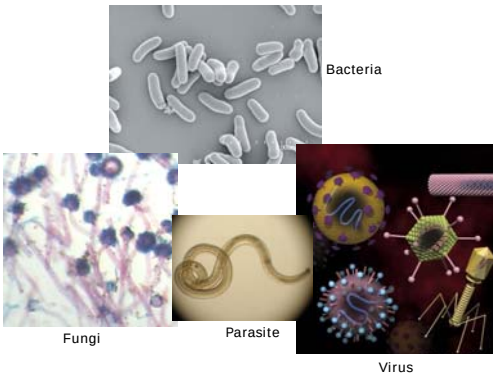
Kenneth Murphy and Casey Weaver

Janeway's Immunobiology

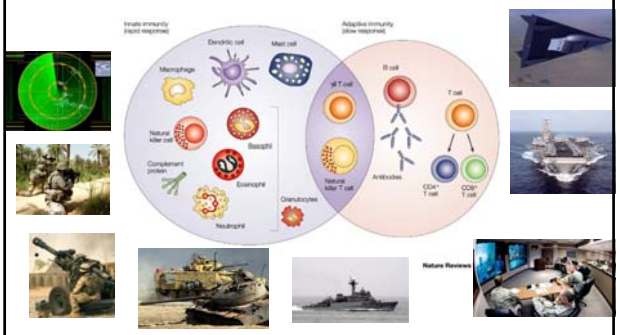
NINTH EDITION

CHAPTER 1
Basic Concepts in Immunology



Pathogens; disease causing microorganisms

Immune response is a self defense mechanism



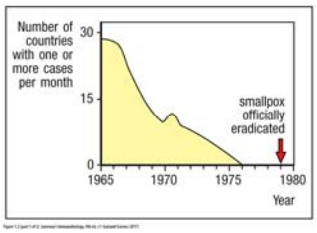
How does the body set up the defense system?

How does the body eliminate the invader and cure itself?

How and why do we develop long-lasting immunity to many infectious diseases?

Importance of vaccination

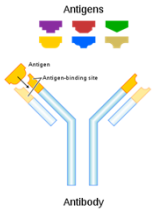
Variola major/minor



Basic immunological concepts

Antigen; originally defined as any molecule that binds specifically to and generate antibody

Antibody; found in blood or other bodily fluids of vertebrates, and used by the immune system to identify and neutralize foreign objects, such as bacteria and viruses.



Innate immune response; immediately available to combat a wide range of pathogens but does not lead to lasting immunity and is not specific for any individual pathogen.
Adaptive immune response; a specific immune response such as the production of antibodies against a particular pathogen leading immunological memory.

Immune response

Functions of the immune response

Innate

Adaptive

- Immunological recognition — Innate immune system
- Immune effector function — Clear out pathogen
- Immune regulation — Protect body from the immune response
- Immunological memory — Long-lasting immunity

WBC
leukocytes

RBC

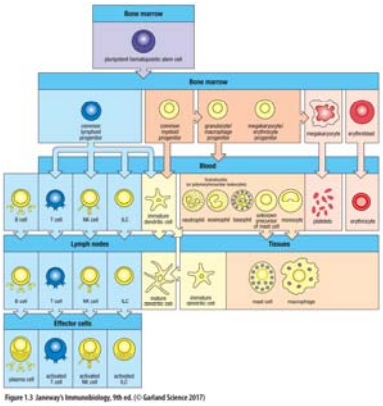


Figure 1.3 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

Myeloid cells in innate and adaptive immunity

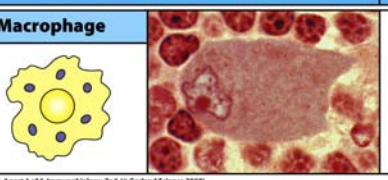
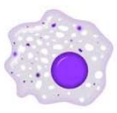
Cell	Activated function
Macrophage 	Phagocytosis and activation of bactericidal mechanisms Antigen presentation

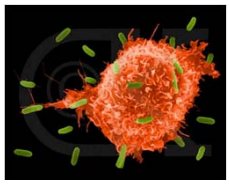
Figure 1-4 part 1 of 6 Immunobiology, 7ed. (© Garland Science 2008)

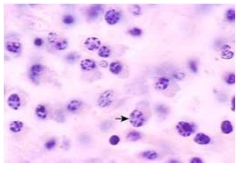
Adaptive immunity (T cell)

Resident in almost all tissues
Mature form of monocytes
An important first defense in innate immunity

Macrophage; phagocytosis







Myeloid cells in innate and adaptive immunity

Cell	Activated function
Dendritic cell 	Antigen uptake in peripheral sites Antigen presentation

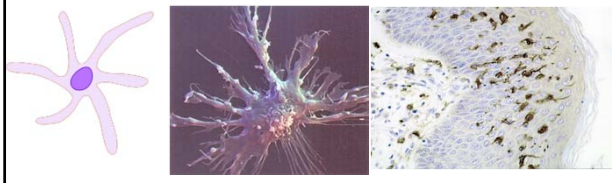
Figure 1-4 part 2 of 6 Immunobiology, 7ed. (© Garland Science 2008)

Adaptive immunity (T cell)

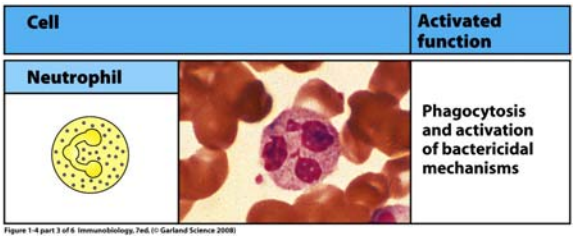
Mechanism of antigen uptake; macropinocytosis
Immature DCs migrate through the bloodstream.

APC (antigen presenting cells); cells that can present antigens to inactive T lymphocytes and activate them.

Dendritic cell; antigen presentation



Myeloid cells in innate and adaptive immunity

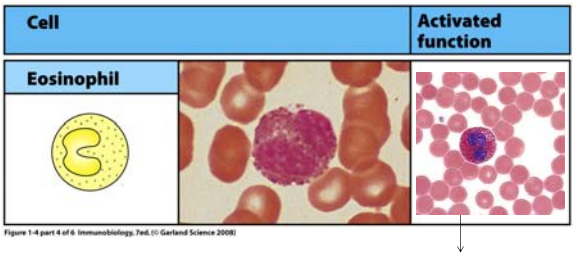


granulocytes

Polymorphonuclear neutrophils

The most abundant type of white blood cells and essential part of the innate immune system. Hallmark of acute inflammation.

Myeloid cells in innate and adaptive immunity

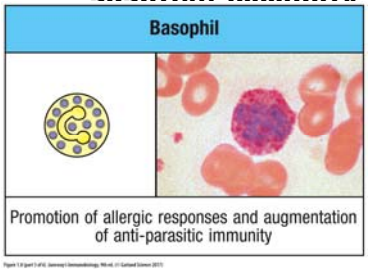


granulocytes

Allergic response

Against parasites which are too large to be ingested by macrophages or neutrophils

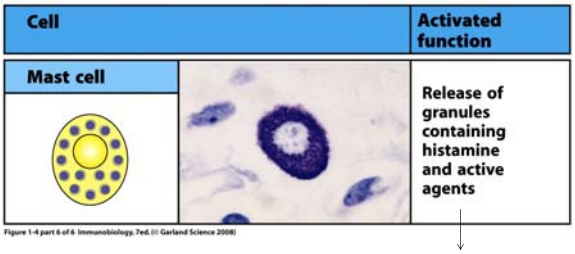
Myeloid cells in innate and adaptive immunity



granulocytes

Least common granulocytes (0.01-0.3% WBC)

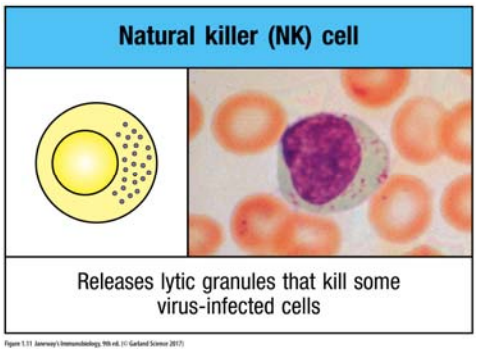
Myeloid cells in innate and adaptive immunity



Allergic response

Mast cell has large granules in their cytoplasm

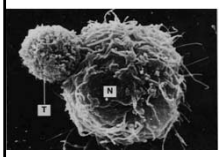
Resident cell of several types of tissues

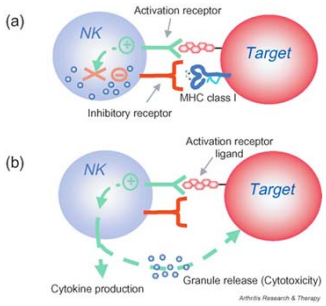


These cells are able to recognize and kill some abnormal cells; tumor cells, cells infected with viruses.

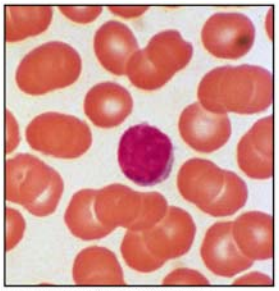
They kill cells by releasing small cytoplasmic granules of proteins called perforin and granzyme that cause the garget cell to die by apoptosis.

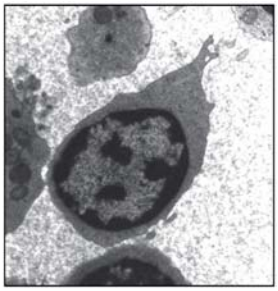
NK cell; big killer cell as innate immunity





Lymphocytes are mostly small and inactive cells

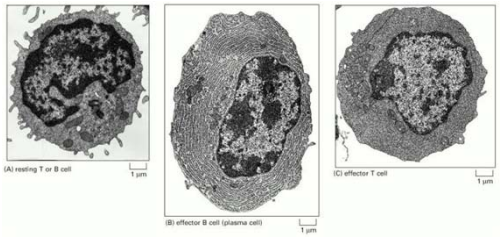




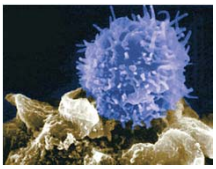
Condensed chromatin
Relative absence of cytoplasm
Small size

Naïve lymphocytes; lymphocytes that have not yet been activated by antigen.

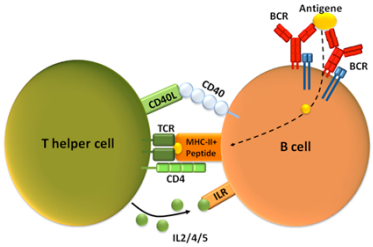
Effector lymphocytes; lymphocytes become activated and have differentiated further into fully functional lymphocytes.



T cells and B cells

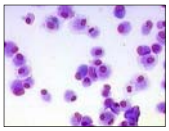


T-DC interaction

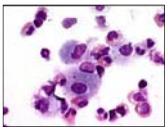


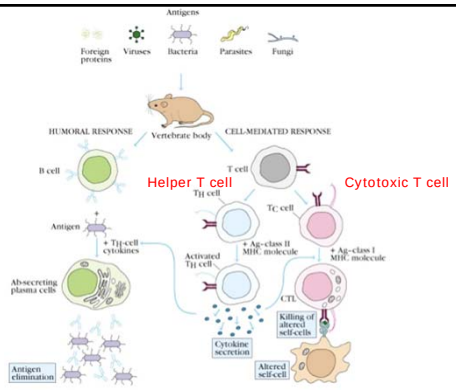
T-B interaction

Healthy control

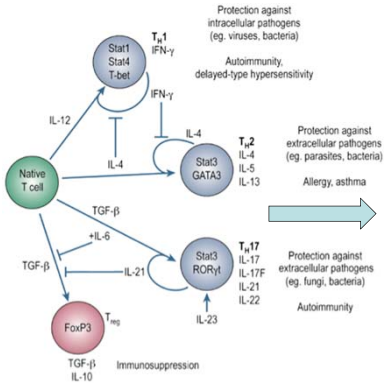


Eosinophilic pneumonia



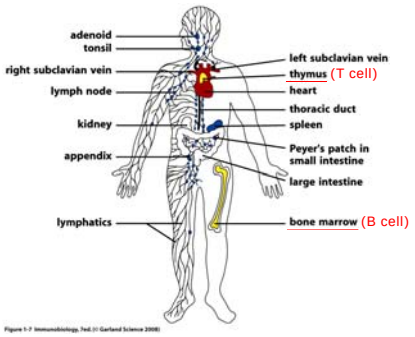


Adaptive immunity; B cell, T cell mediated antigen specific response



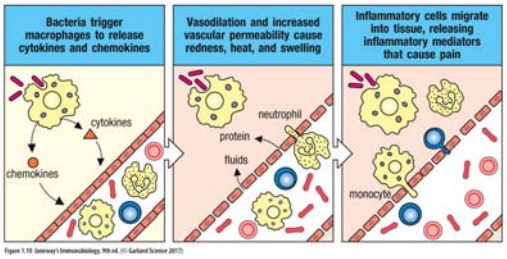
Memory T cells; Responsible for the long-lasting immunity

Regulatory T cells; suppress the activity of other lymphocytes and help control immune responses



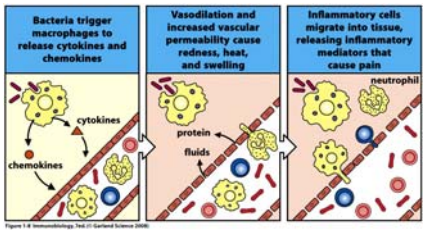
Central or Primary lymphoid organs; where lymphocytes are generated
Peripheral or Secondary lymphoid organs; where mature naïve lymphocytes are maintained and adaptive immune responses are initiated

Cytokines and chemokines



Cytokine; a protein that is secreted by cells and affects the behavior of nearby cells bearing appropriate receptors.
Chemokine; secreted proteins that attract cells bearing chemokine receptors from out of the bloodstream into infected tissue.

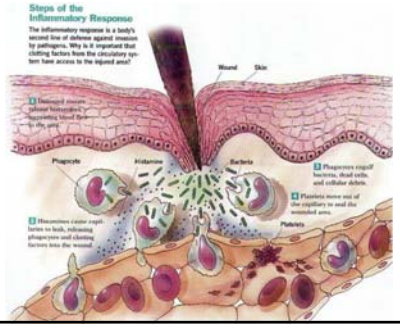
Cytokines and chemokines



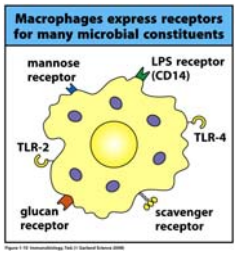
Cytokine; a protein that is secreted by cells and affects the behavior of nearby cells bearing appropriate receptors.
Chemokine; secreted proteins that attract cells bearing chemokine receptors from out of the bloodstream into infected tissue.
Complement-coated microbes are recognized and bound by specific complement receptors on macrophages.

Inflammatory response

Inflammatory response recruits more effector cells and molecules of the innate immune system out of the blood and into the tissues.



Initial discrimination between self and nonself by innate immune system



PAMPs (pathogen associated molecular patterns)
PRRs (pattern recognition receptors)
Recognize structures which are common to many pathogens

To obtain adaptive immune response to purified antigens, killed bacteria or bacterial extracts had to be mixed with the antigen. This additional material was termed an **adjuvant** because it helped the response to the immunizing antigen.

Activated dendritic cells with the adjuvant as well as the antigens express high levels **of co-stimulatory molecules**, which provide signals that act together with antigen to stimulate T lymphocyte.

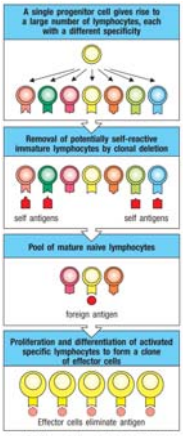
Immature DC

Ag

adjuvant

Mature, activated DC

Clonal selection

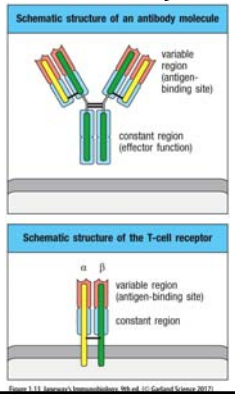


Clonal expansion; On binding antigen, the cell is activated to divide and to produce many identical progeny.

Clonal deletion; Lymphocytes that are potentially self-reactive are removed before they can mature.

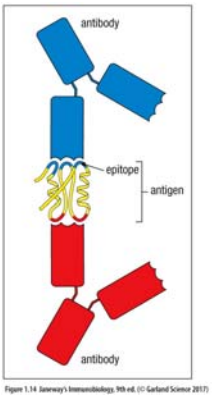
Postulates of the clonal selection hypothesis
Each lymphocyte bears a single type of receptor with a unique specificity
Interaction between a foreign molecule and a lymphocyte receptor capable of binding that molecule with high affinity leads to lymphocyte activation
The differentiated effector cells derived from an activated lymphocyte will bear receptors of identical specificity to those of the parental cell from which that lymphocyte was derived
Lymphocytes bearing receptors specific for ubiquitous self molecules are deleted at an early stage in lymphoid cell development and are therefore absent from the repertoire of mature lymphocytes

Structure of antibody

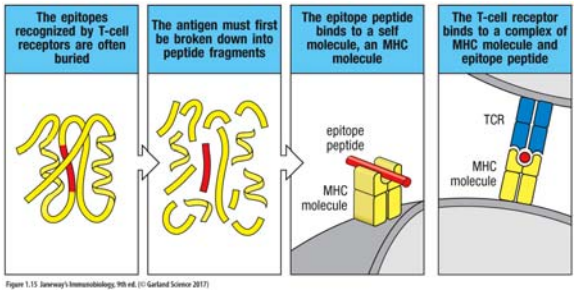


Antigen and epitope

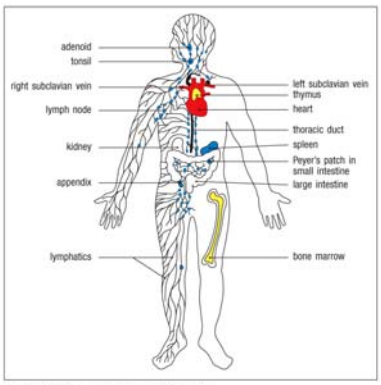
Epitope; A small part of the antigenic molecule which is recognized by an individual antigen receptor or antibody.



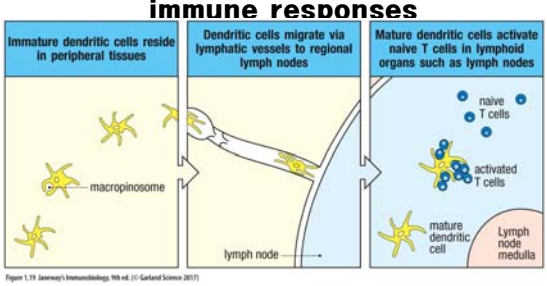
T cell receptor binds a complex of antigen fragment and MHC



MHC molecules; major histocompatibility complex, which is a protein which could present a peptide antigen to T cells

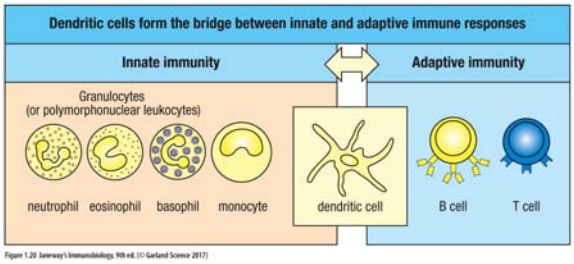


Dendritic cells initiate adaptive immune responses

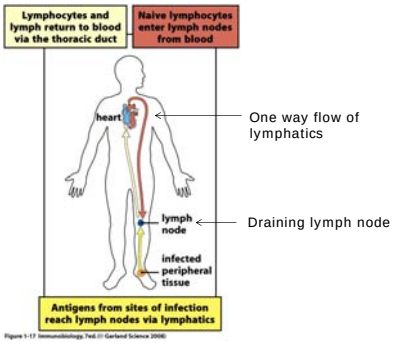


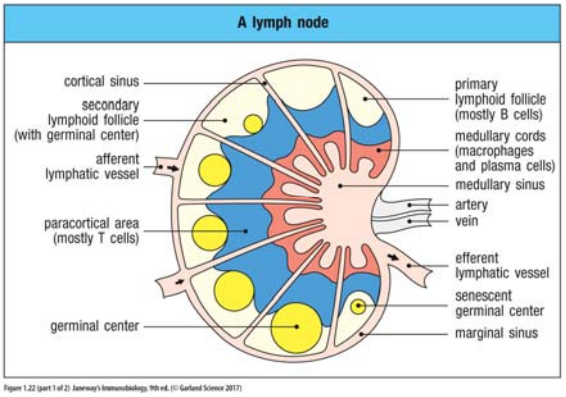
Immature DCs are continually taking up extracellular material, including virus particles and bacteria by the receptor independent mechanism of macropinocytosis.

DCs migrate to peripheral lymphoid tissues and displays antigens to T cells with costimulatory molecules.

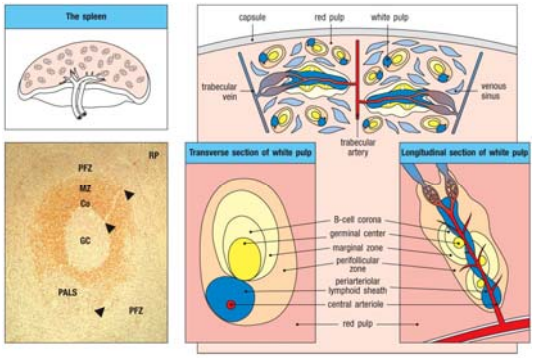


Circulating lymphocytes encounter antigen in peripheral lymphoid organs





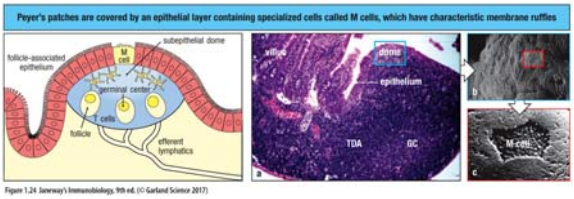
Organization of the lymphoid tissues of the spleen



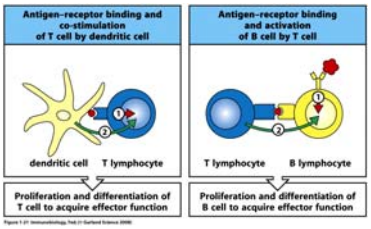
MALT (mucosal associated lymphoid tissues)
GALT (gut associated lymphoid tissues)
NALT (nasal associated lymphoid tissues)
BALT (bronchus associated lymphoid tissues)

Most pathogens enter the body through mucosal surfaces.
Antigens from the air, food, and the natural microbial flora of the body
Mucosal surfaces are protected by an extensive system of lymphoid tissues.

Organization of a Peyer's patch in the gut mucosa



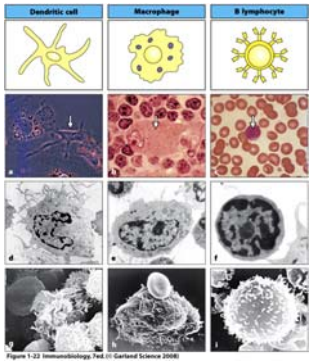
Two signals are required for lymphocytes activation



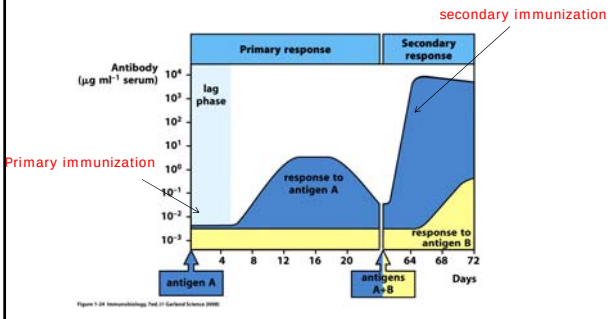
-> Interaction with other cells as well as with antigen is necessary for lymphocyte activation.

Anergy; contact with antigen without accompanying co-stimulatory molecules inactivates naïve lymphocytes.

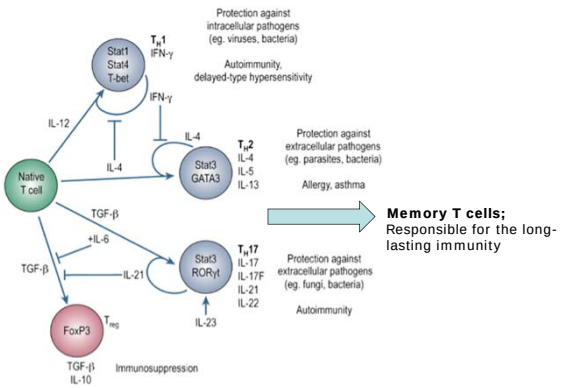
APC (antigen presenting cell)



Immunization and antibody response



Memory cells; significant number of activated antigen specific B cells and T cells persist after antigen has been eliminated.



Regulatory T cells; suppress the activity of other lymphocytes and help control immune responses

Effector module	Cell types, functions, and mechanisms
Cytotoxicity	NK cells, CD8 T cells
	Elimination of virally infected and metabolically stressed cells
Intracellular immunity (Type 1)	ILC1, T_H1 cells
	Elimination of intracellular pathogens; activation of macrophages
Mucosal and barrier immunity (Type 2)	ILC2, T_H2 cells
	Elimination and expulsion of parasites; recruitment of eosinophils, basophils, and mast cells
Extracellular immunity (Type 3)	ILC3, T_H17 cells
	Elimination of extracellular bacteria and fungi; recruitment and activation of neutrophils

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Antibodies deal with extracellular forms of pathogens and their toxic products

Humoral immunity; Antibodies are found in the fluid component of blood, or plasma, and in extracellular fluids.

Neutralization; Most direct way that antibodies can protect against pathogens by binding to them and blocking their access to cells. This is important for protection against viruses.

Opsonization; Phagocytes have receptor that bind the stems of the antibodies coating the bacterum, leading to phagocytosis.

Complement activation; Constant regions of antibodies bound to bacterial surfaces form receptors for the first protein of the complement system, leading complement activation.

Antibodies deal with extracellular forms of pathogens and their toxic products

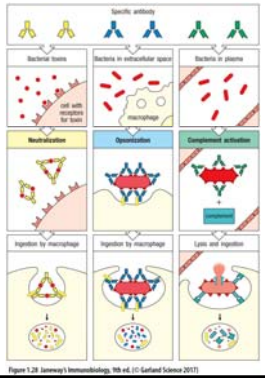


Figure 1.28 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

MHC molecules display peptide fragments of antigens

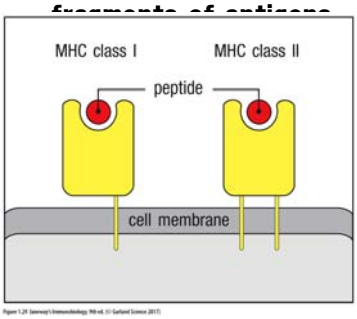


Figure 1.29 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

They have slightly different structures but both have an elongated cleft in the extracellular surface of the molecule, in which a single peptide is trapped during the synthesis and assembly of the MHC molecule inside the cell.

MHC class I

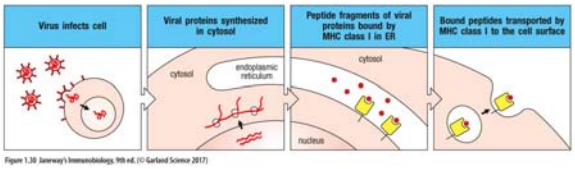


Figure 1.30 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)

MHC class I molecules collect peptides derived from proteins synthesized in the cytosol and are thus able to display fragments of viral proteins on the cell surface. All cells express MHC I.

MHC class II molecules bind peptides derived from proteins in intracellular vesicles, and thus display peptides derived from pathogens living in macrophage vesicles or internalized by phagocytic cells and B cells. DC, macrophages, B cells express MHC II.

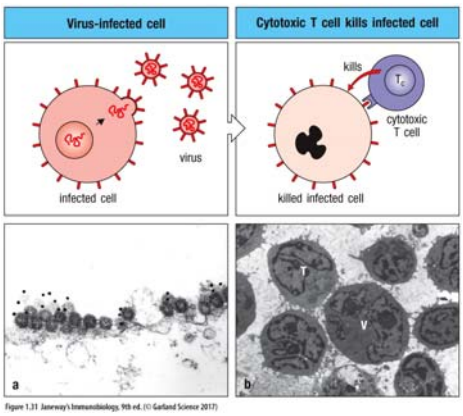
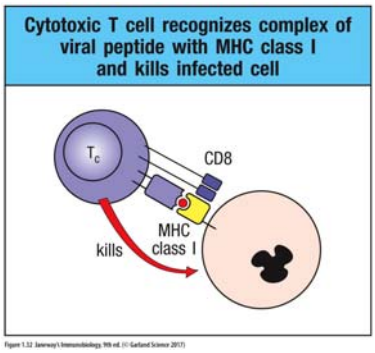
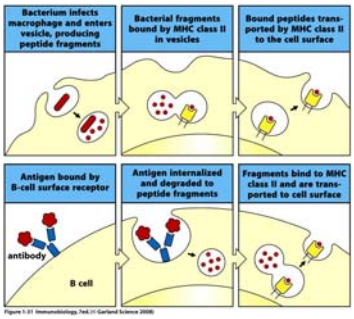


Figure 1.31 Janeway's Immunobiology, 9th ed. (© Garland Science 2017)



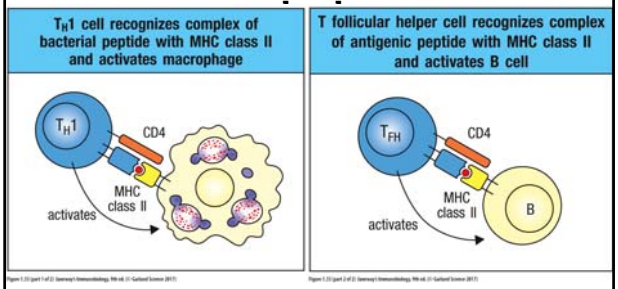
Cell-mediated immune response; Some bacteria and parasites, and all viruses replicate inside cells there they can not be detected by antibodies. T cells are responsible for destruction of these invaders.

MHC class II



MHC class II molecules bind peptides derived from proteins in intracellular vesicles, and thus display peptides derived from pathogens living in macrophage vesicles or internalized by phagocytic cells and B cells.

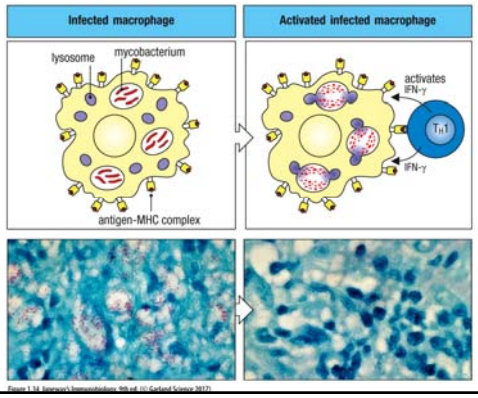
CD4 and CD8 T cells recognize peptides bound to different classes of MHC



CD4 and CD8 are known as coreceptors.

CD8 molecule binds preferentially to MHC class I molecules, whereas CD4 binds preferentially to MHC class II molecules.

Mechanism of host defense against intracellular infection by mycobacteria



Immune response can be beneficial or harmful

Antigen	Effect of response to antigen	
	Normal response	Deficient response
Infectious agent	Protective immunity	Recurrent infection
Innocuous substance	Allergy	No response
Grafted organ	Rejection	Acceptance
Self organ	Autoimmunity	Self tolerance
Tumor	Tumor immunity	Cancer

Successful vaccination