Angiogenesis is required for tumor growth and metastasis when tumor reaches more than 1 mm in diameter. Our primary interest is to further investigate the mechanism of PI3K in angiogenesis and tumorigenesis. Our recent study shows that PI3K and Akt in cancer cells play an important role in regulating tumor growth and angiogenesis through VEGF and HIF-1 expression. PI3K regulates VEGF and HIF-1 expression through HDM2 and p70S6K1 in human cancer cells, and PTEN inhibits VEGF and HIF-1 expression. We also shows the important role of PI3K and Akt expressed in human endothelial cells in regulating angiogenesis and tumor growth, and the potential inhibition of the PI3K/Akt pathway in cancer prevention and therapy, tumorigenesis and angiogenesis.

Expression of CD40 on glioma and the relationship with tumor angiogenesis

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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 in vivo [3]. Moreover, ligation of CD40 results in the production of several angiogenesis factors, including VEGF [4], and promotes a VEGF-dependent angiogenesis re-action [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 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 patterns of soluble VEGF. The expression of CD40 and VEGF are correlative to 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.

Relationship between β-tubulin mRNA expression and sensitivity to docetaxel in malignant effusions from non small-cell lung cancer (NSCLC) and gastric cancer patients

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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

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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

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