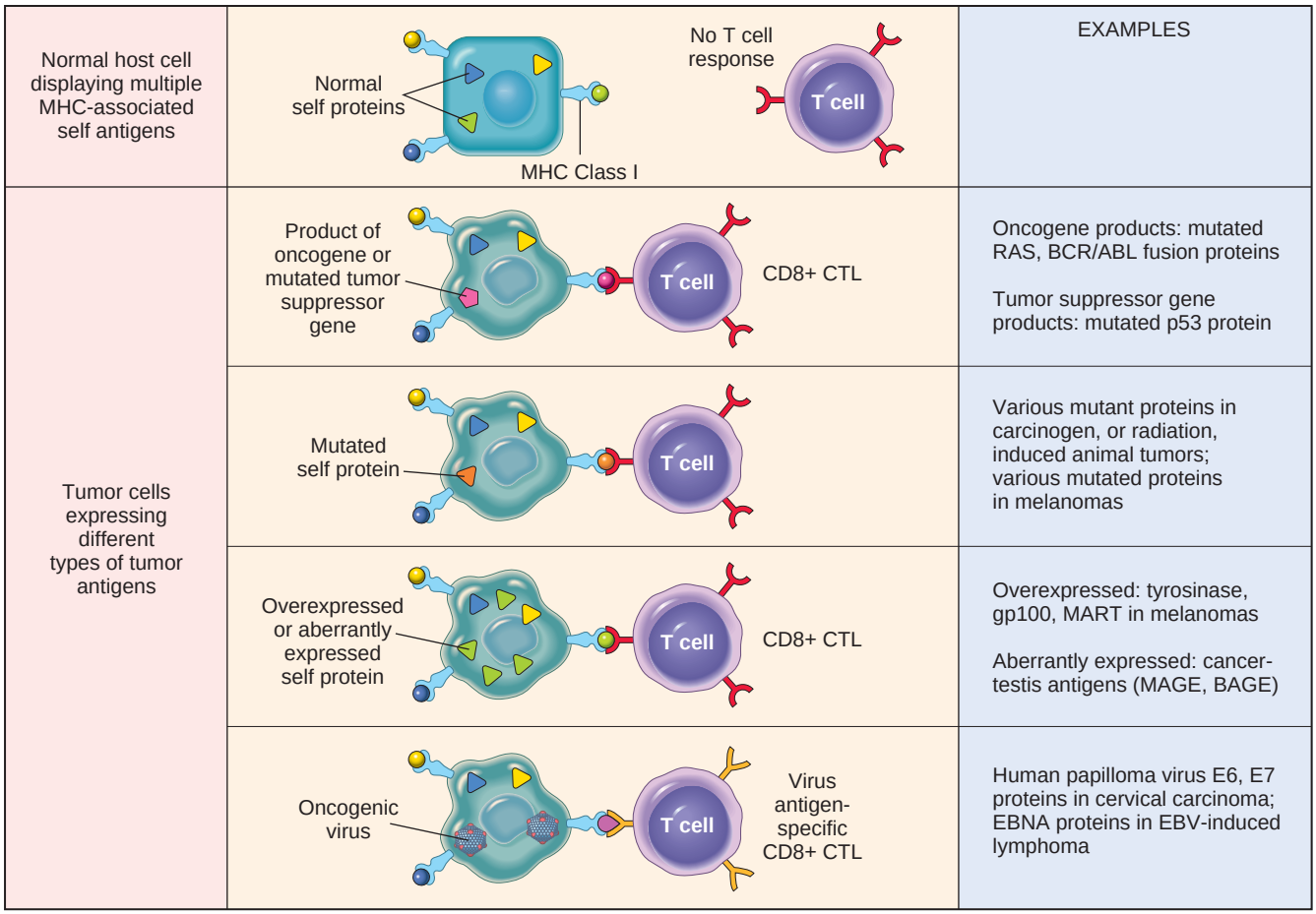

Figure 7-39 Tumor antigens recognized by CD8+ T cells. (Modified from Abbas AK, Lichtman AH: Cellular and Molecular Immunology, 5th ed. Philadelphia, WB Saunders, 2003.)

- **Overexpressed or aberrantly expressed cellular proteins.** Tumor antigens may also be normal cellular proteins that are abnormally expressed in tumor cells. One such antigen is tyrosinase, an enzyme involved in melanin biosynthesis that is expressed only in normal melanocytes and melanomas. It may be surprising that the immune system is able to respond to this normal self-antigen. The probable explanation is that tyrosinase is normally produced in such small amounts and in so few normal cells that it is not recognized by the immune system and fails to induce tolerance. Another group of tumor antigens, the *cancer-testis antigens*, are encoded by genes that are silent in all adult tissues except germ cells in the testis—hence their name. Although the protein is present in the testis it is not expressed on the cell surface in an antigenic form, because sperm do not express MHC class I antigens. Thus, for all practical purposes these antigens are tumor specific. Prototypic of this group is the melanoma antigen gene (MAGE) family. Although originally described in melanomas, MAGE antigens are expressed by a variety of tumor types. For example, MAGE-1 is expressed on 37% of melanomas and a variable number of lung, liver, stomach, and esophageal carcinomas. There are several other members of the MAGE family, variously called RAGE, GAGE, and other fanciful acronyms.
- **Tumor antigens produced by oncogenic viruses.** Several viruses are associated with cancers. Not surprisingly, these viruses produce proteins that are recognized as foreign by the immune system. The most potent of these antigens are proteins produced by latent DNA viruses; examples in humans include human papilloma virus (HPV) and Epstein-Barr virus (EBV). There is abundant evidence that CTLs recognize antigens of these viruses and that a competent immune system plays a role in surveillance against virus-induced tumors because of its ability to recognize and kill virus-infected cells. In fact, the concept of immune surveillance against tumors is best established for DNA virus-induced tumors.
- **Oncofetal antigens.** Oncofetal antigens are proteins that are expressed at high levels on cancer cells and in normal developing (fetal) tissues. Although originally believed to be completely specific for tumors and fetal tissues, as techniques for detecting these antigens have improved, it became clear that their expression in adults is not limited to tumors. Amounts of these proteins are increased in tissues and in the circulation in various inflammatory conditions, and they are even found in small quantities in normal tissues. There is no evidence that oncofetal antigens are important inducers or targets of antitumor immunity. However, oncofetal proteins