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Characterization of Biopharmaceuticals

Any fool can know. The point is to understand.

Albert Einstein

9.1 Background

Biopharmaceuticals are complex, large-molecular-weight, variable-structure, dynamic protein and antibody molecules as compared with pharmaceutical products, wherein a fixed structure is always present. Some prominent examples include cytokines, antibodies, and hormones.

Cytokines are a broad and loose category of small proteins (~5–20 kDa) that are important in cell signaling. They are released by cells and affect the behavior of other cells. Cytokines can also be involved in autocrine signaling. Cytokines include chemokines, interferons, interleukins, lymphokines, and tumor necrosis factor but generally not hormones or growth factors (despite some terminology overlap). Cytokines are produced by a broad range of cells, including immune cells such as macrophages, B lymphocytes, T lymphocytes, and mast cells, as well as endothelial cells, fibroblasts, and various stromal cells. A given cytokine may be produced by more than one type of cell. Cytokines act through receptors and are especially important in the immune system. They modulate the balance between the humoral and cell-based immune responses, and they regulate the maturation, growth, and responsiveness of particular cell populations. Some cytokines enhance or inhibit the action of other cytokines in complex ways. They are different from hormones, which are also important cell signaling molecules, in that hormones circulate in much lower concentrations and hormones tend to be made by specific kinds of cells.

An antibody, also known as an immunoglobulin (Ig), is a large, Y-shaped protein produced by plasma cells that are used by the immune system to identify and neutralize pathogens such as bacteria and viruses. The antibody recognizes an antigen, via the variable region. Each tip of the “Y” of an antibody contains a paratope that is specific for one particular epitope (similarly analogous to a key) on an antigen, allowing these two structures to bind together with precision. Using this binding mechanism, an antibody can tag a microbe or an infected cell for attack by other parts of the immune system or can neutralize its target directly (e.g., by blocking a part of a microbe that is essential for its invasion and survival). The ability of an antibody to communicate with the other components of the immune system is mediated via its Fc region (located at the base of the “Y”), which contains a conserved glycosylation site involved in these interactions. The production of antibodies is the main function of the humoral immune system.