Genetic diversity of the human blood group systems

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The genetic diversity of human blood group systems is an important event programmed by nature that arouses interest and is aligned with modern biology. The variability of blood group antigens that characterize the systems, series and collections reveals the polymorphic nature of these systems and creates a challenge to understand what their biological importance is within the context of the evolution of populations. Understanding the modulating effect of erythrocyte antigenic variability in health, susceptibility and resistance to disease is one path that can be followed[1,2].

Serological methods have been used for decades to demonstrate the diversity of human blood group antigens and to improve our understanding of immunogenic aspects; they have enabled us to establish their roots and the genetic pattern of inheritance[3,4]. The use of molecular methods to investigate blood group systems has unraveled the molecular basis of erythrocyte antigenic structural diversity and revealed that the structure is based on mechanisms that extend from single nucleotide polymorphisms to insertions, deletions, inversions, intra- and intergenic recombinations and alternative splicings[5].

The use of different research methods has led to an accumulation of knowledge about the genetic and antigenic diversity of human blood group systems. Hence, it is possible to understand the importance of the diversity and how this can be applied in transfusion medicine and in other areas of interest[2,6]. Advances resulting from this knowledge contribute to the development of new technologies applied to transfusion medicine[7] and provide the background for the discovery of new blood group systems[8].

The genetic diversity of human blood group systems is extensive. The number of blood group antigens increased from just over 200 in 2000 to 339 in 2013. Of this total, 297 are distributed in 33 blood group systems recognized by the Nomenclature Committee of the International Society of Blood Transfusion (ISBT)[4]. Meanwhile, more than 1250 alleles of the genes controlling the erythrocyte antigen expression have been described[9]. The knowledge of the genetic diversity of blood group systems is consolidated and is continually renewed by the discovery of new antigenic and allelic variants.

The combined use of different research methods was crucial to the advancement of knowledge of blood group systems and the characterization of the Dombrock system (12p13.2), in its different aspects, adequately illustrates this situation. The behavior of anti-Do^a, anti-Do^b, anti-Jo^a, anti-Gy^a and anti-Hy was revealed by hemagglutination and the confirmation that a glycoprotein anchored in the red blood cell plasma membrane containing the corresponding antigens was determined by immunoblotting. Knowledge resulting from the cloning of genes favored the establishment of protocols for genotyping and transfection experiments allowed the development of monoclonal antibodies useful in determining the phenotypes of this system. Furthermore, the application of microarray techniques in the laboratory routine has facilitated the identification of large numbers of blood donors[10]. The combined effect of these methods shows that the Dombrock system is complex at its genetic, antigenic and immune levels.

The Dombrock system was analyzed in Brazilians with the methods used, as well as establishing the frequencies of common alleles, revealing new alleles[11,12]. These studies concluded that Dombrock alleles are heterogeneous and highlighted the importance of analyzing populations from different areas of the country to determine the haplotypes possible and refine genotyping protocols to clarify the Dombrock status of blood donors.

This issue of the *Revista Brasileira de Hematologia e Hemoterapia* presents a study conducted in the State of Minas Gerais, Brazil, which shows that the frequencies of some alleles of the Dombrock system show regional differences[13]. The observed frequencies of the DO*A-WL and DO*B-WL alleles were lower than those reported by Baleotti el al. in a population in the State of São Paulo, Brazil[12]. These differences may be the result of the distinct genetic backgrounds that make up the populations of these two Brazilian states.

Comparative analysis of the Dombrock system between Brazilian and American descendants from Africans also found differences in the allele frequencies[11]. The JO allele was more common than the HY allele in Brazil, but the opposite was observed in New York. These differences reinforce the view that the Dombrock system is very complex and appears

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to reflect the different origins of the Africans who came to Brazil and to North America[14].

The accumulation of knowledge about the genetic diversity of the human blood group systems also offers new opportunities for research in genetics, biochemistry, immunology and anthropology and has contributed to changes in transfusion medicine practices[6]. Moreover, this has favored the understanding of many aspects of immune hemolytic transfusion reactions in animal models[15].

In conclusion, the knowledge on the genes and alleles responsible for the diversity of antigens that comprise human blood group systems aid the understanding of the biological role played by these molecules in the development and maintenance of homeostasis of living systems.

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