Autologous CT7/MAGE-A3/WT1 mRNA-Electroporated Langerhans-Type Dendritic Cells

National Cancer Institute

Source

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An autologous tumor cell vaccine containing CD34+ hematopoietic progenitor cell (HPC)-derived Langerhans-type dendritic cells (LCs) electroporated with mRNA encoding the full-length cancer-testis antigens, CT7 and melanoma-associated antigen 3 (MAGE-A3), and the self-differentiation tumor antigen, Wilms tumor 1 (WT1) with potential immunomodulating and antineoplastic activity. The autologous CT7/MAGE-A3/WT1 mRNA-electroporated Langerhans-type dendritic cells are prepared by drawing a blood sample containing the CD34+ HPCs from a cancer patient. The CD34+ HPCs are treated with a combination of cytokines which specifically support LC development, and the LC population is enriched and expanded ex vivo. The cultured LCs are allowed to mature for one day and then electroporated separately with CT7, MAGE-A3 or WT1 mRNA before final maturation. Upon intradermal administration into the patient, the mature LCs may activate cell-mediated immunity and induce both cytotoxic CD8+ T cells and CD4+ helper T cells against cancer cells expressing CT7, MAGE-A3 and WT1 tumor antigens. This may result in the immune-mediated inhibition of tumor cell proliferation, leading to tumor cell death. CT7 and MAGE-A3 are tumor-specific proteins overexpressed in a number of cancers but not in healthy tissues other than testis and placenta. WT1 is a transcription factor important in development and cancer pathogenesis, which is overexpressed in a variety of cancers, including multiple myeloma, leukemia, ovarian cancer, malignant mesothelioma, neural tumors and renal carcinoma.