2002.

Occurrence

Caucasians	<0.01%
Blacks	4%

Expression

Cord RBCs	Presumed expressed
Altered	Weak on R^N

Molecular basis associated with DAK antigen

Encoded by *RHD*DIIIa*, *RHD*DOL*, and *RHCE*CeRN*[1]. See System pages.

Effect of enzymes and chemicals on DAK antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Presumed resistant

In vitro characteristics of alloanti-DAK

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-DAK

Transfusion reaction	Presumed significant
HDFN	Presumed significant

Comments

Many examples of anti-DAK exist in multispecific sera.

Reference

[1] Reid ME, et al., 2003. DAK, a new low-incidence antigen in the Rh blood group system. Transfusion;43: 1394–7.

LOCR Antigen

Terminology

ISBT symbol (number)	RH55 (004055 or 4.55)
Obsolete name	700053
History	Described in 1994, and became part of the Rh blood group system in 2002. Name was derived from two families in which HDFN occurred.

Occurrence

Only five LOCR+ probands, all European, have been reported.

Expression

Cord RBCs	Presumed expressed

Antithetical antigen

Rh26 (**RH26**)

Molecular basis of LOCR antigen[1]

Amino acid	Ser96 in Rhce
Nucleotide	A at bp 286 in exon 2 of *RHCE*ce*

Effect of enzymes and chemicals on LOCR antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Presumed resistant
Acid	Resistant

In vitro characteristics of alloanti-LOCR

Immunoglobulin class	IgG
Optimal technique	37°C; IAT; enzymes

Clinical significance of alloanti-LOCR

Transfusion reaction	No data
HDFN	Moderate

Comments

Travels with ce, and the c or e may be weakened[2].

References

[1] Coghlan, G., et al., 2006. Molecular basis of the LOCR (Rh55) antigen. Transfusion 46, 1689–1692.

[2] Coghlan, G., et al., 1994. A "new" low-incidence red cell antigen, LOCR, associated with altered expression of Rh antigens. Transfusion 34, 492–495.

CENR Antigen

Terminology

ISBT symbol (number)	RH56 (004056 or 4.56)
History	Described in 2004, and named "CE" after *RHCE*/RhCE and "NR" from the initials of the proband.

Occurrence

Only one CENR+ proband, a Caucasian woman with a CENR+ daughter has been reported.

Expression

Cord RBCs	Presumed expressed

Molecular basis of CENR antigen[1]

Associated with *RHCE*Ce–D*(6–10) with 122A>G in exon 1 (Gln41Arg).
See System pages.

Effect of enzymes and chemicals on CENR antigen on intact RBCs

Ficin/Papain	Resistant (enhanced)
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant
Acid	Resistant

In vitro characteristics of alloanti-CENR

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-CENR

No data. Only one example of anti-CENR has been found.

Comments

Anti-CENR was identified in a serum containing anti-D^W (RH23) and anti-Rh32. An eluate, made by adsorbing the reactive anti-D^W/Rh32 serum onto CENR+ RBCs, was reactive with D^W+ and Rh32+ RBCs. However, the CENR+ RBCs were shown to be D^W− and Rh32− by tests with several examples of these specificities.

Reference

[1] Westhoff, C.M., et al., 2004. A new hybrid *RHCE* Gene (CeNR) is responsible for expression of a novel antigen. Transfusion 44, 1047–1051.

CEST Antigen

Terminology

ISBT symbol (number)	RH57 (004057 or 4.57)
History	Named in 2009 when it was shown to be antithetical to JAL: "CE" for RhCE, and "ST" from the name of the antigen-negative proband.

Occurrence

Most populations	100%

The CEST– phenotype was found in people with African ancestry.

Expression

Cord RBCs	Expressed

Antithetical antigen

JAL (**RH48**)

Molecular basis of CEST antigen[1,2]

Amino acid	Arg114 and Leu245
Nucleotide	C at bp 34 and C at bp 733

See System pages.

Effect of enzymes and chemicals on CEST antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant

In vitro characteristics of alloanti-CEST

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-CEST

No data because antibody is rare.

References

[1] Lomas-Francis, C., et al., 2009. JAL (RH48) blood group antigen: serological observations. Transfusion 49, 719–724.

[2] Westhoff, C., et al., 2009. The JAL Antigen (RH48) is the result of a change in RHCE that encodes Arg114Trp. Transfusion 49, 725–732.

CELO Antigen

Terminology

ISBT symbol (number)	RH58 (004058 or 4.58)
History	Named in 2011 when it was shown to be antithetical to Crawford. “CE” from RhCE, and “LO” from the first two antigen-negative probands.

Occurrence

Three CELO– probands have been reported; they were of African or Hispanic ancestry.

Expression

Cord RBCs	Expressed

Antithetical antigen

Crawford (**RH43**)

Molecular basis of CELO antigen[1]

Amino acids	Trp16, Gln233, Leu245 in Rhce
Nucleotides	G at bp 48, C at bp 697, and C at bp 733 in *RHCE*ce* (*RHCE*ceCF*)

See System pages.

Effect of enzymes and chemicals on CELO antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant

In vitro characteristics of alloanti-CELO

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-CELO

No data available because the antibody specificity is rare.

Comments

CELO– RBCs are also hr^S +/– VS+ and hr^B–.

Reference

[1] Halter Hipsky, C., et al., 2011. *RHCE*ceCF* encodes partial c and partial e but not CELO an antigen antithetical to Crawford. Transfusion 51, 25–31.

CEAG Antigen

Terminology

ISBT symbol (number)	RH59 (004059 or 4.59)
History	Named in 2009: “CE” for RhCE, “A” for Ala, and “G” for Gly.

Occurrence

The only CEAG– proband was of African ancestry.

Molecular basis of CEAG antigen[1,2]

Amino acid	Ala85 in Rhce
Nucleotide	C at bp 254 in exon 2 of *RHCE*ce*
CEAG–	Gly85 and G at bp 254

See System pages.

Expression

Cord RBCs	Expressed

Effect of enzymes and chemicals on CEAG antigen on intact RBCs

Ficin/Papain	Resistant
Trypsin	Resistant
α-Chymotrypsin	Resistant
DTT 200 mM	Resistant

In vitro characteristics of alloanti-CEAG

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-CEAG

No data are available because only one anti-CEAG has been described.

Comments

CEAG– RBCs also lack hr^B (**RH31**) and have a partial e antigen[2].

References

[1] Vege, S., et al., 2009. A novel 254 G>C (Ala85 Gly) change associated with partial Rhe and alloanti-e [abstract]. Transfusion 49 (Suppl.) 15A–15A.

[2] Westhoff, C.M., et al., 2010. Frequency of *RHCE*ce*(*254G>C*) in African-American patients and donors [abstract]. Transfusion 50 (Suppl.), 145A–146A.