Modifying Oncolytic Adenovirus for Osteosarcoma Treatment

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Osteosarcoma, most commonly found in children, originates in the bones and spreads throughout the body over time. Over the last 30 years, the mortality rate for osteosarcoma has not improved, so new treatments are needed. Due to the similarities between human and canine osteosarcoma, cancer immunotherapy treatment concepts used for canines, such as oncolytic adenoviruses, may be applied to improve treatment in humans further. Oncolytic adenovirus CAV2-AU-M2 can infect and kill canine osteosarcoma cells. Additionally, it produces and secretes anti-PD-1 sdAb (single domain antibody) upon cell lysis. Anti-PD-1 sdAb stimulates the immune system in the tumor microenvironment (TME) by reversing T-cell deactivation. However, the cell lysis and, thus, secretion of anti-PD1 sdAb is limited in cells infected with CAV2-AU-M2 due to the depletion of the E3 gene in the adenovirus. Therefore, CAV2-AU-M3, an enhanced oncolytic canine adenovirus, is being developed to resolve this issue. Fc-conjugated anti-PD1 HcAb with a secretory signal is inserted between fiber and E4 in CAV2-AU-M3. Along with our viruses' cytolytic and infective properties, we also aim to analyze their ability to kill cancer stem cells, thus reducing metastasis. Before assaying the viruses for stem cell killing, we must identify stem cell populations in our model of canine osteosarcoma cell lines. We do this by assaying the expression of stem cell marker mRNA in canine osteosarcoma cell lines. Based on the data, we can determine whether they can be used in tumor spheroid formation assays to characterize the oncolytic virus's ability to kill stem cells.

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