treatment with decitabine and TSA increased docetaxel sensitivity in MCF-7 and MDA-MB-231 cells ($P < 0.05$). An array of 84 genes identified 5 genes decreased in resistant cells whose expression was upregulated after decitabine and TSA treatment ($P < 0.05$). Western analysis confirmed expression changes in only one gene, SERPINE1, in docetaxel-resistant cells.

Conclusions: Docetaxel resistance is associated with changes in the DNA methylation machinery. Inhibiting DNA methylation and histone deacetylation, in combination, overcomes resistance of breast cancer cells to docetaxel. Our findings indicate that decreased SERPINE1 expression is associated with docetaxel resistance.

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O-12 TRANSLATIONAL EXPLORATION OF PIK3/Akt pathway activation in early invasive breast cancer

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The phosphatidylinositol 3-kinase (PI3K)/Akt pathway is a frequently deregulated pathway in breast cancer (BC). Akt arguably relays a plethora of extracellular signals to modulate diverse biologic effects, including cell proliferation, growth, motility, and survival, downstream of PI3K activation. However, complexity and diversity in the upstream/downstream arms of this pathway challenge considerably the clinical evolvement of effective therapies.

This study aims to study expressions of PIK3CA and phospho-Akt1 (pAkt) in BC, with respect to proteins upstream/downstream of Akt activation, clinicopathologic parameters, and disease outcome. PIK3CA and pAkt (ser473) were evaluated by immunohistochemistry on tissue microarrays containing 1202 early invasive BC with long term follow-up.

In this study, pAkt overexpression was associated with patients' age, estrogen and androgen receptors, cytokeratin (CK)18, CK19 and PTEN expression. Loss of pAkt was correlated with higher grade, CK5/6, p53 and Ki-67 labelling index. Luminal-like tumours displayed more pAkt positivity than triple negative/basal-like subtypes. However, pAkt overexpression was not associated with breast cancer-specific (BCSS) or metastasis-free survival (MFS). Four combinatorial phenotypes were identified based on PIK3CA and pAkt expression, with considerable proportions being $PIK3CA^{-}/pAkt^{+}$ or $PIK3CA^{+}/pAkt^{-}$. These phenotypes were significantly associated with BCSS ($p = 0.001$) and MFS ($p = 0.002$).

Although pAKT is an oncogene that correlated with poor prognostic variables, it was not a prognostic marker. Combinatorial phenotypic groups of PIK3CA/pAkt denoted, at translational level, functional complexity within the upstream and downstream network of Akt activation with significant impact on patients' outcome. These findings may help developing adequate therapeutic regimens against specific components of this key signalling pathway.

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O-13 *D-gLUCURONYL C5-EPIMERASE* INHIBITS BREAST CANCER CELLS PROLIFERATION THROUGH THE TUMOUR SUPPRESSOR GENES ACTIVATION

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D-Glucuronyl C5-epimerase (GLCE) is one of the key enzymes of the biosynthesis of heparan sulphate proteoglycans. Down-regulation of *GLCE* expression in human breast tumours and cancer cell lines suggested a possible involvement of the gene in breast carcinogenesis. To test the hypothesis, we ectopically expressed GLCE in breast cancer cells MCF7 and showed that re-expression of *D-glucuronyl C5-epimerase* significantly inhibited proliferative activity of MCF7 cells according to CyQUANT NF Cell Proliferation Assay and did not affect the viability of the cells in Colony Formation Test. The antimitotic effect of *D-glucuronyl C5-epimerase* in human breast cancer cells probably is realised via the activation of tumour suppressor genes SYK (+8.1-fold), BRCA1 (+3.5-fold), p53 (+3.3-fold) and E2F1 (+3.00-fold) and change of a balance of pro- and anti-apoptotic factors BCL2 (+4.2-fold), NFKB1 (+2.6-fold) and TNF (+4.6-fold) (PathFinder RT Profiler PCR Array). Also, *GLCE* re-expression in MCF7 cells considerably changed expression of some genes involved in angiogenesis (IL8, IFNB1, TNF and TGFB1) and invasion/metastasis (SYK, NME1, S100A4) suggesting a possible antimetastatic effect of *GLCE in vivo*.

In summary, the ability of the *D-glucuronyl C5-epimerase* to suppress proliferation of breast cancer cells through the affecting different key genes involved in cell cycle regulation, angiogenesis and invasion/metastasis molecular pathways supposes the gene as a new potential candidate for diagnosis and treatment of breast cancer.

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O-14 EXPRESSION AND ACTIVATION OF Akt AND NFkB IN BREAST CANCER PATIENTS

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Background: It is postulated that Akt activates the Nf-kB pathway to promote tumour growth and survival in breast cancer cells.

Material and methods: Tissue microarray technology was employed to analyse tissue from 426 breast cancer patients. Immunohistochemistry was performed using antibodies for pAkt (phosphorylated at serine 473), NF- kB and pNFkappaB (phosphorylated at serine 536). Expression was assessed using the weighted histoscore method by two independent scorers.

Results: Median age was 62 years, median tumour size was 20 mm, 48% were pathologically graded G2 and 31% G3 and 48% were lymph node positive. Ninety-eight patients had unilateral