

Public Lecture by Dr. Boris R. Minev
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New Views Of Cancer Vaccine Development
April 17, 2002 at 6:00 p.m. in the Garren Auditorium, Basic Science Building
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The possibility for the development of cancer vaccines was first recognized in 1893 by the New York surgeon William Coley who reported the regression of several human sarcomas following immune stimulation with a bacterial toxin. Renewed interest in cancer vaccines today is based on two recent advances which have allowed the design of more specific vaccine approaches: improved molecular techniques for the identification of target tumor-associated antigens, and better understanding of the mechanisms involved in antigen processing, presentation, and T cell activation. Among the body's potential defenses are white blood cells called cytotoxic

T lymphocytes (CTL). CTL can recognize and kill cancer cells, but only if they see complexes of protein fragments (peptides) attached to special molecules (MHC molecules) on the surface of the cancer cells. The peptide-MHC complexes are made inside the cancer cells and are then exported to the cancer cell surface. The same process occurs in a normal antigen-presenting cell of the immune system, which can stimulate CTL against the tumor. The identification of peptides derived from tumor-associated antigens (TAA) in melanoma and other cancers has been an important development in the field of tumor immunology. A variety of approaches have been used for the identification of TAA. We used several modern approaches to identify a new melanoma gene (MG50) coding for at least six antigenic peptides recognized by human cytotoxic T lymphocytes. We also reported recently the identification of two peptides from the human telomerase reverse transcriptase (hTERT). We demonstrated in this study that the hTERT-specific CTL of normal individuals and patients with prostate cancer specifically lysed a variety of cancer cell lines, suggesting the existence of precursor CTL for hTERT in both healthy individuals and in cancer patients. Since telomerase activity is increased in the vast majority of human tumors, our findings could contribute to the generation of universal telomerase-based cancer vaccines.

Recently several peptides specific for human cancer cells have been discovered. Unfortunately most attempts to treat patients with cancer with these peptides have not yet been successful. One major reason may be that the peptides have not been able to reach the specific part of the cell where they associate with the MHC molecules. We developed "signal sequence" protein fragments, which can bring the cancer-specific peptides exactly to the part of the cell where MHC-peptide complexes are formed. We were the first to demonstrate that mice immunized with a vaccine composed of signal sequences attached to peptides could reject their experimental tumors and survive. More recently, we found that the addition of signal sequences to a peptide from the human melanoma antigen MART-1 greatly enhances its efficiency as a vaccine.

This lecture summarizes the most recent findings and the future directions in designing cancer vaccines. The most promising approaches to cancer vaccine development and the possible clinical applications of the new vaccines will be discussed.

