470 Gene- and Cell-Based Therapy in Clinical Medicine

Katherine A. High, Marcela V. Maus

Gene therapy is a novel area of therapeutics in which the active agent is a nucleic acid sequence rather than a protein or small molecule. One of the most powerful concepts in modern molecular medicine, gene therapy has the potential to address a host of diseases for which there are currently no available treatments. Because delivery of naked DNA or RNA to a cell is an inefficient process, most gene therapy is carried out using a vector, or gene delivery vehicle. These vehicles have generally been engineered from viruses by deleting some or all of the viral genome and replacing it with the therapeutic gene of interest under the control of a suitable promoter, but nonviral delivery vehicles such as lipid nanoparticles have also been used **(Table 470-1)**. Gene therapy strategies can thus be described in terms of three essential elements: (1) a gene delivery vehicle; (2) a gene to be delivered, sometimes called the transgene; and (3) a physiologically relevant target cell to which the DNA or RNA is delivered. The series of steps in which the vector and donated DNA or RNA enter the target cell and express the transgene is referred to as *transduction*. Gene delivery can take place in vivo, in which the vector is directly injected into the patient, or, in the case of hematopoietic, immune, and some other target cells, ex vivo, with removal of the target cells from the patient, followed by return of the gene-modified autologous cells to the patient after manipulation in the laboratory. The latter approach effectively combines gene transfer techniques with cellular therapies **(Chap. 484)**.

TABLE 470-1 Characteristics of Commonly Used Gene Delivery Vehicles