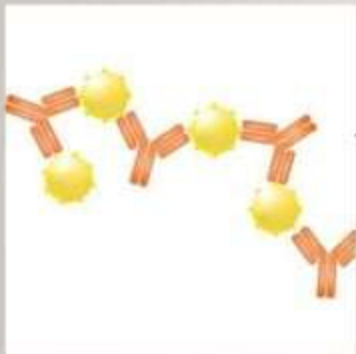
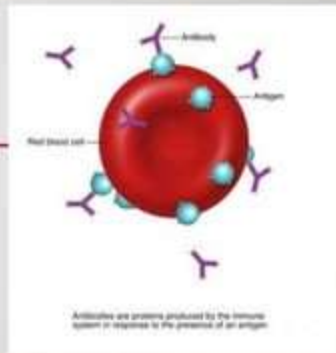


# ANTIGENS AND ANTIBODIES



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Blood... is it the same for everyone?

Why do we do all the blood bank investigations?

What decides the difference?

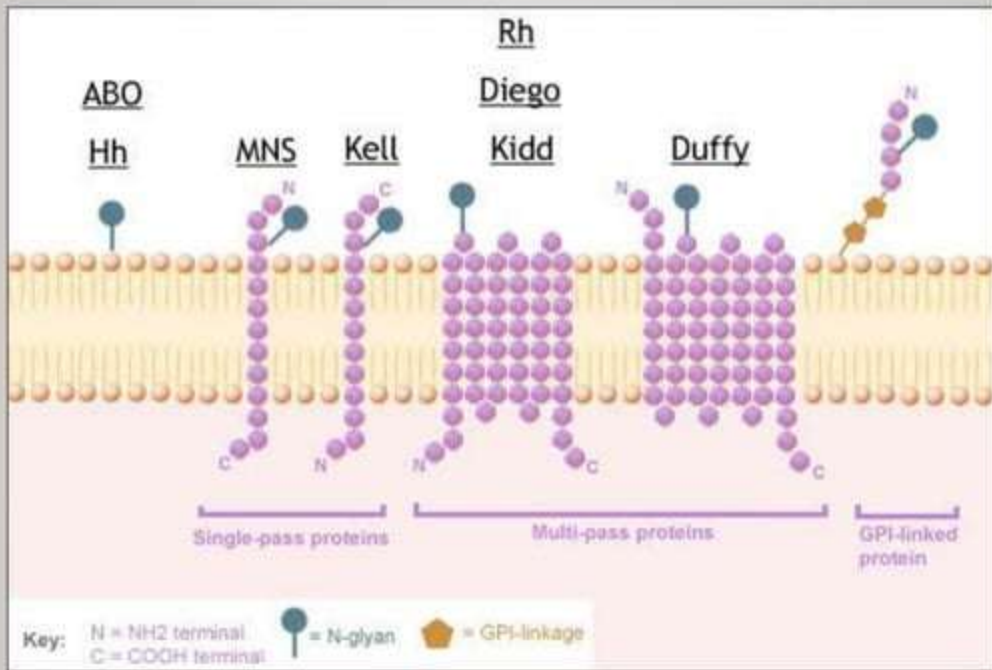
- Before the 1900s, it was thought that all blood was the same, a misunderstanding that led to frequently fatal transfusions of animal blood into humans and hazardous transfusions of blood between people.
- cells that make up the body's tissues and organs are covered with surface markers, or antigens. They are different from one person to the other.

# ANTIGEN

- Surface marker
- An antigen is any substance to which the immune system can respond.
- If the immune system encounters an antigen that is not found on the body's own cells, it will launch an attack against that antigen. Conversely, antigens that are found on the body's own cells are known as "self-antigens", and the immune system does not normally attack these.
- when patients receive blood transfusions, their immune systems will attack any donor red blood cells that contain antigens that differ from their self-antigens. Therefore, ensuring that the antigens of transfused red blood cells match those of the patient's red blood cells is essential for a safe blood transfusion.

## RED CELL ANTIGENS

- Found on RBC surface
- They determine the blood groups
- Blood group antigens are either sugars or proteins  
(ABO- sugars; RH- proteins)



- Aside from the sugar (glycan or carbohydrate) antigens, the red blood cell membrane contains three types of protein that carry blood group antigens: single-pass proteins, multi-pass proteins, and glycosylphosphatidylinositol (GPI)-linked proteins.

## Red blood cell antigens determine your blood group

- The antigens expressed on the red blood cell determine an individual's blood group.
- The main two blood groups are called ABO (with blood types A, B, AB, and O) and Rh
- The functions of many of the blood group antigens are not known, and if they are missing from the red blood cell membrane, there is no ill effect. This suggests that if the blood group used to have a function, e.g., one particular blood group antigen made red blood cells more resistant to invasion from a parasite, it is no longer relevant today.
- But the presence or absence of red blood cell antigens becomes extremely important when from different people mixes, e.g., when a patient receives a blood transfusion from a blood This also happens when a mother becomes pregnant because during labor, a small amount of fetal blood enters her circulation. In these circumstances, exposure to the foreign antigens on red blood cells can trigger immune reactions.



- It is not possible to completely remove the danger of adverse reactions when blood from two people mix, but the danger can be minimized. Before a blood transfusion takes place, the blood to be donated must be "typed and cross matched" with the patient's blood to ensure immune compatibility.
- In pregnancy, the risk of the mother's immune system attacking the foreign antigens present on her fetus' red blood cells is prevented by giving the mother antibodies to cover fetal red blood cell antigens and removing them from the mother's circulation before her immune cells find them

## The classification of blood cell antigens

- Traditionally, newly discovered red blood cell antigens were named alphabetically (e.g. ABO, MNS, P) or were named for the first person who produced antibody against them (e.g. Diego).
- In 1980, The International Society of Blood Transfusion (ISBT) Working Party on Terminology for Red Cell Surface antigens was formed to create a standard for blood group. Under this terminology, each blood group antigen has a number, and it belongs to a blood group system, a collection, or a series.

## Blood groups

- A blood group system contains antigens controlled by a single gene (or by multiple closely loci), and the system is genetically distinct. At the time of writing, there are 22 blood group systems, including the ABO, Rh, and Kell blood groups which contain antigens that can provoke the most severe transfusion reactions.
- Each blood group antigen is assigned a six-digit number by the ISBT. The first three digits represent the blood group (e.g., ABO is 001, Rh is 004), and the last three identify the antigen in the order it was discovered. For example, for ABO, the A antigen was the first to be discovered and has the number 001.001 whereas the B antigen was next and is designated 001.002.

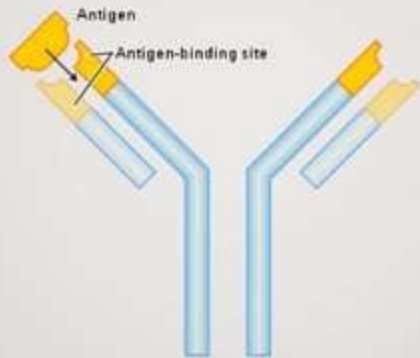
## Collections

- A collection contains antigens that are related in some way, e.g., by genetics or biochemistry, they do not meet the criteria to form a blood group. Once a collection of antigens can be to be genetically distinct, they are given the status of a blood group. At the time of writing, are six collections of antigens.

## RED CELL ANTIBODIES

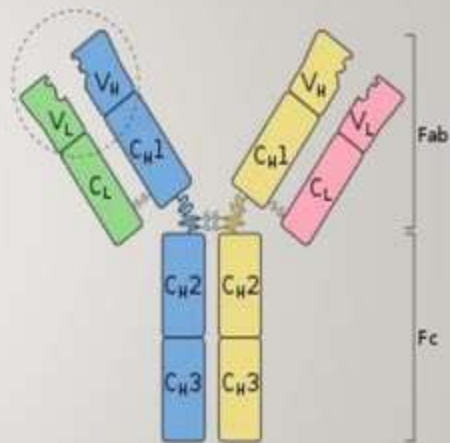
- **Blood group alloimmunization** is “triggered” when a person lacking a particular antigen is exposed to this antigen during transfusion or pregnancy or transplantation. (Immune antibodies)
- An **antibody (Ab)**, also known as an **immunoglobulin (Ig)**, is a large, Y-shaped protein produced by the immune system.
- Naturally occurring : appear within the first years of life.
- antibody's *class* or *isotype*: **IgA**, **IgD**, **IgE**, **IgG**, or **IgM**.
- The class determines the function triggered by an antibody after binding to an antigen, in addition to some structural features.

## Antigens



## Antibody

- Structurally an antibody is also partitioned into two antigen-binding fragments (Fab), containing one  $V_L$ ,  $V_H$ ,  $C_L$ , and  $C_H1$  domain each, as well as the crystallisable fragment (Fc), forming the trunk of the Y shape.
- In between them is a hinge region of the heavy chains, whose flexibility allows antibodies to bind to pairs of epitopes at various distances, to form complexes.
- The variable domains can also be referred to as the  $F_V$  region. It is the subregion of Fab that binds to an antigen.



ABO BLOOD GROUP SYSTEM



*anti-A antibodies*

*B antigens*



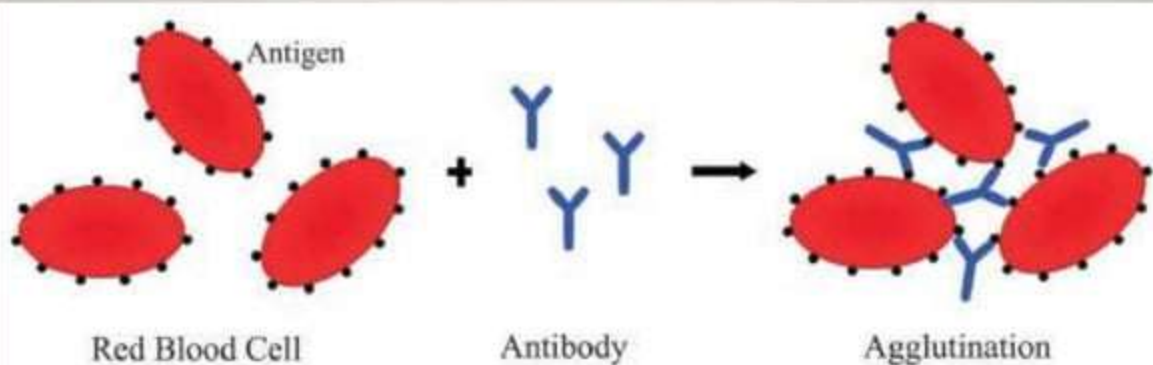


Figure 1 – Representation of the hemagglutination reaction. Blood group antigens and antibodies form a clumping of erythrocytes (modified from Parslow et al., 2004)<sup>(3)</sup>



- Assignment 01

1. Describe the structure of Immunoglobulin
2. Describe the functions of an antibody

Email the answers with following details, to [mkrishnapillai@yahoo.com](mailto:mkrishnapillai@yahoo.com)

- a. Name
- b. Roll number

# HLA- HUMAN LEUCOCYTE ANTIGENS

- Important part of the immune system and is controlled by genes located on chromosome 6.
- Surface proteins
- Two classes mainly:
  - ✓ Class I HLA: HLA-A, HLA-B, and HLA-C

Transmembrane glycoproteins on the surface of all nucleated cells. Consists of an alpha heavy chain bound to a beta-2 microglobulin molecule.

Antigen-presenting cells for CD8 T cells

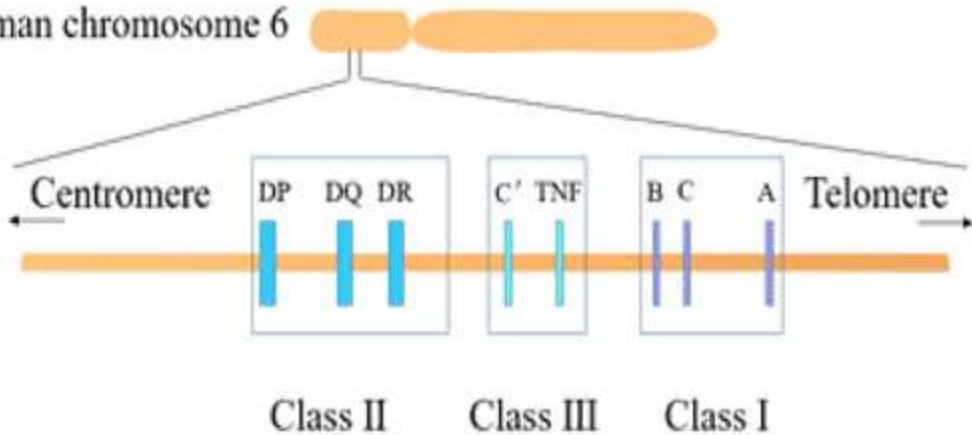
- ✓ Class II HLA: HLA-DP, -DQ, or -DR

Found on dendritic cells, mononuclear phagocytes, some endothelial cells, thymic epithelial cells, and B cells.

Antigen-presenting cells for CD4 T cells

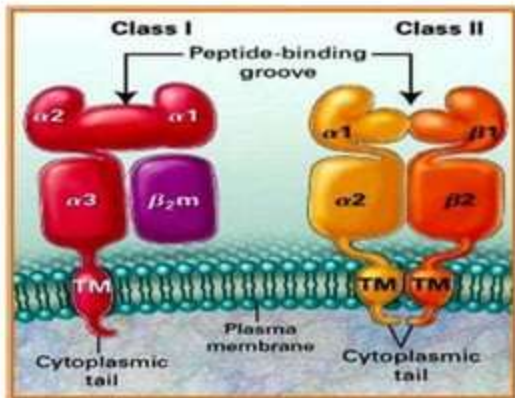
**class III region** of the genome encodes several molecules important in inflammation; they include complement components C2, C4, and factor B; tumor necrosis factor (TNF)-alpha; lymphotoxin; and three

Human chromosome 6



# HLA class I and class II antigens

- Monomer with non-covalently associated subunit ( $\beta_2m$ )
- Presents antigenic peptides to CD8+ T cells
- Expressed by all nucleated cells



- Heterodimer
- Presents antigenic peptides to CD4+ T cells
- Restricted expression on antigen presenting cells (dendritic cells, B cells, macrophages)
- Inducible on other cells (endothelium and epithelium)

# HLA AND DISEASES

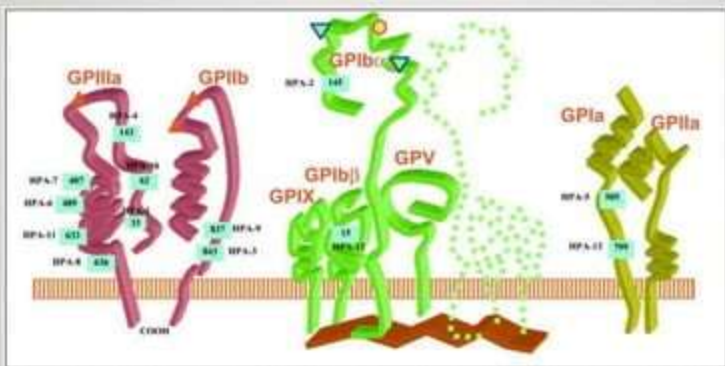
- Psoriasis to HLA-C\*06:02
- Ankylosing spondylitis and reactive arthritis to HLA-B27
- Narcolepsy to HLA-DR2 and HLA-DQB1\*06:02
- Type 1 diabetes mellitus to HLA-DQ2 and HLA-DQ8
- Multiple sclerosis to HLA-DR2
- Rheumatoid arthritis to HLA-DR4

## HLA ANTIBODIES

- Formed following exposure- Sensitization: pregnancy, after receiving a blood transfusion or organ transplant.
- Important role in deciding solid organ transplant.

# HPA-HUMAN PLATELET ANTIGENS

- **platelet specific antigens** that reside on surface membrane glycoproteins
- Other antigens- ABO, P, Le



Only one half of the GPIb-IX-V complex is shown. The HPA polymorphisms and hereditary defects are schematised according to the legend

Glanzmann's thrombasthenia: ▲

Bernard-Soulier syndrome: ▼

von Willebrand's disease-platelet form: ●

HPA polymorphism: 83T

# HPA ANTIBODIES

Produced following exposure

Neonatal alloimmune thrombocytopenia => Haemolytic disease of fetus and neonate

post-transfusion purpura



<i>Antigen</i>	<i>Glycoprotein</i>	<i>Encoding Gene</i>	<i>Phenotypic frequency</i>
<i>HPA-1a, HPA-1b</i>	GPIIIa	ITGB3	72% 1a/1a
			26% 1a/1b
			2% 1b/1b
<i>HPA-2a, HPA-2b</i>	GPIIb	GPIBA	85% 2a/2a
			15% 2a/2b
			1% 2b/2b
<i>HPA-3a, HPA-3b</i>	GPIIb	ITGA2B	37% 3a/3a
			48% 3a/3b
			15% 3b/3b
<i>HPA-4a, HPA-4b</i>	GPIIIa	ITGB3	>99.9% 4a/4a
			<0.1% 4a/4b
			<0.1% 4b/4b
<i>HPA-5a, HPA-5b</i>	GP1a	ITGA2	88% 5a/5a
			20% 5a/5b
			1% 5b/5b

**Table 1:** Commonly implicated human platelet antigens (HPA) in fetal and neonatal allo-immune thrombocytopenia (FNAIT). Adapted from: Roback JD. Technical Manual. American Association of Blood Banks (AABB); 2014.

## ASSIGNMENT 02

1. What are the methods available for HLA typing?
2. What are the methods available for HLA antibody detection?

Email the answers with following details, to [mkrishnapillai@yahoo.com](mailto:mkrishnapillai@yahoo.com)

- a. Name
- b. Roll number

- 
- Questions?

# THANK YOU!

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- Assignments should be emailed on or before 18.01.2021