3-P-276

Cytotoxicity of arsenite in combination with bufadienolide compounds against human glioblastoma cell line U-87

Jingmei Li, Bo Yuan, Meiyan Xuan, Hidetomo Kikuchi, Katsuyoshi Sunaga, Shinya Kamiuchi, Yasuhide Hibino, Hirokazu Matsuzaki, Mari Okazaki

Fac. Pharm. & Phamceu. Sci., Josai Univ.

Exploring novel therapeutic approaches is critically needed for the treatment of glioblastoma, due to concerns over its invasiveness and drug resistance. Trivalent arsenic derivative (arsenite, As^{III}), and two bufadienolide compounds, arenobufagin (Areno) and gamabufotalin (Gama) have been reported to induce cytotoxicity in glioblastoma cells. Herein, the cytotoxicity of As^{III} combined with Areno or Gama was evaluated in the human glioblastoma cell line U-87. A dose-dependent cytotoxicity was observed in the cells treated by As^{III}, Areno and Gama, respectively. Enhancement of cytotoxicity was induced by As^{III} combined with Areno or Gama, and synergistic cytotoxic effects of clinically achieved concentrations of As^{III} combined with Areno were further observed. Apoptosis induction accompanied by a downregulation of proform of caspase-9 and caspase-3 was observed following the treatment with the combined regimen of As^{III} and Areno. The combined regimen also caused enhanced necrosis as evidenced by a clear increase in LDH release and propidium iodide-positive cell populations. In comparison to each single drug treatment, the combined regimen apparently downregulated the expression level of p-Akt, p-mTOR; and upregulated the expression level of LC3. Collectively, the combined regimen of As^{III} and Areno exhibited a unique multivalent cytocidal effects against U-87 cells by triggering apoptotic, necrotic and autophagic cell death, suggesting that developing a new combination regimen of As^{III} and Areno may offer benefits to patients with glioblastoma.

As^{III}とブファジエノライド化合物のヒト膠芽腫細胞U-87に対する細胞毒性における併用効果

○李 婧美、袁 博、玄 美燕、菊地 秀与、須永 克佳、神内 伸也、日比野 康英、松﨑 広和、岡﨑 真理

城西大・院薬