1. Which of the following cytokines is characteristically produced by Th2 cells?
   A. IFN-γ
   B. TNF-α
   C. Lymphotoxin (LT)
   D. IL-4

2. Which of the following originate directly from thymic precursors rather than peripheral T helper cell precursors?
   A. Tr1
   B. Th3
   C. iTreg
   D. nTreg

3. Cytokines sharing the common β chain (βc) belong to which family of receptors?
   A. Class I
   B. Class II
   C. TNF family
   D. IL-1/TLR

4. Cytokines that bind members of the TNF family of receptors include:
   A. IL-2/IL-4/IL-7
   B. IL-1/IL-33/IL-18
   C. FasL/CD40L/APRIL/RANKL
   D. IFN-β/IL-10

5. Which cytokine signal pathway utilizes SMADs?
   A. IL-2
   B. TGF-β
   C. IL-17
   D. TNF-α

6. What is the most potent inducer of TNF-α by monocytes?
   A. Lipopolysaccharide
   B. ssRNA
   C. dsRNA
   D. profiling

7. Which of the following has been shown to inhibit production of IL-4?
A. Vitamin A, cysteinyl leukotriene receptor antagonists, and biotin
B. Vitamin D and B-agonists
C. Para-phenylenediamine
D. Vitamin E, aspirin, and parthenolide

8. Which of the following receptors shares the β subunit of the IL-5 receptor?
A. IL-6 receptor and IL-10 receptor
B. IL-4 receptor and IL-13 receptor
C. IL-3 receptor and GM-CSF receptors
D. IL-13 receptor and IL-21 receptor

9. Which of the following does IL-6 use as for secondary signaling?
A. Erk
B. Lyk
C. P40
D. gp130

10. Which of the following is a Type III interferon?
A. IFN-α
B. IFN-β
C. IFN-γ
D. IFN-λ

Answers
1. D, pages 294-295
When activated, Th1 cells produce IFN-γ, TNF-α, LT (also known as TNF-β), and IL-10. IL-4 is a Th2 cytokine.

2. D, pages 295-296
nTreg cells originate directly from thymic precursors. The other 3 regulatory cells listed originate from peripheral T helper cell precursors.

3. A, page 301
Cytokines sharing the common β chain (as well as those sharing the common γc and gp130-utilizing) belong to the Class I hematopoietin cytokine receptor family.

4. C, page 301
FasL/CD40L/APRIL/RANKL bind the TNF family receptors which signal using NF-κB, TRAF6, MyD88, IRAK, and IRAK4. IL-2/IL-4/IL-7 bind Class I receptors that all share the common γc chain and signal through JAK/STAT. IL-1/IL-33/IL-18 bind the IL-1/TLR receptors which signal using TRAF6, MyD88, IRAK, etc. And, IFN-β/IL-10 bind the Class II receptors that signal through JAK/STAT.

5. B, page 301
TGF-β binds the TGF-β receptors which signal through SMAD. IL-2 signals via JAK/STAT. IL-17 signals via TRAF6/JNK/Erk/AP-1/NF-κB. And, TNF-α signals via
6. A, page 343
“The most potent inducer of TNF-α by monocytes is lipopolysaccharide (LPS), acting through TLR4.”

7. D, page 327, Figure 9-22
“Vitamin E, aspirin, and parthenolide have been shown to inhibit the expression of IL-4, whereas they have no effects on the production of Th1 cytokines.”

8. C, page 327
“…the β subunit of the IL-5 receptor is also found in IL-3 and GM-CSF receptors…”

9. D, page 329
“IL-6 is probably the best studied of the cytokines that use gp130 in their signaling complexes. Other cytokines that signal through receptors containing gp130 are IL-11, IL-27, IL-31, ciliary neurotrophic factor, cardiotrophin-1….”

10. D, page 41
“The recently identified type III interferon group consists of three IFN-λ molecules called IFN-λ1, IFN-λ2, and IFN-λ3 (also called IL-29, IL-28A, and IL-28B, respectively).:

Allergy and Immunology Review Corner: Chapter 10 of Immunology IV: Clinical Applications in Health and Disease, by Joseph A. Bellanti, MD.

Chapter 10: Immunogenetics

Prepared by David Scott, MD, Scripps Clinic, Scripps Green Hospital Program, and Monica Bhagat, MD, University of Pennsylvania

1. Which of the following is not characteristic of MHC class I molecules?
   A: Binds peptides of 10-30 residues or more
   B: Antigen-binding cleft consists of an α1 and α2 domain
   C: Distributed on all nucleated cells
   D: CD8 binds to the α3 region

2. MHC-I and MHC-II molecules are best induced by which cytokine?
   A: IFN-gamma
   B: TGF-beta
   C: IL-10
   D: IL-2

3. Match the following diseases with their associated susceptibility-inducing alleles.
   i. Ankylosing spondylitis
   ii. Celiac disease
iii. Goodpasture  
iv. Lupus  
v. Rheumatoid arthritis
A. B27, DR11, DR2, Cw6, DR4  
B. B27, D51, DR2, DR3, DQ6  
C. DR2, DR4, DR3, DR3, DR4  
D. B51, DR3, DR2, DR3, DR4  
E. B27, DR3, DR2, DR3, DR4

4. Which of the following is not a risk factor for GVHD?
A. HLA mismatch  
B. High numbers of T cells transfused from donor  
C. Younger age of donor or host  
D. Differing genders between donor and recipient

5. For solid organ transplantation, what is the best description of the implication of recipient antibodies to donor HLA-DR, DQ?
A. Absolute contraindication to transplant  
B. High titer is a relative contraindication to transplant  
C. Does not affect transplant  
D. Can be overcome by antecedent host myeloablative therapy

6. Which region of the MHC includes several genes involved in the complement cascade?
A: MHC-I  
B: MHC-II  
C: MHC-III  
D: MHC-IV

7. Once endogenous antigens are processed by the proteasome and resultant peptides are trimmed by cytosolic proteases, what proteins are responsible for translocating the antigenic peptides to the endoplasmic reticulum?
A. TAP1  
B. TAP2  
C. Both TAP1 and TAP2  
D. Tapasin

8. Which of the following statements is false regarding MHC-II deficiency?
A. There are four known genetic types of MHC-II deficiency.  
B. Patients with this disease do not have a laboratory profile consistent with severe combined immunodeficiency.  
C. This disease may lead to the development of autoimmune diseases including sclerosing cholangitis.  
D. There is a complete lack of antibody production in this disease.

9. In processing exogenous antigens, this protein occludes the MHC-II cleft and prevents
peptidases from loading until the molecule is in the lysosomal or late endosomal compartment containing the peptides.

A. Tapasin
B. CLIP
C. Invariant chain
D. TAP1

10. The following statements about hyperacute rejection of a graft are all true except for:
A. Hyperacute rejection of a graft is due to preformed antibodies to ABO or MHC antigens on the graft.
B. Hyperacute rejection of grafts occurs more frequently than acute rejection of grafts.
C. In those patients with multiple anti-MHC antibodies, hyperacute rejection may sometimes be prevented by the use of plasmapheresis of the recipient prior to transplant.
D. In hyperacute rejection, pathology is limited to the actual graft itself and does not involve any of the vasculature of the organ.

**Answers**

1. A, page 373, Table 10-3
   In Summary, MHC-I molecules have the following properties: Polypeptide chains consist of a single α chain (44–47 kD) noncovalently linked to the β2-microglobulin chain (12 kD). They are present on all nucleated cells. Their antigen-binding clefts are composed of α1 and α2 domains. Their binding site for T cell co-receptor is CD8 on the α3 region. The size of the peptide-binding cleft accommodates peptides of 8–11 residues. Whereas, the MHC-II molecules have the following properties: Polypeptide chains consist of a single α chain (32–34 kD) noncovalently linked to a single β chain (29–32 kD). They are present on APC’s. Their antigen-binding clefts are composed of α1 and β2 domains. Their binding site for T cell co-receptor is CD4 on the β2 region. The size of the peptide-binding cleft accommodates peptides of 10–30 residues or more.

2. A, page 370
   “Interferon-γ (INF-γ) increases the expression of MHC-I or MHC-II molecules and can induce the expression of MHC-II molecules on certain cell types that do not normally express them. This may be very important both in normal immunologic function and in autoimmunity.”

3. E, page 377
   Addison’s disease  DR3
   AS  B27
   Behcet’s syndrome  B51
   Celiac disease  DR3, DQA1*0501, DQβ1*0201
   Congenital adrenal hyperplasia  B47
   Dermatitis herpetiformis  DR3
   Graves’ disease  DR3
   Hashimoto’s disease  DR11
   Hereditary hemochromatosis  A3/B14
   Insulin-dependent diabetes mellitus  B35, Cw04
Idiopathic membranous GN   DR3
MS                   DR2, DQ6
Myasthenia Gravis    DR3
Narcolepsy           DR2, DQB1*0602
Psoriasis vulgaris   Cw6
Pemphigus vulgaris   DRB1*0402-DQB1*0302, DRβ1*1401-DQβ1*0503
RA                   DR4
SLE                   DR3
Sarcoidosis          DRβ1*1101

4. C, page 382
All of the listed factors are considered to be risk factors for developing GVHD except for younger age. Instead, older age of donor or host is considered to increase the risk of GVHD. The reason for this is not further explained in this chapter.

5. B, page 380, Table 10-6
In summary, although the presence of antibodies to HLA-A, B, or C is an absolute contraindication to transplant, the presence of antibodies to HLA-DR or DQ, even at high titers, is considered only a relative contraindication. Other autoantibodies cross-reacting with donor do not typically affect the transplant, unless they are directed at the actual transplanted organ.

6. C, page 369
“The MHC has three regions: MHC-I, MHC-II, and MHC-III. The MHC-III region includes several genes involved in the complement cascade (C4A, C4B, C2, and FB), the TNF-alpha and TNF-beta (LT alpha) genes, the CYP21 gene that encodes an enzyme in steroid metabolism, the HSP70 gene that encodes a chaperone, and many other genes of unknown immunological function.”

7. C, page 371
“Endogenous antigens are processed by the proteosome. This complex of proteases typically generates peptides of four to twenty amino acids with a hydrophobic carboxy terminus. After trimming of the peptide by cytosolic proteases, the antigenic peptides are translocated to the ER by the transporters associated with antigen processing (TAP1 and TAP2 molecule). Tapasin physically links the MHC-I molecules and the TAP transporters.”

8. D, page 384
“There are four known genetic types of MHC-II deficiency including CIITA, RFXANK, RFX5, and RFXAP. Patients with MHC-II deficiency do not have severe combined immunodeficiency because they often produce immunoglobulin and their T cells are capable of sustaining proliferation after stimulation with mitogens. In spite of this, their infection pattern resembles that seen in patients with SCID. This is because they have significant compromise in both functional immunoglobulin production and functional T cell responses. As is true for many patients with immunodeficiencies, patients with MHC-II deficiency develop autoimmune disease more frequently than others. Sclerosing
cholangitis is the most common of the autoimmune diseases.”

9. B, page 373
“The newly synthesized molecules transit the ER and the Golgi. After passage of the ligloaded MHC-II-DM complex through the Golgi into the late endosomes, the invariant chain is cleaved by acid proteases, leaving a residual peptide called Class II-associated invariant chain peptide (CLIP) in the MHC-II cleft. At that point, HLD-DM molecules remove CLIP from the cleft and stabilize the molecule while the peptide is loaded into the cleft. The fully loaded MHC-II molecule is recruited to the surface and serves to stimulate predominantly CD4 positive T cells.”

10. D, page 380
“Hyperacute rejection is due to preformed antibodies to ABO or MHC antigens on the graft. Hyperacute rejection due to antibodies and complement activation has been one of the major obstacles to using xenotransplants therapeutically. In hyperacute rejection, the graft rapidly becomes tender and swollen. Arterioles may also show necrosis or thrombosis. The goal of the pre-transplant cross-matching is to avoid this type of rejection and has been responsible for making this complication rather rare. Recent work using plasmapheresis of the recipient prior to transplant and IVIG, however, has allowed some patients with multiple anti-MHC antibodies to safely receive a kidney transplant.”