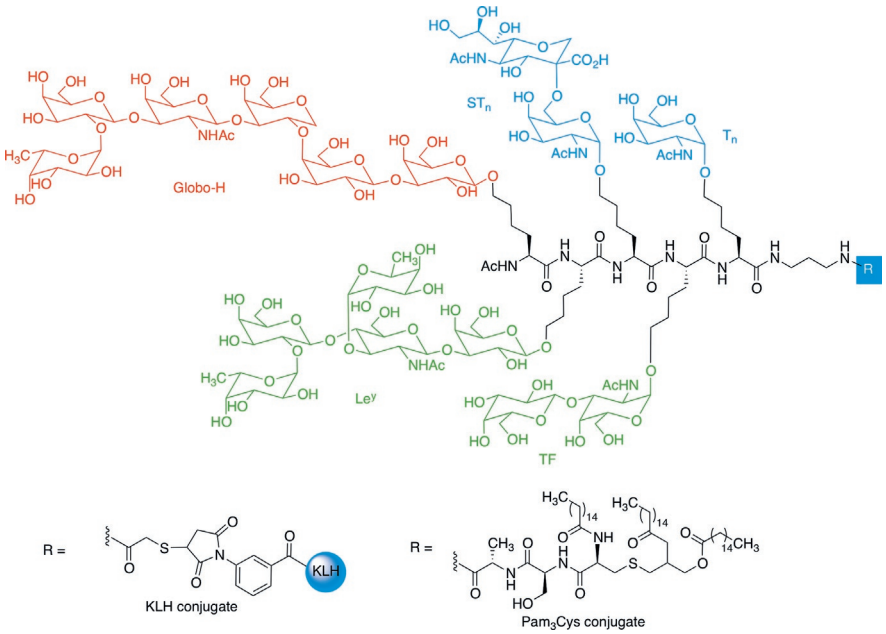

FIGURE 12.10

Two examples of unimolecular multivalent cancer vaccines.

Heat shock proteins (Hsps) are among the most ubiquitous soluble intracellular proteins and have a key role in immunologic phenomena, allowing their use for cancer immunotherapy. The autologous Hsp–peptide vaccine HSPPC-96 (Vitespen®, formerly Oncophage®) is a protein peptide complex consisting of GP96, a 96-kDa Hsp, and an array of GP96-associated cellular peptides.[86] Immunization with HSPPC-96 entered a phase II multicenter clinical trial, which showed that it may be clinically beneficial on recurrent glioblastoma multiforme (GBM) patients because it induces T-cell-specific immunity against those peptides.[87]

NeuVax is another peptide-based vaccine that has begun a phase III trial aimed at preventing or delaying the recurrence of breast cancer. It works by harnessing the patient's own immune system to seek out and attack any cells that express HER2/neu, a protein associated with tumors in breast, ovarian, pancreatic, colon, bladder, and prostate cancers. It consists of an E75 synthetic peptide initially isolated from HER2/neu proto-oncogene combined with the immune adjuvant, GM-CSF (rhGM-CSF from yeast).[88] Another group of interesting candidates as vaccination antigens are antiapoptotic proteins such as inhibitors of apoptotic signals (IAPs) and Bcl-2 because they enhance the survival of cancer cells and facilitate their escape from cytotoxic therapies.[89] The transmembrane protein mucin 1 (MUC1), a glycoprotein that is widely overexpressed in lung, breast, prostate, and colorectal cancers, has been targeted in different vaccines against NSCLC that have been clinically studied. Tecemotide (emepepimut-S, BLP25) is a synthetic lipopeptide formed by 27 amino acids, the first 25 of which are derived from the MUC1 sequence. This lipopeptide is used as the antigen in a liposomal therapeutic cancer vaccine known as Stimuvax (liposomal BLP25 vaccine,