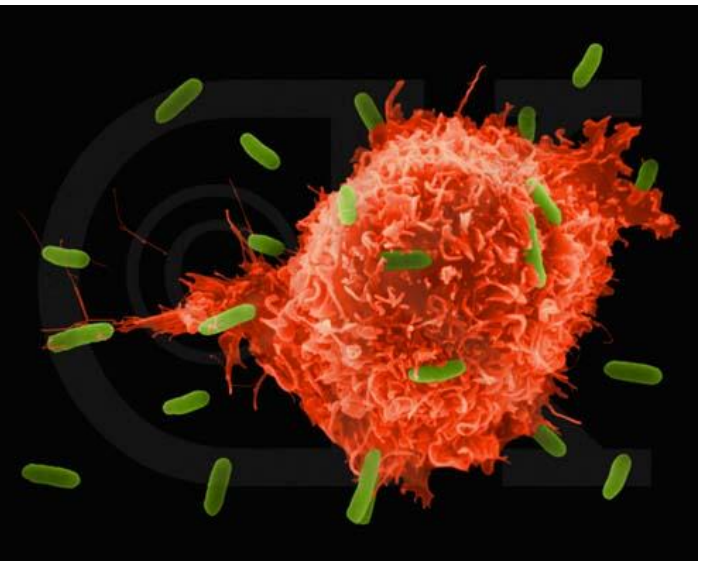
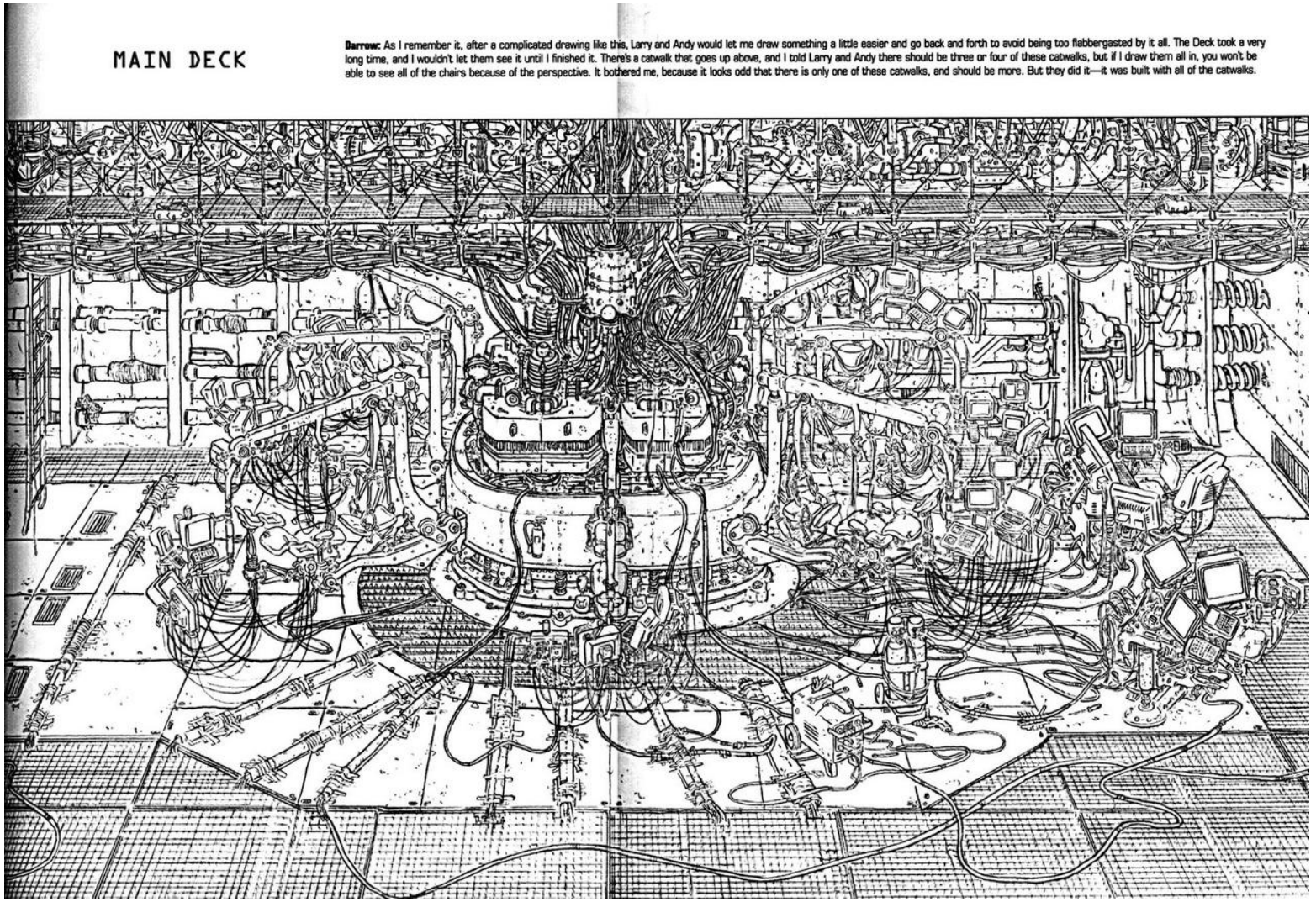
Overview of Immunological Concepts



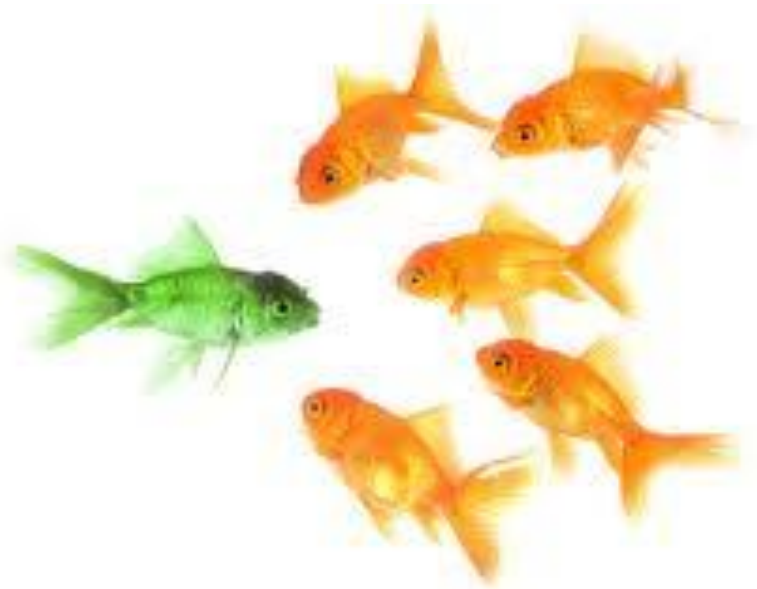
Dr. Issa Abu-Dayyeh

Why is Immunology difficult??

1- Details


MAIN DECK
Barrow: As I remember it, after a complicated drawing like this, Larry and Andy would let me draw something a little easier and go back and forth to avoid being too flabbergasted by it all. The Deck took a very long time, and I wouldn't let them see it until I finished it. There's a catwalk that goes up above, and I told Larry and Andy there should be three or four of these catwalks, but if I draw them all in, you won't be able to see all of the chairs because of the perspective. It bothered me, because it looks odd that there is only one of these catwalks, and should be more. But they did it—it was built with all of the catwalks.

2-Exceptions



3-An evolving science

4-A network!

The Immune system

First line of defense??

Innate Immune System

First Line of defense

Epithelial Barriers:

Skin ($2m^2$)

Mucosal membranes ($400m^2$)

Innate Immune System

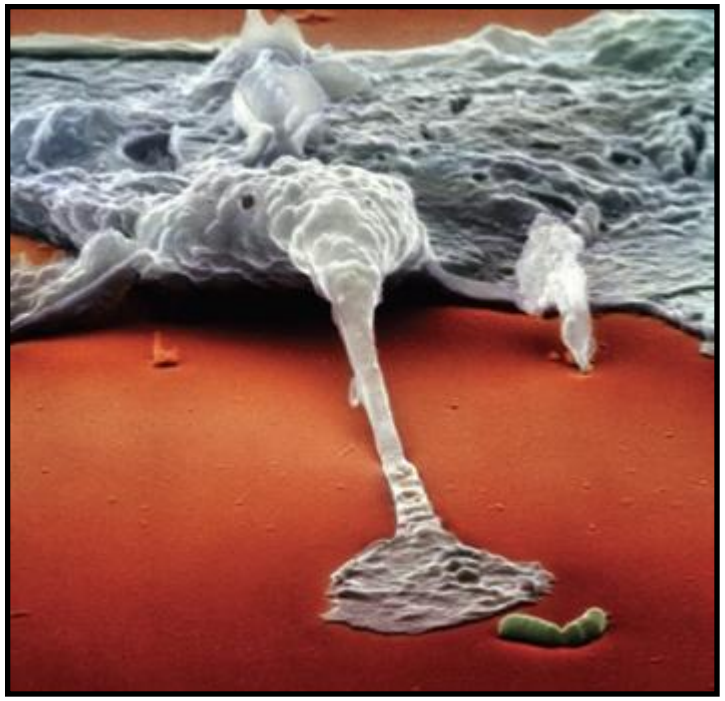
500 million years old!

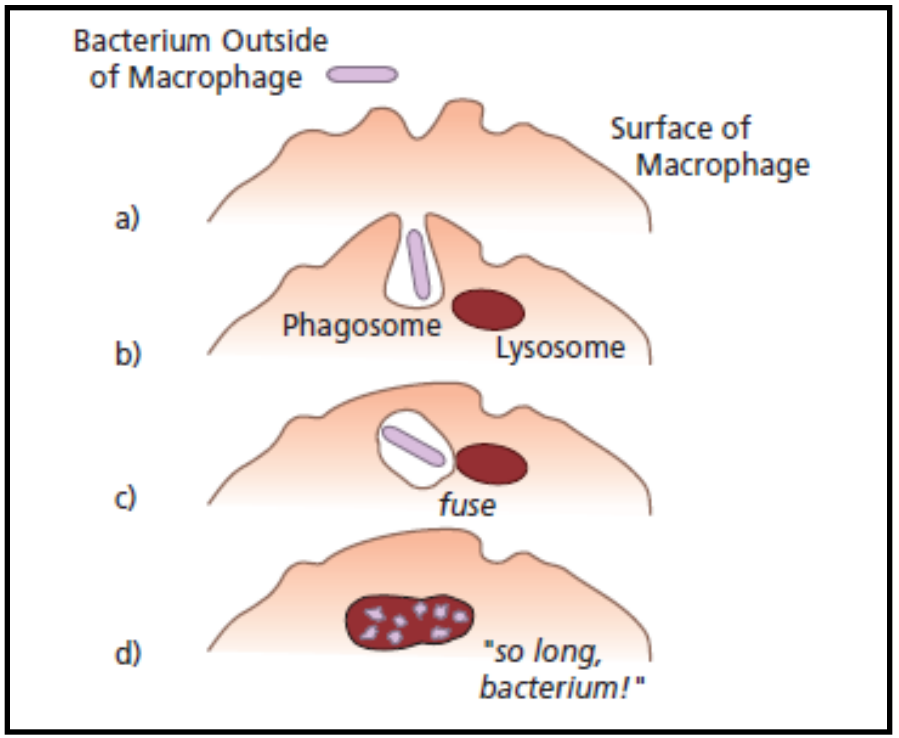
Molecules: Complement

Cells: Neutrophils, Macrophages, DCs, NK etc.

Erythema and edema

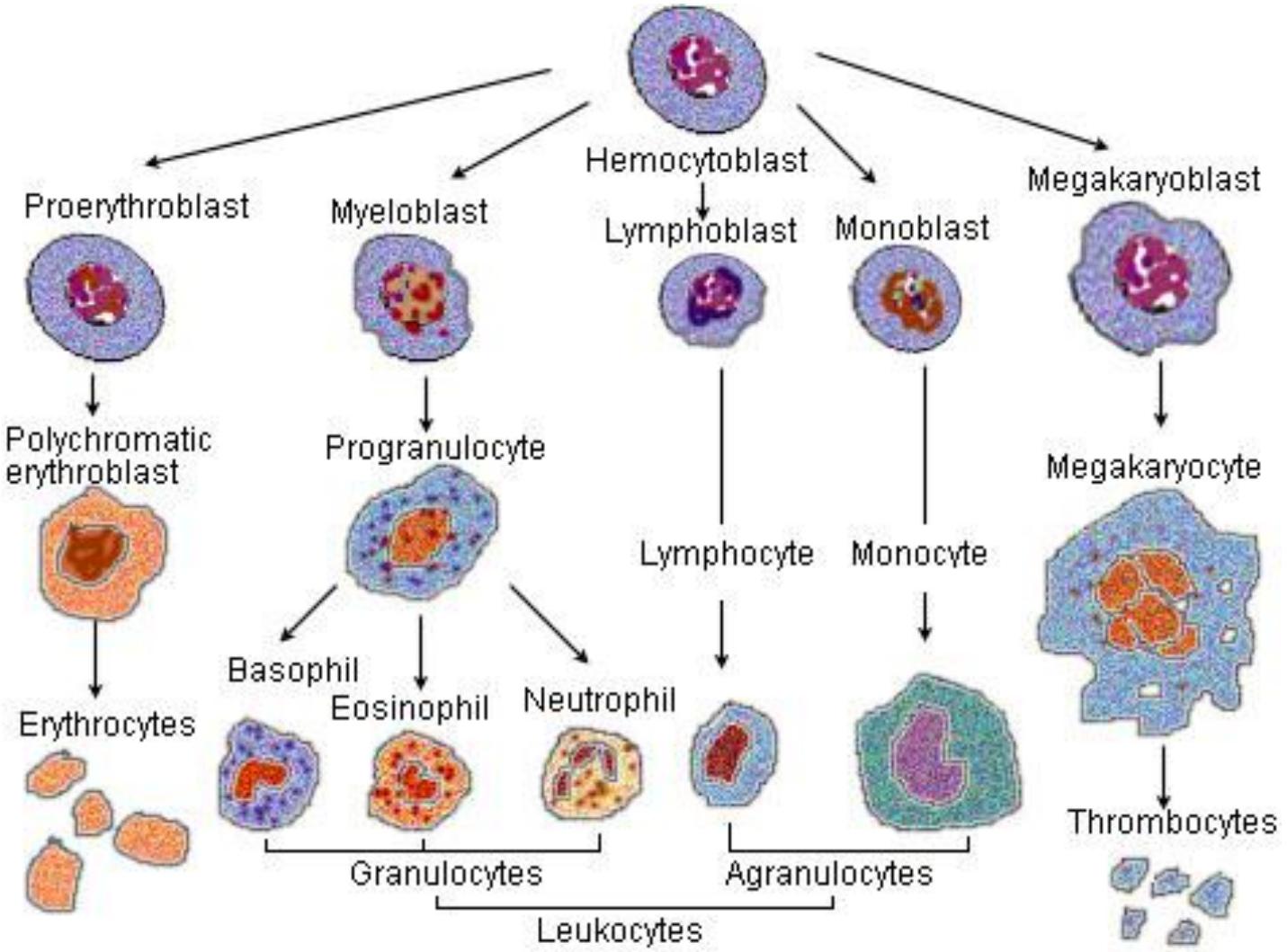
The Macrophage





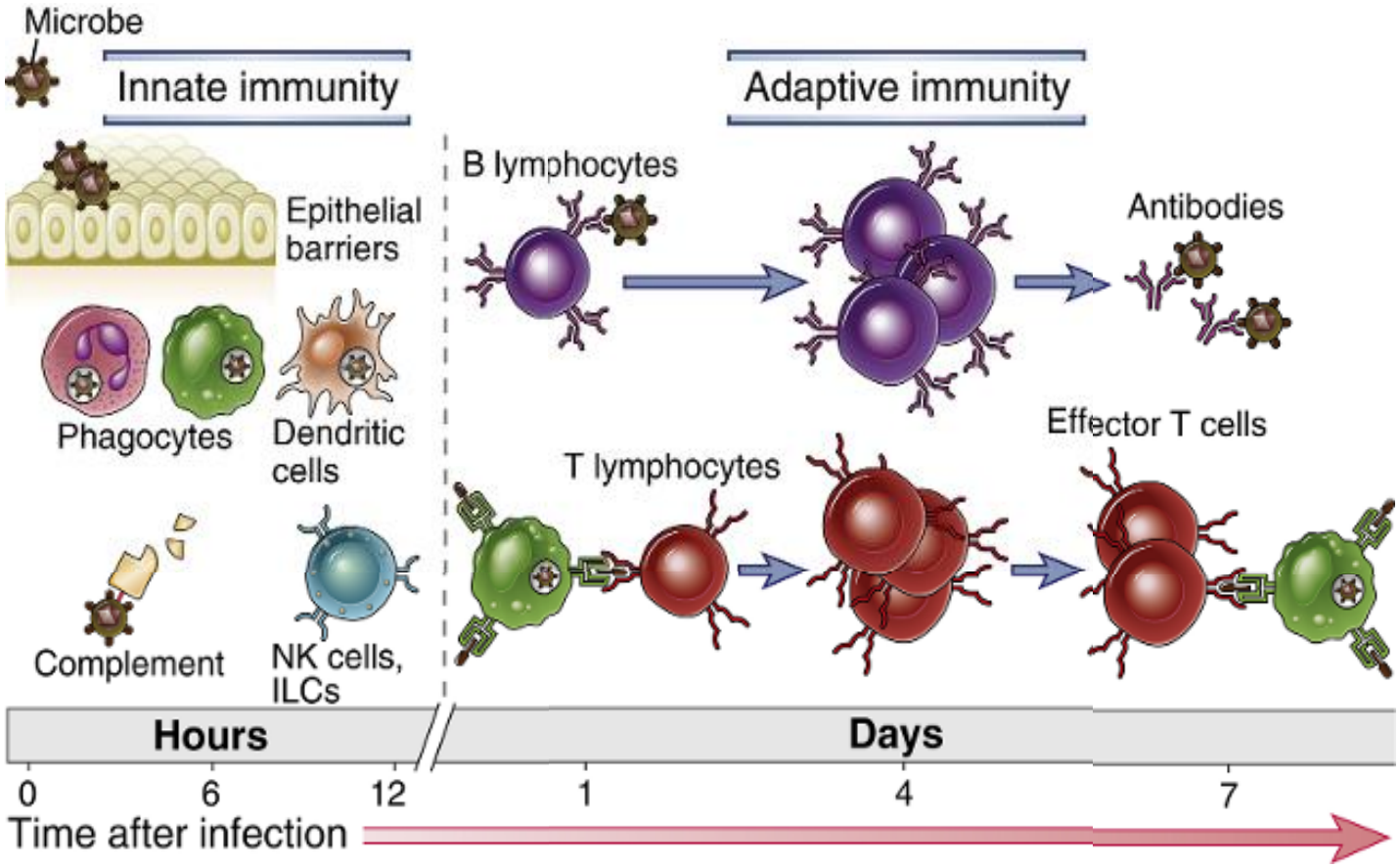
Where do Macrophages and other immune cells come from?

Bone Marrow


Hemocytoblast
Proerythroblast
Myeloblast
Lymphoblast
Monoblast
Megakaryoblast
Polychromatic erythroblast
Progranulocyte
Megakaryocyte
Lymphocyte
Monocyte
Basophil
Eosinophil
Neutrophil
Erythrocytes
Thrombocytes
Granulocytes
Agranulocytes
Leukocytes

Second Line of Defense??

Adaptive Immune System

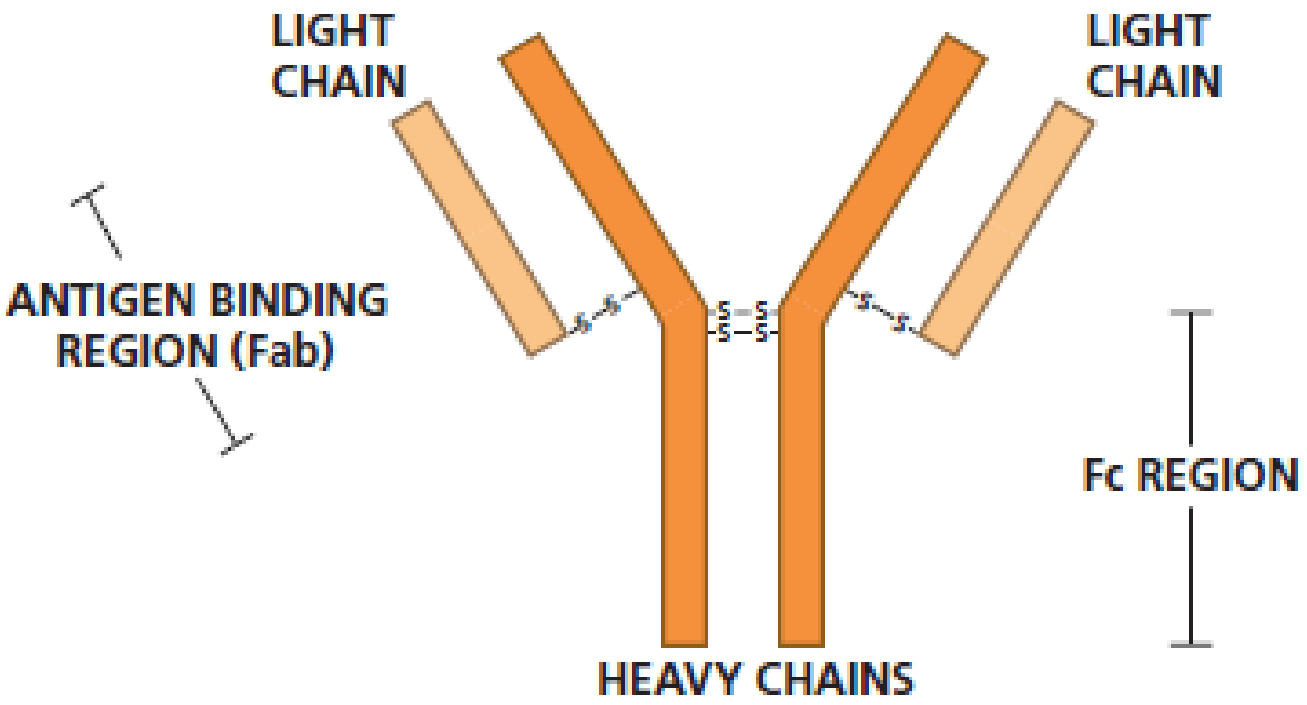

Microbe
Innate immunity
Adaptive immunity
Epithelial barriers
B lymphocytes
Antibodies
Phagocytes
Dendritic cells
T lymphocytes
Effector T cells
Complement
NK cells, ILCs
Hours
Days
0
6
12
1
4
7
Time after infection

Adaptive Immune system

Most probably developed to protect us against viruses

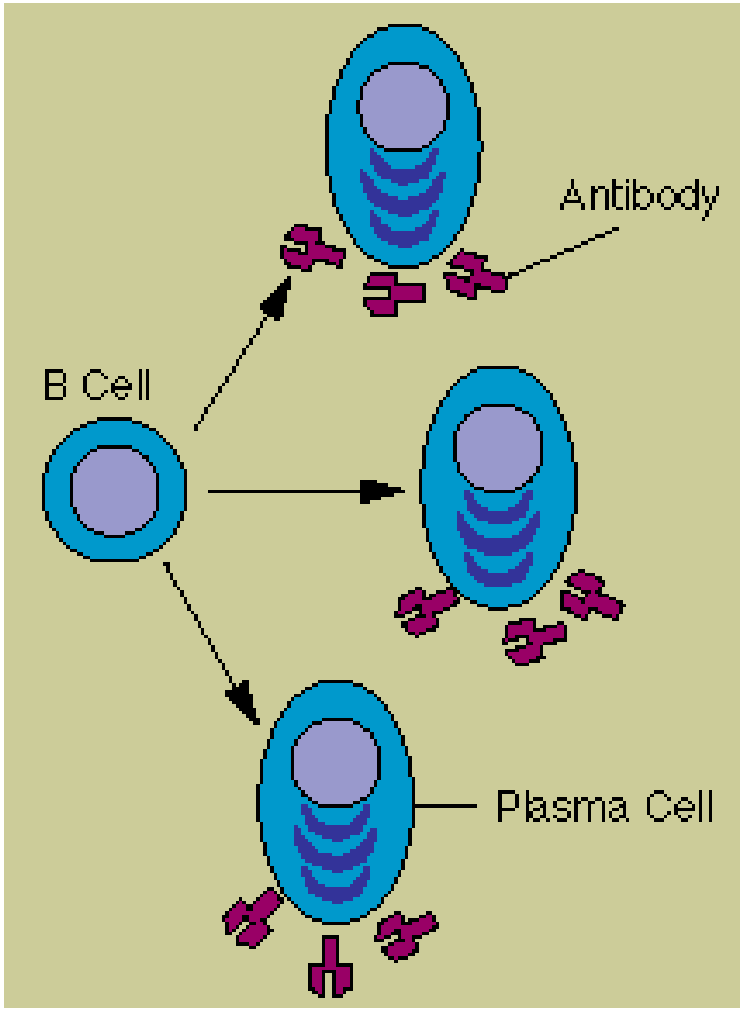
Edward Jenner 1796 Experiment.

What causes immunity to smallpox??



Antibodies!!

B cells Produce Antibodies



Generating Antibody Diversity

- Around 100 million different antibodies are needed to cover antigen variety.
- 10,000 heavy chain genes mixed with 10,000 light chain genes.

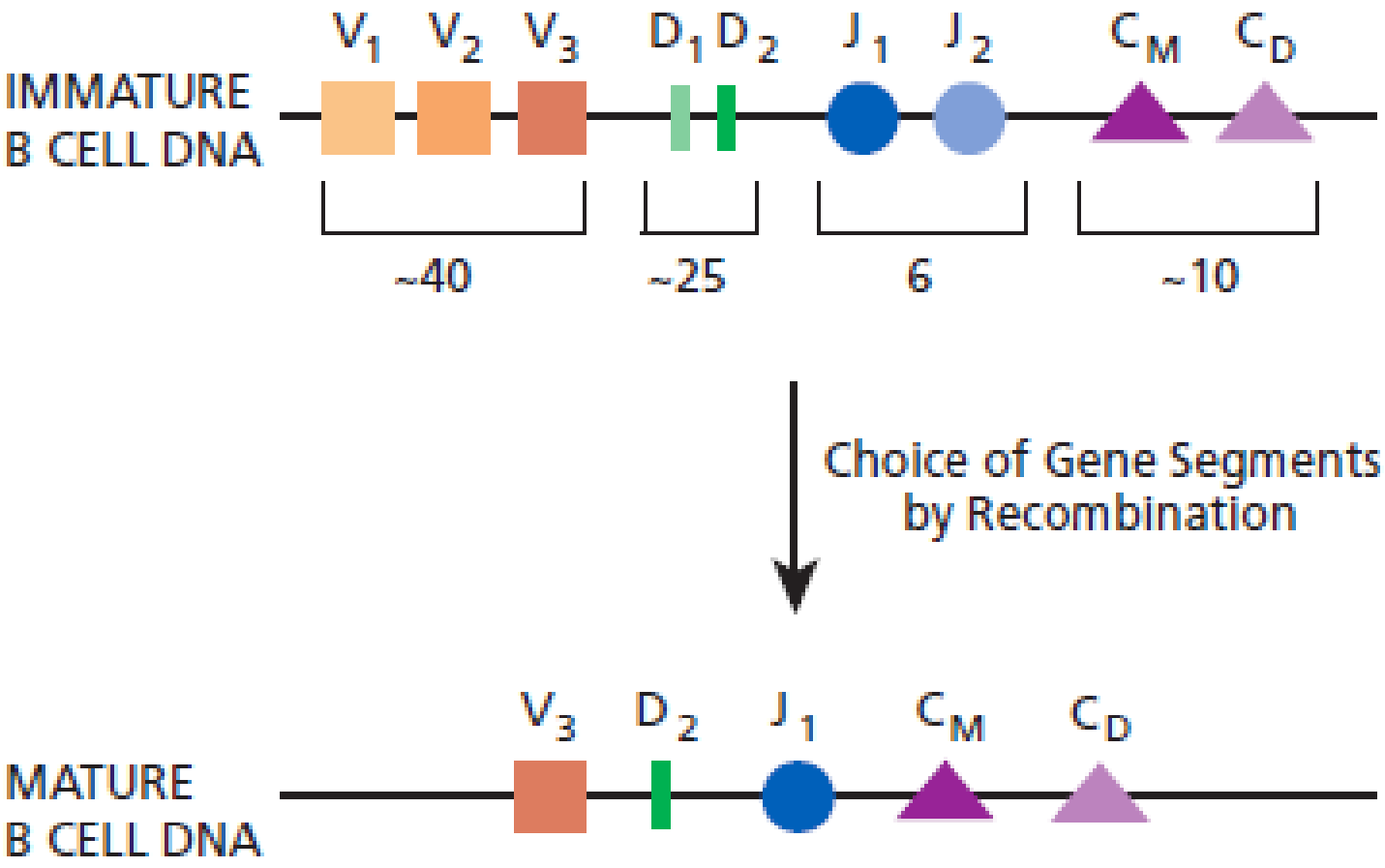
- Total of 20,000 genes required to generate this diversity.

- How many genes do we have???

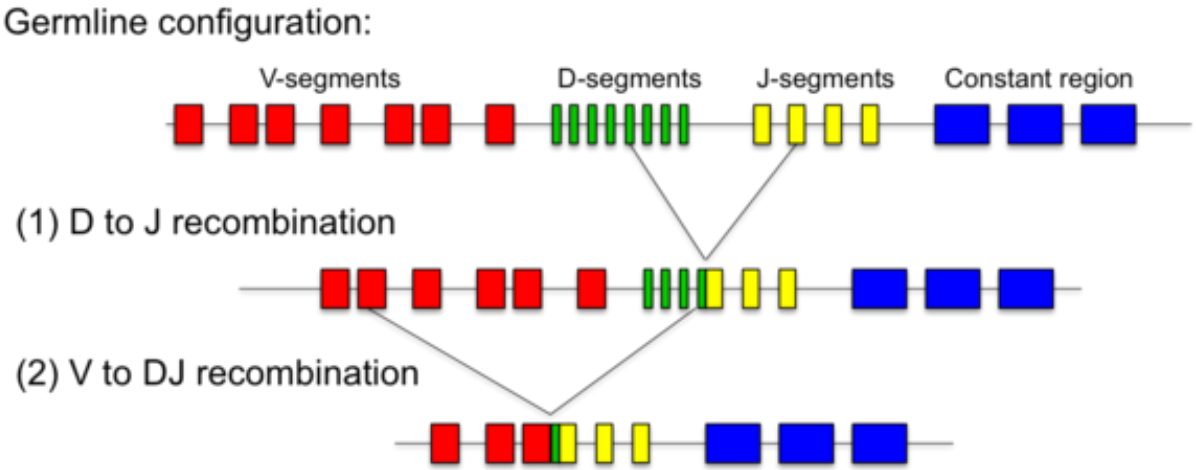
Riddle Solved!!

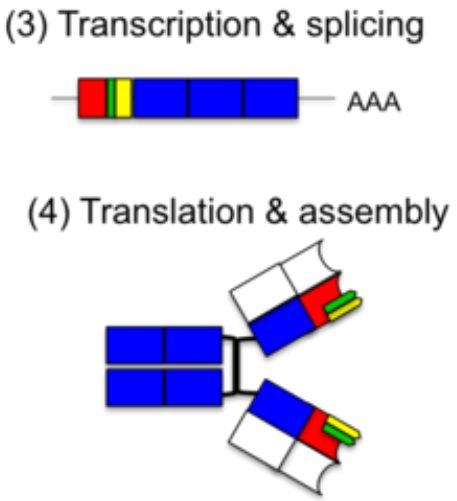
Susumu Tonegawa, 1977

Modular Design



VDJ recombination





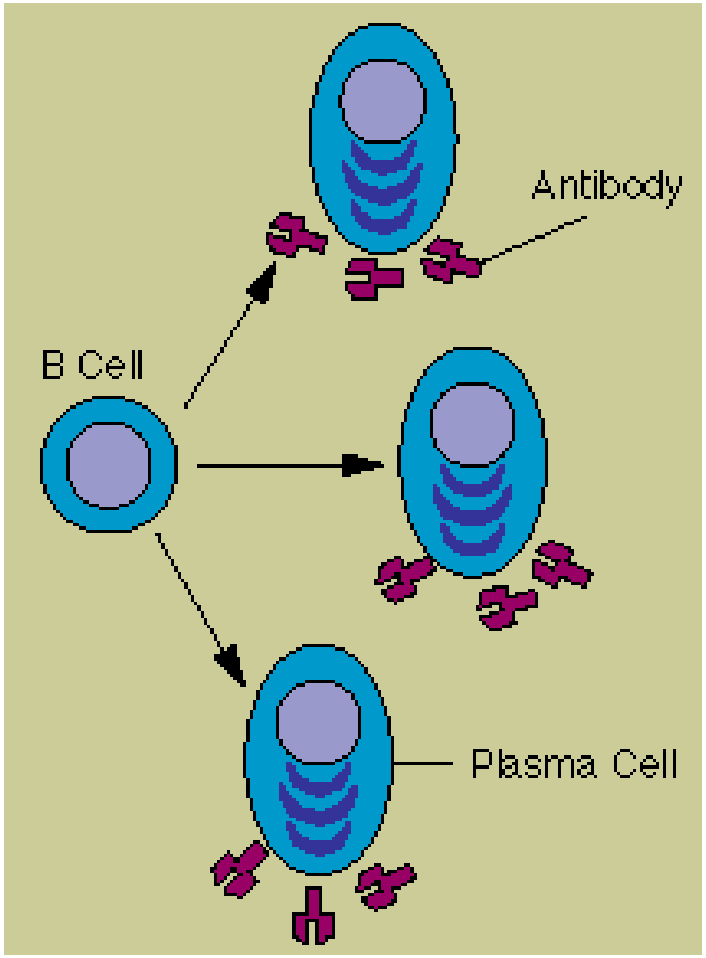
Problem of numbers?

- We have around 3 billion B cells in circulation targeting around 100 million antigens.

- So, 30 B cells per Antigen.

- How can we have enough B cells to fight off an infection???

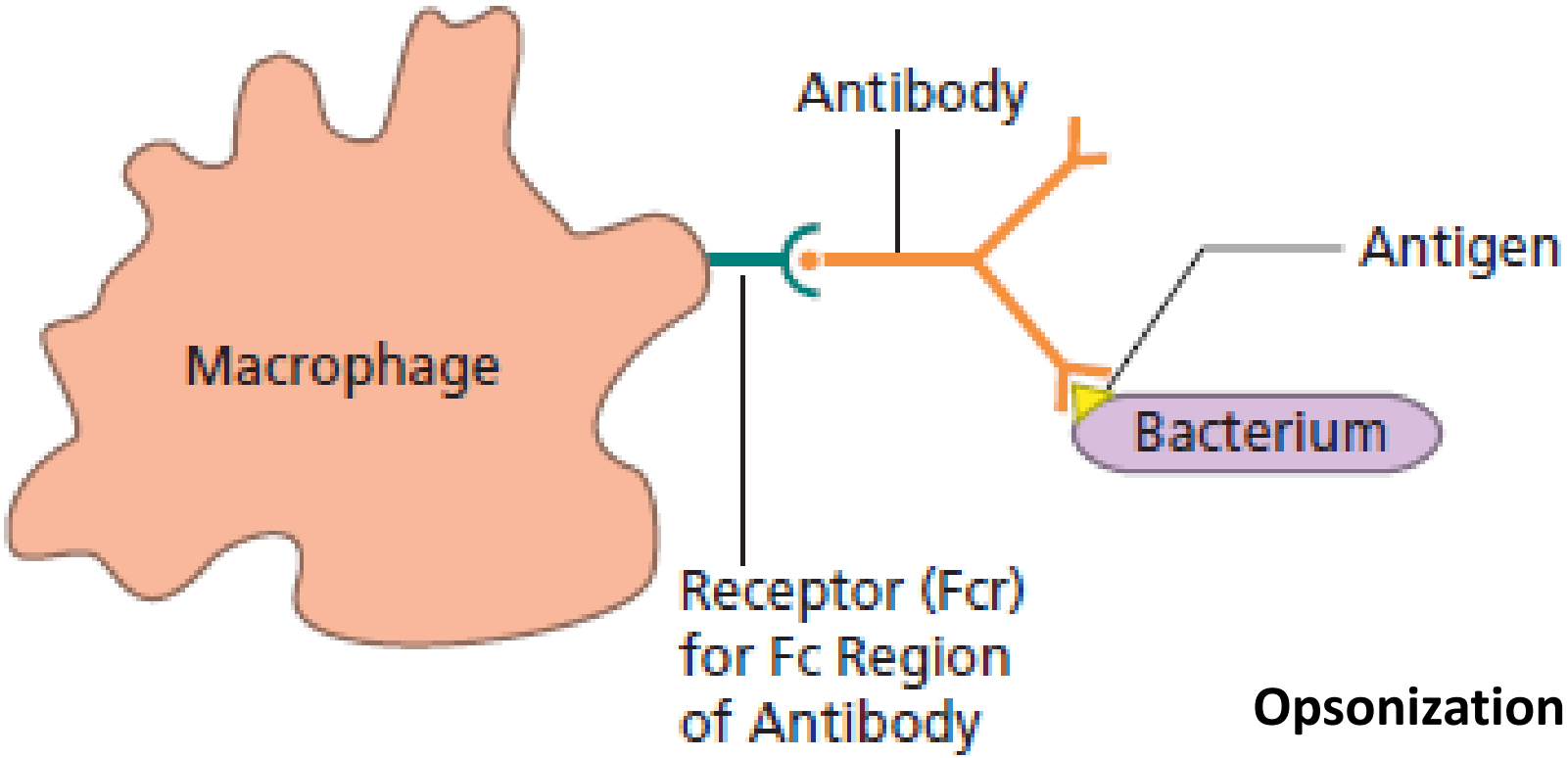
Clonal Expansion



1 cell division/ 12 hours
Within one week……
20,000 B cells secreting the same antibody!!!

One B cell produces around 2000 Abs/sec

How do Antibodies kill???

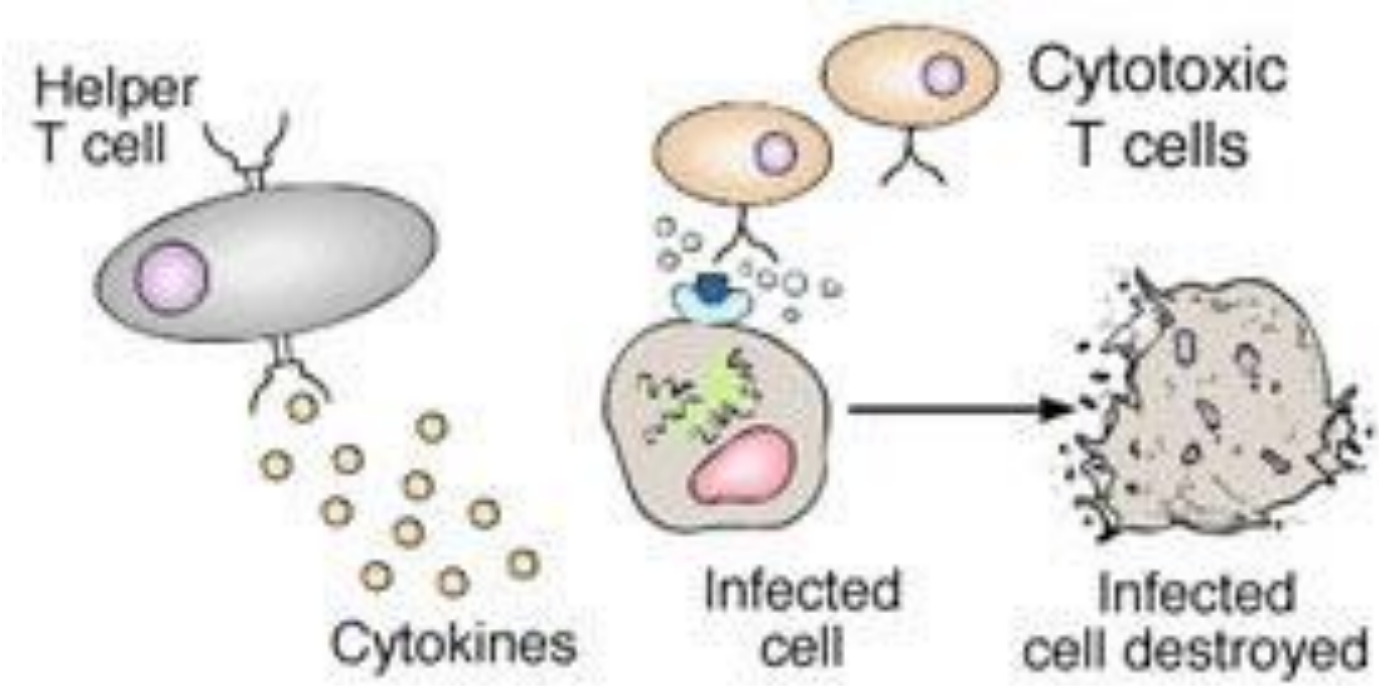


Opsonization

Antibodies can block viral replication too!!

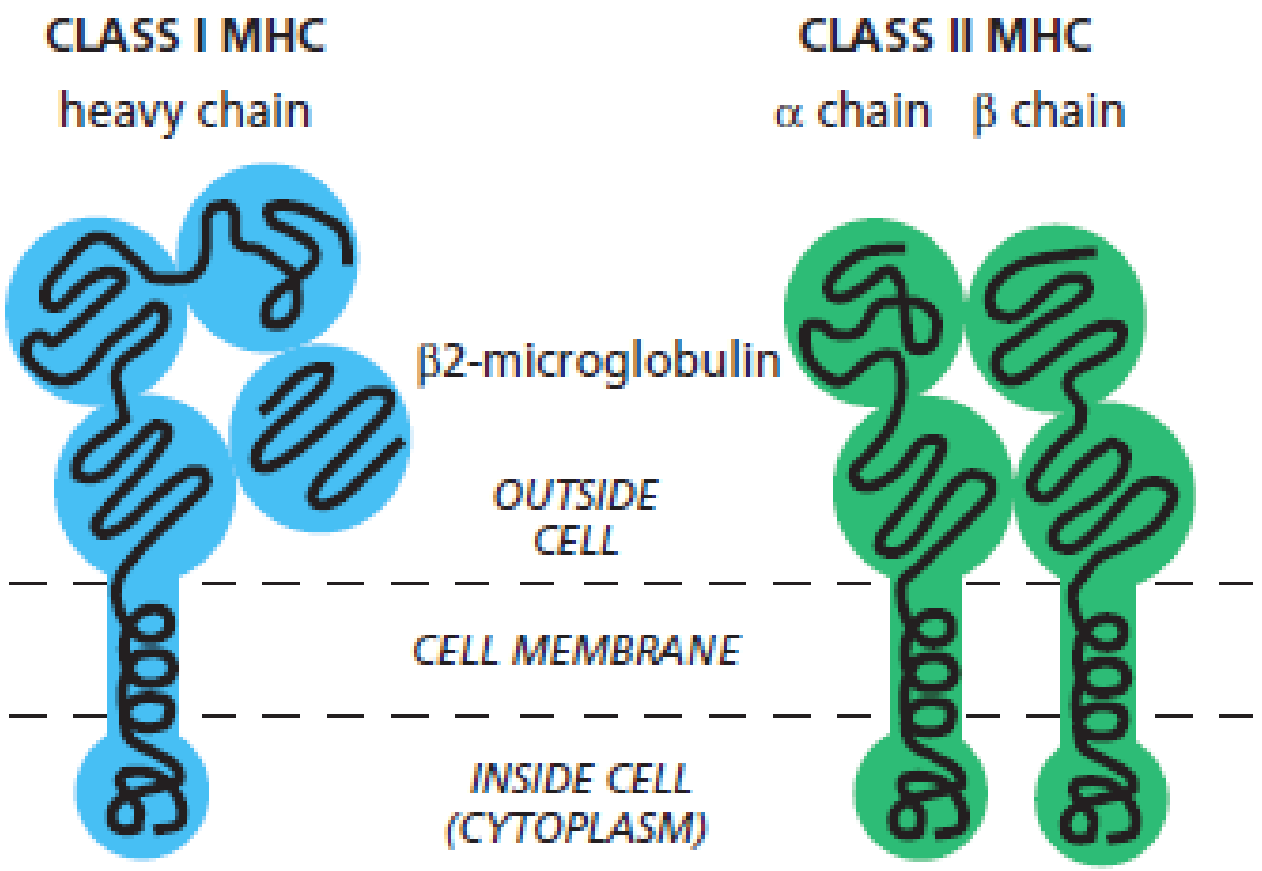
T cells

Matures in the thymus
Comprises: Cytotoxic T cells, Helper T cells, and regulatory T cells.



How can T cells “see” infected cells?

Antigen Presentation
By APCs.



MHC molecules

Seen by
cytotoxic T cells

~9 a.a

MHC class I

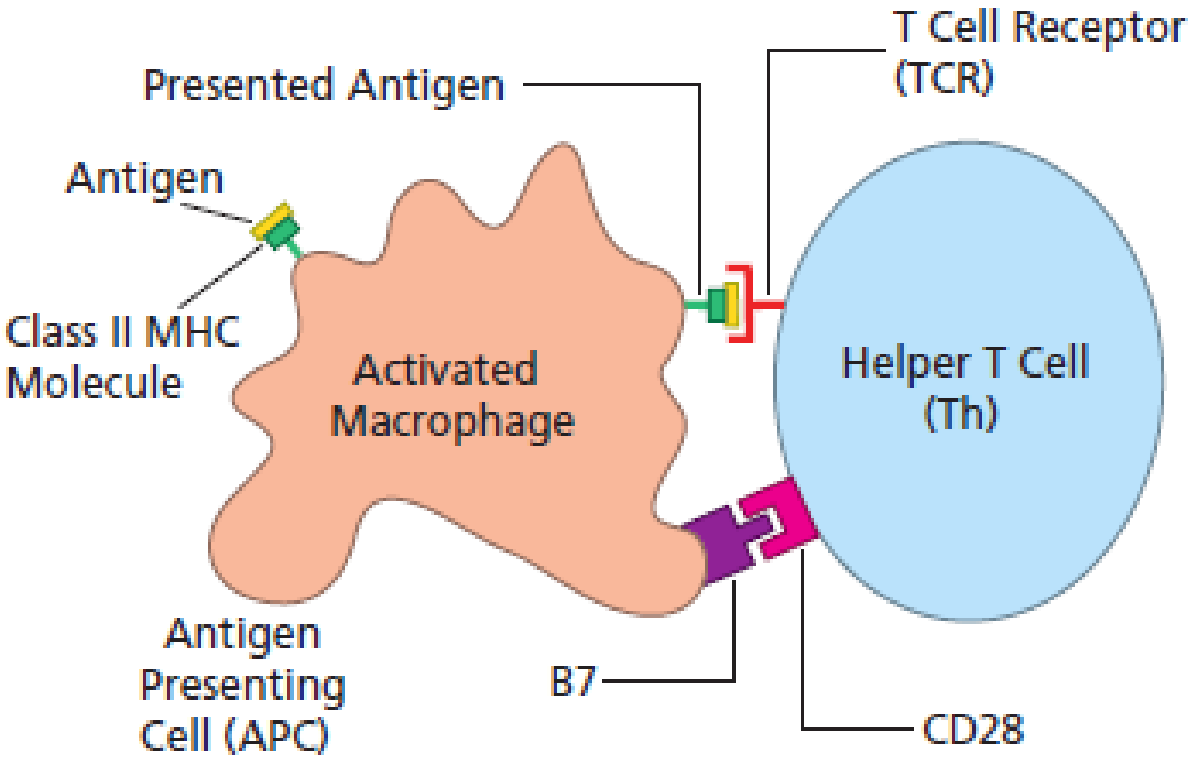
Seen by
Helper T cells

~20 a.a

MHC class II

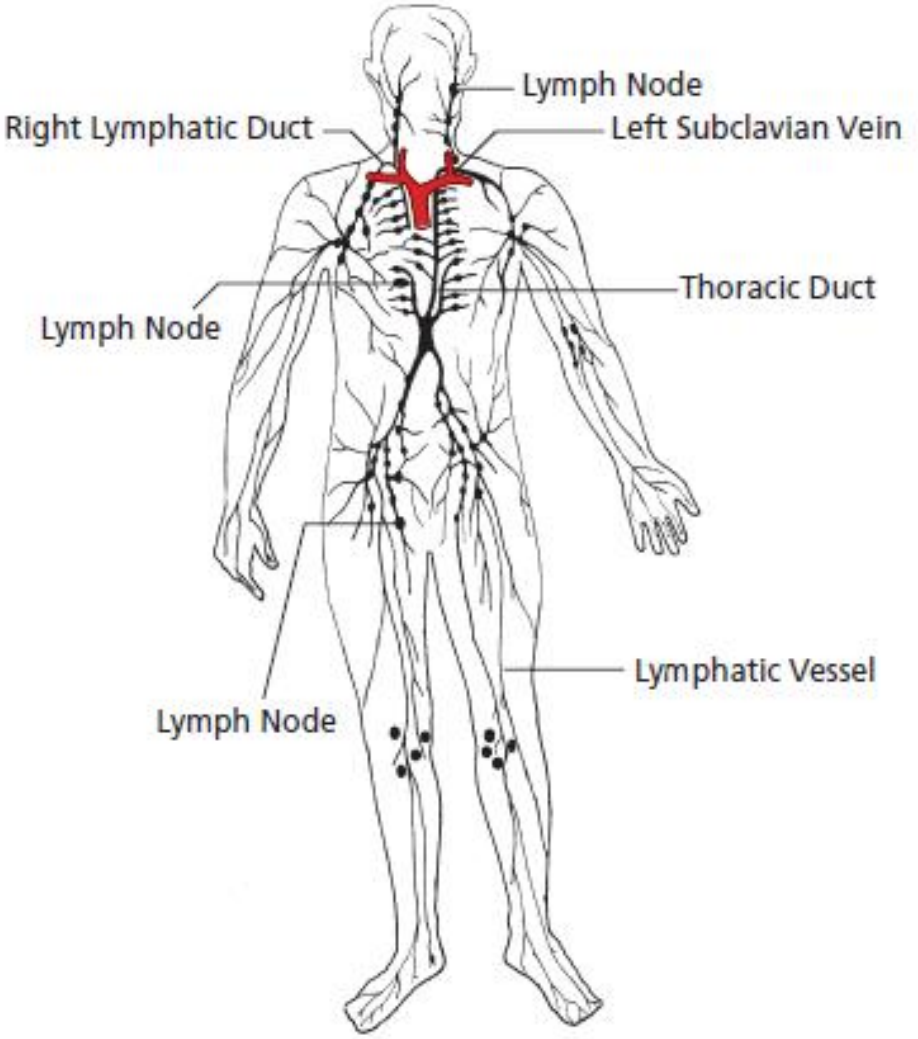
How can we control lymphocyte activation???

- Two-Key System!!!



How can APCs and lymphocytes meet??

Lymph nodes!!



Features of Innate and Adaptive Immunity

Characteristics	Innate	Adaptive
Specificity	For molecules shared by groups of related microbes and molecules produced by damaged host cells	For microbial and nonmicrobial antigens
Diversity	Limited; germline encoded	Very large; receptors are produced by somatic recombination of gene segments
Memory	None	Yes
Nonreactivity to self	Yes	Yes
Components		
Cellular and chemical barriers	Skin, mucosal epithelia; antimicrobial molecules	Lymphocytes in epithelia; antibodies secreted at epithelial surfaces
Blood proteins	Complement, others	Antibodies
Cells	Phagocytes (macrophages, neutrophils), natural killer cells, innate lymphoid cells	Lymphocytes

Innate vs. Adaptive systems

- Innate defends non-specifically and buys time for adaptive immune system to kick in if needed.

- Innate immune system decides which cells should respond, where, and when!

- The innate immune system rules!

THANK YOU!

QUESTIONS??