Abstract

Pancreatic cancer (PC) is a highly aggressive malignancy with limited treatment options and poor prognosis. Carcinoembryonic antigen-related cell adhesion molecule 6 (CEACAM6) protein is abundantly expressed in PC cells and has been linked to tumor growth and metastasis. This research intends to provide insights into the cytotoxic effect of the CEACAM6-mediated targeted therapy using anti-CEACAM6 heavy-chain antibody (HCAb) and secondary-ADC (2°Ab-MMAE) by distinguishing the morphological changes and examining the viability of PC cell line AsPC-1 using MTT assay. Based on the result, it can be deduced that the HCAb successfully internalized the 2°Ab-MMAE as it showed dose-dependent killing effects denoted by cell shrinkage, cell blebbing, and fragmentation into membrane-bound apoptotic bodies. The concentrations of HCAb (0.001, 0.01, 0.1, 1, 10, and 20 nM) resulted in 0.41 ± 0.11, 0.67 ± 0.06, 0.63 ± 0.07, 0.32 ± 0.10, 0.22 ± 0.04, and 0.23 ± 0.03% viable cells, respectively. The half maximal inhibitory concentration (IC_{50}) of HCAb/2°Ab-MMAE was determined to be approximately 0.57 nM, following 96 hrs of drug exposure. An anomaly outcome with an unknown fault was detected at 0.001 nM HCAb. Anti-CEACAM6 HCAb can nevertheless represent a feasible therapeutic strategy for targeted therapy in PC. Further investigations are needed to rectify the deviation and refrain from misleading conclusions by the replication of the MTT assay.

Keywords: pancreatic cancer, CEACAM6, ADC, HCAb, 2°Ab-MMAE