Hypoxia protect tumor cells from apoptosis by Egr-1 stabilizing microtubules

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Cancer is a major health problem worldwide. It was hard to be eliminated even after adjuvant chemoembolisation, chemotherapy or radiotherapy. This poor prognosis may be related to the hypoxic environment the tumor cells survive, which can protect them from death by insensitive to the therapy. Our data showed that hypoxia can protect tumor cells from apoptosis through an Egr-1 dependent pathway. When HepG2 cells were grown under hypoxic environment, the cell activity is much higher than that under normoxia. The cells were enriched in G2/M stage; meanwhile they were not sensitive to UV radiation which could normally induced cell apoptosis. We found that Egr-1, an early response transcription factor, was up regulated after short-term hypoxic treatment. Over expression of Egr-1 could exert the same protecting function like hypoxia. Hypoxia could protect microtubules from disassembly not only in cold incubation, but also during nocodazole treatment. The protecting function of hypoxia was also dependant on wild type Egr-1 over expression, but not on dominant negative Egr-1 over expression, which means that Egr-1 could work without its transcriptional function. Our result suggested a novel mechanism that how hypoxia involved in cancer progression and it may provide a new insight for the cancer therapy.

Keywords: Hypoxia, Egr-1, Microtubule, Apoptosis.

Drug resistance and apoptosis-inducing strategies in cancer therapy

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Background & Objective: Previously it has been shown that NF-κB is activated in tumour cells after chemotherapy. Moreover the activated NF-κB leads to upregulation of inhibitor of apoptosis protein (c-IAPs). This alteration of apoptosis transduction pathway may contribute to drug resistance of tumour cells. In this study we observed the relationship between activation of NF-κB, upregulation of IAPs (livin and survivin) and drug-resistance of gastric cancer cells. Meanwhile we investigated Paoniflorin’s (traditional chiness medicine) inhibition of NF-κB in human gastric cancer cells and its role in the induction of cell apoptosis.

Methods: Activation of NF-κB was detected in SGC7901 cells (wild typp) and SGC7901/VCR cells (drug resistance) by ELISA technique. Protein expression of NF-κB, livin and survivin were assessed by Western blotting. Paoniflorin was diluted to different concentrations and worked on the gastric cancer cells. Flow cytometry was used for evaluation of apoptosis of tumour cells.

Results: The expression of NF-κB and its activation were enhanced in SGC7901/VCR compared to SGC7901 cells. Livin and survivin were overexpressed in SGC7901/VCR cells. Apparent inhibition of NF-κB activity in nuclear and cytopasm was found in the cells with Paoniflorin treatment. The inhibition of NF-κB exhibited in time and dose dependant pattern. Moreover Paoniflorin had a promotion on 5-FU induced cell apoptosis.