Adaptive Immunity

Overview

Innate Immunity		Adaptive Immunity (Chapter 17)
First line of defense	**Second line of defense**	**Third line of defense**
• Intact skin • Mucous membranes and their secretions • Normal microbiota	• Phagocytes, such as neutrophils, eosinophils, dendritic cells, and macrophages • Inflammation • Fever • Antimicrobial substances	• Specialized lymphocytes: T cells and B cells • Antibodies

Fig 16.1

Antibodies

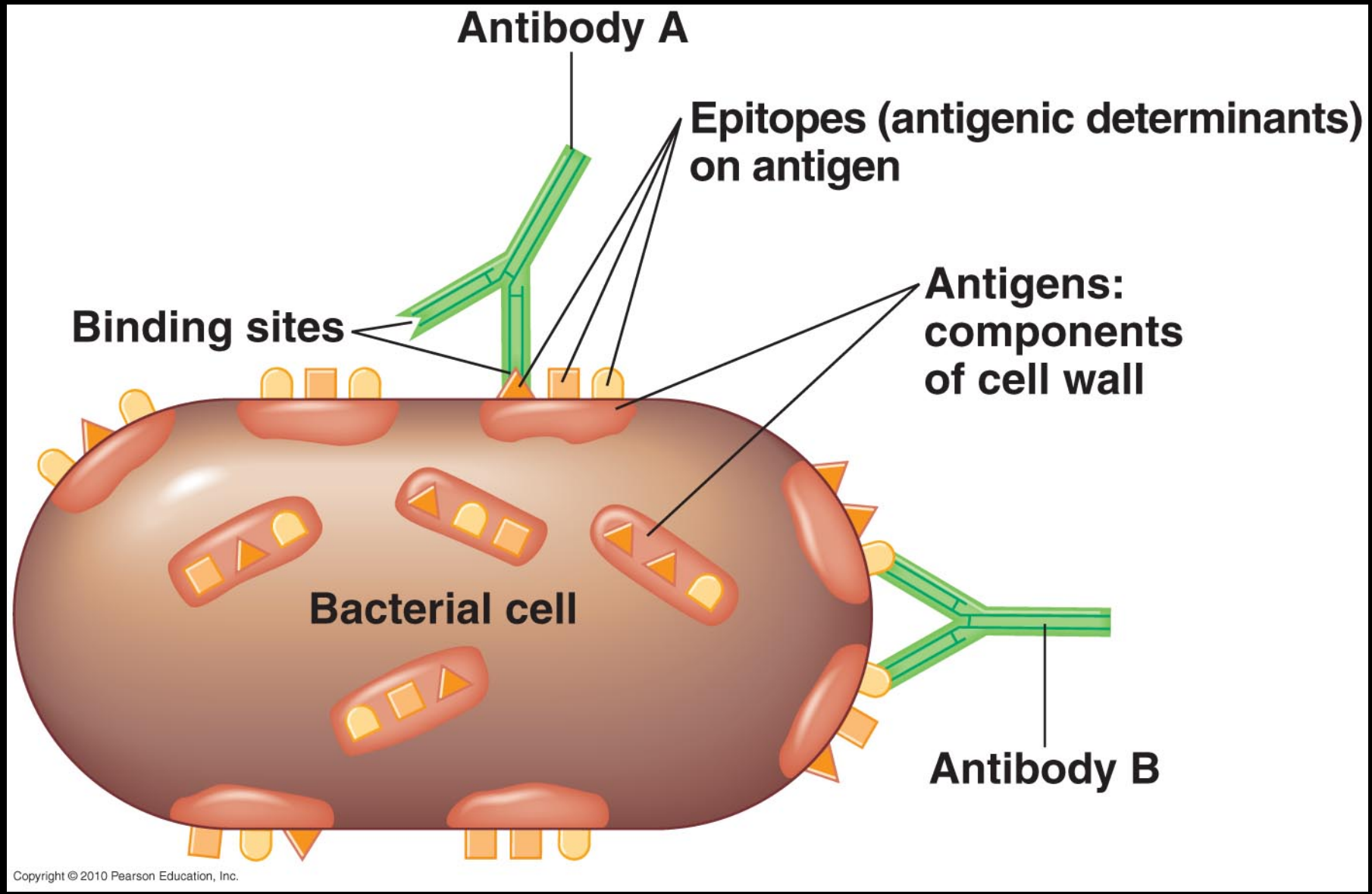


Fig 17.1

Antibodies

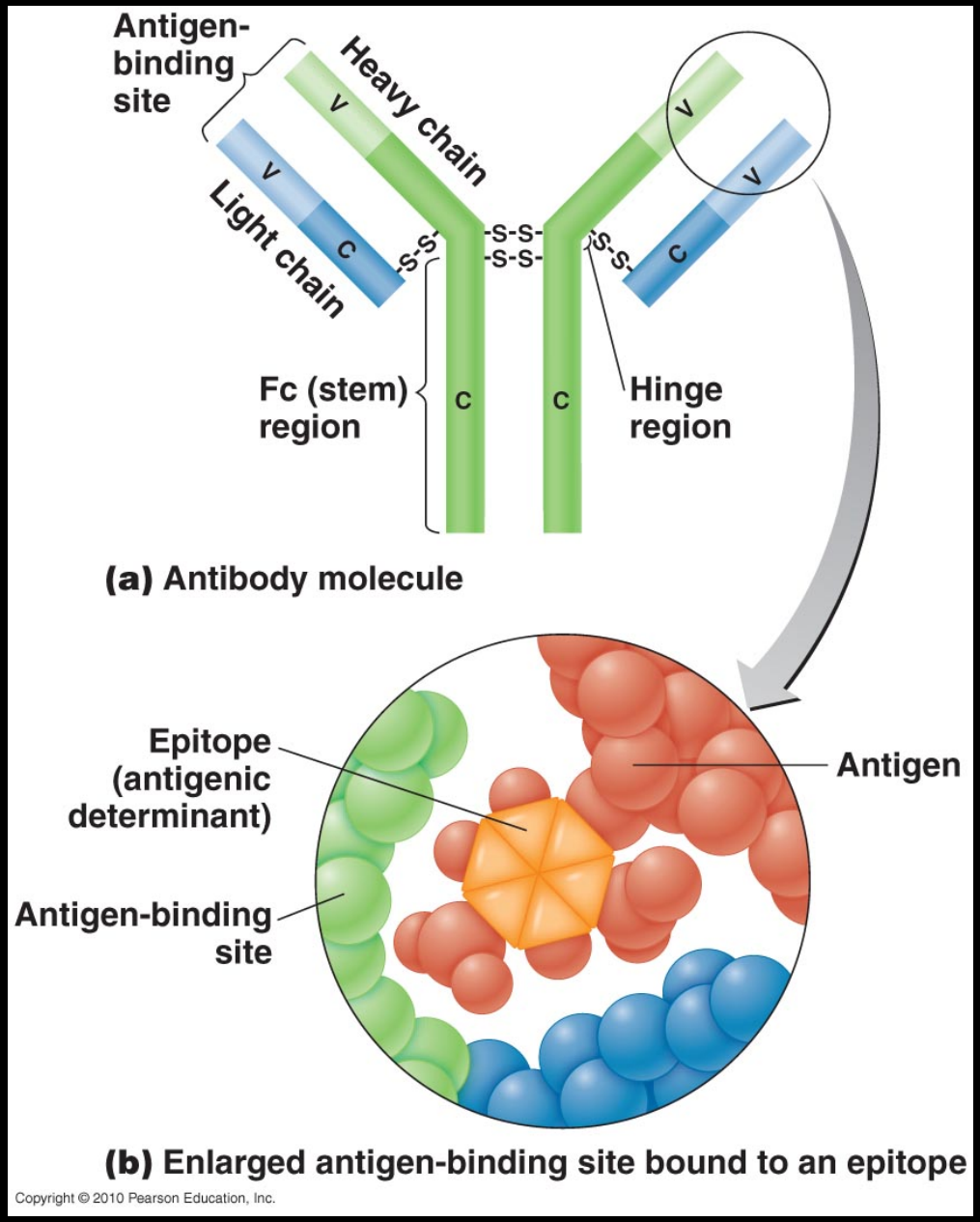
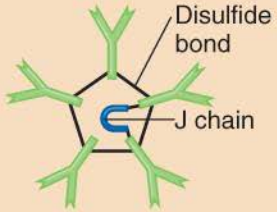
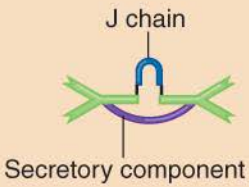


Fig 17.3

Table 17.1 A Summary of Immunoglobulin Classes

Characteristics	IgG	IgM	IgA	IgD	IgE
					
Structure	Monomer	Pentamer	Dimer (with secretory component)	Monomer	Monomer
Percentage of Total Serum Antibody	80%	5–10%	10–15%*	0.2%	0.002%
Location	Blood, lymph, intestine	Blood, lymph, B cell surface (as monomer)	Secretions (tears, saliva, mucus, intestine, milk), blood, lymph	B cell surface, blood, lymph	Bound to mast and basophil cells throughout body, blood
Molecular Weight	150,000	970,000	405,000	175,000	190,000
Half-Life in Serum	23 days	5 days	6 days	3 days	2 days
Complement Fixation	Yes	Yes	No†	No	No
Placental Transfer	Yes	No	No	No	No
Known Functions	Enhances phagocytosis; neutralizes toxins and viruses; protects fetus and newborn	Especially effective against microorganisms and agglutinating antigens; first antibodies produced in response to initial infection	Localized protection on mucosal surfaces	Serum function not known; presence on B cells functions in initiation of immune response	Allergic reactions; possibly lysis of parasitic worms

*Percentage in serum only; if mucous membranes and body secretions are included, percentage is much higher.
†May be yes via alternative pathway.

Table 17.1

B-cell activation

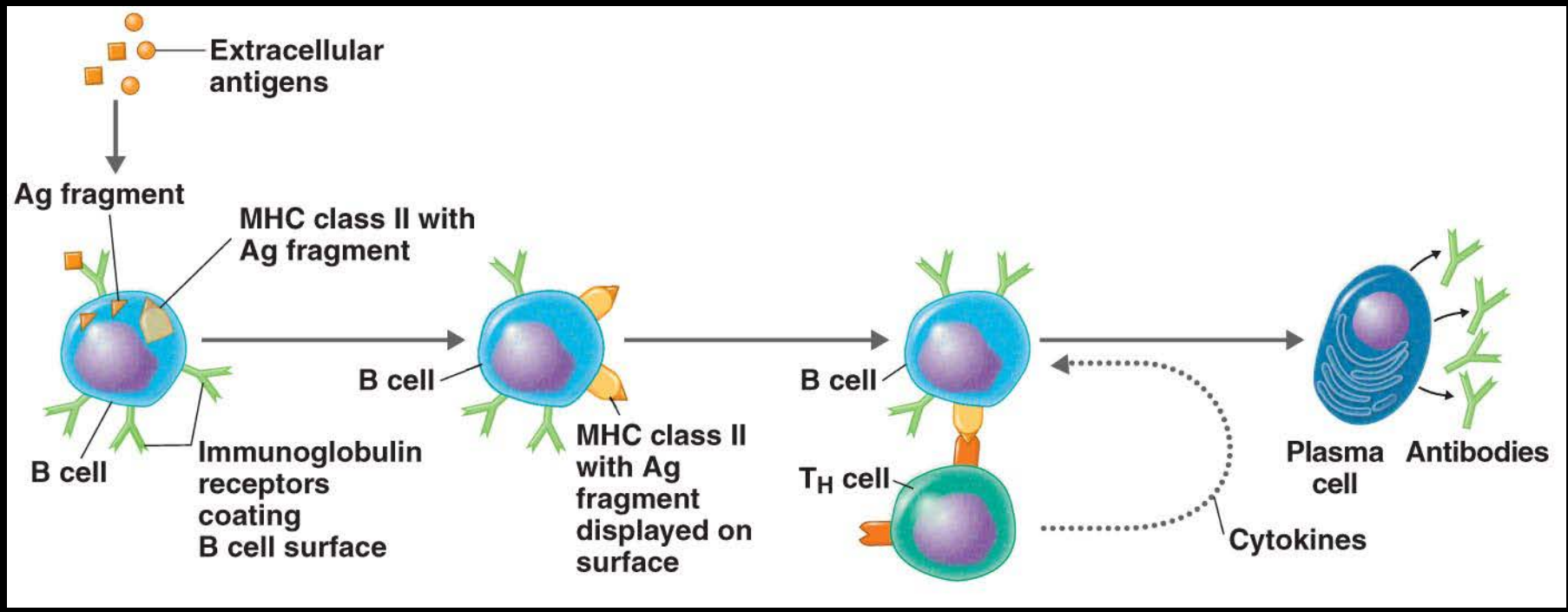


Fig 17.4

Clonal selection, expansion, differentiation

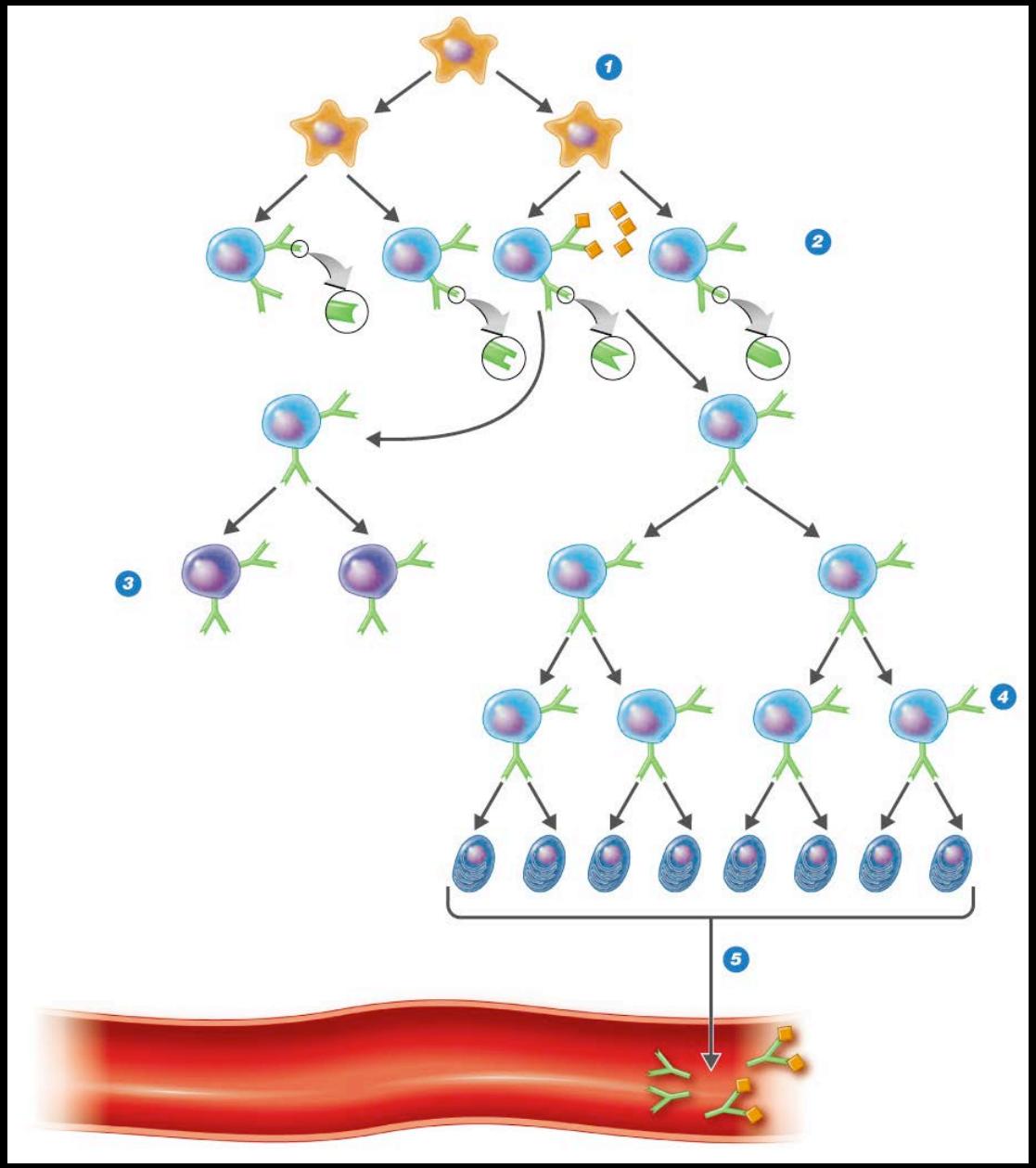


Fig 17.5

Antibody-binding

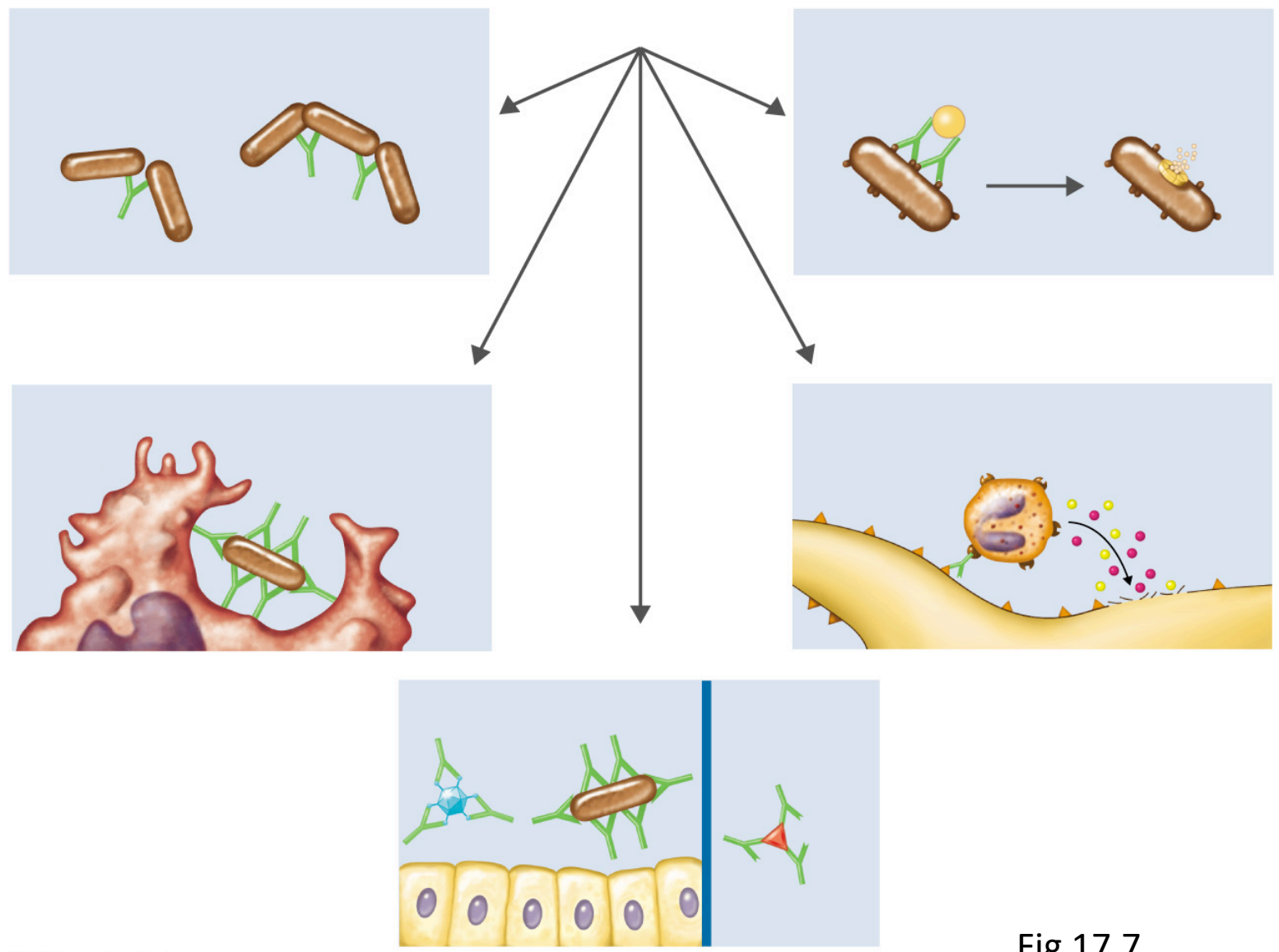
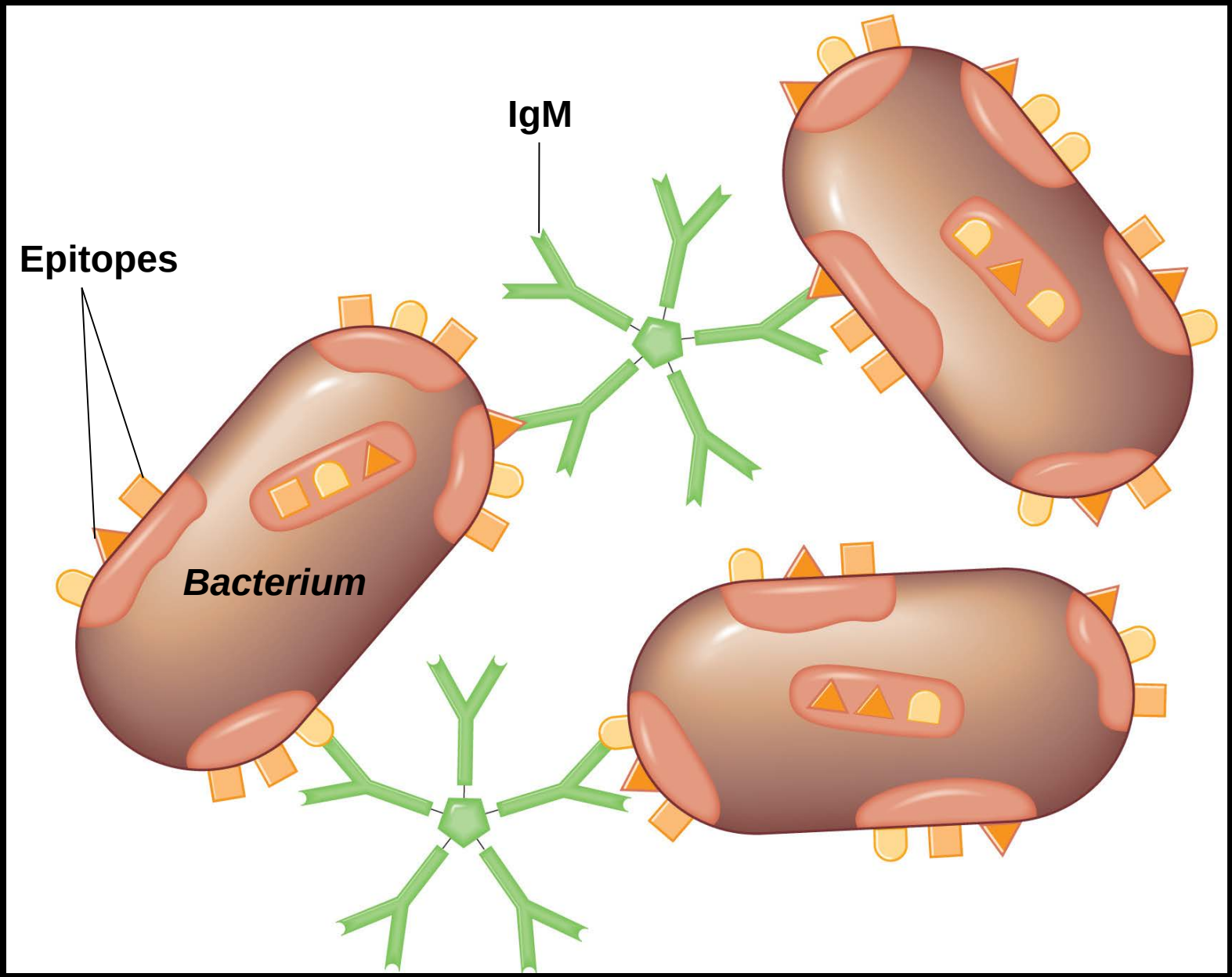
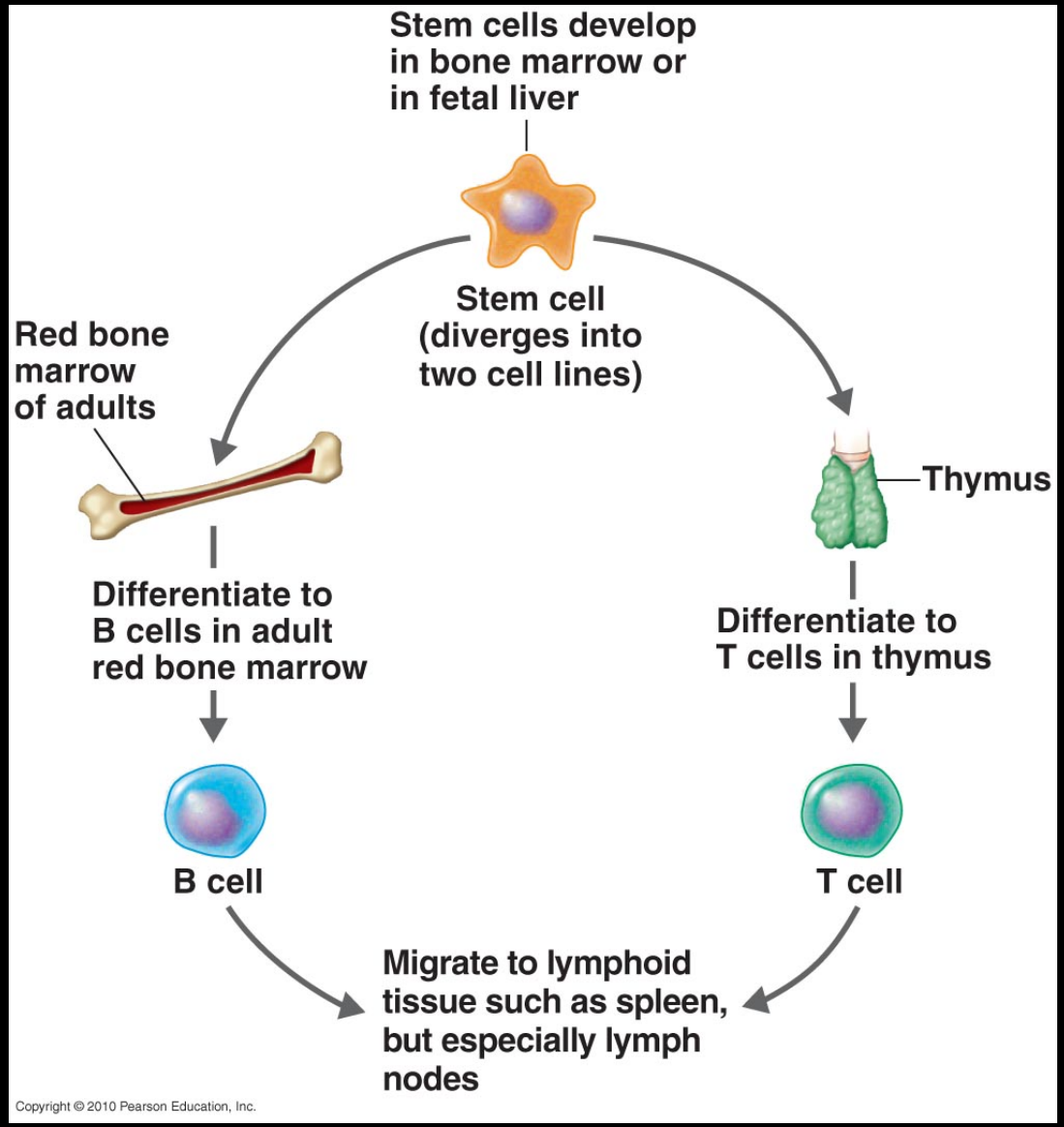


Fig 17.7

Figure 18.5 An agglutination reaction.



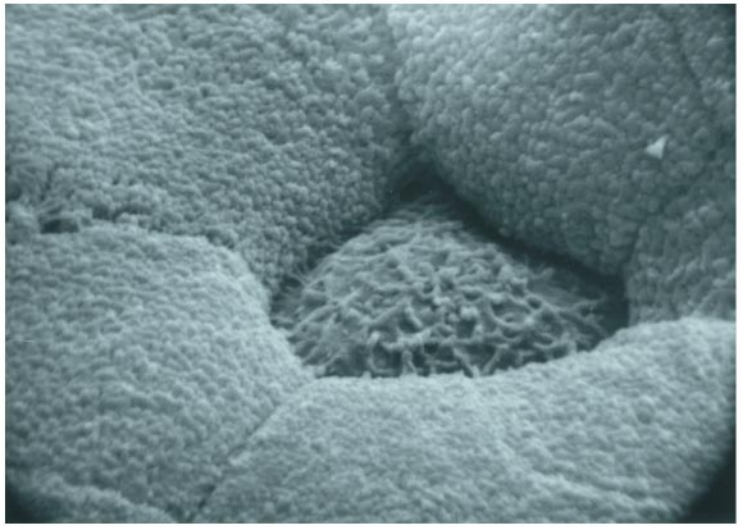
B-cells vs T-cells



Can also detect cancer cells: www.cancerimmunity.org/peptide/mutations/

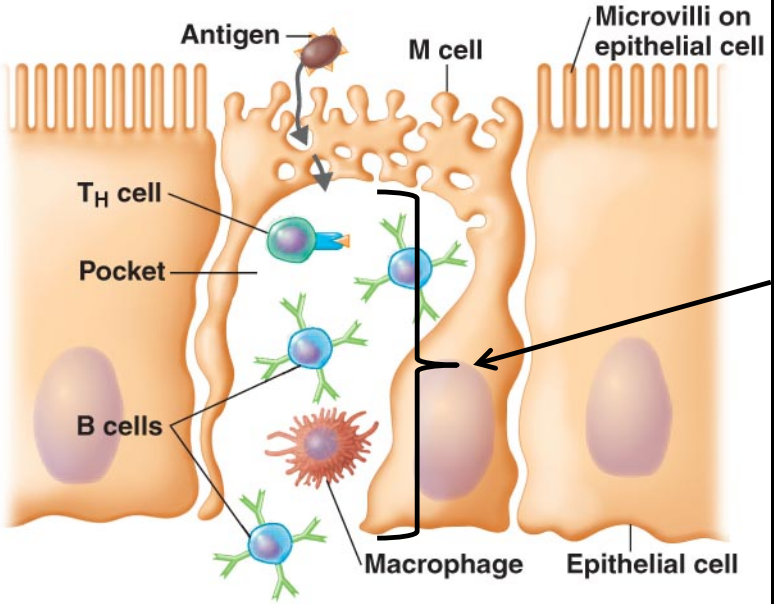
Fig 17.8

M cells



(a) M cell on Peyer's patch. Note the tips of the closely packed microvilli on the surrounding epithelial cells.

SEM 1 μm



(b) M cells facilitate contact between antigens passing through the intestinal tract and cells of the body's immune system.

Peyer's patch

Fig 17.9

Apoptosis

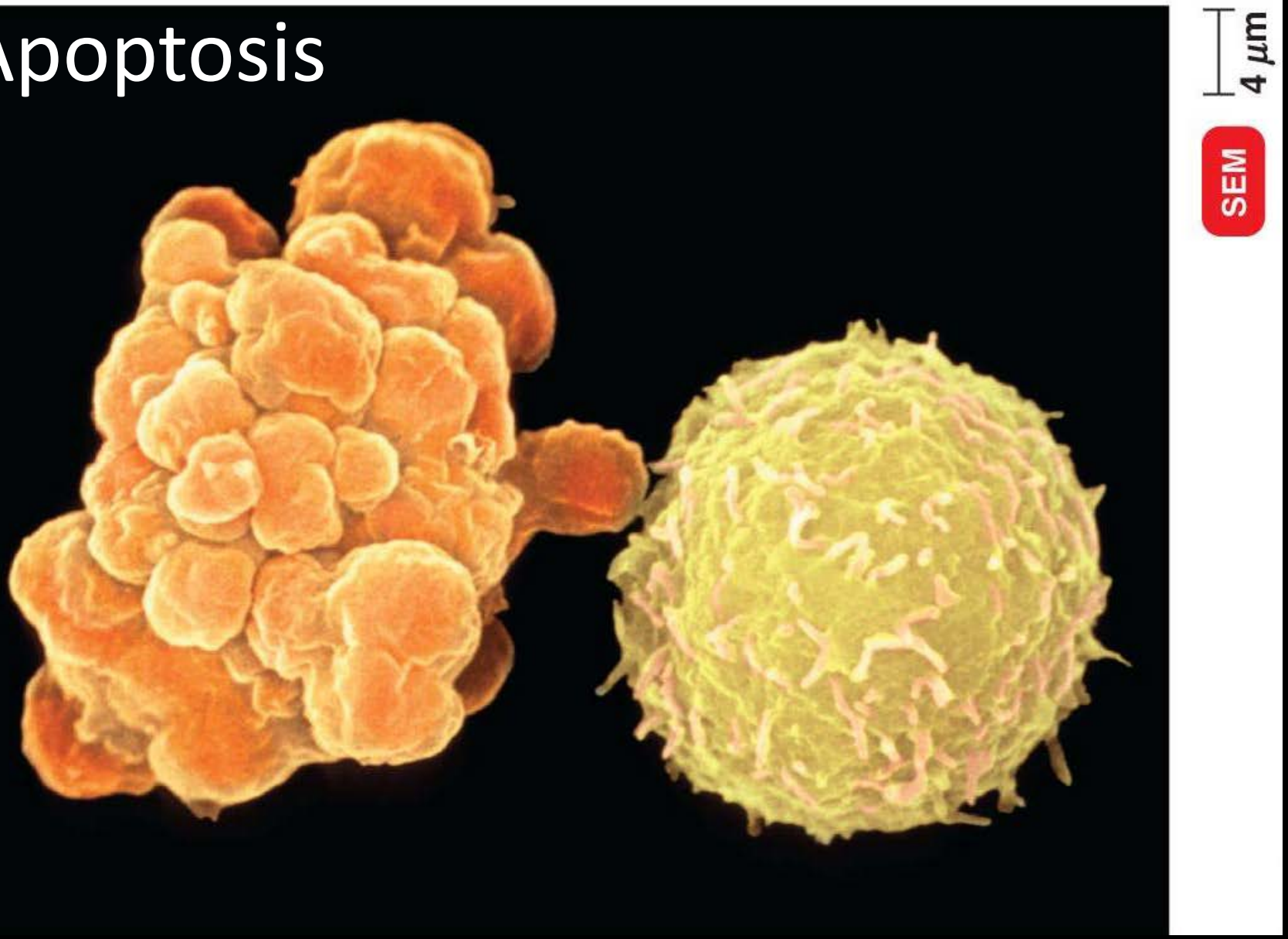


Fig 17.13 Cell on left undergoing apoptosis. Normal cell on right.

Two video clips from Howard Hughes Medical Institute (HHMI)

Clip 1
Clip 2

Dendritic cell

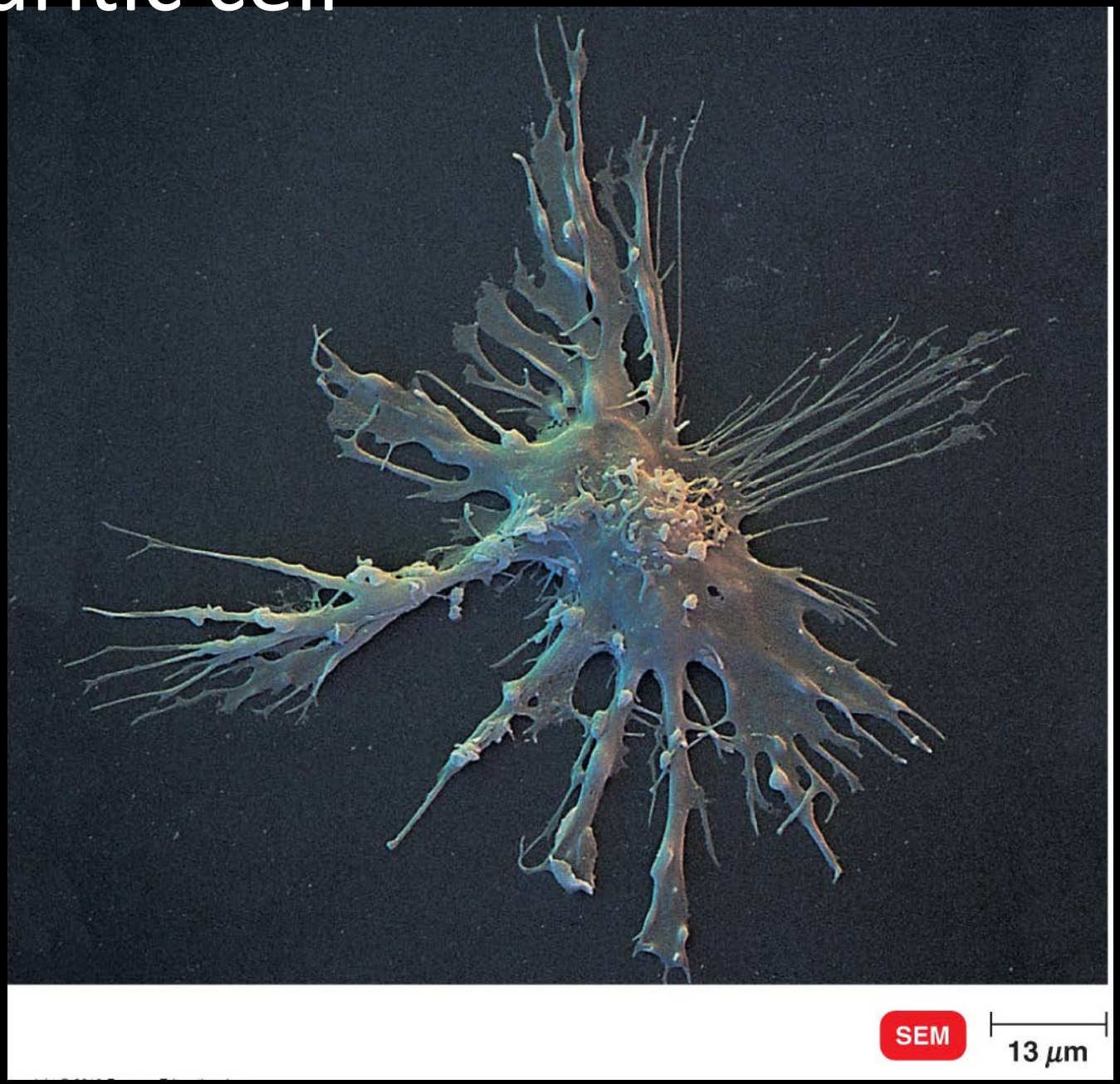


Fig 17.14

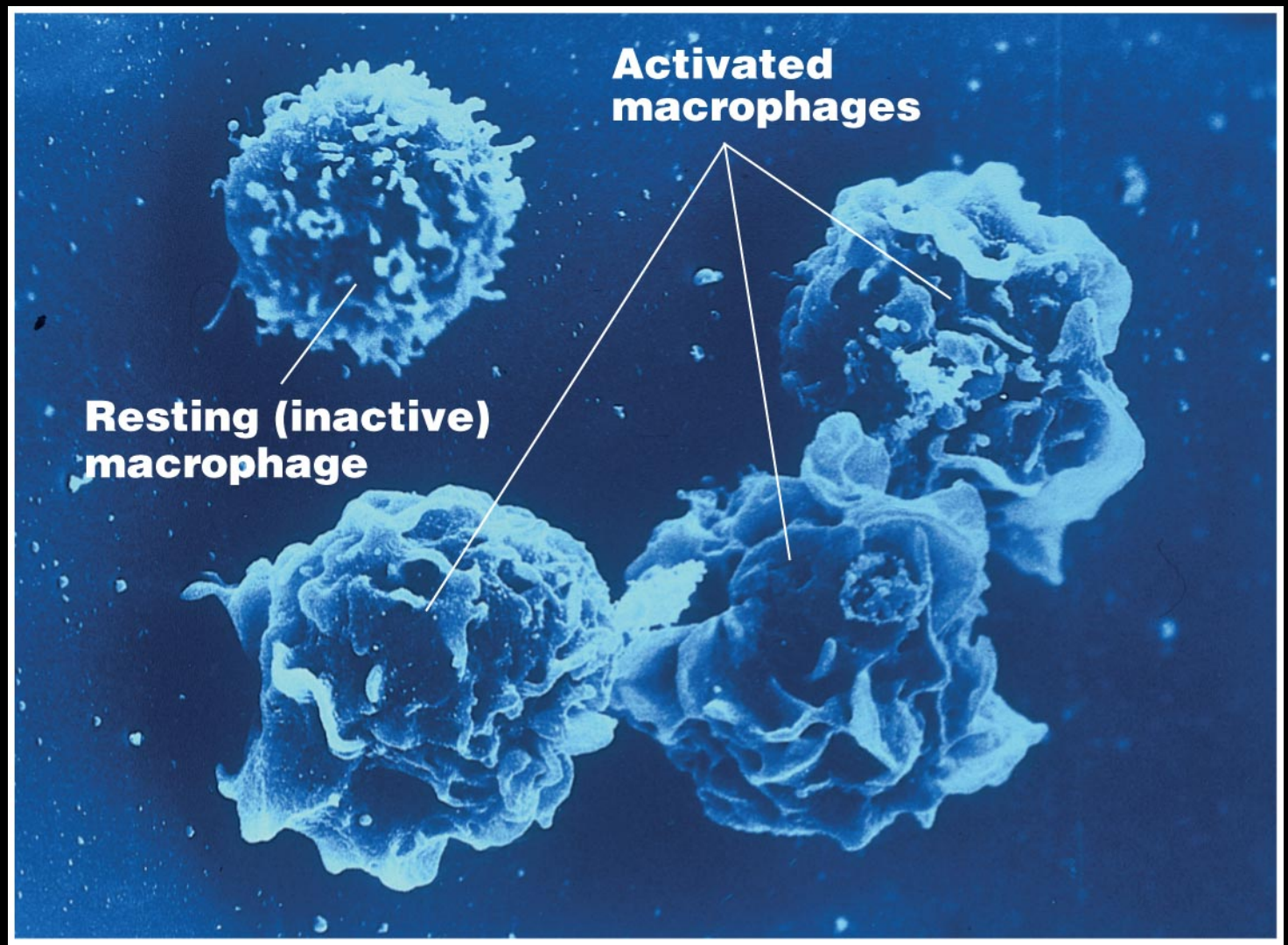


Fig 17.15

Varieties of Macrophage Activation

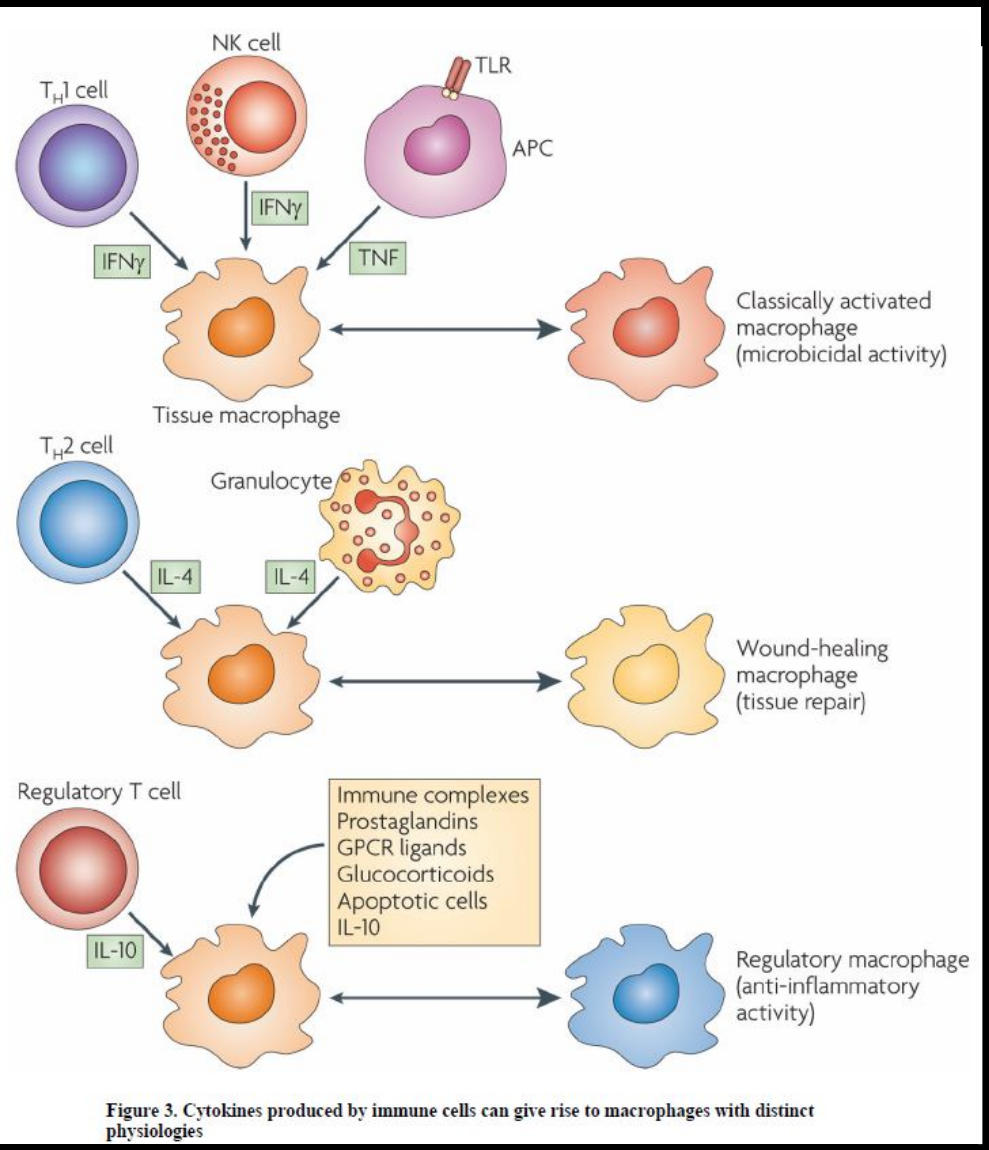


Figure 3. Cytokines produced by immune cells can give rise to macrophages with distinct physiologies

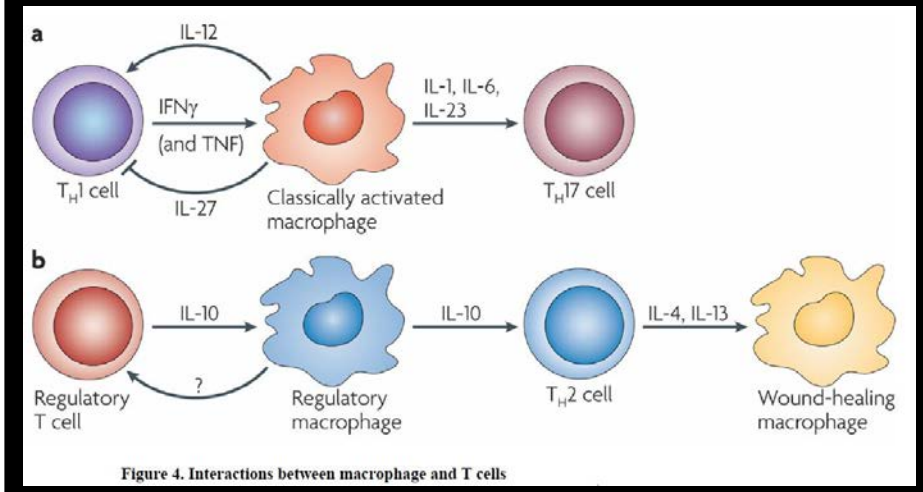


Figure 4. Interactions between macrophage and T cells

Mosser & Edwards. 2008. *Nat Rev Immunol.*

Nature. 1988 Jul 21;334(6179):260-2.

Deactivation of macrophages by transforming growth factor-beta.

Tsunawaki S[1], Sporn M, Ding A, Nathan C.

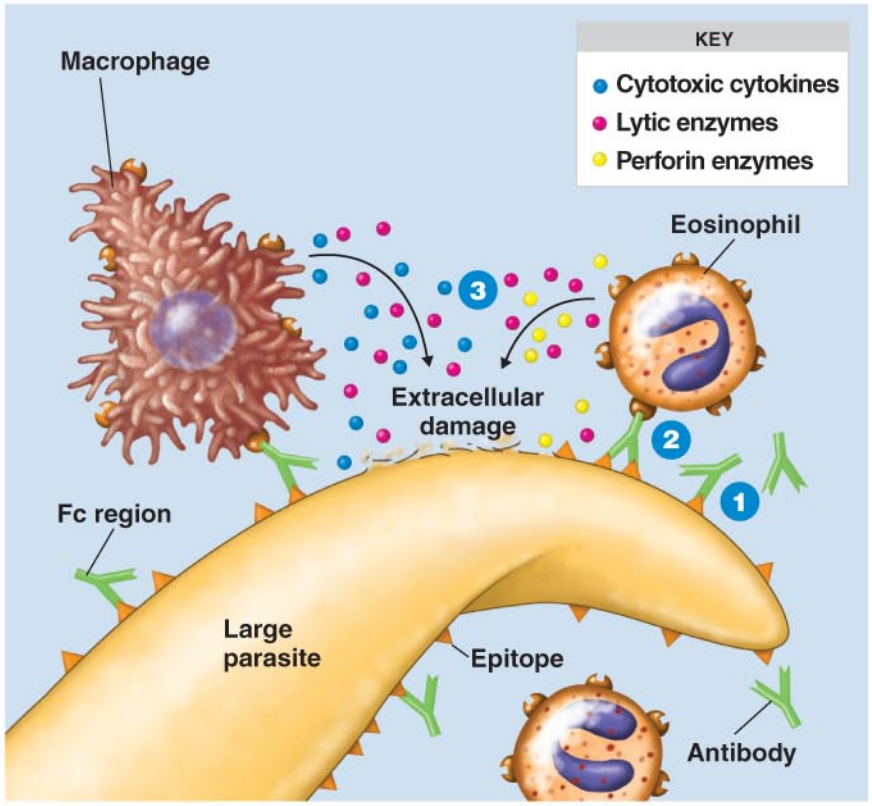
Author information

Abstract

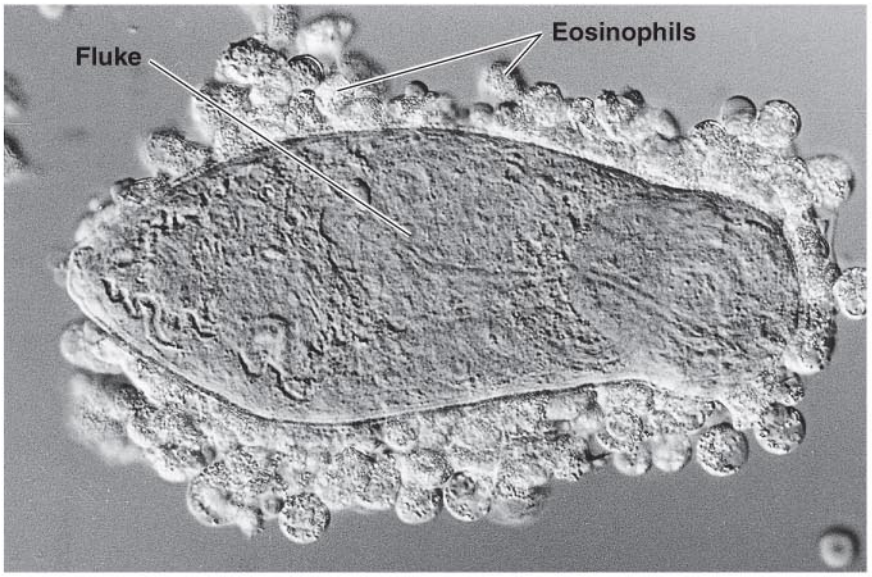
Macrophage activation--enhanced capacity to kill, in a cell that otherwise mostly scavenges--is essential for host survival from infection and contributes to containment of tumours. Both microbes and tumour cells, therefore, may be under pressure to inhibit or reverse the activation of macrophages. This reasoning led to the demonstration of macrophage deactivating factors from both microbes and tumour cells. In some circumstances the host itself probably requires the ability to deactivate macrophages. Macrophages are essential to the healing of wounds and repair of tissues damaged by inflammation. Yet the cytotoxic products of the activated macrophages can damage endothelium, fibroblasts, smooth muscle and parenchymal cells (reviewed in ref. 6). Thus, after an inflammatory site has been sterilized, the impact of macrophage activation on the host might shift from benefit to detriment. These concepts led us to search for macrophage deactivating effects among polypeptide growth factors that regulate angiogenesis, fibrogenesis and other aspects of tissue repair. Among 11 such factors, two proteins that are 71% similar proved to be potent macrophage deactivators: these are transforming growth factor-beta 1 (TGF-beta 1) and TGF-beta 2.

http://www.ncbi.nlm.nih.gov/pubmed/3041283

Antibody-dependent cell-mediated cytotoxicity (ADCC)



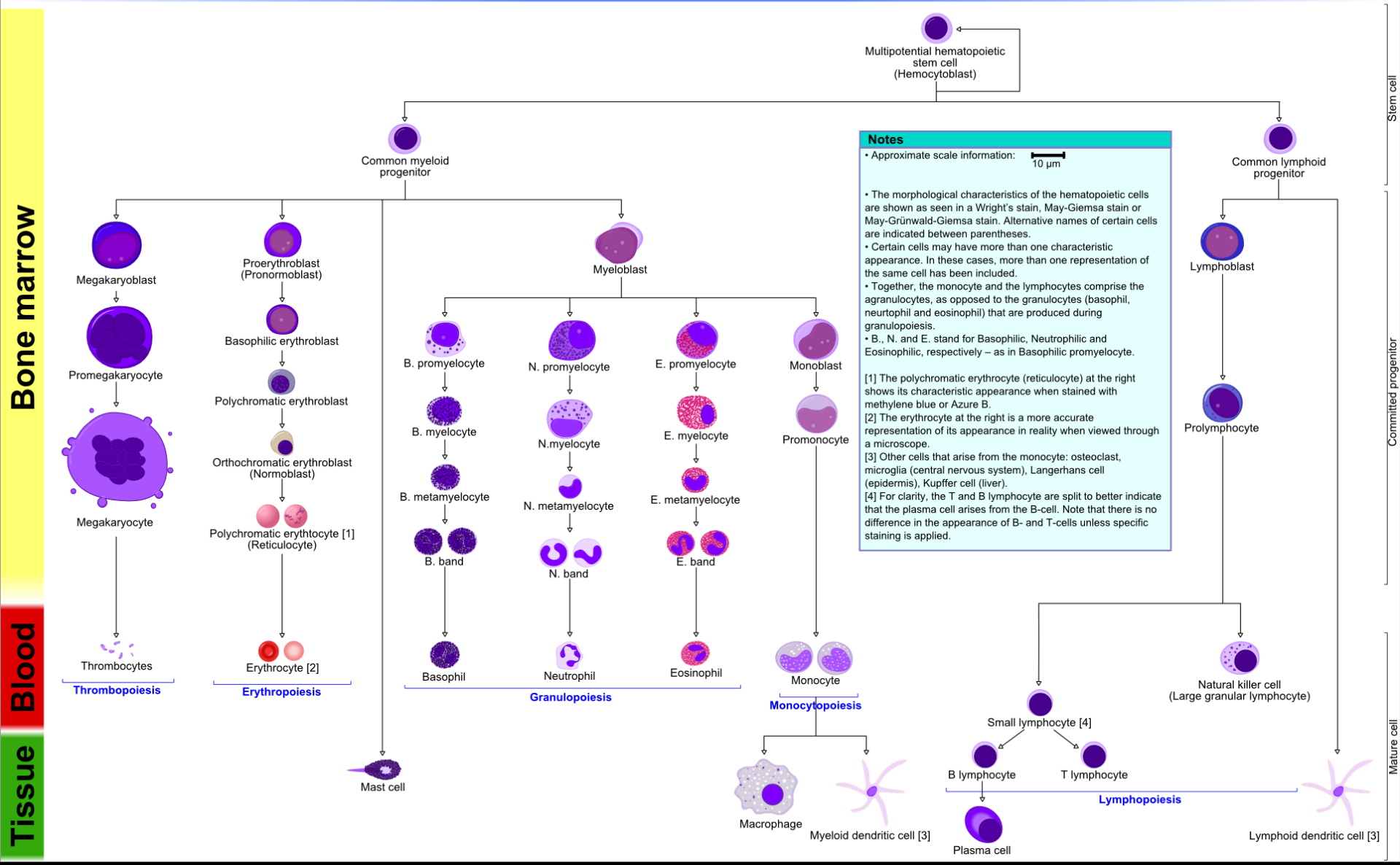
(a) Organisms, such as many parasites, that are too large for ingestion by phagocytic cells must be attacked externally.



(b) Eosinophils adhering to the larval stage of a parasitic fluke

Fig 17.16

Hematopoiesis in humans



wikipedia.org

Immunological memory

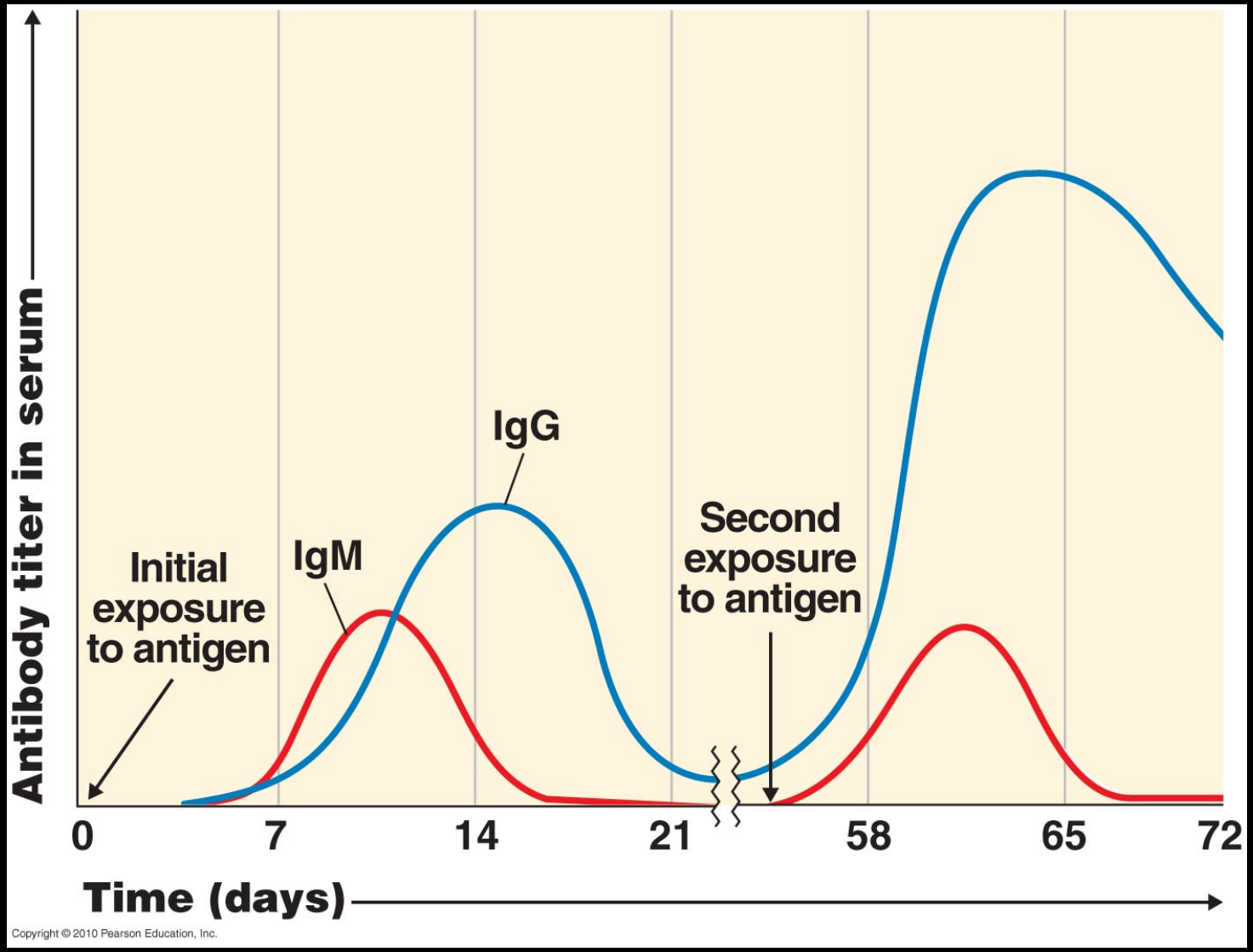


Fig 17.17

Types of adaptive immunity

http://www.cel-sci.com/passive_immunotherapy.html

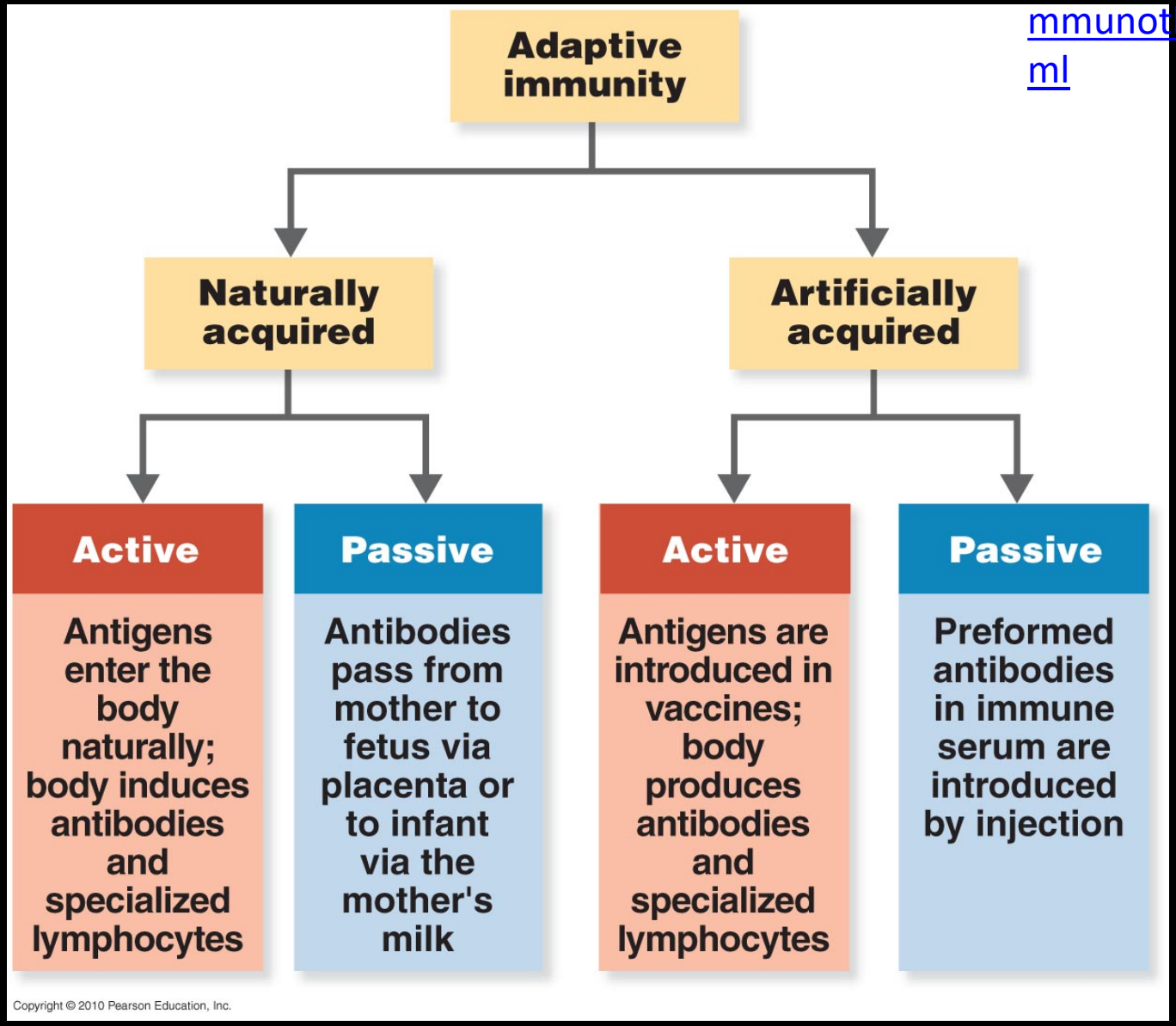


Fig 17.18

Example of passive artificial immunity

MONOCLONAL ANTIBODY THERAPY (mAb)

Monoclonal antibody (mAb) therapy, the most widely used form of cancer immunotherapy today, is a form of **passive** immunotherapy. Monoclonal antibodies often do not require the patient's immune system to take an active role in fighting the cancer.

Monoclonal antibodies are considered targeted therapy. Targeted immunotherapy is therapy directed to a **single target** on a cancer cell, usually an antigen or a receptor site on the cancer cell, or it is directed at a cancer specific enzyme or protein.

Monoclonal antibodies bind only to cancer cell-surface specific antigens. When an antibody recognizes the antigen against which it is directed, they fit together like two pieces of a puzzle setting off a cascade of events leading to tumor cell death.

- Examples of monoclonal antibodies include: Avastin, Erbitux, Rituxan, Herceptin, Mylotarg, Campath, Zevalin, Bexxar, Vectibix.

http://www.cel-sci.com/passive_immunotherapy.html

Issues

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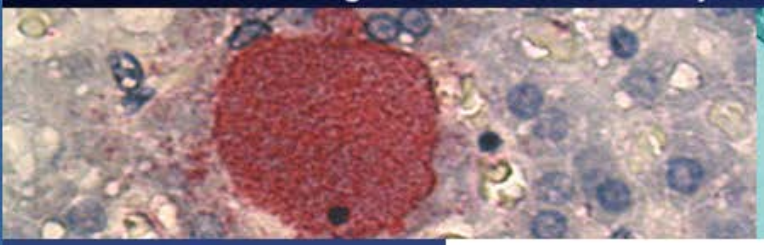

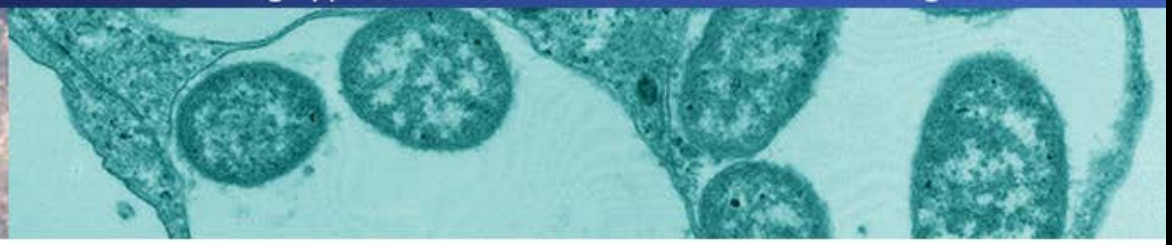

Home
Research Themes
Developmental Projects
New Opportunities
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Research Themes

Passive Immunotherapeutics

Chair: *Arturo Casadevall (Albert Einstein College of Medicine)*

Establish and optimize new technologies for producing high affinity animal and humanized neutralizing monoclonal antibodies for passive administration. Identify requirements for antibody-mediated immunity to establish broad principles applicable to multiple systems.

Projects:

* Optimization of mAbs to staphylococcal enterotoxin B for treatment: *Bettina Fries (Albert Einstein College of Medicine)*
* Development of new passive immunization strategies for anthrax: *Arturo Casadevall (Albert Einstein College of Medicine)*
* Development of mAb therapeutics against biothreat and emerging disease agents: *Thomas Briese (Columbia University)*
* Development of mAb immunotherapy for genetically modified plague: *James Bliska (Stony Brook University)*

Inter-project collaborators

- *Rafi Ahmed (Emory University)*
- *Moonsoo Jin (Cornell University)*
- *Matteo Porotto (Cornell University)*
- *Jeffrey Ravetch (Rockefeller University)*
- *Patrick Wilson (University of Chicago)*

http://www.nbc.columbia.edu/research_themes.html

Review

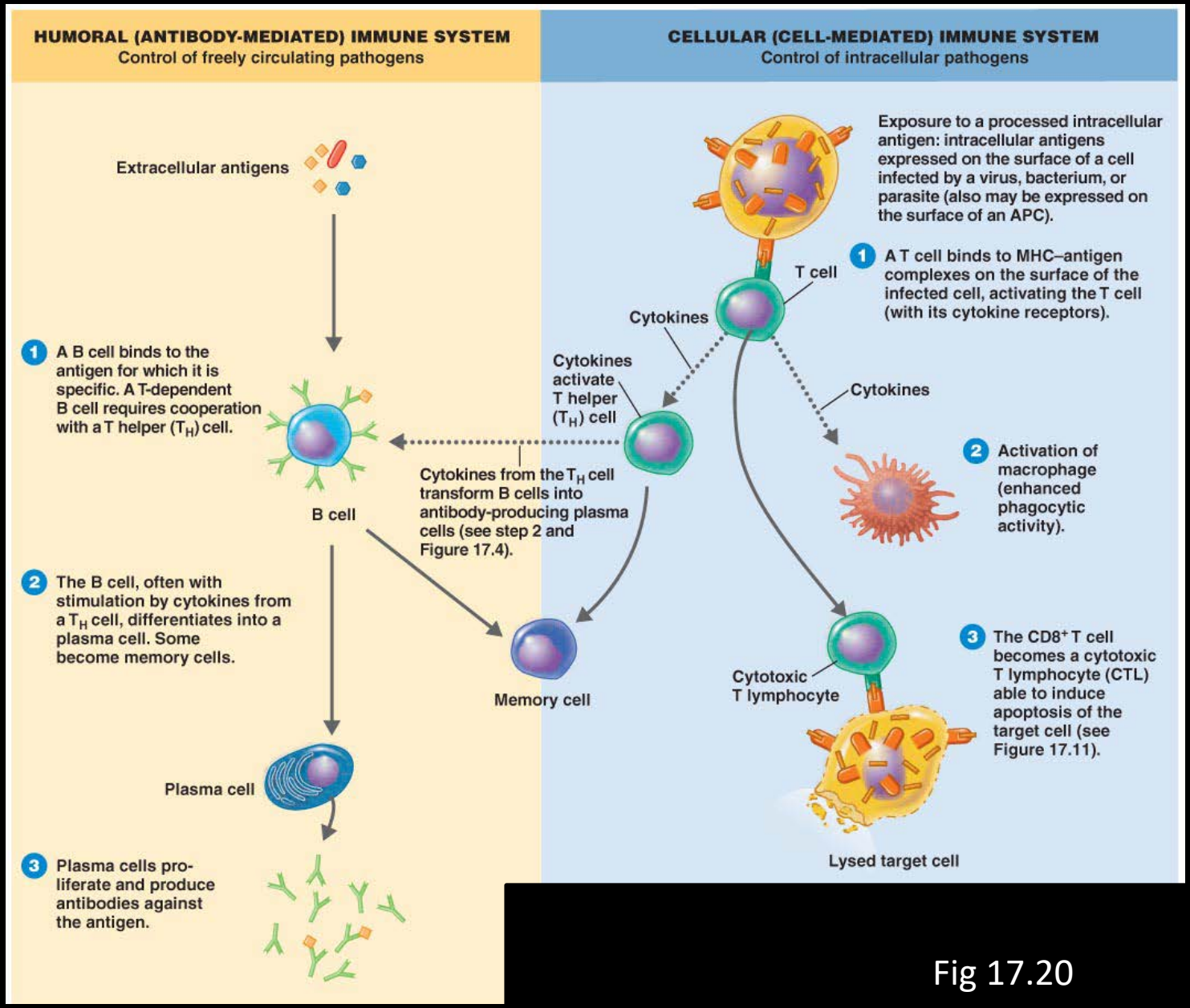

Fig 17.20

Review

Immune System, part 1: Crash Course
Immune System, part 2: Crash Course
Immune System, part 3: Crash Course