

Differential Infection of Primary Human B-Cells and EBV Positive B-Lymphoma Cell Lines by Recombinant AAV Serotypes

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Abstract : B-cell proliferative disorders often occur among persons that are T-cell compromised. These disorders are primarily EBV+ and can first present with a focal lesion. Direct introduction of oncolytic viruses into localized tumors provides theoretical advantages over chemotherapy and immunotherapy by reducing systemic toxicity, to which the immunocompromised host is most vulnerable. Widely studied as a vehicle for gene therapy, AAV has only rarely been applied to treat cancer. As a prelude to development of a therapeutic vehicle, we assessed the ability of 15 distinct recombinant AAV serotypes (rAAV1, rAAV2, rAAV3b, rAAV4, rAAV5, rAAV6, rAAV6.2, rAAV6TM, rAAV7, rAAV8, rAAVrh8, rAAV9, rAAVrh10, rAAV39, rAAV43) bearing eGFP to infect human B-cell tumor lines compared with primary B-cells in vitro. Enhanced infection of tumor lines by AAV 6.2 was demonstrated by flow cytometry. EBV superinfection of EBV negative B-cell tumor lines increased susceptibility to AAV6.2 infection. As proof of concept, AAV6.2 bearing HSV-1 thymidine kinase in place of eGFP eliminated tumor cells upon exposure to ganciclovir.

Keywords : AAV, gene therapy, lymphoma, malignancy, tropism

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