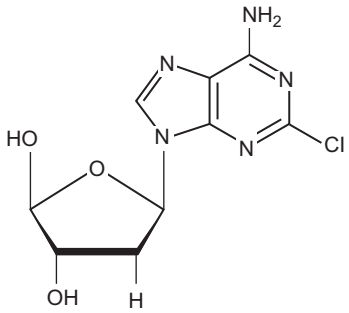
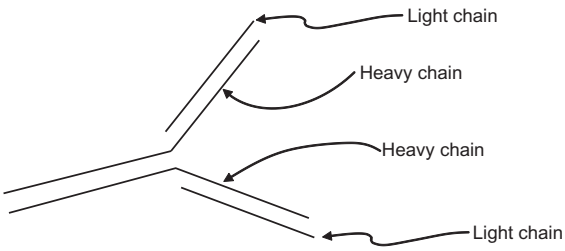


f. Origins of Therapeutic Antibodies

Antibodies designed with the aid of animal models are used to treat various cancers and immune diseases. For example, antibody drugs include trastuzumab (Herceptin®) (47), which binds to epidermal growth factor, and which is used to treat breast cancer. Antibody drugs also include bevacizumab (Avastin®) (48), which binds to vascular endothelial growth factor receptor (VEGFR), and is used to treat a variety of cancers. Moreover, an antibody drug used to treat various immune diseases is natalizumab (Tysabri®) (49). This antibody binds to a protein called integrin, which occurs on the surface of white blood cells. Natalizumab is used to treat two autoimmune diseases, multiple sclerosis and Crohn's disease.

Developing antibody drugs includes the step of refining the polypeptide sequence of the antibody into a drug suitable for administering to humans (50,51,52). This refinement step is called humanization (53). Humanization refers to the process of using genetic engineering to convert any protein of animal origin to a protein that can be injected into people, where the injected protein fails to elicit an immune reaction against itself.

Antibodies take the form of four polypeptides, two light chains and two heavy chains, as indicated in the diagram below. The first light chain and first heavy chain are covalently attached to each other by disulfide bonds, to form a first complex. The second light chain and second heavy chain are covalently attached to each by disulfide bonds to form a second complex. The first complex and second complex are also covalently attached to each other by way of disulfide bonds.



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