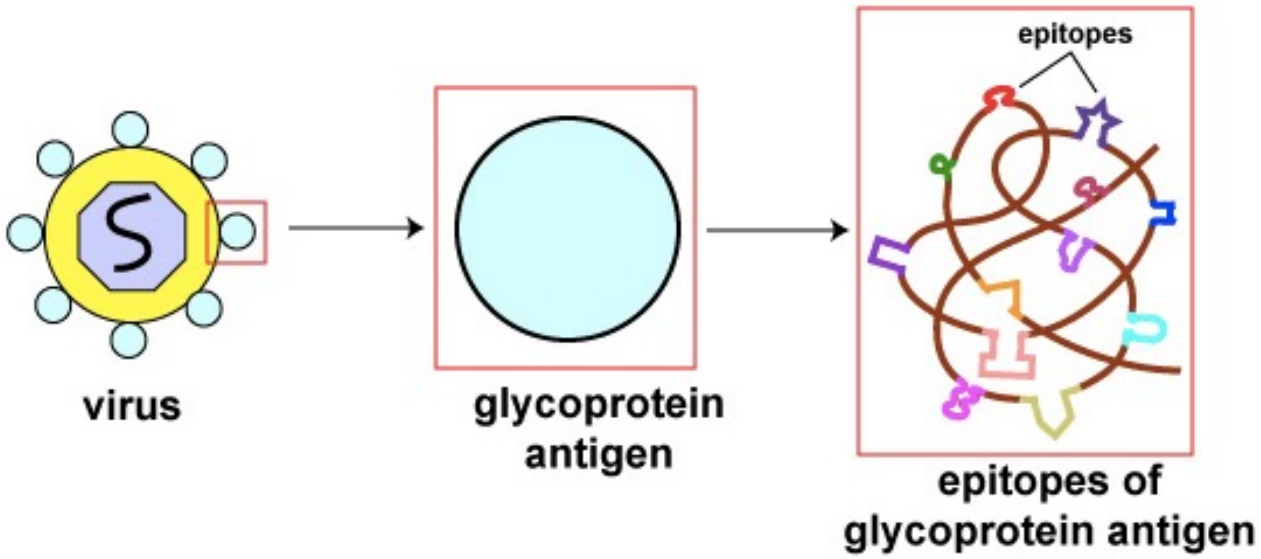
Adaptive Immunity

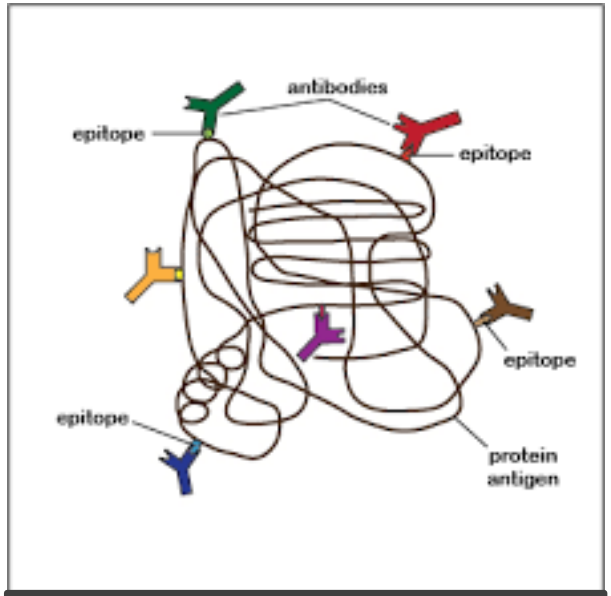
The Adaptive Immune system responds to pathogens by specifically recognizing antigens.

Antigens are molecules from pathogens that can be recognized by the immune system (though non-pathogens can also be antigens).
Importantly, only smaller pieces of antigens (called epitopes or antigenic determinants) are actually **recognized** by the **T cells and B cells** of the adaptive immune system.

The adaptive immune system responds to pathogens

Pathogens are bacteria, viruses and parasites capable of triggering disease in hosts.





Antibodies binding to epitopes

Pathogen* → antigens → epitopes

*Pathogens are made up of many different antigens.
Each antigen can have many epitopes (antigenic determinants)

Adaptive Immunity
vs
Innate Immunity

Both Innate and Adaptive Immune System

Provide Self/nonself differentiation

But ONLY the adaptive immune system has memory and precise antigen specificity

Characteristics of Adaptive Immunity

The adaptive immune system…….

1. can distinguish small differences in antigens.
   Thus, it has greater specificity than innate.
2. takes 5-7 days to initiate antigen specific adaptive immune response when 1st exposed to pathogen.
   Thus, it takes longer than innate immunity.
3. creates immune cells that will provide a faster immune response when infected again with same pathogen.
   Thus, it has memory (unlike innate).

Immune memory

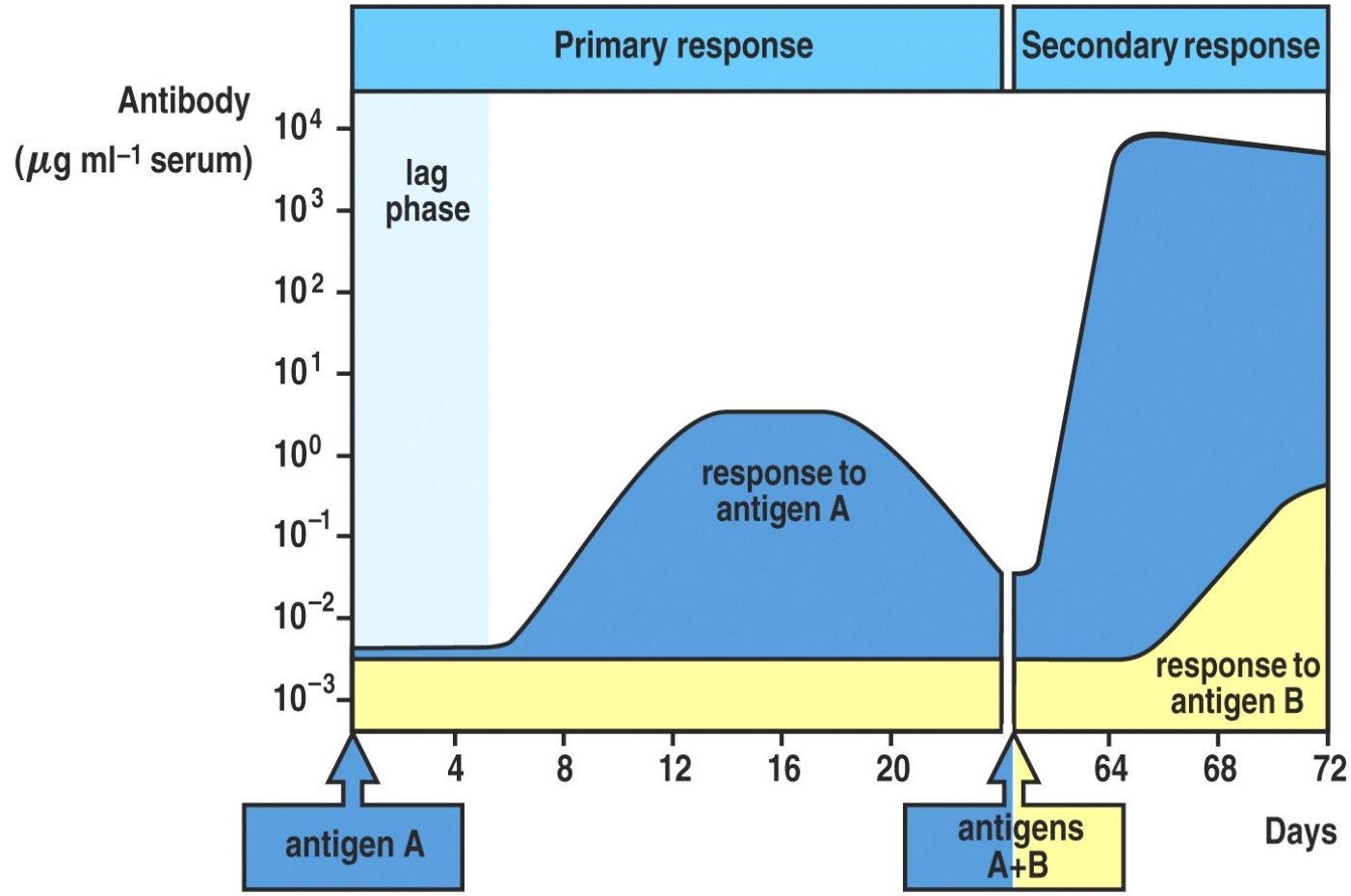


Figure 1-20 Immunobiology, 6/e. (© Garland Science 2005)

Immunological memory. The second exposure to an antigen results in a more potent immune response.

The adaptive immune response to antigen "A" (specific pathogen) is more rapid during the 2nd exposure because of memory.

Adaptive immunity

Adaptive immunity has specificity and memory and provides the primary mechanism for differentiating self "antigens" versus non-self or foreign antigens.

This means the adaptive immune system must determine if a pathogen is foreign and harmful (pathogenic) versus foreign and not harmful (non-pathogenic).

Adaptive immune responses initiation

PRIMARY infection= first exposure

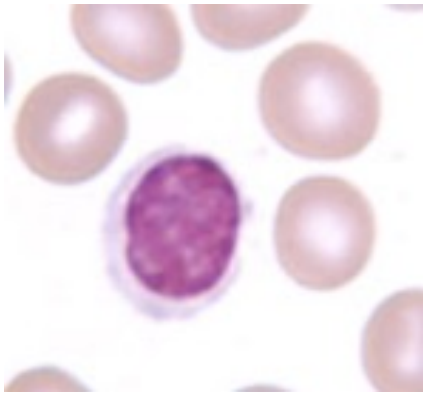
The adaptive immune response takes a few days (3-7 days to initiate during a primary infection. The T and B cells against antigens of a pathogen must be activated and expanded (proliferate) in spleen or lymph node and then spread throughout body to fight the pathogen.

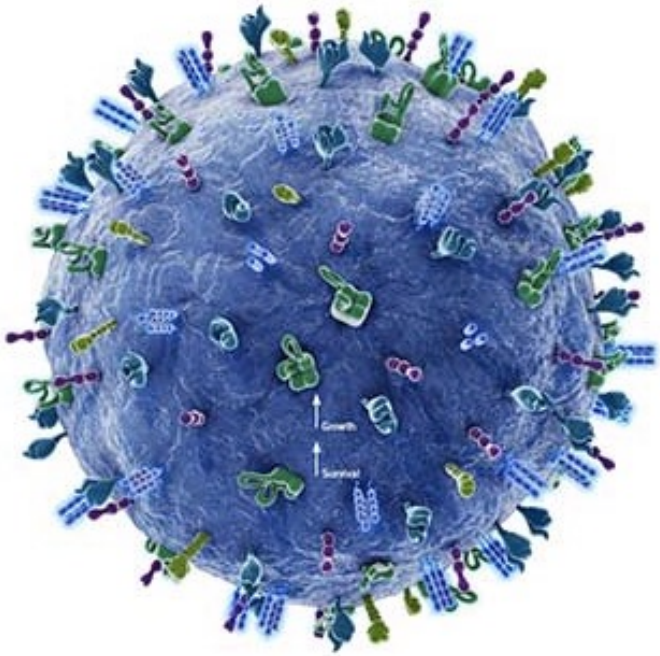
SECONDARY infection= any subsequent exposure

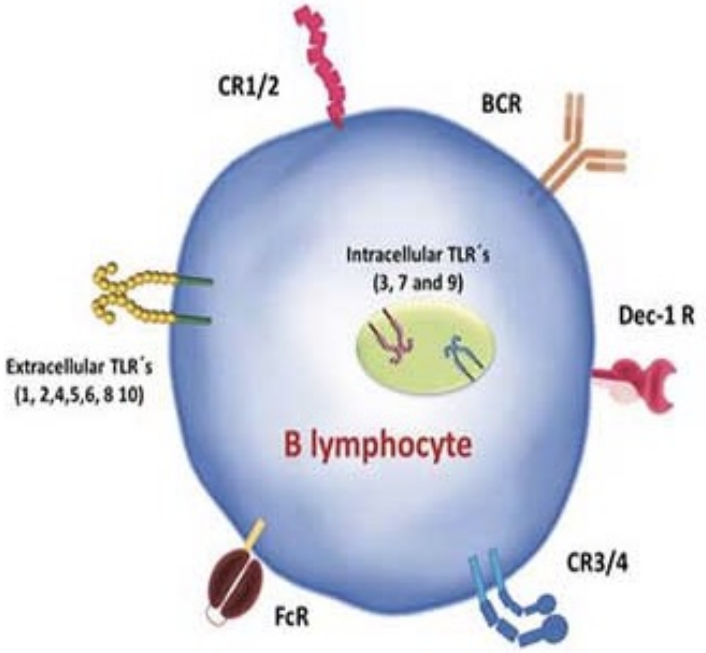
The second time you are exposed to a pathogen, the adaptive immune response happens more quickly (1-3 days) because of adaptive immune memory cells. The more rapid immune response in a secondary exposure is because you have memory T cells and memory B cells which can be activated more quickly when they recognize the pathogen.

Cells of the Adaptive Immune System

Lymphocytes







T lymphocyte or T cell

B lymphocyte/B cell

***Macrophages and Dendritic cells play important roles in ACTIVATING adaptive immunity but do not form memory cells.

Adaptive Immunity

B cell mediated immunity:

Antibodies produced by B-cell interact with pathogens and their toxic products in the blood or other extracellular spaces of the body.

T-cell mediated immunity:

T cells only recognize antigen as a small peptide fragment (peptide) bound to an MHC molecule and displayed at the cell surface.

The THREE tools of the adaptive immune response

1. Antibodies made by B cells.
2. Cytokines made by T helper cells.
3. Killing of infected cells by cytotoxic T cells (CTLs).

B Cells

Antibody-mediated immune response

◆The main function of B cells is to produce antibodies.

◆B cells are the only cells capable of producing antibodies.

No B cells=No antibodies

When a person has no antibodies, the person has increased susceptibility to infections with viruses and extracellular bacterial pathogens.

Antibody structure

Antigen binding region

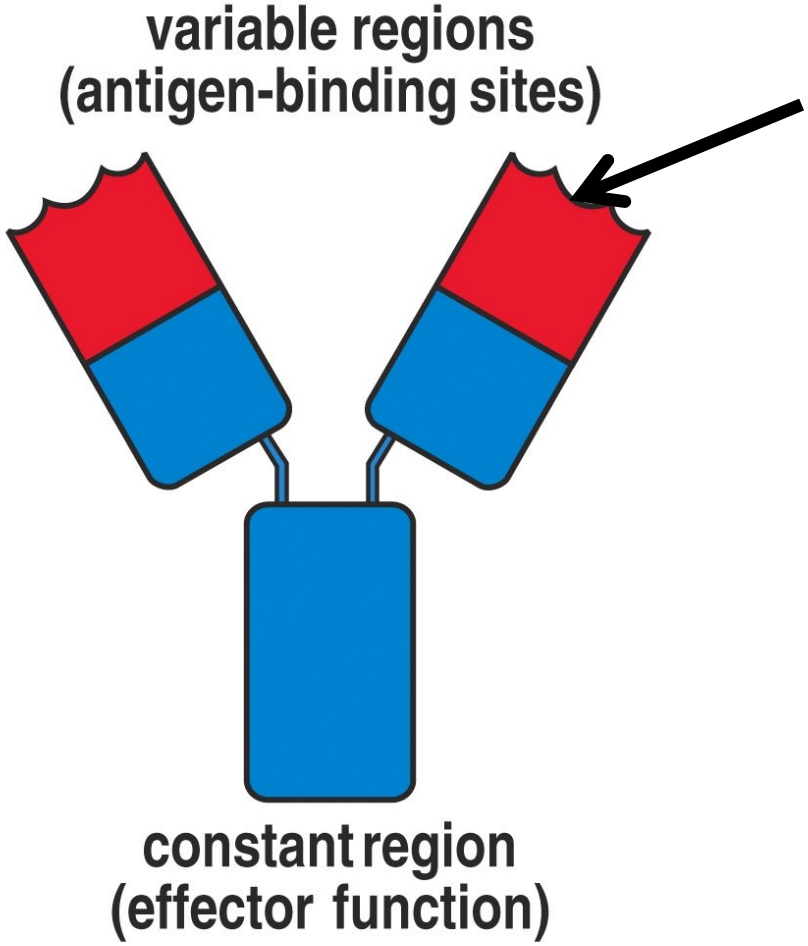


Figure 1-16 Immunobiology, 6/e. (© Garland Science 2005)

Structure of single antibody molecule

One part of ab (Fab) binds specifically to antigens (pieces of pathogens).

◆This Fab part is highly variable. It was estimated that a human can generate ~100,000,000,000 ($=10^{11}$) different kinds of antibodies.

◆An individual B cell only produces a single kind of antibody.

◆ Each antibody has the specific ability to bind only ONE antigen.

Antibody structure

Antibody Isotypes Determined by Constant Region

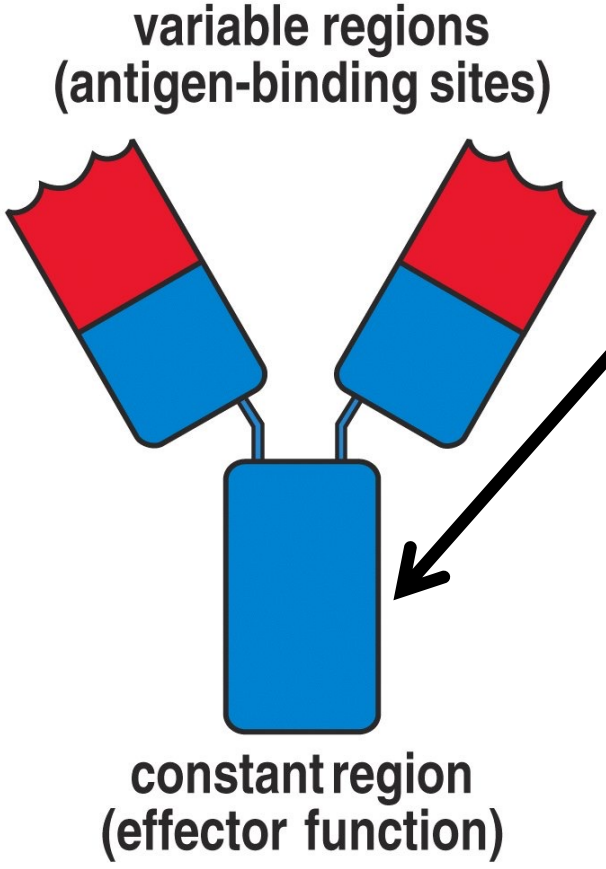


Figure 1-16 Immunobiology, 6/e. (© Garland Science 2005)

The other part of antibodies is called the constant region (Fc).

Only a handful of different constant regions that can be found on antibodies and they result in different "types" or isotypes of antibodies.

Four main antibody isotypes
IgM, IgG, IgA, IgE

Functions of antibodies

1.Neutralization. Antibodies bind to antigens on pathogen or toxin and block toxin function.

2.Opsonization. Antibody molecules enhance phagocytosis.

3.Complement binds to antibodies molecules bound to pathogen or infected cells and enables lysis or phagocytosis.

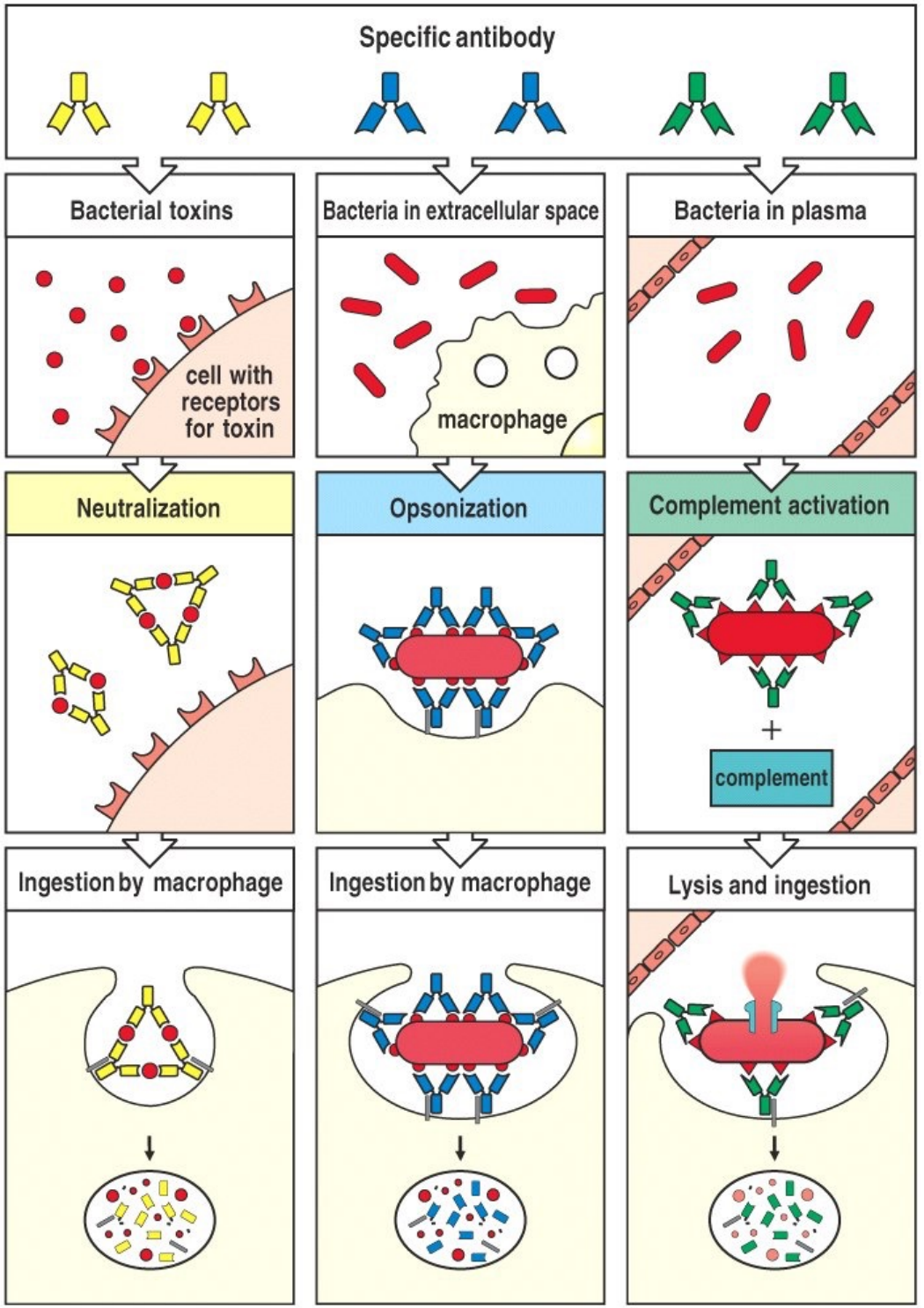
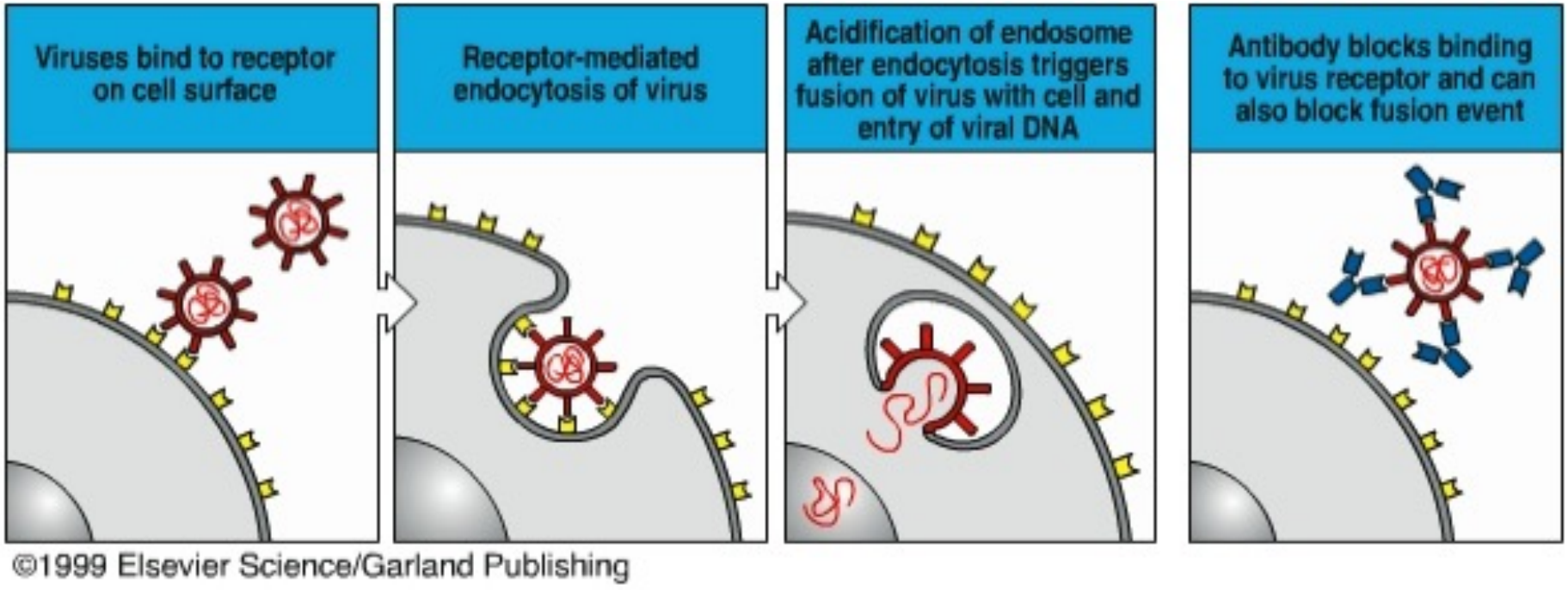


Figure 1-24 Immunobiology, 6/e. (© Garland Science 2005)

Antibody Effector Functions

Neutralization

Neutralizing abs block active site for adherence, entry into host cell, or active site of toxin



Neutralizing antibodies are usually high affinity (=better binding) and primarily IgG and IgA.

Antibody Effector Functions

- Opsonization.

Fc of antibody binds to FcReceptor on phagocytic cells to provide enhanced uptake.

- Complement Activation.

Complement protein binds to Fc receptors.

1. Leads to increased uptake-- opsonization
2. Full complement pathway activation leads to cell lysis of pathogen or infected cell by pore formation.

T cells have a specialized T cell Receptor

- All T cells are activated by a very special receptor on their surface called the T cell receptor (TCR).
- Each T cell expresses only one unique TCR but will express 1000's copies of that same TCR.
- TCRs have a variable region and a constant region (like antibodies).
- Like antibodies, TCRs are incredibly diverse. The body can make $>10^{11}$ different TCRs each capable of binding to a unique antigen.

However, in contrast to antibodies, TCRs only recognize antigen when the antigen is presented by specialized molecules called MHC.

MHC= Major Histocompatibility

- MHC molecules perform the job of displaying fragments of pathogens on the host cell surface.

- Dendritic cells (DCs), B cells and macrophages (macs) are specialized in the job of presenting antigens to T helper cells. Often, they are called professional antigen presenting cells.
- DCs and macs are very good at engulfing pathogens (by phagocytosis), digesting it, and presenting it on their cell surface.
- MHC molecules are called HLA (human leukocyte antigen) in humans

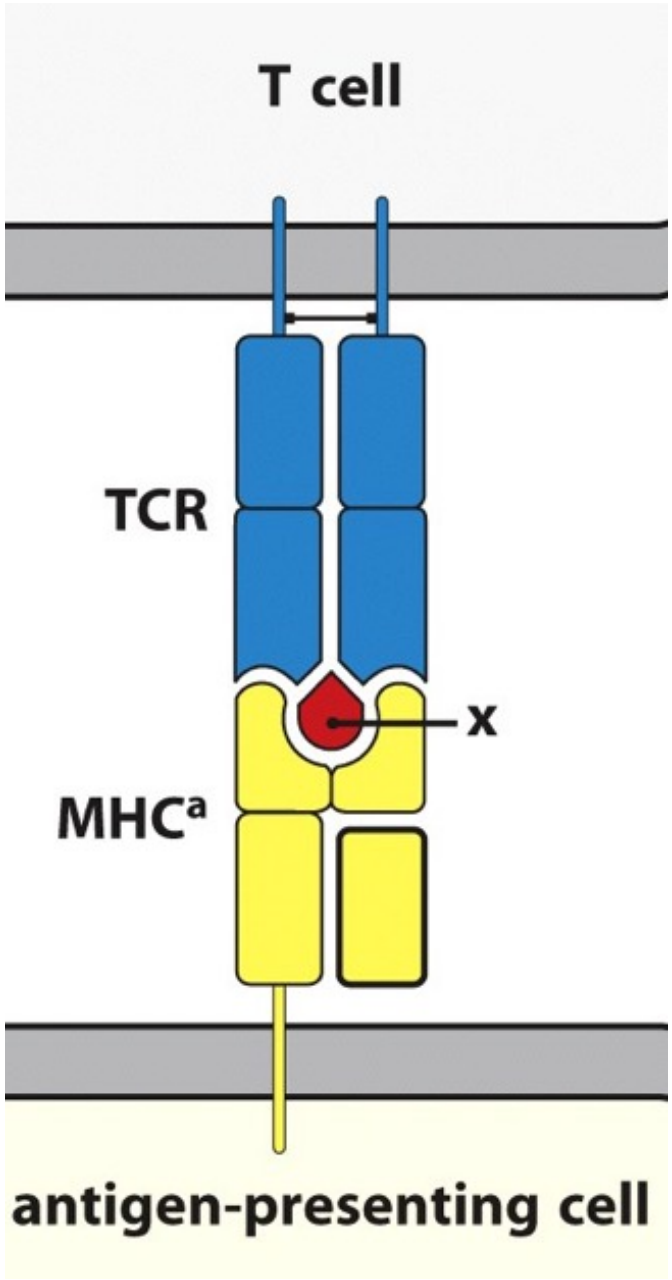
MHC restriction

T cell receptor only recognizes antigen in the "context of" self MHC:

<u>MHC restriction</u>: the fact that a peptide can only be recognized by a given T cell if it is bound to a particular self-MHC.

Red part binding to MHC 

is the antigen (peptide of pathogen) also binding to activate the TCR.



Two main types of T cells

- Cytotoxic T cells- The function of cytotoxic T cells is to specifically kill virally-infected cells. Also called CD8 T cells because they express a unique receptor molecule called CD8 on their cell surface.

- T helper cells- THE primary function of Thelper cells is to produce cytokines.

  These cells are also called CD4 T cells because they express a special receptor molecule called CD4 on their cell surface.

T helper cells

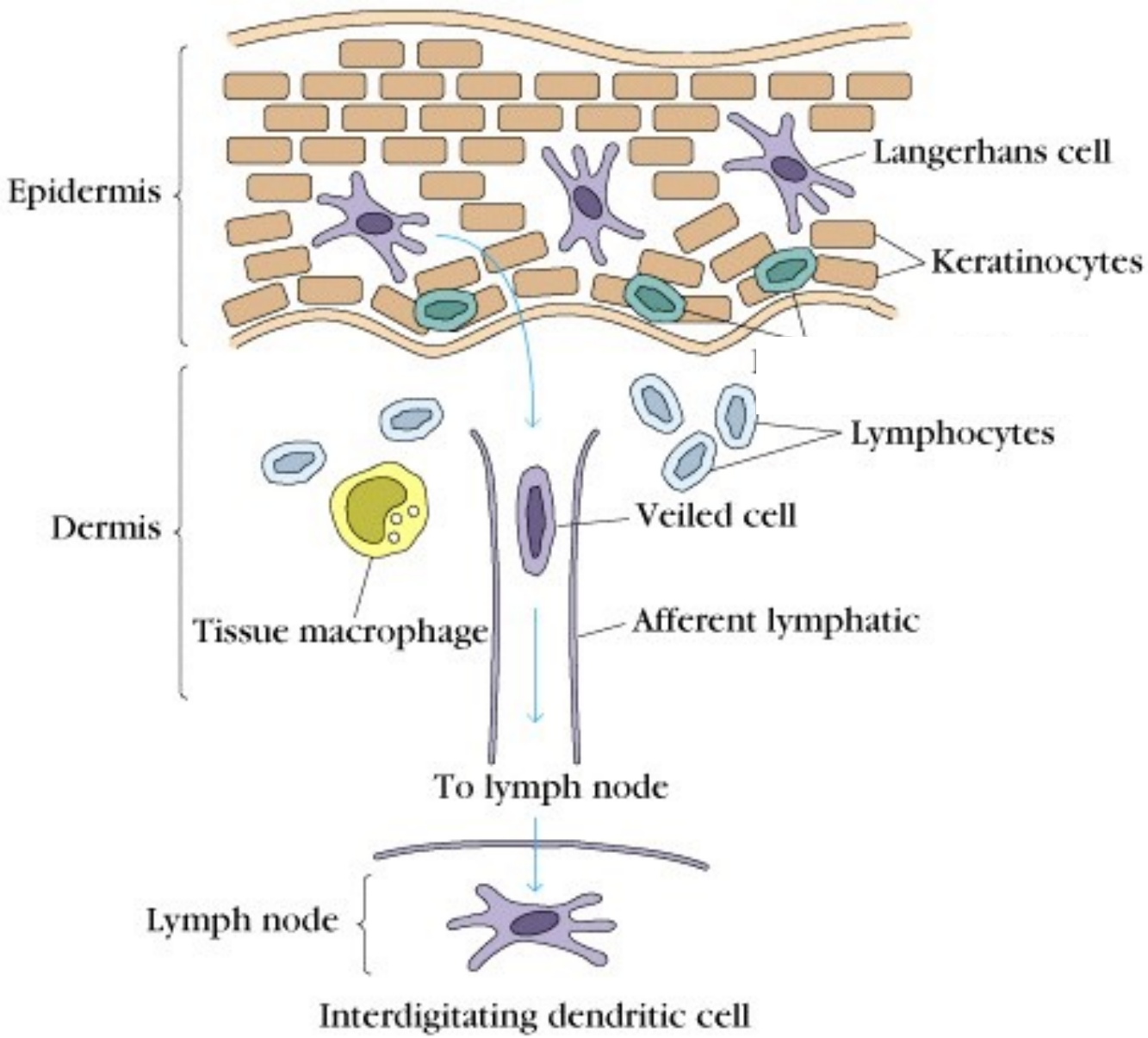
Helper T (Th) cells are considered the master regulators of adaptive immune responses.

Key immune cells need cytokines produced by Th cells in order to be "activated". Th cytokines are mostly DIFFERENT than innate immunity cytokines.

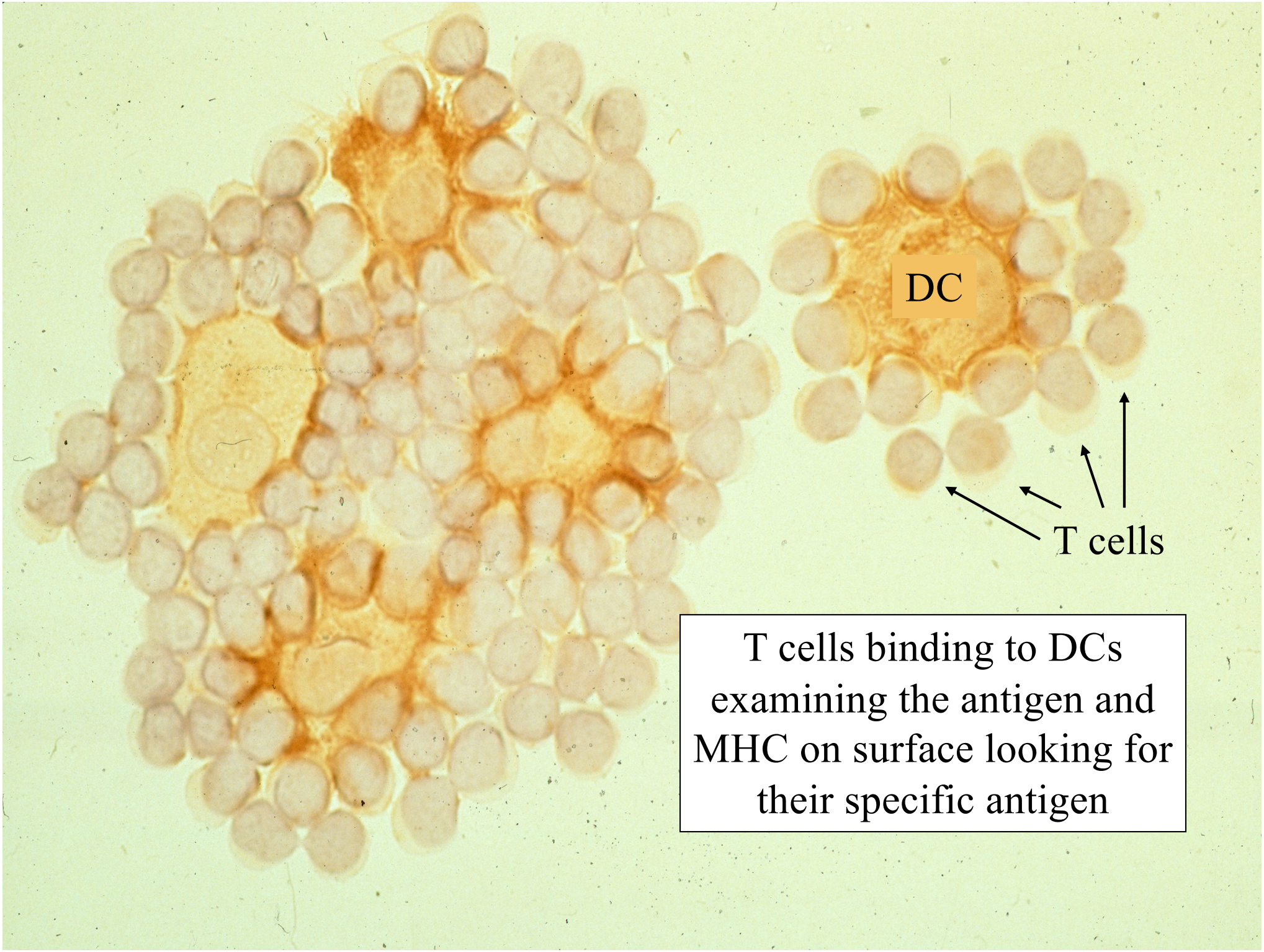
<u>Thelper cytokines are needed for:</u>

- B cells to produce antibodies
- Cytotoxic T cells in order to become maximally effective killers
- Macrophages to kill off pathogens inside

Dendritic cells Activate Naïve T cells to Initiate Adaptive Immune Response

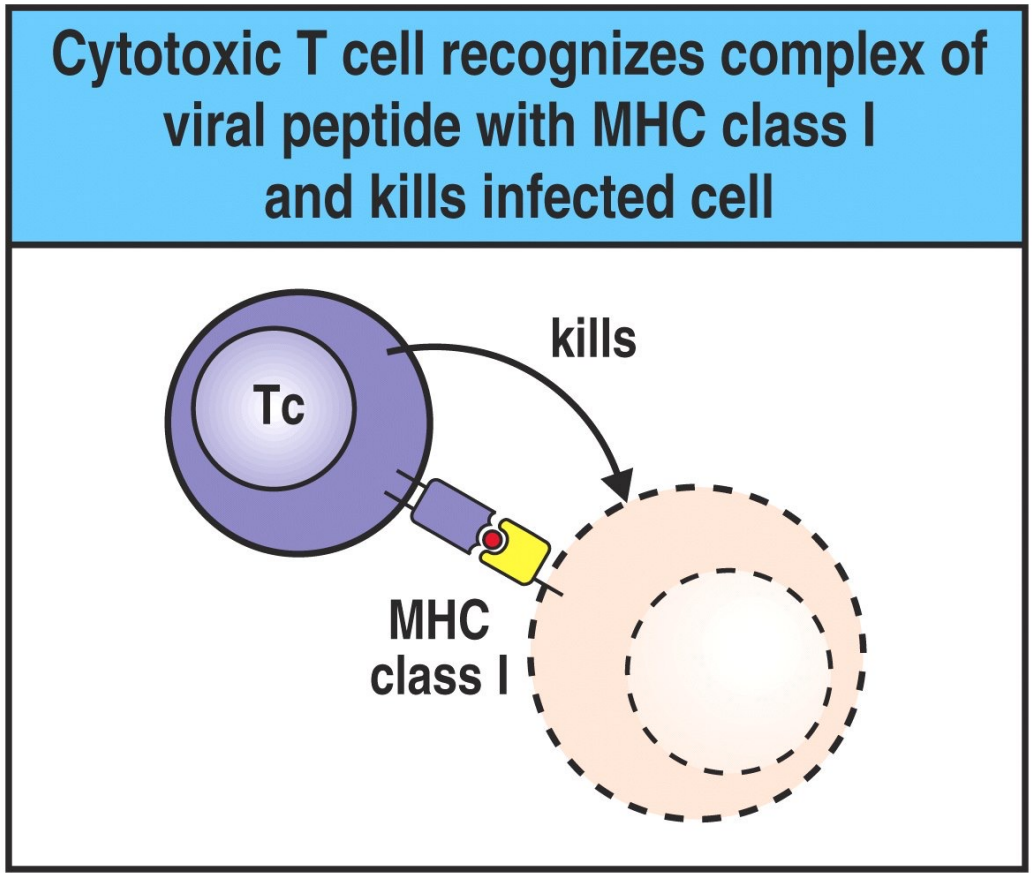


Dendritic cells pick up pathogens (meaning different antigens) at sites of infection
and bring it to the regional lymph nodes or spleen.



T cells binding to DCs examining the antigen and MHC on surface looking for their specific antigen

Activation of Cytotoxic T cells



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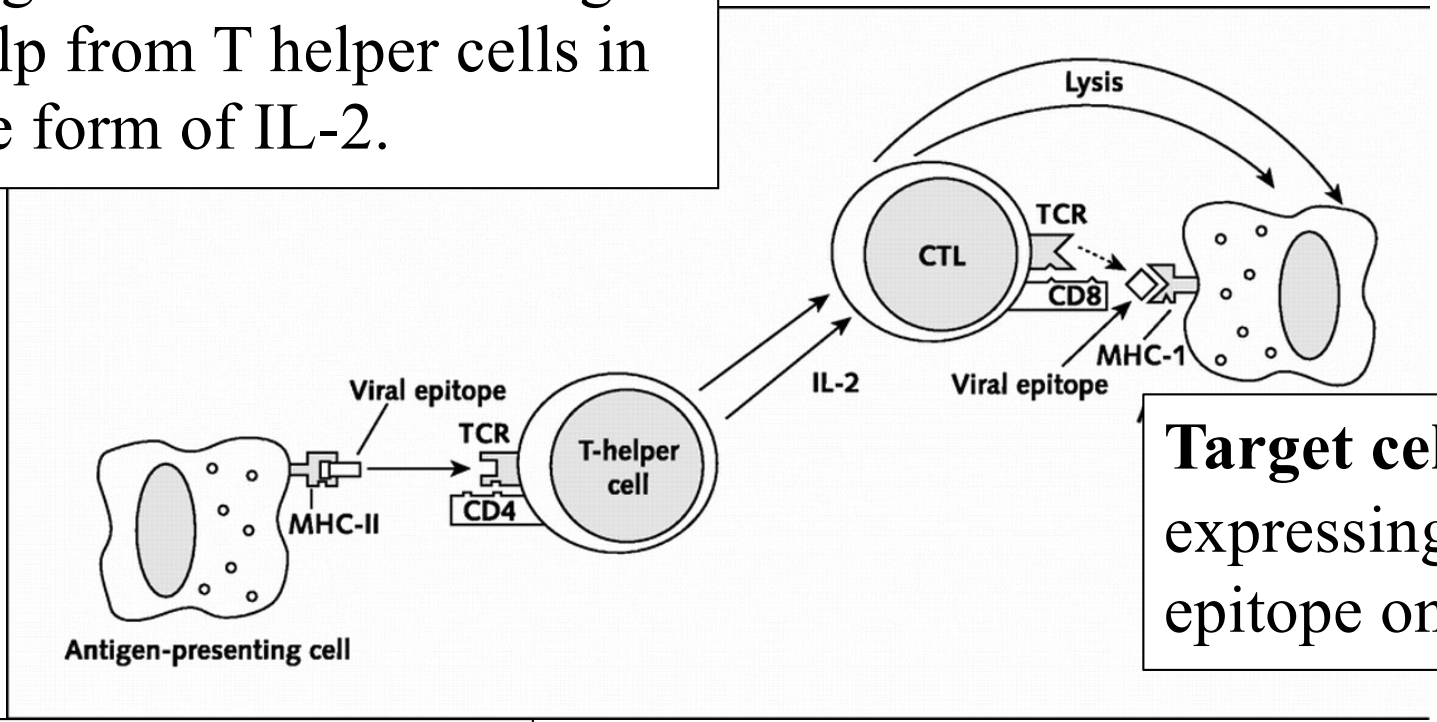
Activated cytotoxic T lymphocytes are known as CTLs. When the TCR of a specific CTL recognizes the antigen presented on MHC by an infected cell, the CTL kills the infected cell.

Activation of Cytotoxic T cells

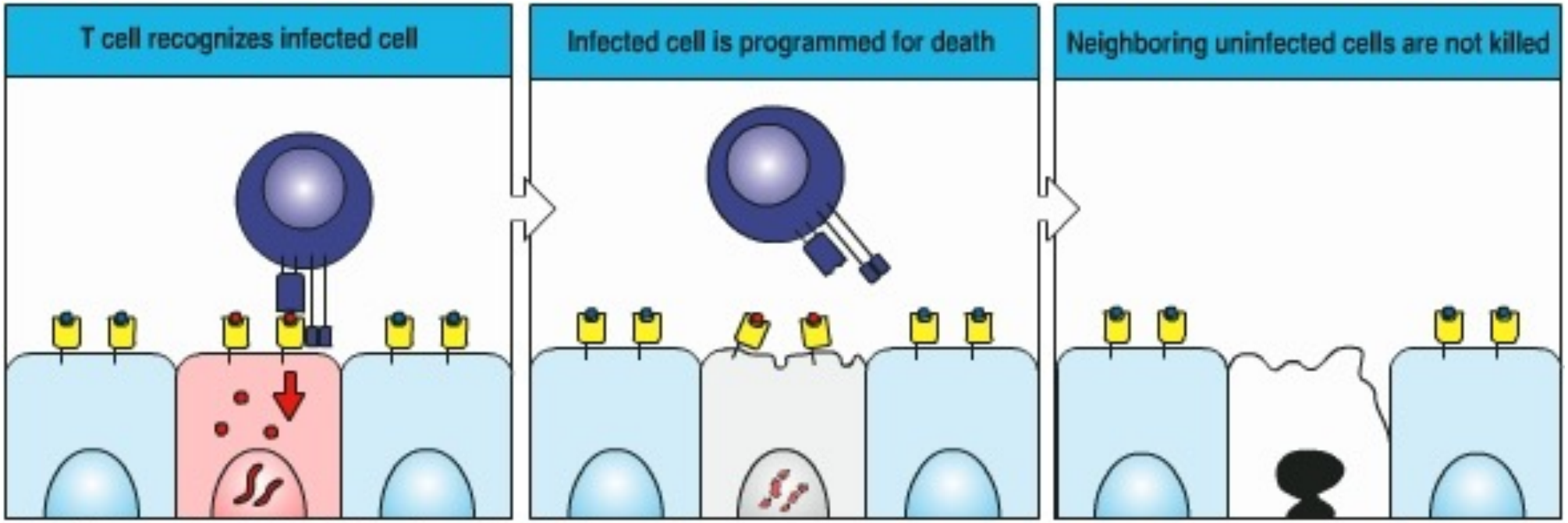
The effector function of activated CTLs is lysis of target cells. CTLs must get help from T helper cells in the form of IL-2.



Target cell expressing viral epitope on MHC

Dendritic cell expressing viral epitope on MHC

CTL Killing
is very specific killing



The antigen specific killing of infected target cells allows for reduced bystander killing of uninfected cells.