**Allergy and Immunology Review Corner:** Chapter 7 of *Immunology IV: Clinical Applications in Health and Disease*, by Joseph A. Bellanti, MD.

**Chapter 7: T Lymphocytes and Cell-Mediated Immunity**

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1. In this figure, which surface markers are typical of this cell population indicated by the blue arrow?
   A. CD3- CD4- CD8-
   B. CD3- CD4+ CD8-
   C. CD3+ CD4- CD8-
   D. CD3+ CD4+ CD8+

![Flow cytometry diagram]

2. Name one newborn screening method currently being utilized in some states to screen for a specific immunodeficiency?
   A. Microarray chip IgE assay
   B. T cell immunophenotyping
   C. PCR for TRECS
   D. CD40 functional expression assay

3. Lymphocyte enumeration studies reveal a patient with T-B+NK- phenotype. What is the underlying defect associated with this phenotype?
   A. IL-7R deficiency
   B. Common gamma chain defect
   C. MHC I deficiency
   D. ADA deficiency

4. IL-4, IL-5, IL-6, IL-10, IL-13 are secreted by which T cell type?
   A. Th1
   B. Th2
C. Th3
D. Treg

5. What is the usual ratio of CD4+ T cells to CD8+ T cells?
   A. 1:1
   B. 1:2
   C. 2:1
   D. 4:1

6. On what chromosome or chromosomes are the genes for the T cell receptor located?
   A. Chromosome 5
   B. Chromosome 6
   C. Chromosome 2 and chromosome 22
   D. Chromosome 7 and chromosome 14

7. Which of the following is a negative regulator of T cell activation?
   A. CD28
   B. ICOS
   C. CD152
   D. CD40 ligand

8. Which of the following transcription factors is ultimately suppressed by cyclosporine
   and tacrolimus
   A. NFAT
   B. NF-κB
   C. GATA 3
   D. RORγt

9. What is the main transcription factor for T-helper 3 cells?
   A. T-bet
   B. FOXP3
   C. RORγt
   D. STAT3

10. What is the main cytokine produced by T-helper 3 cells?
    A. IL-2
    B. IL-17
    C. IL-10
    D. TGF-β

**Answers**
1. D, pages 217-18, Figure 7-7
   The “upper right quadrant is where double positive T cells are found. These double positive cells express a fully rearranged T cell receptor….”

2. C, page 222
“T cell receptor-excision circles (TRECS) are the leftover products of TCR rearrangement during the DP stage that consists of circular DNA containing spliced-out intervening D, J, and C segments. Thymic output can be monitored by a PCR-based assay that is sensitive enough to detect TRECS…in the proposed screening program for SCID.”

3. B, page 249. Table 7-5
X-linked SCID common gamma chain defect. “Lacks T cells, NK cells; has B cells”

4. B, page 235
“Th2 cells secrete IL-4, IL-5, IL-6, IL-10, IL-13”

5. C, page 212
“In humans, circulating CD4+ T cells outnumber CD8+ T cells by approximately 2:1.”

6. D, page 215
“In humans, the genes for the T cell receptor are found on chromosome 7 and chromosome 14….“

7. C, page 232
“The most important negative regulator for global T cell activation is the CTLA4 (CD152) molecule, the high avidity receptor for CD80/26 (also referred to as B-7.1/B-7.2).”

8. A, page 248
“The agents cyclosporine and FK506, or tacrolimus, are known as calcineurin-based immunosuppressives since they both target the signaling pathway coupling calcium flux to induction of the transcription factor NFAT, which is critical for IL-2 production in activated T cells.”

9. B, page 236. Table 7-3
The transcription factor associated with T-helper 3 cells is FOXP3.

10. D, page 236. Table 7-3
The main cytokine produced by T-helper 3 cells is TGF-β.

**Allergy and Immunology Review Corner:** Chapter 8 of *Immunology IV: Clinical Applications in Health and Disease*, by Joseph A. Bellanti, MD.

**Chapter 8:** The Mucosal Immune System in Health and Disease

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1. Which of the following best represents the name and function of M Cells?
   A. Microfold Cells; act as antigen-presenting cells
B. Mucosal Cells; where switching of IgM- to IgA-bearing B cells predominate
C. Microfold Cells; luminal antigens are taken up by these cells and are delivered to adjacent APCs
D. Mediator Cells; such as mast cells and NK cells

2. Which of the following is NOT a region in the GALT where Dendritic Cells may be found?
A. In a region of the Peyer’s Patch immediately below the M cells, referred to as the SED
B. In an intraepithelial location as a set of specialized DC subsets that extend dendrites between the tight junctions of enterocytes that can sample luminal contents
C. In lymphoid follicles scattered throughout the lamina propria
D. In mammary lymphoid tissues

3. Which of the following is NOT an immunoregulatory role of Retinoic Acid in the mucosal immune system?
A. May capture antigens in the external secretions, at the epithelial surface, or attach to antigen located within the mucosal lamina propria
B. Induces addressing-associated homing receptors on T and B cells
C. Induces a subset of forkhead box P3 (FOXP3)+ regulatory T cells
D. Provides important signals that induce differentiation and class switching of IgA-producing B cells

4. Which of the following statements concerning regulatory lymphocytes is FALSE?
A. CD4+ Tregs are abundant in mucosal lymphoid tissues, there they downregulate Th1 and Th2 responses.
B. CD4+ Tregs are characterized by CD25 expression, CTLA-4 binding, and by the production of regulatory cytokines (IL-11 and TGF-alpha).
C. Expression of CD25 on T cells is associated with natural regulatory functions
D. FOXP3 is the key regulatory gene in the development of CD25+ Tregs

5. Which of the following findings are characteristic in patients with selective IgA deficiency?
A. Recurrent ear infections, sinusitis, bronchitis and pneumonia
B. Autoimmune diseases, such as Rheumatoid Arthritis, SLE and ITP
C. Allergic diseases, such as asthma and food allergies
D. Susceptibility to the development of anti-IgA-related anaphylactoid reactions to blood transfusions, and other blood or plasma products containing small amounts of IgA
E. All of the above

6. Bronchus-associated lymphoid tissues (BALT) aim to avoid sensitization by inhaled antigens and this is accomplished in part via which of the following cells?
A. TCR1 T cells
B. Natural killer T cells
C. M cells
D. Goblet cells

7. All of the following cytokines play a role in stimulating production of alpha and beta defensins except for:
A. IL-1
B. TNF-alpha
C. LPS
D. IL-6

8. Advantages of sublingual immunotherapy (SLIT) include all of the following except:
A. Fewer doctor visits
B. Avoidance of injections
C. Fewer side effects
D. Requires lower concentration of allergen doses

9. Which type of T-cell is predominant in the MALT?
A. Alpha-beta T cells
B. Natural killer T cells (NTK)
C. Gamma-delta T cells
D. Treg cells

10. Which of the following correctly describes lymphocyte recirculation to effector sites in regards to the gut-associated lymphoid tissues (GALT)?
A. Antigen is captured by M cells → transfer of antigen to SED area of Peyer’s patch → cognate interaction with T and B cells → migration of these cells out of the Peyer’s patch through efferent lymphatics to enter the mesenteric lymph nodes (MLN).
B. Transfer of antigen to SED area of Peyer’s patch → antigen is captured by M cells → cognate interaction with T and B cells → migration of these cells out of the Peyer’s patch through efferent lymphatics to enter the mesenteric lymph nodes (MLN).
C. Cognate interaction with T and B cells → transfer of antigen to SED area of Peyer’s patch → antigen is captured by M cells → migration of these cells out of the Peyer’s patch through efferent lymphatics to enter the mesenteric lymph nodes (MLN).
D. Antigen is captured by M cells → transfer of antigen to SED area of Peyer’s patch → migration of these cells out of the Peyer’s patch through efferent lymphatics to enter the mesenteric lymph nodes (MLN). → cognate interaction with T and B cells.

Answers
1. C, page 259
“Of particular importance within the mucosal surface are specialized epithelial cells, called microfold (M) cells, located in the epithelium overlying follicles of the Peyer’s Patches. The M cells are characterized by an invagination at the basolateral membrane, which forms a “pocket” normally occupied by lymphocytes and APCs referred to as the Subepithelial Dome (SED). There contain all of the immunocompetent cells that are required for the initial generation of an immune response, i.e., T cells, B cells, and APCs. Soluble and particulate luminal antigens are taken up by M cells and are delivered to adjacent APCs.”
2. D, page 261-262
“Of particular importance in mucosal immunity are the DCs, which are found as a pleomorphic set of several populations of APCs in several sites of the intestine and associated lymphoid tissues. In the GALT, DCs are found in at least 3 separate locations: (1) in a region of the Peyer’s Patch immediately below the M cells, referred to as the SED; (2) in an intraepithelial location as a set of specialized DC subsets that extend dendrites between the tight junctions of enterocytes that can sample luminal contents; and (3) in lymphoid follicles scattered throughout the lamina propria.” Additionally, Mammary-associated lymphoid tissues are separate from Gut-associated lymphoid tissues (GALT).

3. A, pages 263-264
“Retinoic Acid (RA), produced by gut dendritic cells or from dietary sources, not only induces addressin-associated homing receptors on T and B cells, but also provides important signals that induce differentiation and class switching of IgA-producing B cells. Retinoic acid also induces a subset of fork box P3 (FOXP3)+ regulatory T cells, which are important for maintaining immune tolerance in the gut.” Page 273: “SIgA may capture antigens in the external secretions, at the epithelial surface, or attach to antigen located within the mucosal LP”.

4. B, page 274
“CD4+ Tregs are abundant in mucosal lymphoid tissues, where they downregulate Th1 and Th2 responses. These cells are characterized by CD25 expression, CTLA-4 binding, and by the production of regulatory cytokines (IL-10 and TGF-beta). Expression of CD25 on T cells is associated with natural regulatory function; CD25 is the alpha-chain of the IL-2 receptor and is also a marker of T cell activation. FOXP3 is the key regulatory gene in the development of CD25+ Tregs, which can be induced in the periphery, and their conversion into Tregs is dependent on TGF-beta.”

5. E, page 283
“Common infections observed in symptomatic patients with selective IgA deficiency are recurrent ear infections, sinusitis, bronchitis, and pneumonia. People with selective IgA deficiency may be more susceptible to allergic diseases such as asthma and food allergies. The spectrum of autoimmune disorders seen in individuals with selective IgA deficiency include rheumatoid arthritis, systemic lupus erythematosus, and immune thrombocytopenic purpura. As the case study described in this chapter demonstrates, patients with IgA deficiency are more susceptible to the development of anti-IgA-related anaphylactoid reactions to blood transfusions, immunoglobulin replacement therapy, and the administration of other plasma products containing small amounts of IgA.”

6. D, page 272
“BALT refers to the bronchial lymphoid aggregates and the less-organized lymphoid tissue in humans and other species. About 10 to 20 percent of the interstitial lymphocyte pool is composed of T cells. There is a priority to avoid inflammation within the bronchial lumen or mucosa. TCR1 T cells promote tolerance to inhaled antigens, and also
alveolar macrophages exert an anti-proliferative effect on T cells, preventing antigen presentation at the mucosal surface.”

7. D, page 261
“These include alpha and beta defensins, which are produced by Paneth cells and epithelial cells, respectively, and which together provide a protective defensin network against most bacteria and many viruses. Although...proinflammatory cytokines such as IL-1, TNF-alpha, and bacterial LPS play a role in their activation.”

8. D, page 283
“It is claimed that the advantages of this immunotherapy include avoiding injections, fewer doctor visits, and lower side effects. However, the therapy requires four to five months to yield results. Apparently, SLIT is safe and effective, but perhaps less effective than injection immunotherapy, since it needs up to 300x higher allergen doses, and its long-term efficacy is unclear.”

9. C, pages 270-271
“The most common T cell receptor (TCR alpha-beta) is made up of alpha and beta chains and is found on about 95 percent of circulating T cells. A second type of TCR (TCR gamma-delta) has gamma and delta chains and is found on about 5 percent of circulating T cell, but is the predominate cell type in the MALT found within the population of lymphocytes known as IELs. The gamma-delta T cells are particular in that they do not seem to require antigen processing and MHC presentation of peptide epitopes for activation, although some recognize MHC-1B molecules.”

10. A, page 266
“In the case of the GALT, antigen is captured by M cells and is transferred to DCs in the SED area of the Peyer’s patch (PP) where they engage in cognate interaction with T cells and B cells. This is followed by the migration of these cells out of the PP through the efferent lymphatics to enter the local mesenteric lymph nodes (MLN). Activated cells undergo differentiation, and effector cells travel through lymphatics to enter the circulatory system through the thoracic duct. From the blood, the T and B cells seed the lamina propria of the small intestine and mucosae of other remote effector sites.”