

**Skin, Eyes, Respiratory Tract, Digestive Tract, Genitourinary Tract**

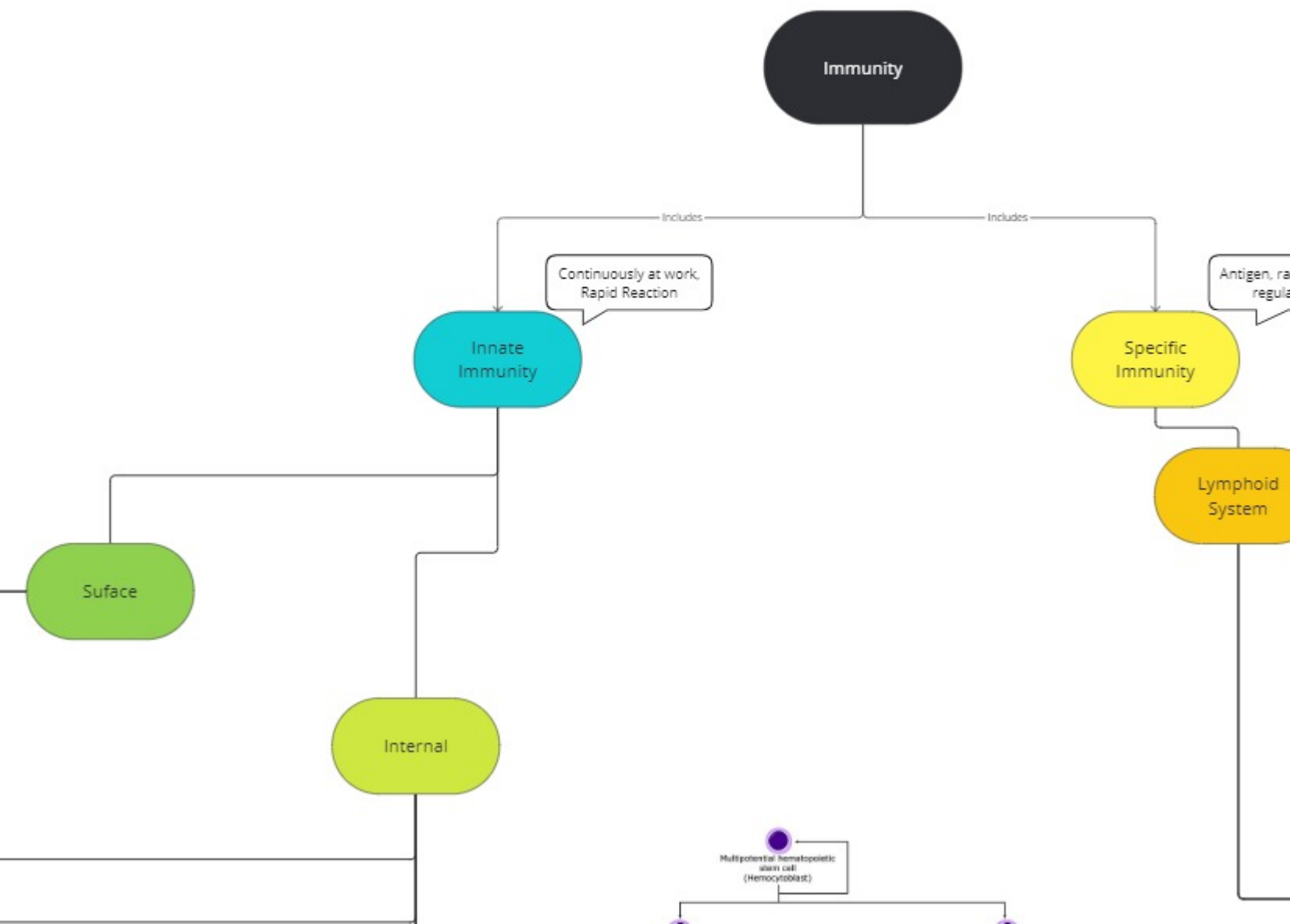
- low pH (acidic)
- enzymes
- antimicrobial peptides (defensins)
- temperature (fever)

### Complement

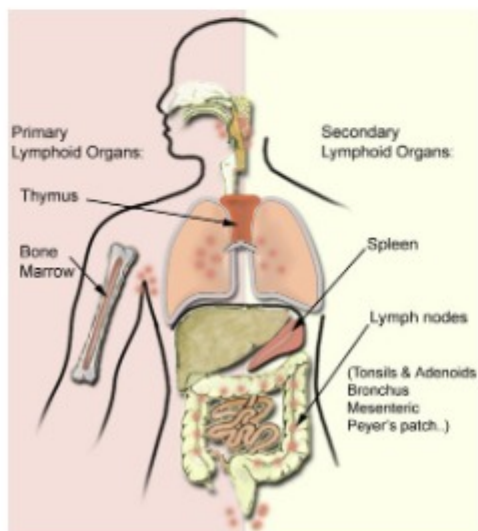
- system that is used as an "alarm and a weapon"

Complement fragments include: C3a, C3b, C3d, C4a,  
and C5a,

MAC (membrane attack complexes, aka lytic units) is  
made, leading to lysis or apoptosis of cells



randomly generated,  
not induced, inducible



**Antigen:** Substance recognized  
by the immune system



### Alternate/Properdin Pathway

- activated by bacteria and bacterial products
- after starting, cascade continues similar to classical pathway

### Lectin Pathway

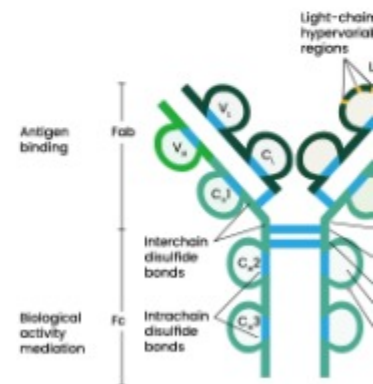
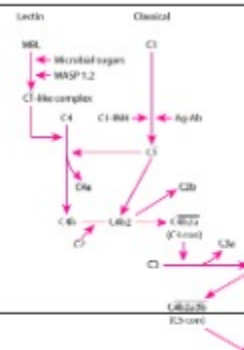
- activated by lectin binding to sugars on the bacterial/fungal cell surface
- mannose binding protein binds to nonreducing sugars, such as mannose, fucose, and glucosamine on bacterial, fungal and other surfaces
- after cleavage of components, joins the classical pathway

### Classical Pathway

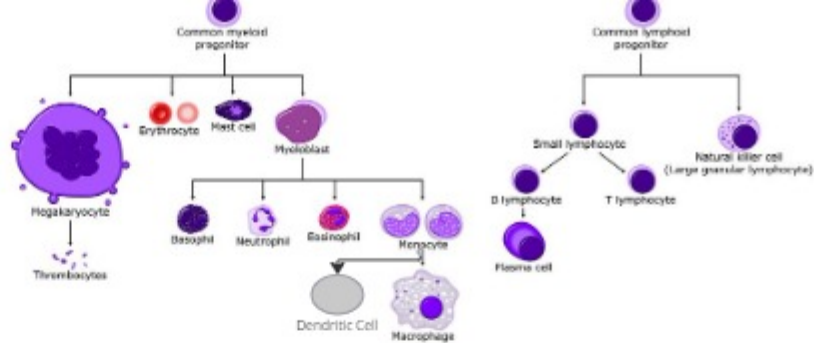
- activated by complexes of antibodies and antigens
- binding of C1 to Fc part of antibody (which is bound to the cell surface antigens/immune complex with soluble antigens)

### MAC (Membrane Attack Complex)

- aka lytic unit
- complex formation leads to apoptosis or hypotonic lysis of cells







### Macrophages

Living cells, can come from either embryonic yolk sac or marrow-derived monocytes

- phagocytic, phagocytosis of debris and microbes
- antigen presentation to T cells
- secretes cytokines for maintenance, repair, antimicrobial activity, or to promote inflammation
- kill phagocytosed bacteria
- markers include: Fc, CR1, CR3, MHC2
- activated by IFN- $\gamma$  (classical activation) made by NK cells and CD4/CD8 T cells
- Chronic stimulation can lead to fusion of macrophages, leading to multinucleated giant cells and large macrophages (epithelioid cells) which surround infections and form a granuloma

### Natural Killer (NK) Cells

- kill antibody-decorated cells and virus infected/tumor cell
- Innate Lymphoid cell, large granular lymphocytes
- Markers include: Fc (with a special one for IgG), KIR, complement receptors for ADCC, and NK-specific inhibitory & activating receptors
- Antibody dependent cellular cytotoxicity (ADCC), so they only kill cells coated with antibodies, doesn't recognize antigens nor need antigen presentation
- activated early in infection
- granules contain perforin (pore forming protein), and granzymes (esterases, also found in cytotoxic T cells)

### NKT Cells

- similar to both NK cells and T cells
- express NK cell receptors, TCR, and CD3
- Responsible for rapid response to infection though cytokine release

NK and T cells produce IFN- $\gamma$ , which activates macrophages and DCs to enforce a protective TH1 cycle of cytokines & local cellular inflammatory reactions

### Dendritic Cells

- most potent APC
- initiates and determines nature of T cell response
- "octopus like tendrils"
- Subclasses: Langerhans cells

**Apoptosis:** controlled cell death, can be induced by granzymes found most commonly in CD8 T cells

### Immature Dendritic Cells

- capture and phagocytose

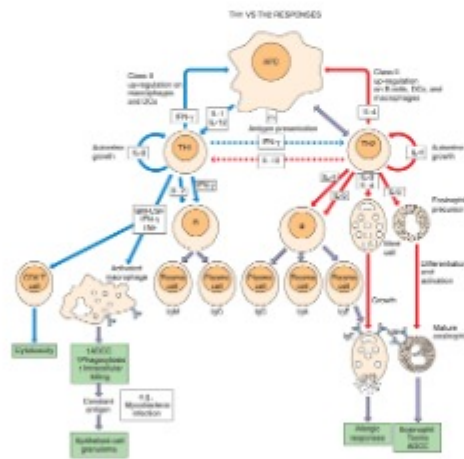


## T Cell

- Mature in the thymus
- Markers include: CD2, CD3, TCR (T Cell Receptor, including CD4 and CD8), cytokine receptors, and adhesion proteins
- Regulate, suppress, and activate immune and inflammatory responses by cell-to-cell interactions and by releasing cytokines
- directly kill virally infected cells, foreign cells, and tumors via apoptosis
- TCR complex is made of the TCR and CD3

Can differentiate into

Can differentiate into



## CD4 T Cells

- Interact with MHC2 on APC's to become activated
- aka Helper T Cells
- release cytokines
- TH0 make cytokines, promote lymphocyte growth and activate DCs
- TH1 response happens as an early response to infection, activating cellular and antibody responses. It also amplifies local inflammation reactions and delayed hypersensitivity reactions by activating macrophages, NK cells, and CD8 cytotoxic T cells.
- TH2 response is the normal T cell response, happening after infection through antibody mediated responses. It promotes antibody production to antigenic debris through IL2.
- TFH (follicular helper T cells) relay cytokine responses (TH1/TH2) to B cells, promoting production of proper antibodies
- Treg Cells are antigen specific suppressor cells, they suppress over the top reactions, keeping T cell responses under control, as

## CD8 T Cells

- interact with MHC1 on all nucleated cells
- aka Cytotoxic T Cell, aka Killer T Cells
- Contain granules that contain granzymes (esterases) and perforin (pore forming protein), which induces apoptosis
- Suppressor T cells can suppress through inhibitory cytokines and MHC1 molecules

## Memory T/B Cells

- long live antigen responsive cells, prepared for future attack by preserving "recipe" for specific antibodies/function

## Im

- provide infection ag blood, neut elimin
- can also ac antibody
- made of 2
- 5 forms, t IgM, and IgA
- Has a vari
- Fc part (the of molecu receptors c

### B Cell

- mature in bone marrow  
Activated by antigens and T cells  
Markers include: surface antibody, MHC2  
- Produce antibody  
- internalize, process, and present antigens to T cells to get help

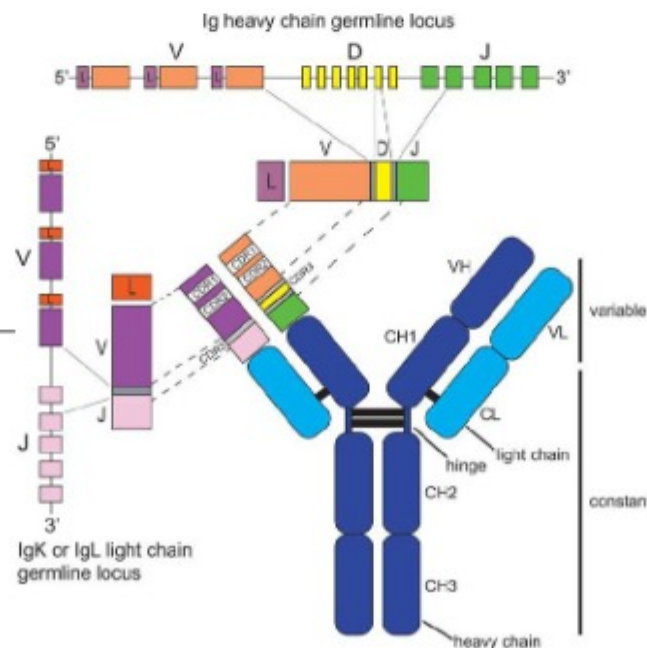
Can differentiate into

### Plasma Cells

- antibody factories

### Immunoglobulins/Antibodies

protection from rechallenge by an agent, block spread of the agent in the body, neutralize virulence factors, and facilitate elimination of the infectious agent. They also act as stimulators for appropriate B-cell activation and as stimulators for antibody factories to grow and make more antibodies. They are composed of two heavy and 2 light chains, connected by disulfide bonds. There are four types: IgG, IgM, IgA, and IgE. IgG is the most common (IgG, IgM, IgA) whereas the other two are not (IgD and IgE). The variable binding region which is used to identify different antigens. The constant region (stem) fixes complement and binding to cell surface immunoglobulin receptors on macrophages, NK cells, T cells, etc.





Inducer, Cells (producer and responder), Time course, Outcome, Cytokines

### INTERLEUKIN-1

Macrophages ,  
Fibroblasts, endothelial  
cells & few epithelial cells

Stimulates expression of  
endothelial adhesion  
molecules  
Emigration of neutrophils &  
macrophages  
Secretion of other cytokines  
Fever

@VijayPatho

### INTERLEUKIN-6

Macrophages, Fibroblasts  
endothelial cells & few  
epithelial cells

Systemic Response:  
Production of  
Acute Phase Reactants  
from liver  
Particularly important in  
inducing B-Cells to  
differentiate into antibody  
producing Cells (Plasma  
Cells)

### INTERLEUKIN-17

T Lymphocytes

Recruitment of  
neutrophils and  
monocytes  
Secretion of other  
cytokines like **IL-6, G-CSF,**  
**GM-CSF, IL-1 $\beta$ , TNF- $\alpha$ ,**  
**chemokines**

### Phagocytosis

- bacteria or fungus by macrophages and neutrophils
- 3 steps: attachment, internalization, digestion
- attachment: mediated by receptors for carbohydrates (like lectin), fibronectin, and receptors for opsonins (IgG and complement binding)
- internalization: plasma folds around particle/microbe (forming a phagosome)
- digestion: vacuole fuses with lysosomes/ granules, which allow for digestions of the vacuole contents
- process can be done with or without antibodies depending on specific

phagocytes and  
phagocytosis, and digestion  
of pathogens for cell surface  
receptors, like for mannose  
and surrounds the  
(phagocytic vacuole)  
with the primary  
lysosomes inactivation and  
the contents  
without oxygen  
consumption

(skin), dermal interstitial cells, and  
others located in the liver,  
thymus, spleen, and germinal  
centers of lymph nodes  
- produce large amounts of  
cytokines in response to viral and  
other infections  
- come from monocytes or stem  
cells  
- these are the only APC's that can  
initiate an immune response with  
a naive T lymphocyte, and they  
determine the response type  
- Mature DC's are antigen  
presenting, able to initiate an  
antigen-specific T-cell response

antigen, releasing cytokines to  
activate other immune responses  
- considered matured when  
activated by inflammatory  
cytokines  
- when mature, move to lymph  
nodes (where T cells are)  
- Presents antigen on MHC1 and  
MHC2  
- Langerhans are an example of  
Immature DC's, which stay in the  
skin until activation, becoming a  
mature DC

- CD is "cluster of differentiation"  
how monoclonal antibodies  
- MHC is "major histocompatibility  
complex" and is found on all  
cells  
- CD can be used to identify  
subsets, thymocytes, and  
and CD8, in T cells, which  
cells, which  
- MHC can be used to identify  
subsets, thymocytes, and  
and MHC2, in T cells, which  
nucleated cells, which  
ones that  
- MHC1 and

#### APC's (antigen presenting Cells):

- Monocytes
- Immature Dendritic Cells
- Dendritic Cells
- Langerhans Cells
- Macrophages



**CD and MHC**

ter of differentiation", which are  
lonal antibodies identify specific  
antigens

major histocompatibility complex",  
und on all cells with a nucleus  
be broken down into different  
e most common two being CD4  
a which CD4 is meant for helper  
ile CD8 is meant for cytotoxic  
functions






be broken down into different  
most common two being MHC1  
in which MHC1 is present on all  
ells (which is important for even  
are infected), whereas MHC2 is  
reserved for APC's  
CD8 interact, and MHC2 and CD4  
interact

keeping T cell responses under control, as  
well as helping development of memory T  
cells

sciencenotes.org

## 5 Types of Antibodies


Antibodies or immunoglobulins (Ig) are Y-shaped proteins that recognize unique markers (antigens) on pathogens.

 <p><b>IgA</b></p> <p>Secreted into mucous, saliva, tears, colostrum. Tags pathogens for destruction.</p>	 <p><b>IgD</b></p> <p>B-cell receptor. Stimulates release of IgM.</p>	 <p><b>IgE</b></p> <p>Binds to mast cells and basophils. Allergy and antiparasitic activity.</p>	 <p><b>IgG</b></p> <p>Binds to phagocytes. Main blood antibody for secondary responses. Crosses placenta.</p>	 <p><b>IgM</b></p> <p>Fixes complement. Main antibody of primary responses. B-cell receptor. Immune system memory.</p>
--	--	---	--	---

- antibody can

- VDJ gene se  
make varia  
directional rec

- variation (b  
where a sw  
changes the  
region), bu



### **Immunogenetics**

recognize at least  $10^8$  structures, but  
can still focus responses  
gments are genetically recombined to  
tions of variable regions, promoting  
ombination and loss of the intervening  
DNA sequences  
be need) can result in class switching,  
itch site is physically changed, which  
function of the antibody molecule (Fc  
t not the specificity (variable region)