well as ER and PgR status should be re-evaluated on surgical specimens after PST.

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Comparison of HER-2 and Hormone Receptor Expression in Primary Breast Cancers and Metastases

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Background: Recent retrospective reviews suggest that the estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor type 2 (HER2) receptor may differ between the primary and recurrence or distant metastases. In these reports, the rate of discordance for ER, PR and HER2 status ranged between 10 and 30%.

Methods: 42 patients who had tissue samples for both primary and metastatic lesions were eligible for our stud. ER, PR, and HER2 status were determined by immunohistochemistry (IHC) and/or FISH.

Result: The sites of biopsied recurrent/metastatic lesions are regional soft tissue (21.4%), lymph nodes (30.1%), lung (26.1%), bone (16.6%), brain (4.8%), and ovary (2.4%).

Discordance for ER was 11% (n = 5). Among these, 7.1% (n = 3) patients had ER-positive primary tumor but ER-negative metastasis and 4.8% (n = 2) had ER-negative primary but ER-positive metastasis. Discordance for ER was 19% (n = 8). Among these, 14.3% (n = 6) had PR-positive primary but PR-negative metastasis and 4.8% (n = 2) had PR-negative primary and PR-positive metastasis. HER-2 status was known in both primary tumor and metastasis in 34 patients. Among these patients, 15.9% (n = 2) had discordant results. Among these discordant cases, two had negative primaries and positive metastasis and no cases had positive primaries and negative metastasis.

We analyzed the discordance in receptor status between primary and recurrent lesion, by subtypes. 21 patients were defined as luminal type (ER and/or PR+, HER2−), 3 patients were defined as Luminal HER2 type (ER and/or PR+, HER2+), 12 patients were defined as HER2 type (ER−, PR−, HER2+), and 6 patients were defined as Triple negative (TN) type (ER−, PR−, HER2−). Discordance rate in Luminal, Luminal HER2, HER2, and TN was 48%, 0%, 8%, and 16%. There was no significant difference in the rate of discordance according to subtypes.

Conclusions: In the management of recurrent or metastatic breast cancer, we may consider tissue sampling of the metastatic lesions, and identify changes in ER, PR or HER2 status, which could lead to more appropriate therapy.

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DPAGT1 Regulation with Polyprenol in MCF-7 Breast Cancer Cells: Possible Therapeutic Approach to E-cadherin Loss Prevention

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Background: Dysregulation of DPAGT1 (Dolichyl-phosphate (UDP-N-acetylglucosamine) N-acetylglucosaminephosphotransferase 1 (GlcNAc-1-P transferase) causes disturbances in E-cadherin expression. In breast carcinomas, loss of E-cadherin correlates with high tumour grade and risk of metastasis. The resent results are in favour of the idea that N-glycosylation in cancer cells is limited by Dolichyl Phosphate Cycle (DPC) intermediates. The aim of the present study is to investigate the effect of Polyprenol (PP), which provides a Dolichol Phosphate (DolP) substitute on regulation of E-cadherin expression in MCF-7 breast cancer cells.

Materials and Methods: Breast cancer cell lines, MCF-7 and MCF-7/ADR were used. PP concentration in the culture medium made up 10^{-2}–10^{-6}. Immunohistochemical and Western blotting methods were used to detect the changes in the expression levels of E-cadherin and DPAGT1 expression. Intermediates of DPC fractions were analysed by HPLC method.

Results: Overexpression of DPAGT1 was 4-fold higher in MCF-7 and 7-fold higher detected in MCF-7/ADR cells than in human mammary epithelial cells (HMEC). Resistant MCF-7/ADR cells differ from sensitive ones MCF-7 in E-cadherin content lost by 3−4 times. It was caused by dolichol-chain shortening and abberant N-glycosylation of E-cadherin in DPC. The study showed 8.5-fold DPC intermediates decrease in MCF-7/ADR cells and 3.6-fold DPC intermediates decrease in MCF-7 cells. Treatment of MCF-7 cells with PP resulted in downregulation of DPAGT1. It is established that PP in the concentration 10^{-4} M could overcome DPAGT1 overexpression which leads to regulation of E-cadherin N-glycosylation.

Conclusions: N-glycosylation is one of the regulators of E-cadherin tumor suppressive activity by affecting the stability of AJs and the assembly of TJs. The findings indicate that DPAGT1 overexpression in MCF-7 and extensive overexpression in MCF-7/ADR can be overcomed by PP, which provides a DolP substitute for DPAGT1 normal expression, N-glycosylation and E-cadherin loss prevention. Polyprenol could be a promising agent for metastasis control in breast cancer.

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Breast Cancer with PIK3Ca Mutations Associated with a Favorable Prognosis in Patients Treated with Tamoxifen Alone

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Background: PI3K/AKT pathway plays a critical role in the tumorigenesis and aggressiveness of human breast cancer. Mutations of *PIK3CA* gene that encodes the PI3K catalytic subunit have been found in approximately 30% of breast cancer. Mutations occur predominately in two 'hot spots' in exon 9 and 20, encoding the helical domain and kinase domain, respectively and constitutively activate downstream signals. Cross-talk between the estrogen receptor and PI3K/Akt pathways are thought to be resistant to hormonal therapy. However some previous studies showed good prognosis in ER positive breast cancer patients with *PIK3CA* mutation. This may be a result of heterogeneous treatment populations in ER/*PIK3CA* mutation positive patients. To clarify this controversy, we sought to examine interaction between *PIK3CA* mutation and breast cancer outcomes in patients who are treated with adjuvant tamoxifen alone.

Material and Methods: Frozen samples from 133 consecutive patients treated with tamoxifen alone as an adjuvant therapy were analyzed for *PIK3CA* mutations using DNA direct sequencing in exon 9 and exon20.

Results: We identified 45 (34.1%) mutations of 133 tumor samples. Of the 45 mutations, 18 (13.6%) and 27 (20.5%) were observed in exon 9 and exon 20, respectively. *PIK3CA* mutation status was not significantly associated with clinicopathologic features such as tumor size, lymph node status, or grade. Patients with *PIK3CA* mutations did not have a worse prognosis compared with those without mutations, but it is not statistically significant due to small number of events.

Conclusions: In our findings, breast cancer with *PIK3CA* mutations associated with a favorable prognosis in patients treated with tamoxifen alone. This may help stratify patients likely to benefit endocrine therapy alone. Further studies are needed to confirm this association.

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Relation Between CpG Methylation 14−3-3-sigma and Nodal Positive Status in Breast Cancers

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Background: 14−3-3 sigma is induced in response to DNA damage, and causes cells to arrest in G(2). Hypermethylation of CpG islands located in the promoter regions of tumor suppressor genes is now firmly established as an important mechanism for gene inactivation. Our objective is to study the relation of 14−3-3 sigma gene promoter hypermethylation and nodal status in sporadic breast cancer.

Material and Methods: This is a prospective study we quantified methylation levels of promoter 14−3-3σ gene in 107 women with breast cancer and 108 control subjects by Real Time QMS-PCR SYBR green and analyzed association with prognostics factor in breast cancer.

Results: Median age was 58 years (32−88); 69% were postmenopausal women. Nodal involvement N0; 63%, N1; 30%, N2; 7%), tumor size (T1; 58%, T2; 35%, T3; 4%, T4; 4%) and grade G1; 20%, G2; 37%, G3; 30%). The methylation of 14−3-3σ were 60% of sporadic breast cancer patients and were 34% of normal breast ($p = 0.0047$). The methylation of 14−3-3σ gene in serum was markedly related with T3−4 stage ($p < 0.05$), nodal positive status ($p < 0.05$) and poor outcome. With a median follow up 6 years we saw more probability of developing distance metastasis in patients with methylation 14−3-3σ ($p > 0.05$).

Conclusions: Hypermethylation of the 14−3-3σ a promoter is an early and frequent event in breast neoplastic transformation, leading to the suggestion that silencing of 14−3-3σ may be an important event in tumor progression and particularly in breast carcinogenesis. Therefore, it is possible that loss of σ expression contributes to malignant transformation by impairing the G_2 cell cycle checkpoint function, thus allowing an accumulation of genetic defects. Perhaps in the detection of CpG methylation of 14−3-3σ may be used for diagnostic and prognostic purposes.