FIT Board Review Corner – December 2015

Welcome to the FIT Board Review Corner, prepared by Sarah Spriet, DO, and Tammy Peng, MD, senior and junior representatives of ACAAI’s Fellows-In-Training (FITs) to the Board of Regents. The FIT Board Review Corner is an opportunity to help hone your Board preparedness.

Review Questions

Allergy and Immunology Review Corner: Cellular and Molecular Immunology, 8th Edition
By Abul K. Abbas, MBBS, Andrew H. H. Lichtman, MD, PhD and Shiv Pillai, MBBS, PhD.

Chapter 14 (pages 294-316): Regional Immunity: Specialized Immune Responses in Epithelial and Immune Privileged Tissues
Prepared by Niti Agarwal, MD, New York and Presbyterian Hospital

1. Which of the following pairs are correct regarding immunity in the gastrointestinal tract?
   a. M cells: luminal antigen processing
   b. Paneth cells: neutralization of microbes in the lumen
   c. Secretory IgA/IgM: defensin production
   d. Intestinal epithelial cells: luminal antigen sampling

2. DC subsets in the GI tract have which of the following important functions?
   a. Mesenteric antigen sampling
   b. T cell tolerance induction and effector T cell activation
   c. Induction of B cell IgG class switching
   d. Imprinting gut homing phenotypes of strictly B cells

3. Which of the following tissues encompasses the greatest number of lymphocytes?
   a. Bone marrow
   b. Spleen
   c. Skin
   d. GI tract

4. Which of the following statements is accurate in regards to IGA class switching in the gut?
   a. IgA class switching can occur by only T cell dependent mechanisms
   b. DCs in the subepithelial dome of Peyers patches capture bacterial antigens delivered by M cells and migrate to interfollicular zone where they present antigen to CD8+ T cells
   c. TLR ligand activated DCs induce IgA class switch through factors such as BAFF, APRIL, and TGF-B
   d. B cell class switching to IgA is stimulated primarily through TGF-beta

5. IBD is thought to be related to which of the following immune mechanisms?
   a. Defects in innate immunity to gut commensals such as defensins and NOD2 cytoplasmic innate immune sensors
   b. Abnormalities primarily in the TH2 and TH17 immune response
c. Adequate T reg mediated suppression of immune responses to commensal organisms
d. Mutations in select genes relating to cell apoptosis

6. Which of the following immunodeficiency is a result of FOXP3 mutations resulting in failure to develop proper T regulatory response leading to immune dysregulation, polyendocrinopathy, enteropathy, and autoimmunity?
   a. Complete DiGeorge
   b. Nethertons Disease
   c. Deficiency of Interleukin 1 receptor antagonist
   d. IPEX

7. Which of the following is considered an immune privileged site?
   a. Brain
   b. Conjunctiva
   c. Scrotum
   d. Skin

8. Which of the following pairs is correct regarding the cutaneous immune system?
   a. Epidermis: innate immune defense function/physical barrier protection to microbial invasion
   b. Keratinocytes: mixed population of mast cells, macrophages, and DCs mediating inflammatory response
   c. Dermis: secrete defensins as well as inflammatory cytokines to various PAMPs and DAMPs
   d. Keratinocytes: IL-18 and IL-22 induce expression of defensins in keratinocytes

9. Which describes the function of alveolar macrophages best?
   a. Maintaining an anti-inflammatory phenotype
   b. Activate T cell responses as well as antigen presentation of airway Dendritic cells
   c. Expression of IL-5, nitric oxide, and TGF-beta
   d. Highly phagocytic compared with resident macrophages

10. Skin homing molecules include which of the following?
    a. CCR3
    b. CC10
    c. CLA
    d. CCL26

Answers
M cells involved with luminal antigen processing is correct. Paneth cells are involved with defensing production, Secretory IgA/IgM involved with neutralization of microbes in the lumen. Intestinal epithelial cells are involved with mucus secretion, and finally, DC subsets are involved with luminal antigen sampling amongst other functions.

DC subsets in the GI tract are involved with lamina propria antigen sampling, T cell tolerance induction and effector T cell activation, induction of B cell IgA class switching, and imprinting gut homing phenotypes of both B and T cells.

3. B, page 294, Figure 13-2.
The spleen has greatest numbers of lymphocytes, followed by bone marrow and GI tract which have similar numbers, followed by skin.

4. C, page 303, Figure 13-7.
Antigens that are presented to B cells are generally presented in their intact, native conformation and IgA class switching occurs through both T cell dependent and independent mechanisms. DCs in the subepithelial dome of Peyers patches capture bacterial antigens delivered by M cells and migrate to interfollicular zone where they present antigen to CD4+ T cells. TLR ligand activated DCs induce IgA class switch through factors such as BAFF, APRIL, and TGF-B. B cell class switching to IgA is stimulated through action of both TGF-beta and through T cell CD40L binding to B cell CD40.

IBD is thought to be due to many different immune mechanisms including the following: Defects in innate immunity to gut commensals such as defensins and NOD2 cytoplasmic innate immune sensors, abnormalities primarily in the TH1 and TH17 immune response, inadequate T reg mediated suppression of immune responses to commensal organisms, and mutations in select genes relating to cell autophagy.

IPEX also known as immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX), including severe gut inflammation as well as autoimmunity, is due to FOXP3 mutations leading in failure of Tregs to develop.

Immune privileged sites are tissues where immune responses are not readily initiated, including the brain, anterior chamber of the eye, and testis. Mechanisms include tight junctions of endothelial cells in blood vessels at these sites, local production of immunosuppressive cytokines, and expression of cell surface molecules that inactivate or kill lymphocytes.

Epidermis is involved with innate immune defense function/physical barrier protection to microbial invasion. Keratinocytes secrete defensins as well as inflammatory cytokines to various PAMPs and DAMPs, and the dermis has a mixed population of mast cells, macrophages, and DCs mediating inflammatory response. Additionally, IL-17 and IL-22 induce expression of defensins in keratinocytes.

Alveolar macrophages represent the majority of free cells within the alveolar spaces. These cells are functionally distinct from macrophages in most other tissues in that they maintain an anti-inflammatory phenotype. They express IL-10, NO, and TGF-beta, and are poorly phagocytic compared with resident macrophages. Alveolar macrophages inhibit T cell responses as well as the antigen presentation function of CD103+ airway DCs.
CLA, CCR4, and CCR 10 are all examples of skin-homing molecules. In addition, T cell expression of CCR4 and CCR10 which bind to chemokines CCL17 and CCL27 are also required for T cell trafficking to the skin.