Kobe Maristela
BIOL 483

Biology 483- Infection, Immunity and Evolution of Disease
Spring 2021
Homework 11

Directions: Read the following sections in "The Immune System" by Parham and answer the questions below each section.

For the 3rd edition
Read Chapter 4, but with a special focus on these sections:

- **Generation of immunoglobulin diversity in B cells before encounter with antigen**
- **4-7 The DNA sequence encoding a V region is assembled from two or more gene segments**
- **4-8 Random recombination of gene segments produces diversity in the antigen binding sites of immunoglobulins**
- **Figure 4.34**
- **Summary**

What is a gene segment? What are the 3 general types of gene segments for immunoglobulin genes?

- A gene segment comprises of genes sequentially arrayed along the chromosome. Each segment codes for a specific or alternate version of parts of a protein.
  - For immunoglobulin genes each segments contains an alternative version of a part of the immunoglobulin V region
- Immunoglobulin genes are found at the chromosomal locations: the heavy-chain locus on chromosome 14, the κ light-chain locus on chromosome 2 and the λ light-chain locus on chromosome
- The three general types of gene segments for immunoglobulin genes are
  - Variable (V), Joining (J), and Diversity (D) gene segments

What is somatic recombination?

Somatic recombination is the process during the development of B cells in which the arrays of V,D, and J segments are cut and spliced by DNA recombination.

In general terms, how is VDJ-joined rearranged DNA created?

V, D, and J genes that are joined together are randomly selected, which results in numerous different combinations of the gene segments. The randomness aids in rearranging the cut and rejoined DNA. Strict requirements of the recombination in the heavy chain DNA cannot join V directly to J without the involvement of D gene segment thus it results in the rearrangement of DNA being created.

Read Chapter 6, but with a special focus on these sections:

- **Figures 6.1, 6.2, 6.4, 6.5, 6.6, 6.11**
- **6-1 B-cell development in the bone marrow proceeds through several stages**
- **6-2 B-cell development is stimulated by bone marrow stromal cells**

Kobe Maristela
BIOL 483

- **6-7 B-cells have to pass two main check points in their development in the bone marrow**
- **Summary**

What are the anatomical locations for B cell development?

B cell development first start in the bone marrow then is carried in the blood to lymph nodes, the spleen, Peyer's patches, and other secondary lymphoid tissues

What are the key stages of B cell development? What kinds of gene rearrangements occur over these developmental stages?
For example, compare the Heavy and Light chain gene rearrangements that occur at the Early pro-B cell stage relative to the Immature B cell stage.

- B cell development can be divided into six distinct stages:
  - Stage 1 → Generation of diverse and clonally expressed B-cell receptors in the bone marrow
    - Repertoire assembly
  - Stage 2 → Alteration, elimination or inactivation of B-cell receptors that bind to components of the human body
    - Negative selection
  - Stage 3 → Promotion of a fraction of immature B cells to become mature B cells in the secondary lymphoid tissues
    - Positive selection
  - Stage 4 → Recirculation of mature B cells between lymph, blood, and secondary lymphoid tissues
    - Searching for infection
  - Stage 5 → Activation and clonal expansion of B cells by pathogen-derived antigens in secondary lymphoid tissues
    - Finding infection
  - Stage 6 → Differentiation to antibody-secreting plasma cells and memory B cells in secondary lymphoid tissue
    - Attacking infection
- Gene rearrangement occurs over multiple development stages:
  - Early Pro-B cell
    - Heavy chain genes: D-J rearrangement | Light chain genes: Germline | Ig Status: None
  - Late Pro-B cell
    - Heavy chain genes: V-DJ rearrangement| Light chain genes: Germline | Ig Status: None
  - Large pre-B cell
    - Heavy chain genes: VDJ rearranged | Light chain genes: Germline | Ig Status: μ heavy chain is made
  - Small pre-B cell
    - Heavy chain genes: VDJ rearranged | Light chain genes: V-J rearranging | Ig Status: μ chain in endoplasmic reticulum
  - Immature B cell
    - Heavy chain genes: VDJ rearranged | Light chain genes: VJ rearranged | Ig Status: μ heavy chain. λ or κ light chain. IgM on surface

Kobe Maristela
BIOL 483

What are stromal cells and what do they do?

- Stromal cells are supportive cells in providing specialized microenvironments in the growth of B cells, in addition, they also act as connective tissue for any organs.
- Stromal cells have two main functions:
  - Stromal cells make specific contacts with the developing B cells through the interaction of adhesion molecules and their ligands.
  - Stromal cells produce growth facts that act on the attached B cells.

What happens at the various check points for B cells? Why are check points useful/important?

- B cells have two determining checkpoints during their development
  - 1st Checkpoint → selects for functional heavy chains
  - 2nd Checkpoint → selects for function light chains
- These checkpoints are important in the development of B cells as they prevent dysfunctional cells from making it through development. Cells that fail checkpoints will die by apoptosis.

For the 4th and 5th editions—same questions as above

Read Chapter 4, but with a special focus on these sections:

- **Generation of immunoglobulin diversity in B cells before encounter with antigen**
- **4-7 The DNA sequence encoding a V region is assembled from two or more gene segments**
- **4-8 Random recombination of gene segments produces diversity in the antigen binding sites of immunoglobulins**
- **Figure 4.36**
- **Summary**

Read Chapter 6, but with a special focus on these sections:

- **Figures 6.1, 6.2, 6.4, 6.5, 6.6, 6.11**
- **6-1 B-cell development in the bone marrow proceeds through several stages**
- **6-2 B-cell development is stimulated by bone marrow stromal cells**
- **6-7 Developing B-cells pass two check points in the bone marrow**
- **Summary**