Immunology 101 for the Non-Immunologist

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Society for Immunotherapy of Cancer

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What is Immunity?

*protection of one organism against another

*elimination or control of the offending organism

*setting up conditions so the offending organism does not cause problems down the road

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What is the Immune System?

*network of many different types of proteins, cells, tissues and organs

*function depends upon highly regulated interactions between these proteins, cells, tissues and organs

*success depends upon a coordinated attack on the invading organism

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Major roles of the immune system?

PATHOGENS - disease causing organisms
bacteria, viruses, fungus, parasites and prions

The challenge: * The variety of pathogens is endless
* Pathogens are largely made of the same stuff as us

CANCER - aberrant, uncontrolled cell growth
gene mutations, oncogenes

The challenge: * The variety of cancer is endless
* Cancer cells are made of nearly exactly the same stuff healthy cells

How can the immune system deal with so many different pathogens/cancers?

*The immune system has no prior "knowledge" of what all these different pathogens might be

*The pathogens are always changing (mutating/evolving)

Therefore, the immune system must anticipate new problems and adapt to an ever changing world of pathogens.

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Dealing with endless antigens…..

Susumu Tonegawa
1987 Nobel Prize

The answer is that the immune system can make a ridiculous number of different "detectors"

Detectors = proteins that can specifically bind antigens: T cell receptor (TCR) and B cell receptor (BCR/antibodies)

1,000,000,000,000,000,000 Pathogen "detectors"

10,000,000,000,000 Cells in the human body

30,000 Genes in the genome

V(D)J RAG-mediated recombination

An example of autoimmunity
Type 1 diabetes - "juvenile diabetes"

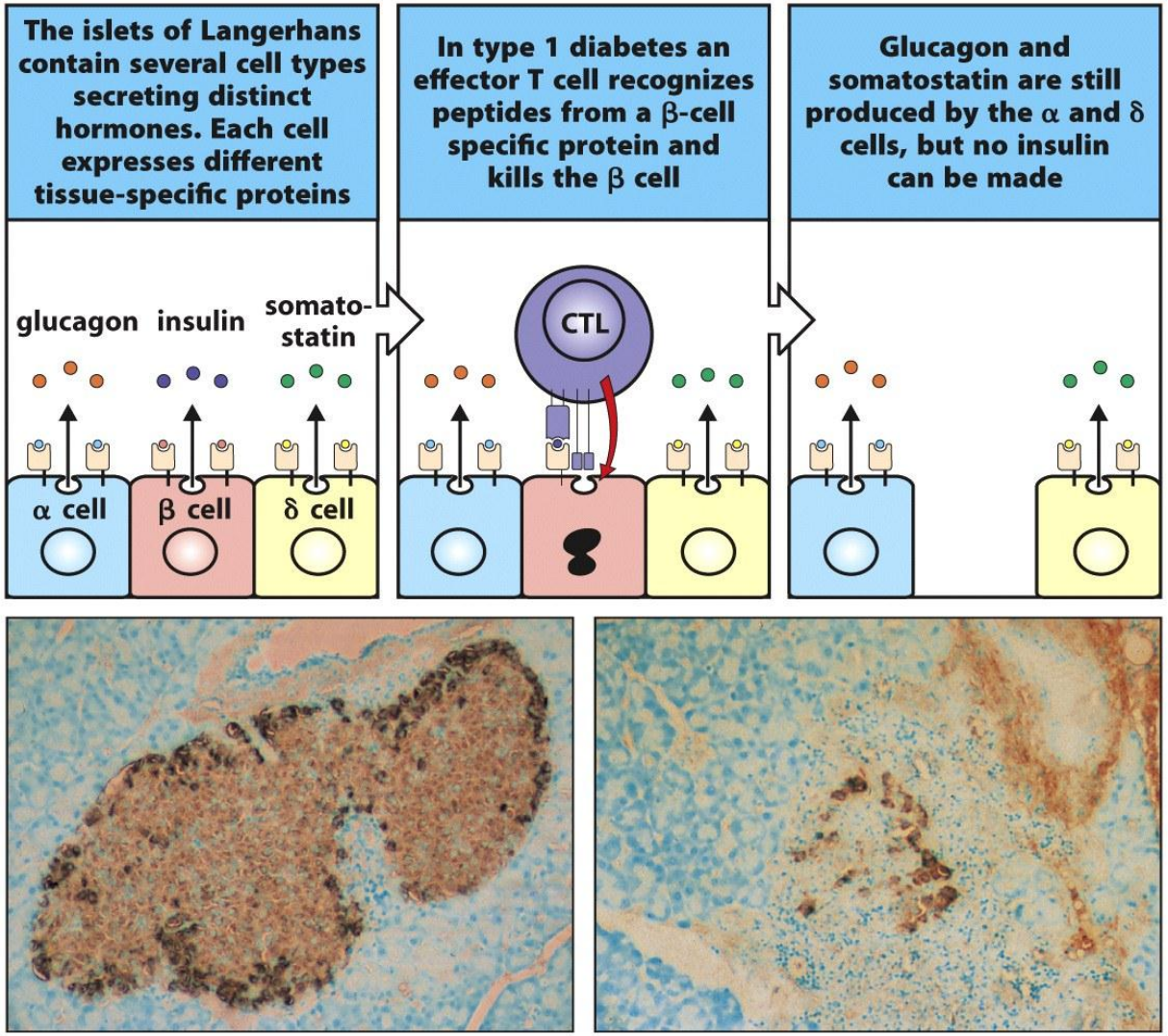

Figure 15.26 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Cells of the immune system kill insulin producing β cells resulting in Type 1 diabetes

The immune system remembers

One of the major benefits of an adaptive immune system

*Effector T cells and antibodies persist for weeks after exposure to antigen – "protective immunity"

*Second exposure to the same antigen produces a much faster response

*Second response is referred to as **Immunological Memory**

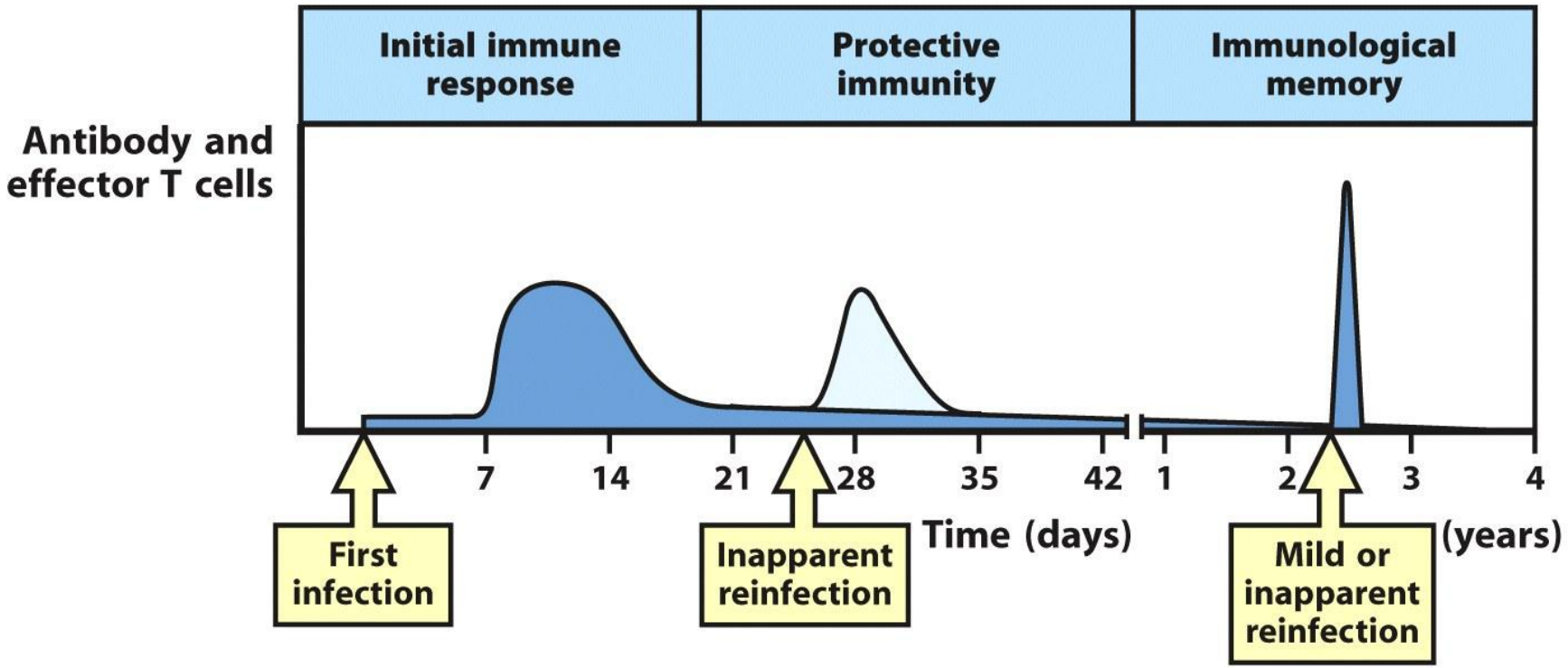

Figure 11.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

The single most important question that the immune system must answer over and over:

Is this cell/tissue/protein "self" or is it "non-self"?

Self – uninfected, healthy, normal (i.e. no genetic mutations)

Non-self – viruses, bacteria, fungus, parasites, etc., cells that are infected by these pathogens and diseased cells (cancer)

***If the immune system answers this question incorrectly:**

-the disease will not be cleared

-or, possibly worse - autoimmunity

Autoimmunity - the destruction of healthy tissues leading to very nasty diseases

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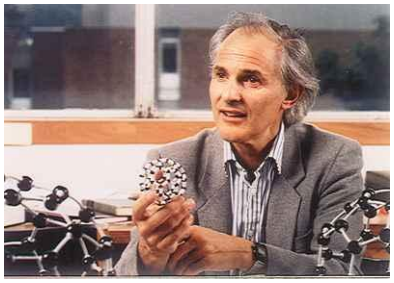
Is this cell/tissue/protein "self" or is it "non-self"?

"Tolerance"

Peter Medawar – 1960 Nobel Prize



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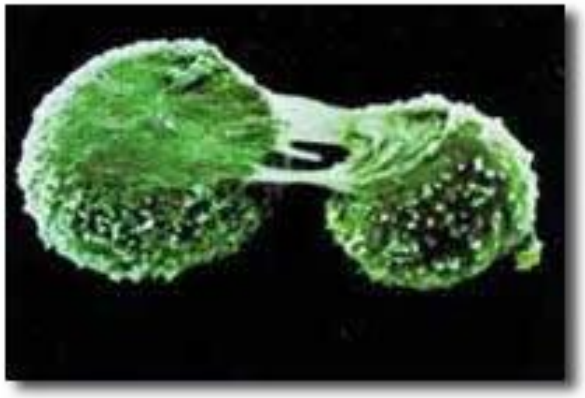
B lymphocytes: B cells

- Antibody producing cells that respond to an antigen stimulation
- Antibodies can provide protective immunity for decades

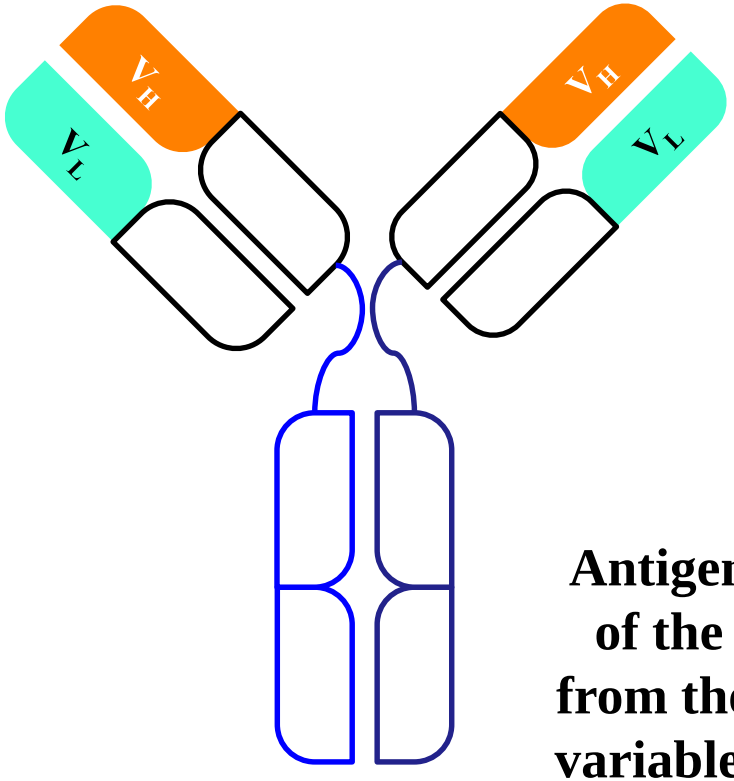


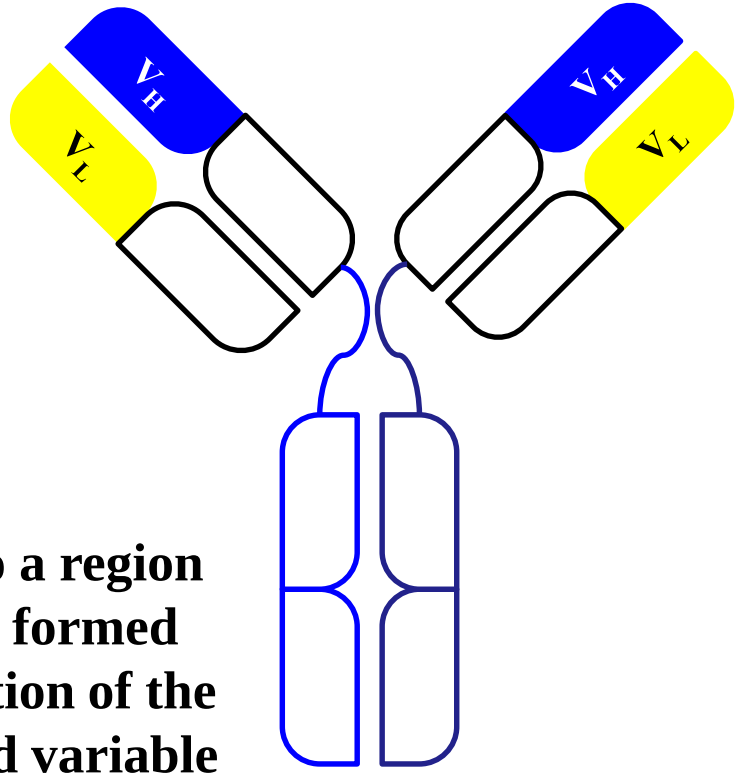
B Cells dividing

Antigen Receptors

Receptor = pathogen detector

Antibodies



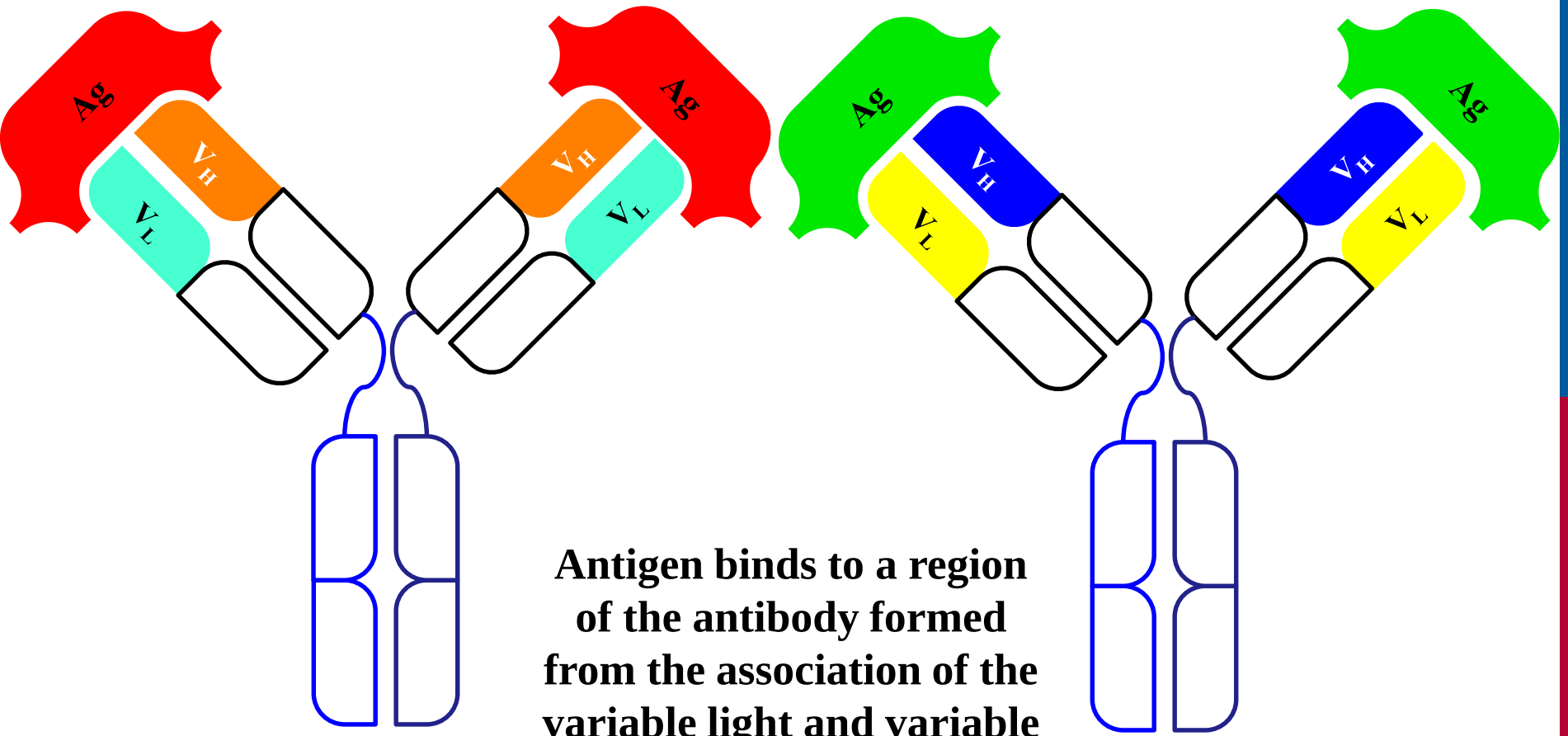


Antigen binds to a region of the antibody formed from the association of the variable light and variable heavy regions

Antigen Receptors

Receptor = pathogen detector

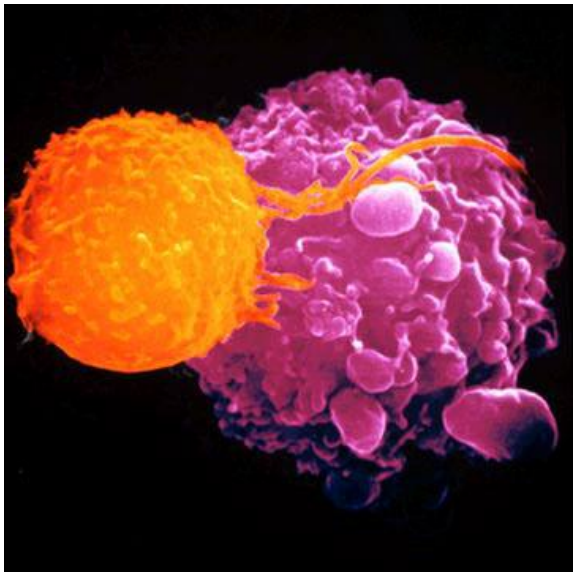
Antibodies



Antigen binds to a region of the antibody formed from the association of the variable light and variable heavy regions

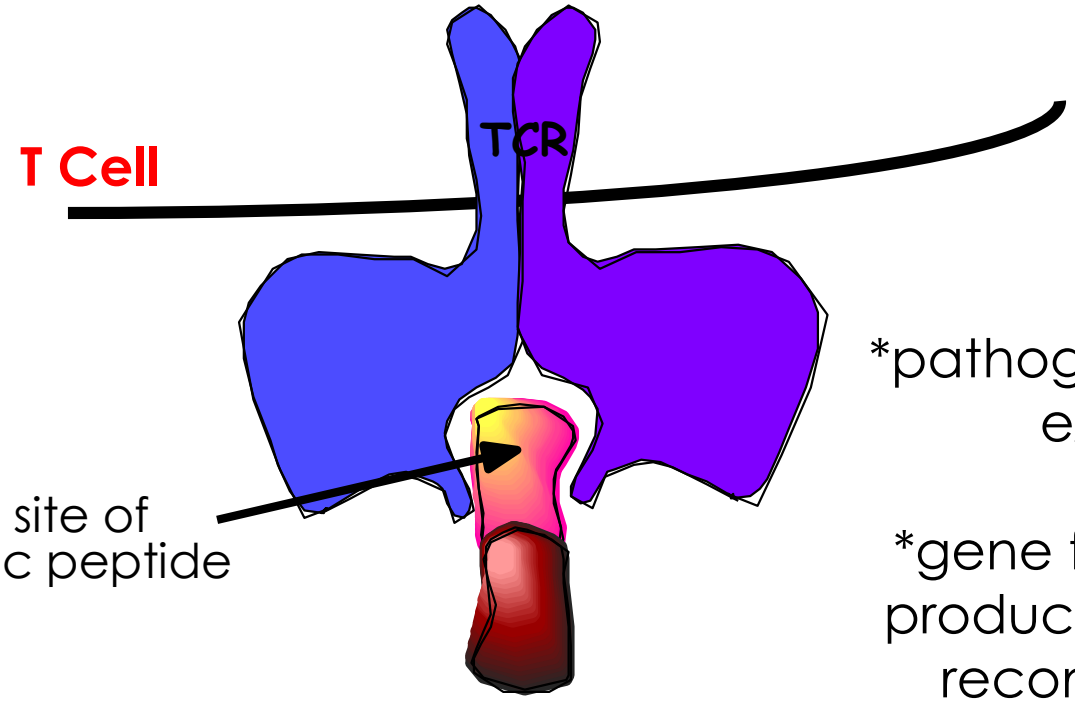
T lymphocytes: T cells

- following maturity, T cells migrate to various lymphoid organs where they await contact with antigens
- basis for cell-mediated immunity



T cell (orange) killing
a cancer cell

T cell Antigen Receptor (TCR)



TCR contact site of immunogenic peptide

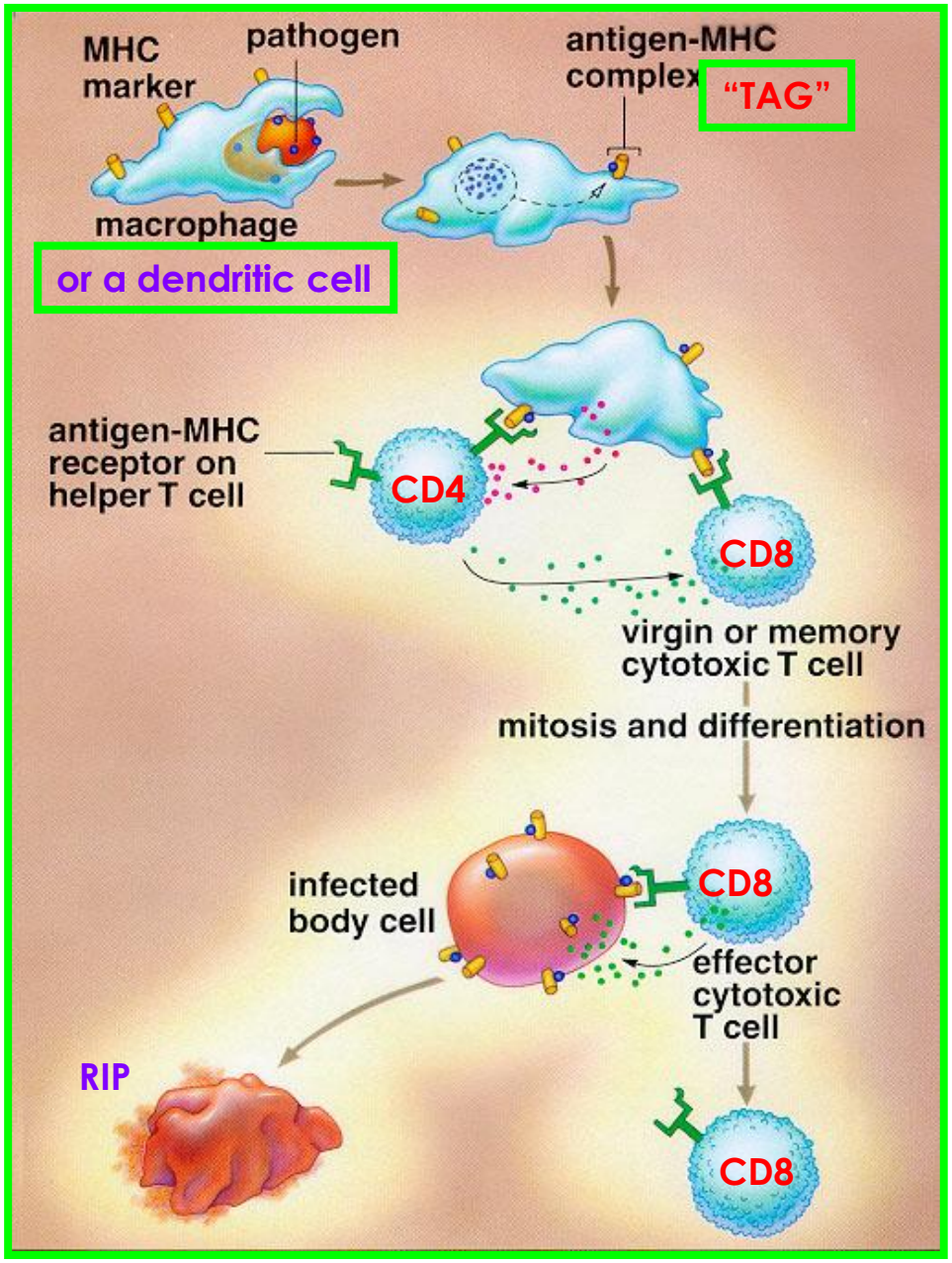
TCR

*pathogen detector expressed by T cells

*gene for TCRs are produced by V(D)J recombination

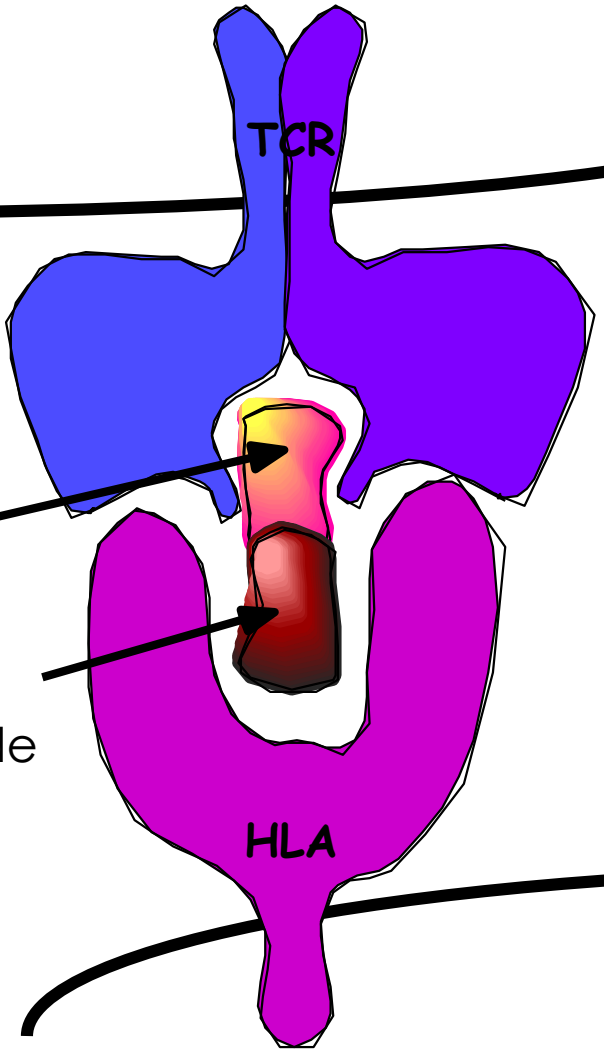
Cells must be "tagged" as infected to activate the immune response

The "Tags" are fragments of the antigen (pathogen) bound to MHC or HLA



Major Histocompatibility Molecules (MHC) or Human Leukocyte Antigens (HLA)

T cell Antigen Receptor (TCR)



TCR contact site of immunogenic peptide

HLA contact site of immunogenic peptide

TCR

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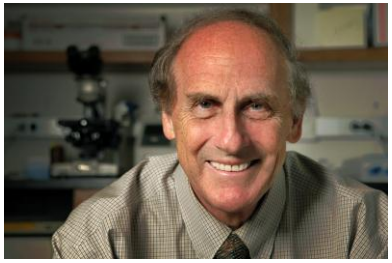
Antigen Presenting Cell (**APC**)

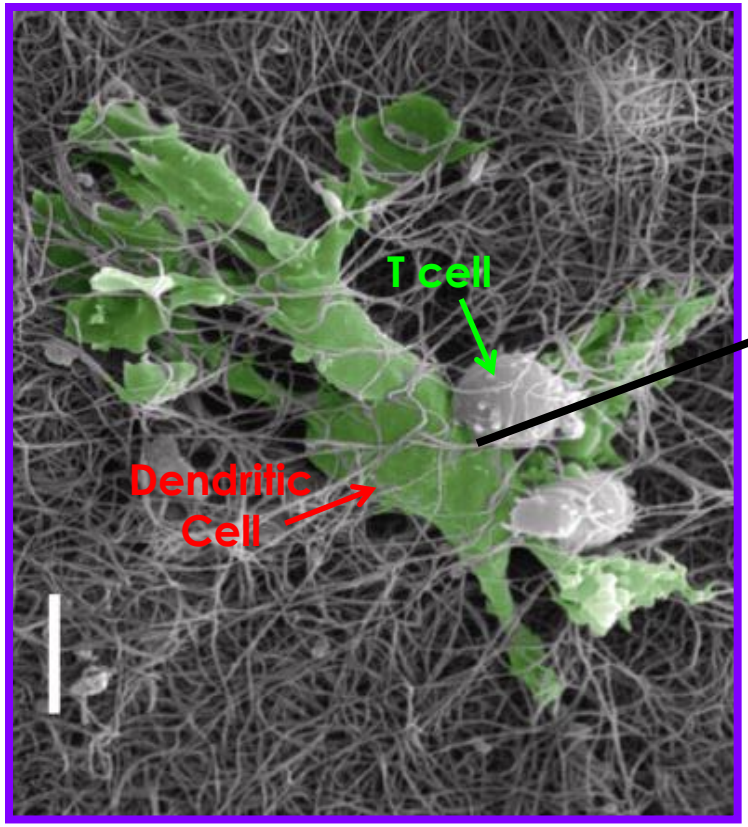
Most important = dendritic cells (DCs)

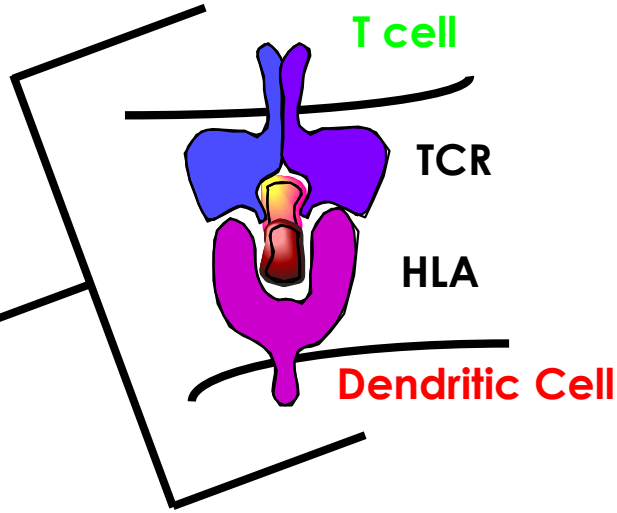


Ralph Steinman
2011 Nobel Prize

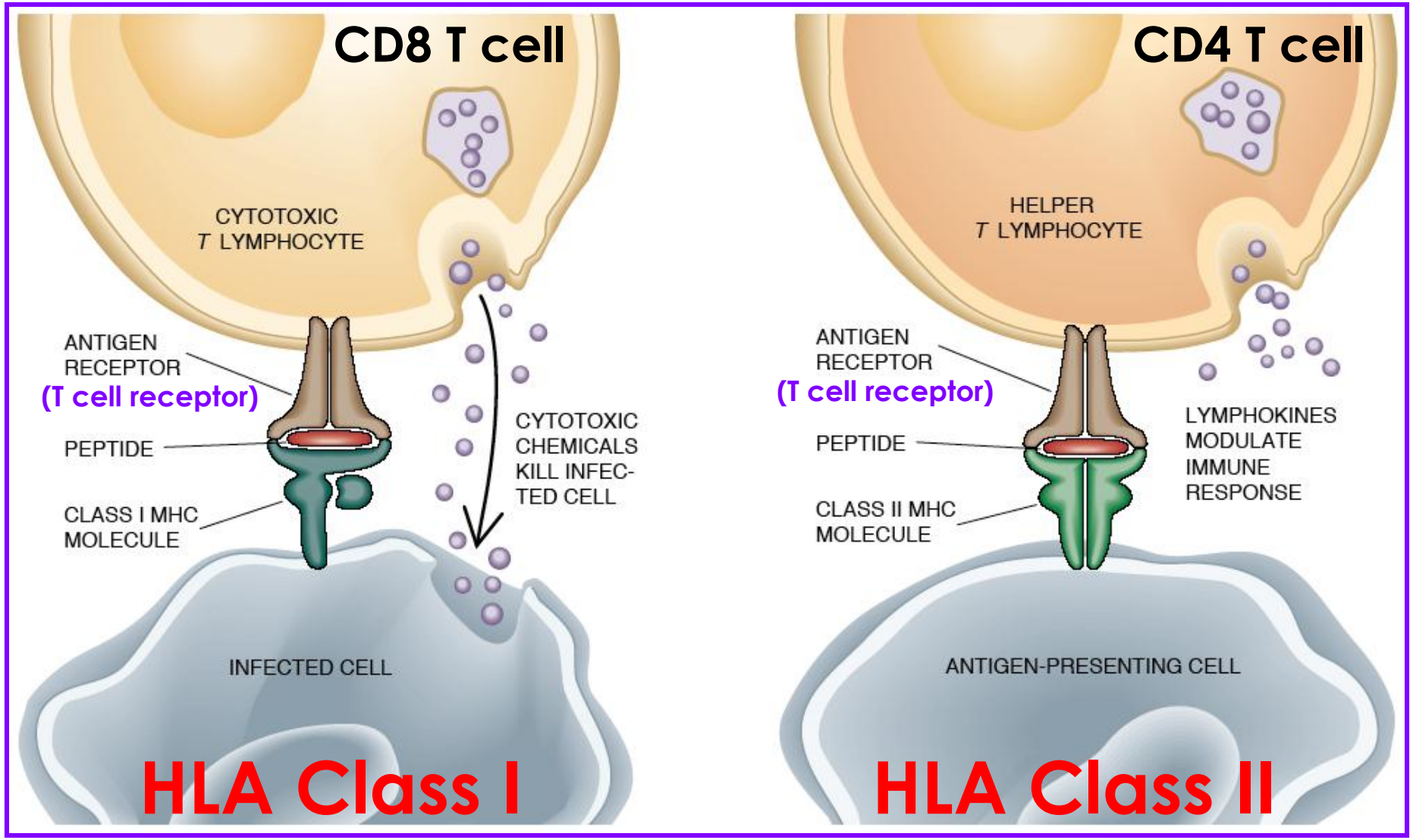
Dendritic cells (DCs)

Have a variety of functions including phagocytosis, secretion of cytokines and **antigen presentation**.





Two major types of T cells (CD8 and CD4) and two major types of HLA (Class I and Class II)



The immune system is actually two distinct systems

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"The immunologist's dirty little secret"
C.A. Janeway. Jr

"Clean" antigens will not activate the immune response
They must be mixed with *adjuvants*

		Acquired Immune system
		Needs to be 'primed' before it can work to its full effectiveness. Only really effective after it has seen a possible infective agent before.
Speed of Response		Slow (>week)
Response		Highly Specific Antigen Dependent
Memory		Yes

The immune system is actually two distinct systems

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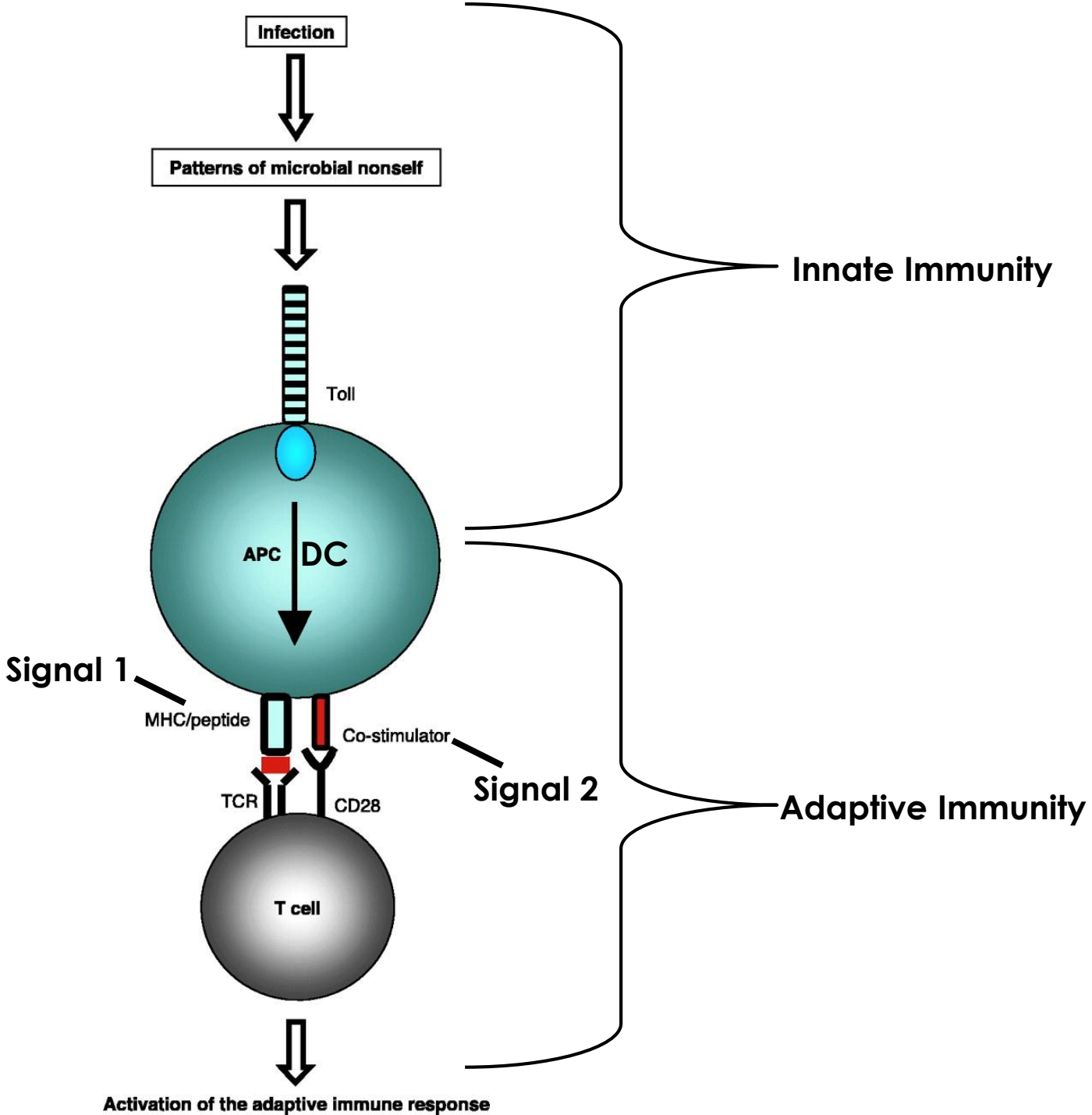
"Clean" antigens will not activate the immune response
They must be mixed with *adjuvants*

	Innate Immune system	Acquired Immune system
	Is always working to protect the body and does not require any special preparation to stop infection.	Needs to be 'primed' before it can work to its full effectiveness. Only really effective after it has seen a possible infective agent before.
Speed of Response	Immediate	Slow (>week)
Response	Non-Specific Antigen Independent	Highly Specific Antigen Dependent
Memory	No	Yes


Infection
Patterns of microbial nonself
Toll
APC
DC
Signal 1
MHC/peptide
Co-stimulator
Signal 2
TCR
CD28
T cell
Activation of the adaptive immune response
Innate Immunity
Adaptive Immunity