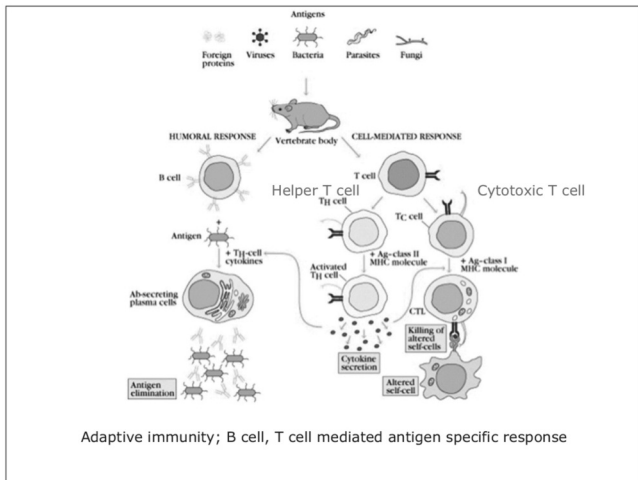
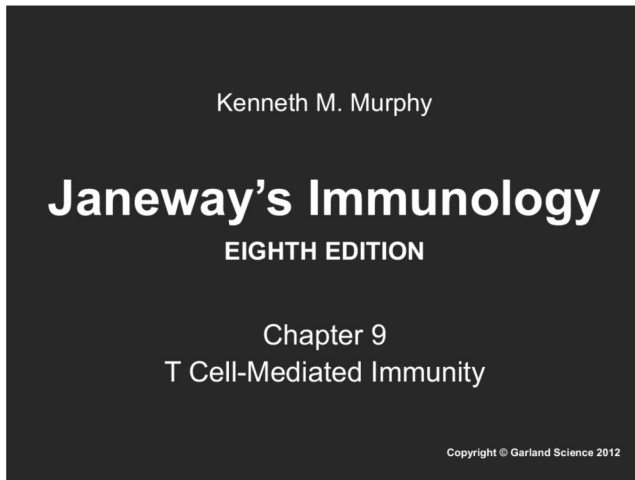




Naïve T cells; Mature recirculating T cells that have not yet encountered their specific antigens

Effector T cells; Activated and differentiated T cells after encounter their specific antigens

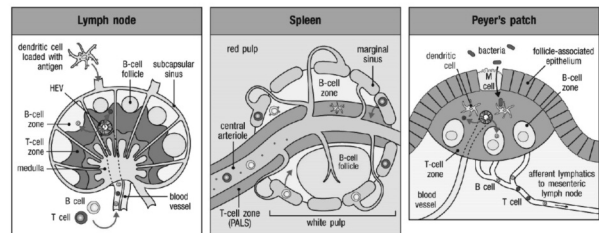
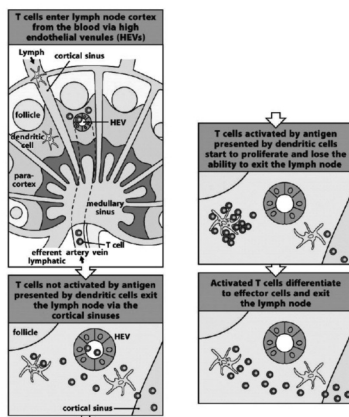
Memory T cells; generated from primary T cell response which are long-lived cells that give an accelerated response to antigen, which yields protection from subsequent challenge by the same pathogen.

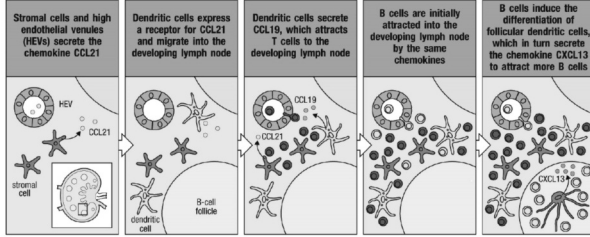
Roles of effector T cells

	CD8 cytotoxic T cells	CD4 T _H 1 cells	CD4 T _H 2 cells	CD4 T _H 17 cells	T _{reg} cells	CD4 regulatory T cells (various types)
Types of effector T cell						
Main functions in adaptive immune response	Kill virus-infected cells	Activate infected macrophages. Provide help to B cells for antibody production	Provide help to B cells for antibody production, especially switching to IgE	Enhance neutrophil response. Promote barrier integrity (skin, intestine)	B-cell help. Isotype switching. Antibody production	Suppress T-cell responses
Pathogens targeted	Viruses (e.g. influenza, rabies, vaccinia). Some intracellular bacteria	Microbes that persist in macrophage vesicles (e.g. mycobacteria, listeria, Leishmania donovani, Pneumocystis carinii). Extracellular bacteria	Helminth parasites	Klebsiella pneumoniae. Fungi (Candida albicans)	All types	

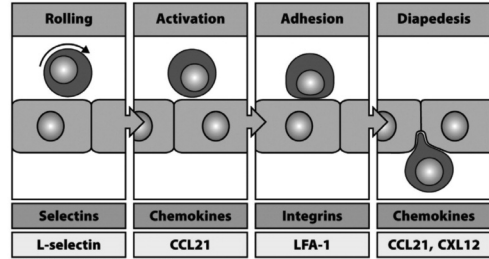
Figure 9.1 Janeway's Immunobiology, 8th ed. (© Garland Science 2012)

Entry of naïve T cells and APCs into PLNs



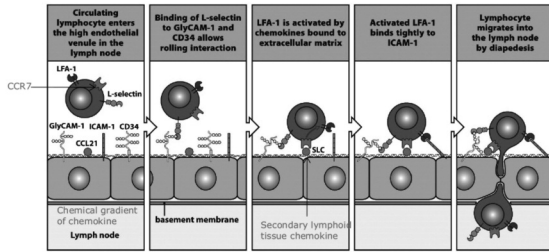


Lymphocytes entry into lymphoid tissues depends on chemokines and adhesion molecules

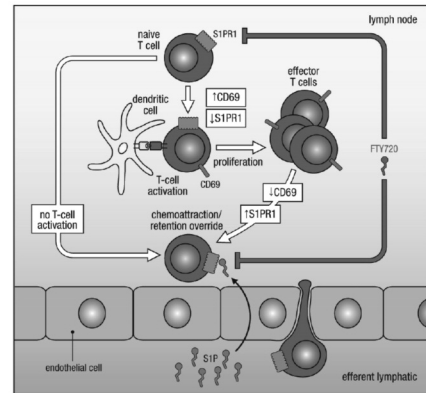


L-selectin (Cd62L); leukocytes
P-selectin (CD62P), E-selectin (Cd62E); vascular endothelium

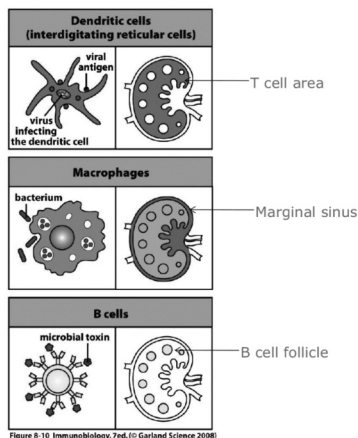
Lymphocytes entry into lymphoid tissues depends on chemokines and adhesion molecules



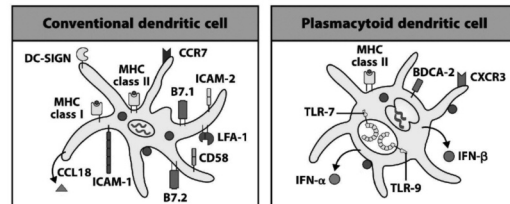
ICAM-2 is expressed constitutively on all endothelial cells, whereas on the absence of inflammation, ICAM-1 is expressed only on the high endothelial cells of peripheral lymphoid tissues.



APCs are distributed differentially in the lymph node

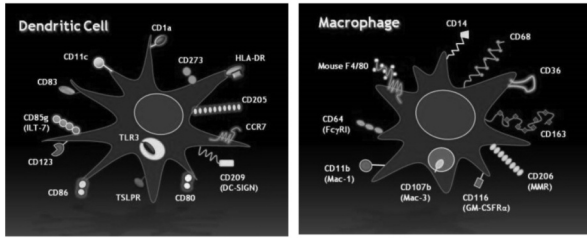


There are two different functional classes of DCs



Conventional dendritic cells; primarily concerned with activation of naive T cells.

Plasmacytoid dendritic cells; primarily for viral infections and secrete large amounts of class I interferons. These cells are less efficient in priming naive T cells.



The predominant leukocyte integrin is a separate marker for dendritic cell and macrophage.

CD11c is a marker for DC
CD11b is a marker for Macrophage, resting macrophage do not express MHCII and B7.

The different routes of antigen processing and presentation by DCs

	Routes of antigen processing and presentation by dendritic cells				
	Receptor-mediated phagocytosis	Macro-pinocytosis	Viral infection	Cross-presentation after phagocytosis or macropinocytosis	Transfer from incoming dendritic cell to resident dendritic cell
Type of pathogen presented	Extracellular bacteria	Extracellular bacteria, soluble antigens, virus particles	Viruses	Viruses	Viruses
MHC molecules loaded	MHC class II	MHC class II	MHC class I	MHC class I	MHC class I
Type of naive T cell activated	CD4 T cells	CD4 T cells	CD8 T cells	CD8 T cells	CD8 T cells

Figure 8-12 Immunobiology, 7ed. (© Garland Science 2008)

Transfer antigen to resident DCS in PLN

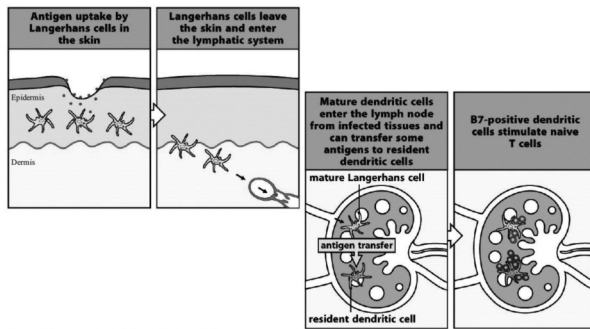


Figure 8-13 Immunobiology, 7ed. (© Garland Science 2008)

Becoming potent APC

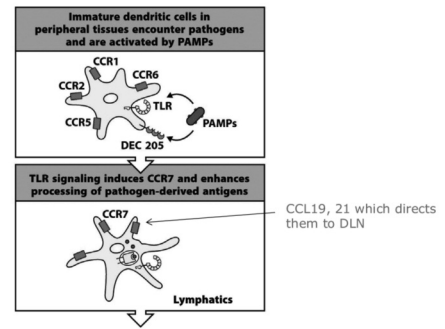


Figure 8-14 part 1 of 3 Immunobiology, 7ed. (© Garland Science 2008)

Becoming potent APC

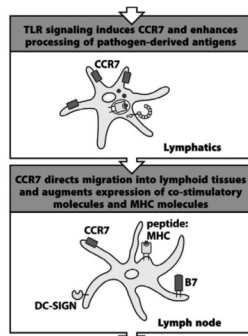


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Becoming potent APC

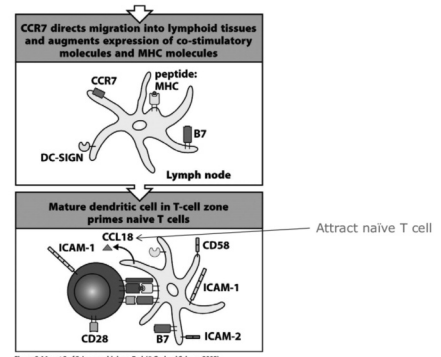


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B cells as APC to present specific antigen

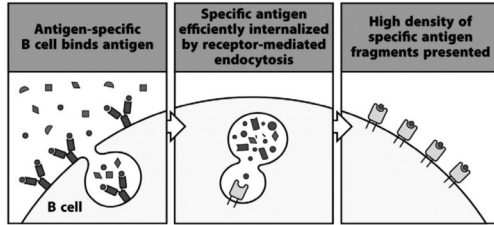


Figure 9-15 Immunobiology, 7th ed. (© Garland Science 2008)

Macrophages cannot take up soluble antigens efficiently. B cells are uniquely adapted to bind specific soluble molecules by receptor mediated endocytosis.

	Dendritic cells	Macrophages	B cells
Antigen uptake	+++ Macropinocytosis and phagocytosis by tissue dendritic cells	+++ Macropinocytosis +++ Phagocytosis	Antigen-specific receptor (Ig) ++++
MHC expression	Low on tissue-resident dendritic cells High on dendritic cells in lymphoid tissues	Inducible by bacteria and cytokines - to +++	Constitutive increases on activation +++ to +++++
Co-stimulation delivery	Inducible High on dendritic cells in lymphoid tissues ++++	Inducible - to +++	Inducible - to +++
Location	Ubiquitous throughout the body	Lymphoid tissue Connective tissue Body cavities	Lymphoid tissue Peripheral blood
Effect	Results in activation of naive T cells	Results in activation of macrophages	Results in delivery of help to B cell

Figure 9-19 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Cell adhesion molecules mediate the initial interaction of naïve T cells with APCs.

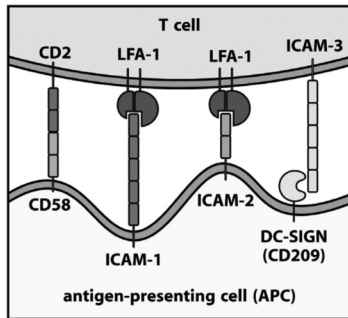


Figure 9-17 Immunobiology, 7th ed. (© Garland Science 2008)

Transient adhesive interactions can be stabilized by specific antigen recognition

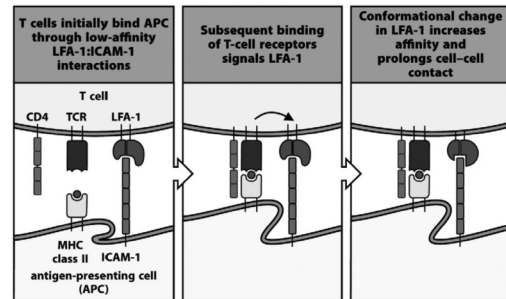


Figure 9-18 Immunobiology, 7th ed. (© Garland Science 2008)

Three kinds of signals are involved in activation of native T cells by APCs

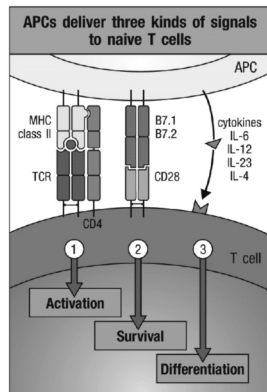


Figure 9-22 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

CD28 dependent co-stimulation of activated T cells induces expression of the T cell growth factor interleukin-2 and the high affinity IL-2 receptor

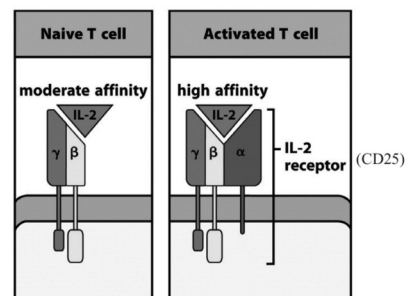


Figure 9-20 Immunobiology, 7th ed. (© Garland Science 2008)

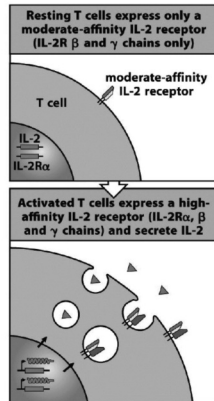


Figure 8-21 part 1 of 3 Immunobiology, 7ed. (© Garland Science 2008)

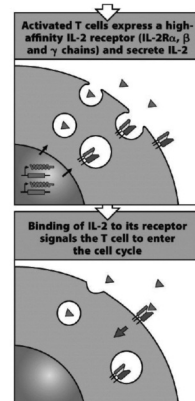


Figure 8-21 part 2 of 3 Immunobiology, 7ed. (© Garland Science 2008)

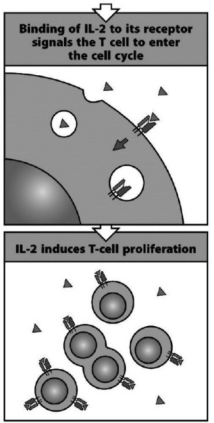


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Signal 2 can be modified by additional co-stimulatory pathways

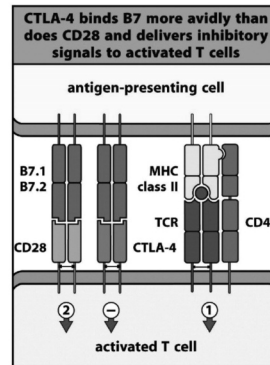


Figure 8-22 Immunobiology, 7ed. (© Garland Science 2008)

ICOS-ICOSL:
Activated T cells induce ICOS for their proliferation and helper T cell function.

4-1BB-4-1BBL:
Activated T cells induce 4-1BB for their activation.

Ligands are expressed on APCs including DCs, B cells, and macrophages.

Functional inactivation or clonal deletion of peripheral T cells

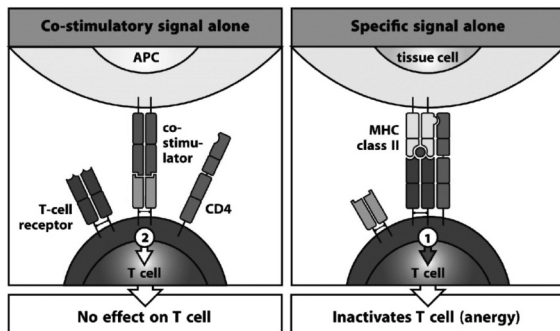


Figure 8-23 Immunobiology, 7ed. (© Garland Science 2008)

Decreased TcR signaling through induction of GRAIL and Cbl

Molecular mechanism of anergy in T cells is not fully understood

Active effector T cells can respond to their target cells without costimulation

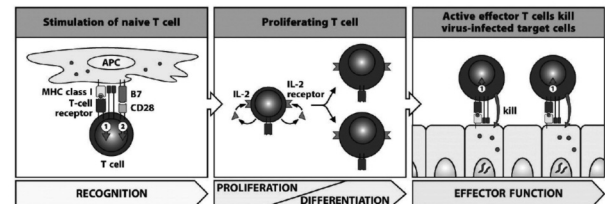
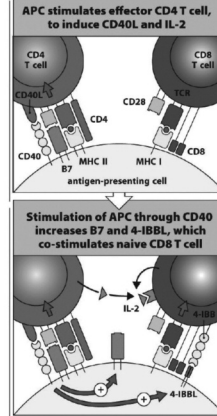
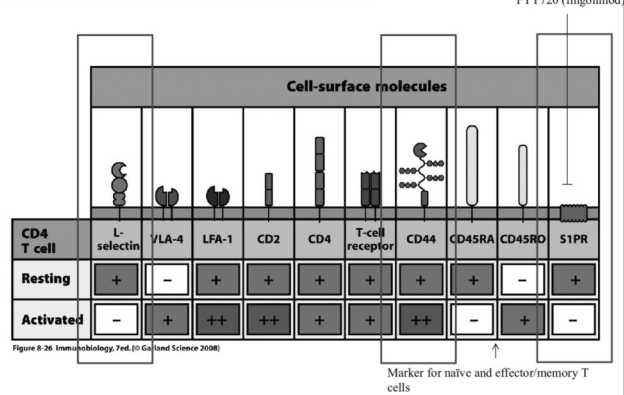


Figure 8-25 Immunobiology, 7ed. (© Garland Science 2008)

Effector T cells; low L-selectin, high LFA-1, VLA-4

-> This allows T cells recirculate through lymph nodes and bind to vascular endothelium results these T cells enter sites of infection.

Activation of T cells changes the expression of several cell surface molecules



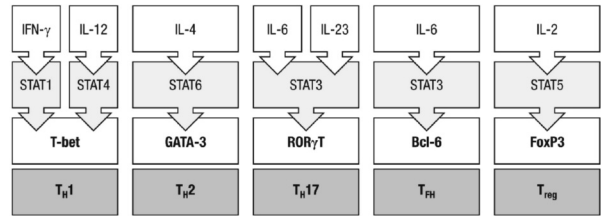
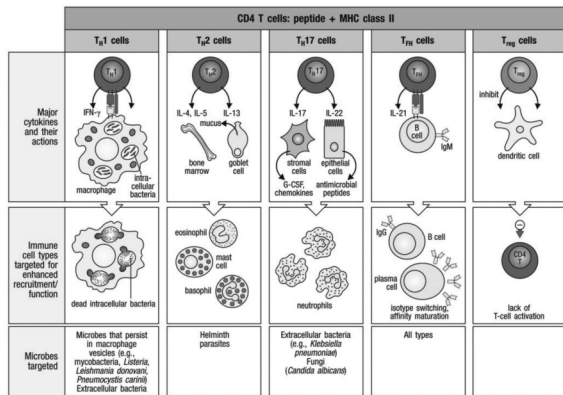
Most CD8 T cell responses require CD4 T cells

Native CD8 T cell differentiate into cytotoxic cells.

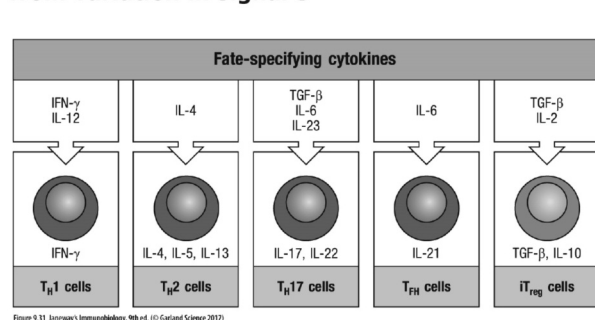
The CD4 T cell help is needed to compensate for inadequate costimulation of naive CD8 T cells by the virus infected antigen presenting cell.

CD40 on DC and CD40L on CD4 T cell induces B7 in dendritic cell and enables it to costimulate the naive CD8 T cell directly.

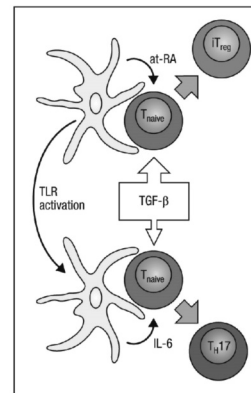
T cell molecule 4-1BB and 4-1BBL on activated APC enhances costimulatory signals in both direction.



Several distinct types of effector T cells coming from variation in signal 3



Balance between iTreg and Th17



CD4 T cell subsets can cross-regulate each other's differentiation through the cytokines

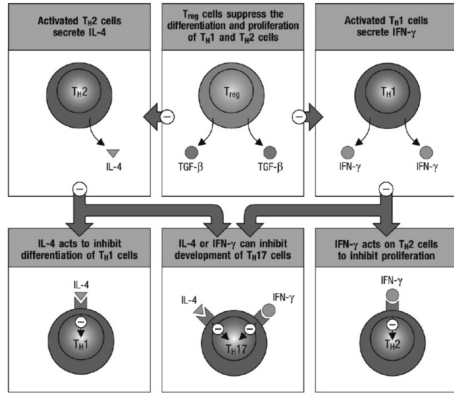
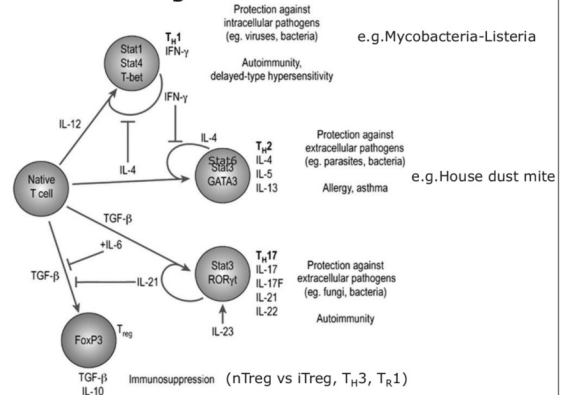
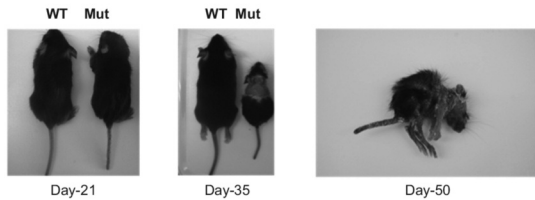


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Several distinct types of effector T cells coming from variation in signal 3



Scurfy mouse ; Without Tregs...



Interactions of T cells with their targets initially involve nonspecific adhesion molecules

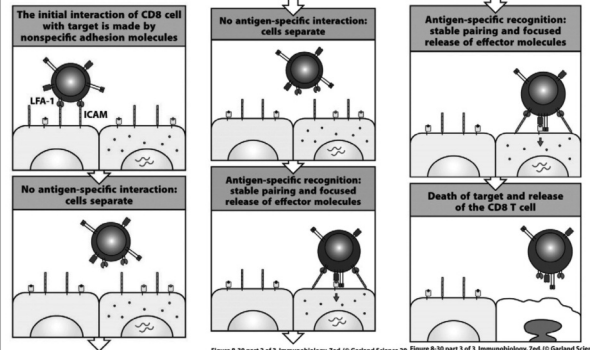


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Immunological synapse

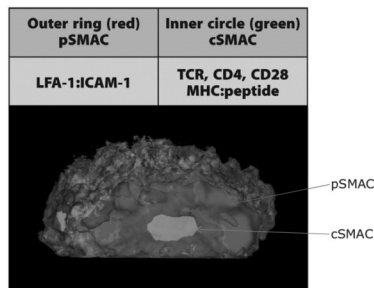


Figure 9-31 Immunobiology, 7th ed. (© Garland Science 2008)

Cell-cell contact forming what is called the supramolecular adhesion complex (SMAC) or the immunological synapse.

Peripheral SMAC (pSMAC), central SMAC (cSMAC)

The cellular polarization of cytotoxic T cells

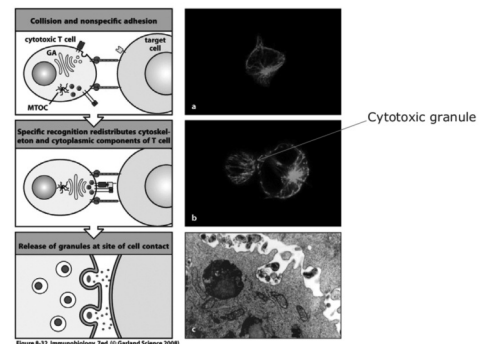


Figure 9-32 Immunobiology, 7th ed. (© Garland Science 2008)

Effector molecules produced by effector T cells

CD8 T cells: peptide + MHC class I		CD4 T cells: peptide + MHC class II							
Cytotoxic (killer) T cells		T _H 1 cells		T _H 2 cells		T _H 17 cells		T _H 22 cells	
Cytotoxic effector molecules	Others	Macrophage-activating effector molecules	Others	Barrier immunity activating effector molecules	Others	Barrier immunity activating effector molecules, neutrophil recruitment	Others	Suppressive cytokines	Others
Perforin Granzymes Granulysin Fas ligand	IFN- γ LT- α TNF- α	IFN- γ GM-CSF TNF- α CD40 ligand Fas ligand	IL-3 LT- α CXCL2 (GRO α)	IL-4 IL-5 IL-13 CD40 ligand	IL-3 GM-CSF IL-10 TNF- β IL-22 COL11 (retardin) COL17 (SARF)	IL-17A IL-17F IL-22 CD40 ligand	IL-3 TNF- α CXCL20	IL-10 TGF- β	IL-35

Figure 9.39 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Cytokine	T-cell source	B cells	T cells	Macrophages	Hematopoietic cells	Other tissue cells	Effect of gene knockout
Interleukin-2 (IL-2)	Naive T _H 1, some CD8	Stimulates growth and J-chain synthesis	Growth and differentiation	—	Stimulates NK cell growth	—	Impaired T _H 1 cell development and function
Interleukin-3 (IL-3)	T _H 1, T _H 2, CTL	Differentiation of B ₂ 20 myeloma (mouse)	Induces T _H 1 differentiation	Activates B ₂ 20 myeloma	Activates NK cells	Activates T _H 17 cells and class II	Impaired B ₂ 20 myeloma, some thymocytes
Lymphokine-4 (IL-4, TNF- β)	T _H 2, some CTL	Inhibits	Kills	Activates, induces B ₂ 20 production	Activates neutrophils	Kills fibroblasts and tumor cells	Absence of lymph nodes, thymic atrophy
Interleukin-4 (IL-4)	T _H 2, T _H 1	Activates growth of B ₂ 20, IgE production	Growth, survival	Promotes marginal zone macrophage activation	Promotes growth of mast cells	—	No T _H 2
Interleukin-5 (IL-5)	T _H 2	—	—	—	—	—	Reduced eosinophils
Interleukin-13 (IL-13)	T _H 2	—	—	—	—	—	Impaired eosinophil expansion
Interleukin-17 (IL-17)	T _H 17	Promotes IgG ₁ , IgG ₂ , IgM, IgA (mouse)	—	—	Stimulates osteoblast and epithelial cells to secrete osteocalcin	—	Impaired osteoblast differentiation
Interleukin-22 (IL-22)	T _H 17	—	—	—	—	—	Impaired epithelial defense
Transforming growth factor- β (TGF- β)	T _H 2	Inhibits growth, IgA secretion (mouse)	Inhibits activation	Activates neutrophils	Activates dendritic cells	Inhibits/activates cell growth	Impaired T _H 1 cell development, multi-organ autoimmunity and death ~10 weeks
Interleukin-10 (IL-10)	T _H 2, T _H 1, T _H 17, T _H 22, T _H 1, CTL	Inhibits growth, IgA secretion (mouse)	Inhibits activation	Activates neutrophils	Activates dendritic cells	Inhibits/activates cell growth	—
Interleukin-3 (IL-3)	T _H 1, T _H 2, T _H 17, T _H 22, T _H 1, CTL	Inhibits growth, IgA secretion (mouse)	Inhibits activation	Activates neutrophils	Activates dendritic cells	Inhibits/activates cell growth	—
Tumor necrosis factor- α (TNF- α)	T _H 1, T _H 2, T _H 17, T _H 22, T _H 1, CTL	Inhibits growth, IgA secretion (mouse)	Inhibits activation	Activates neutrophils	Activates dendritic cells	Inhibits/activates cell growth	—
Granulocyte-macrophage colony-stimulating factor (GM-CSF)	T _H 1, T _H 2, T _H 17, T _H 22, T _H 1, CTL	Inhibits growth, IgA secretion (mouse)	Inhibits activation	Activates neutrophils	Activates dendritic cells	Inhibits/activates cell growth	—

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Cytotoxic CD8 T cells can induce apoptosis in target cells

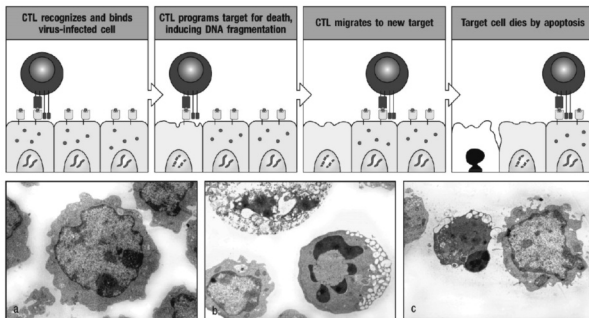


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Apoptosis by cytotoxic granule to target cells

Apoptosis by fas and fas ligand interaction to kill lymphocytes
-> important for maintaining lymphocytes homeostasis

Cytotoxic effector proteins

Protein in granules of cytotoxic T cells	Actions on target cells
Perforin	Aids in delivering contents of granules into the cytoplasm of target cell
Granzymes	Serine proteases, which activate apoptosis once in the cytoplasm of the target cell
Granulysin	Has antimicrobial actions and can induce apoptosis

Figure 9.42 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Cytotoxic granules are modified lysosomes that contain at least three distinct classes of cytotoxic effector proteins that are expressed specifically in cytotoxic T cells.

Cytotoxic effector proteins

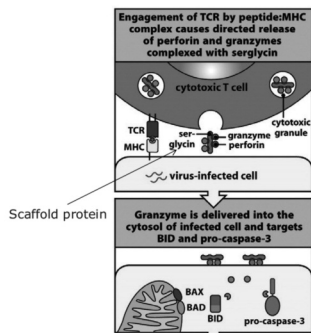


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Cytotoxic effector proteins

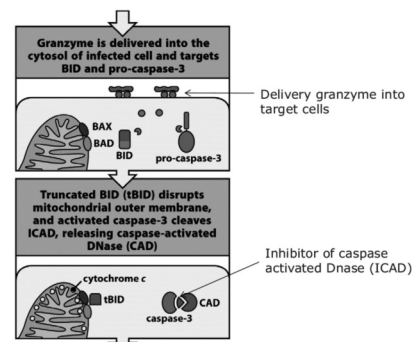
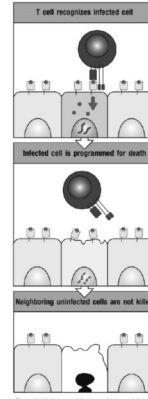
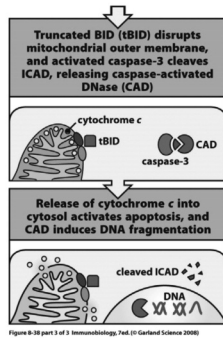


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Cytotoxic effector proteins



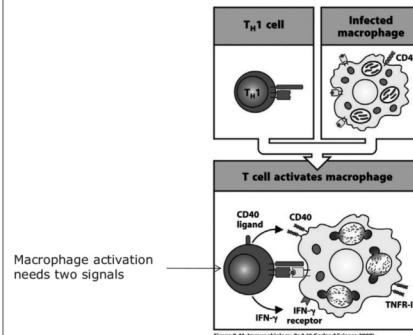
Cytokines from CD8 T cells

IFN- γ inhibits viral replication directly and induces the increased expression of MHC I. Also activates macrophages.

TNF- α and **LT- α** can synergize with IFN- γ in macrophage activation and in killing some target cells through their interaction with TNFR-I which induces apoptosis.

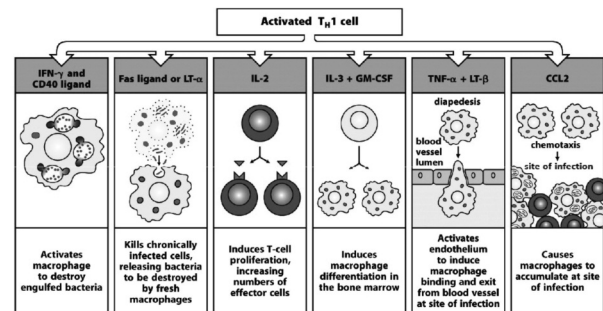
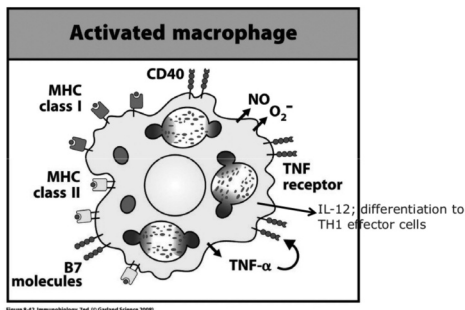
TNF- α also activates vascular endothelium and increases vascular permeability which leads to increased entry of proteins or cells to tissues.

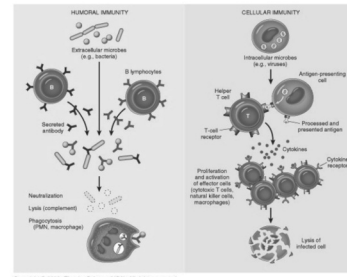
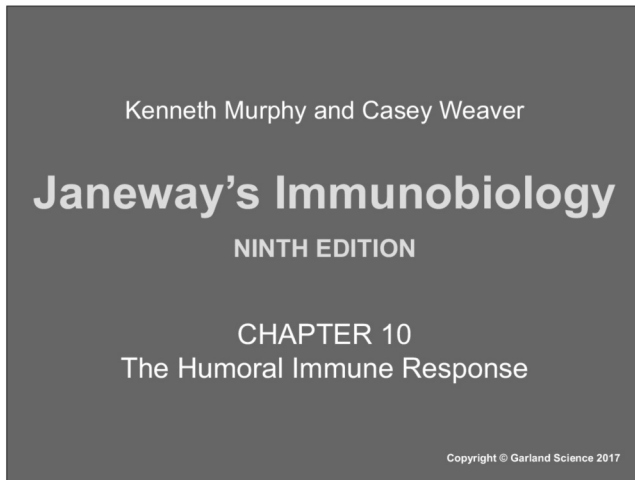
Macrophage activation by TH1 cells



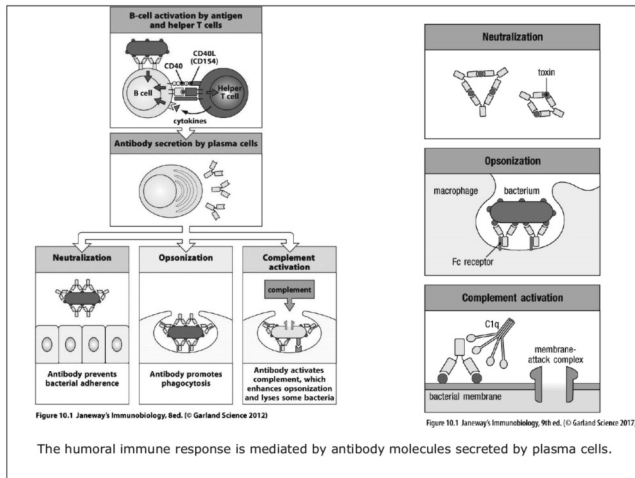
TH2 cells are inefficient macrophage activators because they produce IL-10, a cytokine that can deactivate macrophages

Potent antimicrobial effector macrophage

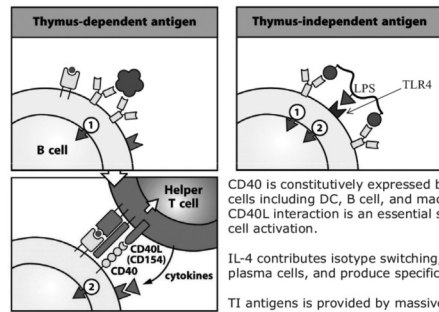




The extracellular spaces are protected by the humoral immune response, in which antibodies produced by B cells cause the destruction of extracellular microorganisms and prevent the spread of intracellular infections.



B cell activation needs 2 signals

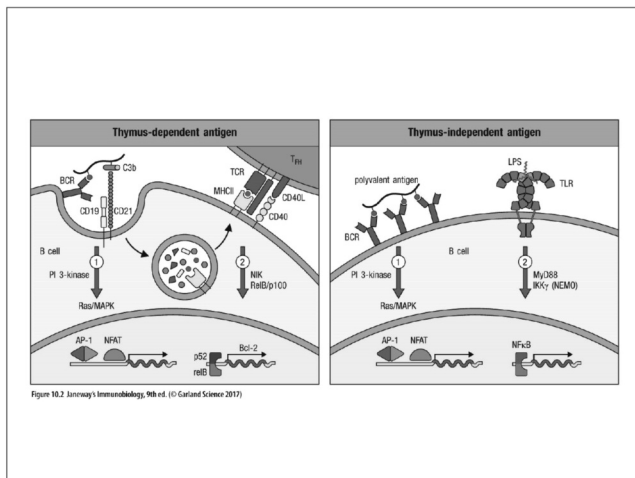


CD40 is constitutively expressed by antigen presenting cells including DC, B cell, and macrophage. CD40-CD40L interaction is an essential signal for resting B cell activation.

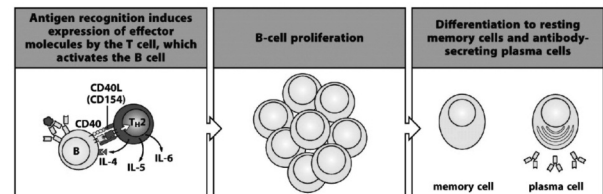
IL-4 contributes isotype switching, differentiation into plasma cells, and produce specific antibodies.

TI antigens is provided by massive cross-linking of BcR or by recognition of a common microbial constituent when a B cell binds repeating epitopes on the bacterial cell. (e.g. LPS). Second signal can be delivered through TLRs.

B cell receptor binds native proteins, glycoproteins, and polysaccharides, whole virus particles and bacterial cells by recognizing epitopes on their surfaces.



Armed helper T cells stimulate the proliferation and differentiation of B cells



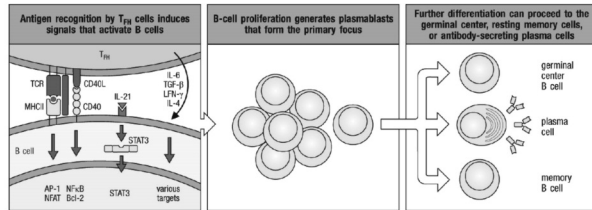


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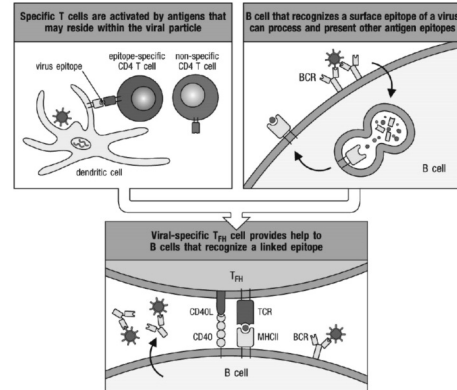


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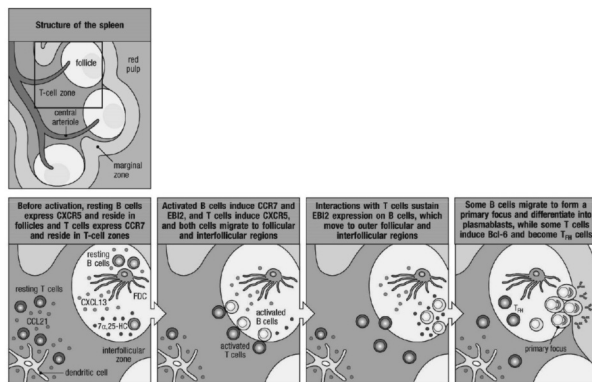


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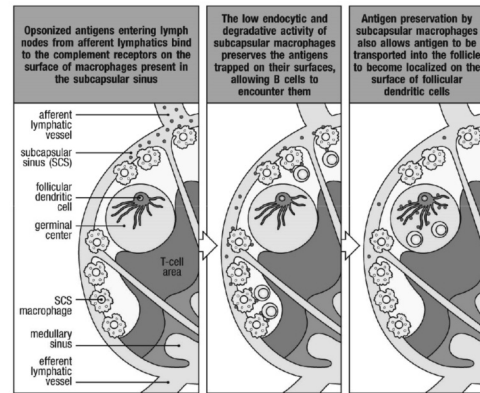


Figure 10.7 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

B-lineage cell	Intrinsic properties			Inducible by antigen stimulation		
	Surface Ig	Surface MHC class II	High-rate Ig secretion	Growth	Somatic hypermutation	Class switch
Resting B cell	High	Yes	No	Yes	Yes	Yes
Plasmablast	High	Yes	Yes	Yes	Unknown	Yes
Plasma cell	Low	Yes	Yes	No	No	No

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Linked recognition

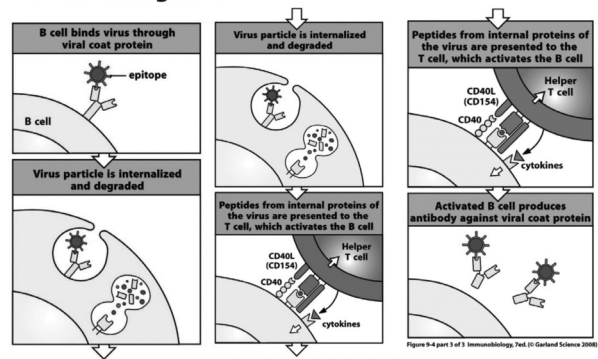


Figure 9-4 part 1 of 3 Immunobiology, 7th ed. (© Garland Science 2008)

Figure 9-4 part 3 of 3 Immunobiology, 7th ed. (© Garland Science 2008)

A given B cell can only be activated by helper T cells that respond to the same antigen. The peptide recognized by the T_H cell is likely to differ from the protein epitope recognized by the B cell's antigen receptor.

Protein antigens attached to polysaccharide antigens allow T cells to help cognate B cells

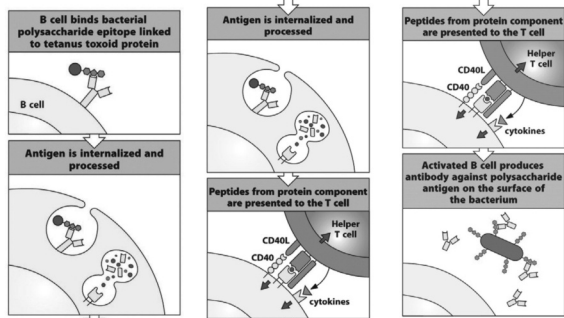
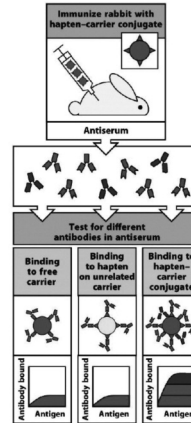


Figure 10.5 part 2 of 4 Janeway's Immunobiology, 8th ed. (© Garland Science 2012)

Hapten



Hapten; A small molecule that can elicit an immune response only when attached to a large carrier such as a protein.

Accidental coupling of a hapten to a protein is responsible for the allergic responses shown by many people to the antibiotic penicillin, which reacts with host proteins to form a coupled hapten that can stimulate an antibody response.

Linked recognition works to preserve self-tolerance, since autoreactive antibodies will arise only if self-reactive T_H and self-reactive B cells are present at the same time.

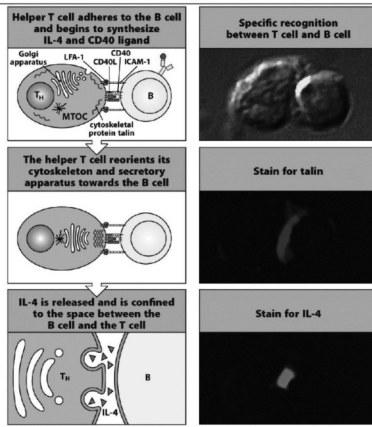


Figure 9-6 Immunobiology, 7th ed. (© Garland Science 2008)

CD40-CD40L interaction activates B cell proliferation, immunoglobulin class switching, and somatic hypermutation. It also increases expression of B7 molecule.

The area of T-B cell contact

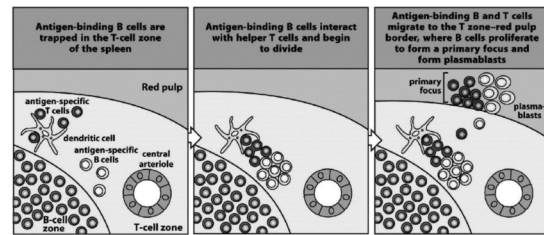


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Native T cells and B cells home to different regions.

T cells differentiated into helper T cells after encountering APCs.

B cells specific for the same antigen encounter it, they are arrested in T cell zone, near the T-B zone border.

Initially proliferated B cells migrate to the border of T cell zone and the red pulp, they continue to proliferate and differentiate into plasmablasts, forming **primary focus** of clonal expansion.

Antigen-binding B cells meet T cells at the border between the T-cell area and a B-cell follicle in secondary lymphoid tissues.

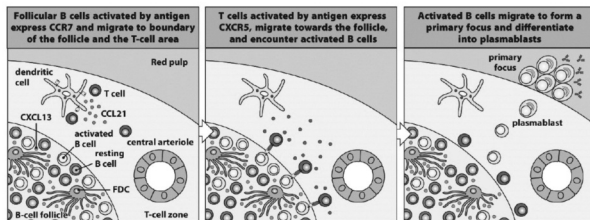
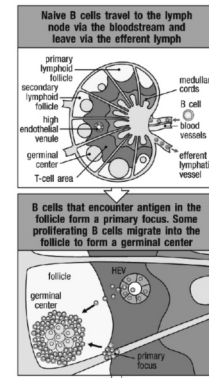


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Follicular dendritic cell (FDC): a specialized cell type secrete CXCL13 to attract naïve B cells expressing CXCR5. The FDC is a nonphagocytic cell of nonhematopoietic origin.

Germinal center



Activated B cells form germinal centers in lymphoid follicles.

Germinal centers mainly composed of proliferating B cells and 10% of antigen specific T cells

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Germinal center

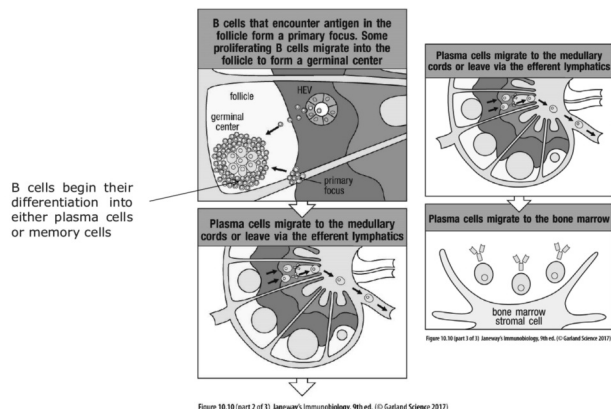
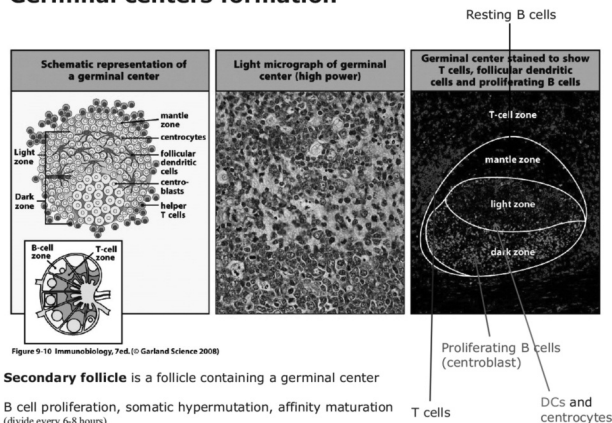


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Germinal centers formation



Schematic representation of a
with a germinal center

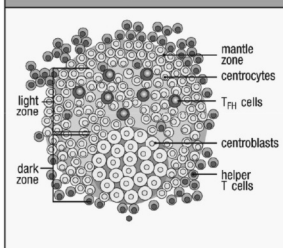
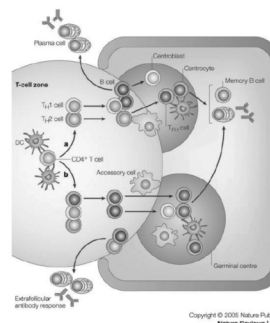
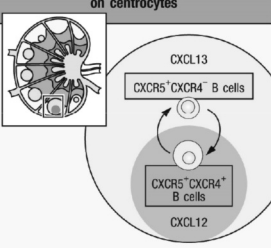


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Cyclic reentry of cells into the dark zone is dependent on reexpression of CXCR4 on centrocytes



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Follicular helper T cell; are antigen experienced CD4 T cells found in the B cell follicles of secondary lymphoid organs. TFH cells are found within B cell follicles and mediate antigen specific naïve or memory B cell activation, which triggers germinal center formation.

Initially rapidly proliferating B cells reduce their expression of IgD and these B cells are termed **centroblast**. As time goes on, some B cells reduce their rate of division and begin to express higher levels of IgD termed **centrocyte** and they arise from centroblast.

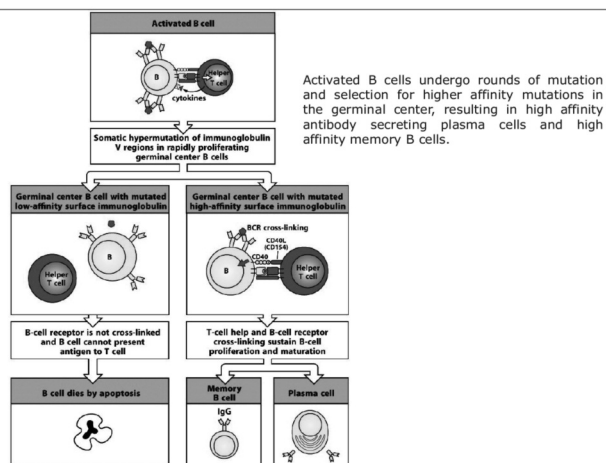


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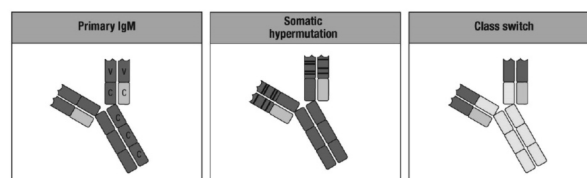
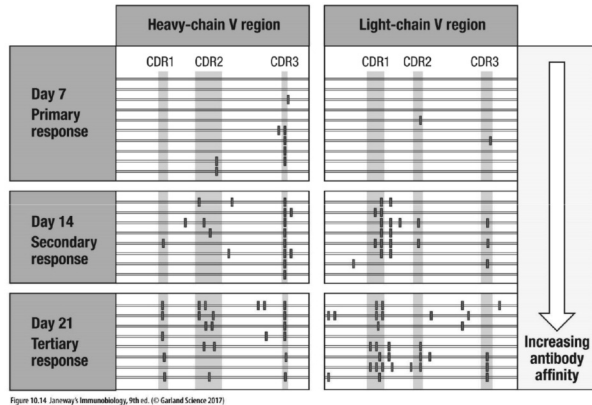
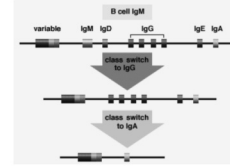


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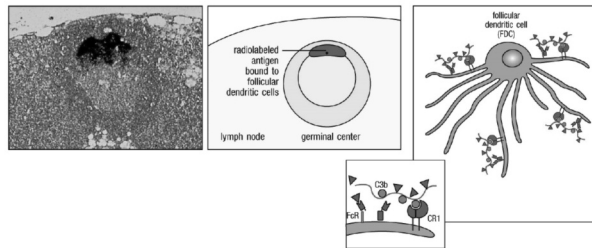


All naïve B cells express cell surface IgM and IgD, and IgM is the first antibody secreted.



IgM is less than 10% of the immunoglobulin found in plasma.
IgG is the most abundant.

Follicular DC recognize immune complexes



Antigen trapped by Follicular DC stored for long periods in the form of immune complexes and sustain germinal center B cell proliferation.

Role of cytokines in regulating expression of antibody classes

Cytokines	IgM	IgG3	IgG1	IgG2b	IgG2a	IgE	IgA
IL-4	Inhibits	Inhibits	Induces		Inhibits	Induces	
IL-5							Augments production
IFN- γ	Inhibits	Induces	Inhibits		Induces	Inhibits	
TGF- β	Inhibits	Inhibits		Induces			Induces
IL-21		Induces	Induces				Induces

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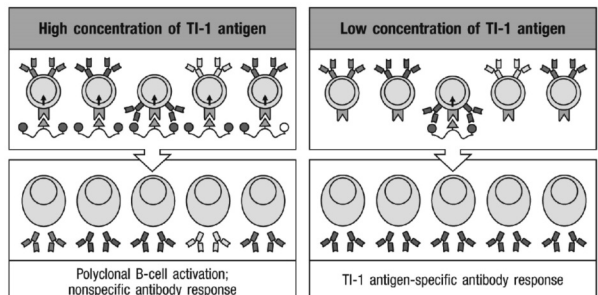
TD antigens (thymus dependent antigen): antibody responses to protein antigens require antigen specific T cell help. These antigens are unable to induce antibody responses in animals or humans without T cells. It typically involve antigen-specific T cell help.

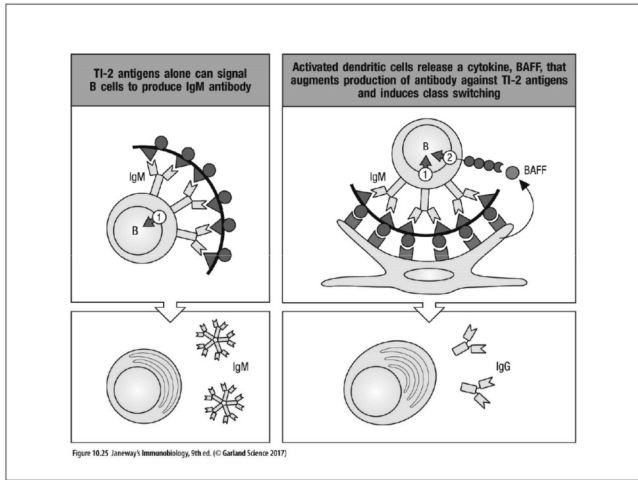
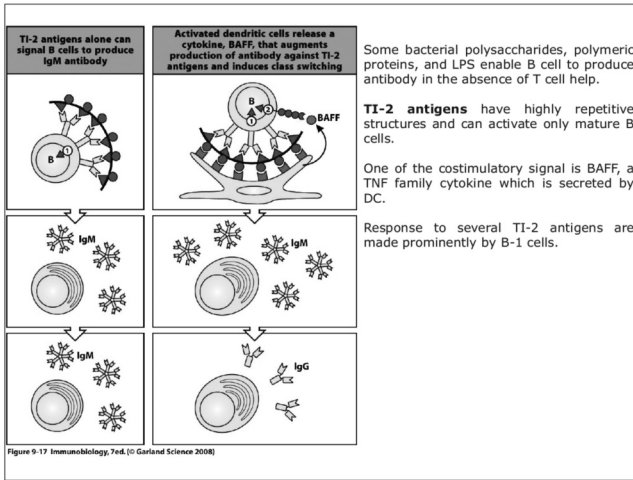
TI antigens (thymus independent antigen): Some microbial constituents such as bacterial polysaccharides can induce antibody production in the absence of helper T cells.

Some bacterial polysaccharides, polymeric proteins, and LPS enable B cell to produce antibody in the absence of T cell help.

Thymus independent antigens (TI antigens)

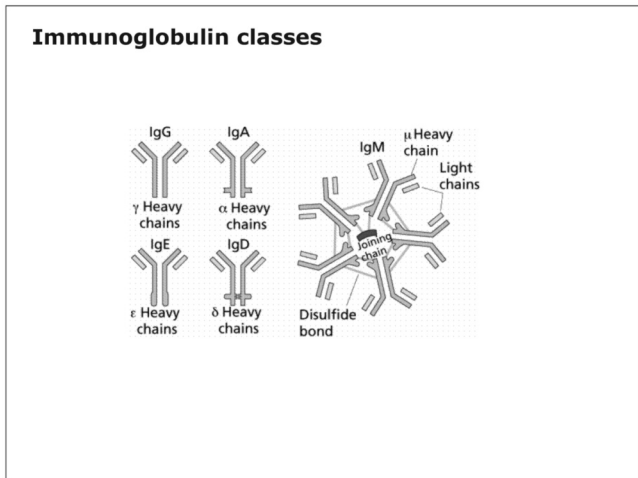
TI-1 antigens possess an intrinsic activity that can directly induce B cell division. TI-1 antigen is **B cell mitogen**. ; **LPS, bacterial DNA, etc.**





	TD antigen	TI-1 antigen	TI-2 antigen
Antibody response in infants	Yes	Yes	No
Antibody production in congenitally athymic individual	No	Yes	Yes
Antibody response in absence of all T cells	No	Yes	Yes
Primes T cells	Yes	No	No
Polyclonal B-cell activation	No	Yes	No
Requires repeating epitopes	No	No	Yes
Examples of antigen	Diphtheria toxin Viral hemagglutinin Purified protein derivative (PPD) of <i>Mycobacterium tuberculosis</i>	Bacterial lipopolysaccharide <i>Brucella abortus</i>	Pneumococcal polysaccharide <i>Salmonella</i> polymerized flagellin Dextran Hapten-conjugated Ficoll (polysaccharide)

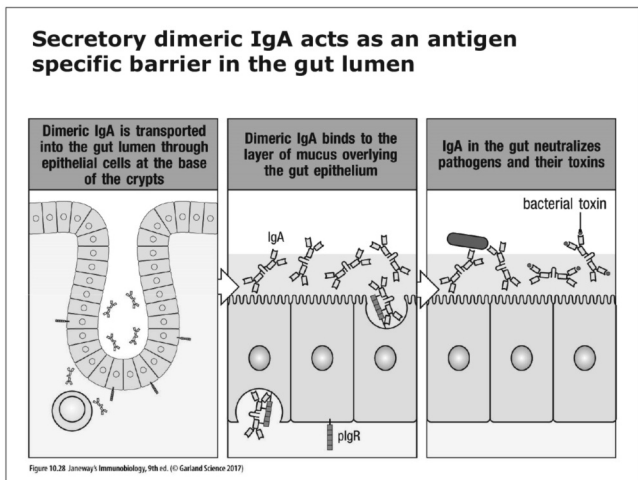
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Each human immunoglobulin class has specialized functions and a unique distribution

Functional activity	IgM	IgD	IgG1	IgG2	IgG3	IgG4	IgA	IgE
Neutralization	+	-	++	++	++	++	++	-
Opsonization	+	-	++	+	++	+	+	-
Sensitization for killing by NK cells	-	-	++	-	++	-	-	-
Sensitization of mast cells	-	-	+	-	+	-	-	+++
Activates complement system	+++	-	++	+	+++	-	+	-
Distribution	IgM	IgD	IgG1	IgG2	IgG3	IgG4	IgA	IgE
Transport across epithelium	+	-	-	-	-	-	+++ (secreted)	-
Transport across placenta	-	-	+++	+	++	+/-	-	-
Diffusion into extravascular sites	+/-	-	+++	+++	+++	+++	++ (monomers)	+
Mean serum level (mg·ml ⁻¹)	1.5	0.04	9	3	1	0.5	2.1	3×10 ⁻⁶

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Selective distribution of immunoglobulin classes in the body

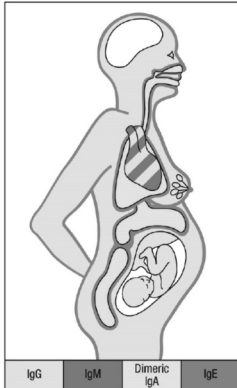


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Dimeric IgA predominates in secretions across epithelia, including breast milk.

IgG and monomeric IgA are the major antibodies in extracellular fluid within the body.

IgE is found mainly associated with mast cells just beneath epithelial surfaces.

The fetus receives IgG from the mother by transplacental transport.

Disease	Organism	Toxin	Effects <i>in vivo</i>
Tetanus	<i>Clostridium tetani</i>	Tetanus toxin	Blocks inhibitory neuron action, leading to chronic muscle contraction
Diphtheria	<i>Corynebacterium diphtheriae</i>	Diphtheria toxin	Inhibits protein synthesis, leading to epithelial cell damage and myocarditis
Gas gangrene	<i>Clostridium perfringens</i>	Clostridial toxin	Phospholipase activation, leading to cell death
Cholera	<i>Vibrio cholerae</i>	Cholera toxin	Activates adenylate cyclase, elevates cAMP in cells, leading to changes in intestinal epithelial cells that result in loss of water and electrolytes
Anthrax	<i>Bacillus anthracis</i>	Anthrax toxic complex	Increases vascular permeability, leading to edema, hemorrhage, and circulatory collapse
Botulism	<i>Clostridium botulinum</i>	Botulinum toxin	Blocks release of acetylcholine, leading to paralysis
Whooping cough	<i>Bordetella pertussis</i>	Pertussis toxin Tracheal cytotoxin	ADP-ribosylation of G proteins, leading to lymphoproliferation Inhibits cilia and causes epithelial cell loss
Scarlet fever	<i>Streptococcus pyogenes</i>	Erythrogenic toxin Leukocidin Streptolysins	Vasodilation, leading to scarlet fever rash Kill phagocytes, allowing bacterial survival
Food poisoning	<i>Staphylococcus aureus</i>	Staphylococcal enterotoxin	Acts on intestinal neurons to induce vomiting. Also a potent T-cell mitogen (SE superantigen)
Toxic-shock syndrome	<i>Staphylococcus aureus</i>	Toxic-shock syndrome toxin	Causes hypotension and skin loss. Also a potent T-cell mitogen (TSST-1 superantigen)

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Neutralization of toxins by IgG antibodies protects cells from their damaging action

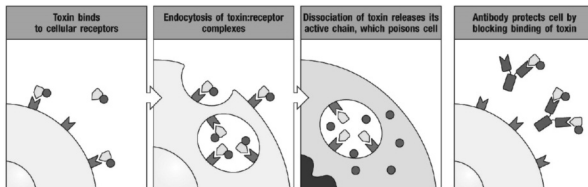


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Many bacteria cause their damaging effects by elaborating toxic proteins. One part of the toxin molecule binds a cellular receptor. Another part of the toxin molecule enters the cytoplasm and poisons the cell.

Diphtheria and tetanus toxins are bacterial toxins.

Viral infection of cells can be blocked by neutralizing antibodies

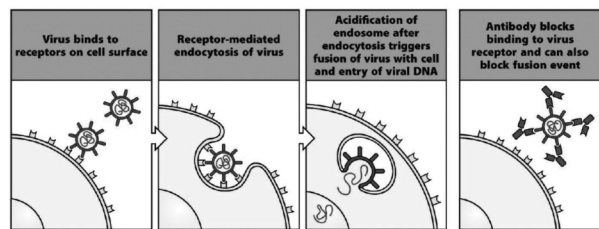


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For some viruses this fusion event takes place on the cell surface. For others it can occur only within the more acidic environment of endosomes.

Antibodies bound to viral surface proteins neutralize the virus, inhibiting either its initial binding to the cell or its subsequent entry.

bacterial infection of cells can be blocked by neutralizing antibodies

Many bacterial infections require an interaction between the bacterium and a cell surface receptor.

The attachment process involves very specific molecular interactions between bacterial adhesins and their receptors on host cells.

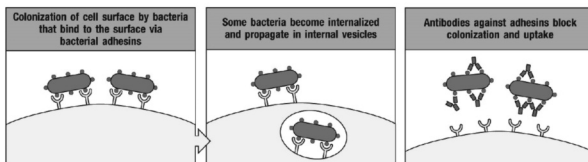


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Complement system is initiated by antibody response

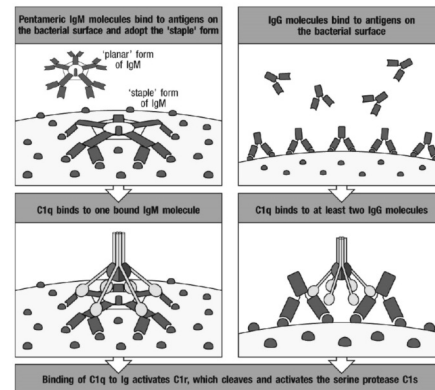


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Erythrocyte CR1 helps to clear immune complexes from the circulation

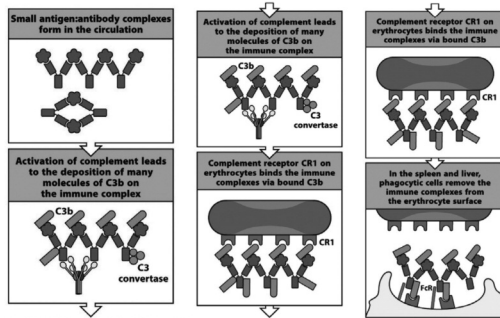


Figure 9-29 part 1 of 3 Immunobiology, 7ed. (© Garland Science 2008) Figure 9-29 part 2 of 3 Immunobiology, 7ed. (© Garland Science 2008) Figure 9-29 part 3 of 3 Immunobiology, 7ed. (© Garland Science 2008)

Receptor	FcγRI (CD64)	FcγRII-A (CD32)	FcγRII-B2 (CD32)	FcγRII-B1 (CD32)	FcγRIII (CD16)	FcεRI	FcαRI (CD23)	FcαRII (CD89)	FcμR
Structure	α 72 kDa	α 40 kDa			α 50-70 kDa	α 45 kDa	α 55-75 kDa	α 70 kDa	
Binding	IgG1	IgG1	IgG1	IgG1	IgG1	IgE	IgE	IgA1, IgA2	IgA, IgM
Order of affinity	1) IgG1-IgG3 2) IgG4 3) IgG2	2 × 10 ⁶ M ⁻¹ 1) IgG1 2) IgG3-IgG2* 3) IgG4	2 × 10 ⁶ M ⁻¹ 1) IgG1-IgG3 2) IgG4 3) IgG2	2 × 10 ⁶ M ⁻¹ 1) IgG1-IgG3 2) IgG4 3) IgG2	5 × 10 ⁶ M ⁻¹ IgG1-IgG3	10 ¹⁰ M ⁻¹	2-7 × 10 ⁷ M ⁻¹ (monomer) 2-7 × 10 ⁶ M ⁻¹ (monomer)	10 ⁷ M ⁻¹ IgA1-IgA2	3 × 10 ⁶ M ⁻¹ 1) IgA 2) IgM
Cell type	Macrophages Neutrophils Eosinophils	Macrophages Neutrophils Eosinophils Platelets Langerhans cells	Macrophages Neutrophils Eosinophils	B cells Mast cells	NK cells Eosinophils Macrophages Neutrophils Mast cells	Mast cells Basophils	Eosinophils B cells	Macrophages Eosinophils Neutrophils	Macrophages B cells
Effect of ligation	Uptake Stimulation Activation of respiratory burst Induction of killing	Uptake Granule release (eosinophils)	Uptake Inhibition of stimulation	No uptake Inhibition of stimulation	Induction of killing (NK cells)	Secretion of granules	Degranulation	Uptake Induction of killing	Uptake

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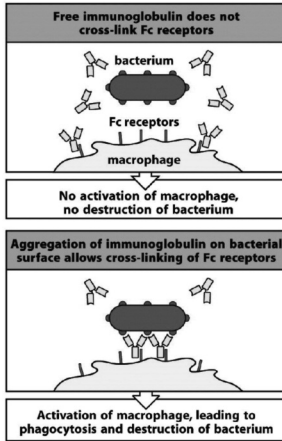


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Free immunoglobulin vs. bound antibody

Free immunoglobulin molecules bind most Fc receptors with very low affinity and can not cross-link Fc receptors.

Antigen bound immunoglobulin binds to Fc receptors with high avidity because several antibody molecules that are bound to the same surface bind to multiple Fc receptors on the surface of the accessory cell.

Fc and complement receptors on phagocytes trigger the uptake and degradation of antibody coated bacteria

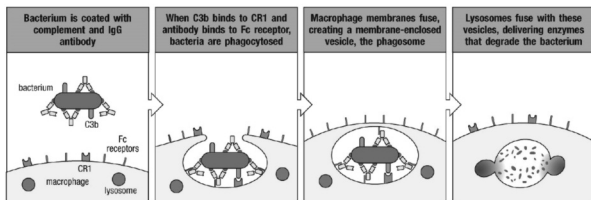


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Many bacteria resist phagocytosis by macrophages and neutrophils. Bacteria coated with IgG and complement are more readily ingested than those coated with IgG alone.

The stimulation of phagocytosis by complement coated antigens binding complement receptors is particularly important early in the immune response, before isotype-switched antibodies have been made.

Fc receptors activate NK cells to destroy antibody coated targets

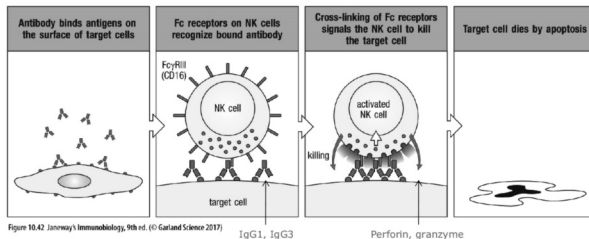


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Antibody dependent cell mediated cytotoxicity (ADCC): The destruction of antibody coated target cells by NK cells because of recognition by Fc receptor

Nonphagocytic cells-NK cells, eosinophils, basophils, and mast cells are triggered to secrete stored mediators when their Fc receptors are engaged.

IgE cross linking on mast cell leads to a rapid release of inflammatory mediators

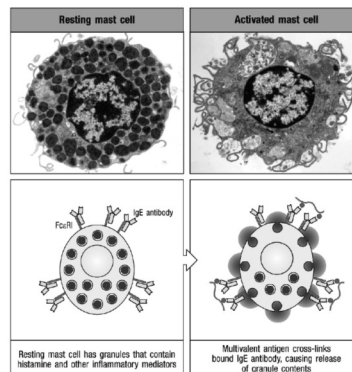


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Synthesize and release lipid mediators such as prostaglandin D2 and leukotriene C4.

Secretes cytokines such as TNF-α, initiating a local inflammatory response.

Degranulation releases the stored histamine, causing a local increase in blood flow and vascular permeability that quickly leads to an accumulation of fluid and blood proteins, including antibodies, in the surrounding tissue.