Enhancement of radio-sensitization in prostate cancer cells using bacterial toxin

Chih-Ho Lai[1,2], Yuh-Shyan Tsai[2,3], Jer-Tsong Hsieh[2]

[1]Graduate Institute of Basic Medical Science and School of Medicine, China Medical University, Taichung, Taiwan; [2]Department of Urology, University of Texas Southwestern Medical Center, Dallas, Texas, USA; [3]Department of Urology, Medical College and Hospital, National Cheng Kung University, Tainan, Taiwan

Prostate cancer (PCa) is one of the most malignancies in male in western developed countries and its incidence is rising in Taiwan. Although most patients can be cured by surgery and radiotherapy, more than 30,000 patients were died of the disease in the United States annually. Ionizing radiation (IR) is employed frequently in the management of several tumor types, including advanced PCa. DAB2IP (DOC-2/DAB2 interactive protein) is a potent growth inhibitor for PCa by inducing apoptotic pathway. By knocking down endogenous DAB2IP levels, PCa cells become resistance to IR-induced apoptosis. Our results showed that cytolethal distending toxin (CDT), a genotoxin which produced by *Campylobacter jejuni*, converted radio-resistance to susceptible phenotype. Combined treatment of CDT and IR induced cell death through ATM-dependent DNA damage checkpoint responses in radio-resistant PCa. Moreover, CDT significantly enhanced IR-induced tumor growth delay was observed in an animal experimental model. These findings indicate that CDT can be administered with IR to overcome radio-resistant PCa, particularly in DAB2IP-deficient phenotype.

Keyword: prostate cancer, cytolethal distending toxin, ionizing radiation, radio-resistant