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IMMUNOLOGY

REVIEW THE CONCEPTS

1. a. Pathogenic strains of *Staphylococcus aureus* secrete collagenases that can break down connective tissue, allowing entry of the bacteria.
   b. Envelope viruses such as HIV have proteins that mediate fusion of the viral envelope with the host cell membrane, resulting in delivery of the viral genetic material into the host cell.

2. Leukocytes are made in the bone marrow and circulate throughout the body in the bloodstream. Leukocytes can leave the bloodstream and enter lymph nodes and lymphoid organs. Here, they interact with other cells and molecules that activate immune responses. Activated cells can leave the lymph system and recirculate through the bloodstream. Pathogenic invaders evoke chemical signals that can cause functionally active leukocytes to leave the circulation, move into tissues, and attack pathogenic invaders or destroy virus-infected cells.

3. Examples of mechanical defenses include the skin, epithelia, mucus and cilia in the nose and airways, and the exoskeleton in arthropods. Chemical defenses include low pH in the stomach, lysozyme in tears, and other antimicrobial secretions.

4. The classical complement cascade is antibody dependent. Immune complexes initiate this response via recruitment of C1q. This is the firststepinacascadeofproteolytic events. Recruitment of C1q allows recruitment of C1r and C1s and enables activation of their proteolytic activity. The next step involves proteolytic activation of a complex

between C2 and C4. This activation yields C3 convertase that, in turn, activates C3. Activated C3 unleashes the activities of C5–C9, ultimately resulting in the formation of a pore-forming protein complex that can attack pathogenic cells by inserting itself into biological membranes and rendering them permeable. The alternative pathway bypasses the initial steps and is not antibody dependent. This pathway starts with the spontaneous hydrolysis of the thioester bond of the C3 component of complement. An alternative C3 convertase can be formed upon interaction between the spontaneously activated C3 component and microbial surfaces. The steps downstream of C3 activation are the same as the classical pathway.

5. Decoration of particulate antigens with antibodies enhances phagocytosis. This process is called opsonization. In this process, antibodies attach to a virus or microbial surface by binding to their cognate antigen. Specialized phagocytic cells such as dendritic cells or macrophages can recognize the constant regions of bound antibodies by means of Fc receptors. Fc-receptor-dependent events allow the dendritic cells and macrophages to more readily inject and destroy antigenic particles.

6. Somatic recombination of *V* gene segments both completes an intact *V* segment and also places the promoter sequences of the rearranged *V* gene within controlling distance of enhancer elements required for the *V* gene transcription. In this way, B cells ensure that only rearranged *V* genes are transcribed.

7. Once a heavy-chain gene has undergone a successful recombination, it forms a complex with two surrogate light chains, λ5 and VpreB in association with Igα and Igβ. This pre-B cell receptor complex shuts off RAG expression. Since RAG expression is required for recombination, no further recombination can take place until RAG expression is reinitiated.

8. Class switch involves recombination of the gene segment for the heavy chain constant regions. The exons that encode the μ and δ heavy chains are immediately downstream of the VDJ cluster. Alternative splicing determines whether a μ or a δ chain will be produced. Downstream of the μ/δ combination are the exons that encode all of the other different isotypes. Each of these exons is preceded by repetitive sequences that promote recombination. To switch from IgM to any of the other isotypes, there is a recombination event that deletes all the intervening DNA to place the exon of any particular heavy chain constant region downstream of the VDJ cluster. (This process affects only the heavy chain.)

9. Along with other signals, T lymphocytes provide signals to antigen-activated B cells that induce expression of activation-induced deaminase (AID). AID deaminates cytosine residues to uracil. Thus, with every round of B cell replication there is a potential for mutations to accumulate. Mutations that improve the affi nity of the immunoglobulin for antigen convey a selective advantage. Those B cells whose antibodies have a higher affi nity for antigen tend to proliferate more. Thus, the overall affi nity of a population of B cells for a particular antigen increases over time. This phenomenon is called the affi nity maturation of the antibody response.

10. Both MHC Class I and MHC class II proteins are glycoproteins essential for immune recognition. Class I MHC proteins are present on all cells. In humans, Class I MHC proteins are coded by the HLA-A, HLA-B, and HLA-C loci. Class II MHC proteins are present only on antigen-presenting cells, including B cells, dendritic cells, and macrophages. In humans, class II MHC proteins are coded by six HLA-D genes.
    Cytotoxic T cells use Class I molecules as their restriction elements. T helper cells use Class II MHC molecules as their restriction elements.

11. The Class I MHC pathway presents cytosolic antigens.
    Step 1: Acquisition of antigen is synonymous with the production of proteins with errors (premature termination, misincorporation).
    Step 2: Misfolded proteins are targeted for degradation through conjugation with ubiquitin.
    Step 3: Proteolysis is carried out by the proteasome. In cells exposed to interferon γ, the catalytically active β subunits of the proteasome are replaced by interferon-induced active β subunits.
    Step 4: Peptides are delivered to the interior of the ER via the dimeric TAP peptide transporter.
    Step 5: Peptide is loaded onto newly made class I MHC molecules within the peptide-loading complex.
    Step 6: The fully assembled class I MHC–peptide complex is transported to the cell surface via the secretory pathway.

12. The Class II MHC pathway presents antigens delivered to the endocytic pathway.
    Step 1: Particulate antigens are acquired by phagocytosis and nonparticulate antigens by pinocytosis or endocytosis.
    Step 2: Exposure of antigen to the low pH and reducing environment of endosomes and lysosomes prepares the antigen for proteolysis.
    Step 3: The antigen is broken down by various proteases in endosomal and lysosomal compartments.
    Step 4: Class II MHC molecules, assembled in the ER from their subunits, are delivered to endosomal/lysosomal compartments by means of signals contained in the associated invariant (Ii) chain. This delivery targets late endosomes, lysosomes, and early endosomes, ensuring that class II MHC molecules are exposed to the products of proteolytic breakdown of antigen along the entire endocytic pathway.
    Step 5: Peptide loading is accomplished with the assistance of DM, a class II MHC-like chaperone protein.
    Step 6: Peptide-loaded Class II MHC molecules are displayed at the cell surface.

13. T cells that have receptors that could interact with self-MHC complexed with a particular self-peptide are identified by combining to form self-peptide MHC complexes within the thymus. If any of these combinations surpass a threshold that triggers the T-cell receptor, those cells die via an apoptotic pathway before leaving the thymus.

14. T-cell-related autoimmune diseases are associated with particular alleles of Class II MCH proteins because MHC recognition is required for T-cell attack.

15. Professional antigen-presenting cells such as dendritic cells and macrophages phagocytize pathogens and process antigens into small peptides. Interaction with pathogens activates professional antigen-presenting cells to migrate toward lymph nodes and increase the activity of their endosomal/lysosomal proteases. They also secrete cytokines that can stimulate naïve T cells. The professional antigen-presenting cells process antigens from the phagocytized pathogens into small peptides and display in the form of peptide-MHC complexes. Together with the stimulating cytokines, this sets up conditions for T cells to be activated. In the lymph nodes, B cells bind to antigens via their B-cell receptors, internalize the immune complex, and process it for presentation via the Class II MHC pathway. Activated T cells that recognize the same antigen bind to the B-cell complex, leading to B-cell differentiation and high-affinity antibody production.

16. Innate immune response:
    - Pathogen invades
    - Effector cells recognize the pathogen
    - Effector cells remove the pathogen

    Adaptive immune response:
    - Pathogen invades
    - Antigen-presenting cells identify the pathogen
    - Antigen-presenting cells travel to lymphoid organs
    - Antigen-presenting cells display antigen to lymphocytes
    - Lymphocytes proliferate and differentiate to effector cells
    - Effector lymphocytes clear pathogen

17. Passive immunization is when an antibody is administered to a person who cannot generate their own immune response, either because they do not have time (as in a snake bite toxin) or because their immune system is compromised (as in patients with an immune deficiency). Maternal antibodies passed through the placenta to a fetus are also an example of passive immunization.

18. Use noninfectious virus-like particles (virus capsid proteins devoid of any genetic material) to mimic the intact virion.

19. The vaccine is injected into the patient in order to produce a primary immune response (antibody production) that will (hopefully) neutralize the pathogen if you are exposed to it a second time. (Note: The vaccine must contain the most current strain in order to protect you; you can still get the fluafterreceivingafl u shot due to the many types of infl uenza.)

20. A polyclonal antibody can be made by injecting purifiedproteinofinterestintoa mammalian model (e.g., mouse, goat, or rabbit). The mammal will produce antibodies against the protein that will be present in the blood of the animal. The blood can be drawn from that animal and purifiedintoserumbyremovalof blood cells and platelets. The serum can be used directly or the antibody can be further purifi ed.
A monoclonal antibody can be made by injecting purifiedproteinofinterest into a mammalian model. The mammal is allowed to produce an antigen response and then the spleen is harvested. The spleen cells are dissociated and the immune B cells are fused with myeloma cells creating hybridomas, an immortal line. Each hybridoma creates a unique antibody.

21. Plasma cells synthesize and secrete antibody molecules in response to infection. It is this ramped-up production of secreted antibodies that underlies the effectiveness of the adaptive immune response in eliminating pathogens. Without plasma cells, the adaptive immune response would not be able to bind pathogen. The innate immune system targets antibody/antigen complexes for clearance, so without antibodies, the immune system would be unable to clear pathogens.