Berberine induces human tongue squamous carcinoma cell apoptosis through PI3K-regulated ER stress pathway

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Until now, oral cavity squamous cell carcinoma (OSCC) is the most common head-and-neck cancer, which accounts for approximately 3% of all newly diagnosed cancer cases. OSCC is high mortality according to be characterized by a high degree of local invasiveness and a high rate of metastasis. Despite of recent advances in surgical, radiotherapy, and chemotherapy treatment protocols, it has been discussed that OSCC could not be eradicated. Berberine is a natural alkaloid. Recently, berberine has been showed to inhibit metastasis in lung cancer cells, and cytotoxic in glioma, prostate and nasopharyngeal cancer cells. However, the therapeutic effects and the possible mechanisms of berberine in OSCC are still unclear. Results found that berberine significantly decreased cell viability in human tongue squamous carcinoma derived SAS cells line. Besides, berberine increased the ER-stress signals, including Grp94, CHOP, Xbp-1 mRNAs and proteins. Further, the pro-caspase-12 protein level was decreased, and the caspase-12 mRNA level was increased. In mitochondrial pathway, berberine increased Bax, Bak, Bid mRNAs and proteins

levels and decreased Bcl-2 mRNAs and proteins levels. Besides, the pro-caspase-9, pro-caspase-7, and pro-caspase-3 proteins level was decreased. We also found that phospho-AKT protein level was decreased after berberine treatment in cells. Besides, LY294002, the inhibitor of phosphoinositide 3-kinases (PI3Ks), promoted ER-stress and mitochondrial related apoptosis signals. Through this study, suggested that berberine may a useful compound in inhibition of OSCC through PI3K-AKT regulated ER-stress and mitochondrial pathways.