Poster

[P26-9] P26-9: Oncologic drugs (5): Pharmacokinetics, TDM practice

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[P26-9-4] Protodioscin induces mitochondria mediated apoptosis through endoplasmic reticulum stress and reactive oxygen species-dependent pathway in human cervical cancer cells

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Background

Natural foods and herbal medical have played a central role in the treatment of cancers. Protodioscin (PD), a main steroidal saponin purified from various plants and foods, shows various biological functions including anticancer effects. Therefore, we investigated the therapeutic effects and molecular mechanisms of PD on human cervical cancer cells.

Materials &Methods:

Human cervical cancer HeLa and C33a cells were used as the cell model. Cell viability was performed using MTT assay. The cell apoptosis was assessed using the Annexin V-FITC apoptosis assay. The mitochondrial membrane potential, endoplasmic reticulum stress, and reactive oxygen species were measured by cytometry with JC-1, endoplasmic reticulum (ER) assay, or DCF-DA stain, respectively. The protein expression levels were detected by western blotting.

Results

PD was found to inhibit cell viability and induce the cell apoptosis of HeLa and C33a cells in dose-dependent manner. PD also significant increased the activation of caspase-8, -3, -9, -PARP and Bax, decreased Bcl-2 expression. Moreover, PD induced loss of mitochondrial dysfunction, activated the reactive oxygen species stress and ER stress signaling pathway, including the increased expression of Bip (Grp78), phosphorylated of eIF-2α, and induced ATF-4 binding to the CHOP promoter. In addition, PD increased the levels of reactive oxygen species stress, which was blocked by NAC (ROS antagonist) and Grp78 inhibitor (salu) inhibited PD-induced cell death and cell apoptosis signaling. Interestingly, PD induced phosphorylation of JNK1 and p38MAPK and inhibition of JNK1/p38MAPK activity also significantly abolished cell death and ER stress signaling.

Conclusions

Taken together, these findings suggest that induction of ER stress via a p-eIF-2α/ATF4/CHOP, and ROS-dependent pathway may be an important mechanism by which PD induces apoptosis in human cervical cancer cells