

DLK1/EPHA2/HBB/NRP1/RGS5/TEM1 Peptide-pulsed Alpha-type-1 Polarized Dendritic Cell Vaccine

National Cancer Institute

Source

National Cancer Institute. *DLK1/EPHA2/HBB/NRP1/RGS5/TEM1 Peptide-pulsed Alpha-type-1 Polarized Dendritic Cell Vaccine*. NCI Thesaurus. Code C113807.

A cell based cancer vaccine composed of mature polarized dendritic cells (alphaDC1) pulsed with six human leukocyte antigen (HLA)-A2-presented tumor blood vessel antigen (TBVA)-derived peptides, with potential immunostimulatory and antineoplastic activities. Dendritic cells (DCs) were treated with a "type-1 polarizing cytokine cocktail", including interleukin-1beta, tumor necrosis factor alpha (TNF-a), interferon-alpha (IFN-a), IFN-gamma and polyinosinic:polycytidylic acid (pl:C) to produce mature alpha type-1 polarized DCs (alphaDC1) that are capable of producing high levels of interleukin-12p70 (IL-12p70). The alphaDC1 are subsequently pulsed with TBVA-derived peptides, including delta-like homologue 1 (DLK1) 310-318, EPH receptor A2 (EPHA2) 883-891, beta-globin (HBB) 31-39, neuropilin-1 (NRP1) 433-441, regulator of G-protein signaling 5 (RGS5) 5-13 and tumor endothelial marker 1 (TEM1) 691-700. Upon administration, these DCs are able to induce a potent cytotoxic T-lymphocyte (CTL) response against the TBVAs expressed on tumor-associated stromal cells, which results in stromal cell lysis and inhibition of angiogenesis. Disrupting the surrounding tumor vasculature inhibits tumor cell growth and survival. alphaDC1 are able to induce a potent tumor antigen-specific CTL response due to their high co-stimulatory activity and the secretion of anti-cancer cytokines, such as IL-12p70.