JR Blood Group System

Number of antigens 1

High prevalence	Jr^a

Terminology

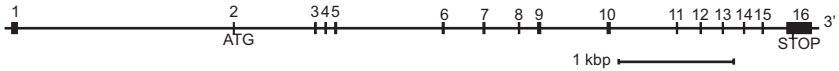
ISBT symbol (number)	JR (032)
CD number	CD338
History	The Jr^a antigen was promoted from the 901 Series of High-Incidence antigens to a System in 2012, when it was shown that *ABCG2* null alleles define the Jr(a–) phenotype[1].

Expression

Tissues	Highly expressed in placenta (syncytiotrophoblasts). Low expression in epithelial cells of small and large intestines, liver ducts, colon, lobules of the breast, endothelial cells of veins and capillaries, and brain microvessel endothelium, stem cells, lung, and in the apical membrane of proximal tubules of the kidney. It is unregulated in breast and brain tumors.

Gene

Chromosome	4q22.1
Name	*JR* (*ABCG2*)
Organization	16 exons spread over approximately 68.6 kbp of gDNA
Product	Jr glycoprotein (ATP-binding cassette, sub-family G, member 2 [ABCG2]; breast cancer resistance protein [BCRP])



The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00034-X

Database accession numbers

GenBank	NM_004827.2 (DNA)
Entrez Gene ID	9429

Molecular bases of silencing *JR* [JR_{null} (Jr(a–), JR:–1)] phenotype[1–3]

The reference allele, *ABCG2* (Accession number NM_004827.2) encodes Jr^a (JR1). Nucleotide differences from this reference allele, and amino acids affected, are given.

Allele name	Exon	Nucleotide	Restriction enzyme	Amino acid	Ethnicity (prevalence)
*ABCG2*01N.01* or *JR*01N.01*	4	376C>T	*Rsa*I–	Gln126Stop	Asian (Many)
*ABCG2*01N.02* or *JR*01N.02*	7	706C>T	*Bsm*FI–	Arg236Stop	Europeans (Few)
*ABCG2*01N.03* or *JR*01N.03*	7	736C>T	*Taq*I–	Arg246Stop	(Few)
*ABCG2*01N.04* or *JR*01N.04*	4	337C>T	*Tsp*45I+	Arg113Stop	(Rare)
*ABCG2*01N.05* or *JR*01N.05*	7	784G>T	*Nla*III+	Gly262Stop	(Few)
*ABCG2*01N.06* or *JR*01N.06*	13	1591C>T	*Hpy*188I–	Gln531Stop	(Rare)
*ABCG2*01N.07* or *JR*01N.07*	2	187_197del ATATTATCGAA		Ile63TyrfsStop	(Rare)
*ABCG2*01N.08* or *JR*01N.08*	6	542_543insA		Phe182ValfsStop fsStop	(Rare)
*ABCG2*01N.09* or *JR*01N.09*	7	730C>T		Gln244Stop	(Rare)
*ABCG2*01N.10* or *JR*01N.10*	7	791_792delTT		Leu264His fsStop	(Few)
*ABCG2*01N.11* or *JR*01N.11*	8	875_878dupACTT		Phe293Leu fsStop	(Rare)

Amino acid sequence

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MSSSNVEVFI  PVSQGNTNGF  PATASNDLKA  FTEGAVLSFH  NICYRVKLKS   50
GFLPCRKPVE  KEILSNINGI  MKPGLNAILG  PTGGGKSSLL  DVLAARKDPS  100
GLSGDVLING  APRPANFKCN  SGYVVQDDVV  MGTLTVRENL  QFSAALRLAT  150
TMTNHEKNER  INRVIQELGL  DKVADSKVGT  QFIRGVSGGE  RKRTSIGMEL  200
ITDPSILFLD  EPTTGLDSST  ANAVLLLLKR  MSKQGRTIIF  SIHQPRYSIF  250
KLFDSLTLLA  SGRLMFHGPA  QEALGYFESA  GYHCEAYNNP  ADFFLDIING  300
DSTAVALNRE  EDFKATEIIE  PSKQDKPLIE  KLAEIYVNSS  FYKETKAELH  350
QLSGGEKKKK  ITVFKEISYT  TSFCHQLRWV  SKRSFKNLLG  NPQASIAQII  400
VTVVLGLVIG  AIYFGLKNDS  TGIQNRAGVL  FFLTTNQCFS  SVSAVELFVV  450
EKKLFIHEYI  SGYYRVSSYF  LGKLLSDLLP  MRMLPSIIFT  CIVYFMLGLK  500
PKADAFFVMM  FTLMMVAYSA  SSMALAIAAG  QSVVSVATLL  MTICFVFMMI  550
FSGLLVNLTT  IASWLSWLQY  FSIPRYGFTA  LQHNEFLGQN  FCPGLNATGN  600
NPCNYATCTG  EEYLVKQGID  LSPWGLWKNH  VALACMIVIF  LTIAYLKLLF  650
LKKYS                                                     655
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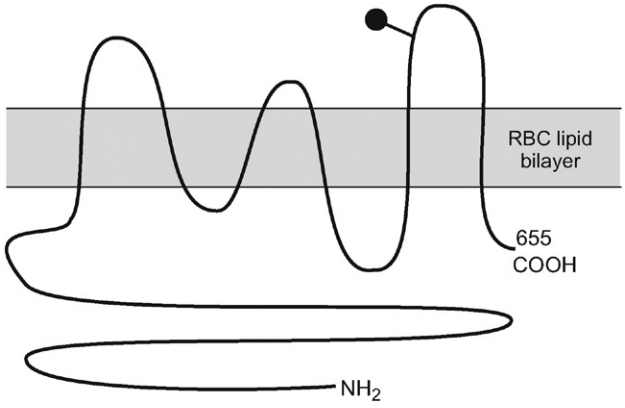
Carrier molecule

A multipass membrane glycoprotein with one nucleotide-binding domain (NBD; residues 1 to ~396), followed by one membrane-spanning domain (MSD; residues ~397 to 655). The functional molecule is likely a homodimer.



M_r (SDS-PAGE)	72,000 reduced; 180,000 non-reduced
CHO: N-glycan	Three potential; one likely
Cysteine residues	12

Function

ABCG2 is an ATP-dependent transport protein that has broad substrate specificity (including for urate). It is involved in multidrug resistance in tumor cells, particularly in breast cancer, and may function in the defense of normal cells against toxic agents, and have a role in folate homeostasis. Transport of PPIX

suggests that ABCG2 may be important for homeostasis of endogenous porphyrins. The abcg2 expression in mice conferred a survival advantage during hypoxia.
Xenobiotic transporter that may play an important role in the exclusion of xenobiotics from the brain; may be involved in brain-to-blood efflux; appears to play a major role in the multidrug resistance phenotype of several cancer cell lines. When overexpressed, the transfected cells become resistant to mitoxantrone, daunorubicin, and doxorubicin, display diminished intracellular accumulation of daunorubicin, and manifest an ATP-dependent increase in the efflux of rhodamine.
Significant expression of this protein has been observed in the placenta, which may suggest a potential role for this molecule in placenta tissue[4,5].

Disease association

The Gln126Stop and Gln141Lys variants of ABCG2 are associated with an increased risk for gout[5].

References

[1] Zelinski, T., et al., 2012. ABCG2 null alleles define the Jr(a–) blood group phenotype. Nat Genet 44, 131–132.
[2] Reid, M.E., et al. 2012. The JR Blood Group System (ISBT 032): Molecular Characterization of Three New Null Alleles. Transfusion, submitted.
[3] Saison, C., et al., 2012. Null alleles of *ABCG2* encoding the breast cancer resistance protein define the new blood goup system Junior. Nat Genet 44, 174–177.
[4] Doyle, L.A., et al., 1998. A multidrug resistance transporter from human MCF-7 breast cancer cells. Proc Natl Acad Sci USA 95, 15665–15670.
[5] Woodward, O.M., et al., 2011. ABCG transporters and disease. FEBS Journal 278, 3215–3225.

Jr^a Antigen

Terminology

ISBT symbol (Number)	JR1 (032001 or 32.1)
Obsolete names	Junior; 900012; 901005
History	The first five examples of anti-Jr^a were reported in 1970. Named for the first maker of anti-Jr^a, Rose Jacobs, and not for "Junior" as some believed.

Occurrence

All populations	>99%

The Jr(a–) phenotype has been found mostly in Japanese and other Asians, but also in persons of northern European extraction, Bedouin Arabs, and in one Mexican.

Expression

Cord RBCs	Expressed

Molecular basis associated with Jr^a antigen

See "Molecular basis of JR_{null} [Jr(a–), JR:–1] phenotype" in the System pages.

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

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

In vitro characteristics of alloanti-Jr^a

Immunoglobulin class	IgG more common than IgM
Optimal technique	IAT
Complement binding	Some

Clinical significance of alloanti-Jr^a

Transfusion reaction	^{51}Cr cell survival studies indicated reduced RBC survival; a patient with anti-Jr^a developed rigor after transfusion of 150mL of cross-match incompatible blood
HDFN	Positive DAT but usually no HDFN; however, one fatal case of HDFN[1]

Comments

Siblings of patients with anti-Jr^a should be tested for compatibility, and the patient urged to donate blood for cryogenic storage when his/her clinical state permits.

Reference

[1] Peyrard, T., et al., 2008. Fatal hemolytic disease of the fetus and newborn associated with anti-Jr^a 48, 1906–1911.