Oncolytic Activity of Engineered Adenovirus Ad-TERT in Glioblastoma Multforme

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Glioblastoma multiforme (GBM), a grade IV astrocytoma, has an elevated level of hTERT. Ad-TERT, a promising oncolytic adenovirus type 5 variant where E1A regulating components have been replaced with hTERT promoter, is engineered to advantage of differential hTERT activity. E1A gene products are necessary for viral replication, so regulating E1A activity aids in improving targeting of and viral reproduction in cancer cells while passing over noncancerous ones. While the Ad-TERT and wild-type adenovirus type 5 have been found in other cancers to have similar cytotoxic effects in tumor cells, Ad-TERT has been found to be significantly less cytotoxic to normal cells, displaying increased selectivity for replication in tumor cells. Ad-TERT shows great promise as a better oncolytic virotherapy, yet it has not yet been investigated in GBM. The inadequacy of conventional and burgeoning treatments in GBM necessitates a new, effective treatment. GBM's increased hTERT activity indicates that Ad-TERT could be more successful than the wild type virus in targeting and destroying tumor cells. Astrocyte and GBM cells were infected with both normal adenovirus type 5 and Ad-TERT. Comparison of oncolytic activity was determined through quantifying E1A gene product levels with in-cell ELISA, and E1A protein levels were found to be significantly lower in astrocytes infected with Ad-TERT ($p<0.05$). A fluorescent cytotoxicity assay found a significantly increased percentage of dead cells in astrocytes infected with Ad-Null when compared with controls and Ad-TERT ($p<0.05$). Ad-TERT was found to improve targeting and killing of glioblastoma cancer cells only.

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