ABSTRACT

Neuroblastoma (NB) is a primary malignant tumor of the peripheral sympathetic nervous system. High-risk NB is characterized by *MYCN* amplification and human telomerase reverse transcriptase (*hTERT*) rearrangement, contributing to hTERT activation and poor outcome. For targeting hTERT-activated tumors, we developed two oncolytic adenoviruses, OBP-301 and tumor suppressor p53-armed OBP-702, in which the hTERT promoter drives expression of the viral *E1* gene for tumor-specific virus replication. Here, we demonstrate the therapeutic potential of the hTERT-driven oncolytic adenoviruses OBP-301 and OBP-702 using four human MYCN-amplified NB cell lines (IMR-32, CHP-134, NB-1, LA-N-5) exhibiting high hTERT expression. OBP-301 and OBP-702 exhibited a strong antitumor effect in association with autophagy in NB cells. Virus-mediated activation of E2F1 protein suppressed MYCN expression. OBP-301 and OBP-702 significantly suppressed the growth of subcutaneous CHP-134 tumors. Thus, these hTERT-driven oncolytic adenoviruses are promising antitumor agents for eliminating MYCN-amplified NB cells via E2F1-mediated suppression of MYCN protein.