

Zebularine and trichostatin A sensitized human breast adenocarcinoma cells towards tumor necrosis factor-related apoptosis inducing ligand (TRAIL)-induced apoptosis

ABSTRACT

Tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) is a promising cancer therapeutic agent due to its selective killing on cancer cells while sparing the normal cells. Nevertheless, breast adenocarcinoma cells can develop TRAIL resistance. Therefore, this project investigated the anti-cancer effects of the combination of epigenetic drugs zebularine and trichostatin A (ZT) with TRAIL (TZT) on the human breast adenocarcinoma cells. This treatment regimen was compared with the natural anti-cancer compound curcumin (Cur) and standard chemotherapeutic drug doxorubicin (Dox). As compared to TRAIL treatment, TZT treatment hampered the cell viability of human breast adenocarcinoma cells MDA-MB-231 significantly but not MCF-7 and immortalized non-cancerous human breast epithelial cells MCF10A. Unlike TZT, Cur and Dox treatments reduced cell viability in both human breast adenocarcinoma and epithelial cells significantly. Nevertheless, there were no changes in cell cycle in both TRAIL and TZT treatments in breast adenocarcinoma and normal epithelial cells. Intriguingly, Cur and Dox treatment generally induced G2/M arrest in MDA-MB-231, MCF-7 and MCF10A but Cur induced S phase arrest in MCF10A. The features of apoptosis such as morphological changes, apoptotic activity and the expression of cleaved poly (ADP) ribose polymerase (PARP) protein were more prominent in TRAIL and TZT-treated MDA-MB-231 as compared to MCF10A at 24 h post-treatment. Compared to TZT treatment, Cur and Dox treatments exhibited lesser apoptotic features in MDA-MB-231. Collectively, the sensitization using Zeb and TSA to augment TRAIL-induced apoptosis might be an alternative therapy towards human breast adenocarcinoma cells, without harming the normal human breast epithelial cells.

Keyword: Cell biology; Epigenetics; Cancer research; Tumour necrosis factor-related apoptosis inducing ligand (TRAIL); Zebularine; Trichostatin A; Breast cancer; Apoptosis