I Blood Group System

Number of antigens 1

High prevalence I

Terminology

ISBT symbol (number)	I (27)
Obsolete names	207; Ii collection
History	The I antigen was placed in a system in 2002, when mutations of the *I* gene encoding the glycosyltransferase responsible for converting i-active straight oligosaccharide chains to I-active branched chains were identified.

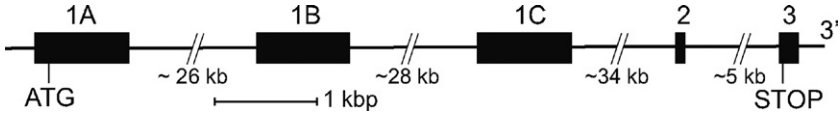
Expression

Soluble form	Human milk, saliva, amniotic fluid, urine, ovarian cyst fluid (small amounts in serum/plasma)
Other blood cells	Lymphocytes, monocytes, granulocytes, platelets
Tissues	Wide tissue distribution

Gene

Chromosome	6p24.2
Name	*I* (*GCNT2, IGnT*)
Organization	3 exons spread over approximately 100 kbp of gDNA; three forms of exon 1 are differentially spliced to give one of three transcripts: IGnTA, IGnTB or IGnTC[1,2,3]
Product	6-β-*N*-acetylglucosaminyltransferase (β6GlcNAc-transferase, β6GlcNAc-T); the branching enzyme for I antigen expression on RBCs is encoded by *IGnTC*; expression of I antigen on lens epithelium is encoded by *IGnTB*

The Blood Group Antigen (3/e). DOI: http://dx.doi.org/10.1016/B978-0-12-415849-8.00029-6



Database accession numbers

GenBank	NM_145655.3; AF458026 (mRNA)
Entrez Gene ID	2651

Molecular bases of weak I antigen

Homozygosity or compound heterozygosity for weakened expression of *GCNT2* alleles leads to the I+^{W} phenotype. The reference allele, *GCNT2*01* (Accession number NM_145655.3) encodes I (I1). Nucleotide differences from this allele, and amino acids affected, are given.

Allele encodes	Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
I+^{W}	*GCNT2*01W.01*	1C	243T>A	Asn81Lys	Caucasians, Taiwanese (Rare)
I+^{W}	*GCNT2*01W.02*	1C	505G>A	Ala169Thr	Caucasians (Rare)
I+^{W}	*GCNT2*01W.03*	1C	683G>A	Arg228Gln	Caucasians (Rare)

Molecular bases of silencing of *GCNT2*

Homozygosity or compound heterozygosity for silent *GCNT2* alleles leads to the I– (adult i) phenotype. Differences from *GCNT2*01* reference allele (accession number NM_145655.3) are given.

Allele name	Exon	Nucleotide	Amino acid	Ethnicity (prevalence)
*GCNT2*01N.01*	3	1049G>A	Gly350Glu	Japanese, Taiwanese (Rare)
*GCNT2*01N.02*	3	1154G>A	Arg385His	Japanese, Taiwanese (Rare)
*GCNT2*01N.04*	1C 2	816G>C; 1006G>A	Glu272Asp; Gly336Arg	(Rare)
*GCNT2*01N.05*	2	984G>A	Trp328Stop	Arabs (Rare)
*GCNT2*01N.06*	1B, 1C, 2, 3	del exons 1B, 1C, 2, 3	No protein	Taiwanese (Rare) Pakistani (Rare)
*GCNT2*01N.07*	1C	651delA	Val244Stop	Japanese (Rare)
*GCNT2*01N.08*	2	935G>A	Gly312Asp	Persian Jews (Rare)

Amino acid sequence for IGnTC β6GlcNAc-transferase[1,2,3]

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MNFWRYCFFA  FTLLSVVIFV  RFYSSQLSPP  KSYEKLNSSS  ERYFRKTACN   50
HALEKMPVFL  WENILPSPLR  SVPCKDYLTQ  NHYITSPLSE  EEAAFPLAYV  100
MVIHKDFDTF  ERLFRAIYMP  QNVYCVHVDE  KAPAEYKESV  RQLLSCFQNA  150
FIASKTESVV  YAGISRLQAD  LNCLKDLVAS  EVPWKYVINT  CGQDFPLKTN  200
REIVQHLKGF  KGKNITPGVL  PPDHAIKRTK  YVHQEHTDKG  GFFVKNTNIL  250
KTSPPHQLTI  YFGTAYVALT  REFVDFVLRD  QRAIDLLQWS  KDTYSPDEHF  300
WVTLNRVSGV  PGSMPNASWT  GNLRAIKWSD  MEDRHGGCHG  HYVHGICIYG  350
NGDLKWLVNS  PSLFANKFEL  NTYPLTVECL  ELRHRERTLN  QSETAIQPSW  400
YF                                                         402
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Carrier molecule

The *GCNT2* gene product adds β6GlcNAc to i-active, linear oligosaccharide chains of repeating *N*-acetyllactosamine units on glycolipids and glycoproteins on RBCs, and to glycoproteins in plasma (see figure in Section III). Present on proteins with polylactosamine-containing N-glycans (band 3, glucose transporter, etc.)[4].
A range of copy numbers per RBC has been reported[4].

Function

Not known.

Disease association

A decreased expression of I antigen and concomitant increased expression of the reciprocal i antigen are associated with leukemia, Tk polyagglutination, thalassemia, sickle cell disease, HEMPAS, Diamond Blackfan anemia, myeloblastic erythropoiesis, sideroblastic erythropoiesis, and any condition that results in stress hematopoiesis. Congenital cataracts are associated with a lack or marked reduction of I antigen on RBCs and lens[2]. Caucasians without cataracts have a markedly reduced β6GlcNAc-transferase activity[1]. Asians with cataracts have no β6GlcNAc-transferase activity[2,3]. Anti-I is associated with cold hemagglutinin disease (CHAD) and pneumonia due to *Mycoplasma pneumoniae*.

Phenotypes associated with I antigen and the reciprocal i antigen

RBCs	Antigen expression		Occurrence
	I	i	
Adult	Strong	Weak	Common
Cord	Weak	Strong	All
i Adult	Trace	Strong	Rare

Comments

I antigens occur at the branching points of A-, B-, and H-active oligosaccharide chains.

Branching is under developmental control regulated by phosphorylation of key residues in the C/EBPα transcription factor, which acts on the *GCNT2* promoter. Once the gene is activated, the level of the I antigen expression on RBCs of the newborn child begins to increase[5].

References

[1] Yu, L.-C., et al., 2001. Molecular basis of the adult i phenotype and the gene responsible for the expression of the human blood group I antigen. Blood 98, 3840–3845.

[2] Yu, L.C., et al., 2003. The molecular genetics of the human I locus and molecular background explaining the partial association of the adult i phenotype with congenital cataracts. Blood 101, 2081–2087.

[3] Inaba, N., et al., 2003. A novel I-branching β-1,6-*N*-acetylglucosaminyltransferase involved in human blood group I antigen expression. Blood 101, 2870–2876.
[4] Cooling, L., 2010. Polyactosamines, there's more than meets the "Ii:" a review of the I system. Immunohematology 26, 133–155.
[5] Yu, L.C., Lin, M., 2011. Molecular genetics of the blood group I system and the regulation of I antigen expression during erythropoiesis and granulopoiesis. Curr Opin Hematol 18, 421–426.

I Antigen

Terminology

ISBT symbol (number)	I1 (027001 or 27.1)
Obsolete names	900026; 207001; Individual
History	Reported in 1956; named I to emphasize the high degree of the "Individuality" of blood samples failing to react with a potent cold agglutinin. Placed in a collection with i antigen in 1990, and made a one-antigen system in 2002 when the gene encoding the branching transferase was cloned.

Occurrence

Adults	>99%

Reciprocal antigen

i [See Ii Collection (**207**)].

Expression

Cord RBCs	Weaker than on adult RBCs; frequently appear to be I-negative
Altered	Weakened on RBCs produced under hematopoietic stress, and on South East Asian ovalocytes (see also Disease association).

Molecular basis associated with I antigen

See System pages for molecular bases associated with I-negative (adult i) phenotype.

Effect of enzymes and chemicals on I antigen on intact RBCs

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

Acid	Resistant

In vitro characteristics of anti-I

Immunoglobulin class	IgM (rarely IgG)
Optimal technique	RT or 4°C
Complement binding	Yes; some hemolytic

Clinical significance of anti-I

Transfusion reaction	No (may need to infuse through an approved blood warmer). Increased destruction of I+ RBCs transfused to people with the adult i phenotype and alloanti-I
HDFN	No

Autoanti-I

Most people have cold-reactive autoanti-I in their plasma.
A common specificity in CHAD and pregnancy.

Comments

So-called compound antigens have been described: IA, IB, IAB, IH, IP1, ILe^{bH}.
Alloanti-I is rare because the I– (adult i) phenotype is rare.