Cancer Nanovaccine

Xiaoyuan (Shawn) Chen

Center for Nuclear Medicine and Molecular Imaging (CNMMI), Shandong Cancer Hospital and Institute, Shandong First Medical University and Shandong Academy of Medical Sciences

The fundamental mechanisms regulating immune activation and tolerance have laid the foundational groundwork for modern cancer immunotherapy. Harnessing these principles, the field has revolutionized oncology, with strategies aimed at unleashing a potent and durable antitumor immune response. Among these, tumor vaccines represent a promising modality designed to prime the immune system against tumor-specific or tumor-associated antigens. Here we provide a comprehensive analysis of the evolving landscape of tumor vaccines, encompassing a wide array of platforms including peptide-based vaccines, dendritic cell (DC) vaccines, viral vector-based vaccines, nucleic acid (DNA and RNA) vaccines, and whole-cell vaccines. We critically examine their mechanisms of action, and the challenges that have limited their widespread clinical success, such as tumor heterogeneity, insufficient antigen delivery, and immunosuppressive microenvironments. In addition, a paradigm shift is emerging with strategies to generate tumor-associated antigens (TAAs) directly within the tumor microenvironment (TME), which bypasses the need for predefined antigens and leverages the patient's complete and personalized antigen repertoire. We explore innovative methods for *in situ* TAA generation, including immunogenic cell death (ICD) inducers (*e.g.*, phototherapy, and certain chemoradiotherapies), which release tumor antigens in an immunostimulatory context. Furthermore, we discuss the role of *in situ* vaccination through intratumoral delivery of pattern recognition receptor agonists (e.g., TLR, STING agonists) and engineered vectors that trigger localized tumor destruction and antigen presentation. By integrating critical insights from both classic vaccine strategies and *in situ* vaccination techniques, we aim to chart a path toward the next generation of highly personalized and effective cancer immunotherapies.