Johns Hopkins Engineering

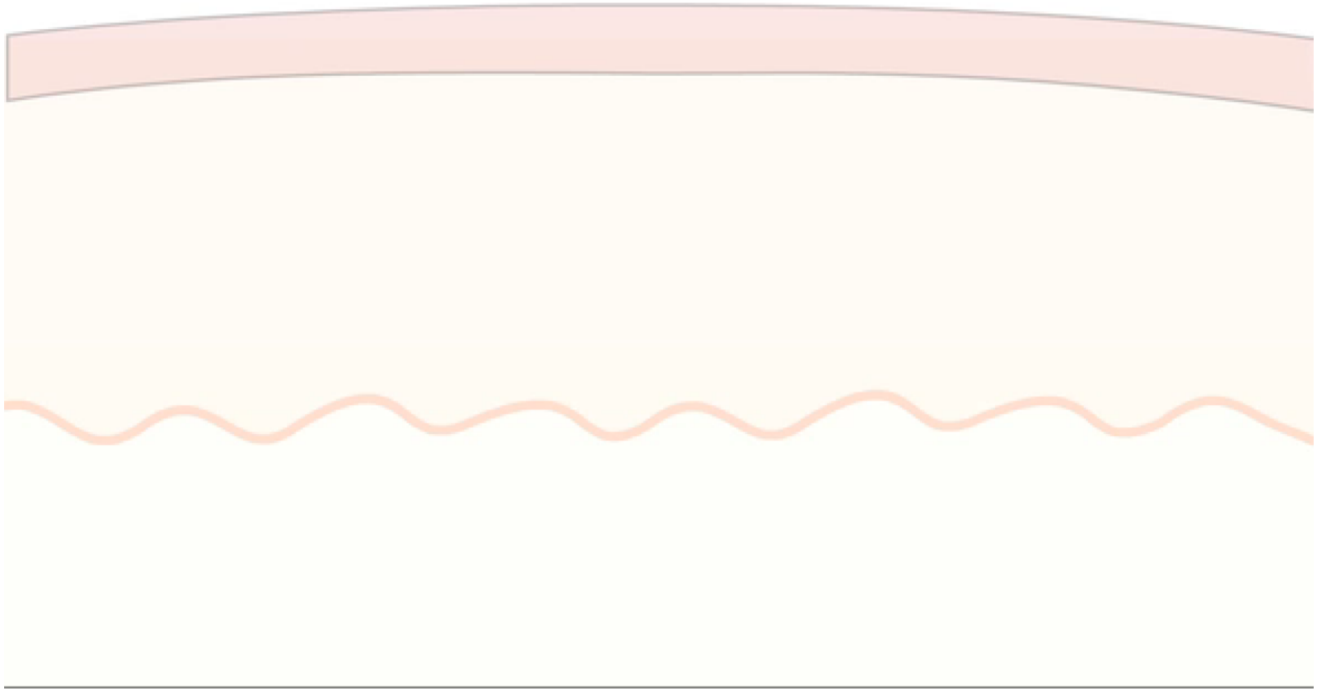
Immunoengineering

Module 2/Lecture 2F

Immune Response to Pathogens - Summary

JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

Review



Summary

	Phases of the immune response		
	Immediate (0–4 hours)	**Early (4–96 hours)**	**Late (96–100 hours)**
	Nonspecific Innate No memory No specific T cells	Nonspecific + specific Inducible No memory No specific T cells	Specific Inducible Memory Specific T cells
Barrier functions	Skin, epithelia, mucins, acid	Local inflammation (C5a) Local TNF-α	IgA antibody in luminal spaces IgE antibody on mast cells Local inflammation
Response to extracellular pathogens	Phagocytes Alternative and MBL complement pathway Lysozyme Lactoferrin Peroxidase Defensins	Mannan-binding lectin C-reactive protein T-independent B-cell antibody Complement	IgG antibody and Fc receptor-bearing cells IgG, IgM antibody + classical complement pathway
Response to intracellular bacteria	Macrophages	Activated NK-dependent macrophage activation IL-1, IL-6, TNF-α, IL-12	T-cell activation of macrophages by IFN-γ
Response to virus-infected cells	Natural killer (NK) cells	IFN-α and IFN-β IL-12-activated NK cells	Cytotoxic T cells IFN-γ

Figure 11.29 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

	Pathological agent	Disease	Humoral immunity				Cell-mediated immunity	
			IgM	IgG	IgE	IgA	CD4 T cells (macrophages)	CD8 killer T cells
Viruses	Herpes zoster	Chickenpox						
	Epstein–Barr virus	Mononucleosis						
	Influenza virus	Influenza						
	Polio virus	Poliomyelitis						
Intracellular bacteria	*Rickettsia prowazekii*	Typhus						
	Mycobacteria	Tuberculosis, leprosy						
Extracellular bacteria	*Staphylococcus aureus*	Boils						
	Streptococcus pneumoniae	Pneumonia						
	Neisseria meningitidis	Meningitis						
	Corynebacterium diphtheriae	Diphtheria						
	Vibrio cholerae	Cholera						
Fungi	*Candida albicans*	Candidiasis						
Protozoa	*Plasmodium* spp.	Malaria						
	Trypanosoma spp.	Trypanosomiasis						
Worms	Schistosome	Schistosomiasis						
Toxins	*Corynebacterium diphtheriae*	Diphtheria						
	Clostridium tetani	Tetanus						

Figure 11.15 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

What does a T cell need for activation?

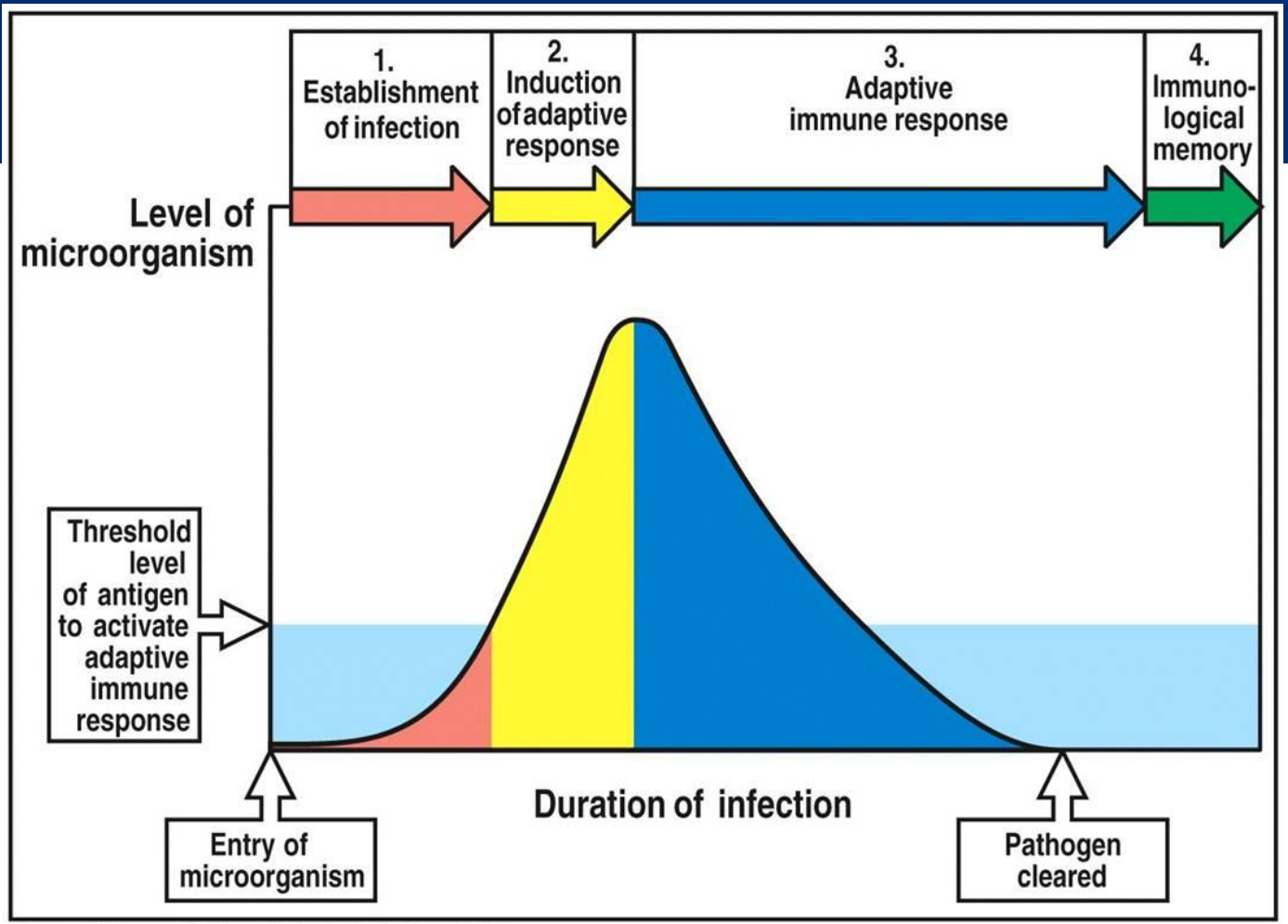


Figure 10-1 Immunobiology, 6/e. (© Garland Science 2005)

Dynamic Response

Phases of the immune response			
Response		**Typical time after infection to start of response**	**Duration of response**
Innate immune response	Inflammation, complement activation, phagocytosis and destruction of pathogen	Minutes	Days
Adaptive immune response	Interaction between antigen-presenting dendritic cells and antigen-specific T cells: recognition of antigen, adhesion, co-stimulation, T-cell proliferation and differentiation	Hours	Days
	Activation of antigen-specific B cells	Hours	Days
	Formation of effector and memory T cells	Days	Weeks
	Interaction of T cells with B cells, formation of germinal centers. Formation of effector B cells (plasma cells) and memory B cells. Production of antibody	Days	Weeks
	Emigration of effector lymphocytes from peripheral lymphoid organs	A few days	Weeks
	Effector cells and antibodies eliminate the pathogen	A few days	Weeks
Immunological memory	Maintenance of memory B cells and T cells and high serum or mucosal antibody levels. Protection against reinfection	Days to weeks	Can be lifelong

Figure 1.34 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immunological Memory

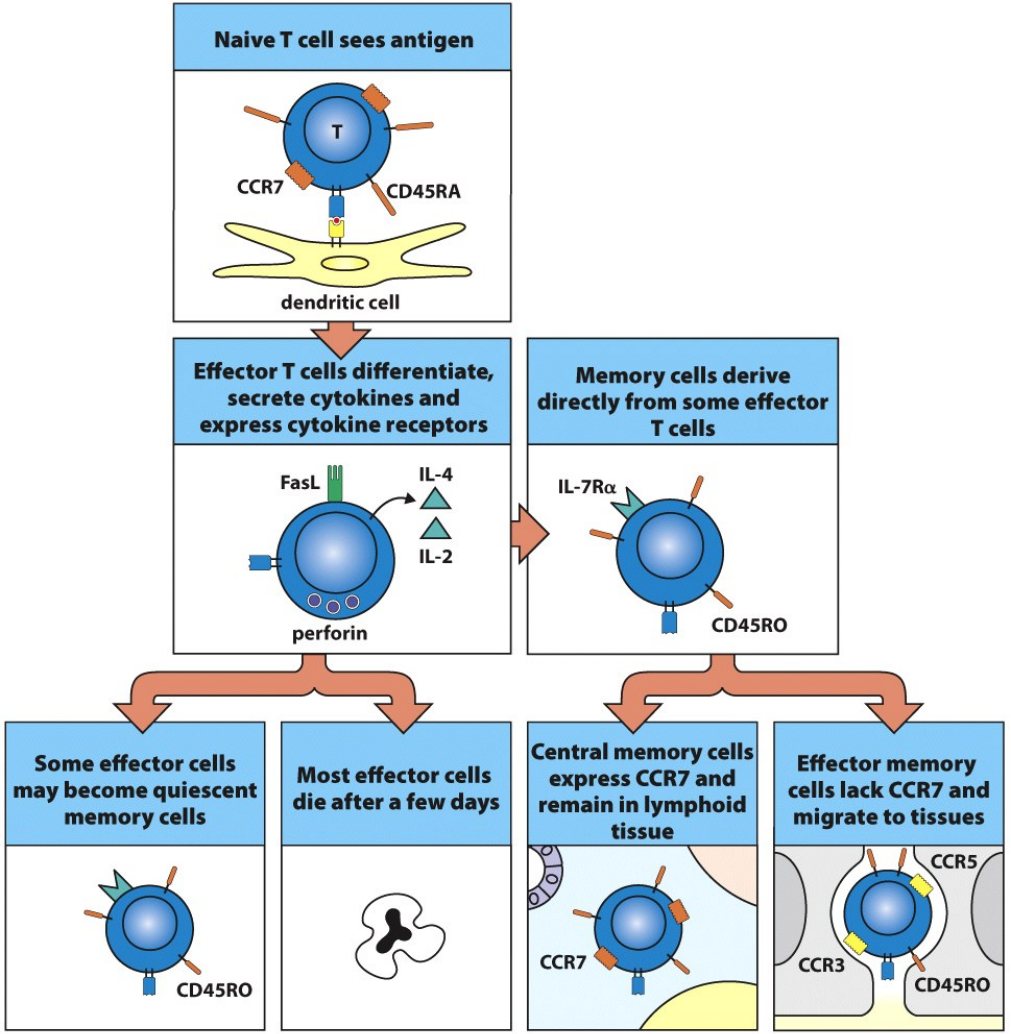


Figure 11.25 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immunological Memory

- Leads to **more** antigen-specific cells present
- Antigen-specific cells are **more sensitive** to stimulation
- **Tissue resident** antigen-specific cells

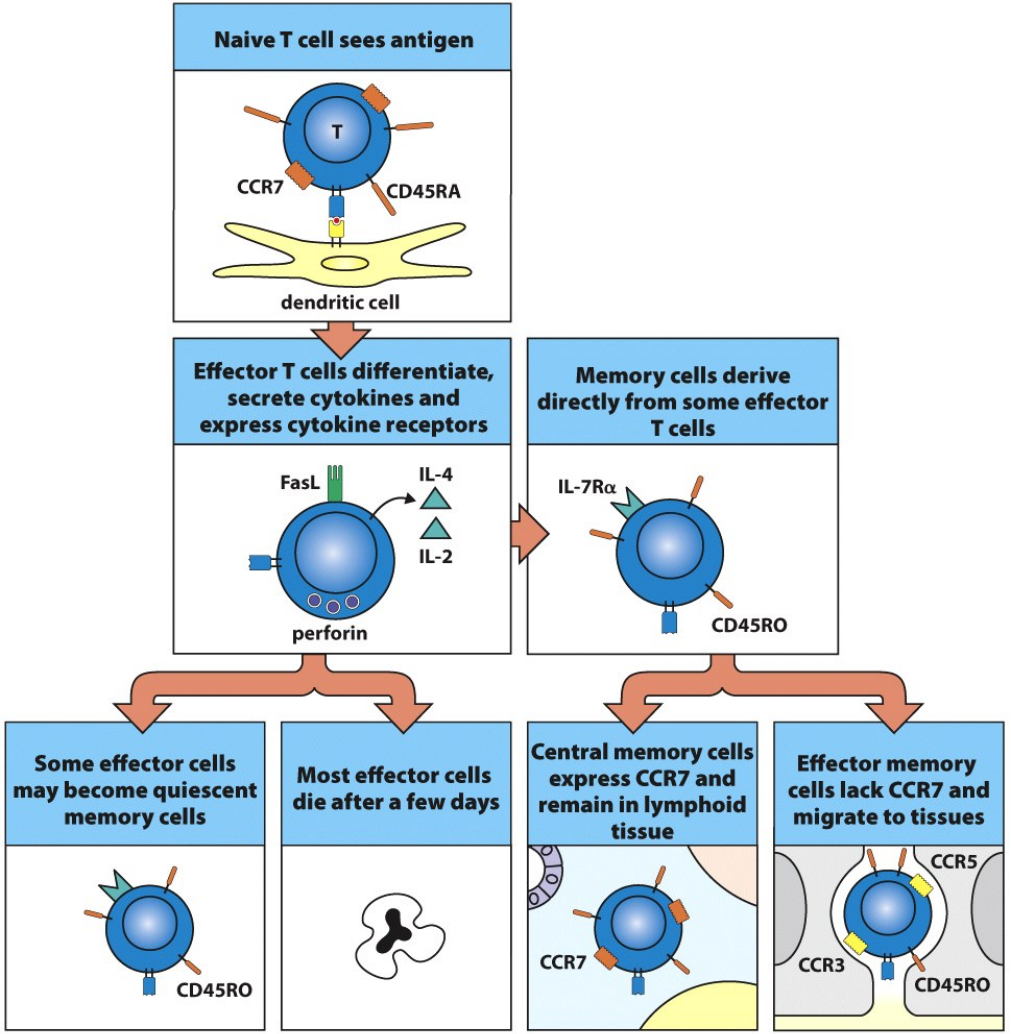


Figure 11.25 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immunological Memory

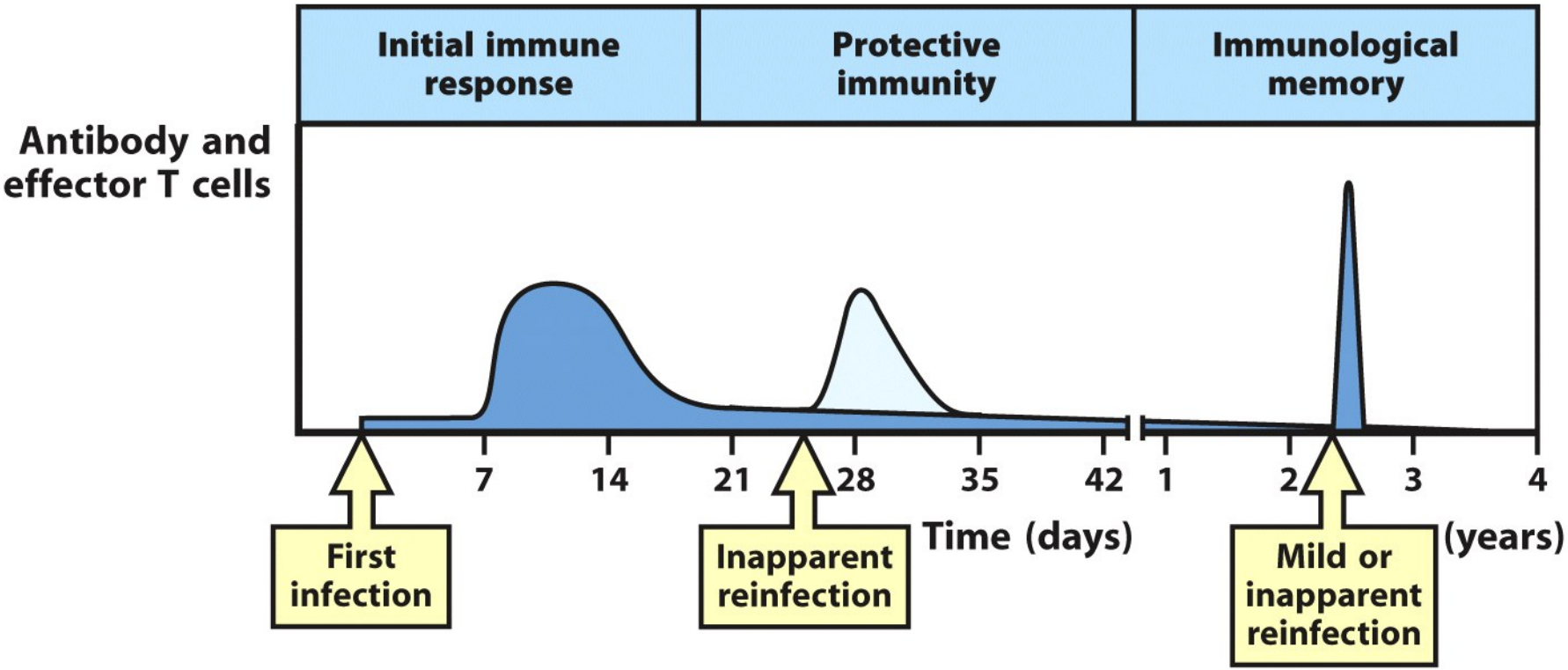


Figure 11.16 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Vaccines

Disease	Baseline 20th Century Pre-Vaccine Annual Cases	2009 Cases	Percent Decrease
Measles	503,282	71	99.9%
Diphtheria	175,885	0	100%
Mumps	152,209	1,991	98.7%
Pertussis	147,271	13,214	91.0%
Smallpox	48,164	0	100%
Rubella	47,745	3	99.9%
Haemophilus influenzae type b, invasive	20,000	35	99.8%
Polio	16,316	0*	100%
Tetanus	1,314	18	98.6%

https://www.niaid.nih.gov/research/vaccine-benefits

Vaccines

- Replicate the infection without the actual infection and need:

1) Antigen from pathogen

2) Danger signal

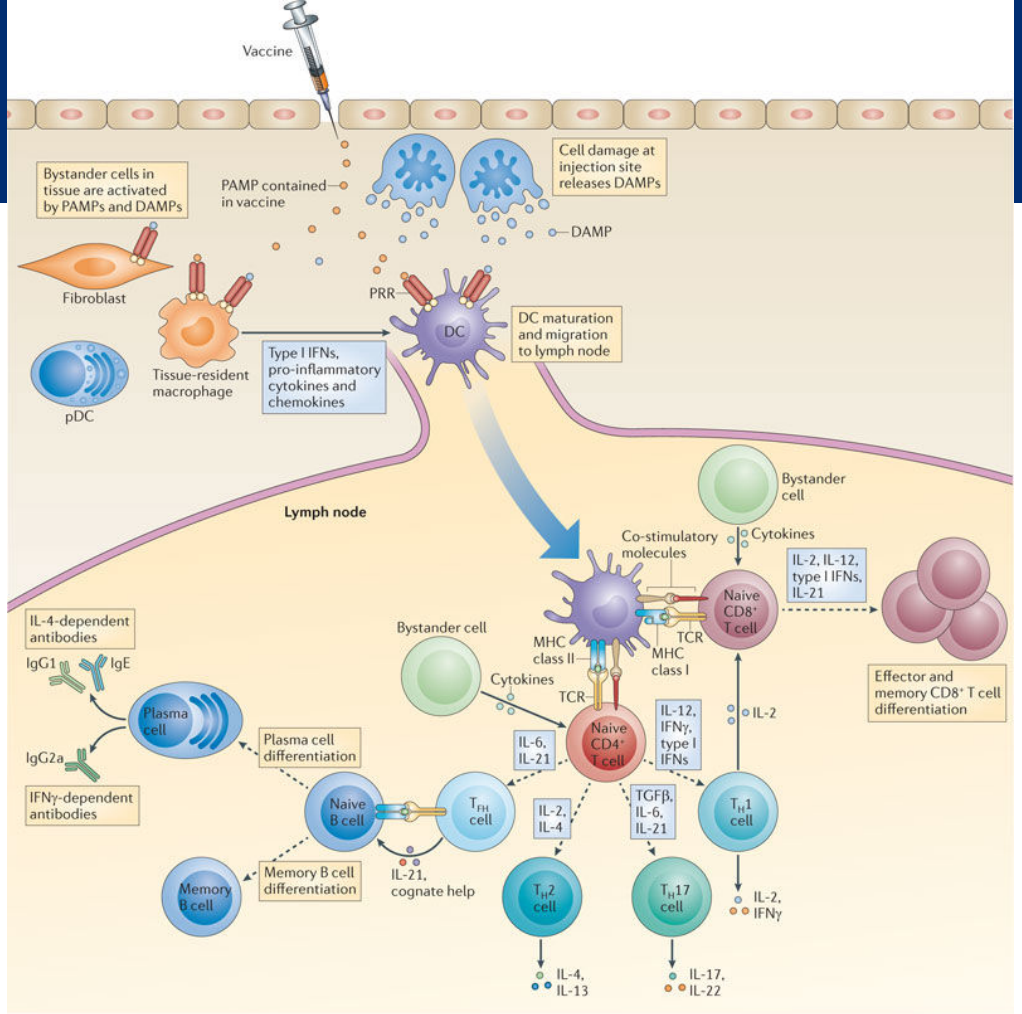
Vaccine Types

Scientists take many approaches to designing vaccines against a microbe. These choices are typically based on fundamental information about the microbe, such as how it infects cells and how the immune system responds to it, as well as practical considerations, such as regions of the world where the vaccine would be used. The following are some of the options that researchers might pursue:

- Live, attenuated vaccines
- Inactivated vaccines
- Subunit vaccines
- Toxoid vaccines
- Conjugate vaccines
- DNA vaccines
- Recombinant vector vaccines

https://www.niaid.nih.gov/research/vaccine-types

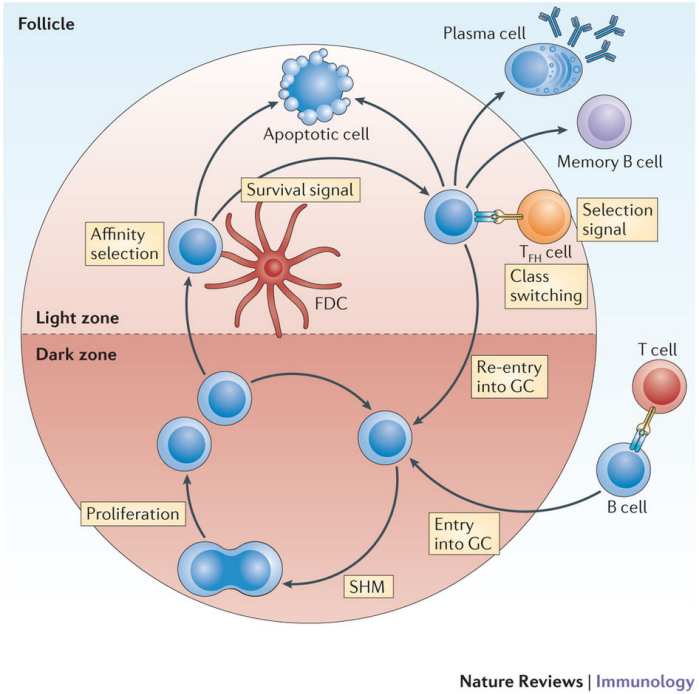
Vaccines



Nature Reviews | Immunology

Desmet, Christophe J., and Ken J. Ishii. "Nucleic acid sensing at the interface between innate and adaptive immunity in vaccination." *Nature reviews. Immunology* 12.7 (2012): 479.

Vaccines & Memory



Nature Reviews | Immunology

Heesters, Balthasar A., Riley C. Myers, and Michael C. Carroll. "Follicular dendritic cells: dynamic antigen libraries." *Nature Reviews Immunology* 14.7 (2014): 495-504.

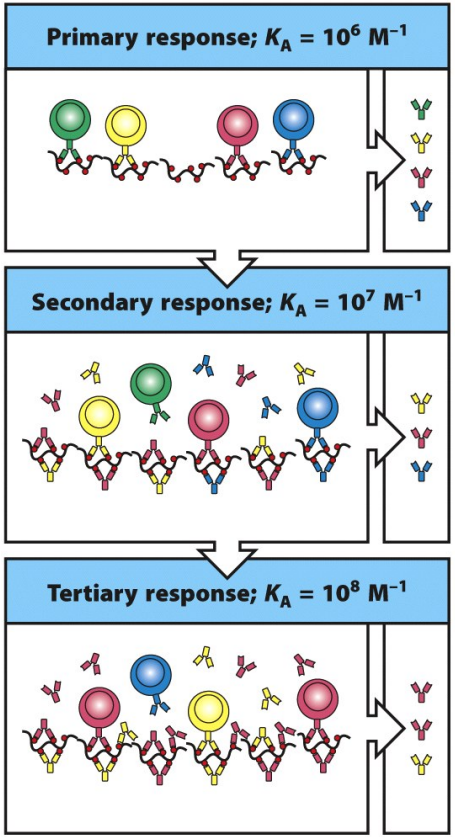


Figure 11.20 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

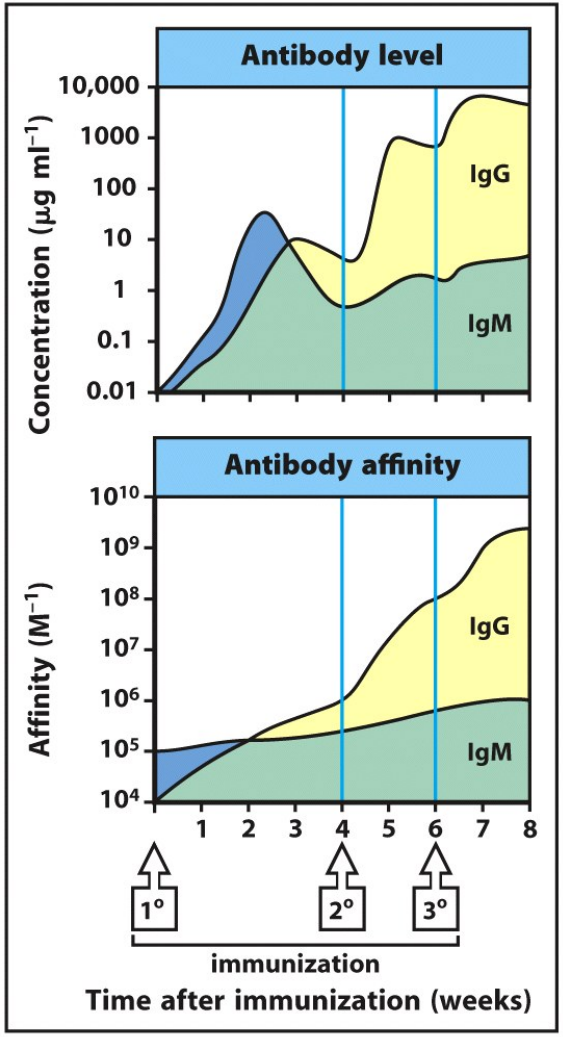


Figure 11.19 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Vaccine Effect on B cells

	Source of B cells	
	Unimmunized donor Primary response	Immunized donor Secondary response
Frequency of antigen-specific B cells	$1:10^4 - 1:10^5$	$1:10^2 - 1:10^3$
Isotype of antibody produced	IgM > IgG	IgG, IgA
Affinity of antibody	Low	High
Somatic hypermutation	Low	High

Figure 11.18 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Immune Cell Lineages

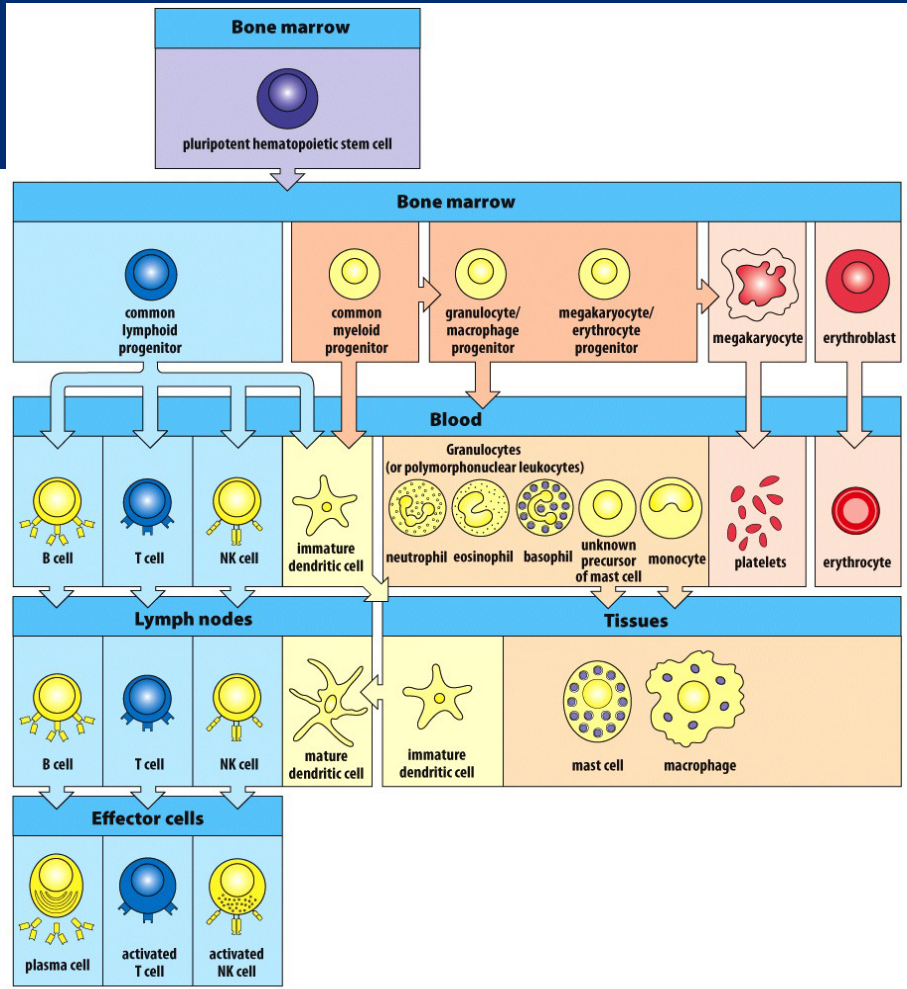


Figure 1.3 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Types of CD4+ T cells

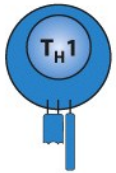
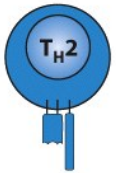
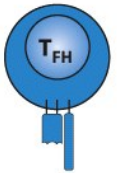
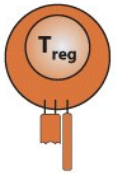
	CD8 cytotoxic T cells	CD4 T_H1 cells	CD4 T_H2 cells	CD4 T_H17 cells	T_{FH} cells	CD4 regulatory T cells (various types)
Types of effector T cell						
Main functions in adaptive immune response	Kill virus-infected cells	Activate infected macrophages Provide help to B cells for antibody production	Provide help to B cells for antibody production, especially switching to IgE	Enhance neutrophil response Promote barrier integrity (skin, intestine)	B-cell help Isotype switching Antibody production	Suppress T-cell responses
Pathogens targeted	Viruses (e.g. influenza, rabies, vaccinia) Some intracellular bacteria	Microbes that persist in macrophage vesicles (e.g. mycobacteria, *Listeria*, *Leishmania donovani*, *Pneumocystis carinii*) Extracellular bacteria	Helminth parasites	*Klebsiella pneumoniae* Fungi (*Candida albicans*)	All types	

Figure 9.1 Janeway's Immunobiology, 8ed. (© Garland Science 2012)

Summary

- List examples of pathogens and routes of infection
- Identify major cellular and protein components of the immune response to pathogens and their function
- Describe how information is communicated by the immune system
- Explain differences between the immune response to bacteria and viruses and explain how infection is resolved
- Define immunological memory and context with vaccines