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The expression of COX-2 in cells of invasive ductal carcinoma and adjacent non-cancerous ductal epithelia in human breast

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Background: Cyclooxygenase-2 (COX-2) is an inducible enzyme that converts arachidonic acid to prostaglandins. Aberrant expression of COX-2 and prostaglandins has been observed in many cancers, including colon and breast cancers, and 40% of human breast cancers show overexpression of COX-2. The aim of this study was to analyze the expression of COX-2 and c-erbB-2 in breast cancers.

Materials and Methods: The expression protein and mRNA of COX-2 and c-erbB-2 was examined in 56 breast tissue including microscopically normal epithelium and invasive ductal carcinomas (IDC) using immunohistochemical (IHC) method and RT-PCR. The results were compared with the prognostic parameters of breast cancer including tumor grade, growth pattern, lymph node metastasis, and the expression of ER and Ki-67.

Results: The COX-2 mRNA was expressed in 83.3% of cancer cell and also expressed in 88% of adjacent non-cancerous tissue (ANCT). The expression of COX-2 mRNA was closely associated with that of c-erbB-2 mRNA in IDC ($p = 0.000$). However the expression of mRNA and protein of COX-2 and c-erbB-2 were not associated with other prognostic parameters of breast cancer.

Conclusions: The association between the expression of COX-2 mRNA and that of c-erbB-2 suggests that Her2/neu gene induces the COX-2 expression in breast cancer and overexpression of COX-2 is involved in the breast cancer development. Though the cells of ANCT are normal in morphology, their molecular alteration (overexpression of COX-2) suggests that these cells have transformed already. In the breast tissue that was taken for any reason, we recommend to study the status of COX-2 expression.

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DNA ploidy in relationship with EZH2 expression as markers of breast carcinomas

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Prediction of breast cancer progression is still a clinical problem of major concern. During the last years biomarkers has been used for the assignment of the biological behavior of breast tumors but only few of them have been proven to be clinically useful. Therefore, new prognostic factors more precise and reliable are needed and new strategies should be considered.

The polycomb group protein enhancer of zeste homologue (EZH2) has been reported as an aggressive breast cancer marker. Its expression was further associated with tumor size, hormone receptor status and advanced stage of the disease.

The aim of this study was to investigate the value of the expression of EZH2 in relationship with DNA ploidy in order to predict the potential role of the above markers in tumor aggressiveness.

Materials: We studied 62 imprints of breast carcinomas immunocytochemically with the use of EZH2 antibody. DNA ploidy was measured with Image Plus Software on imprint smears with the Thionin Feulgen procedure in order to be used for image analysis. The prevalence of EZH2 expression and DNA ploidy was then correlated with clinicopathological parameters.

Results: Overexpression of EZH2 was observed in 72.8% of breast carcinomas and was strongly associated with standard pathology predictors of clinical outcome including tumor size ($p = 0.003$), stage ($p < 0.0001$) negative ER/PR status ($p < 0.001$) and positive lymph nodes status ($p < 0.001$) but not HER2 protein expression.

Aneuploid tumors were correlated with positive expression of EZH2 ($p = 0.039$), poorly differentiated carcinomas ($p = 0.001$), lymphnodes metastasis ($p < 0.0001$) and positive Ki-67 expression ($p = 0.025$). Multivariate statistical analysis revealed that from all studied parameters only EZH2 expression was significantly associated with lymphnodes status and aneuploidy ($p < 0.0001$ respectively).

Conclusions: This pilot study provides good evidence that EZH2 expression and DNA ploidy, could be markers of poor prognosis and suggests that both of them could be of significant interest for targeted therapy in patients with breast carcinomas.

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Correlation between hormonal receptors and HERr2 status of primary and metastatic breast cancer according to the metastatic organ involved

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Background: The estrogen receptor (ER) is expressed in approximately two thirds of newly diagnosed breast cancers while Her2 overexpression occurs in approximately 20%. Both markers are important predictive factors regarding therapeutic decisions. Various studies have shown that the ER/Her2 phenotype of primary breast cancer may undergo a natural biologic drift in recurrent or metastatic disease and it is possible that these changes may influence tumor response to endocrine or anti-Her2 therapy. However it is not known whether the metastatic organ involved and assessed may influence the biologic drift.

Objective: Our main objective was to address the question of whether there is a difference in the prevalence of biologic shift between primary and metastatic tissue according to the metastatic organ involved.

Material and Methods: We evaluated the ER, progesteron receptor (PR) and Her2 phenotype of metastatic breast cancers and compared it with the ER, PR and Her2 status of the primary tumor in 25 cases. In this analyses the most frequent site of metastasis was the liver (13 cases) followed by bone (5 cases), both skin and lung (3 cases) and lymph node at distant site (1 case).

Results: Of the 25 specimens analyzed we found discordance between primary and metastatic site in 15 cases. The discordance rate between different metastatic site was: liver − 46% (6/13), bone − 60% (3/5), lung − 67% (2/3), skin and lymph node − 100% (3/3 and 1/1). Hormonal receptors, especially ER receptor, was the most frequent changed parameter between primary and metastatic tissue (32%) followed by progesteron (24%) and Her2 (4%). In 3 cases the ER receptor expression was lost and in one the Her2 expression changed from positive to negative.

Conclusion: A significant number of patients show discordant expression of molecular markers between primary and metastatic disease being this disagreement independent of the site of metastasis. Considerations regarding this variation and its influence to tumor response, namely endocrine therapy, must be explored.

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Expression and characterization studies of the LIV-1 family members in female breast cancer patients of Malaysia

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SLC39A is a family of zinc transporters and LIV-1 is one of the subfamily that comprises of nine members. All the nine members show similarities to the ZIP (Zrt-Irt-like Proteins, SLC39A) super family, especially in the region associated with their ability to transport zinc intracellular. However, using phylogenetic tree software, analysis shows that although the nine members are in a family, some members are group separately, suggesting differences in their function. In these first finding shows that SLC39A12 and SLC39A13 which were cloned respectively into pcDNA5/FRT/V5-His-TOPO and electrophoresis analysis shows SLC39A12 gene is approximately 1962 base pairs, produces 73 kDalton recombinant proteins, whilst SLC39A13 gene is approximately 1094 base pairs, produces 43 kDalton recombinant proteins. Confocal microscopy study demonstrated that transiently expressed, anti V5-tagged to respective SLC39A12 and SLC39A13, were localized to the plasma membrane of Chinese Hamster Ovary cells treated under non-permeabilised condition, interestingly, SLC39A12 protein expresses more in endoplasmic reticulum in the permeabilised condition. These results suggest that their locations may also regulate zinc homeostasis differently in cells. We proceed with another novel investigation to study if the hormone treatments for our breast cancer patients influence the expression of the LIV-1 family members. A preliminary result shows that in our 100 female breast cancer patients' samples indicates a strong correlation with all the members of subfamily LIV-1 for SLC39A4 and SLC39A5.