Preclinical Study of PD1-based TWIST1 Vaccination Approach – Promoting its Translation into Clinical Use

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Objectives:

1. Use electroporation to deliver the human PD-1-based TWIST1 tumor antigen vaccine (huPD1-TWIST1) vaccine and evaluate its immunogenicity and antitumor activity in mouse models; and
2. Establish a nanoparticle-mediated in-vivo vaccine delivery system.

Background:

Previous study by the research institution highlighted the advantages of using adeno-associated viruses as vectors to deliver soluble PD-1 protein-TWIST1 (sPD1-TWIST1) vaccines in inducing tumor-specific killing cells. This research project aims to explore the characteristics of huPD1-TWIST1 in inducing tumor-specific killing cells. This research project would utilize a PD-1-enhanced DNA vaccine technology for the treatment of human mesothelioma. This is a targeted therapy specifically targeting dendritic cells, utilizing a DNA vector encoding the specific tumor antigen TWIST1 protein, which is fused with sPD1. When PD-1 binds to the PD-1 ligand (PD-L1) on dendritic cells, it can effectively deliver tumor antigens to dendritic cells and trigger the secretion of the cell signaling molecule IL-12 and induce a strong TWIST1-specific CD8+ T cell immune response against mesothelioma.

Methodology:

1. Delivered huPD1-TWIST1 vaccine into mice using electroporation and investigated its immunogenicity and efficacy.
2. Explored different DNA/RNA vaccine delivery systems to replace electroporation.

Impact:

If the research results are positive, the research institution might launch a clinical trial to demonstrate the efficacy of the sPD1-TWIST1 vaccine in patients with mesothelioma.

Result and Conclusion:

1. Administration of the vaccine inhibited the growth of mouse mesothelioma. Vaccination with the huPD1-TWIST1 vaccine or its derivative enhanced TWIST1-specific T cell responses in mice models. Combination therapy with a CTLA-4 antibody significantly improved therapeutic efficacy, achieving 50-80% tumor-free survival.
2. An in-house lipid nanoparticles delivery platform has been established to deliver the vaccines effectively.