Pseudolaric acid B

Pseudolaric acid B (PAB), a diterpene acid isolated from the root and trunk bark of Pseudolarix kaempferi Gordon (Pinaceae), was found to inhibit cell growth in a variety of cancer cell lines, but to date the effect of PAB on neuroglioma remains unclear.

In a study, Wang et al., found Pseudolaric acid B (PAB) inhibited the viabilities of glioma cells in vitro and in vivo, which was accompanied by abnormal increases of intracellular ferrous iron, H2O2 and lipid peroxidation, as well as depletion of GSH and cysteine. In vitro studies revealed that the lipid peroxidation and the cell death caused by PAB were both inhibited by iron chelator deferoxamine, but exacerbated by supplement of ferric ammonium citrate. Inhibition of lipid peroxidation with ferrostatin-1 or GSH rescued PAB-induced cell death. Morphologically, the cells treated with PAB presented intact membrane, shrunken mitochondria with increased membrane density, and normal-sized nucleus without chromatin condensation. Mechanistically, PAB improved intracellular iron by upregulation of transferrin receptor. The increased iron activated Nox4, which resulted in overproduction of H2O2 and lipid peroxides. Moreover, PAB depleted intracellular GSH via p53-mediated xCT pathway, which further exacerbated accumulation of H2O2 and lipid peroxides. Thus, PAB triggers Ferroptosis in glioma cells and is a potential medicine for glioma treatment [1)].

MTT analysis confirmed that PAB inhibited neuroglioma A172 cell growth in a time- and dose-dependent manner. In addition, PAB influenced the aggregation of tubulin in A172 cells. Meanwhile following PAB treatment, a higher percentage of cells accumulated in the G2/M phase from 12 to 48 h, while at 36 h, cell cycle slippage into the G0/G1 phase, and at 48 h, slippage into the S phase was observed using flow cytometric analysis. Corresponding protein expression was consistent with the cell cycle alteration as detected by western blotting, and it was speculated that cell cycle slippage was related to reduced effectiveness of PAB which warrants further investigation. Meanwhile PAB induced cell death by regulating p38, ERK and JNK expression and activating the DNA damage response. Therefore, PAB plays an antitumor role in A172 cells, and may be a candidate drug for neuroglioma therapy [2)].

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Wang Z, Ding Y, Wang X, Lu S, Wang C, He C, Wang L, Piao M, Chi G, Luo Y, Ge P. Pseudolaric acid B triggers Ferroptosis in glioma cells via activation of Nox4 and inhibition of xCT. Cancer Lett. 2018 Apr 24. pii: S0304-3835(18)30288-X. doi: 10.1016/j.canlet.2018.04.021. [Epub ahead of print] PubMed PMID: 29702192.
2)
Song F, Yu X, Zhang H, Wang Z, Wang Y, Meng X, Yu J. Pseudolaric acid B inhibits neuroglioma cell proliferation through DNA damage response. Oncol Rep. 2017 Aug 1. doi: 10.3892/or.2017.5861. [Epub ahead of print] PubMed PMID: 28765951.