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Cancer vaccines: methods for inducing immunity

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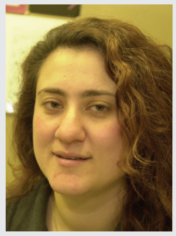

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"Currently, great emphasis for tumor immunotherapy is based predominantly on genetic engineering techniques, which have made the difficult/impossible techniques a reality, and successful tumor immunotherapy is now a realistic goal."

There is an active interest in tumor immunotherapy. Studies over 35 years ago involving tumor cell lysates with or without adjuvant have now re-emerged, and patients have been shown to generate immune responses to tumor antigens. Currently, great emphasis for tumor immunotherapy is based predominantly on genetic engineering techniques, which have made the difficult/impossible techniques a reality, and successful tumor immunotherapy is now a realistic goal. Several tumor antigens have been identified (e.g., melanoma antigens, p53, MUC1, Her2/neu, carcinoembryonic antigen and polysaccharides) that can be produced in large amounts by recombinant techniques, either as fusion proteins in bacterial or other systems, or as soluble molecules in eukaryotic systems. Furthermore, synthetic peptides can be made to parts of the tumor antigen that are presented by either class I or class II MHC molecules. Cytokines have been described and there is much more knowledge of how the immune system functions, in particular how cellular immune responses are generated and how peptides can be presented by class I or class II molecules. This knowledge has led to the peptide approach to tumor immunotherapy. Dendritic cells (DCs) have also emerged and have been shown to play a central role in generating immune responses in patients with cancer. Various other methods have also been applied for the generation of optimal immune responses, such as DNA vaccines, combination gene therapy, hybrid cell vaccination, tumor cell vaccination and cell-free vaccines. In addition, there are several methods of measuring cellular immunity: cytotoxic T lymphocyte, T-cell proliferation (including more quantitative carboxyfluorescein succinimidyl ester assays), intracellular and extracellular cytokine production by cells in culture using either ELISA or multiplex and flow cytometry and, more recently, polyfunctional T-cell assays, ELISPOT and MHC class I/II tetramers to follow immune activation. Thus, there is an enormous amount of information and reagents available for guiding vaccine development in the context of cancer immunotherapy.

This special issue on cancer vaccines focuses on a number of recent and promising approaches used for applying cancer vaccines in the context of immune therapy. These include:

- Tumor cell fusions (Gong and colleagues)
- Antigen delivery by targeting C-type lectin receptors expressed by DCs (Pietersz and colleagues)
- DC-based cancer vaccines (Dauer and colleagues)
- Multiepitope approaches for a p53-based vaccine (DeLeo and Whiteside)
- Use of modified Ankara virus-based vaccines (Acres and Bonnefoy)
- Use of heat-shock proteins as tumor vaccines (Calderwood and colleagues)
- Targeting cytochrome p450 CYP1B1 (Luby)
- Use of *Listeria monocytogenes* as a novel cancer vaccine platform (Brockstedt and Dubensky)
- Use of particulate-based vaccines to deliver antigens (Plebanski and colleagues)

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In addition, there are a number of reviews that focus on other vaccine aspects, which include:

- Recent vaccine therapies for renal cancer (Amato)
- EGFRvIII as a novel target for tumor immunotherapy studies (Li and Wong)
- MUC1 as a target for tumor immunotherapy and methods used in animal models and in human clinical trials (Apostolopoulos and colleagues)
- Immunotherapy for HCV (Lang and Weiner)
- Melanoma-based vaccines (Riley and Agarwala)
- DNA-based vaccines (Bodles-Brakhop and Draghia-Akli)
- Carcinoembryonic antigen-based vaccines (Marshall and colleagues)
- Telomerase-based cancer vaccines (Beatty and Vonderheide)
- Human papillomavirus-based vaccines (Insinga and colleagues)

There is a plethora of information available to explore the development of novel immunization approaches for cancer. Collectively, this information will allow more rational advancement in understanding the immune effects of a particular immunization strategy and promote a greater understanding of the role of specific immune induction to impact a particular cancer phenotype. Ultimately, a combination of these new immunization strategies, the determination of tumor antigens and the use of newer immune-monitoring tools, as described in this issue, will serve to improve immunizations as adjunctive strategies for the treatment of cancer or as vaccines to prevent cancer development in high-risk populations.