Vaccinating Against Cancer

By Meghan Delmastro-Greenwood, Ph.D.

Vaccinations provide the immune system with the necessary education to battle and defend the body against specific targets, called antigens. Each immunization stimulates the immune response and establishes memory to protect against subsequent infections. Although the majority of current vaccines target infectious diseases, extending this technology to battle cancer is a rapidly advancing area of research.

Tumor-targeting, antigen-based vaccines range in composition from peptides to DNA. Peptide-based vaccines directly deliver peptides (small pieces of proteins) derived from tumor antigens to promote a specific immune response against the cancer. In contrast, in DNA-based vaccines, host cells take up plasmid DNA (short loops of DNA). These cells then use the DNA to produce cancer-specific proteins, which are then expressed on the surface of cells. These proteins cause the immune system to regard the cells as foreign and consequently attack the cells along with the tumor area. Therefore, both methods hold promise for prophylactically and therapeutically treating cancer.

In the past year, several studies have investigated the potential use of tumor vaccines in various cancers. Peptide vaccines emerged as a method to incorporate specific cancer antigens, similar to infectious disease vaccination. However, because of the need for combinatorial stimulation of the immune cells, it is often necessary to utilize adjuvants and/or other treatments (i.e. cytokines, chemotherapy, antibodies) to promote the most effective peptide-based immunization. For example, in patients with advanced colorectal cancer, a peptide-cocktail immunization accompanied with chemotherapy increased patient survival, particularly when the stimulated immune cells were specific for both antigens present in the cocktail (1). Additionally, the use of peptide mimotopes, which mimic inherent tumor antigens, in association with natural cancer antigens can expand tumor-specific T cells and boost tumor clearance (2).

Unlike peptide-based vaccines, immunizations with DNA plasmids allow for prolonged tumor-specific responses, as plasmids are not as rapidly cleared from the body as peptides. In a model of metastatic melanoma, DNA-based vaccines effectively enhanced cytotoxic T cells, which are critical for killing cancerous cells (3). Similarly, injection of plasmids encoding HER2/neu-coding DNA plasmids protected mice against tumor growth (4). This type of strategy can be used prophylactically in breast cancer, for example, as HER2/neu is well-established as a biomarker of disease development and therapeutic target.

Though tumor vaccines are currently being used in both mouse models and advanced stages of cancer, several challenges exist. First, tumor vaccines, whether they be peptide or DNA-based, must target specific tumor antigens. Not all tumor antigens will stimulate the immune system; hence the need for appropriate combinatorial therapies and potent adjuvants. Second, the early identification of cancer biomarkers is necessary to generate prophylactic vaccines. Established tumors require powerful immune responses, and current vaccine strategies may not be robust enough to eliminate ongoing cancers. Pretreatment of high-risk individuals may thus be a better method for preventing tumor development. Lastly, like any vaccine, enduring protection against tumors is difficult. Incorporating different immunization doses, strategies, and locations alone or in combination with other drugs may become the most efficacious vaccine. Nonetheless, cancer vaccines remain a heavy research interest and will continue to progress in an effort to be used in a variety of patients, regardless of cancer duration or type.

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References

1. Sugiura F, Inoue K, Okuno K, Sukegawa Y: [Clinical study of Peptide-cocktail vaccination with tegafur-uracil/leucovorin for advanced colorectal cancer]. Gan To Kagaku Ryoho 2012;39:1760-1762
2. Buhrman JD, Jordan KR, U'Ren L, Sprague J, Kemmler CB, Slansky JE: Augmenting Antitumor T-Cell Responses to Mimotope Vaccination by Boosting with Native Tumor Antigens. Cancer Res 2012
3. Kang TH, Mao CP, La V, Chen A, Hung CF, Wu TCP: Innovative DNA Vaccine to Break Immune Tolerance against Tumor Self-Antigen. Hum Gene Ther 2012
4. Nguyen-Hoai T, Kobelt D, Hohn O, Vu MD, Schlag PM, Dorken B, Norley S, Lipp M, Walther W, Pezzutto A, Westermann J: HER2/neu DNA vaccination by intradermal gene delivery in a mouse tumor model: Gene gun is superior to jet injector in inducing CTL responses and protective immunity. Oncoimmunology 2012;1:1537-1545