Molecular assays as tools to facilitate new discoveries and to enhance immunohematology in daily transfusion practice

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The practice of transfusion medicine saves lives, but approximately 2-4% of transfused patients develop alloantibodies against red blood cell antigens, becoming alloimmunized. The alloimmunization index is 10 times higher in transfusion-dependent patients such as those with sickle cell anemia or thalassemia.

The determination of red blood cell phenotype by hemagglutination in alloimmunized patients can be lengthy, complex, and produce results difficult to interpret. The elucidation of the molecular basis for most red cell antigens in recent years allows the use of molecular assays to determine the presence or absence of alleles for various blood groups (genotype) and predict the red cell phenotype. Genotype determination can be used to resolve complex cases where serological determination of the blood recipients' phenotype is impaired either by lack of reagents or by other limitations of hemagglutination due to the presence of alloantibodies in the patient's blood. In those instances, the determination of genotype helps to predict the red cell antigen that can be expressed, providing a more thorough characterization of the blood type.

Often blood group genotyping in the care of transfusion-dependent patients is of great clinical benefit because it allows for the use of better-matched blood, reducing the risk of hemolytic transfusion reactions, especially delayed transfusion reactions due to existing alloantibodies, and prevents new alloimmunization events. The prevention of hemolytic reactions can by itself reduce transfusion requirements by ensuring better survival of the transfused erythrocytes and decreasing the risk of other transfusion adverse reactions such as potential exposure to infectious diseases and transfusion-related acute lung injury[1-3].

There is solid evidence indicating that matching genotype can provide an extra layer of safety and efficacy to the care of transfusion-dependent and/or chronically transfused patients. The use of genotype is also cost-effective in terms of time and resources associated with complex serologic workups and a higher number of transfused red blood cell units.

Molecular testing is rapidly advancing and offers tremendous help as a powerful tool with potential advantages in the identification of rare red blood cell donors and finding antigen matches for chronically transfused patients. However, it should be noted that, regardless of the test protocols used, genotyping predicts a blood type but does not determine the phenotype the way serologic tests do. In some instances, the genotype will not correlate with the serotype because the simple presence of a gene does not mean that the gene will be expressed as an antigen on the red blood cell membrane. A large number of genetic events may silence or weaken the expression of antigens encoded by an allele. Thus, the profile of a gene needs to be completely elucidated, and appropriate assays need to be performed to look for genetic changes that may alter the predicted phenotype.

This field is growing exponentially and molecular events associated with the specific expression of most alleles have been identified for all described blood group systems in various ethnic groups. Therefore, molecular methods must be used with caution in antigen and antibody investigations because the serological problem may involve the inheritance of a null allele, a hybrid gene or a new variant.

Genetic analysis of blood group variants within a given population is an important step that provides basic knowledge and ultimately increases the accuracy of prediction of red cell phenotype by genotype determination.

The Kell blood group is very relevant in transfusion practice because it is highly immunogenic, frequently causes alloimmunization and may cause hemolytic disease of the fetus and newborn (HDFN)[4]. Kell antigen phenotyping is hampered by technical limitations and genotyping can be of great assistance to solve this problem. The development of easy and efficacious strategies for KEL genotyping is fundamental to provide the needed information about the allelic frequency in multiethnic populations and to identify individuals with rare genotypes such as K*1/K*1 and K*3/K*3[5].

The more we know about the frequency and molecular background of variants in a given population, the more accurate will be genotype/phenotype results, and the better will be the care provided for those in need.

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References

1. Westhoff CM. Molecular testing for transfusion medicine. Curr Opin Hematol. 2006; 13(6):471–5.
2. Westhoff CM, Sloan SR. Molecular genotyping in transfusion medicine. Clin Chem. 2008;54(12):1948–50.
3. Moulds J. Future of molecular testing for red blood cell antigens. Clin Lab Med. 2010;30(2):419-29.
4. Santiago JC, Ramos-Corpas D, Oyonarte S, Montoya F. Current clinical management of anti-Kell alloimmunization in pregnancy. Eur J Obst Gynecol Reprod Biol. 2008;136(2):151–4.
5. Arnoni CP, Muniz JG, de Paula TA, Person RD, Gazito D, Baleotti Jr W, et al. An easy and efficient strategy for KEL genotyping in a multiethnic population. Rev Bras Hematol Hemoter. 2013;35(2):99-102

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