Antibody and Humoral Immune Response

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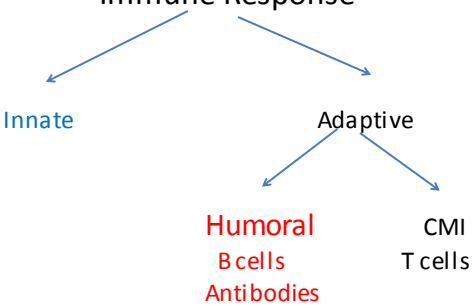
Objectives

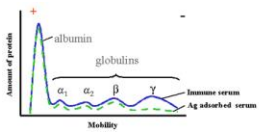
- Antibody structure
- Different classes of antibodies
- Antibody function
- Humoral immune response
  - Ag recognition
  - Activation
  - Effector
- T dependant and T independent Ags
- Primary and Secondary immune response

Immune Response



Humoral Immune response

- Mediated by proteins called antibodies/ Immunoglobulins
- Theses antibodies are secreted by activated B cells which are called plasma cells
- Antibodies are secreted into blood circulation and mucosal fluids
- Produce many effector functions



B lymphocytes

- Mediates humoral immune response
- Generated and matured in bone marrow
- Have the surface markers (proteins)
  - CD (Cluster of differentiation) 19, 20
- Express membrane bound antibodies (IgM, IgD) as receptors for antigen
- Once activated, they proliferate and differentiate into plasma cells and secrete antibodies

Antibodies/ Immunoglobulins

- Secreted by plasma cells
- Two types
  - Membrane bound (B cell receptor)
  - Secreted antibodies
- Five classes
  - IgM, IgG, IgD, IgA, IgE
- Structure
  - Biochemistry

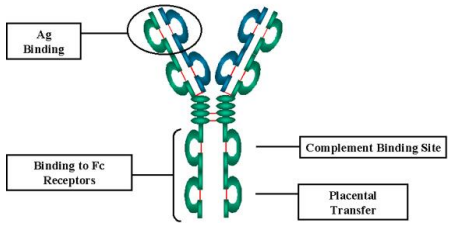
Variable region

- The amino acid sequence in the tips of the "Y" varies greatly among different antibodies.
- This gives the antibody its specificity for binding antigen – "variable region"
- The variable region includes the ends of the light and heavy chains

Constant region

- The constant region (Fc) determines the mechanism used to destroy antigen (effector function).
- Antibodies are divided into five major classes, IgM, IgG, IgA, IgD, and IgE, based on their constant region structure and immune function.

Immunoglobulin Fragments: Structure/Function Relationships



Functions of Antibodies

- Neutrilization
  - Viruses –
  - Toxins
- Opsonization
- Activation of Complements
- ADCC

Humoral Immune Response

Features of Humoral Immune response

- Specificity
  - Specific responses for distinct antigens
- Diversity
  - Respond to a large variety of antigens
- Memory
  - Enhanced response to repeated exposure
- Clonal expansion
  - Keeps pace with rapidly progressing microbes
- Specialization
  - Best response to each of different microbes
- Self limiting response
  - Return to resting state once the infection is eliminated and allow to prepare to respond to new infection

Humoral immune response

- Recognition
- Activation
- Effector

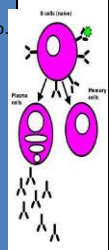
Humoral Immune Response

Recognition → Activation → Effector

By B cell receptor
Recognize proteins, CHO etc. (Antigens) of m.o.

Clonal expansion and differentiate to plasma &memory cells

Abs secreted by plasma cells
Memory cells



Recognition of Antigens in Adaptive Immune Response

- By surface receptors on B/T lymphocytes
  - Clonally distributed
  - Each clone has a unique specificity for a specific Ag
  - Massive number of receptors
  - Recognize millions of different antigens
  - Following recognition, transmit a biochemical signal to the inside of the cells

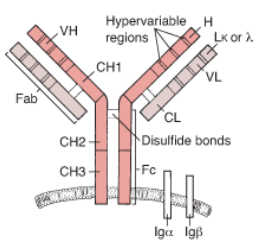
Ag Recognition

- B cells can recognize unprocessed Ags
- TCR only identifies peptide fragments of an Ag (processed Ag) displayed by a special unit called MHC molecules on APC/nucleated cells

B cell Receptor

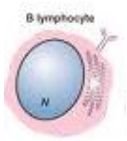
- They are membrane bound Abs (IgD & IgM)
- Act as receptors for Ags
- Able to recognize shapes/conformations of proteins, lipids, carbohydrates, nucleic acids (antigens) of microbes
- Can identify native antigens as they are (without processing)

B cell Receptor



B cell receptor	T cell receptor
Can identify • unprocessed (native) Ags • Not combined with MHC • Recognize proteins, CHO, lipids etc	Recognize Ags that are • Processed Ags • Combined with MHC molecules • Only peptides "MHC restricted"

Ag recognition



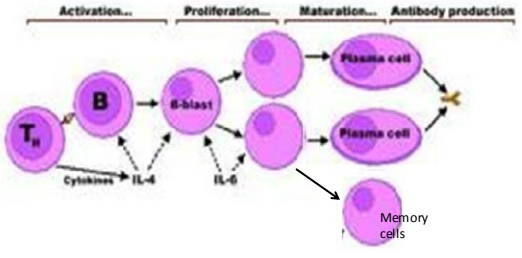
- BCR has 2 roles after Ag binding
  - Transmit signal for its activation
  - Deliver Ag into sites for processing for MHC II presentation
    (Act as professional APC)

Activation

- After recognition, B cells need 2 signals for activation
- Signal 1 – Binding of Ag to BCR
- Signal 2
  - For proteins Ags – signal from activated T cell
  - For CHO, lipids etc. - m.o. or accessory cell will provide 2nd signal

Effector phase

After activation of B cells
↓
proliferation
↓
differentiate into plasma cells
↓
produce Abs
↓
Abs circulate and enter site of infection
B cells home to peripheral L.O.
Memory cells home to germinal centres



Effector functions of Abs

- IgG
  - Neutralization of microbes and toxins
  - Opsonization
  - Activation of classical pathway of complement
  - ADCC
  - Placental transfer to neonate
- IgM
  - Activation of classical pathway of complement
- IgA
  - Provides mucosal immunity (neutralization of microbes and toxins
- IgE
  - Defense against helminths (larger parasites)
  - Mast cell degranulation (allergic reaction)

Antigens

Protein antigens (T-dependent)

- Needs T-cell (T-helper cell) help for activation
- Protein antigens
- Elicit a strong antibody response

Non protein Ags (T-independent)

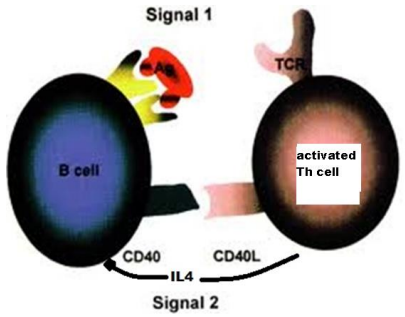
- No need of T cell help
- Lipids, carbohydrates and other non-protein antigens
- Elicit a weaker antibody response

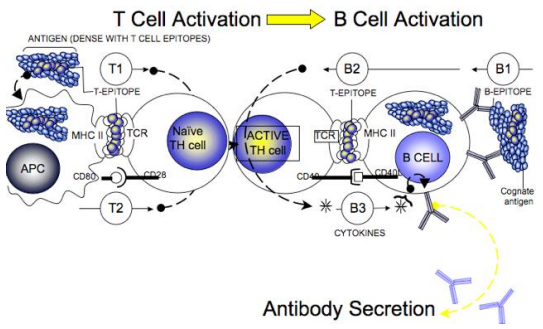
Help from T_H cells (T-dependent Antigens)

- Important for
  - Class switching
  - Affinity maturation
  - Memory

Help from T_H cells

- Naive B cells are activated by activated T helper cells by providing 2nd signal
- Both cells recognize same Ag – "linked recognition"



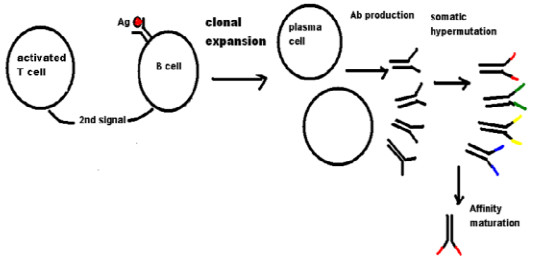


T dependant Ags

- After activation by the 2 signals B cells move to germinal centre and proliferate ⟶ clonal expansion
- During proliferation get point mutations in the gene coding "V" region – "Somatic Hypermutation"
- Produce different Abs with different a. acids in V region
- B cells that produce Abs that have highest affinity to the specific Ag will be selected

" Affinity Maturation"

Affinity maturation



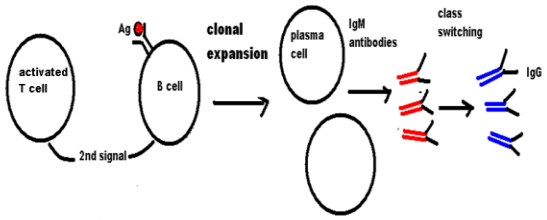
T dependant Ags

- Due to the cytokines by T_H cells
- Change in genes coding heavy chain
- Change in the Fc portion of Ab
- Produce different Ab classes with different Fc portion

"Class/ Isotope Switiching"

IgM ⟶ IgG, IgA, IgE

Class switching



T dependant Ags

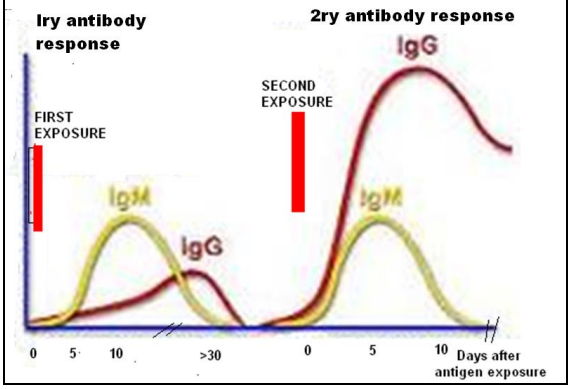
- Somatic hypermutation
- Affinity maturation
- Isotope Switing (IgM ⟶ IgG)
- Memory cells

T independent Ags

- Little/ No Somatic hypermutation
- Little/ No Affinity maturation
- Little/ No Isotope Switching (IgM is the main Ab))
- No Memory cells

Primary and secondary Immune Response

Primary	Secondary
• Ab response for first exposure	• Ab response for subsequent exposures
• Smaller amount of Abs	• Larger amounts of Abs
• Smaller peak	• Larger peak
• 5-10 days lag period	• 1-3 days lag period
• Usually IgM > IgG	• IgG > IgM
• Lower average affinity	• Higher afinity



Summary

- B cells and their receptors
- Humoral immune response
  - Ag recognition
  - Activation
  - Effector
- Functions of antibodies
- T dependant and T independent Ags
- Affinity maturation and class switching
- Primary and Secondary immune response