Role of Phosphatase of Regenerating Liver-3 in the Metastasis of Melanoma Cells

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Phosphatase of regenerating liver (PRL-3) has been widely proposed to facilitate metastasis in many cancer types. Our study demonstrated that B16 melanoma cells transfected with PRL-3 cDNA showed a fibroblast-like morphology and an enhanced cell migratory ability, whereas PRL-3-specific antisense oligodeoxynucleotide and the phosphatase inhibitors sodium orthovanadate or bpV blocked the effect of PRL-3. PRL-3 also facilitated lung and liver metastasis of B16 cells in mice. Moreover, we used PRL-3-siRNA to specifically reduce the expression of PRL-3 in B16-BL6 cells. PRL-3-siRNA significantly inhibited cell adhesion and migration, but had no effect on cell proliferation. While in the spontaneous metastatic tumor model in vivo, PRL-3-siRNA treatment remarkably inhibited the proliferation of primary tumor, prevented tumor cells from invading the draining lymph nodes, and prolonged the life span of mice. Furthermore, a series of Myc tagged PRL-3 wild type or mutant plasmids were expressed in B16F1 cells to investigate the relationship between PRL-3’s cellular localization and metastasis. We found that CCVM motif is critical for the localization of PRL-3 on cell plasma membrane and the lung metastasis of melanoma. In particular, Cystine170 is the key site for prenylation in this process. These observations provide strong evidence that PRL-3 truly plays a causal role in tumor metastasis, and that inhibiting PRL-3 will improve the treatment of malignant tumors. The cellular localization of PRL-3 is highly correlated with its function in tumor metastasis, and inhibition of prenylation for PRL-3 might be a new approach to cancer therapy.

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Predictive markers for anti-HER therapies

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Anti-HER2 therapy brings enormous benefits to breast cancer patients. It can reduce the tumor burden significantly and improves the survival outcome as well. Her-2 positive tumor had been a poor prognostic subtype but nowadays it wouldn’t be true anymore. In addition to anti-HER2 monoclonal antibody, HER tyrosine kinase inhibitors have been involved in the treatment modality where the prognostic outcomes of HER2 positive patients would be improved further. To the next step, particularly for individualization of the treatment, the prediction of these HER2 therapies is necessary. For this purpose, we have investigated on the predictive markers for anti-HER therapies. For example, total HER2 protein expression levels, especially homo-dimers, in the primary tumors were found to be potent predictive markers for the survival in metastatic breast cancer patients. In addition, ADCC activity was demonstrated to be engaged in the anti-tumor activity of anti-HER2 antibody therapy. Furthermore, disorders in PI3 kinase related molecules seem to be involved in clinical response to anti-HER tyrosine kinase inhibitor treatment. Taken together, it seems becoming to be possible to predict the response and treatment outcomes of anti-HER therapies, which would provide further benefits to HER2 positive breast cancer patients.

Expression of tissue inhibitor of matrix metalloproteinases-1 (TIMP-1) and TIMP-3 protein in invasive breast carcinoma: correlations with prognostic factors

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Introduction: Our aim was to study the expression pattern of tissue inhibitor of metalloproteinases (TIMP)-1 and 3 protein in invasive breast carcinoma, and their clinic-pathological and prognostic value as well as its relation to endocrine therapy.

Methods: Immuno-histochemistry was performed on paraffin embedded tissue specimens from 153 invasive breast carcinomas to detect the proteins TIMP-1 and 3, estrogen receptor (ER), progesterone receptor, p53, c-erbB-2, and Bcl-2.

Results: TIMP-1 and 3 proteins were immune-detected in the cytoplasm of the malignant cells and the peritumoral stroma, as well as...