3. Antigen Receptors and Generation of Antibody/T-Cell Receptor Diversity

LEARNING OBJECTIVES:

1. Become familiar with the principles of adaptive immunity.
2. Understand the concept of clonal selection of antigen-specific lymphocytes.
3. Become familiar with the structure of the immunoglobulin molecule and its special features that allow antigen recognition and binding.
4. Understand the mechanisms that generate immunoglobulin and T-cell receptor diversity, i.e. combinatorial and junctional diversity.
5. Recognize the practical use of monoclonal antibodies in clinical research and patient treatment.

SUMMARY

1. The adaptive or acquired immune response is the response of antigen-specific lymphocytes to antigen, including the development of immunological memory. The process is mediated by the clonal selection of antigen-specific lymphocytes.

2. Immunoglobulins (or antibodies) produced by B cells, and T-cell receptors produced by T cells, are the highly variable recognition molecules of adaptive immunity. The antigen-binding region consists of hypervariable loops and can have diverse structures that allow binding to a large variety of antigen-epitopes.

3. The antigen-binding region (variable region) of the heavy chain of the antibody molecule is assembled from multiple gene segments, namely variable (V), diversity (D), and joining (J) genes, by somatic DNA recombination. Light chains are assembled from V and J genes.

4. The diversity of antibodies and T-cell receptors is generated by gene rearrangement through somatic DNA recombination. The random combination of multiple V, D, and J gene segments yields combinatorial diversity. Junctional diversity is the result of terminal deoxynucleotidyl transferase (TdT)-mediated, nontemplated addition of nucleotides during the recombination process. Random pairing of heavy and light chains adds further combinatorial diversity. It is estimated that these processes could give rise to 10^{11} different antibody specificities that comprise the antigen receptor repertoire of ‘naïve’ B cells.

5. Monoclonal antibodies that recognize an antigen with high-specificity and high-affinity are extremely useful in research, diagnosis, as well as in the treatment of certain diseases and cancers.