Review Questions: Janeway's Immunobiology 8th Edition by Kenneth Murphy

- Chapter 14 (pages 571-606): Allergy and Allergic Diseases— prepared by Tara Shankar, MD, Children's Hospital of Pittsburgh of UPMC, and Andrew Nickels, MD, Mayo School of Graduate Medical Education
- Chapter 15 (pages 611-663): Autoimmunity and Transplantation— prepared by Erin Kempe, MD, Ohio State University Hospital, and Monica Bhagat, MD, University of Pennsylvania

Allergy and Immunology Review Corner: Chapter 14 of Janeway's Immunobiology 8th Edition by Kenneth Murphy.

Chapter 14 (pages 571-606): Allergy and Allergic Diseases

Prepared by Tara Shankar, MD, Children's Hospital of Pittsburgh of UPMC, and Andrew Nickels, MD, Mayo School of Graduate Medical Education

1. Which of the following are associated with decreased risk of atopy?
   A. Helminth infection
   B. RSV infection
   C. Hepatitis A infection
   D. Diesel exhaust exposure

2. A 20 year old male with history of multiple food allergies and persistent erythroderma is admitted for staphylococcal cellulitis. Laboratory evaluation reveals high serum IgE levels. What defect is thought to be responsible for this disease?
   A. Lack of costimulation by CD40 ligand
   B. Lack of the protease inhibitor SPINK5
   C. STAT 3 deficiency
   D. RAG 1 mutation

3. What is unique to IgE in terms of its receptor binding properties?
   A. The majority is found soluble in body fluids
   B. It does not require cross-linking to activate cells
   C. It binds with high affinity to FceRII
   D. It is captured by the FceRI receptor in the absence of bound antigen

4. Which of the following is a true statement about mast cells?
   A. They mature in the bone marrow
   B. They are found only in mucosal epithelia
   C. Activation depends on Kit activation of PI 3 kinase
   D. Their role is limited to IgE driven pro inflammatory responses

5. A 32yo female presents for evaluation of rash. She describes erythematous, pruritic wheals that have occurred daily for the past 10 weeks, typically with individual wheals resolving within 24 hours or with use of benadryl. A laboratory workup reveals anti-FceRI antibodies.
What type of hypersensitivity reaction is this?
A. Type I
B. Type II
C. Type III
D. Type IV

6. Deficiency is which of the following protein or molecule has been associated with atopic dermatitis?
A. IL-5
B. Filaggrin
C. Major Basic Protein
D. Eosinophil cationic protein

7. A 23 yo F presents to your office for a 1 year follow up for allergic rhinitis. Her symptoms are not controlled despite optimal medical management. Together with the patient, the decision is made to initiate subcutaneous immunotherapy for treatment of allergic rhinitis. Which of the following most accurately reflects a key mechanism of action to immunotherapy?
A. Induction of regulatory T Cells secreting IL-10 and/or TGF-β
B. Induction of IgG2, selectively promoted by IL-8
C. Induction of B-Cell class switching by down regulation of IL-5 receptor
D. Down regulation of IL-8 and IL-10 expression by circulating helper T-Cells

8. Omalizumab is a commercially available anti-IgE antibody medication. It binds to the Fc region of free IgE. In clinical trials, it has been shown to reduce circulating IgE levels by more than 95% as well as which of the following?
A. Increase circulating Th1 cells
B. Down regulate the numbers of high-affinity IgE receptors on basophils and mast cells
C. Increase IgE-mediated antigen trapping by dendritic cells.
D. Decrease B-Cell class switching to IgE producing plasma cells.

9. Contact dermatitis is a classic form of delayed type hypersensitivy. Divalent cations such as nickel have been observed as a common cause of delayed type hypersensitivity in humans. Divalent cations can alter the conformations or the peptide binding of MHC class II molecules, and thus promote a T-cell response. In humans, nickel can also bind to what receptor and produce a pro-inflammatory response?
A. TCR
B. CXCR3
C. LFA-1
D. TLR-4

10. Which of the following MHC Class II allele is strongly associated with Celiac Disease?
A. HLA-C
B. HLA-DR1
C. HLA-DQ2
D. HLA-DR5
Answers
1. C, page 580
A history of infection with...hepatitis A virus...also seems to have a negative association with atopy.

2. B, page 576
Netherton’s syndrome, which is characterized by high levels of IgE and multiple allergies. The defect in this disease is the lack of a protease inhibitor called SPINK5 which is thought to inhibit the proteases released by bacteria such as Staphylococcus aureus.

3. C, page 583
IgE is an exception, because it is captured by the high-affinity Fce receptor (FceRI) in the absence of bound antigen.

4. C, page 584
Mast cell activation depends on the activation of PI3-kinase in mast cells by Kit.

5. B, page 589
It seems likely that from one-third to one-half of the cases of chronic urticaria are caused by autoantibodies against either the alpha chain of FceRI or against IgE itself and are thus due to autoimmunity. Interaction of the autoantibody with the receptor triggers mast-cell degranulation, with resulting urticaria. This is an example of a type II hypersensitivity reaction.

6. B, page 593
Deficiency Filaggrin has been recently associated with atopic dermatitis. Filaggrin is an epidermal protein that binds to keratin fibers in epidermal cells, contributing to the physical barrier at the skin surface that keeps skin waterproof and prevents the entry of airborne allergens.

7. A, page 956
Mechanisms of Immunotherapy are complex, but the key to success seems to be the induction of regulatory T-Cells secreting IL-10 and/or TGF-β, which skews the response away from IgE production. In insect venom immunotherapy, it has been shown that immunotherapy induces the increase production of IL-10 and in some cases TGF-β, as well as the induction of IgG isotypes, particularly IgG4, an isotype selectively promoted by IL-10.

8. B, page 597
In addition to reducing circulating IgE levels by more than 95%, Omalizumab also was shown to down regulate the numbers of high-affinity IgE receptors on basophils and mast cells.

9. D, page 603
In addition to altering the conformations or the peptide binding of MHC class II molecules, and thus promote a T-cell response, divalent cations can bind TLR-4 and produce a pro-inflammatory response.

10. C, page 602
Celiac disease shows an extremely strong genetic predisposition, with more than 95% of patients expressing the HLA-DQ2 class II MHC allele.

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**Chapter 15 (pages 611-663): Autoimmunity and Transplantation**

*Prepared by Erin Kempe, MD, Ohio State University Hospital, and Monica Bhagat, MD, University of Pennsylvania*

1. Which of the following tissue types exhibits immune privilege:
   A. Appendix
   B. Dermis
   C. Retina
   D. Thymus

2. In immune privileged tissues, regulatory T-cell responses are induced by which of the following cytokine signals:
   A. TGF-β in the absence of IL-6
   B. TGF-β in the presence of IL-6
   C. IFN-γ and TNF-α
   D. IL-4 and IL-13

3. What cytokine is secreted by peripheral regulatory T cells and reduces activation of self-reactive T cells?
   A. IFNγ
   B. IL-10
   C. IL-22
   D. TNFα

4. Which of the following autoimmune conditions is the result of autoantibodies directed toward a cell-surface receptor?
   A. Goodpasture syndrome
   B. Hashimoto thyroiditis
   C. Myasthenia gravis
   D. Systemic lupus erythematosus

5. A defect in what gene results in the autoimmune syndrome IPEX (immune dysregulation, polyendocrinopathy, enteropathy, X-linked)?
   A. AIRE
   B. CTLA-4
   C. FoxP3
   D. FAS

6. Natural Treg cells develop in the thymus in response to which of the following?
A. Strong stimulation by self antigens that is sufficient to cause deletion
B. Strong stimulation by self antigens that is not sufficient to cause deletion
C. Weak stimulation by self antigens that is not sufficient to cause deletion
D. Weak stimulation by self antigens that is sufficient to cause deletion

7. Which of the following autoimmune diseases CANNOT be transferred across the placenta to the fetus?
   A. Myasthenia gravis
   B. Graves’ disease
   C. Pemphigus vulgaris
   D. Hashimoto’s thyroiditis

8. In the pemphigus vulgaris, what is the target autoantigen bound?
   A. Desmoglein-1
   B. BP-280
   C. Desmoglein-3
   D. Both desmoglein-1 and desmoglein-3 may be bound during the progression of this disease

9. One of the disease-susceptibility genes in Crohn’s disease is known as which of the following?
   A. CARD9
   B. NOD1
   C. CARD15
   D. Blau

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    C. CARD15
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**Answers**

1. C, pages 617-618
   See chart on page 617. Some tissue types, including the brain and the eye, are considered immune privileged, in that when antigens from these sites come into contact with autoreactive T cells, they are able to induce tolerance, or a nondestructive response.

2. A, page 618
   In the absence of infection or inflammation, antigen recognized with TGFb induces a regulatory T cell response. However, if antigen is recognized in the presence of TGFb and IL-6, proinflammatory TH17 responses ensue.

3. B, pages 620-621
   Regulatory T cells that encounter their specific self antigen secrete IL-10, which suppresses the response of other autoreactive T cells and reduces inflammatory responses.
4. C, pages 632-633
In myasthenia gravis, autoantibodies against the alpha chain of the acetylcholine receptor in skeletal muscle cells block transmission through the receptor and result in progressive weakness.

5. C, pages 642-643
Fig. 15.32. Mutations in the gene for FoxP3 result in IPEX due to decreased function of regulatory T cells. Mutations in the AIRE gene result in APECED; in CTLA-4 result in multiple diseases like Graves and IDDM; and in FAS lead to ALPS.

6. C, page 62
Fig. 15.9. Tregs develop when they are weakly stimulated in the thymus but not stimulated enough to result in positive selection.

7. D, pages 625-626
Fig 15.14. Hashimoto’s thyroiditis is due to anti-TPO antibodies.

8. D, page 529
In the initial mucosal stage, only dsg-3 is bound, but as the disease progresses to involve generalized skin, dsg-1 may be bound as well. Dsg-1 is only bound in a milder form of this condition known as pemphigus foliaceus.

9. C, pages 647-648
NOD2 (also known as CARD15) is a known Crohn’s disease disease-susceptibility gene. Blau syndrome is defined by granuloma formation in the skin, eyes, and joints and is thought to be due to a gain of function mutation in NOD2. Crohn’s disease is thought to be due to a loss of function in NOD2.

10. C, page 657
Preformed alloantibodies against blood group antigens and/or polymorphic MHC alleles can bind vascular endothelial antigens on vascularized graft tissues, leading to rapid initiation of complement and blood clotting cascades. This results in acute vessel thrombosis and graft death.