

Kell K/k Antigen (KEL) Genotyping

TO DETERMINE THE NUMBER OF K (KEL1) ALLELE COPIES AND RISK FOR SEVERE HEMOLYTIC DISEASE

Disease Overview

- The Kell blood group is comprised of 27 antigens found on a red blood cell membrane glycoprotein (Kell glycoprotein).
- The K/k (*KEL1/KEL2*) polymorphism, otherwise known as the Kell/Cellano polymorphism, results from a point mutation in the extracellularly located C-terminal portion of the Kell glycoprotein.
- The most clinically significant of the Kell antigens, K (*KEL1*), has the potential to cause hemolytic disease of the fetus and newborn (HDFN) or severe hemolytic transfusion reactions.
- HDFN may occur in K-negative mothers (k/k) carrying a K-positive fetus from the transfer of maternal antibodies to the K antigen across the placental barrier. Symptoms may be seen as early as 20 weeks gestation and include hydrops and severe anemia due to suppression of erythropoiesis and alloimmune hemolysis.
- Over half of HDFN cases that occur due to anti-K antibodies are caused by multiple blood transfusions or a previous pregnancy with a K-positive baby.
- Transfusion of girls and women of reproductive age with K-positive blood should be avoided; however, donated blood is not routinely screened for Kell antigens in the United States.
- Alloimmunization due to the potent K immunogen should be considered after ABO and RhD blood group antigen incompatibilities; anti-K is responsible for up to 30 percent of antibody-mediated, severe fetal anemia.

Epidemiology

- Approximately 9 percent of Caucasians and 2 percent of African-Americans are K-positive; K homozygosity is rare. K frequency in other ethnic groups is unknown.
- Approximately 4 percent of K-negative mothers (k/k) will deliver a K-positive fetus.

Genetics

- The *KEL* gene is located on chromosome 7q33.
- A C>T nucleotide change at *KEL* position 578 results in an amino acid substitution Thr193 (k) to Met193 (K).
- Autosomal dominant inheritance; K-positive phenotypes result from heterozygosity or homozygosity for K.

Indications for Ordering

- Fetal testing when the mother has clinically significant alloantibody and the father of the pregnancy is either heterozygous for K or not available for testing.

- Paternal testing in a K RBC antigen-positive individual to determine K heterozygosity or homozygosity when his reproductive partner is K-negative by RBC antigen typing. (If the father of the pregnancy is determined to be homozygous for the K allele, all of his offspring can be assumed to be K-positive, negating the need for fetal *KEL* testing).

Interpretation

- K-negative: predicts a K-negative phenotype.
- K-homozygous or heterozygous: predicts a K-positive phenotype.

Methodology

- Polymerase chain reaction and fluorescent monitoring using hybridization probes to detect the c.578C>T (p.Thr193Met) change.
- Analytical sensitivity and specificity are 99 percent.
- Clinical sensitivity is 99 percent for the K allele.

Limitations

- Kell antigens other than K/k are not evaluated by this assay.
- Clinical specificity may be compromised by rare primer-site mutations.
- Bloody amniotic fluid samples may give false-negative results due to maternal cell contamination.

Related Test

Antigen Testing, AHG- Specify Individual RBC Antigen (0013298)

References

- Poole J, et al. A *KEL* gene encoding serine at position 193 of the Kell glycoprotein results in expression of *KEL1* antigen. *Transfusion* 2006;46(11):1879–85.
- Santiago JC, et al. Current clinical management of anti-Kell alloimmunization in pregnancy. *Eur J Obstet Gynecol Reprod Biol* 2007 (e-pub ahead of print).
- Vaughan JI, et al. Inhibition of erythroid progenitor cells by anti-Kell antibodies in fetal alloimmune anemia. *N Engl J Med* 1998;338(12):798–803.

Test Information

0051644 Kell Antigen Genotyping (KEL1/KEL2)

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.