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Epigenetic modification and differentiation induction of malignant glioma cells by natural products

Malignant glioma (MG) is a poor prognosis disease because of inevitable recurrence after operation, radiotherapy and chemotherapy. Searching a more effective treatment modality is urgently needed. Our previous studies have shown the activities of natural products against MG stem cells. It is interesting to further elucidate the underlying molecular mechanisms. Epigenetic modification has been proposed to be a potential novel anticancer strategy and could lead to differentiation induction of cancer cells. We thus explore the effects of market available natural products such as Oligo-Fucoidan (OF) and human urine extract (CDA-2) on this paradigm in the MG cell lines including Grade III MG cells (U87MG) and Grade IV MG cells (GBM8401, DBTRG) and compared to immortalized astrocyte cell line SVGp12. The results show that both OF and CDA-2 markedly suppresses the proliferation of MG cells and only slightly affects that of SVGp12 cells. CDA-2 inhibits the mRNA expression of DNA methyltransferases (DNMTs) accompanied with mRNA induction of neuronal marker MAP2 (microtubule associated protein 2) and astrocyte marker GFAP (glial fibrillary acidic protein). In addition to DNMTs inhibition and GFAP induction, OF also increases the mRNA expression of histone acetyltransferase CRBBP along with drastic induction of oligodendrocyte marker MBP (myelin basic protein) in U87MG cells. Interestingly, combining with synthetic demethylating agent decitabine further synergizes the OF-induced MBP in U87MG cells, while combining with histone deacetylase inhibitor Chidamide significantly augments the OF-induced MAP2 and NeuN in GBM8401 cells. Taken together, CDA-2 and OF could substantially modulate genes critical for epigenetic regulation (DNA methylation and histone acetylation) during induction of various differentiation markers, suggesting the potential for their clinical application. Further clinical trial to evaluate their efficacy in recurrent MG patients is warranted.

Biography

Gi-Ming Lai has an expertise in clinical trial and his research interest is to look for more efficacious cancer therapy by combining drugs or seeking active ingredients of natural products from which are regarding as complementary and alternative medicine.

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