

Discovery of Gene Expressed in Many Cancers and Only Normal Testis

Published date: Feb. 1, 2012

Technology description

Large numbers of expressed sequence tags (EST's) have been cloned from various normal and cancer tissues. Cancer-testis antigens are a distinct class of differentiation antigens that have a restricted pattern of expression in normal tissues. These genes are primarily expressed in the primitive germ cells, spermatogonia, in the normal testis. Malignant transformation is often associated with activation or derepression of silent Cancer-testis genes, and this results in the expression of Cancer-testis antigen in a variable proportion of a wide range of human tumors. Three related genes, termed XAGEs, were recently identified by homology walking using the dbEST database.

The XAGE-1 gene is a human X-linked gene that is strongly expressed in normal testis, Ewing's sarcoma, alveolar rhabdomyosarcoma, as well as breast cancer and other cancers (e.g., lung carcinoma, prostate adenocarcinoma, ovarian carcinoma, pancreatic adenocarcinoma, glioblastoma, etc.). The largest open reading frame of the XAGE-1 transcript encodes a putative protein of 16.3 kD (p16) with a potential transmembrane domain at the amino terminus. In addition, the XAGE-1 transcript contains a second ATG in the reading frame corresponding to residue 66, which would encode a 9 kD protein (p9). In vitro transfection experiments using 293T cells have revealed a 9 kD protein. However, the size of the protein expressed endogenously is not yet known. XAGE-1 shares homology with GAGE/PAGE proteins in the C-terminal end.

The invention relates to the fact that the XAGE-1 gene is expressed in a number of human cancers, specifically: prostate, pancreatic, and ovarian cancers, as well as a large percentage of breast and lung tumors. The protein p9 and p16, immunogenic fragments thereof, analogs of these proteins, and nucleic acids encoding these proteins, fragments, or analogs, can be administered to persons with XAGE-1 expressing cancers to raise or augment an immune response to the cancer. The invention further provides nucleic acid sequences encoding the protein, as well as expression vectors, host cells, and antibodies to the proteins. Further, the invention provides immunoconjugates that comprise an antibody to p16 or to p9, and an effector molecule, such as a label, a radioisotope, or a toxin. The invention also provides methods of inhibiting the growth of XAGE-1 expressing cells by contacting them with immunoconjugates of an anti-p9 or p16 antibody and a toxic moiety. The invention also provides kits for the detection of p9 or p16 proteins in a sample.

Application area

The XAGE-1 gene and encoded protein could be of value in the development of a cancer diagnostic and cancer immunotherapy.

Institution

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