PUMA gene transfection can enhance the sensitivity of epirubicin-induced apoptosis of MCF-7 breast cancer cells

C.-G. Sun1*, J. Zhuang1*, W.-J. Teng1, Z. Wang2 and S.-S. Du3

1Department of Oncology, Weifang Traditional Chinese Hospital, Weifang City, Shandong, China
2Xi Yuan Hospital of the China Academy of Chinese Medical Sciences, Beijing, China
3Beijing Normal University, Beijing, China

*These authors contributed equally to this study.
Corresponding authors: Z. Wang/ S.-S. Du
E-mail: wangzhong_w@163.com / dushushan_dss@yeah.net

Received July 3, 2014
Accepted December 5, 2014
Published May 29, 2015
DOI http://dx.doi.org/10.4238/2015.May.29.6

ABSTRACT. We explored whether p53 upregulated modulator of apoptosis (PUMA) gene transfection could enhance the sensitivity of epirubicin-induced apoptosis of MCF-7 breast cancer cells. The liposome-mediated recombinant eukaryotic expression vector PU-MA-pCDNA3 and empty vector plasmid were stably transfected into MCF-7 cells. Epirubicin (0.01-100 μM) was applied to MCF-7, MCF-7/PUMA, and MCF-7/pCDNA3 cells for 72 h. The MTT assay was used to calculate the cell survival rate in each group, and the 50% inhibitory concentration (IC50) was calculated. The IC50 values of epirubicin in MCF-7, MCF-7/PUMA, and MCF-7/pCDNA3 cells were 13 ± 1.4, 1.8 ± 0.2, and 10.7 ± 1.3 μM, respectively. The sensitivity of MCF-7/PUMA cells to epirubicin increased 7.2-fold. Epirubicin-induced apoptosis in MCF-7 cells dose-dependently, but MCF-7/PUMA cell-induced apoptosis was more significant compared to controls. Low
concentrations of epirubicin (0.1 μM) caused low levels of apoptosis of MCF-7/pCDNA3 (1.15 ± 0.26%) and MCF-7 cells (0.9 ± 0.24%), but significantly induced apoptosis of MCF-7/PUMA cells (6.44 ± 1.46%). High epirubicin concentration (1 μM) induced apoptosis in each group, but the epirubicin MCF-7/PUMA apoptosis rate (35.47 ± 9.36%) was significantly higher than that of MCF-7 (12.6 ± 3.73%) and MCF-7/pCDNA3 (15.2 ± 5.17%) cells (P < 0.01). Flow cytometry and TUNEL assays for apoptosis detection showed similar results. PUMA protein expression in MCF-7/PUMA cells was significantly higher than that in MCF-7 and MCF-7/pCDNA3 cells by Western blot analysis. Therefore, stable transfection of PUMA can significantly enhance epirubicin-induced apoptosis sensitivity of MCF-7 breast cancer cells.

**Key words**: PUMA gene; Breast cancer; MCF-7 cells; Apoptosis