ヒトグリオブラストーマ細胞における生理活性天然物由来物質およびその新規誘導体の殺細胞作用

Cytocidal effect of bioactive natural products and its novel derivatives against human glioblastoma cell

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【Aims】Glioblastoma is one of the most common and lethal form of primary brain tumors, and characterized by fast infiltration, rapid growth and resistance to conventional therapies. Despite advances in the understanding of the disease progression, genomics and clinical behavior, the natural history of treated glioblastoma remains very poor with 5-year survival rates of approximately 5%. Considering the sustained development of metastasis, tumor recurrence and drug resistance, there is an urgent need for the novel therapeutic approaches to combat glioblastoma. To provide a novel insight into therapeutic strategies against glioblastoma, the cytotoxicity of trivalent arsenic derivative (arsenite, As^{III}), which has shown superior therapeutic efficacy for acute promyelocytic leukemia, and two active bufadienolide compounds, gamabufotalin (GBF) and arenobufagin (Areno) was investigated in glioblastoma cell line U-87. Ferulic acid (FA) and caffeic acid (CA) have been demonstrated to exhibit antitumor activity. In order to develop novel FA derivatives (FADs) with great potential for cancer prevention and therapy, the cytocidal effect of three newly synthesized FADs was also investigated in U-87 cells.【Methods】Following treatment for 48 h with various concentrations of each bioactive natural product, cell viability was detected by WST-1 assay.【Results and discussion】Consistent with our previous reports, As^{III}, GBF as well as Areno exhibited a dose-dependent cytotoxicity against U-87 cells, reconfirming that these compounds may serve as promising therapeutic agents to combat glioblastoma. Among FADs, only FAD041 and FAD059 displayed lower cytotoxicity against the cells compared to As^{III}, GBF and Areno. Almost no cytocidal effect was observed in FAD004, FA as well as CA, possessing structural similarity with FADs. Further investigations are ongoing in our laboratory by focusing on the molecular mechanisms underlying the cytotoxicity of As^{III}, GBF and Areno, each alone or in combination.