

# Johns Hopkins Engineering

## Immunoengineering

Module 2/Lecture 2E

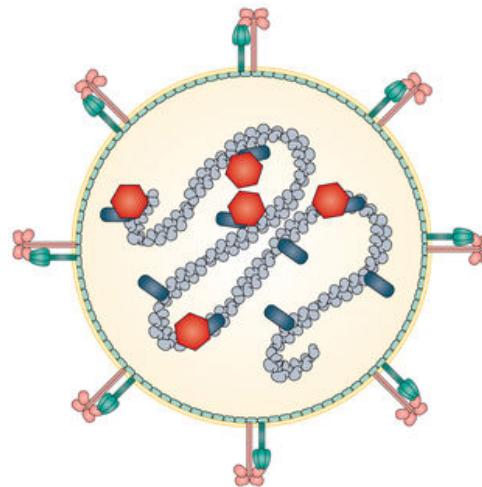
**Immune Response to Pathogens: Viral Immune Response**



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# Viruses

a



Fusion (F) protein

Large (L) protein

Haemagglutinin (H) protein

Phosphoprotein (P)

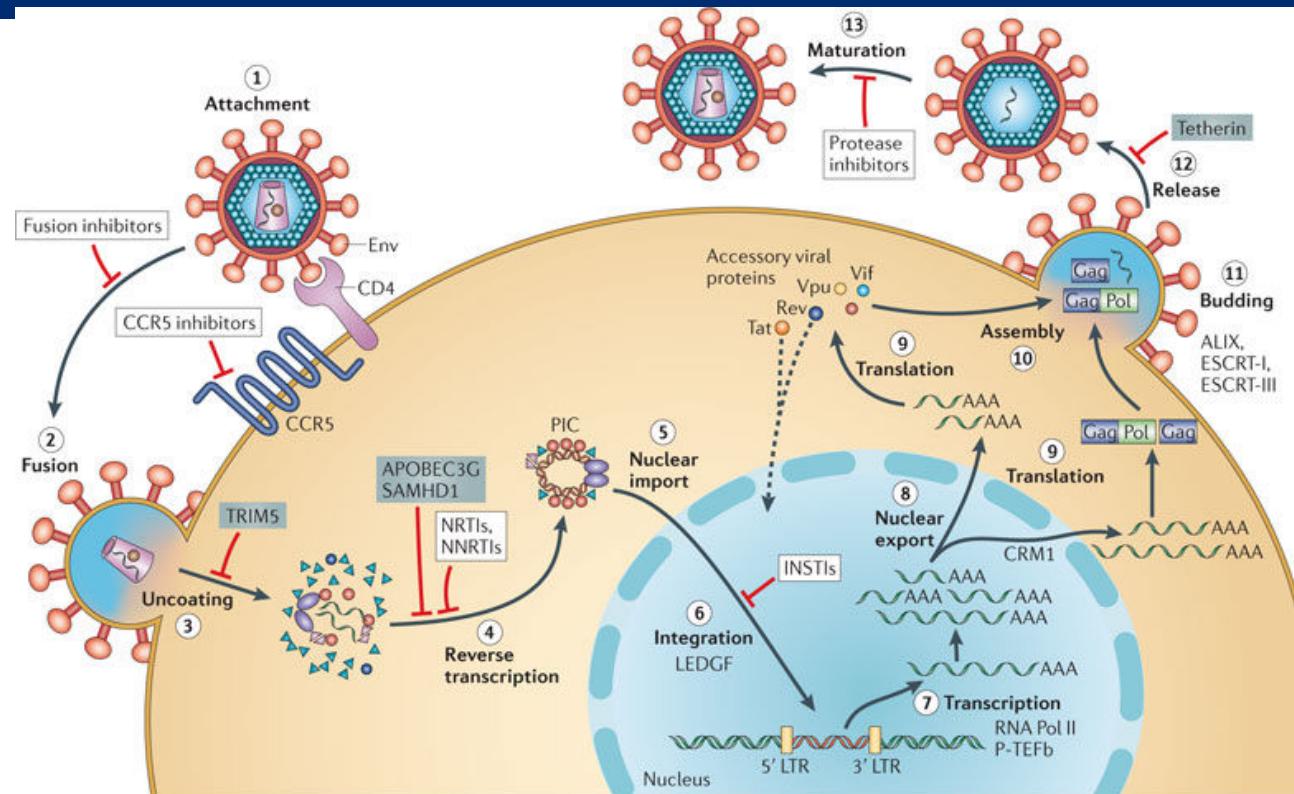
Matrix (M) protein

Nucleocapsid (N) protein

Lipid bilayer

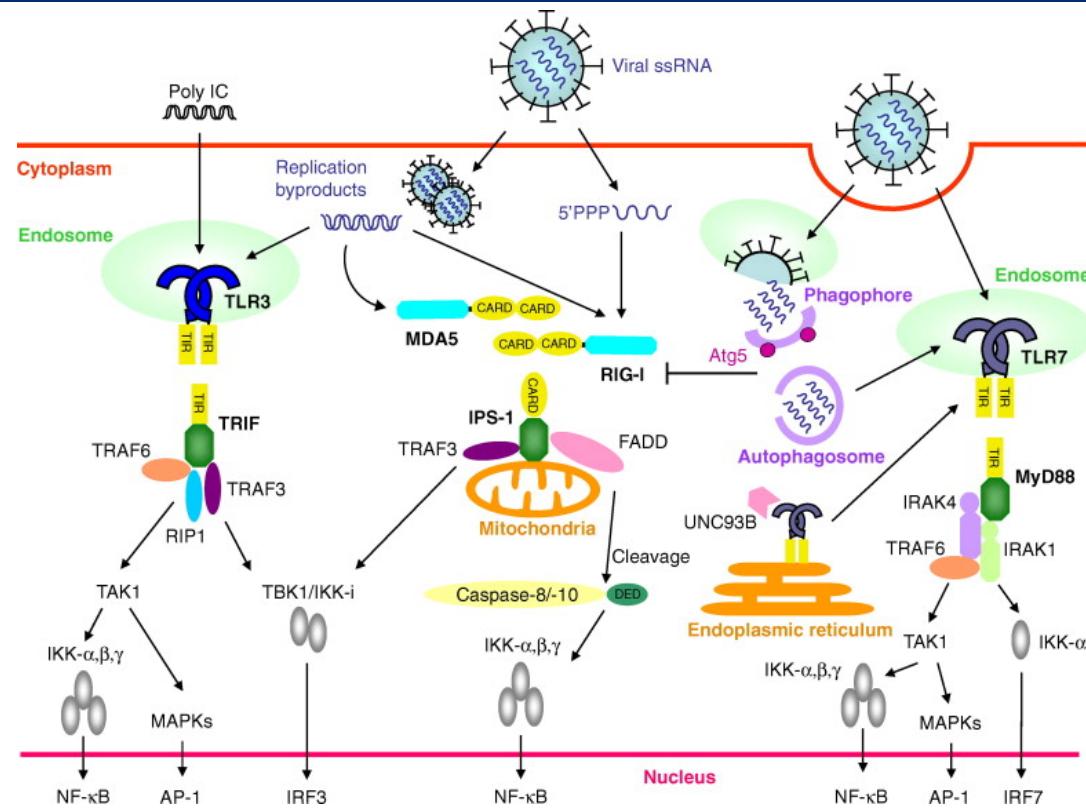
Nature Reviews | Disease Primers

# Viral Infection



# This is war!

# TLR Signaling Alerts the Innate Immune System



# Dendritic Cells Carry Information of Viral Infection

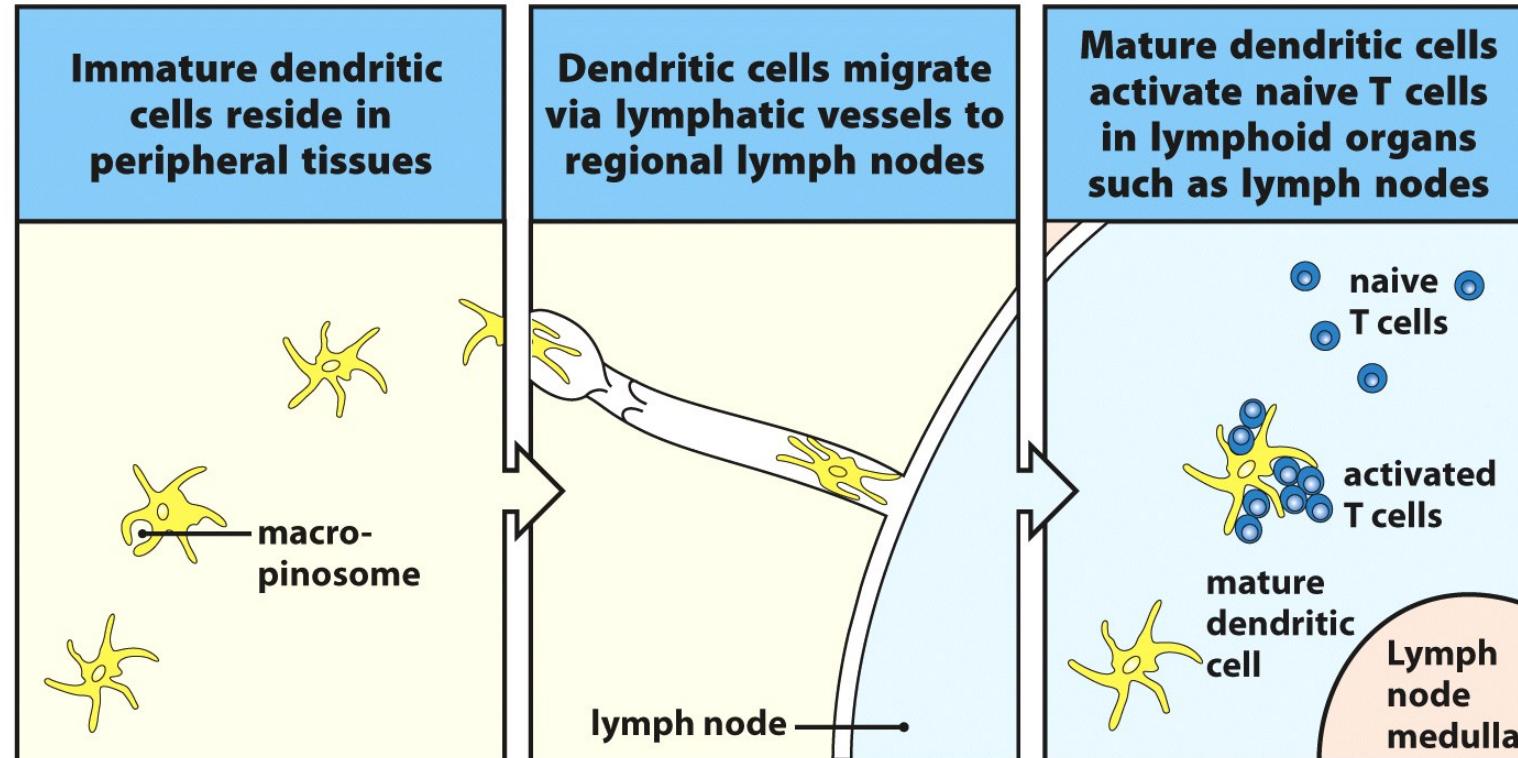


Figure 1.11 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# CD4+ T cell and APC interaction

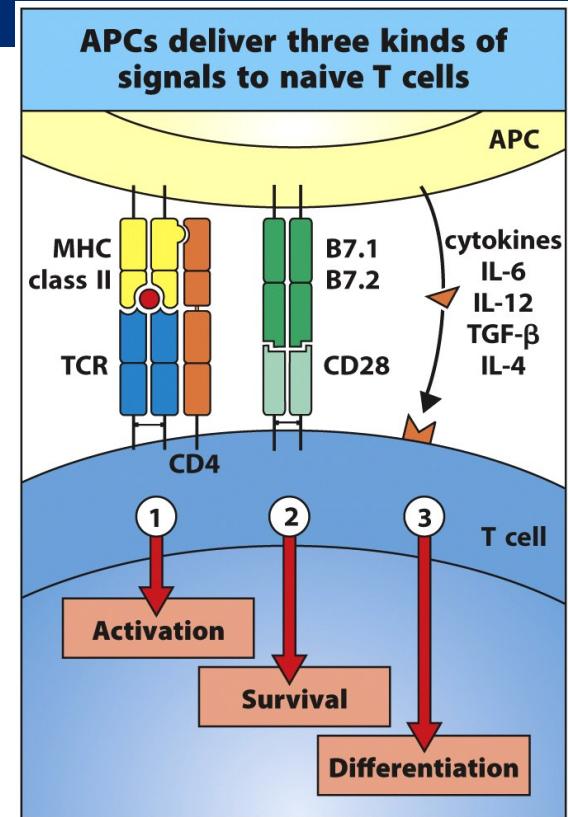
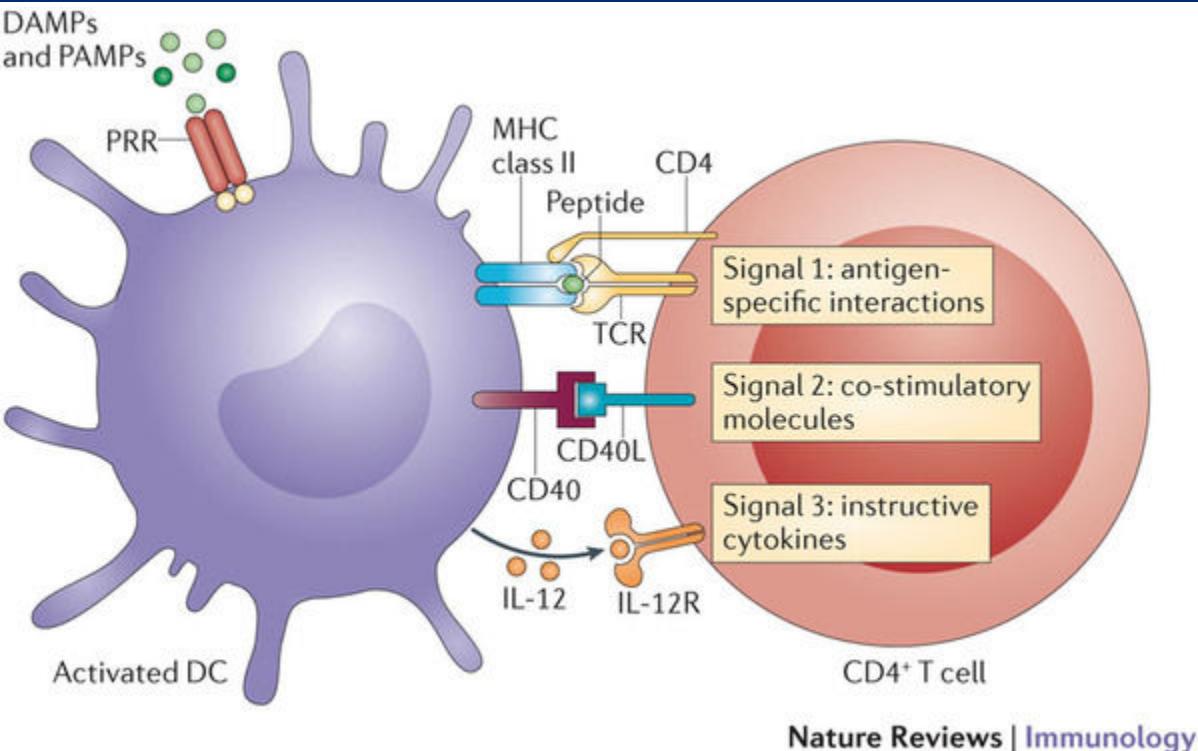


Figure 9.19 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Kambayashi, Taku, and Terri M. Laufer. "Atypical MHC class II-expressing antigen-presenting cells: can anything replace a dendritic cell?." *Nature reviews. Immunology* 14.11 (2014): 719.

# Routes of Antigen Processing for Dendritic Cells for CD4+ T cells

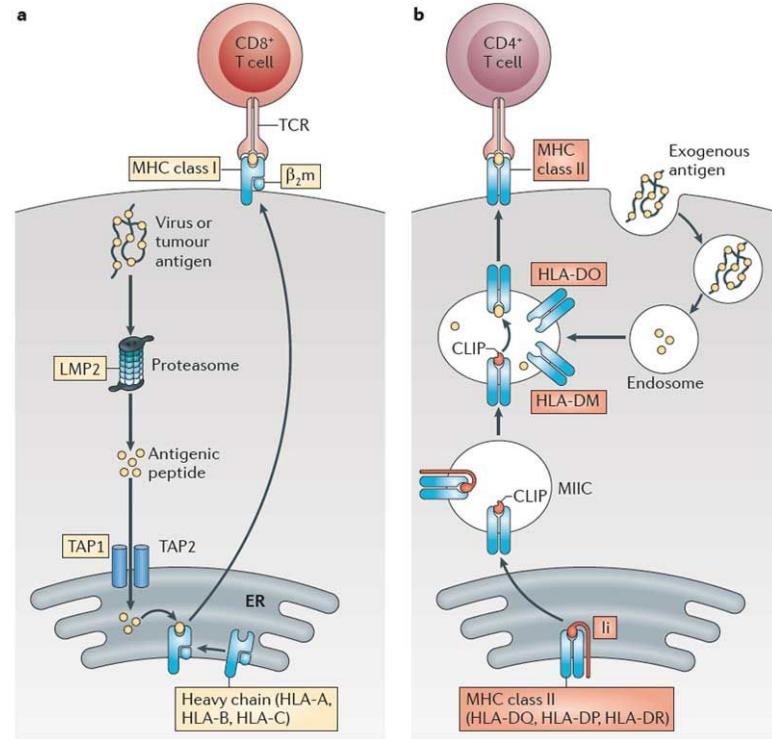
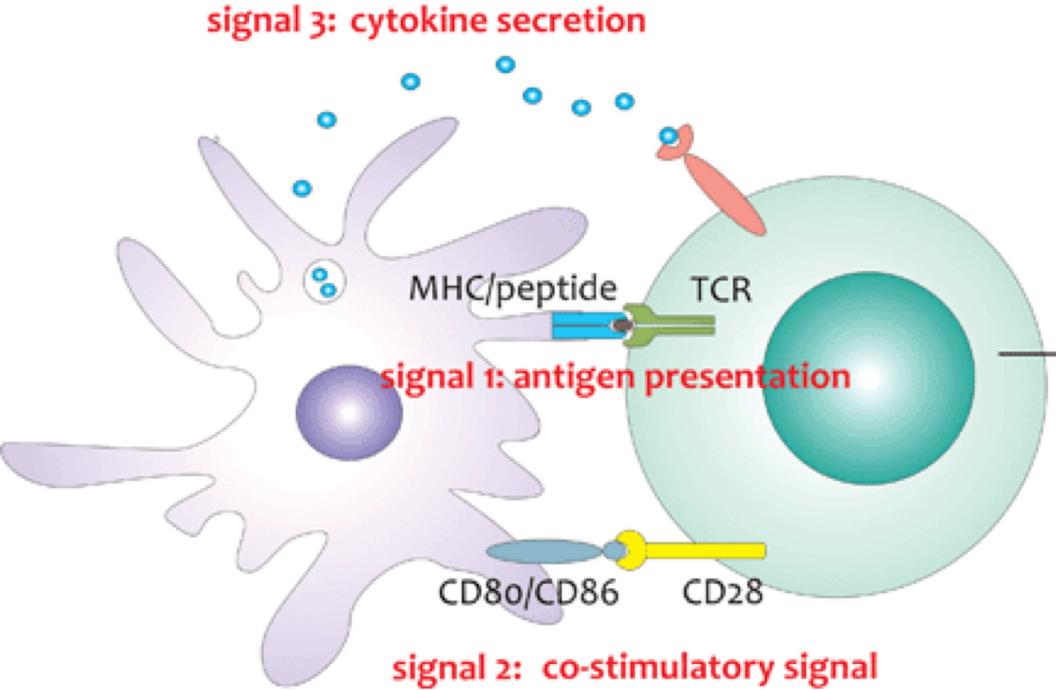
	Receptor-mediated phagocytosis	Macropinocytosis
Type of pathogen presented	Extracellular bacteria	Extracellular bacteria, soluble antigens, virus particles
MHC molecules loaded	MHC class II	MHC class II
Type of naive T cell activated	CD4 T cells	CD4 T cells

The diagram shows two main pathways for dendritic cells to capture antigens:

- Receptor-mediated phagocytosis:** This pathway involves a dendritic cell engulfing a long, rod-shaped bacterium. The bacterium is shown with a wavy surface, likely representing flagella.
- Macropinocytosis:** This pathway involves a dendritic cell taking up several small, circular vesicles containing red dots, representing soluble antigens or virus particles.

Figure 9.12 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# CD8+ T cell and APC interaction



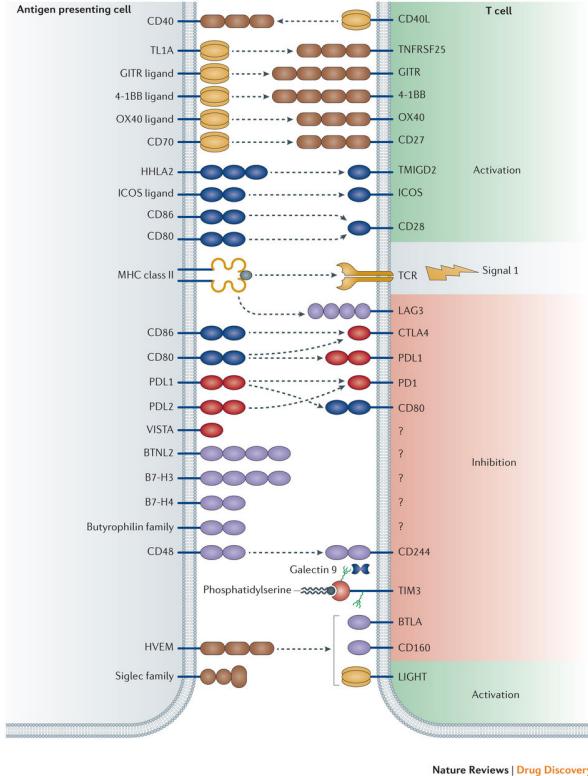
Nature Reviews | Immunology

De Koker, Stefaan, et al. "Designing polymeric particles for antigen delivery." *Chemical Society Reviews* 40.1 (2011): 320-339.

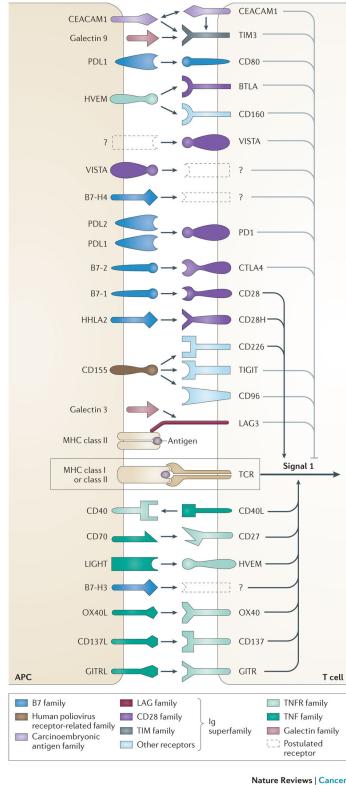
# Routes of Antigen Processing for Dendritic Cells for CD4+ and CD8+ T cells

Routes of antigen processing and presentation by dendritic cells					
Receptor-mediated phagocytosis	Macro-pinocytosis	Viral infection	Cross-presentation after phagocytic or macropinocytic uptake	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

# Numerous co-stimulatory interactions



Nature Reviews | Drug Discovery



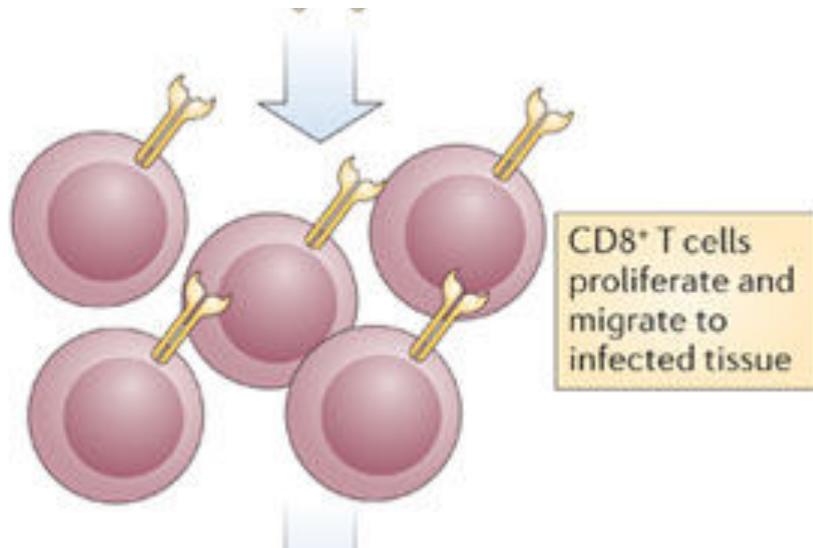
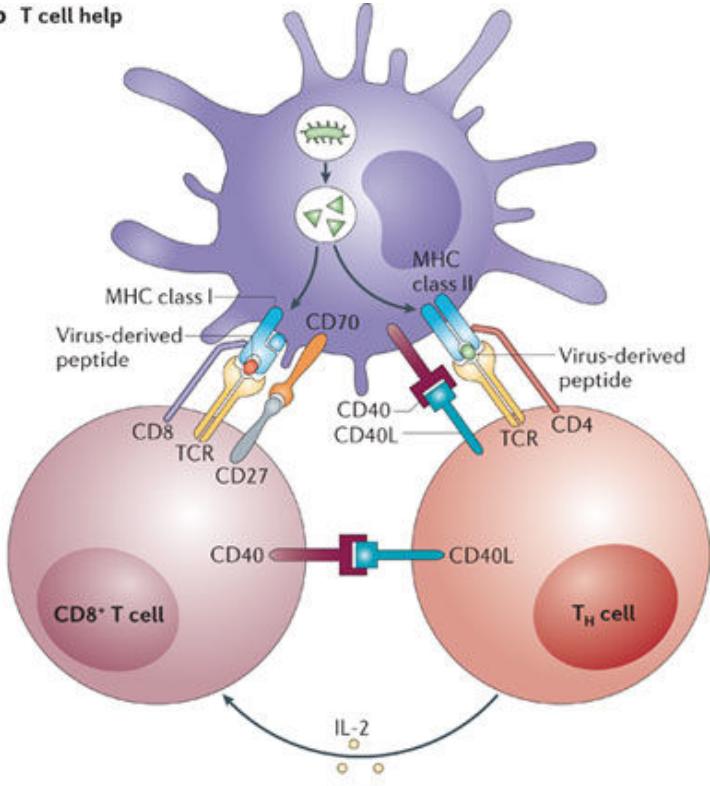
Nature Reviews | Cancer

Melero, Ignacio, et al. "Evolving synergistic combinations of targeted immunotherapies to combat cancer." *Nature Reviews. Cancer* 15.8 (2015): 457.

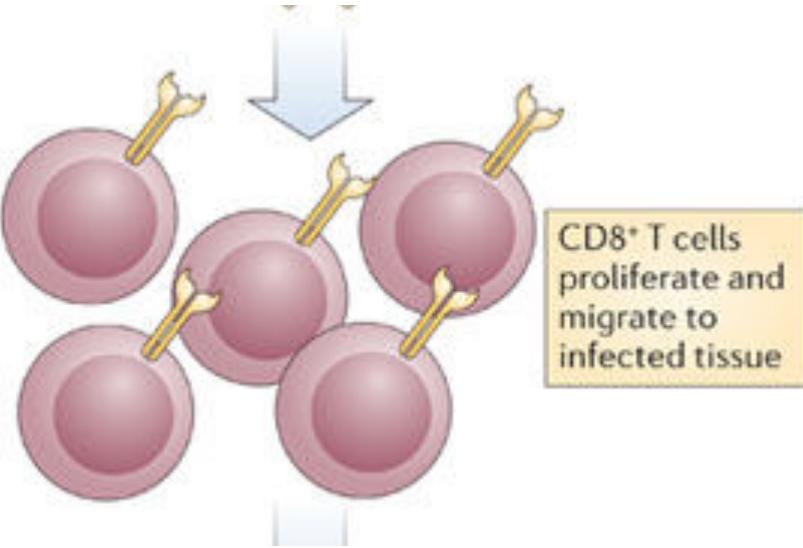
Mahoney, Kathleen M., Paul D. Rennert, and Gordon J. Freeman. "Combination cancer immunotherapy and new immunomodulatory targets." *Nature reviews. Drug discovery* 14.8 (2015): 561.

# CD4+ T cell help

› T cell help



# CD4+ T cell help



65,536 cloned T cells

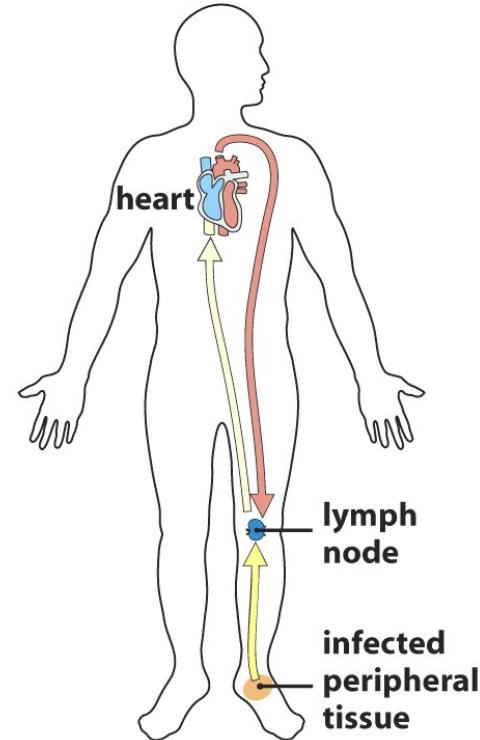
[https://commons.wikimedia.org/wiki/File:M%26T\\_Bank\\_Stadium\\_DoD.jpg](https://commons.wikimedia.org/wiki/File:M%26T_Bank_Stadium_DoD.jpg)

Swain, Susan L., K. Kai McKinstry, and Tara M. Strutt. "Expanding roles for CD4+ T cells in immunity to viruses." *Nature reviews. Immunology* 12.2 (2012): 136.

# Lymphocyte Trafficking

Lymphocytes and lymph return to blood via the thoracic duct

Naive lymphocytes enter lymph nodes from blood

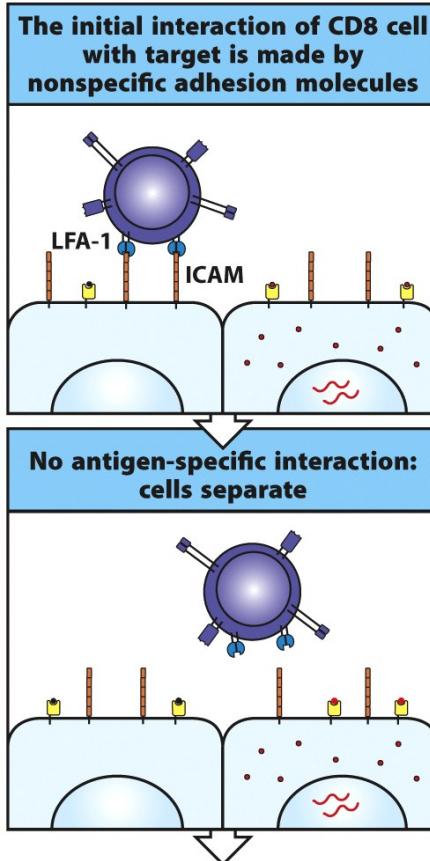


Antigens from sites of infection reach lymph nodes via lymphatics

# Video of Extravasation

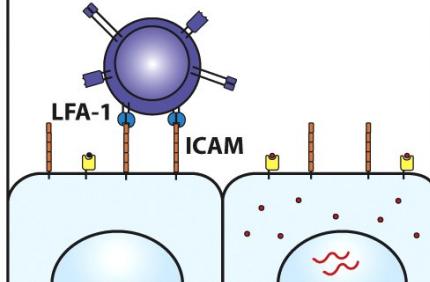
[https://www.youtube.com/watch?v=HiJ\\_tcQJUwM](https://www.youtube.com/watch?v=HiJ_tcQJUwM)

# CD8+ T cell Killing

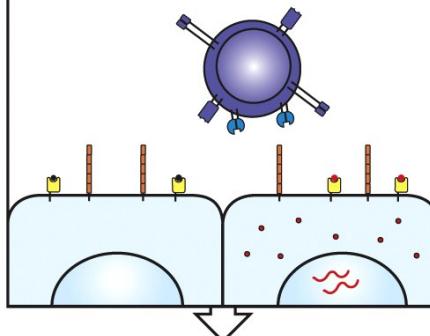


# CD8+ T cell Killing

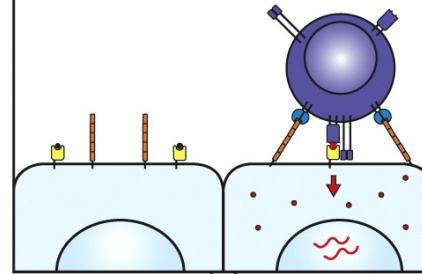
The initial interaction of CD8 cell with target is made by nonspecific adhesion molecules



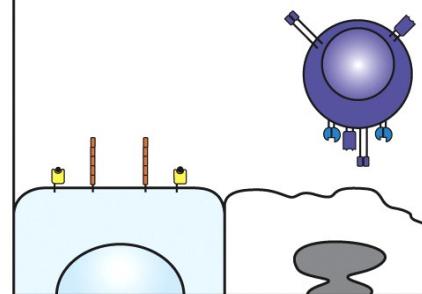
No antigen-specific interaction: cells separate



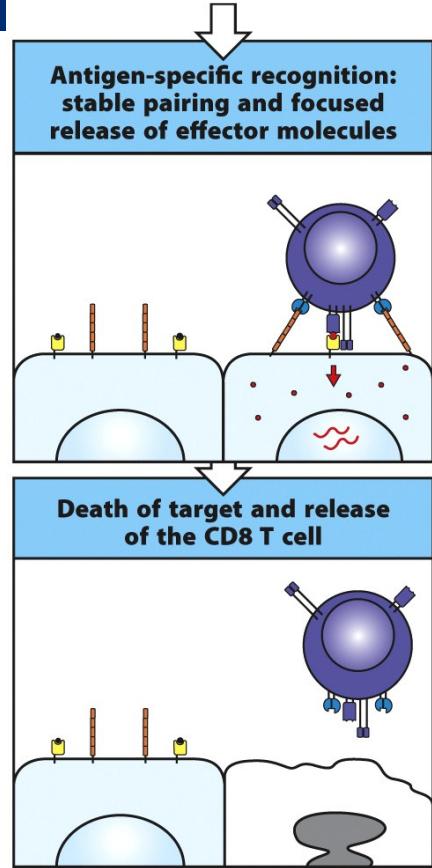
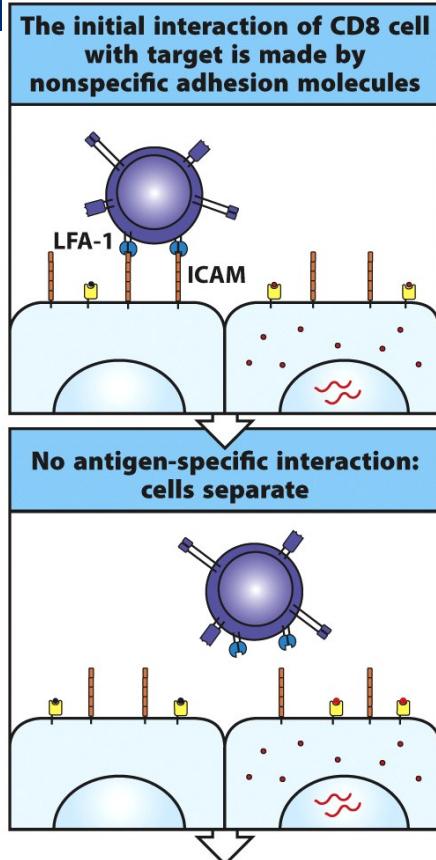
Antigen-specific recognition: stable pairing and focused release of effector molecules



Death of target and release of the CD8 T cell



# CD8+ T cell Killing



Tissue	MHC class I	MHC class II
<b>Lymphoid tissues</b>		
T cells	+++	+*
B cells	+++	+++
Macrophages	+++	++
Dendritic cells	+++	+++
Epithelial cells of the thymus	+	+++
<b>Other nucleated cells</b>		
Neutrophils	+++	-
Hepatocytes	+	-
Kidney	+	-
Brain	+	-†
<b>Nonnucleated cells</b>		
Red blood cells	-	-

# MHC I vs. MHC II

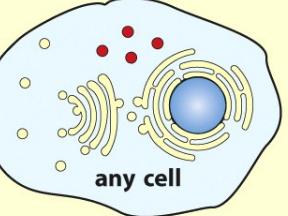
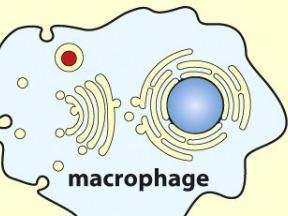
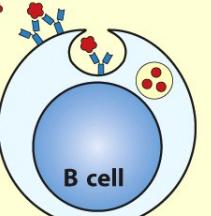
Cytosolic pathogens	Intravesicular pathogens	Extracellular pathogens and toxins
 any cell	 macrophage	 B cell
Degraded in	Cytosol	Endocytic vesicles (low pH)
Peptides bind to	MHC class I	MHC class II
Presented to	Effector CD8 T cells	Effector CD4 T cells
Effect on presenting cell	Cell death	Activation to kill intravesicular bacteria and parasites
		Activation of B cells to secrete Ig to eliminate extracellular bacteria/toxins

Figure 6.2 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# CD8+ T cells Kill Specifically

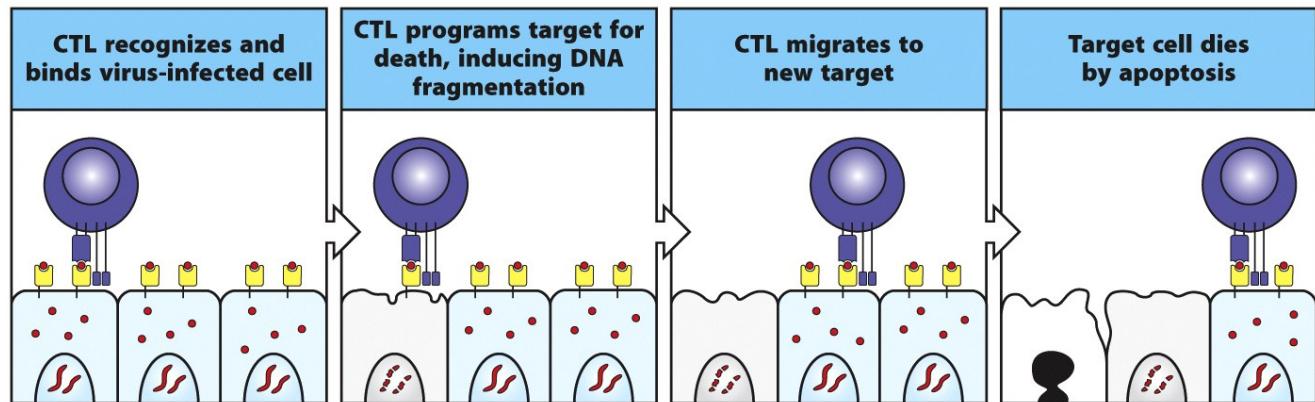
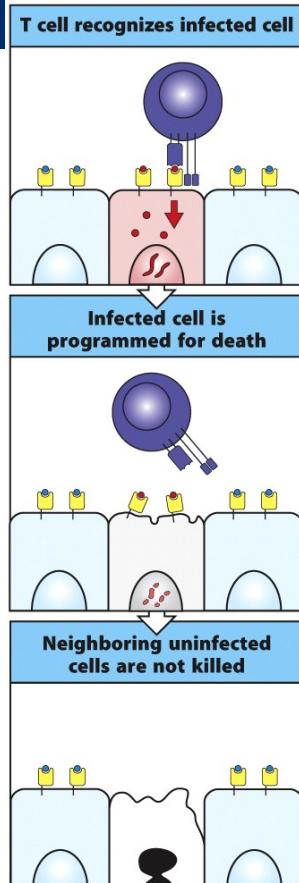


Figure 9.35 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# How CD8+ T cells Kill

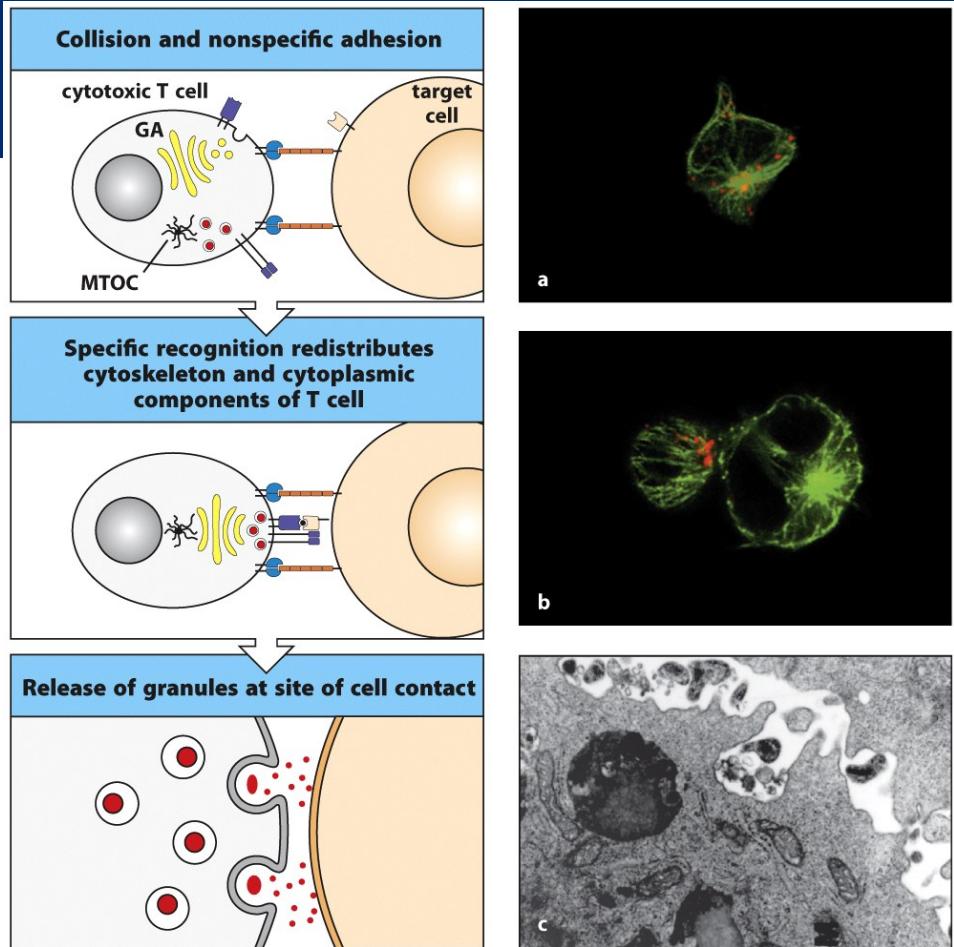


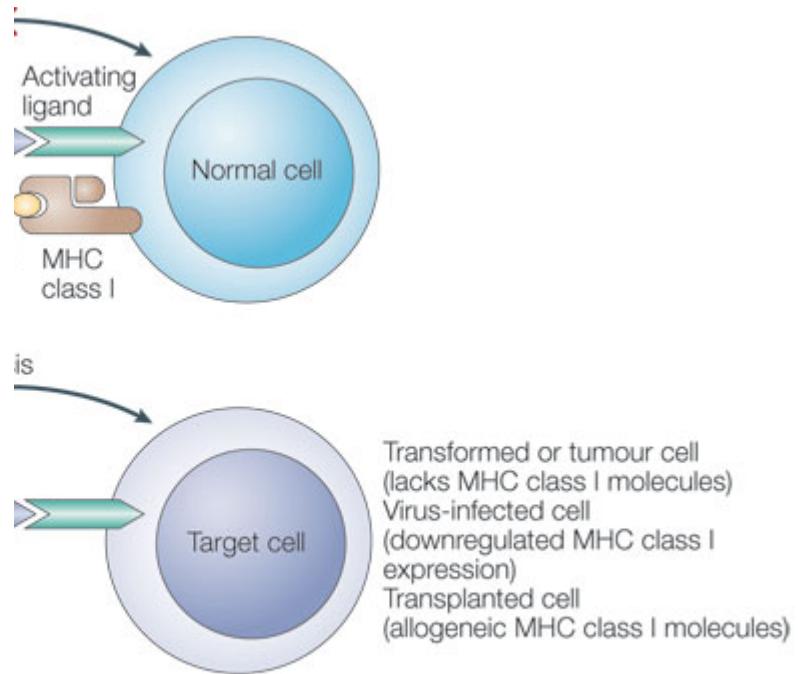
Figure 9.32 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

# How CD8+ T cells Kill

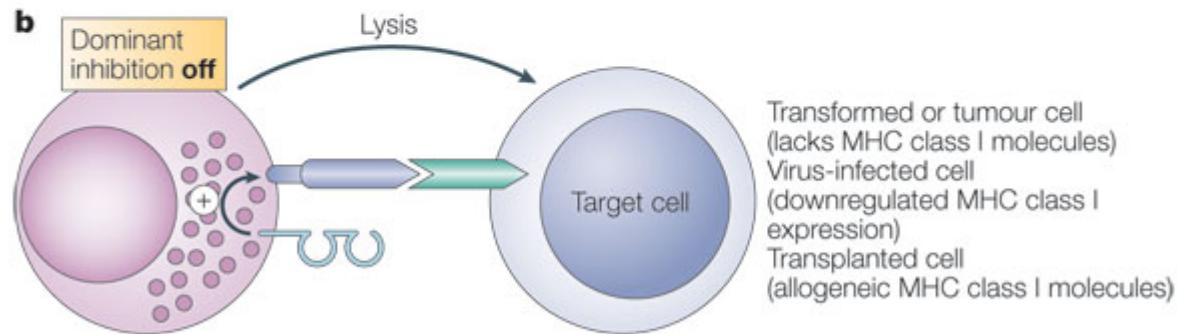
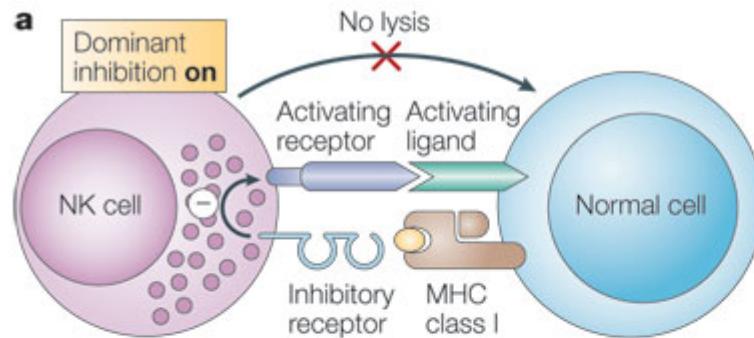
Protein in granules of cytotoxic T cells	Actions on target cells
Perforin	Aids in delivering contents of granules into the cytoplasm of target cell
Granzymes	Serine proteases, which activate apoptosis once in the cytoplasm of the target cell
Granulysin	Has antimicrobial actions and can induce apoptosis

# CD8+ T cell killing

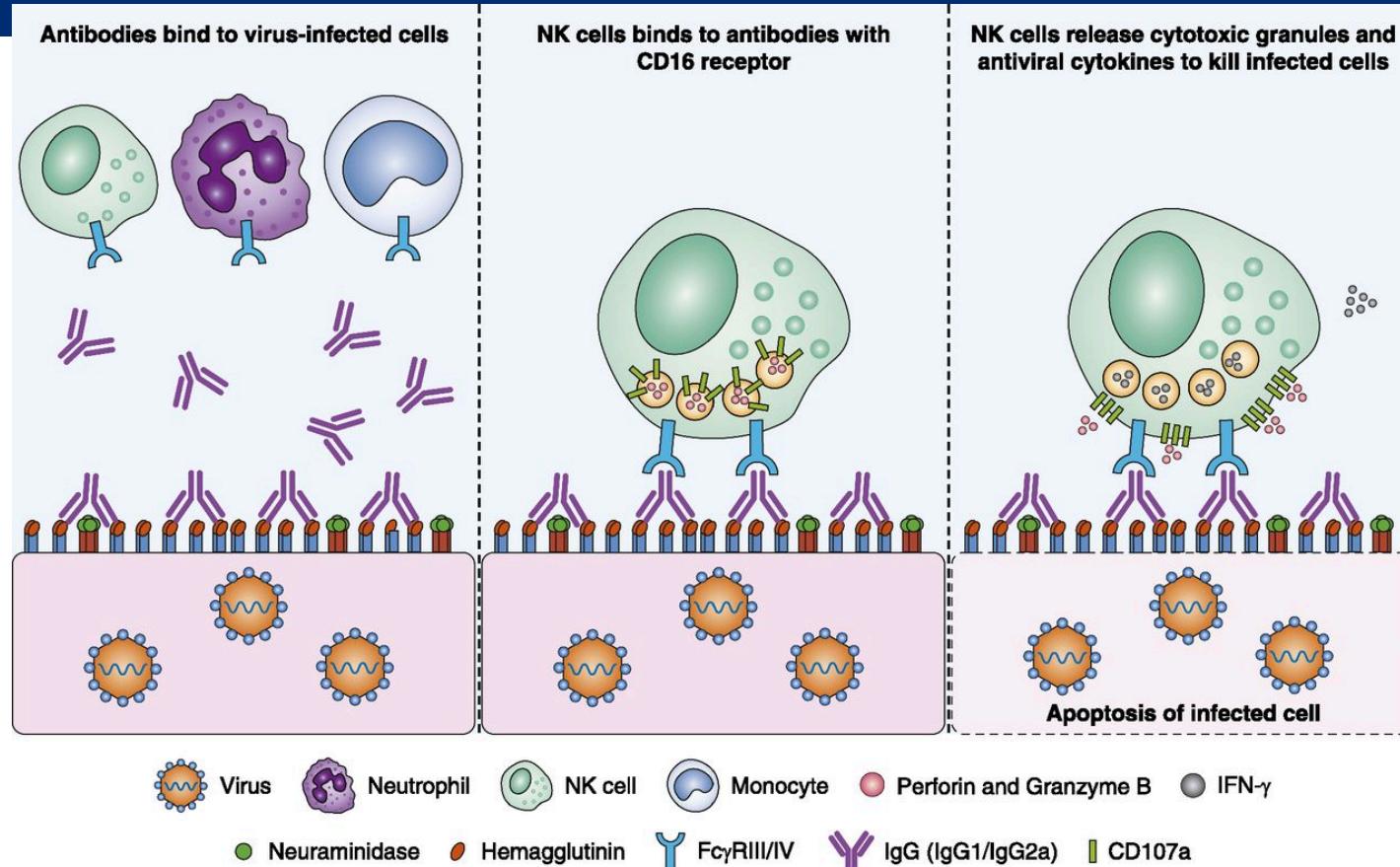
# Viruses Evade CD8+ T cell Attack



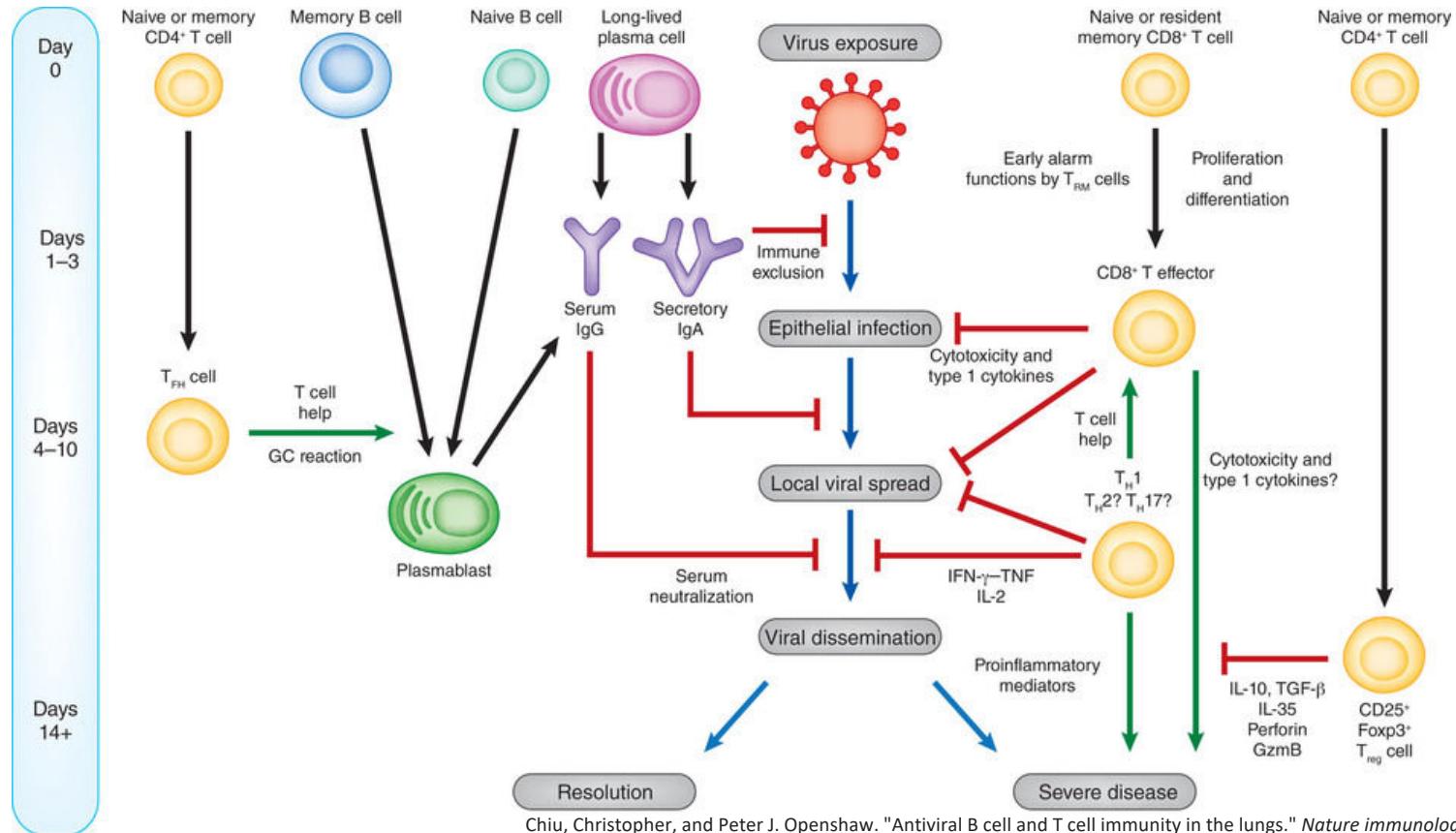
# Natural Killer Cells Kill Cells not Expressing MHC I



# Natural Killer Cells also Have Fc Receptors



# Spreading of the Adaptive Immune Response





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