Journal of Biomedical Sciences | ISSN: 2960-9356
Research Article Peer-review, Open Access

Genomics in Transfusion Medicine: Innovations in Blood Typing, Donor Matching, and Personalized Therapy

Nodirzhonova Z. N. [1]
Ganiev A. K. [2]
Sayfutdinova Z. A. [3],
Hwa Jeong Ha [4]
No Won Park [5]

Abstract

Advancements in genotyping and next-generation sequencing (NGS) are opening new avenues for transfusion medicine, allowing for precise blood group classification, better prediction of rare blood types, and improved donor selection. Studies on genetic distribution across different populations, including those in Denmark, Hainan Province, Manchuria, and India, reveal significant polymorphism in blood group systems, underscoring the importance of genomic data in transfusion strategies.

Keywords: Blood transfusion, PIEZO1, Genotyping, monomorphic distribution, ABO gene.

[1] *1st year student of the Academic Lyceum of Tashkent Medical Academy*

[2] *Head of the Academic Lyceum of Tashkent Medical Academy, PhD*

[3] *Associate Professor of the Department of Hematology, Transfuziology and Laboratory work of Tashkent Medical Academy, PhD*

[4] *Professor/Dept. of Clinical Laboratory Science, Dongnam Health University In Korea, PhD*

[5] *Member of IAC CFIAC, Fellowship International Academey of cytology*

Introduction. Blood transfusion remains one of the most common medical treatments, with standard pre-

transfusion testing based on the ABO and Rh system remaining unchanged for decades. However, the implementation of genomic technologies can significantly improve donor matching, health assessment, blood component characteristics, and the metabolic properties of transfused products [5].

New methods of transfusion therapy are being developed, taking into account the individual characteristics of donors and recipients. As part of the Recipient Epidemiology and Donor Evaluation Study (REDS-III), funded by the National Heart, Lung, and Blood Institute, more than 800,000 genetic markers are being analyzed to study the structure of red blood cells, platelets, HLA, HPA, iron metabolism, and genetic diseases. Genomic approaches have the potential to radically transform donor matching, blood component storage, and the selection of transfusion products, opening new prospects for transfusion medicine [4].

However, the implementation of genomic technologies has the potential to significantly enhance donor-recipient matching, improve health assessments, refine blood component characteristics, and optimize metabolic properties of transfused products. Recent studies, such as the Recipient Epidemiology and Donor Evaluation Study (REDS-III), have analyzed over 800,000 genetic markers to investigate red blood cell structure, platelet compatibility, iron metabolism, and genetic diseases.

Additionally, genomic research has furthered our understanding of hemoglobin regulation, particularly in oxygen transport and hypoxia response mechanisms. The discovery of PIEZO1 as a determinant of the Er blood group highlights the growing relevance of genetic factors in transfusion medicine. Beyond transfusion, genetic insights into traumatic brain injury (TBI) progression and the ABO gene's variability demonstrate the broader impact of genomic studies in clinical medicine.

Over the past decade, DNA-based extended antigen typing and gene sequencing have been increasingly used in medicine. The main goals in this field include training specialists, improving the accessibility of genotyping, and standardizing it for clinical use. Genotyping plays a key role in cases where standard methods fail to confirm compatibility, Rh typing remains inconclusive, allo- and autoantibodies are detected during transplantation, or prenatal testing is required. It is also used to refine the A subgroup classification when selecting kidney and platelet donors. Commercial testing technologies, as well as new methods such as high-density arrays and targeted sequencing (NGS), are being explored, opening new opportunities for diagnostics and personalized medicine [3].

At the same time, it is essential to consider rare blood groups and disease predisposition. The genetic distribution and status of twelve rare blood groups among the Li people in Hainan Province remain stable. The Duffy, Diego, Kidd, Dombrock, MNS, and Lutheran systems exhibit polymorphism and have unique characteristics that distinguish them from other regions and ethnic groups. In contrast, the Kell, Colton, Scianna, Ethan, Knops, and Indian blood groups are characterized by a monomorphic distribution [2].

Studies have shown that in the Harbin region of Manchuria, the GYPB (S/s), Duffy, Dombrock, Diego, Kidd, and Mur blood groups exhibit significant polymorphism, whereas the Kell, Scianna, Colton, Lutheran, and Ye groups are characterized by oligomorphism. Additionally, the Dombrock and Kidd systems in this region have unique gene distribution patterns [6].

In the southern regions of India, the prevalence of blood group antigens differs significantly from the rest of the country. Regional variations in phenotype distribution play a crucial role in ensuring timely treatment for patients with alloimmunization [7].

The high accuracy of genetic prediction for certain blood types supports its application to the DBDS cohort and potential donor groups in other countries with minimal methodological adjustments. Genetic typing accurately determines clinically significant blood groups and Rh factors (C/c and E/e), but it has not yet fully replaced serological tests for blood transfusion, although serological methods themselves are not entirely reliable. The accuracy of genetic prediction allows for the reduction of potential donors with rare blood groups and facilitates correlation studies. Since genetic data cover more than 180,000

individuals (about 3% of Denmark's population), the antigen distribution in this cohort is considered representative. This study presents estimated blood group antigen levels in Denmark, and the genetically determined antigen status of 90,000 DBDS donors is available to researchers and the regional blood bank for further studies and donor strategy development [1].

Next-generation sequencing (NGS) will complement serological and molecular methods and may eventually replace them entirely, providing fast and comprehensive analysis for screening and identifying rare blood samples [9].

The timing for describing PIEZO1 as a genetic determinant of the Er blood group system could not have been more appropriate. On October 4, 2021—presumably around the time the authors were gathering their data at the International Blood Group Reference Laboratory in Bristol, UK—Ardem Patapoutian was announced in Stockholm as the 2021 Nobel Prize laureate in Physiology or Medicine for his discoveries related to two mechanically activated ion channels, Piezo1 and Piezo2. Similar to piezoelectric crystals, where electric charges are generated upon mechanical deformation, transmembrane Piezo proteins convert mechanical forces into ion flow across cell membranes. This cellular mechanotransduction plays a crucial physiological role in somatosensation (touch perception, proprioception, and pulmonary respiration), erythrocyte volume regulation, vascular physiology, and various human genetic disorders [4].

At any given time during an adult's life, approximately 25 trillion red blood cells (erythrocytes) circulate in the bloodstream. Each erythrocyte cluster contains between 250 to 270 million copies of hemoglobin per cell, enabling oxygen transport and delivery to all tissues—a specialized cellular function essential for life. One of the latest advancements in biochemistry has been the identification of mechanisms that regulate this function by controlling hemoglobin dynamics. Allosteric regulation of hemoglobin conformational changes facilitates oxygen release in response to hypoxia. This process is aided by the stabilization of the tense, deoxygenated state of hemoglobin through the organic phosphate compound 2,3-bisphosphoglycerate (BPG). BPG production via the Rapoport–Luebering shunt occurs due to a redirection of glycolysis, triggered by the activation of bisphosphoglycerate mutase (BPGM), the rate-limiting enzyme of this pathway. However, it has been observed that BPGM activity favors the synthase reaction at an alkaline pH, while the phosphatase reaction becomes dominant in acidic conditions [3].

Traumatic brain injury (TBI) is the most common cause of death and long-term disability in trauma patients. According to the latest data from the Centers for Disease Control and Prevention (CDC), approximately 2.87 million patients seek emergency care, are hospitalized, or die annually due to TBI. Preventing secondary traumatic brain injury and the progression of traumatic intracranial hemorrhage (TIH) are primary treatment goals for these patients. Numerous factors have been associated with TBI progression and worsening clinical outcomes, including systemic arterial hypotension, hypoxia, the presence and greater extent of midline shift upon admission, elevated diastolic and mean arterial blood pressure at admission, bilateral TBI location, larger initial TBI volume, multiple TBIs, pre-existing conditions, older age, coagulopathy, a lower initial Glasgow Coma Scale (GCS) score, and a higher Injury Severity Score (ISS). The most common mechanism of injury in these cases is falling [8].

In modern humans, the common variability of the ABO gene is determined by very few nonsynonymous polymorphisms. The ABO gene encodes a glycosyltransferase that converts the O precursor antigen into A or B antigens.

Only four mutations alter the enzymatic function of glycosyltransferase responsible for A or B antigens. A single deletion can disrupt the enzymatic function of glycosyltransferase, preventing O antigens from being catalyzed into A or B. These common A, B, and O alleles maintain a higher-than-expected level of haplotype diversity—a classic sign of balanced selection [5].

Conclusion. The integration of genomic technologies into transfusion medicine marks a paradigm shift in donor selection, blood component storage, and personalized patient care. The high accuracy of genetic

prediction for blood types supports its widespread application, complementing and potentially replacing traditional serological testing. Next-generation sequencing (NGS) and advanced genotyping techniques provide more precise and comprehensive blood group identification, allowing for better management of rare blood groups and alloimmunization risks.

Population-based genetic studies highlight the importance of understanding blood group variability in different ethnic and geographic groups, which can improve transfusion outcomes and donor recruitment strategies. Moreover, ongoing research into hemoglobin function, cellular mechanotransduction, and traumatic brain injury progression further demonstrates the potential of genomic medicine beyond transfusion therapy. As the field continues to evolve, the standardization, accessibility, and clinical adoption of genetic-based transfusion strategies will be critical in ensuring safer and more effective blood transfusion practices worldwide.

REFERENES:

1. Boccoz SA, Fouret J, Roche M, Lachuer J, Legras-Lachuer C, Corgier BP, Marquette CA. Massively parallel and multiplex blood group genotyping using next-generation-sequencing. Clin Biochem. 2018 Sep;60:71-76. doi: 10.1016/j.clinbiochem.2018.07.010. Epub 2018 Aug 7. PMID: 30092181.
2. Chenna D, Polavarapu I, Shastry S. Prevalence of blood group antigens among regular blood donors: A single center study from South India with a review of national literature. Transfus Apher Sci. 2023 Oct;62(5):103747. doi: 10.1016/j.transci.2023.103747. Epub 2023 Jun 3. PMID: 37316433.
3. D'Alessandro A, Earley EJ, Nemkov T, Stephenson D, Dzieciatkowska M, Hansen KC, Minetti G, Champigneulle B, Stauffer E, Pichon A, Furian M, Verges S, Kleinman S, Norris PJ, Busch MP, Page GP, Kaestner L. Genetic polymorphisms and expression of Rhesus blood group RHCE are associated with 2,3-bisphosphoglycerate in humans at high altitude. Proc Natl Acad Sci U S A. 2024 Jan 2;121(1):e2315930120. doi: 10.1073/pnas.2315930120. Epub 2023 Dec 26. PMID: 38147558; PMCID: PMC10769835.
4. Gassner C. PIEZO1: now also featuring blood group antigens. Blood. 2023 Jan 12;141(2):123-124. doi: 10.1182/blood.2022018186. PMID: 36633886.
5. Kurbonova Z.Ch, Babadjanova Sh.A., Sayfutdinova Z.A., Tojiboyeva D.A. Qon guruhlarini aniqlash usullari va xatoliklarini o‘rganish. Journal of new century innovations. 2023 May;4(28):173-180.
6. Liu Y, Bi DM, Zhao SZ, Yan TY, Lu FL, Wang X, Jiang PY. [Gene Polymorphism 24 Rare Blood Group Antigens of 11 RBC Blood Group Systems in Manchu Population of Harbin Area in China]. Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2017 Dec;25(6):1799-1803. Chinese. doi: 10.7534/j.issn.1009-2137.2017.06.040. PMID: 29262919.
7. Moslemi C, Saekmose SG, Larsen R, Bay JT, Brodersen T, Didriksen M, Hjalgrim H, Banasik K, Nielsen KR, Bruun MT, Dowsett J, Dinh KM, Mikkelsen S, Mikkelsen C, Hansen TF, Ullum H, Erikstrup C, Brunak S, Krogfelt KA, Storry JR, Ostrowski SR, Olsson ML, Pedersen OB. Genetic prediction of 33 blood group phenotypes using an existing genotype dataset. Transfusion. 2023 Dec;63(12):2297-2310. doi: 10.1111/trf.17575. Epub 2023 Nov 3. PMID: 37921035.
8. Tutunjian AM, Arabian SS, Paolino J, Wolfe ES, Mahoney EJ, Hojman HM, Johnson BP, Bugaev N. ABO blood groups do not predict progression of traumatic intracranial hemorrhage. J Clin Neurosci. 2021 Aug;90:345-350. doi: 10.1016/j.jocn.2021.06.023. Epub 2021 Jun 23. PMID: 34275573; PMCID: PMC8290093.
9. Villanea FA, Huerta-Sanchez E, Fox K. ABO Genetic Variation in Neanderthals and Denisovans. Mol Biol Evol. 2021 Jul 29;38(8):3373-3382. doi: 10.1093/molbev/msab109. Erratum in: Mol Biol Evol. 2021 Dec 9;38(12):5835. doi: 10.1093/molbev/msab261. PMID: 33892510; PMCID: PMC8321519.