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Flotillin overexpression is detected in many invasive carcinoma and sarcoma and is a marker of poor prognosis associated with a higher metastatic risk [4-8]. How flotillins participate in the acquisition of invasive and metastatic properties remains to be determined.

Our study aims at identifying how the UFIT pathway influences the membrane remodeling and modifies the trafficking of cargo leading to the acquisition of invasive properties.

We show that flotillins downregulation in invasive cancer cells dramatically inhibit their invasive properties as monitored *in vitro* using a 3D-collagen invasion assay and *in vivo* using zebrafish xenografts. Reciprocally, ectopic up-regulation of flotillins in non-tumoral cells is sufficient to induce their invasive behavior *in vitro* and *in vivo*. We show that flotillins are critical regulators of the trafficking of several cargo amongst them MT1-MMP, a key metalloproteinase responsible for the proteolytic activity of invadopodia [9].

Keywords: flotillins, cancer marker, metastasis, cell invasion.

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CIRCULATING DNA-MARKERS IN LUNG CANCER: CHANGES IN RETROTRASPOSONS METHYLATION STATUS IN RESPONSE THERAPY AND DURING THE POST-TREATMENT FOLLOW-UP

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Background

Malignant cell transformation is accompanied by two processes of DNA methylation changes: hypermethylation in CpG islands of tumor suppressor genes and global hypomethylation in repetitive DNA sequences (retrotransposons) [1, 2]. The composition of circulating DNA (cirDNA) from plasma and cell-surface-bound cirDNA (csb-cirDNA) was shown earlier to be altered in the blood of cancer patients due to accumulation of tumor-specific aberrantly methylated DNA fragments, which are currently considered valuable cancer markers [3, 4].

Material and Methods

The present study compared LINE-1 retrotransposon methylation patterns in free-cirDNA and csb-cirDNA from healthy subjects (n=33) and lung cancer (LC) (n=32) patients, and also from

LC patients during the post-treatment follow-up period. Concentrations of methylated LINE-1 region 1 (LINE-1met) were assayed by real-time methylation-specific PCR. In order to normalize the LINE-1 methylation level, the LINE-1 region 2 concentration was evaluated, which was independent of the methylation status (LINE-1Ind).

Results

The LINE-1 methylation level, determinated as the ratio LINE met/LINE Ind, in csb-cirDNA from LC patients was significantly lower than in csb-cirDNA from healthy subjects (P=0.005). In the total group of LC patients, LINE-1 methylation level was shown to be significantly increased during the follow-up after chemotherapy (P<0.05, paired test) and after surgery comparaed to the methylation level before treatment (P<0.05, paired t-test). The revealed association between LINE-1 methylation level and effect of antitumor therapy was more pronounced in squamous cell lung cancer compared with adenocarcinoma (P<0.05 and P>0.05, respectively). All relapse-free patients within the follow-up period (n=19) were characterized by an increase in LINE-1 methylation level, and patients who experienced disease recurrence (n=13) had decreased levels that corresponded to those observed before treatment.

Conclusion

Our data demonstrate that LINE-1 methylation level determination represents a valuable tool for evaluation of cancer treatment efficiency and post-treatment monitoring.

Keywords: lung cancer, diagnosis, prognosis, oncomarkers, methylation, circulating DNA.

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AUTOMATED IMAGE ANALYSIS IN ASSESSMENT OF E-CADHERIN DOWN-REGULATION DURING EPITHELIAL-MESENCHYMAL TRANSITION IN PROSTATE CANCER

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Experience of using automated image analysis with Aperio software for evaluation of E-cadherin expression is presented. Advantages and limitations of the method are described. Automated analysis makes it possible to distinguish changes in marker expression that may be difficult to assess visually.

Keywords: automated image analysis, Aperio, E-cadherin, epithelial-mesenchymal transition.

Automated image analysis (AIA) is becoming increasingly popular in pathology as it provides some opportunities that are difficult or even impossible to realize by visual staining assessment [1-3]. It is used for a wide variety of applications, but, anyway, can't yet substitute classic pathology.

During epithelial-mesenchymal transition (EMT) epithelial cells transiently acquire some features of mesenchymal ones, this leads to higher invasion, migration and therapeutic resistance.