ABSTRACT

Pancreatic ductal adenocarcinoma (PDAC) have an exceptional ability to invade nerves through pronounced crosstalk between nerves and cancer cells; however, the mechanism of PDAC cell invasion remains to be elucidated. Here, we demonstrate the therapeutic potential of telomerase-specific oncolytic adenoviruses, OBP-301 and tumor suppressor p53-armed OBP-702, against human PDAC cells. Highly invasive PDAC cells exhibited higher levels of phosphorylated ERK1/2 expression independent of KRAS expression; ERK1/2 inhibitor or siRNA treatment significantly reduced the migration and invasion of PDAC cells, suggesting that the ERK signaling pathway is associated with the invasiveness of PDAC cells. OBP-702 infection suppressed ERK signaling and inhibited PDAC cell migration and invasion more efficiently than OBP-301. OBP-702 also effectively inhibited PDAC cell invasion even when invasiveness was enhanced by administration of motility stimulators, such as nerve and neurosecretory factors. Moreover, noninvasive whole-body imaging analyses showed that OBP-702 significantly suppressed tumor growth in an orthotopic PDAC xenograft model, although both viruses were equally effective against subcutaneous tumors, suggesting that OBP-702 can influence the orthotopic tumor microenvironment. Our data suggest that oncolytic virus–mediated disruption of ERK signaling is a promising antitumor strategy for attenuating the invasiveness of PDAC cells.