The challenges of cancer vaccines

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The first therapeutic cancer vaccine has now been approved by the FDA, and a diverse range of therapeutic cancer vaccines directed against a spectrum of tumor-associated antigens are currently being evaluated in clinical trials, according to a review published March 6 in the *Journal of the National Cancer Institute*.

The tumor microenvironment and other immunosuppressive entities can potentially limit the efficacy of vaccines. To counteract this, the use of vaccines with immune checkpoint inhibitors, certain chemotherapeutics and small-molecule targeted therapies, and radiation is being evaluated both in preclinical and clinical studies.

A detailed review by Jeffrey Schlom, Ph.D., of the Laboratory of Tumor Immunology and Biology at the Center for Cancer Research at the National Cancer Institute, outlines the diverse vaccine platforms currently being evaluated preclinically and in randomized phase II and phase III clinical trials. Vaccines were initially evaluated in patients with metastatic disease who had already undergone multiple therapies. But clinical studies have now begun showing that patients will respond better to vaccines when they have been treated with fewer chemotherapeutic regimens and a longer time has elapsed since their last chemotherapy treatment.

The author adds that one of the most intriguing targets for vaccine therapy are molecules linked with cancer "stem cells" or to the epithelial-mesenchymal transition (EMT) process, phenomena which are both associated with drug resistance.

The author writes that the future of therapeutic cancer vaccines will include combination therapies with a range of therapeutic modalities and that current and future clinical trial designs will be comprised of patients with more indolent metastatic disease and treatment in the adjuvant or neoadjuvant settings. "As the long-term safety profiles of therapeutic vaccines are established, they most probably will be used in patients with a high risk of cancer, such as in patients with high-grade prostatic intraepithelial neoplasia who are at risk for the development of prostate cancer, and familial adenomatous polyposis patients who are at risk for the development of colorectal cancer," Schlom writes. "Numerous studies have demonstrated that analysis of the immune infiltrate in colorectal and other cancer biopsies before chemotherapy can serve as a strong independent prognostic indicator for survival."

He adds that insight into the EMT phenotype and genetic mutations of cancer cells are now revealing new targets for cancer vaccines.

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