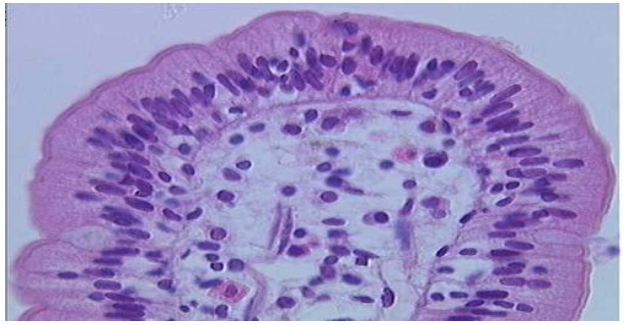
2 Nov 2023,
BT 304
Lecture 36

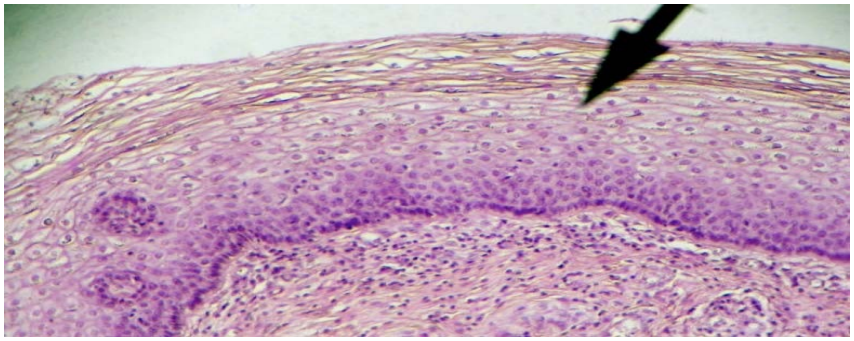
Type I mucosal surfaces are covered by simple epithelium - expresses a simple polymeric Ig receptor (pIgR) that allows dimeric IgA to access the lumen.

- Intestine
- Lungs
- Uterus



Type II mucosal surfaces are covered by stratified squamous epithelium which provides physical protective barriers for activities that are important for the host species.

- Oral cavity
- Vaginal cavity



Defense systems within the gut

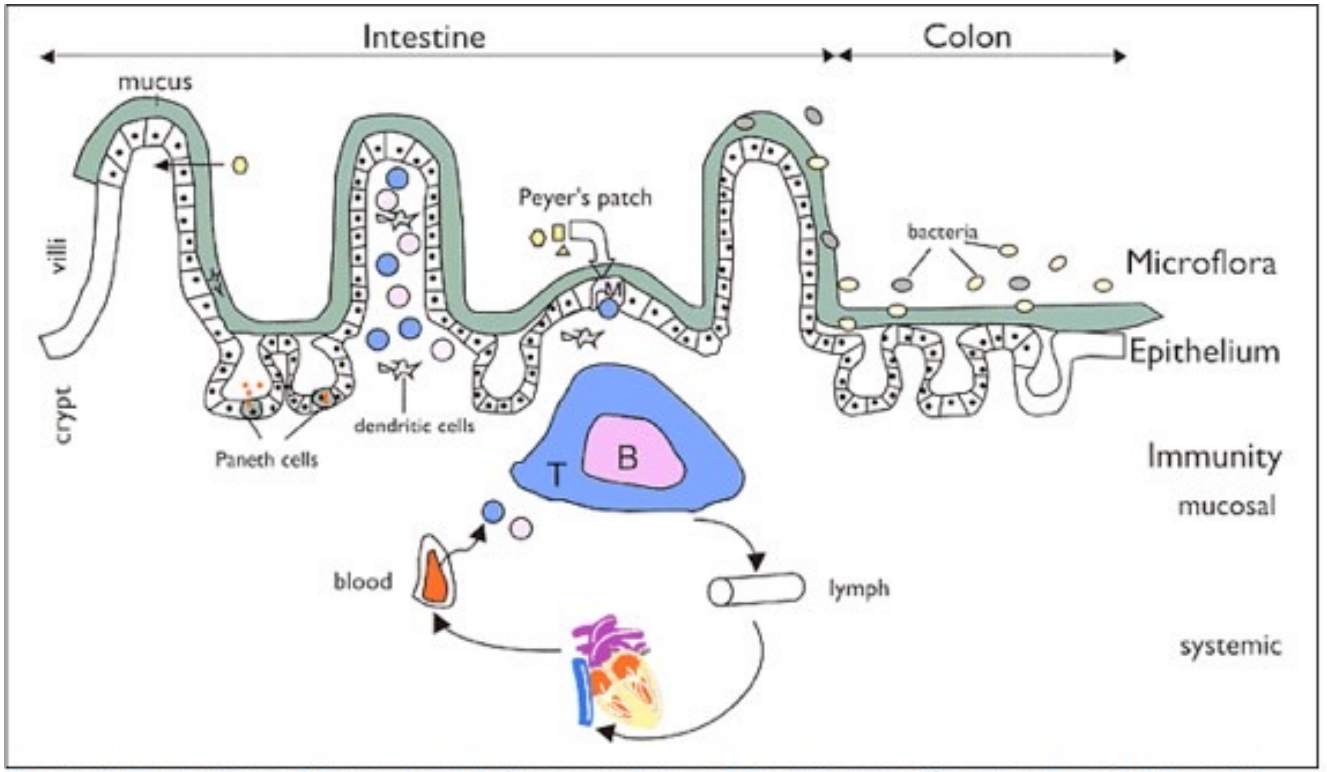


Figure I: Illustration of the natural defense systems of the intestine (Source: DanoneVitapole)

- Nonimmunologic barriers
- Immune system - innate and adaptive
- Gut flora (commensal bacteria)

Barriers to infection in the gut

- Enzymes present in saliva
- Low pH in the stomach
- Bile - stimulates peristalsis
- Intestinal mucus
- Tight junctions joining epithelial cells in the intestine.

Essential components of the intestinal innate immune mechanisms

[EC crosstalk with B cells T-independent]*

Immunoglobulins	Secretory IgA[a]
Antimicrobial peptides and proteins	Defensins, lysozyme, secretory phospolipase A2, angiogenins
Microbial	Commensal intestinal flora
Others	Gastric acid, biliary and pancreatic secretions, mucins

[a] Although by definition belonging to adaptive immunity, sIgA acts in first line mucosal defense, a key feature of innate immunity.

*Epithelial cells (EC) recognize microorganisms and communicate with and orchestrate both innate and acquired immune responses. They can produce different cytokines in response to different commensal bacteria. Uptake of bacteria by epithelial cells has been observed.

Yuan & Walker: J Pediatr Gastroenterol Nutr 38:463-473, 2004

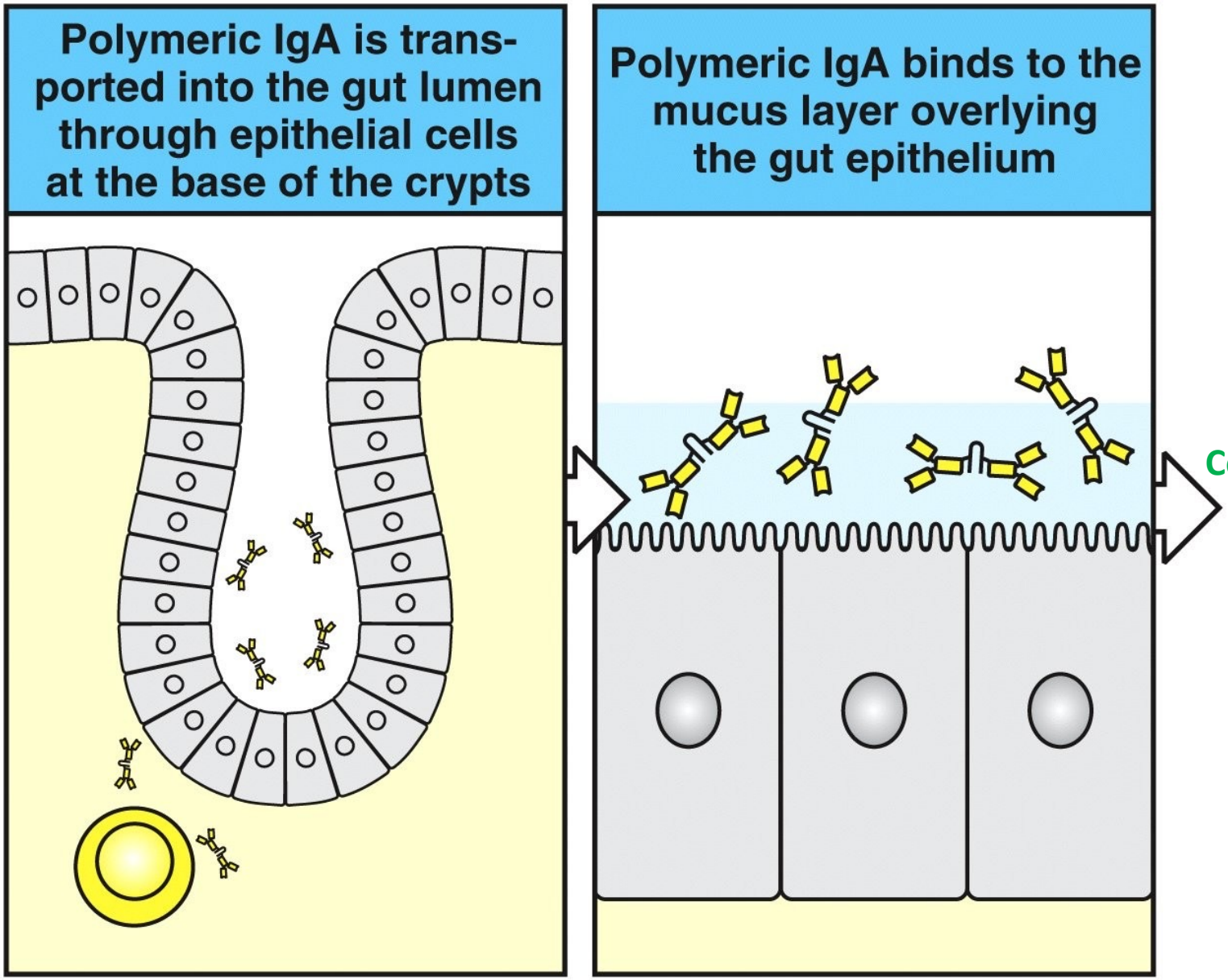


Figure 10-24 part 1 of 2 Immunobiology, 6/e. (© Garland Science 2005)

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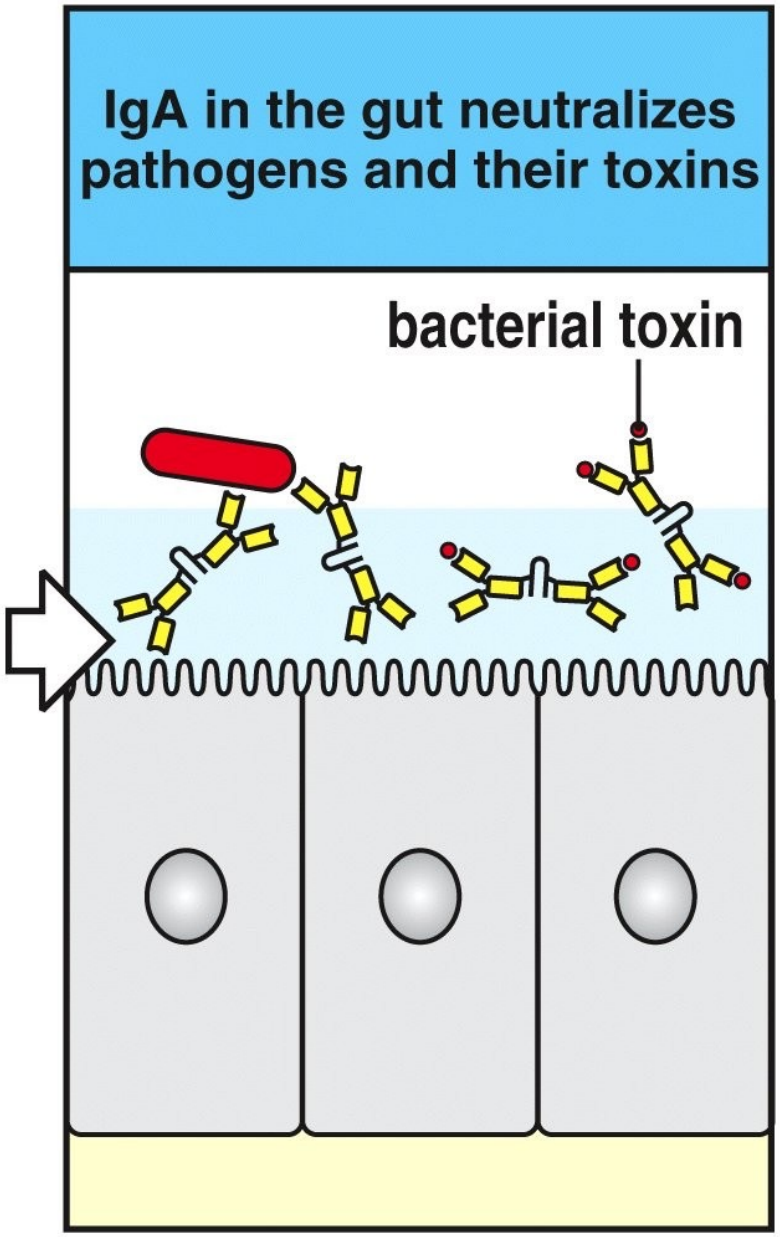
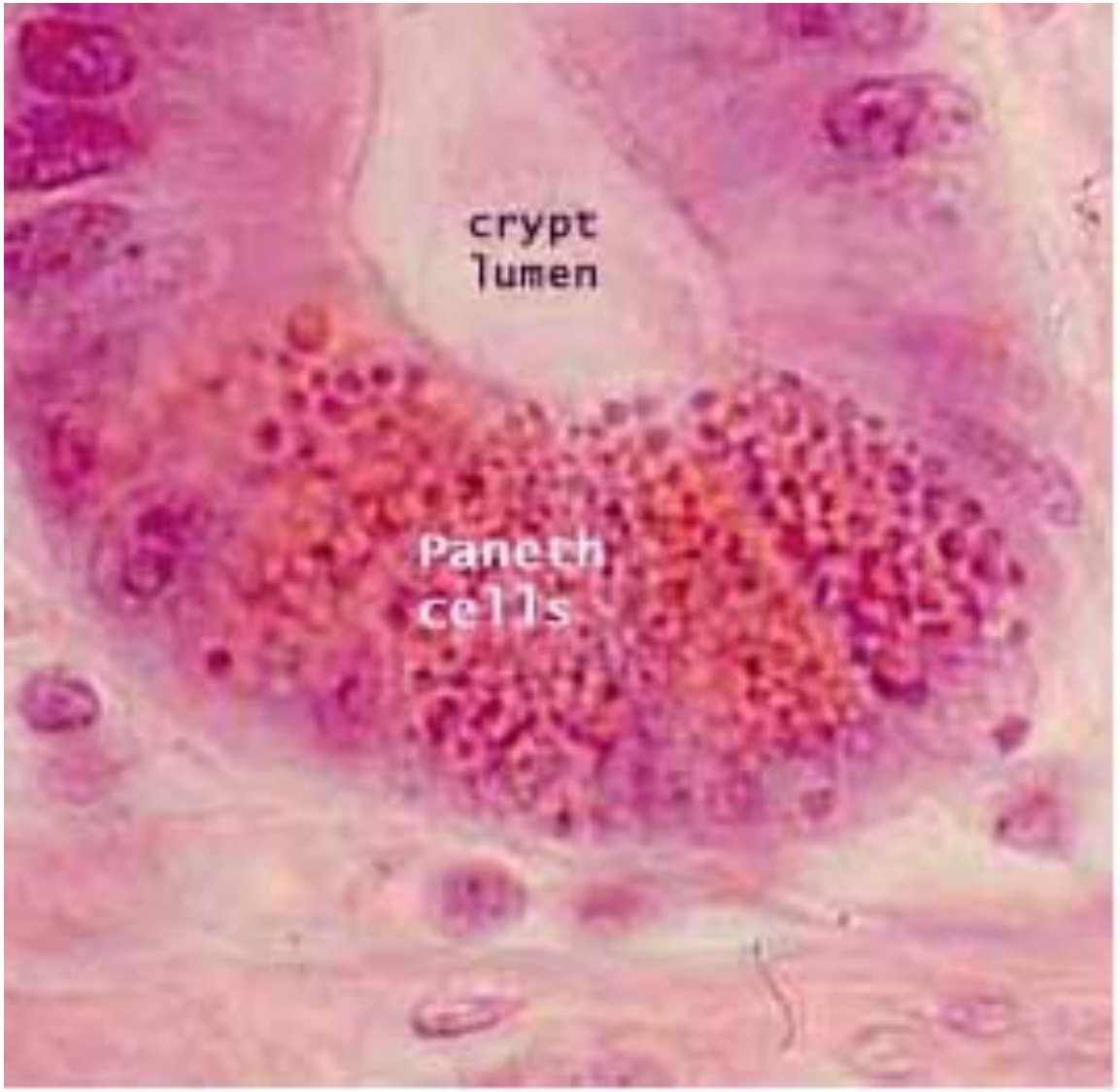
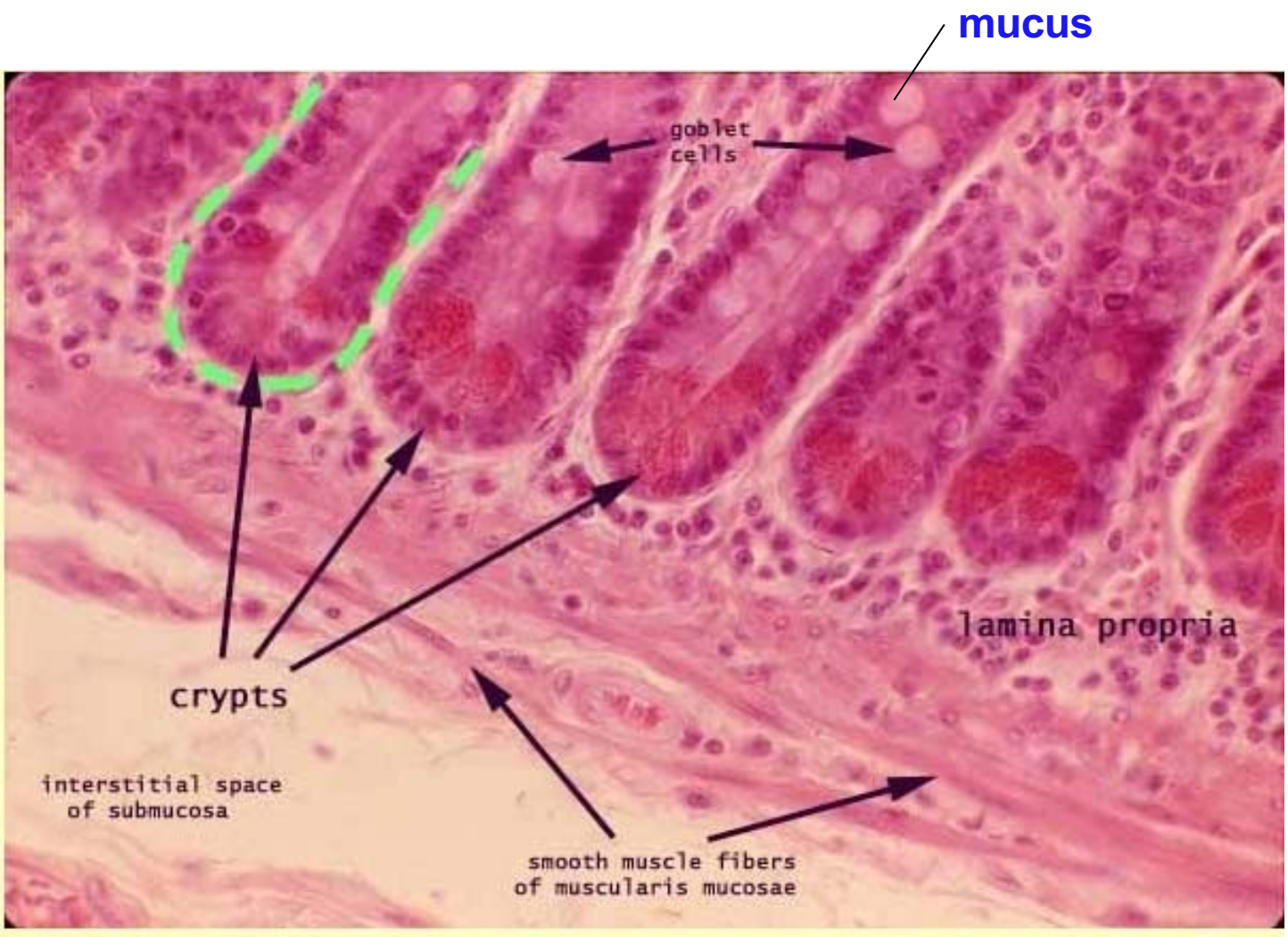


Figure 10-24 part 2 of 2 Immunobiology, 6/e. (© Garland Science 2005)



www.siumed.edu/dking2/gicells.htm



www.siumed.edu/dking2/gicells.htm

Immune response: antigen entry

- Follicle-associated (FAE) M cells (microfold cells)
- Villous M cells (Peyers Patches-independent IgA induction pathway) - located at a distance from PP
- Dendritic cells

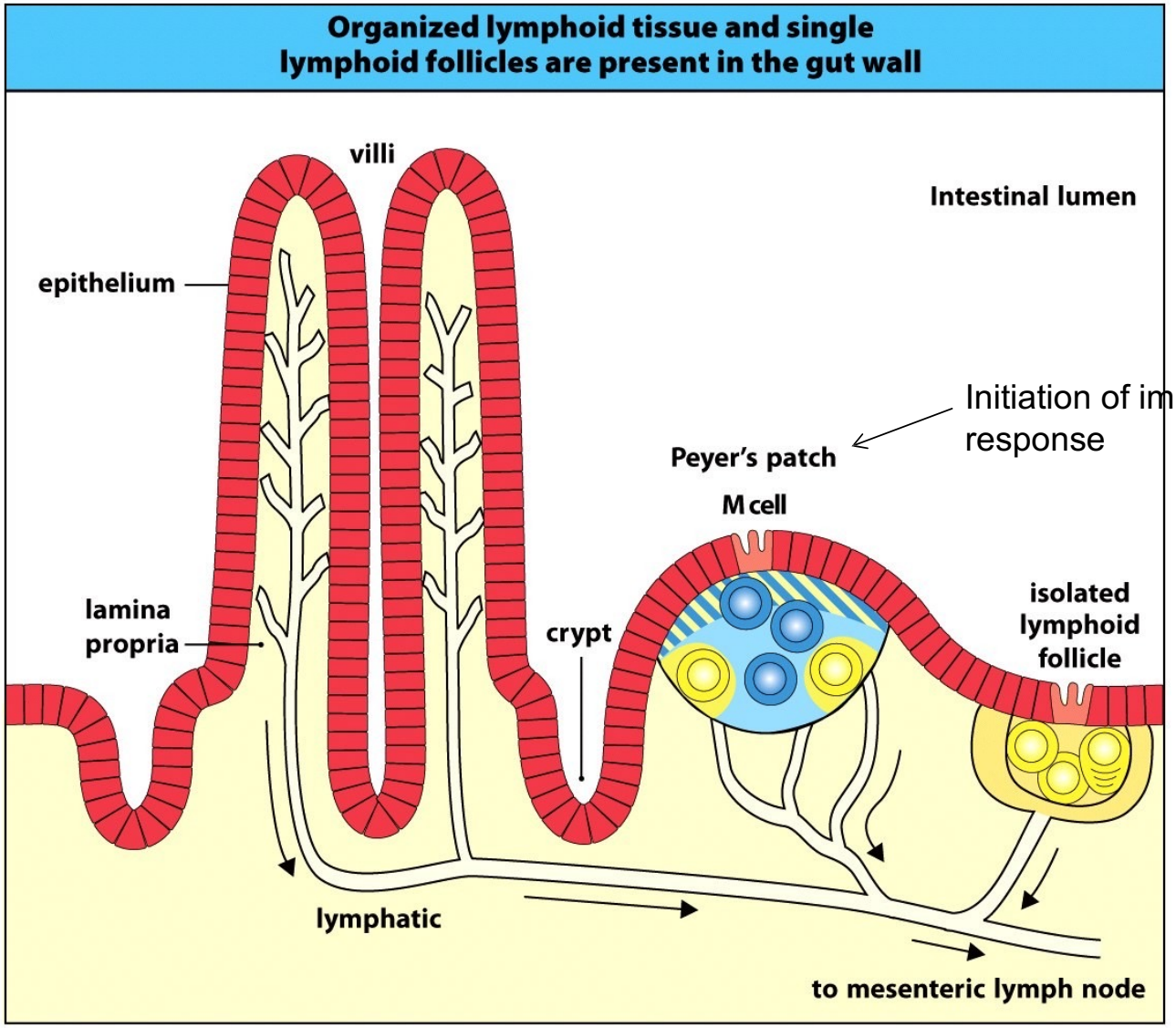


Figure 10.4 part 1 of 2 The Immune System, 3ed. (© Garland Science 2009)

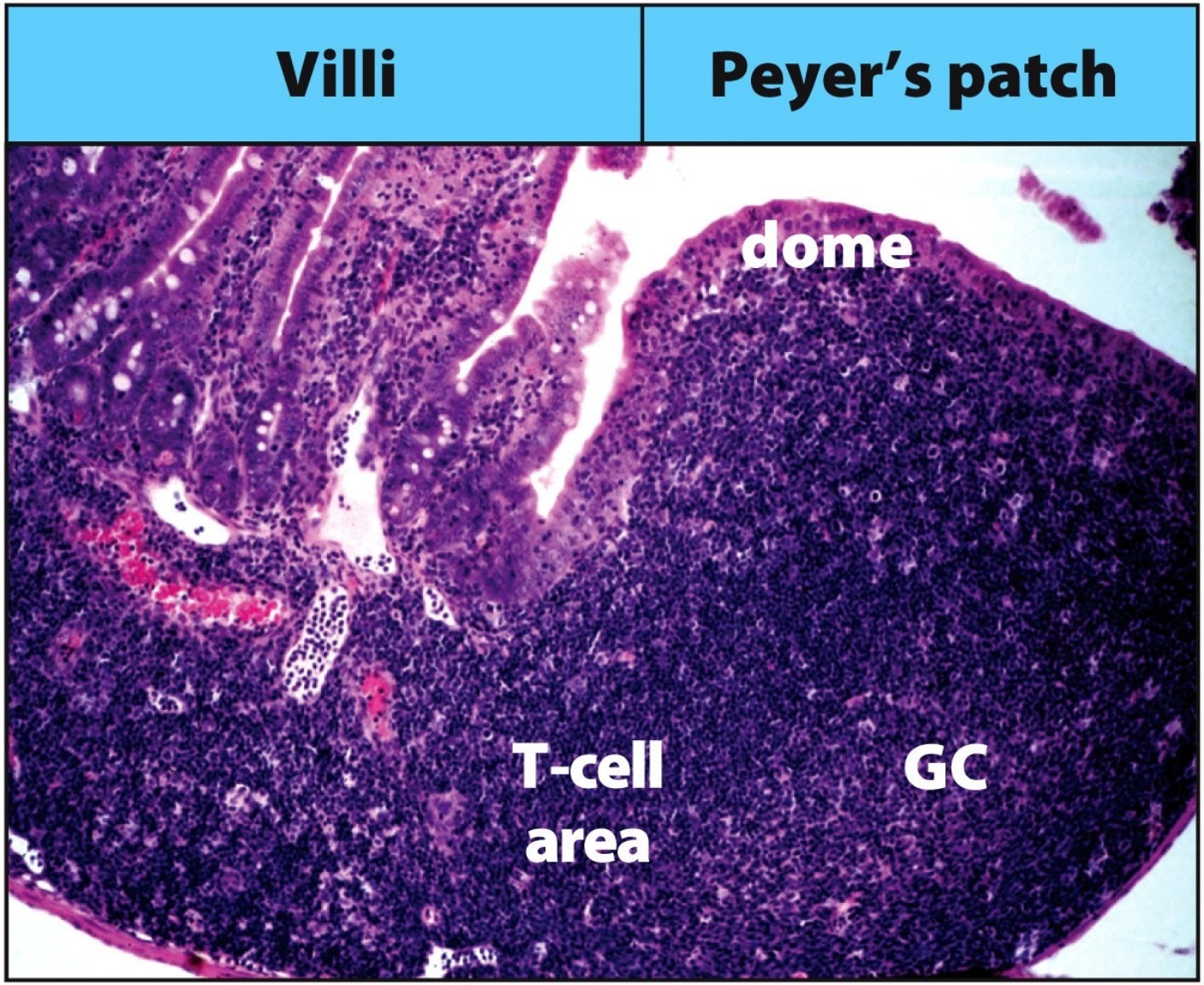


Figure 10.4 part 2 of 2 The Immune System, 3ed. (© Garland Science 2009)

M cells are specialized to transport microorganisms to gut-associated lymphoid tissue

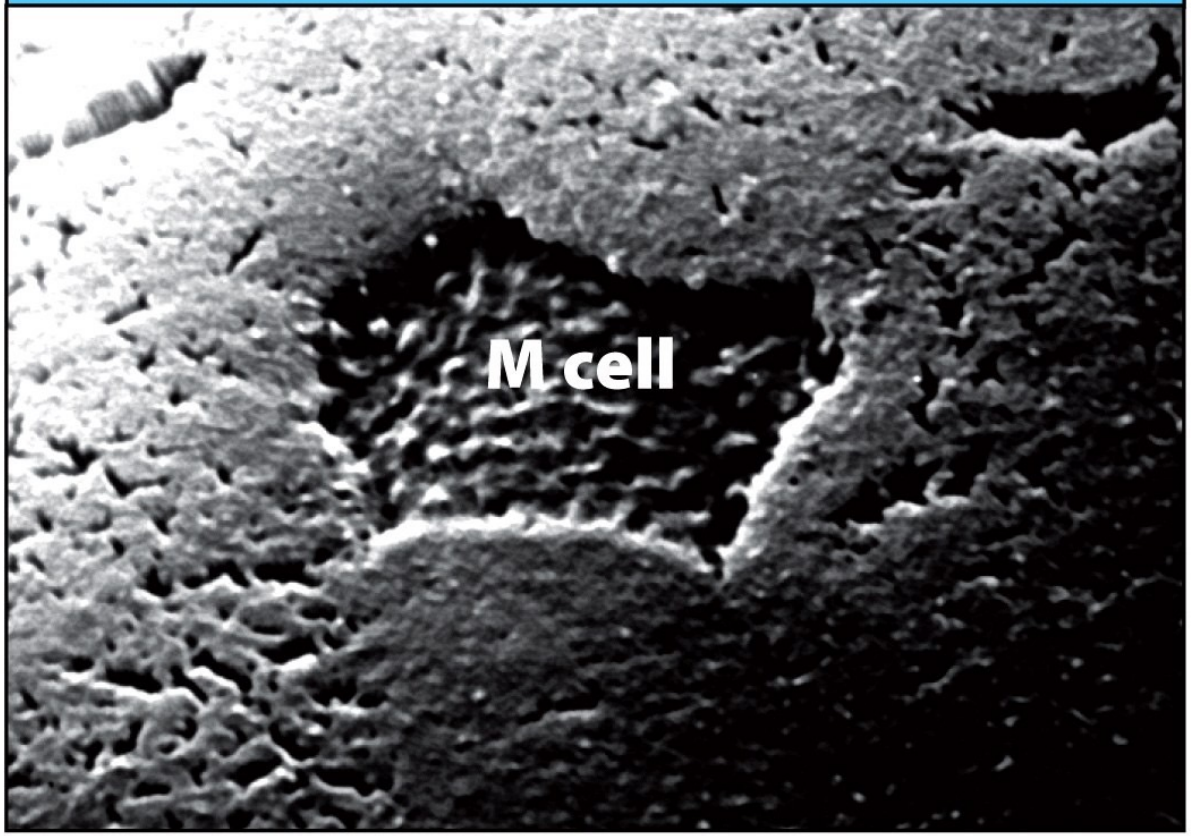
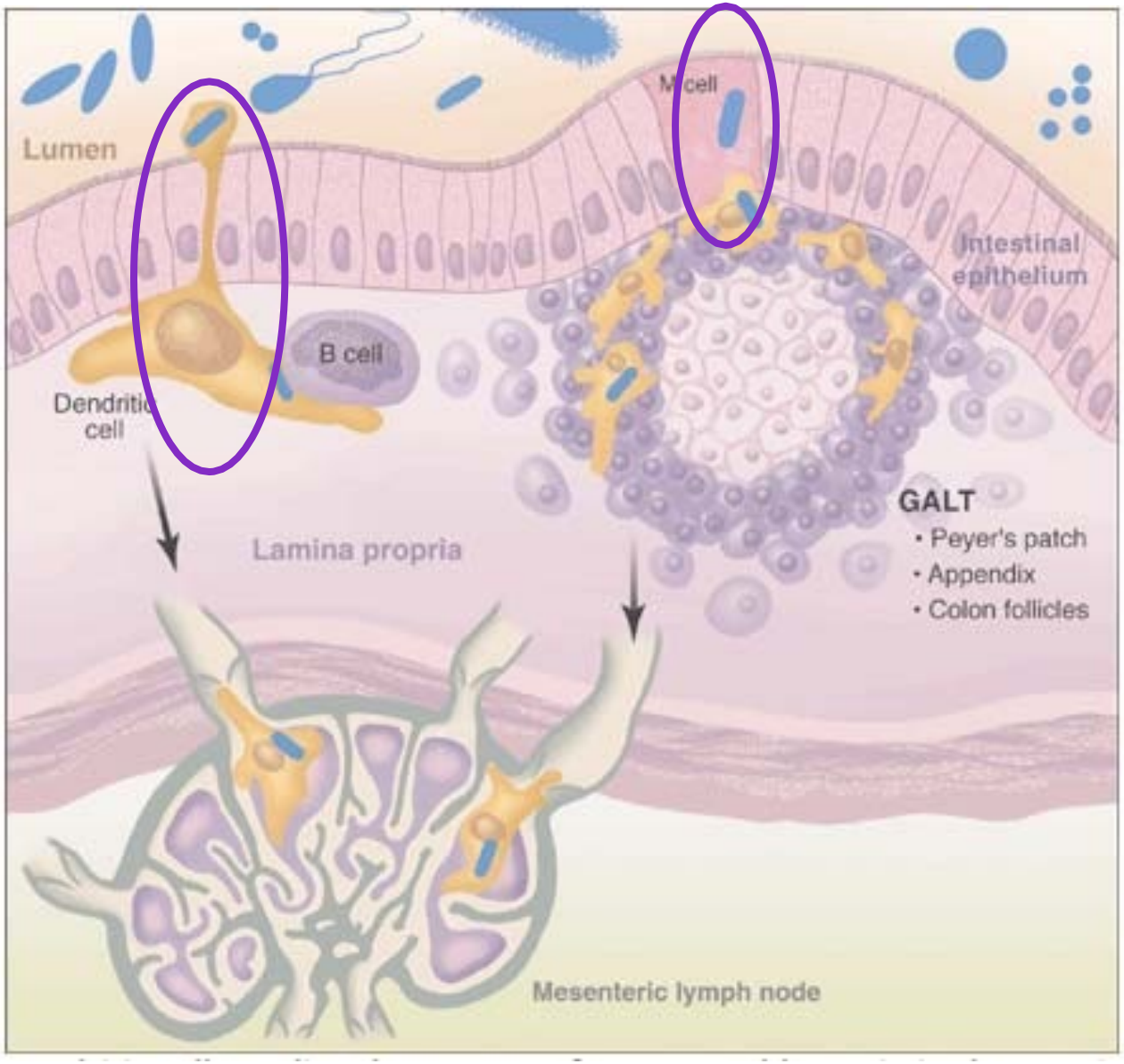


Figure 10.5 The Immune System, 3ed. (© Garland Science 2009)



Kraehenbuhl & Corbett. Science 303:1624-1625, 2004

Sampling of bacteria in lumen

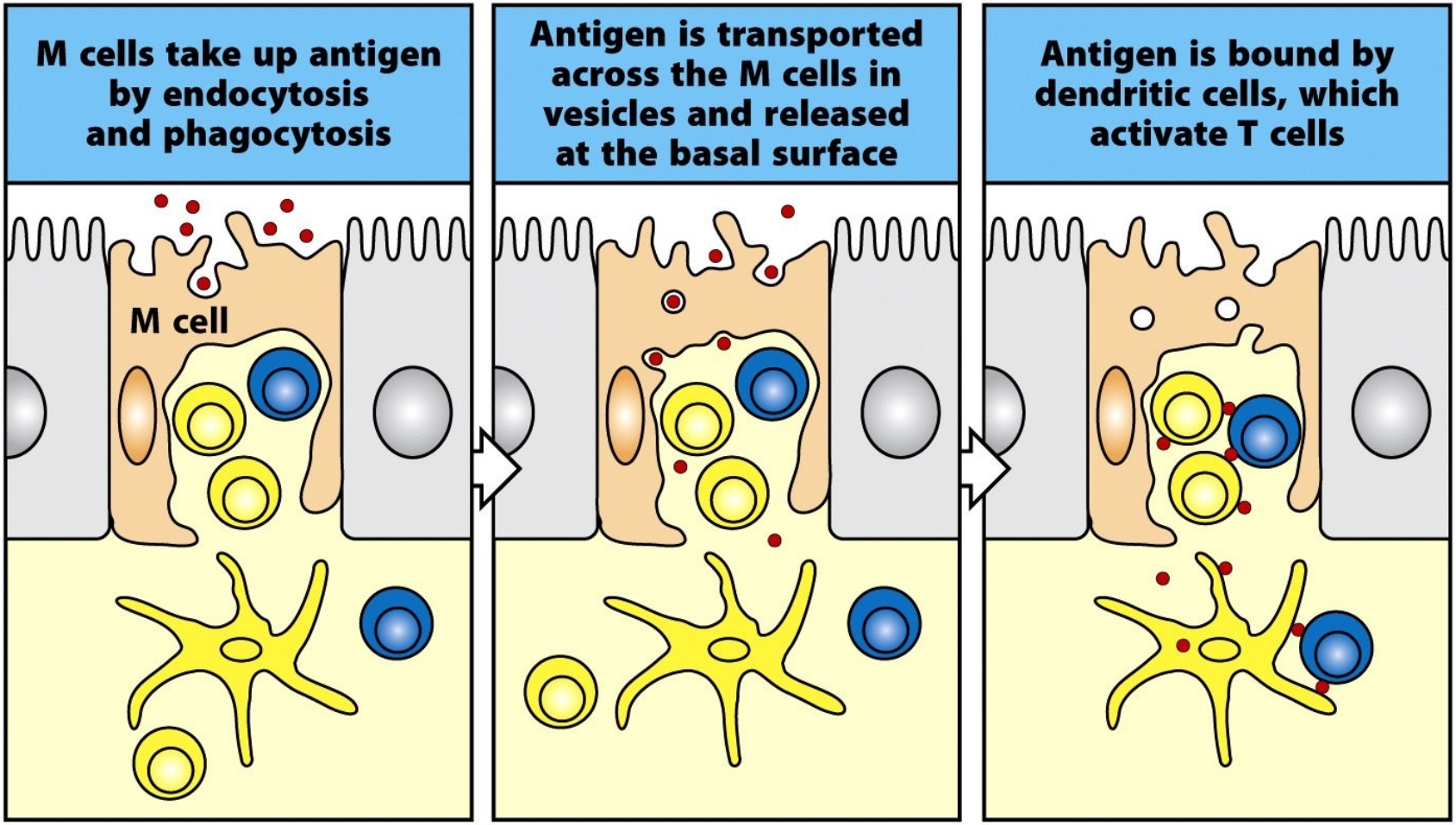
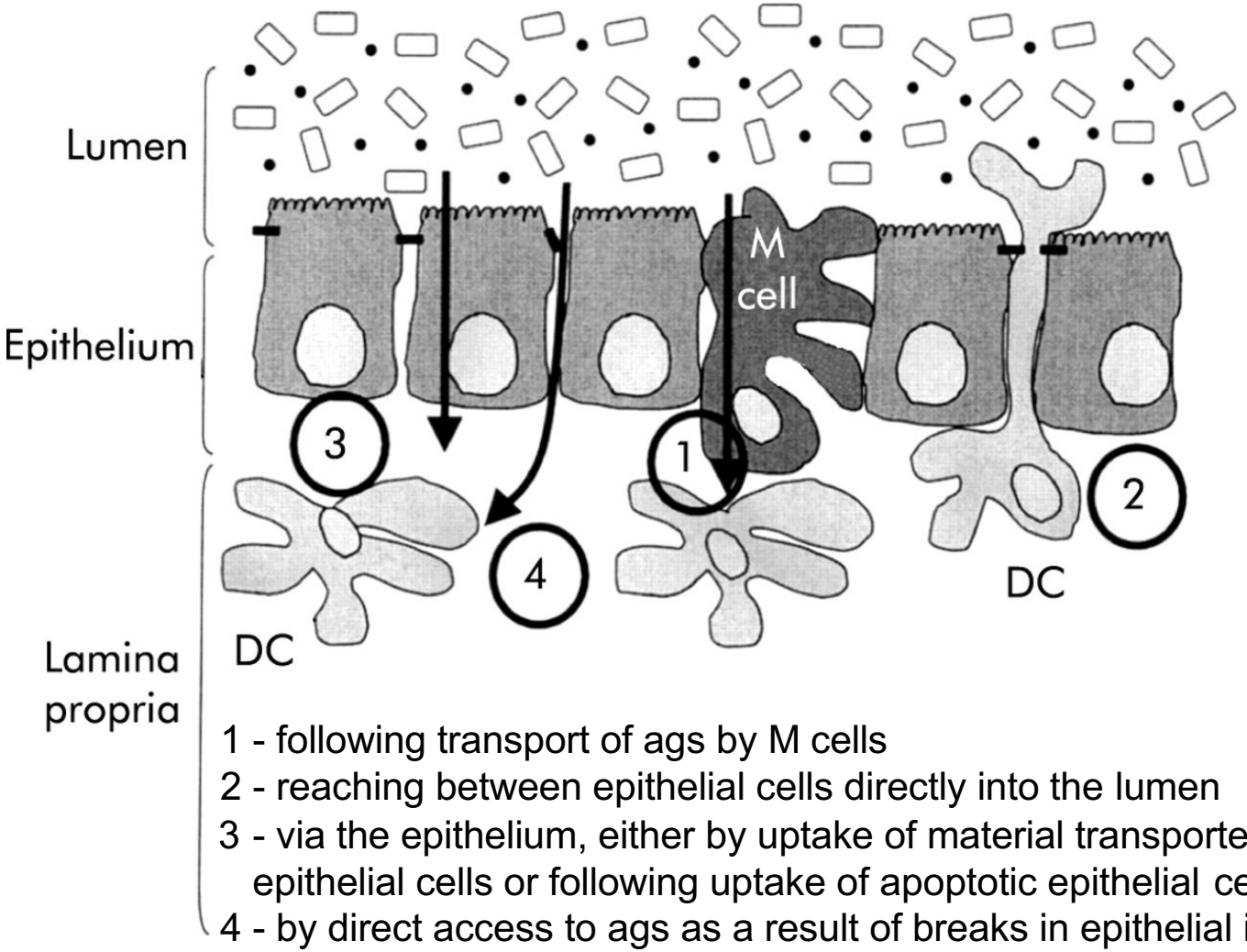


Figure 11-8 part 1 of 2 Immunobiology, 7ed. (© Garland Science 2008)

Gut Dendritic Cells

- Found in cryptopatches, isolated lymph follicles, Peyer's patches, and mesenteric lymph nodes.
- Subsets - seem to depend on chemokine signaling.
- Can protect colonic epithelial integrity by secreting IL-22.

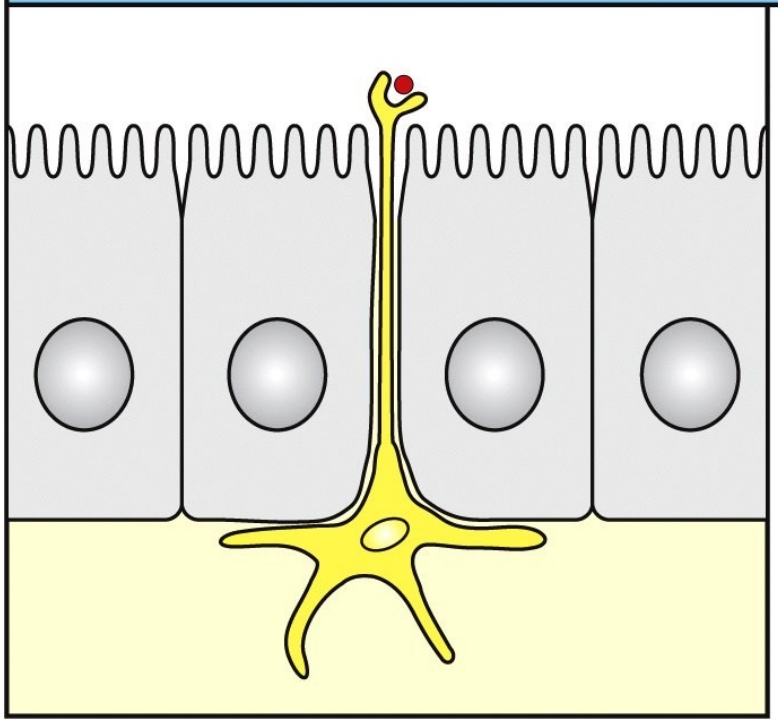
DCs take up antigen:



1 - following transport of ags by M cells
2 - reaching between epithelial cells directly into the lumen
3 - via the epithelium, either by uptake of material transported by epithelial cells or following uptake of apoptotic epithelial cells
4 - by direct access to ags as a result of breaks in epithelial integrity

Stagg, A J et al. Gut 2003;52:1522-1529

Dendritic cells can extend processes across the epithelial layer to capture antigen from the lumen of the gut



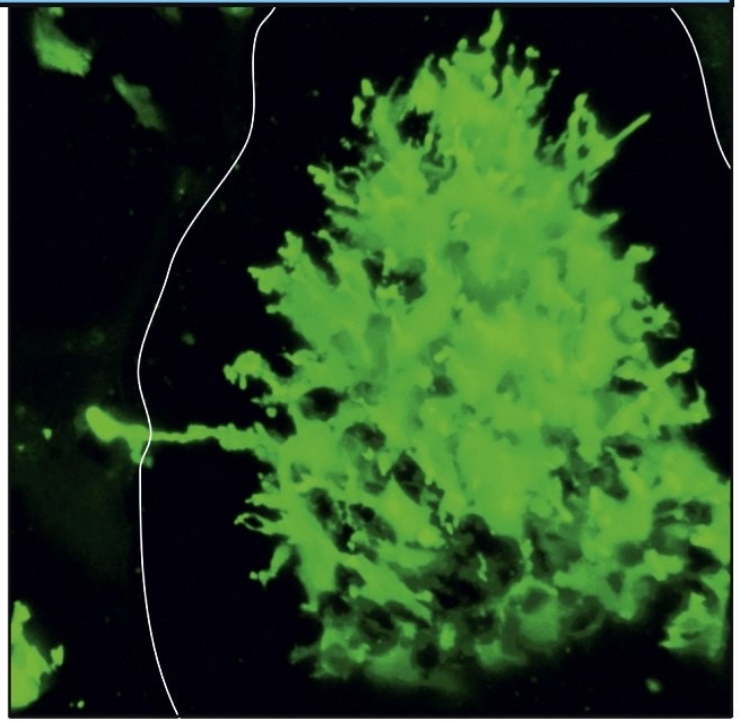


Figure 11-9 Immunobiology, 7ed. (© Garland Science 2008)

Dendritic cells recognize pathogens through pattern recognition receptors (PRRs):

- TLRs (LPS, peptidoglycan, unmethylated CpG motifs, double-stranded viral RNA)
  - TLR2 - Gram positive cell wall components
  - TLR4 - LPS from *E coli* - essential for maturation & cytokine production in LPS-stimulated murine DC
  - TLR5 - Flagellin from Gram negative bacteria
  - TLR9 - CpG motifs from bacterial DNA
- Mannose receptors
- NOD1
  - recognizes muramyl-tripeptides from Gram negative bacteria
- NOD2
  - recognizes muramyl-dipeptides common to all peptidoglycans of all bacteria species

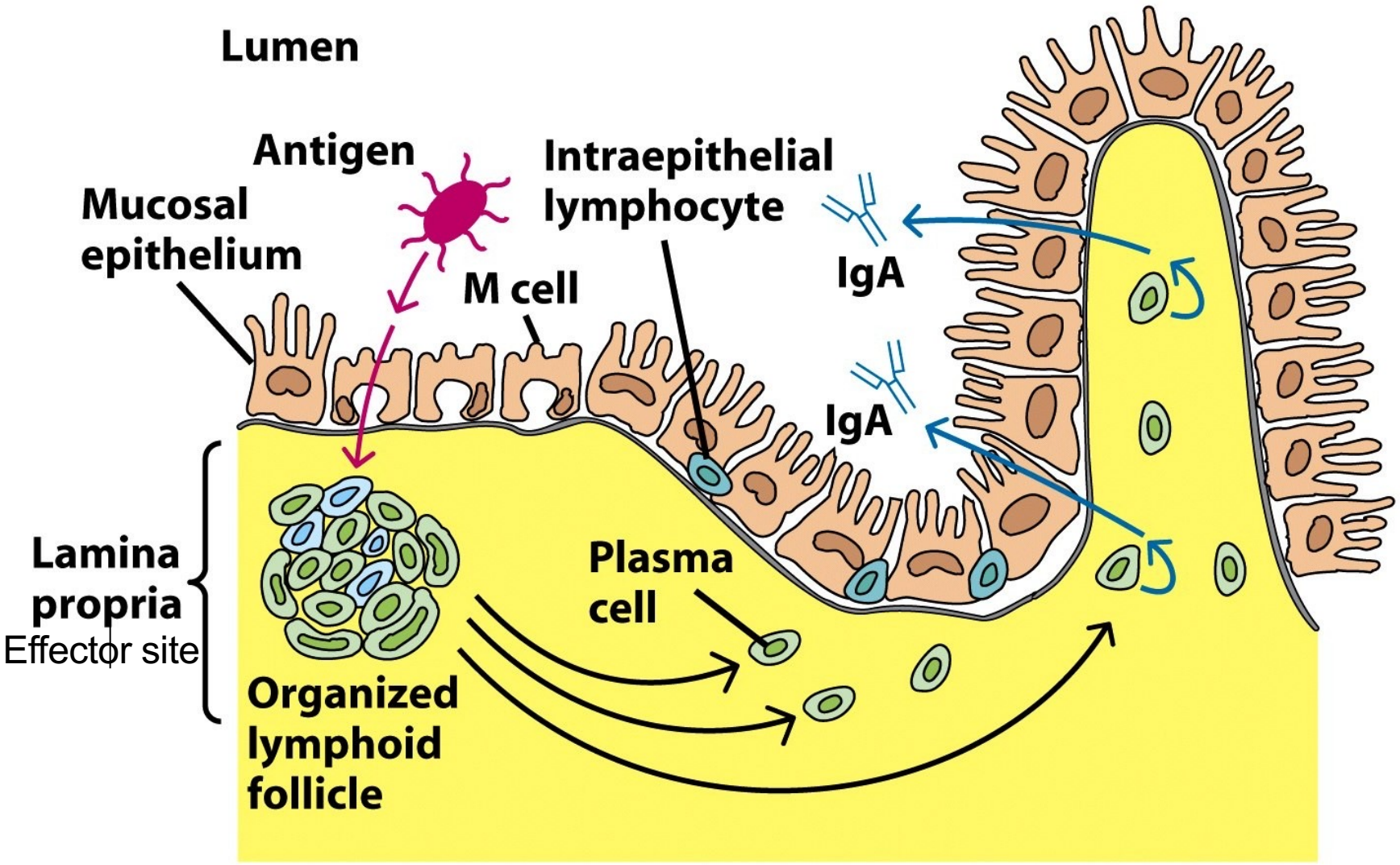
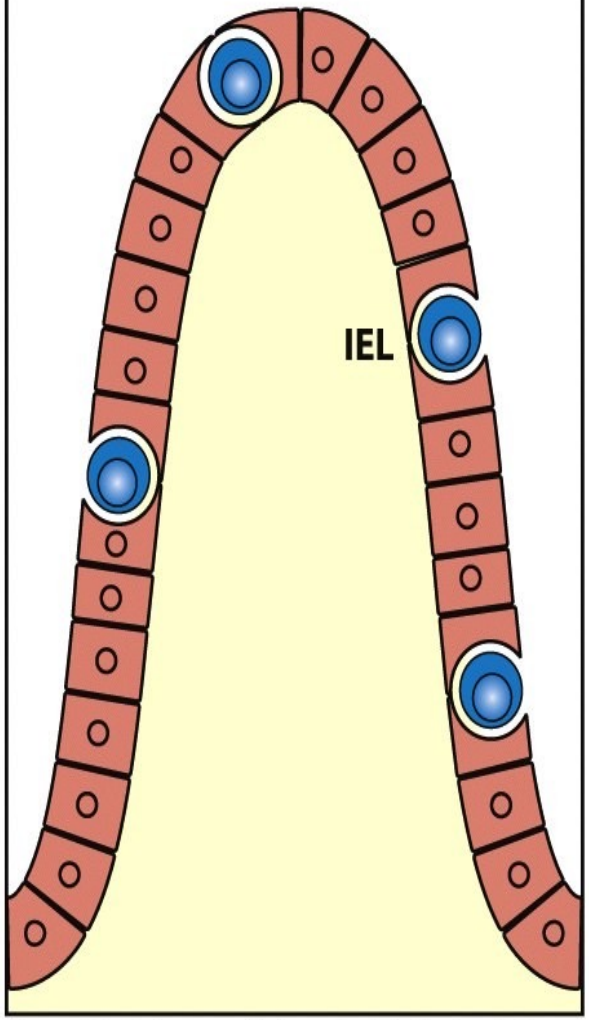
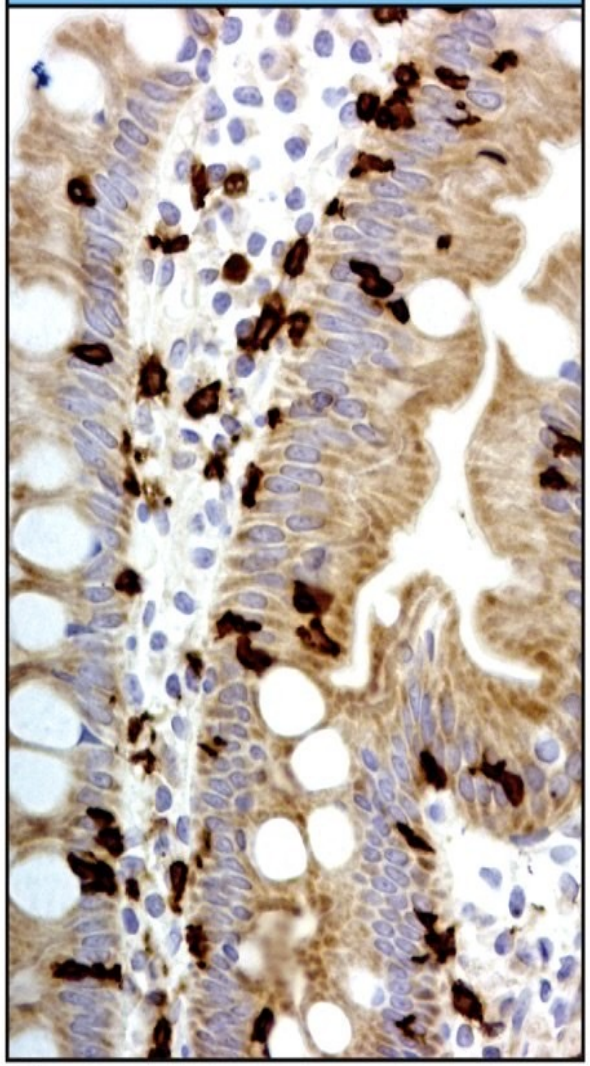


Figure 2-19b
Kuby IMMUNOLOGY, Sixth Edition

Lymphocytes called intra-epithelial lymphocytes (IELs) lie within the epithelial lining of the gut



The intraepithelial lymphocytes are CD8-positive T cells



At higher magnification, the IELs can be seen to lie within the epithelial layer between epithelial cells

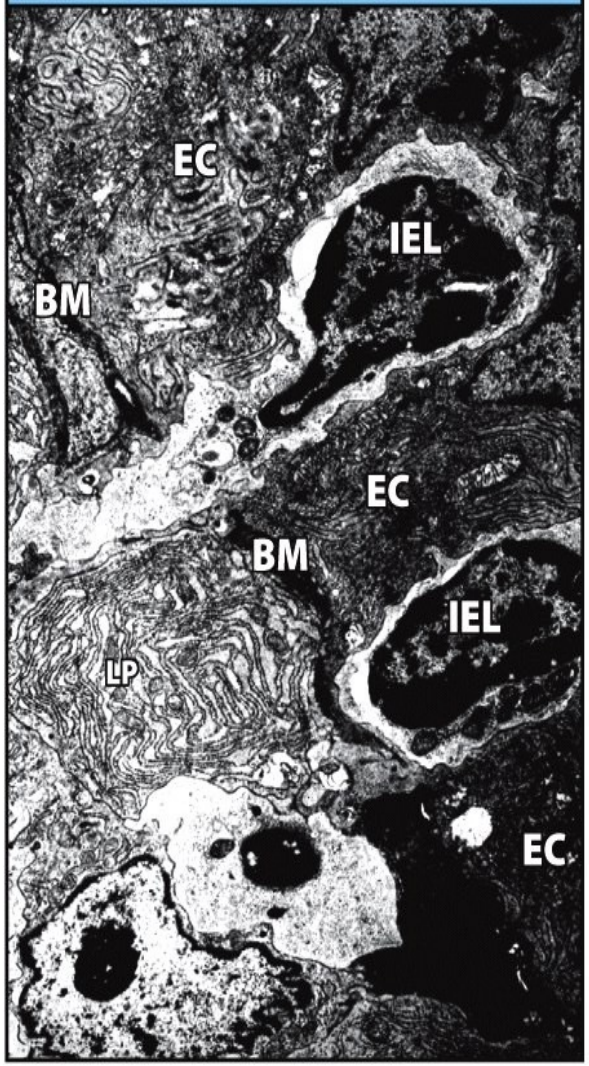


Figure 11-16 Immunobiology, 7ed. (© Garland Science 2008)

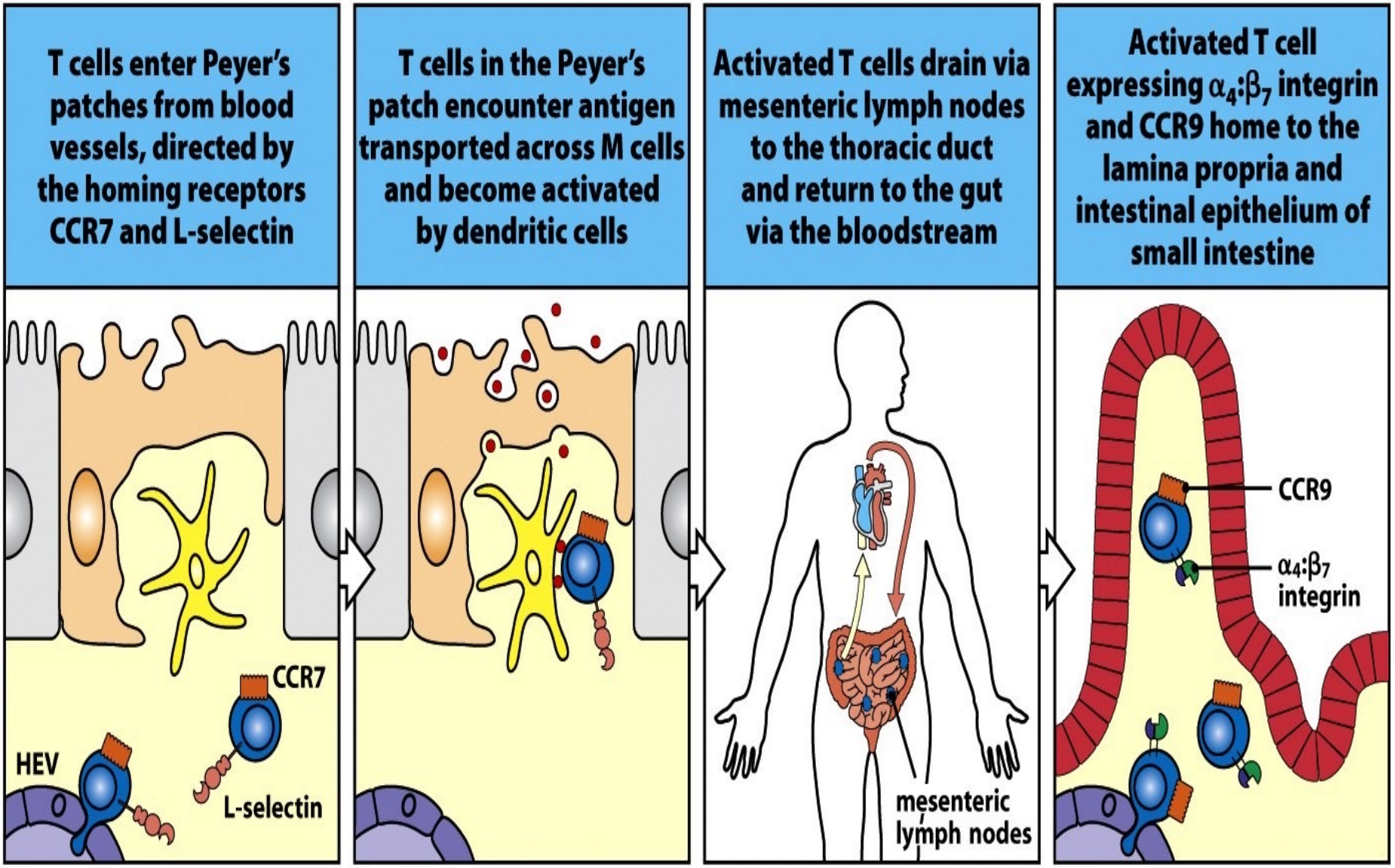


Figure 11-11 Immunobiology, 7ed. (© Garland Science 2008)

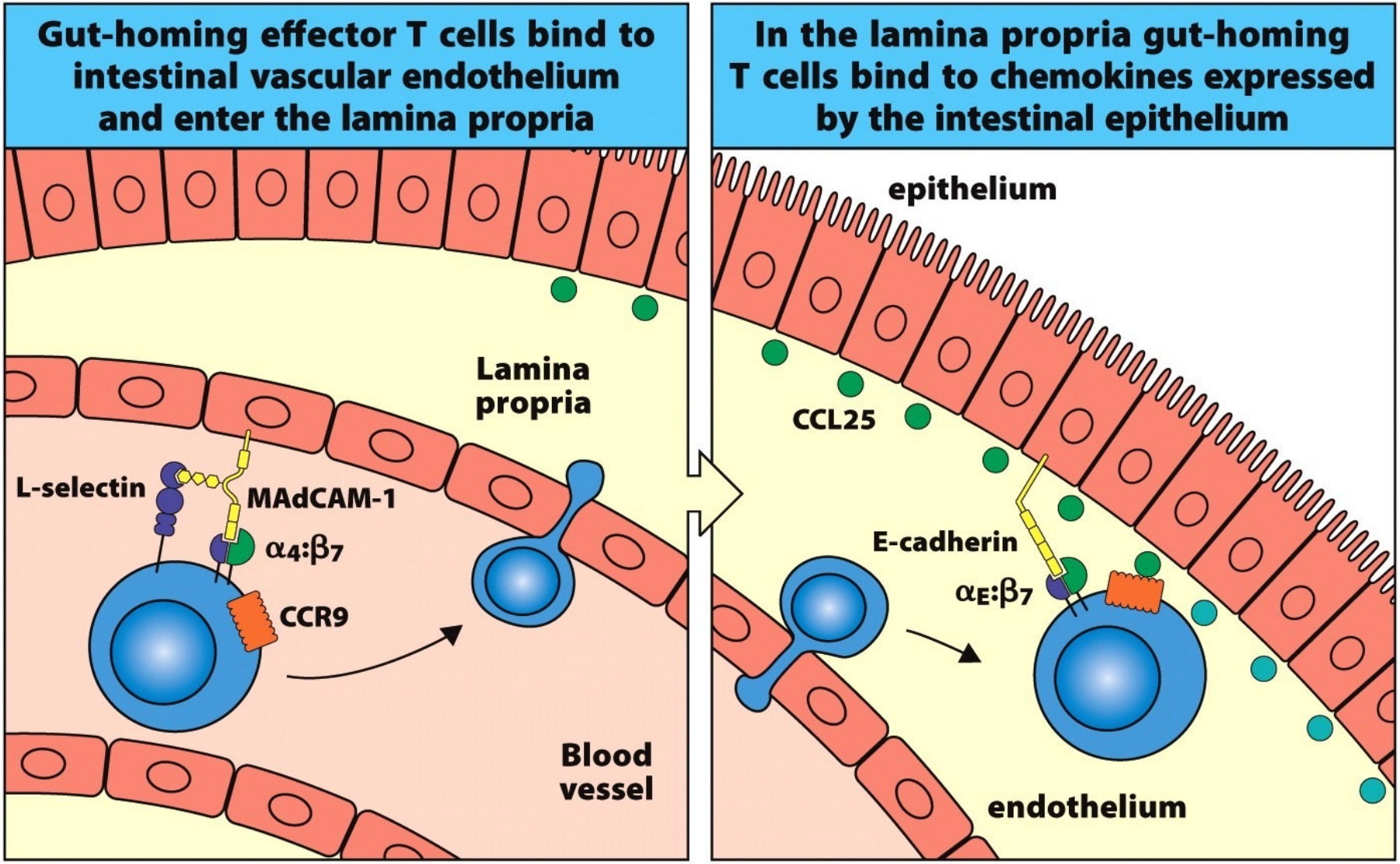


Figure 10.11 The Immune System, 3ed. (© Garland Science 2009)

CCL25 - TECK (Thymus expressed chemokines)- homing of T cells to gut
CCL28 – MEC (mucosae-associated epithelial chemokine) - homing of T cells to mucosal surfaces