

NOVA

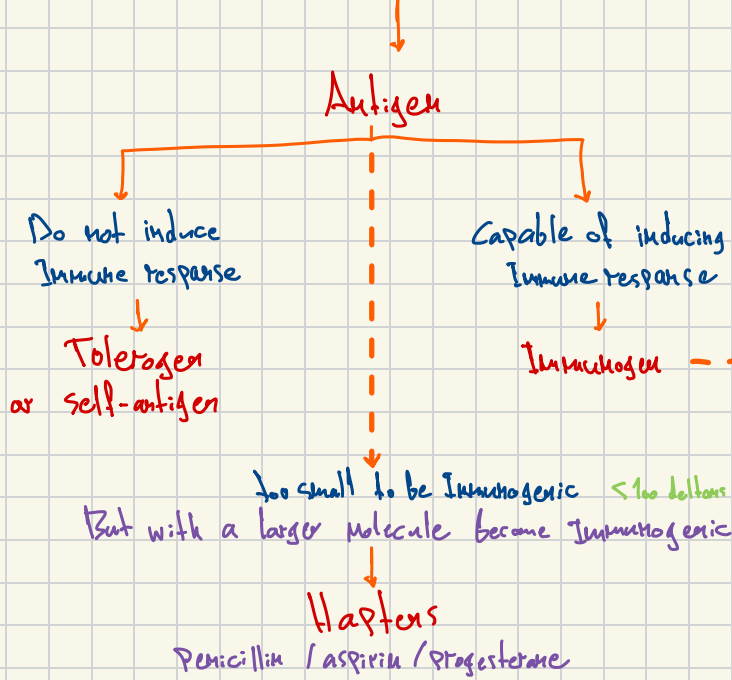
Intensive course

By: Dr. Mohammad alzuraiqi
Telegram: @mzuraiqi

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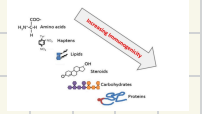
Molecule bind to component of immune system with/without immune response



Factors Increase Immunogenicity;

- Dose
- Route SC < IV < Intra gastric
- Genetic

- Foreignness
- Molecular weight
- Structural complexity

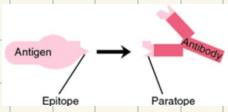


- Adjuvant

[Immunopotentiator / Immuno-booster]

↳ Enhance immune response by;

- extend presence in blood
- Aid absorption by presenting cell
- activate Macrophage / Lymphocytes
- Cytokine production



Epitopes [antigenic determinants]

Site within antigen
integral part of molecule
consist of 4-5 amino acid

Polyvalent; antigen with different epitopes



Multivalent; antigen with same epitopes

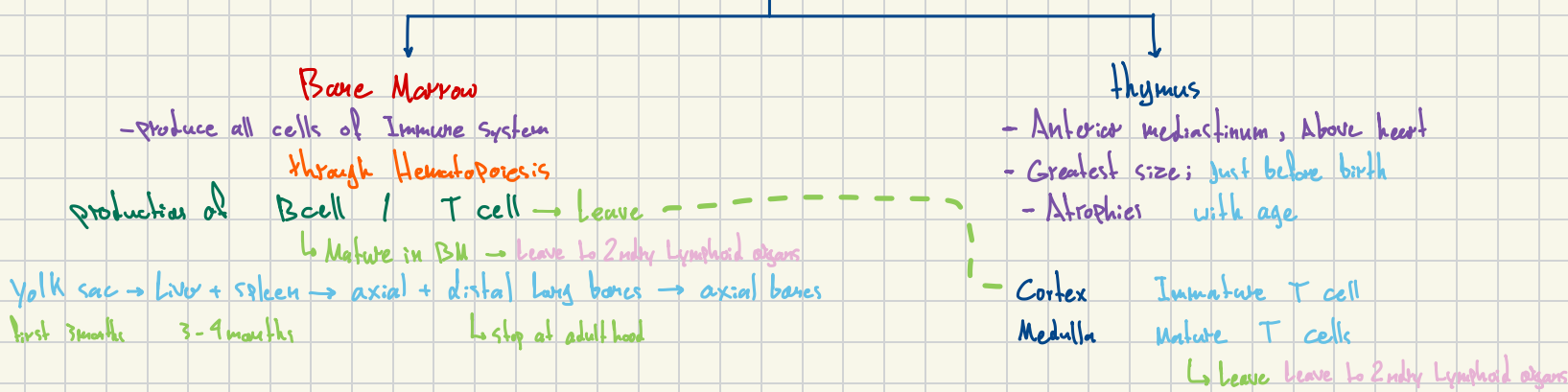


Paratopes;

site within antibody

Acquired Immunity	Active Immunity	Passive Immunity
a. Naturally Acquired Immunity	<ul style="list-style-type: none"> - Antigens enter the body naturally, triggering innate and adaptive immune responses. - Provides long-term protection. 	<ul style="list-style-type: none"> - Antibodies pass from mother to fetus across the placenta. - Infants receive antibodies through breast milk. - Provides immediate short-term protection.
b. Artificially Acquired Immunity	<ul style="list-style-type: none"> - Antigens enter the body through vaccination, prompting innate and adaptive immune responses. - Provides long-term protection. 	<ul style="list-style-type: none"> - Transfer of antibodies from immune individuals to a recipient. - Provides immediate short-term protection.

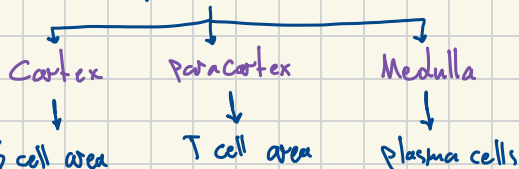
Primary Lymphoid organs
Central Lymphoid organs
Responsible for Synthesis + Maturation



* T cell deficiency + Normal B cells
↳ DiGeorge syndrome [thymic aplasia/hypoplasia]

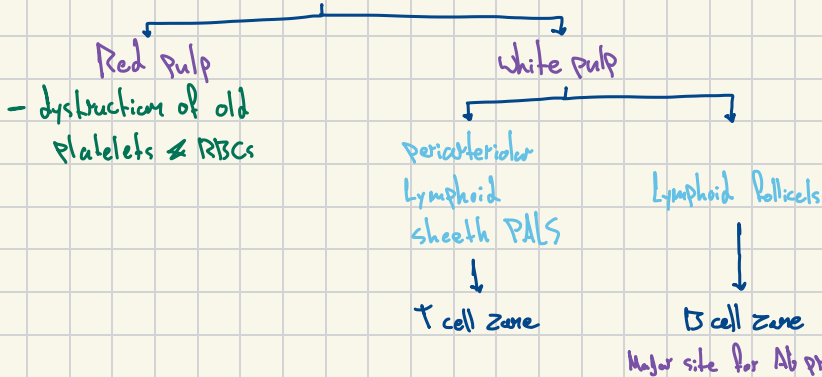
Secondary Lymphoid organs
Peripheral Lymphoid organs
Localize / trap / recognize Ag Site for Ab production

1) Lymph Node



Primary follicles: Mature resting
Secondary follicles: active + Germinal center
↳ develop in response to Ag

2) Spleen



* Plays a major role in phagocytosis of Ab-coated bacteria
* Splenectomy Pt:
↳ susceptible for infection by capsulated bacteria [Pneumococci + Meningococci]

3) Mucosa associated lymphoid tissue [MALT]

- 1) 50% of lymphoid tissue
- 2) in GI / RS / UG
- 3) produce IGA / IgE

MALT in ileum → Peyer's patches
have specialized M cells

Neutrophils:

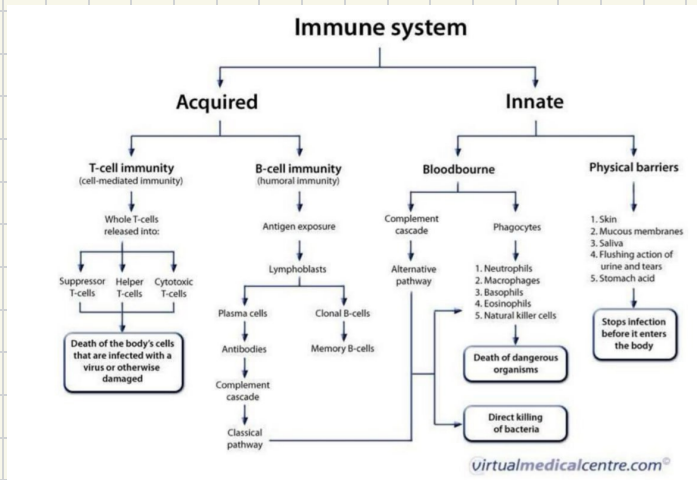
- 1- short life span 6-7hrs
- 2- can't multiply in tissue
- 3- Nucleus → 3-5 connected lobes
Polymorphonuclear Leukocytes
- 5- poorly stained

Monocytes:

- 1- longer half life 3 days
- 2- can multiply in tissue
- 3- Nucleus → kidney shaped
enter tissue → Macrophages
Ag presentation to T cells

Dendritic cells

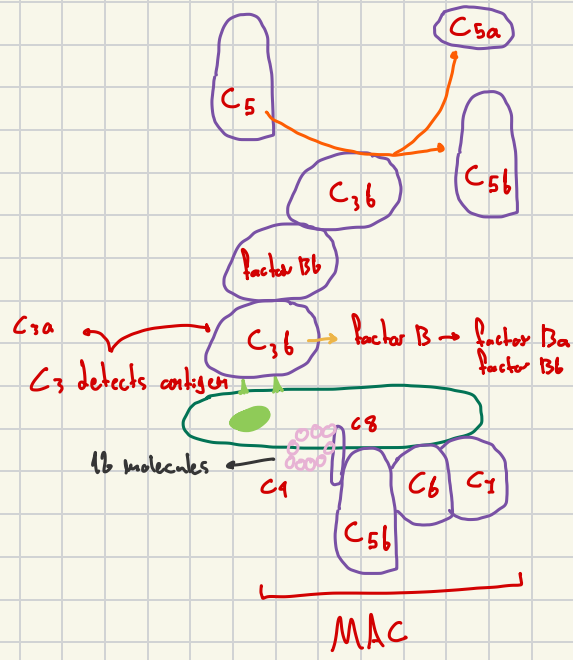
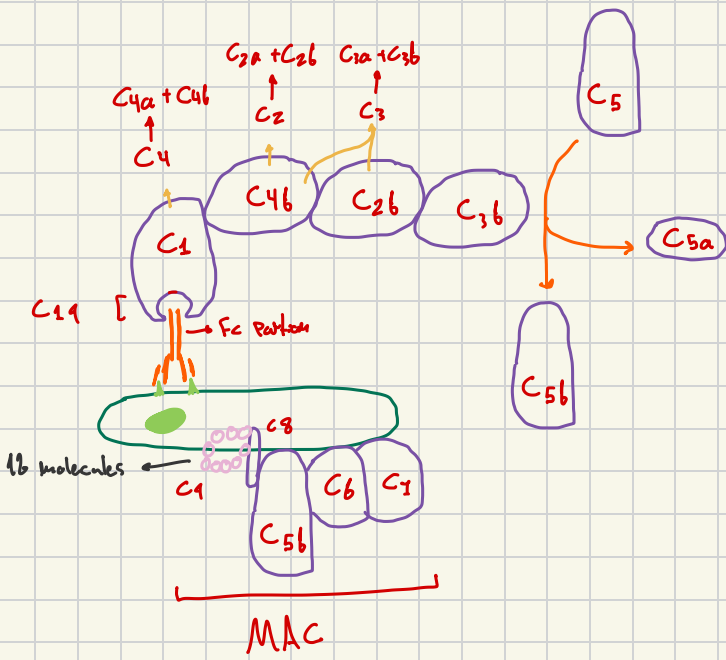
spiny projections
APC



Complement System; proteins [pro enzymes]/Not cells/ produced by liver

1) Classical pathway;
Most potent / activated by antibody IgG/IgM
"Fc portion"

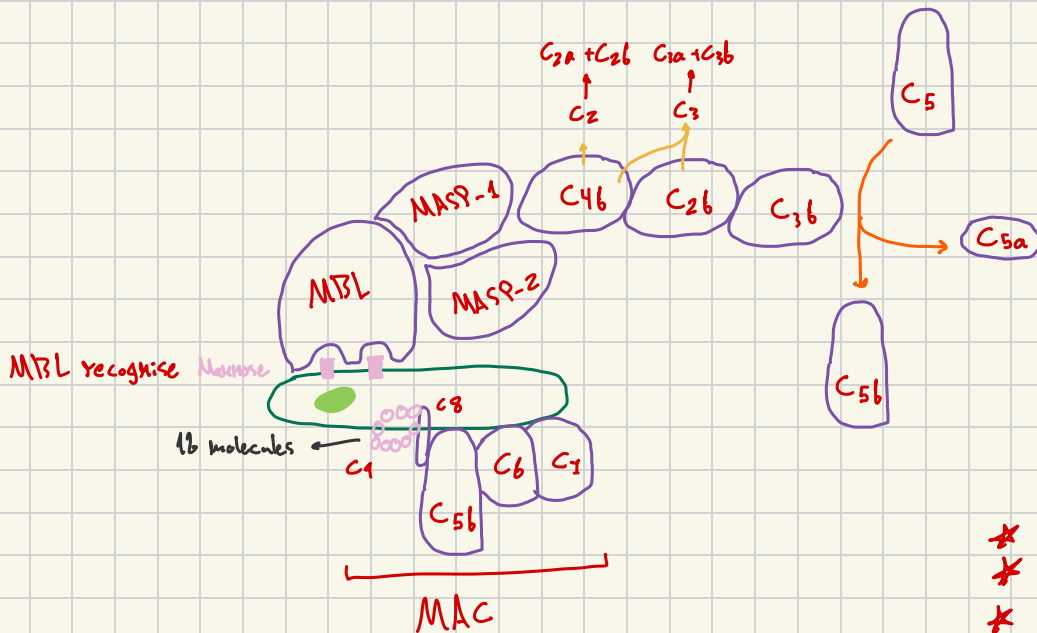
2) Alternative pathway
No previous exposure / spontaneous activation
by Lipoteichoic acid G-
Cell walls of yeast
Viral envelope



- * First complement activated = C1
- * C3 convertase = C4b2b
- * C5 convertase = C4b2b3b

- * First complement activated = C3
- * C3 convertase = C3bBb
- * C5 convertase = C3bBb3b

3) Mannan binding lectin MBL pathway



- * First complement activated = MBL
- * C3 convertase = C4b2b
- * C5 convertase = C4b2b3b

Function of Complement;

$C_{3a} / C_{5a} \rightarrow \rightarrow$ Anaphylatoxins; bind on mast cells
 \rightarrow Release Histamine
 \rightarrow Anaphylaxis
 \rightarrow Chemotaxin attract phagocytic cells
 $C_{3b} \rightarrow \rightarrow$ OPSONIZATION C_{3b} receptor on phagocytic cells

Protection against Complement;

- 1) CD59 / MAC inhibitory protein \rightarrow Inhibit C_9
- 2) Decay accelerating factor (DAF) \rightarrow Inhibit C_{3b} / C_{4b}

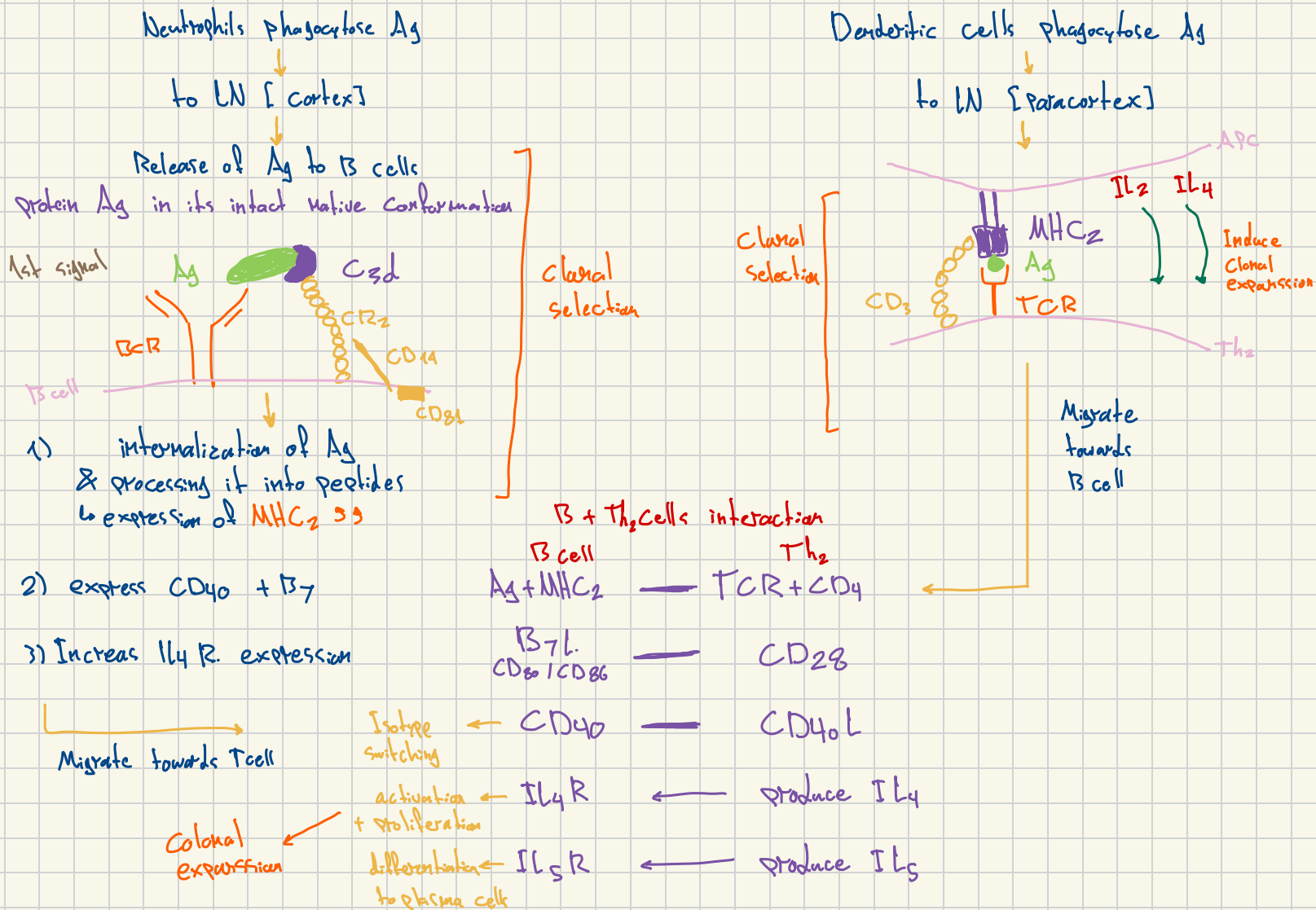
Condition	Definition	Mechanism/Pathophysiology	Key Features/Symptoms
IgA Nephropathy (Berger Disease)	Deposition of IgA in a granular pattern in the mesangium of the renal glomerulus.	IgA activates the alternative complement pathway, causing cell damage, proteinuria, and hematuria.	Typically affects kidneys; associated with defective IgA clearance, often post-upper respiratory tract infections .
Henoch-Schönlein Purpura (HSP)	Systemic form of IgA nephropathy.	Involves multiple systems (skin, connective tissues, joints, GI tract, kidneys) with purpuric rash, arthritis, and abdominal pain.	Predominantly affects children; systemic disease with widespread involvement.
Angioedema	Recurring noninflammatory generalized edema affecting skin, mucous membranes, and organs.	Continuous activation of the classical complement pathway due to C1-inhibitor deficiency . Leads to production of C_{3a} , C_{4a} , C_{5a} , activating mast cells and histamine.	Severe cases cause respiratory swelling and compromised breathing.
Paroxysmal Nocturnal Hemoglobinuria (PNH)	Complement-induced intravascular hemolytic anemia .	Defective membrane protein anchoring DAF leads to complement-mediated hemolysis by failing to block $C_{3/C5}$ convertase and MAC formation.	Causes hemolysis due to increased RBC vulnerability to complement destruction.
C3 Deficiency	Increased susceptibility to staphylococcal infections, particularly in the sinuses and respiratory tract.	Reduced production of C_{3b} impairs opsonization, decreasing phagocytosis of staphylococci.	High sensitivity to staphylococcal infections.
MAC Deficiency	Increased susceptibility to gonococcal and meningococcal infections.	Deficiency in MAC components impairs bacterial killing through the complement system.	High sensitivity to Neisseria infections.

B cell;

1) B cell receptor; $IgM^+ / IgD / Ig\alpha + Ig\beta$

Co receptors; $CD21 / CD14 / CD31 \rightarrow TAPA_1$
or CR2

2) Steps in activating B cell & Th2 "Bidirectional activation"



Isotype switch;

Switch from Membrane bound IgM into secretory $Ig [G, A, M, E, D]$

Mechanism; through allelic exclusion
changing constant part while keeping variable part unchanged

enzyme; activation induced cytidine deaminase **AID**

Hyper IgM syndrome; Inability to switch from IgM
AID deficiency
or Mutation in $CD40$ or $CD40L$

Determination factors;

first exposure IgM
second exposure IgG

Viruses IgG
Bacteria IgE

Mucosal tissue IgA

Somatic Hypermutation / affinity maturation;

to increase Ab affinity for Ag

Mechanism; Point mutation of V genes produces different affinity



Inhibiting B cell;

- $CD32 (Fc\gamma R_2B)$ Negative feedback

- $CD22$

Plasma cells;

- Do not express CD20
- **IL21** help in generation
- home; stay in Medulla of LN or Leave and home in BM

Long Lived

- Maintain Ab production
- ↳ Long life Immunity
- Do Not require Ag stimulation

Short Lived;

- Rapidly formed
- apoptosis after few days

Memory B cell;

- express high levels of anti-apoptotic protein **Bcl-2** Long life span
- CD27** protein
- home in LN or BM without secreting Ab
- ↳ secondary response
- ↳ activation → rapid response

B1 cells; 5-10%

- self renewing
- home in peritoneum / Mucosal site
- Respond to; Non protein Ag
- T cell independent manner

activate by; BCR - Ag
TLR - PAMPs

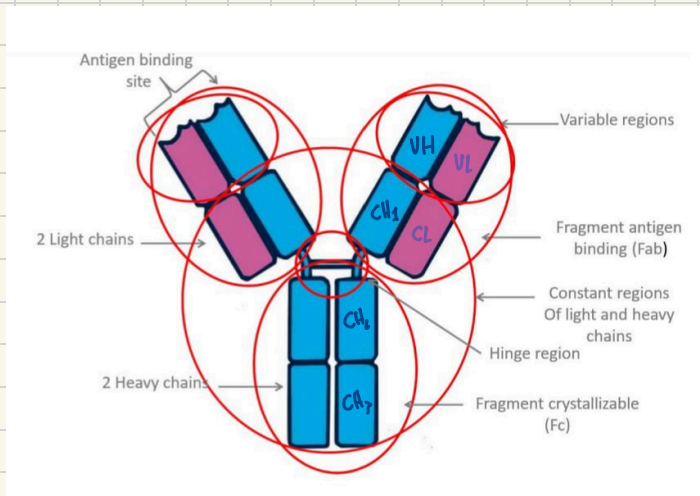
Give short lived plasma cells;

that Do Not undergo ISO type switch

Type of Ab secreted

IgM | IgA | IgG2
(Natural antibodies)

Antibody Structure;



Ab + papain enzyme = 2 Fab 1 Fc

Ab + Mercapto ethanol = tetra peptide

↳ cleavage of disulfide bond

Forces in affinity of Ab-Ag;

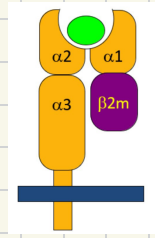
Van der waal / hydrogen / Ionic bonds

Ab	Forms	Functions	Half-Life	Special Notes
IgG	Monomeric	<ul style="list-style-type: none"> - Precipitation reaction - Agglutination - Fetal and neonatal protection - Opsonization - Immobilization of bacteria - Neutralization of bacteria and toxins 	~23 days	Predominant in blood, lymph, CSF, and peritoneal fluid Has four subclasses : IgG1 to IgG4
IgA	Dimeric (secreted) Monomeric (serum)	<ul style="list-style-type: none"> - Neonatal protection against respiratory and GIT infections - Antiviral and agglutinating functions - Cannot fix complement 	~6 days	Serum IgA function is unknown
IgM	Pentameric	<ul style="list-style-type: none"> - First antibody in response to antigen stimulation - Agglutination - Complement fixation 	~10 days	Cannot cross the placenta First antibody produced after 5 months of gestation
IgD	Monomeric	Function unknown	N/A	N/A
IgE	Monomeric	<ul style="list-style-type: none"> - Associated with hypersensitivity/allergy - Increases during parasitic infections 	~2 days	High-affinity receptors on eosinophils

MHC; Major histocompatibility complex
 encoded by large gene family [highly polymorphic]

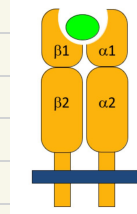
MHC type 1; on all cells

Composition: α chains; $\alpha_1 + \alpha_2 \rightarrow$ have groove for Ag
 43kDa
 $\alpha_3 \rightarrow$ anchored to cell membrane
 β_2 microglobulin; Non MHC encoded
 12kDa
 Non transmembrane
 Non covalent bond
 function \rightarrow stabilize MHCs



MHC type 2; only on APC

Composition: 2 α chains
 $\alpha_1 + \beta_1 \rightarrow$ have groove for Ag
 2 β chains



Function of MHC

- 1) Ag presentation to CTLs
- 2) transplantation
- 3) Autoimmunity

Autograph: Same organism
 allograph: Same species
 Xenograph: different species

* In order for successful transplantation
 to find donor who shares HLA genes

changes that happen to APC after phagocytosis

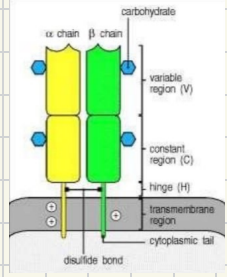
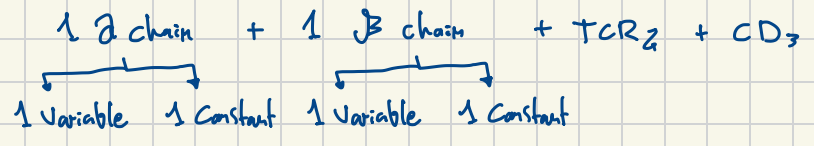
	Dendritic cells	Macrophages	B cells
Antigen uptake	+++ Macropinocytosis and phagocytosis by tissue dendritic cells Viral infection	Phagocytosis +++	Antigen-specific receptor (Ig) ++++
MHC expression	Low on tissue dendritic cells High on dendritic cells in lymphoid tissues	Inducible by bacteria and cytokines - to +++	Constitutive Increases on activation +++ to ++++
Co-stimulator delivery	Constitutive by mature, nonphagocytic lymphoid dendritic cells ++++	Inducible - to +++	Inducible - to +++
Antigen presented	Peptides Viral antigens Allergens	Particulate antigens Intracellular and extracellular pathogens	Soluble antigens Toxins Viruses
Location	Lymphoid tissue Connective tissue Epithelia	Lymphoid tissue Connective tissue Body cavities	Lymphoid tissue Peripheral blood

T cell

T cells involved in

- Intra / extra cellular pathogen immunity
- anti tumor
- Autoimmunity
- Graft rejection

TCR;

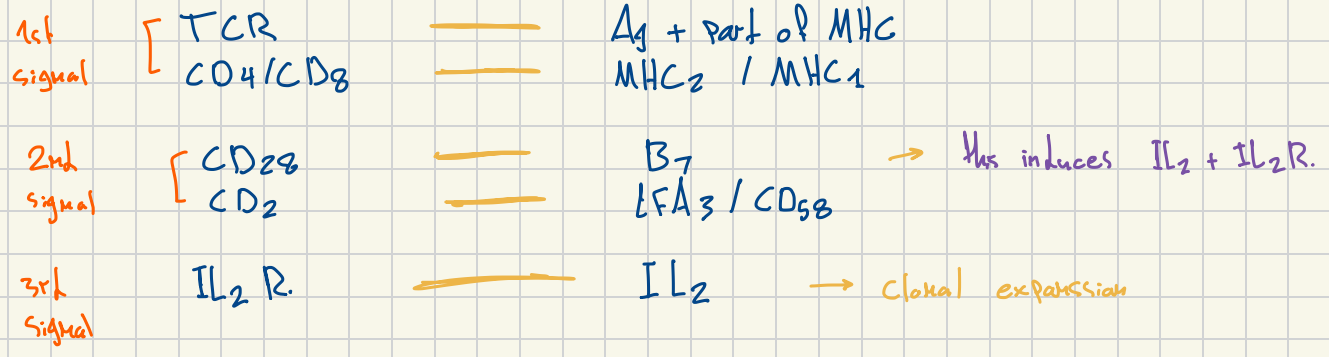


Coreceptor;

- CD4 / CD8
- CD28
- CD2
- CD40L
- IL2 Receptor

CD4 → Th₁ / Th₂ / Th₁₇
 CD8 → Cytotoxic T cell

Signals of activation



Supramolecular activating cluster; or Immunological synapse;

- area of physical contact between T cell + APC
- Intracellular molecules rapidly mobilize to site of contact

absence in any signal T cell anergy & tolerance

CD4 activation; Th₁ / Th₂ / Th₁₇

B cell activation / Ab production → Th₂
 Macrophage / DC activation → Th₁
 Inflammation → Th₁₇

Th₂ activation;
 Type of Ag; allergen / extracellular microbe / worms

activating cytokine; IL₄

Over activation; allergic reaction

cytokine produced; IL₄ B cell activation → IgG₁ / IgE
 IL₅ eosinophilic activation

IL₄ + IL₆ Macrophages Inhibition → Th₁ Inhibition

Th₁ activation;
 Type of Ag; Intracellular pathogen

activating cytokine; IL₁₂ / IFN γ

Over activation; auto immunity

cytokine produced; IFN γ CD₈ activation → Cytotoxic T cell
 Macrophage activation
 Neutrophil activation

activate B cells → IgG_{1/3}

Inhibit IL₄ → Inhibit Th₂

Th₁₇ activation;
 Type of Ag; extracellular bacteria / fungi

Over activation; organ specific autoimmunity

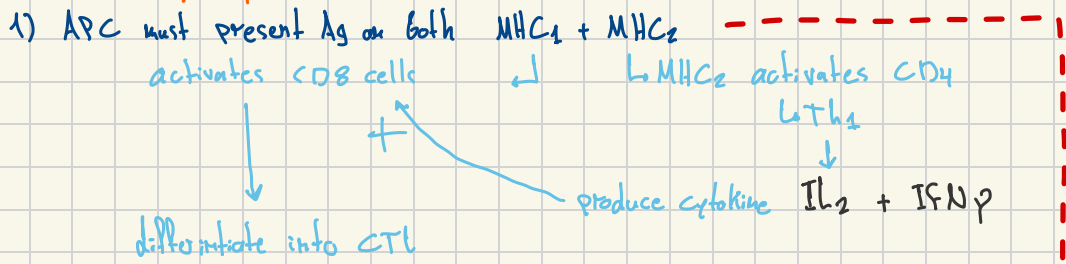
activating cytokine; IL₆ / TGF β

cytokine produced; IL₁₇ Inflammation / activate Neutrophils + Macrophages

30%

CD8;

Indirect activation; By APC



Direct activation; By Infected cells

cells with Intracellular pathogen
 \hookrightarrow express protein on MHC_1 + produce IFN_1
 \hookrightarrow activate CTL to kill

* Cross presentation:

DC phagocytose Infected cell
Tumor cells

\hookrightarrow expressed on MHC_2

How to present on MHC_1 ?

\hookrightarrow Release these proteins to cytosol
 \hookrightarrow expression on MHC_1

Killing by CTL;

- 1) Production of perforins + granzymes \rightarrow enter through pores
 \hookrightarrow Pores in cell membrane
 \hookrightarrow osmotic lysis
 \hookrightarrow activate Caspase + endonuclease
- 2) activation of Fas - FasL [apoptosis pathway]
 FasL on CTL
 Fas on target cell
 \hookrightarrow activation of Caspases \rightarrow cell death

Regulation of T cell

- 1) binding of B7 on CTLA4 instead of CD28
 \hookrightarrow Inhibition
- 2) FasL on NK / Treg
 \hookrightarrow activation of Fas on active T cells
 \hookrightarrow cell death
 "activation induced cell death"
- 3) elimination of Ag \rightarrow passive cell death
- 4) CD4 Treg
- 5) PD1 on T cell
 PDL1 \rightarrow on APC & other cells
 PDL2 \rightarrow only on APC
 \hookrightarrow Inactivate T cell
 or conversion to Treg

* Autoimmune lymphoproliferative Syndrome

Defect in Fas / FasL
 \hookrightarrow defect in apoptosis
 \hookrightarrow Lymphocyte accumulation
 \hookrightarrow Humoral autoimmunity

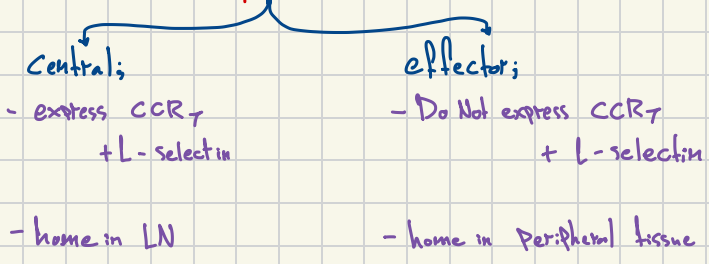
- CD4⁺ Treg;

- 1) Markers \rightarrow CD4 / CD25 / FoxP3
- 2) differentiate from CD4 cells
- 3) Generation;
 - By central tolerance
self antigen recognition in thymus
 - By Peripheral tolerance
self & foreign antigens in peripheral tissue

4) activating cytokines; IL_{10} / $TGF-\beta$

- 5) Function;
- A) IL_2 Consumption
 - B) Reduce APC ability to stimulate T cell
 \hookrightarrow By binding to B7
 - C) secrete Granzymes B
 - D) secrete cytokines
 IL_{10} \rightarrow inhibition of Macrophages / DC / Th_1 / CD8
 \hookrightarrow inhibit IL_{12} \rightarrow inhibit Th_1 / CD8
 \hookrightarrow inhibit MHC_2 + costimulatory molecules
 $TGF-\beta$ \rightarrow inhibit T cell & Macrophages

Memory T cells



* Inappropriate T cell activation;

Super antigen;

- Non specific activation of T cell

↳ massive cytokines release

- Mechanism; Binds on outer part of MHC₂
only binds to V β chain of TCR

instead of both V β & V α

[0.01% → 10%]

- effects; High levels of IL₁ / TNF α / IL₂

→ fever / vascular leakage / toxic shock syndrome

* Privilege site;

areas with No immune response

anterior chamber of eye

+ testes

Mechanism; high levels of

IL₁₀ / TNF β

Migration inhibiting factor

• The immunoglobulin superfamily includes:

- Antigen receptors of T and B cells
- CD3
- Co-receptors CD4 and CD8
- Most Fc receptors
- CD28 and B7 adhesion molecules
- Cytokine receptors
- MHC molecules

