cancer therapy, although results seem to be disappointing.[95] GRNVAC1, a vaccine that has completed phase II clinical trials in patients with acute myelogenous leukemia and metastatic prostate cancer,[96] uses autologous immature DCs that are transduced *ex vivo* with mRNAs encoding a near full-length hTERT protein. After these DCs are matured, they are returned back to patients to elicit a polyclonal anti-hTERT T-cell response.

### 4.6 VACCINES AGAINST ONCOGENIC VIRUSES

Approximately 15–20% of cancers are associated with viral infections. HTLV-1 (adult T-cell leukemia, ATL), human papillomavirus (HPV; cervical, head, neck, and other cancers), HHV-8 (Kaposi's sarcoma), hepatitis B virus (HBV) and hepatitis C virus (HCV) (hepatocellular carcinoma), and Epstein–Barr virus (EBV; Burkitt's lymphoma) are examples of oncogenic viruses.[97] Currently, vaccines against HPV and against HBV are available, and scientific endeavor continues for six other cancer-associated infections, mostly viruses (other infectious agents such as bacteria and parasites are also associated with some types of cancer). These vaccines are based on viral antigens that are modified to make "virus-like particles" that are not infectious and therefore cannot cause disease. Synthetic versions of antigens that modify their chemical structure to stimulate immune responses are also being created in the laboratory for use in cancer preventive vaccines.

The first cancer preventive vaccine, approved by the FDA in 1981, was directed against HBV, an infection that can lead to liver cancer. The Papanicolaou test, developed in the 1920s, was introduced clinically in the 1940s. After its widespread implementation by collecting cells from the cervix to evaluate changes in cellular morphology consistent with preneoplasia or cancer, deaths from cervical cancer declined rapidly. In 1983, it was established that several HPV strains that can be transmitted sexually have oncogenic potential and produce cervical cancers, and also some vaginal, vulvar, anal, penile, and oropharyngeal cancers.[98] The search for vaccines to protect against these HPV infections led to FDA approval in 2006 of Gardasil® and Cervarix®, which protect against 4 and 2 HPV types, respectively. These vaccines cannot prevent the development of all cervical cancers, but they may reduce their incidence by 70%.[99]

## 5 GENE THERAPY

Gene therapy is based on the insertion of a functional gene into the somatic cells of a patient to correct an inborn metabolic error, to repair an acquired genetic abnormality, or to provide a new function to a cell. The main problem associated with gene therapy is the lack of efficient and selective vectors to deliver the genes. Ideally, a gene therapy vector would target a specific tissue with high transduction efficiency, sustaining a stable and regulated gene expression without any side effects or immunogenic responses. These criteria are not yet fulfilled.

Viruses are the most commonly employed vectors used in gene therapy, although they are not ideal because they trigger an immunological response. Nonviral vectors are safer but less efficient. The most promising of these are the synthetic cationic liposomes formed by positively charged amphiphilic molecules in which the positive charges interact electrostatically with negative charges in DNA phosphate groups, forming complexes that can enter the cells. Unfortunately, due to the low efficiency of DNA delivery by these systems, the amount of liposome currently required is too large to allow clinical use.