

To horizon: The use of synthetic O blood group in practical substitutive therapy

Anca Roxana LUPU^a, MD, PhD, Anca CIOBANU^b, MD, Oana CIOCAN^a, MD,
Mihaela CLOSCA-GHEORGHIU^b, MD, Carmen SAGUNA^a, MD,
Irina CARAUSU^c, MD

^a“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

^bAcademy of Medical Science, Bucharest, Romania

^c“Coltea” Clinical Hospital, Bucharest, Romania

ABSTRACT

Donated blood is routinely classified by type as A, B, AB or O and as Rh positive or as Rh negative. In the past, people with Type O/RH negative blood were considered universal blood donors. Blood types are based on the type of a molecule, called agglutinin, found on the surface of red blood cells. People in groups A and B have blood containing one of two different sugar molecules which can trigger an immune response. Those in group O have neither of these “antigens”, while those in group AB have both. Based in the idea that O blood type is an universal donor, scientists have researched for a method to remove the surface proteins on red blood cells and to transform the A, B, AB blood types in the O blood type.

Key words: blood types, agglutinin, type O/Rh negative blood

INTRODUCTION

The blood types represent populations composed of some figurative elements of the blood (erythrocytes, trombocytes, and leucocytes), characterized by certain antigens, identified for the first time on the erythrocytes, but present also in other cells of the human body. The blood types are constant and, as a

general rule, they do not modify by the environment or the age. (2)

Biochemical studies have proved that many blood type antigens are carbohydrates complexes.

Karl Landsteiner has discovered the blood type system ABO, the most important system

Address for correspondence:

Anca Ciobanu, MD, PhD, Academy of Medical Science, 19-21 Stefan cel Mare Street, District 2, Bucharest, Romania
email address: ancaciobanu05@yahoo.com

that must be taken into account in case of blood transfusions and transplants. (4)

The blood type is mainly determined by the ABO system (a group of antigens located on the surface of the erythrocyte). The blood type is determined by the presence or absence of certain inherited antigens on the surface of the erythrocyte ABH (H is a carbohydrate structure located on the surface of the erythrocytes in group O). These antigens can be proteins, carbohydrates, glycoproteins or glycol lipids – considering the blood type; some of these antigens can also be located on the surface of other cells. (4)

They exist in the blood as epitopes on the erythrocytes, but also as soluble glycol-sphingolipids forms tied with the lipoproteins of the plasma. (4)

The ABO system and the Rhesus system can determine more severe immunological reactions than other blood types systems. □

HISTORICAL DATES

The ABO system was discovered in 1901 and the RhD system was discovered in 1937.

Today, International Society for Blood Transfusions (ISBT) acknowledges 29 blood type systems. Up to the present, approx. 400 erythrocyte antigens have been discovered and as many allo antibodies. Among the erythrocyte antigens, the most immune genes are A, B (from the ABO system) and D (from the Rh system). The following are: c, E, C and Kell. (3)

In the past, the persons with blood type O negative were considered as a universal donor (meaning that any person irrelevant of the blood type can receive blood from the O negative blood type without any adverse reaction). In time, the research has proved that even O negative blood type can have antibodies that may cause severe adverse post transfusions reactions.

Based on the idea that O blood type is an universal donor, scientists have looked for a method to transform the A, B and AB blood types in the O blood type.

In 1980 Jack Goldstein and his research team have isolated an enzyme in the coffee beans that could convert B blood type into O blood type. Due to the high costs implicated by this method and to the fact that the acidity

of the environment destroyed the erythrocyte, this study was abandoned. (6)

In 2000 a clinical trial has underlined a method to convert B blood type into O blood type which can be used for transfusions for A and O blood types. This method was also abandoned due to the large number of enzymes necessary for the conversion. (6)

In 2007 a Danish research team has discovered a low-cost and efficient method to convert A, B and AB blood types in O blood type. They discovered a bacterial enzyme that could safely convert the blood types in the O blood type, by alienating sugar molecules on the surface of the erythrocytes in the A, B and AB blood types.(6)

The researchers lead by Prof. Dr. Henrik Clausen from the Copenhagen University have studied ~ 2,500 types of fungi and bacteria to discover this enzyme that can alienate the A and B antigens on the surface of the erythrocytes.

All erythrocytes contain the H antigen. In humans, the ABO gene is polymorphic with A alleles encoding A transferases, B alleles encoding B transferases and O alleles encoding inactive products. The A transferases catalyses the transfer of an N-acetylgalactosamine to acceptor H substrates and the B transferases catalyses the transfer of a galactose to the same substrates (1). For the persons with A blood type the H antigen is converted into the A antigen by the action of α 1,3-N-acetyl-galactosaminyl transferase (GTA). For the persons with B blood type the H antigen is converted into the B antigen by the action of the enzyme α 1,3 N-galactosyl transferase (GTB). If none of the two enzymes is present, the H antigen can not be modified and the blood type will be O.(1)

The scientists discovered a few enzymes (A-zyme) that can alienate GalNac converting the A blood type back to the O blood type. These enzymes are produced by bacteria from the flavo bacteria group – *Elizabethkingia meningoseptum*, which were discovered in 2002. The Copenhagen researchers discovered a recombinant version of this enzyme produced by *Escherichia coli*. A version of B-zyme was identified in the bacteria *Bacteroides fragilis*. This enzyme was produced also by the E.Coli. These two enzymes synthesized by E.Coli were used

to treat the A, B and AB blood to obtain O blood, considered the universal donor. (3)

By action at normal temperature and under neutral pH, these enzymes do not destroy the erythrocytes. It was proved that in approximately one hour they alienate the sugar molecules from the surface of the erythrocytes, and that they can be further washed away. (3)

The research team has initially taken blood from healthy persons, has converted the blood type in O blood type and than has transfused the donors. No adverse reactions were noticed, so this method has become the subject of many clinical trials. □

CONCLUSION

The enzymatic conversion processes represents an achieving of producing universal red blood cells. This discovery opens new perspectives for the blood supply, enhancing the safety of clinical transfusions.

In medicine the clinical transfusions have a large application not only in hematology but also in other specialites (surgical specialites) and blood transfusions, as supported therapy, is important to achieve an efficient response.

REFERENCES

1. Cailleau-Thomas Anne, Le Moullac-Vaidye Beatrice, Rocher Jezabel, et al – Tissue expression of the gene and of the A and B antigens. *Eur J Biochem* 2002; 269:4040-4047
2. Danielescu M – Grupele sanguine. In Paun R – *Tratatat de medicina interna*. Bucuresti: Editura Medicala, 1997; 404-434
3. Liu QP, Sulzenbacher G, Yuan H, et al – *Bacterial glycosidases for the production of universal red blood cells*. Nature Biotechnology Published online: 1 April 2007
4. Hoffman R, Benz EJ Jr, Samford JS, et al – *Hematology – Basic Principles and Practice*, second edition. Churchill Livingstone Inc. 1995; 1947-1974
5. Galel Susan A, Malone JM III, Viele Maurene K – Wintrobe's Clinical Hematology, eleventh edition. Philadelphia: Lippincott Williams&Wilkins, 2004; 832-845
6. Maugh TH II – Scientists convert blood for universal use. *The Seattle Times* 2007; 1-3