Blood Group Immunity Basics

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Introduction to blood types

- Specific molecules on the surfaces of red blood cells
  - Recognition signals
- It’s long been known
  - Can sometimes mix blood from different patients
  - But sometimes mixing blood leads to a fatal response
- 1901, Carl Landsteiner reported the existence of blood types
- Blood type determination ensures that mixing of the same type of blood is okay
- Incorrectly mixed blood will agglutinate
Agglutination of blood

• Due to the presence of antibodies in serum
• Antibodies can attach to antigens on red blood cell (rbc) surface
• Antibodies cause clumping, or agglutination, of improperly typed rbc's
  – Properly typed blood will not agglutinate
Agglutination of erythrocytes

Blood typing principles - ABO

• Type A has O antigen and A antigen
  – Can receive A or O type blood
  – Can donate to A or AB type recipient

• Type B has O antigen and B antigen
  – Can receive B or O type blood
  – Can donate to B or AB type recipient

• Type AB has O, A and B antigens
  – Can receive any type blood
  – Can donate only to type AB recipient

• Type O has only O antigen
  – Can receive only type O blood
  – Can donate to any recipient
What determines blood type?

- Presence of antigens on surface of red blood cells
- Same blood type antigen is found on many cells throughout the body
- Same blood type antigen may be secreted into body fluids
  - secretors
Structures of the ABO blood type antigens

• Lodish, et al., Molecular Cell Biology, 4/e, 2000, W.H. Freeman
Antigens

• An antigen is a molecule that can stimulate an immune response
  – The ‘A’ antigen does not behave as an antigen in a blood type A person

• Immune responses are mediated by the immune system
Why do we generate an immune response against blood type antigens?

• The antigens found on red blood cells
  – Also found on other body cells
  – Also found in foreign substances

• Exposure to a substance with an antigen will stimulate an immune response

• Blood type A will not generate a response against antigen A or O
  – Will respond to an antigen that looks like B antigen

• Blood type B will not generate a response against antigen B or O
  – Will respond to an antigen that looks like A antigen
Immune system

- Cells that have the ability to recognize foreign substances
- The cells of the immune system help the body neutralize and dispose of foreign substances
Parts of the immune system

• Barrriers
  – Epithelium, mucosa, secretions
  – Act to prevent foreign substances from entering the body
  – Non-specific

• Cells
  – Lymphocytes
  – T and B cells
  – Highly specific

• Antibodies
  – Produced by the B cells
Immunity

• Specificity
  – Recognition of a wide variety of antigens
  – Determines ‘Self’ vs ‘non-self’
  – Acts to remove non-self antigens from the body
Bone marrow stem cells

- Stem cells can develop into a variety of cells
- Stem cells in the bone marrow can develop into any of the blood cells
  - Including immune cells

- Artwork originally created for the National Cancer Institute. Reprinted with permission of the artist, Jeanne Kelly. Copyright 1996
What stimulates an immune response?

- Foreign antigen
- Engulfed by macrophage
- Macrophage presents antigen pieces to helper T cell
- Mature helper T cell then helps develop the immune response

http://press2.nci.nih.gov/sciencebehind/immune08.htm
Specificity of immune response

• Only the helper T cells that recognizes the antigen is stimulated
• The specific T cell then divides into more T cells
  – clones
• Now the body has many identical helper T cells that recognize a given foreign antigen
Helper T cells

• Helper T cells stimulate B cells
  – Only the specific B cell that recognizes an antigen
• B cells divide
• B cells secrete antibodies
• Antibodies immobilize and agglutinate antigen
Production of antibodies

- Helper T cells stimulate B cells
- B cells become plasma cells
- Secrete antibodies

[Link](http://press2.nci.nih.gov/sciencebehind/immune/immune08.htm)
Antibodies

• Immunoglobulins (Ig’s)
  – Proteins that recognize antigens
  – Will bind antigens
  – Clumps groups of antigen together for easier disposal
    • Agglutination reaction

• Different classes of antibodies

• Variable regions bind to specific antigen

• http://press2.nci.nih.gov/sciencebehind/immune/immune08.htm
Immunoglobulin IgG

- Two binding sites
  - variable regions
  - Recognize antigen
- Constant region
- Binds two antigens
- Immobilizes them for removal by macrophages

Immunoglobulin structure

- IgM has a pentameric structure
  - Used in blood typing
- IgA has a dimeric structure
  - Found in secretions

Immunoglobulin E

- Associated with the surface of mast cells
- Mediates allergic reactions
- When allergen binds, the mast cells release histamine

Destruction of altered or foreign cells

- Complement
- Cytotoxic T cells

- Bind and recognize antigen on the surface of cells
- Begin process that will destroy the altered cell

Blood type antigen

• Provide **recognition** to the immune system
  – Found on many body cells
• Immune system will not attack cells with the matching blood type antigen
• Derangements in blood type antigen
  – Can occur in cancer
  – Can assist immune system in recognizing and destroying the cancer cells
Blood type antigen

- Recognition
- **Adhesion**
- Cells of organs need to stick together
- Tumor cells- antigens may be deranged
- Lack of adhesion
  - Leads to metastasis
Lectins

- Proteins that bind to carbohydrates
  - specificity
- Lectins are found in foods
  - Wheat germ agglutinin
  - Adheres to nAcetyl-glucosamine
  - Glues bread dough together
- Lectins are found on the surfaces of some Microbes
Microbial lectins

- Microbes have lectins on their surfaces
  - Aids in attachment of microbes to epithelial surfaces
  - Microbes will bind to cells that express their carbohydrate receptor
  - May be blood type carbohydrate

- Many associations between specific blood type and susceptibility to certain microbial infections
Microbial specificity

• Blood type B tends to be disposed to
  – Streptococcus
  – UTI
  – Shigella
  – Amoebiasis
  – pneumonia

• Blood type A tends to be disposed to
  – Otitis media
  – Giardia

• Blood type O tends to be disposed to
  – Helicobacter pylori
  – Candida albicans
  – Cholera
  – Yersinia (plague)
Microbial specificity

• Blood type O tends to be protected from
  – Diphtheria
  – Typhoid
Plant (and other food) lectins

• Some lectins in foods can cause problems to certain blood types
• Some lectins may be protective
  – May compete with harmful lectins for adhesion to cell surfaces
  – May Inhibit the attachment of microbes to epithelial surfaces
Blood types

• ABH/O
• Secretor/non-secretor
• Lewis antigen
• Rhesus antigen
Blood type antigen

- Defined set of carbohydrates
  - Simple sugars attached in certain orders
- Galactose on the end specifies B
- nAcetylgalactosamine on the end - A
- No sugar in the end position specifies O
ABO blood type antigens

• Lodish, et al., Molecular Cell Biology, 4/e, 2000, W.H. Freeman
Glucose

- One simple sugar
- Composed of
  - Carbon
  - Hydrogen
  - Oxygen
- Carbohydrate

http://jcbmac.chem.brown.edu/baird/Chem22/I/concepttest/testF/gluStr.html
Cell surface carbohydrates

- Found on all cell surfaces
- Blood type antigen is found on many cell surfaces
- Provide recognition between cells
- Provide a surface to interact with the world
- Carbohydrates face into the intestine
  - Interact with foods and microbes
ABO blood type

- Blood type present on outside of cell
  - Attached to the membrane of the red blood cell
  - Attached to proteins on the surface of other body cells
  - On the outside of intestinal epithelial cells
    - Directed to the inside of the intestines
    - Faces toward the food
Blood type antigen

• On epithelial surfaces
  – Available for microbes to bind

• Microbes specifically interact with epithelial surface receptor
  – Some of these are the blood type antigen
Secretor

• ~80% are secretors
  – Secreted blood type antigen
  – Into body secretions
    • Tears
    • GI tract
    • Milk
    • Saliva
Benefits of secretion of antigen

- Secreted antigen can bind lectins in secretions
- May be able to inhibit lectin binding to epithelium
- May reduce the binding of microbes to the epithelium
Lewis

• Similar to ABO blood groups
• Found on the surface of leukocytes
• Lewis antigens are important in inflammation
  – Help with cell recognition
  – Leukocytes leave the blood plasma
  – Move to the tissues in inflammation
  – Lewis antigen promotes this movement
Lewis antigen

- Found in the red blood cell
  - Lewis antigen is synthesized in other cells
  - Moves to the red blood cell
  - Attached through lipids

- Can unattach, not a permanent antigen in rbcs
Rhesus

• Another antigen found on red blood cells
• Originally found in rhesus monkeys
• Associated with erythroblastosis fetalis
  – Rh + fetus borne by Rh- mother
  – Incompatible
  – Mother’s immune system will attack the fetus
  – Usually second birth
Rhesus antigen incompatibility

• Only a problem in Rh- mothers
• Only when father is Rh+
  – Some of the offspring may be Rh+
• First birth is usually ok
  – Mother’s immune system is sensitized
• Subsequent births are at risk
• Treated with Rhogam
  – 7 months and at birth
• Can inhibit maternal immune response to Rh antigen
Summary

• Blood type antigens are on the surfaces of many body cells
• Help with recognition of cells
  – Movement of cells through body
  – Immune system self recognition
• Interact with food lectins
• Interact with microbial lectins