Epitopes for Detection of Antibodies Against Tumor Antigens

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Technology description

UCLA researchers have developed a new product for the detection, prognosis and prediction of multiple cancers based on the simultaneous detection of serum antibodies to multiple tumor-associated antigens. The method bypasses the expensive and difficult requirement for purification of individual recombinant TAA proteins by using chemically synthesized peptides of the TAA.

BACKGROUND

Detection of serum-derived antibodies against microbial antigens is routinely used for the diagnosis and prognosis of some infectious diseases. In the past 10 years, strong evidence has emerged to support the theory that the human immune system also mounts spontaneous humoral responses against autologous tumor-associated antigens (TAA). Up to now, there are at least 1800 TAA identified based on recognition by antibodies present in patients sera. These TAA include targets from many cancer types, such as melanoma, renal cancer, Hodgkins disease, esophageal cancer, lung cancer, colon cancer, gastric cancer, breast cancer, prostate cancer and so on.The discovery of these TAA awakens the old hope of finding serological markers for cancer detection, diagnosis and prognosis. However, the development of a sensitive, cost effective and comprehensive cancer diagnostic based on serological profiles to TAA has been limited by practical problems. For example, most of the antigens react with few - or no -- allogeneic sera. This indicates that an effective diagnostic for a given cancer must test for the presence of antibodies to a large number of TAA associated with that cancer. Such a test would require the recombinant production and purification of multiple TAA proteins, which is expensive and difficult to achieve. Multiplying these problems by each cancer for which a screen is desired makes developing a comprehensive test unfeasible.What is needed is a platform solution that enables the sensitive detection of serum antibodies to multiple TAA for multiple cancers.

INNOVATION

The present invention enables the creation of a new product for the detection, prognosis and prediction of multiple cancers based on the simultaneous detection of serum antibodies to multiple TAA. The method bypasses the expensive and difficult requirement for purification of individual recombinant TAA proteins by using chemically synthesized peptides of the TAA. Utilizing prediction software, researchers at UCLA have demonstrated that one can systematically and efficiently predict peptide regions on a TAA that can (1) react to antibodies in a subset of patients with a specific cancer, and (2) effectively distinguish a cancer patient from a negative control as accurately as the recombinant

TAA. This approach of using peptide fragments of TAA to detect their corresponding antibodies in a patients serum can be repeated with any number of TAA to create a panel array of synthetic peptide fragments to provide a sensitive and comprehensive test for multiple cancers.
The UCLA researchers have proven the feasibility of the approach by using their prediction software to identify a peptide fragment of NY-ESO-1, a tumor associated antigen highly expressed in different types of cancers. NY-ESO-1-specific antibodies present in the sera of patients with melanoma, prostate cancer, non-small cell lung cancer, esophageal cancer, gastric cancer, and hepatocellular carcinoma reacted with the synthetic peptide at a frequency similar to their reaction with the recombinant protein. This proof-of-principle demonstrates the feasibility of applying the same methodology to multiple TAA to create an entirely new product line of synthetic TAA fragments for the routine detection, prognosis and prediction of multiple cancers.The UCLA investigators would welcome the opportunity to collaborate with an industrial partner for the continued identification and validation of reactive fragments to other TAA. The UCLA researchers can bring to this collaboration two valuable assets: Know-how in identifying peptide fragments for use in serological detection of cancer; and access to clinical samples and clinical data in different cancer indications.
RELATED MATERIALS
Dominant B cell epitope from NY-ESO-1 recognized by sera from a wide spectrum of cancer patients: Implications as a potential biomarker. Int J Cancer. (2005)

Application area

The approach described above may be used to create an entirely new product line of a library of synthetic TAA fragments. The fragments may be combined and sold as appropriate in panels for the routine screening of multiple types of cancer by a simple serum test (requiring no more than half ml of serum). Further, specialized arrays may be sold for the periodic testing post-diagnosis to assist in the evaluation of prognosis and treatment efficacy.

Advantages

The invention provides a practical, cost-effective method for developing an entirely new product line that fills an unmet market need for a simple test for cancer screening, monitoring prognosis, and predicting progression.
The test provides a platform technology to which additional TAA peptides may be added as they become publicly available or newly identified and validated. The sensitivity and specificity for a specific cancer may be increased with the addition of more TAA for that cancer, and the array may be diversified with the addition of markers for multiple cancers.
The test uses synthetic peptides in lieu of purified recombinant TAA, thereby reducing cost and labor while increasing quality and stability of the reagents.

Peptide probes in the test give increased sensitivity since the decreased number of binding sites on the target antigens results in lower backgrounds. In addition, the peptides are flexible to be coated on most solid surfaces, e.g. gold, plastic for the development of new detection devices.
The prediction software greatly expedites the identification of the optimal fragment for the assay since large numbers of fragments that span the entire TAA do not need to be generated and tested.
By assaying for the presence of serum antibodies to TAA, the patients humoral response serves as a natural signal amplifier and therefore increases the sensitivity of the test. Further, this approach permits the non-invasive screening for TAA that are expressed only in tissues.
The principle of looking at a serological profile to an antigen has been adopted in routine serological tests for infectious agents such as Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), and HIV. Thus, it may be readily adopted for cancer screening as well.

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