response, 5 stable disease and 7 progressive disease. The main side effects were myelosuppression, nausea, vomiting and late-onset diarrhea.

**Conclusion:** The combination of CPT-11 and DDP is effective with tolerable side effects in the treatment of SCC, but further investigation trails are needed.

**Keywords:** small cell carcinoma; irinotecan; chemotherapy

TIMP-1 protects MCF-7 breast cancer cells from paclitaxel-induced apoptosis by decreasing the stability of cyclin B1

Ting Wang a,b, Jing-Huan Lv a, Xiong-Fei Zhang a, Chao-Jun Li 5, Xiao Han a, Yu-Jie Sun a,b,d,*

a Key Laboratory of Human Functional Genomics of Jiangsu Province, Nanjing Medical University, 140 Hanzhong Rd., Nanjing 210029, China
b Department of Cell Biology and Medical Genetics, Nanjing Medical University, 140 Hanzhong Rd., Nanjing 210029, China
c Cancer Center, Nanjing Medical University, 140 Hanzhong Rd., Nanjing 210029, China
d Medical School, Nanjing University, 20 Hankou Rd., Nanjing 210093, China

Paclitaxel (PTX) is a very effective drug in treating tumors. It disturbs microtubule dynamics and impairs the transition of cells from metaphase to anaphase in mitosis, leading to cell death by apoptosis. However, the effectiveness of PTX in cancer chemotherapy is hampered by drug resistance in some patients. Tissue inhibitor of metalloproteinase-1 (TIMP-1) is well known to be capable of inhibiting apoptosis. Elevated tumor tissue TIMP-1 levels have been significantly associated with a poor response to chemotherapy. We hypothesized that TIMP-1 could reduce the sensitivity of breast cancer cells to PTX by inhibiting apoptosis. To test this hypothesis, we first examined the effects of TIMP-1 on the apoptosis induced by PTX and investigated the effects of TIMP-1 on the expression and stability of cyclin B1 that critically regulates the metaphase to anaphase transition during mitosis in MCF-7 breast cancer cells. Our data demonstrate that TIMP-1 could significantly decrease the sensitivity of MCF-7 cells to PTX-induced apoptosis, attenuate mitotic blockage in G2/M, and enhance the degradation of cyclin B1. To further investigate whether the inhibitory effect of TIMP-1 on PTX-induced apoptosis is mediated by lowering levels of cyclin B1, a cyclin B1-expression plasmid was transfected into clone over-expressing TIMP-1. The levels of PTX-induced apoptosis were then analyzed. The data showed that the TIMP-1-based decrease in PTX-induced apoptosis was reversed by cyclin B1. Our data indicate that TIMP-1 can protect breast cancer cells from PTX-induced apoptosis by decreasing the stability of cyclin B1.

**Keywords:** TIMP-1, PTX, apoptosis, cyclin B1, breast cancer.

Background: Several gene expression signatures have been reported to predict patient survival of gastric cancer after surgical resection. However, the prognostic gene lists have overlapped poorly until now. This study conducted an analysis to characterize gene expression profile and developed a survival prediction model.

**Methods:** The gene expression profile was evaluated in fresh frozen tumor tissue obtained from 48 patients with primary gastric cancer. We measured 84 representative genes involved in transformation and tumorgenesis using quantitative reverse transcription polymerase chain reaction (qRT-PCR) and related the results to overall survival.

**Results:** In a univariate analysis, 84 genes were ranked on their ability to predict survival, of which 9 genes were the strongest predictor (p < 0.05). They were PLAU, MAP2K1, THBS1, TWIST1, ITGB5, NME4, ANGPT2, PDGFβ, ITGB1. Then we did a multivariate analysis to further select four genes (ITGB1, PDGFβ, ITGB1, TWIST1) from the above 9 genes for the construction of biomathematics model, which was independent of age, gender, TNM stage and other variables. This model could correctly classify gastric patients into the high-risk group, median-risk group and low-risk group, as well as predict their survival.

**Conclusions:** Measurement of the expression of four genes is probable to predict surgery-related survival. This model may be test further for its potential to improve the selection of the resected gastric cancer patients in adjuvant chemotherapy.

Involvement of mTOR and survivin inhibition in tamoxifen-induced apoptosis in human hepatoblastoma cell line HepG2

Renhua Guo, Tongshan Wang, Hongmei Ge, Yongqian Shu, Zuhu Huang

Department of oncology(RH.G, TS.W, YQ.S), Department of Infectious disease(ZH.H), and Laboratory of molecular biology(HM.G), First Affiliated Hospital of Nanjing Medical University, Nanjing, China

Patients with advanced hepatocellular carcinoma (HCC) have shown to benefit from tamoxifen treatment. The mechanisms of tamoxifen effects in HCC, however, are not yet clearly understood. The PI3K/Akt/mTOR signal pathway is involved in cell proliferation, tumorigenesis, and apoptosis. Over-expression of survivin has played an important role in leading to antiapoptosis. The current study investigated changes in mTOR pathway and survivin expression in hepatocarcinoma cell line HepG2 treated with tamoxifen. We detected apoptosis of hepatocarcinoma cells by flow cytometry assay. Survivin transcription level and p70S6 kinase was demonstrated by PCR, Dual-Luciferase Reporter Assay and Western blot analysis respectively. Our results showed as follows. Tamoxifen leads to apoptosis of the cells, and reduction in survivin expression, as well as a dramatic reduction in the activated form of p70S6 kinase. 20 μM tamoxifen treatment significantly reduces transcription of survivin mRNA. Treating HepG2 cells with rapamycin, a specific mTOR inhibitor, significantly reduce survivin protein level but not affect survivin transcription, which indicated that tamoxifen and rapamycin were synergetic in regards to down-regulation of survivin expression in hepatocellular carcinoma cells. Our results suggest that tamoxifen down-regulate survivin expression in HepG2 cells is mediated by