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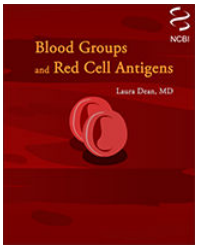

10. The Kidd blood group

The Kidd (JK) glycoprotein is the red blood cell (RBC) urea transporter. Situated in the membrane it rapidly transports urea into and out of RBCs, maintaining the osmotic stability and shape of the RBC in the process. The Kidd glycoprotein is also expressed in the kidney, where it enables the kidney to build up a high concentration of urea which is needed for the kidney to produce concentrated urine.

People who do not produce the Kidd glycoprotein tend not to be able to maximally concentrate urine, but despite this, they are healthy and their RBCs have a normal shape and lifespan.

Antibodies that target Kidd antigens are a significant cause of delayed hemolytic transfusion reactions. Anti-Kidd antibodies are also a cause of hemolytic disease of the newborn (HDN), the severity of the disease varies but tends to be mild in nature.

At a glance

Antigens of the Kidd blood group.

Number of antigens	**3: Jk1 (Jk^a), Jk2 (Jk^b) and Jk3**
Antigen specificity	**Protein** Amino acid sequence determines the specificity of Kidd antigens
Antigen-carrying molecules	**Glycoprotein that transports urea** The Kidd protein is a transmembrane, multi-pass protein that transports urea across the RBC membrane.
Molecular basis	**The SLC14A1 gene encodes the Kidd glycoprotein.** Located on chromosome 18 (18q11-q12), contains 11 exons that span more than 30 kbp of DNA. The SLC14A1 gene has two major codominant alleles, Jk^a and Jk^b, which result from a SNP (838G→A), and the corresponding Jk^a and Jk^b antigens differ by a single amino acid (D280N).
Frequency of Kidd antigens	**Jk^a**: 77% Caucasians, 92% Blacks, and 73% Asians **Jk^b**: 74% Caucasians, 49% Blacks, and 76% Asians **Jk3**: 100% in most populations, >99% in Polynesians (1)
Frequency of Kidd phenotypes	**Jk(a+b+): 50% Caucasians**, 41% Blacks, **49% Asians** **Jk(a+b-):** 26% Caucasians, **51% Blacks**, 23% Asians **Jk(a-b+):** 23% Caucasians, 8% Blacks, 27% Asians **JK(a-b-):** Rare in most populations, found in **0.9% Polynesians** (1)

Antibodies produced against Kidd antigens.

Antibody type	**IgG and IgM** IgG is more common
Antibody reactivity	**Capable of hemolysis** Can bind complement

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Transfusion reaction	**Yes—common cause of delayed hemolytic transfusion reactions.** Anti-Jk^a and anti-Jk^b are dangerous antibodies because they can be difficult to detect in routine blood cross-matches. They are a common cause of delayed hemolytic transfusion reactions. Anti-Jk3 is rare and can cause immediate and delayed hemolytic transfusion reactions.
Hemolytic disease of the newborn	**Yes—typically mild disease.** Anti-Jk^a has been implicated in at least one severe case of HDN, but most cases of HDN caused by the anti-Kidd antibodies are mild in nature.

Background information

History

In 1951, a patient called Mrs. Kidd was found to have produced antibodies targeted against a then unknown red cell antigen during her pregnancy. The marker was present on the RBCs of her fetus, and the maternal antibodies targeted against it caused fatal hemolytic disease in her newborn child.

The protein was given the name Jk^a and was the first antigen to be discovered in the Kidd blood group system. Since this time, two other antigens, Jk^b and Jk3, have been found.

In 1959, the first example of the null phenotype, i.e., Jk(a-b-), was found in a woman who had become jaundiced after a blood transfusion. Her serum was found to contain an antibody that recognized both Jk^a and Jk^b. This antibody was subsequently named anti-Jk3.

Nomenclature

- Number of Kidd antigens: 3
- ISBT symbol: JK
- ISBT number: 009
- Gene symbol: SLC14A1
- Gene name: Solute carrier family 14, member 1

Basic biochemistry

Phenotypes

There are three common Kidd phenotypes: JK(a+b-), JK(a-b+), and JK(a+b+).

The Jk-null phenotype, JK(a-b-), is rare in most populations. Individuals with this blood type are often detected after they have been immunized to Kidd antigens during a previous blood transfusion or pregnancy. After immunization, JK(a-b-) individuals form anti-Jk3, which can cause HDN in subsequent pregnancies and hemolyse donor blood that contains Jk^a and/or Jk^b antigens during a subsequent blood transfusion.

Expression of Kidd antigens

The expression of the Kidd antigens is limited to RBCs and the kidney (in the vasa recta).

Function of Kidd protein

The Kidd protein is a major urea transporter in RBCs. It rapidly transports urea into and out of RBCs and in the process helps to maintain osmotic stability. The urea transport across Kidd null RBC membranes is ~1000 times slower than across normal RBC membranes (2, 3).

The transport of urea by the Kidd glycoprotein in the kidney enables the kidney medulla to maintain a high concentration of urea, which in turn enables the kidney to produce concentrated urine.

However, the absence of the Kidd glycoprotein is not associated with disease. The RBCs in Kidd null individuals have a normal shape and lifespan (3). Individuals with the Jk(a-b-) phenotype are unable to maximally concentrate urine, but it does not cause any other health problems (4).

Clinical significance of Kidd antibodies

The Kidd antibodies are often difficult to detect, making them hazardous in transfusion medicine, where they are suspected to be a common cause of delayed hemolytic transfusion reactions (DHTRs) (5).

Transfusion reactions

Anti-Jk^a can cause severe and fatal hemolytic transfusion reactions (6) but is more commonly associated with less severe DHTRs. It has been estimated that over one-third of DHTRs are caused by anti-Jk^a (7, 8). Case studies have also pointed to anti-Jk^b as being responsible for severe DHTR (9, 10). Anti-Jk3 has also been responsible for causing severe hemolytic transfusion reactions, both immediate and delayed (5).

Hemolytic disease of the newborn

During pregnancy, fetal Kidd antigens are capable of causing alloimmunization of the mother (11). But in contrast to the hemolytic activity of Kidd antibodies in incompatible blood transfusions, anti-Jk^a and anti-Jk^b are only rarely responsible for severe HDN (12). Likewise, anti-Jk3 is a rare cause of HDN, but the first documented case in Mrs. Kidd's newborn was fatal.

Molecular information

Gene

The SLC14A1 gene (Solute carrier family 14, member 1) is a member of the urea-transporter gene family and is located on chromosome 18 (18q12-q21). The gene is organized in 11 exons distributed across than 30kb of DNA. The first three exons and part of the fourth are not translated; exons 4-11 encode the mature Kidd protein.

The Jk^a and Jk^b antigens are the products of two alleles that are inherited in a co-dominant fashion. The Jk^a/Jk^b polymorphism results from a 838G→A transition, resulting in an D280N substitution (13). Based on this, several investigators have suggested different methods for JK genotyping (13–15).

The Jk(a-b-) phenotype is generally inherited as a recessive trait—a number of different mutations have been found to be responsible 16). In the Polynesian population where the null phenotype is less rare, a splice site mutation causes loss of exon 6 from mRNA transcripts and it is unlikely that the truncated Kidd protein produced is transported to the RBC membrane (17). A similar situation holds true in the Finnish population in which another genetic explanation causes the same phenotype (17, 18).

View the sequences of Kidd alleles at the
dbRBC Sequence Alignment Viewer

Protein

The Kidd protein urea transporter is an integral protein of the RBC membrane. It is a transmembrane protein containing 389 amino acid residues. The protein is predicted to span the membrane 10 times with both the N

terminus and C terminus being intracellular. This membrane topology is shared by the anion exchanger that bears the Diego blood group antigens.

The Kidd protein consists of two hydrophobic domains that each span the membrane five times, and they are linked by a large glycosylated extracellular loop. The Asn211 on this third loop carries 1% of ABO antigens found on the RBC. The Jk^a/Jk^b polymorphism is found on the neighboring fourth extracellular loop (19).

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