ABO blood group system

ABO Blood group antigens present on red blood cells and IgM antibodies present in the serum

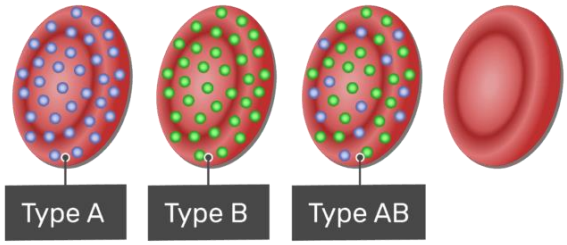
The ABO blood group system is the most important blood type system (or blood group system) in human blood transfusion. The associated anti-A and anti-B antibodies are usually IgM antibodies, which are usually produced in the first years of life by sensitization to environmental substances such as food, bacteria, and viruses. ABO blood types are also present in some other animals, for example chimpanzees, bonobos, and gorillas.

- The ABO blood group system was discovered by Karl Landsteiner in 1900. Landsteiner won the Nobel Prize in Physiology or Medicine in 1930 for this discovery. Landsteiner initially described blood groups A, B, and O; AB was later discovered by Alfred von Decastello and Adriano Sturli in 1902.
- Watkins and Morgan discovered that ABO blood group antigens are determined by specific sugars (N-acetylgalactosamine for A and galactose for B).
- In 1988, Laine's group found that the band 3 protein carries the major ABH substances.
- Yamagamoto's group later identified the exact glycosyl transferase enzymes responsible for A, B, and O antigens.

Inheritance

- A and B are codominant, giving the AB phenotype.
- Blood groups are inherited from both parents.
- The ABO blood type is controlled by a single gene (the ABO gene) with three alleles; i, I^A, and I^B. As both I^A and I^B are dominant over i .

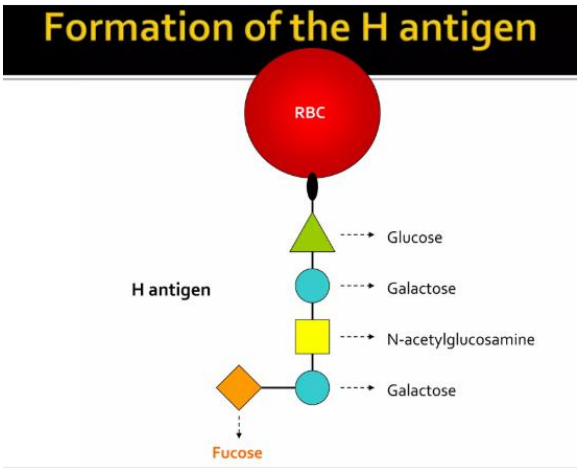
✓ I^A allele gives type A: Individuals with $I^A I^A$ or $I^A i$ have type A blood
✓ I^B allele gives type B: individuals with $I^B I^B$ or $I^B i$ have type B
✓ i allele gives type O : only ii people have type O blood
✓ A type A and a type B couple can also have a type O child if they are both heterozygous ($I^B i$, $I^A i$).
✓ People have both phenotypes, because A and B express a special dominance relationship: codominance, which means that type A and B parents can have an AB child. The cis-AB phenotype has a single enzyme that creates both A and B antigens. The resulting red blood cells do not usually express A or B antigen at the same level that would be expected on common group or B red blood cells, which can help solve the problem of an apparently genetically impossible blood group.



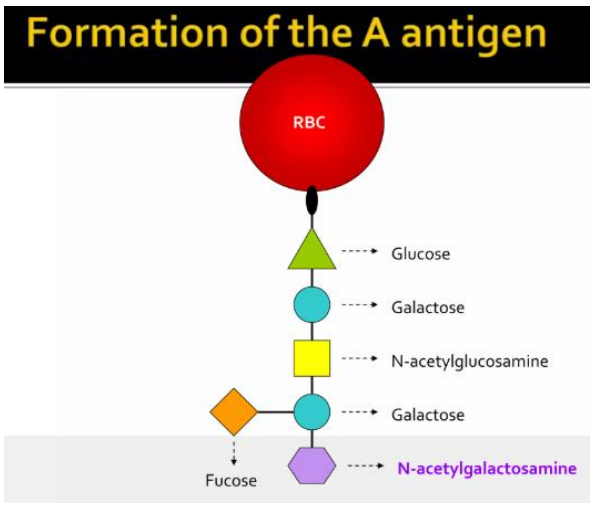
The H antigen

The H antigen serves as the essential precursor for the ABO blood group antigens.

H gene, which is located on chromosome 19 and spans more than 5 kilobases across three exons. the H gene encode a fucosyltransferase enzyme which produce H antigen .This antigen is a carbohydrate sequence primarily attached to the band 3 protein on the red blood cell membrane, and its structure consists of a chain of sugars terminating with an α-L-fucose residue linked to the terminal D-galactose.



ABO antigens, namely A and B, are synthesized from this H antigen by the action of enzymes encoded by the ABO locus on chromosome 9. The three main allelic forms of this gene : A, B, and O—determine the final blood type.

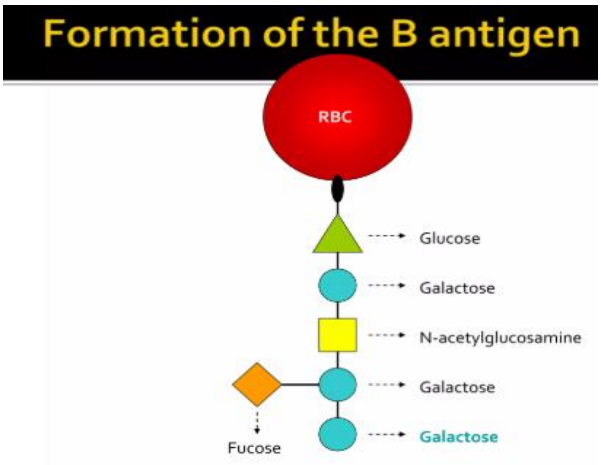


- The A allele encodes a glycosyltransferase that adds an α-N-acetylgalactosamine to the D-galactose end of the H antigen, forming the A antigen.

Subgroups

- A1 and A2 : The A blood type contains about twenty subgroups, of which A1 and A2 are the most common (over 99%). A1 makes up about 80% of all A-type blood, with A2 making up the rest. These two subgroups are interchangeable as far as transfusion is concerned, but complications can sometimes arise, in rare cases when typing the blood

- the B allele encodes a different glycosyltransferase that adds an α-D-galactose to the same position, producing the B antigen.



- In contrast, the O allele is non-functional due to a single guanine deletion at position 261 in exon 6, which causes a frameshift and premature termination of translation, preventing enzyme production. As a result, in individuals with the O blood type, the H antigen remains unmodified.
- rare Individuals do not express antigen H on their red blood cells called bombay phenotype. As H antigen serves as precursor for producing A and B antigens, the absence of H antigen means the individuals do not have A or B antigens as well (similar to O blood group). However, unlike O group, the H antigen is absent, hence the individuals produce isoantibodies to antigen H as well as to both A and B antigens. In case they receive blood from O blood group, the anti-H antibodies will bind to H antigen on RBC of donor blood and destroy the RBCs by complement-mediated lysis.

Serology

Anti-A and anti-B antibodies (called isohaemagglutinins), which are not present in the newborn, appear in the first years of life. They are isoantibodies, they are produced by an individual against antigens produced by members of the same species (isoantigens).

Anti-A and anti-B antibodies are usually IgM type, which are not able to pass through the placenta to the fetal blood circulation.

O-type individuals can produce IgG-type ABO antibodies.

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Origin theories

The origin of ABO antibodies may be linked to environmental and food antigens that have epitopes similar to A and B glycoprotein antigens. Antibodies produced against these antigens in early life can cross-react with ABO-incompatible red blood cells encountered later. Anti-A antibodies are thought to arise from immune responses to influenza virus, whose epitopes resemble the α-D-N-acetylgalactosamine on A glycoproteins, while anti-B antibodies may originate from antibodies against Gram-negative bacteria like E. coli, which cross-react with α-D-galactose on B glycoproteins.

The "Light in the Dark theory" proposes that viruses acquiring host cell membranes, which carry ABO antigens, may transmit these antigens to secondary hosts, eliciting immune responses against non-self-blood antigens and priming newborns to produce neutralizing antibodies. This theory implies a form of communal immunity that reduces the spread of blood antigens within populations, favoring antigenic diversity. However, the diversity of ABO alleles is more likely driven by negative frequency-dependent selection, where rare antigen variants are more easily recognized by the immune system, giving individuals with rare types an advantage in pathogen detection.

Disease associations with ABO blood groups:

Mechanism is currently unclear.

1. Skin cancers: Non-O blood groups (A, B, AB) have lower risk of certain skin cancers compared to O group:
    - 14% reduced risk of squamous cell carcinoma
    - 4% reduced risk of basal cell carcinoma
2. Pancreatic cancer: Type O blood is associated with a reduced risk of pancreatic cancer.
3. Ovarian cancer: Presence of B antigen (blood groups B and AB) is linked with an increased risk of ovarian cancer.
4. Gastric cancer: Blood group A has a higher risk of gastric cancer. Blood group O has the lowest risk.
5. Cholera infection: Individuals with blood group O , Have higher susceptibility to cholera infection. Suffer more severe illness if infected.