Abstract

Immune checkpoint inhibitors, including anti-programmed cell death 1 (PD-1) antibody, provide improved clinical outcome in certain cancers. However, pancreatic ductal adenocarcinoma (PDAC) is refractory to PD-1 blockade therapy due to poor immune response. Oncolytic virotherapy is a novel approach for inducing immunogenic cell death (ICD). We demonstrated the therapeutic potential of p53-expressing telomerase-specific oncolytic adenovirus OBP-702 to induce ICD and antitumor immune responses in human PDAC cells with different p53 status (Capan-2, PK-59, PK-45H, Capan-1, MIA PaCa-2, BxPC-3) and murine PDAC cells (PAN02). OBP-702 significantly enhanced ICD with secretion of extracellular adenosine triphosphate and high-mobility group box protein B1 by inducing p53-mediated apoptosis and autophagy. OBP-702 significantly promoted the tumor-infiltration of CD8+ T cells and the antitumor efficacy of PD-1 blockade in a subcutaneous PAN02 syngeneic tumor model. Our results suggest that oncolytic adenovirus–mediated p53 overexpression augments ICD and the efficacy of PD-1 blockade therapy against cold PDAC tumors. Further *in vivo* experiments would be warranted to evaluate the survival benefit of tumor-bearing mice in combination therapy with OBP-702 and PD-1 blockade.