Cancer stem cells : the new target for fighting cancer from the latest translational research

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Cancer cells are heterogeneous and only a small subpopulation of cancer cells, cancer stem cells (CSCs), possesses the ability to proliferate and to be capable of self-renewal. Increased evidences have suggested that breast cancer stem cells, which characterized by CD44+/CD24−/low, could result in treatment failure. One hypothesis that inhibiting such subpopulation might subsequently improve clinical outcome. Therefore, much attentions should be paid to explore the effective treatments against the subpopulation, which might subsequently result in disease salvage. Potential candidates to eradicate breast cancer stem cells include immune modulation, blocking the key molecules of stem cell proliferation signaling pathway, cells differentiation treatment, and selection of sensitive cytotoxic agents to breast cancer stem cells. Our pilot studies had shown that CD44+/CD24−/low CSCs were resistant to lower concentration of thiopeta, paclitaxel and antracycline compared with non-breast cancer stem cell subset, whereas the chemosensitivity was remarkably reversed by higher concentration of thiopeta and paclitaxel except for antracycline. These results provided some clues that high-dose chemotherapy might be effective to kill thiopeta and the selection of conditioning regimen was crucial in clinic. Cells differentiation therapies have been regarded as the landmark progress in some malignances since it could differentiated primary initial cells into relatively different normal cells. In a experiment the percentage of CSCs could also be significantly decreased with an addition of cell differentiation agent CDA-2. Targeting signal transduction pathways that controls CSCs proliferation and differentiation might be useful to inhibit the proliferation of CSCs. Over-expression of Smo, Shh, and Gli-1 of Hedgehog signaling pathway in breast CSCs was discovered that controls CSCs proliferation and differentiation and might be useful to eliminate CSCs subpopulation. Dendritic cells based immunotherapy and other cellular therapy, which had no prefer to both CSCs subpopulation and other subpopulation, are of promising and some clinical trails have been carrying out in China.

Screening of traditional Chinese medicine with antitumor effect and the isolation of effective chemical constituents from Forsythia suspensa (Thunb) Vhal. (Oleaceae): studying the mechanism of its apoptotic-induction

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Abstract: Traditional Chinese medicine may be a useful model for scientific research because of its standardized system of therapies and long-time practices. Chinese medicine provides a rich pool of novel and efficacious agents for treating a variety of cancer, but few effective constituents have been isolated from drugs and its mechanisms of anticancer activity is still unclear. Here, we have done some experiments on isolating, identification of new effective constituents of Chinese medicine Forsythia suspensa and investigating its mechanism using molecular biochemistry methods are ascendant aspects of drug-development in our country. First, we screened the inhibition effect of 15 traditional medicines selected from Chinese herbology and folk remedy on human digestive cancer cells. We found that Forsythia suspensa used commonly as antibacteria drugs showed good inhibitory effect and it has never been reported before. Next, we used several types of column chromatography to obtain the effective compounds from Forsythia suspensa, which structures were determined by spectroscopic methods. As a result, we obtained several triterpenes. Among these, ambrolic acid and 20(s)-dammar-24-ene-3β, 20-diol-3β-acetate were firstly found to inhibit the proliferation of SGC-7901 cells. Ambrolic acid could induce apoptosis, while 20(s)-dammar-24-ene-3β, 20-diol-3β-acetate could not. Furthermore, the results of western blots showed that ambrolic acid could regulate the protein levels of Bcl-2 family, caspase family, and FAS family. Meanwhile, it also could down regulated the protein level of p-Akt. In conclusion, it was the first time to report the antineoplastic effect and mechanisms of Chinese medicine Forsythia suspension.

Expression of livin in gastric cancer and induction of apoptosis in SGC-7901 cells by shRNA-mediated silencing of livin gene

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Background: Because of increased resistance to apoptosis in tumor cells, inhibition of specific anti-apoptotic factors may provide a rational approach for the development of novel therapeutic strategies. Livin, a novel inhibitor of apoptosis protein family, has been found to be expressed in various malignancies and is suggested to have poorly prognostic significance. However no data are available concerning the significance of livin in gastric cancer. In this study we detected the expression of livin in human gastric carcinoma and investigated the apoptotic susceptibility of SGC-7901 cell by shRNA-mediated silencing of the livin gene.

Methods: The mRNA and protein expression of Livin were analyzed by RT-PCR and western blot assay. The relationship between Livin expression and clinical pathologic parameters was investigated. The small interfering RNA eukaryotic expression vector specific to Livin was constructed by gene recombination, and the nucleic acid was sequenced. Then it was transfected into SGC-7901 cells by Lipofectamin 2000. RT-PCR and Western blot assay were used to validate gene silencing efficiency of Livin in SGC-7901 cells. Stable clones were obtained by G418 screening. The cell apoptosis was assessed by flow cytometry (FCM). Cell growth state and 50 % inhibition concentration (IC50) of 5-FU and cisplatin was determined by MTT method.

Results: The expression of livin mRNA and protein were detected in 19 of 40 gastric carcinoma cases (47.5% %) and SGC-7901 cells, No expression of livin was detected in tumor adjacent tissues and benign gastric lesion. The positive correlation was found between livin expression and poor differentiation of tumors as well as lymph