Xg Blood Group System

Number of antigens 2

Polymorphic	Xg[a]
High prevalence	CD99

Terminology

ISBT symbol (number)	XG (012)
History	The Xg system was established in 1962 when it was found that Xg[a] antigen expression was controlled by the X chromosome.

Expression

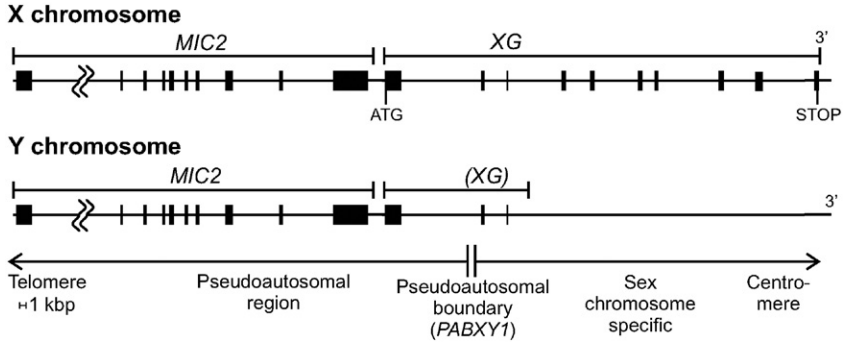
Other blood cells	Xg[a]: expression may be restricted to RBCs CD99: lymphocytes (27,000 sites), platelets (4,000 sites)[1]
Tissues	CD99: fibroblasts, fetal liver, lymph nodes, spleen, thymus, pancreatic islet cells, ovarian granulosa cells, sertoli cells, fetal adrenal, adult bone marrow[2]. Most abundant expression is in the most immature stages of the B cell, T cell, and granulocyte lineages

Gene

XG	
Chromosome	Xp22.33
Name	*XG* (*PBDX*)[2]
Organization	10 small exons distributed over approximately 60 kbp of gDNA. Exon 1 to exon 3 are present in the pseudoautosomal region of the X and Y chromosomes. Exon 4 to exon 10 are only on the X chromosome[2]
Product	Xg[a] glycoprotein

The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00014-4

CD99	
Chromosome	Xp22.2 and Yp11.2
Name	*MIC2* (*CD99*)
Organization	10 exons distributed over 52 kbp of gDNA
Product	CD99



Database accession numbers

	XG	*CD99*
GenBank	NM_175569, AF380356 (mRNA)	M16279
Entrez Gene ID	7499	4267

Molecular basis of Xg phenotype

Molecular basis of Xg(a–) and CD99– phenotypes have not been determined.

Xg^a amino acid sequence

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MESWWGLPCL  AFLCFLMHAR  GQRDFDLADA  LDDPEPTKKP  NSDIYPKPKP   50
PYYPQPENPD  SGGNIYPRPK  PRPQPQPGNS  GNSGGYFNDV  DRDDGRYPPR  100
PRPRPPAGGG  GGGYSSYGNS  DNTHGGDHHS  TYGNPEGNMV  AKIVSPIVSV  150
VVVTLLGAAA  SYFKLNNRRN  CFRTHEPENV                          180
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XG encodes a putative leader sequence of 21 amino acids.

CD99 amino acid sequence

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MARGAALALL  LFGLLGVLVA  APDGGFDLSD  ALPDNENKKP  TAIPKKPSAG   50
DDFDLGDAVV  DGENDDPRPP  NPPKPMPNPN  PNHPSSSGSF  SDADLADGVS  100
GGEGKGGSDG  GGSHRKEGEE  ADAPGVIPGI  VGAVVVAVAG  AISSFIAYQK  150
KKLCFKENAE  QGEVDMESHR  NANAEPAVQR  TLLEK                   185
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MIC2 encodes a signal peptide of 22 amino acids.

Carrier molecule

A single pass type 1 membrane glycoprotein.

	Xg^a glycoprotein	CD99
M_r (SDS-PAGE)	22,000–29,000	32,500
CHO: N-glycan	No sites	No sites
CHO: O-glycan	11 potential sites[2]	11 potential sites[3]
Cysteine residues	3	1
Copies per RBC	9,000 (polyclonal anti-Xg^a) 18–450 (monoclonal anti-Xg^a)	200 to 2,000[3]

Function

CD99 is a cell surface glycoprotein involved in leukocyte migration, T-cell adhesion, and transmembrane protein transport, and also in T-cell death by a caspase-independent pathway. It may have the ability to rearrange the actin cytoskeleton, and may also act as an oncosuppressor in osteosarcoma. Cyclophilin A binds to CD99, and may act as a signaling regulator of CD99[2]. In RBCs the function of CD99 is not known.

Disease association

XG is linked to genes responsible for ichthyosis (*STS*), ocular albinism (*OAI*), and retinoschisis (*RS*).
High levels of CD99 are found in Ewing's sarcoma, some neuroectodermal tumors, lymphoblastic lymphoma, and acute lymphoblastic leukemia[2].

Phenotypes (% occurrence)

Phenotype	Male	Female
Xg(a+)	65.6	88.7
Xg(a–)	34.4	11.3

Phenotypic relationship of Xg^a and CD99 antigens

	Xg^a type	CD99 level
Male	Xg(a+)	High
	Xg(a–)	High or low
Female	Xg(a+)	High
	$Xg(a+^W)$	High
	Xg(a–)	Low

Comments

First blood group system to be assigned to the X chromosome. Family studies with anti-Xg^a helped to define the mechanism responsible for various sex-chromosome aneuploides.

Xg^a and CD99 escape X chromosome inactivation.

XG transcripts were detected in thymus, bone marrow, and fetal liver, and in several non-erythroid tissues: heart, placenta, skeletal muscle, prostate, thyroid, spinal cord, trachea[4].

References

[1] Latron, F., et al., 1987. Immunochemical characterization of the human blood cell membrane glycoprotein recognized by the monoclonal antibody 12E7. Biochem J 247, 757–764.

[2] Tippett, P., Ellis, N.A., 1998. The Xg blood group system: a review. Transfus Med Rev 12, 233–257.

[3] Fouchet, C., et al., 2000a. Quantitative analysis of XG blood group and CD99 antigens on human red cells. Immunogenetics 51, 688–694.

[4] Fouchet, C., et al., 2000b. A study of the coregulation and tissue specificity of *XG* and *MIC2* gene expression in eukaryotic cells. Blood 95, 1819–1826.

Xg^a Antigen

Terminology

ISBT symbol (number)	XG1 (012001 or 12.1)
History	Discovered in 1962 when serum from multiply-transfused Mr. And detected an antigen with a higher prevalence in females than in males; encoded by a locus on the X chromosome. Named after the X chromosome and "g" from "Grand Rapids," where the patient was treated.

Occurrence

Females	89%
Males	66%

Expression

Cord RBCs	Weak
Altered	Weak expression on RBCs from adult females heterozygous for *Xg*^{a}. Weak expression on RBCs from adult males is rare.

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

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

In vitro characteristics of alloanti-Xg^a

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

Clinical significance of alloanti-Xg^a

Transfusion reaction	No
HDFN	No

Autoanti-Xg^a

One example has been reported.

Comments

An uncommon antibody; occurs mostly in monospecific rather than multispecific sera. Some anti-Xg^a are naturally-occurring. Xg^a is a poor immunogen.

For the phenotypic relationship between Xg^a and CD99, see System pages.
Xg^a escapes X chromosome inactivation.

CD99 Antigen

Terminology

ISBT symbol (number)	XG2 (012002 or 12.2)
Obsolete names	12E7; MIC2; E2; HuLy-m6; FMC29; HEC
History	Became part of the Xg blood group system in 2000 because *MIC2* and *XG* are adjacent, homologous genes, and two CD99-negative people were found with the alloantibody.

Occurrence

The only two CD99-negative probands that have been described are Japanese[1].

Expression

Cord RBCs	Weak

Effect of enzymes and chemicals on CD99 antigen on intact RBCs

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

In vitro characteristics of alloanti-CD99

Immunoglobulin class	IgG
Optimal technique	IAT

Clinical significance of alloanti-CD99

There are no data because the antibody is rare.

Comments

CD99 escapes X chromosome inactivation.
CD99 has a phenotypic relationship to Xg^a; see System pages.

Reference

[1] Uchikawa, M., et al., 1995. An alloantibody to 12E7 antigen detected in 2 healthy donors [abstract]. Transfusion 35 (Suppl.), 23S.