Adenovector-transduced AP1903-inducible MyD88/CD40-expressing Autologous PSMA-specific Prostate Cancer Vaccine BPX-201

National Cancer Institute

Source

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A genetically-modified, dendritic cell-based (DCs) vaccine in which the autologous cells are transduced with an adenoviral vector expressing the tumor antigen prostate-specific membrane antigen (PSMA) and a fusion protein composed of synthetic ligand inducible adjuvant iMC composed of a drug-inducible costimulatory CD40 receptor (iCD40) and the adaptor protein MyD88, with potential immunomodulating and antineoplastic activities. The iCD40 contains a membrane-localized cytoplasmic CD40 domain fused to the FK506 modified drug-binding protein 12 (FKBP12). Upon intradermal administration of BPX-201, these DCs accumulate in local draining lymph nodes. Twenty-four hours after vaccination, the dimerizing agent AP1903 is administered. AP1903 binds to the drug binding domain, leading to iMC oligomerization and activation of iCD40 and MyD88-mediated signaling in iMC-expressing DCs. This signaling pathway activates the DCs and stimulates a cytotoxic T-lymphocyte (CTL) response against host tumor cells that express PSMA. PSMA, a glycoprotein secreted by prostatic epithelial and ductal cells, is overexpressed in prostate cancer cells and is used as a tumor marker for both diagnosis and treatment evaluation. MyD88 is involved in interleukin 1 receptor (IL1R) and toll-like receptor (TLR) signaling.