Oncolytic Herpes Simplex Virus-1-encoding GM-CSF

National Cancer Institute

Source

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An ICP34.5-, ICP47-deleted, oncolytic herpes simplex type-1 virus (HSV-1) isolated from the mouth of an HSV-1-infected patient of Chinese Han ethnicity, and encoding the immunostimulating factor cytokine granulocyte-macrophage colony stimulating factor (GM-CSF) with potential immunostimulating and antineoplastic activities. Upon administration, the recombinant human GM-CSF HSV-1 selectively infects and replicates in tumor cells, thereby inducing tumor cell lysis. In addition, GM-CSF attracts dendritic cells (DCs) and may stimulate a cytotoxic T cell response against tumor cells, which results in immune-mediated tumor cell death. Deletion of the gene encoding for ICP34.5 provides tumor selectivity and prevents replication in healthy cells. As ICP47 blocks antigen presentation in HSV-infected cells, deletion of this gene may induce a more potent antitumor immune response in the tumor cells. Additionally, deletion of ICP47 causes increased expression of the HSV US11 gene and allows US11 to be expressed as an immediate early and not a late gene. This further enhances the degree of viral replication and oncolysis of tumor cells. Interruption of the ICP6 gene, which encodes the large subunit of the viral ribonucleotide reductase, in the viral vector also enhances selective replication in tumor cells.