Expression of CD40 on glioma and the relationship with tumor angiogenesis

Xueguang Zhang

Biological Research Institute, Suzhou University, 708 Remin Road, 215007 Suzhou, China

CD40, member of the tumor necrosis factor receptor (TNF-R) gene family is expressed by numerous cell types including most professional antigen-presenting cells (APCs), monocytes, and endothelial cells and so on [1]. Its ligand (CD40L, also called CD154), is predominantly expressed by activated CD4+ T cells and platelets [2]. Interactions between CD40 and CD40L, have repeatedly been found to be of importance in the activation of EC for the expression of adhesion molecules and the production of several proinflammatory cytokines and chemokines in vitro and vivo[3]. Moreover, ligation of CD40 results in the production of several angiogenesis factors, including VEGF [4], and promotes a VEGF-dependent angiogenesis reaction [5]. In our study, the relationship between CD40 and VEGF as well as their contributions to neovascularization under the condition of disoxidation were investigated. The expressions of CD40 and VEGF were studied by S-P immunohistochemistry in about 60 cases of disoxidation were investigated. The expressions of CD40 and VEGF were studied by S-P immunohistochemistry in about 60 cases of glioma. Microvessel density (MVD) was determined by anti-CD34 immunostaining. By FCM, confocal and ELISA analysis, the relationship between CD40 and VEGF on glioma cell lines was studied and the function and significance of CD40 expression on neovascularization and secretion pattern of soluble VEGF in the condition of chemical disoxidation induced by CoCl2 were analyzed. It was found that at the early stage of disoxidation, CD40 molecules and VEGF coexpressed on the membrane of tumor cells, which is in consistent with the secretion pattern of soluble VEGF. The expression of CD40 and VEGF are corelate with each other and their expression levels increase with the severity of malignance of glioma and have close relation with neovascularization. It was proved that under the condition of disoxidation, CD40 and VEGF have close relation with tumor angiogenesis, providing new target molecules and strategies for immunotherapy of tumor.

Aim: Despite the success of docetaxel as an anti-tumor agent, the inter-individual variability in drug response still poses a major impediment to the successful use of this agent in the treatment of cancer. Current knowledge about predictive biomarkers of docetaxel sensitivity in malignant effusions is poor. The aim of this study was to investigate the association between β-tubulin III mRNA expression and chemosensitivity to docetaxel in malignant effusions of NSCLC and gastric cancer.

Method: Real-time quantitative PCR was used to analysis β-tubulin III mRNA expression in thirty-seven malignant effusions prospectively collected. Viable tumor cells obtained from malignant effusions were tested for sensitivity to docetaxel using ATP-TCA assay.

Results: β-tubulin III expression level was inversely correlated with sensitivity to docetaxel in pleural effusions of NSCLC patients (P =0.022). Meanwhile, no correlation was found between β-tubulin III mRNA expression and docetaxel sensitivity in malignant effusions of gastric cancer patient (P > 0.05).

Conclusion: It was demonstrated for the first time that low level of β-tubulin III mRNA expression in malignant effusions was associated with chemosensitivity to docetaxel in NSCLC patients in vitro. The data in this study also provided preliminary evidence for using gene expression in malignant effusions as an approach to predict response to docetaxel chemotherapy in the clinic.

PRL-3 Expression in Cancer

Xiang Gao

Model Animal Research Center, Nanjing University, 210029 Nanjing, China

PRL-3 is expressed at a high level in cancer metastases. We previously reported that overexpression of PRL-3 in mouse melanoma cells resulted in higher migratory mobility. To investigate substrates and signal transduction pathway of PRL-3, we screened the 17.5-day-old mouse embryo library with the bait of PRL-3 in yeast two-hybrid system. Then we identified CSK (C-terminal Src Kinase), a negative regulatory kinase of SRC family tyrosine kinases, as a PRL-3 interacting protein. This physical interaction was verified with co-immunoprecipitation assays. Furthermore, in the transwell assay, RPL-3 partially blocked the endogenous CSK ability to decrease the cell migration, and depletion of SRC could entirely reverse the effect of PRL-3 overexpression. The activity SRC is up-regulated in PRL-3 overexpressing cells. Our findings suggest that PRL-3 increases cell mobility by directly exerting its influence on CSK, which consequently resulted in elevated SRC activity.

The prognostic value of PRL-3 overexpression in colon cancer and the molecular mechanism of PRL-3 promoting cancer cell metastasis

Chengchao Shou

The Key laboratory of cancer research and its application of educational ministry, Peking university school of oncology, 52 Fucheng Road, 100036 Beijing Haidian

Background: High expression of PRL-3 has been implicated in cancer invasion and metastasis, indicating a close link between PRL-3