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The relationship between the expression of cytokeratin 5/6 and clinicopathologic factors in invasive breast carcinoma

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Background: Analysis of gene expression profiling data on breast carcinomas had revealed "molecular subclasses" that had prognostic significance. The basal-like subtype was associated with poor clinical outcomes. We investigated the relationship between the expression of basal-like subtype of breast carcinomas and clinicopathologic factors and defined the clinical implications of this class in invasive breast carcinoma.

Materials and Methods: An immunohistochemical study was performed on tissue microarrays constructed with 91 invasive carcinoma samples. Immunohistochemical stain for estrogen receptor (ER), progesterone receptor (PR), HER2/neu and cytokeratin (CK) 5/6 was performed.

Results: Of total 179 invasive breast carcinomas from 2005 to 2008, 91 cases were tested CK 5/6. The basal-like tumors were 13.2% (12/91). Clinicopathologic factors significantly associated with this subtype were ER, PR and histologic grade ($p = 0.001$, 0.001 and 0.004, respectively). While the other variables, like patient age, tumor size, lymph node involvement, stage and HER2/neu expression were non-signifiicant ($p > 0.05$).

Conclusions: The present sudy demonstrated that the expression for CK 5/6 was more likely to ER(−) and high histologic grade status. Theses were importatnt observations as theses tumors were limiting the range of relevant adjuvant therapies. But these findings should be further assisted by adding more specimens and finally help to facilitate treatment and constant sudies of this tumor subtype. Furthermore, we will try to find out the relationship between CK 5/6 expression and breast cancer stem cells, known as CD44+ and CD24− cells.

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Clinical significance of b-catenin expression in human breast cancer

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Background: Human breast cancer tumorigenesis is associated with one or more distinct mutations in major genes. β-catenin was first identified as a protein associated with E-cadherin in maintaining cell-cell interactions. β-Catenin is a multifunctional protein, which plays a very important role in both cell adhesion and signal transduction in theWnt/β-catenine pathway. Normally, β-catenin is rigorously controlled by upstream regulators in the Wnt/β-catenin signaling cascade. Mutation of the adenomatous polyposis coli (APC) or β-catenin gene results in stabilization of β-catenin and a significant increase in this protein within the cell. Recently it has been known that ER signaling pathways are closely associated with other intracellular signaling pathways such as growth factor and other kinase signaling pathways. ER activity may be influenced by PI3-K pathway. estrogen induces up-regulation of PI3K/Akt through activation of ER in breast cancer cells. In the present study, We investigated the relationship among ER, PR, b-catenin and PTEN expression in normal tissues and breast cancer tissues. In addition, this study were established an experimental in vitro breast cancer study model to examine the effect of GSK-3β on b-catenin expression in human breast cancer MCF-7 cells.

Material and Methods: Study candidates patients who underwent surgery for primary breast cancers from June 2008 to July 2009. The total number of breast cancer patients that had been enrolled during this period was 74. All patients was invasive ductal carcinoma. Cancer and normal tissue were collected from patients with invasive breast carcinoma with informed consent. we studied immunohistochemical staining for b-catenin protein and protein expression against ERa, ERb, p53, PTEN, b-catenin, and b-actin.

Results: ELISA assay for b-catenin from various breast normal and cancer tissues, the b-catenin protein content was significantly increased in cancer tissues. It showed high b-catenin level in ERb-positive breast cancer tissues and ERb expression compared to the adjacent normal tissues. There was a clear correlation between b-catenin and ERb expression in cancer tissues. GSK3b inhibitor induces up-regulation of b-catenin in human breast cancer cells in a ERa-independent manner. Immunohistochemical examination showed that the b-catenin was immunolocalized to the nuclei membrane of cancer cells.

Conclusions: b-Catenin expression was significantly increased in ER-positive cancer tissues. ERb in ERa-positive breast cancer tissues, b-catenin has a clear correlation with ERb expression. These results suggest that ERb might be pivotal role in the β-catenin expression in breast cancer cells. although this needs to be confirmed by additional studies, β-catenin intensity may be the marker of ERb expression.

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Activation of breast cancer cell proliferation by ROR-alpha through aromatase promoter

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Objectives: Aromatase plays an important role on progression of estrogen-dependent breast cancer. Nevertheless, mechanisms controlling the aromatase gene expression have not yet been fully clarified. On the other hand, retinoic acid receptor-related orphan receptor (ROR)α plays an important role on growth and differentiation of many organs by regulating transcription of target genes. We have identified a novel ROR response element on the promoter I.4 of aromatase gene. We have also confirmed a significant positive correlation between RORα and aromatase mRNA levels in the breast cancer specimens. In the present study, we examined the effect of RORα on aromatase gene expression, endogenous aromatase activity and proliferation activity of breast cancer cells.

Methods: RORα expression vector was transfected into MCF7 cell, which is ER-positive breast cancer-derived clonal cell. Expression of aromatase mRNA was examined using quantitative real time RT-PCR. Endogenous aromatase activity was measured by detecting ^{3}HOH, released during aromatization of [1β-^{3}H] androstenedione. Proliferation activity was measured by cell proliferation assay using the CellTiter 96 Aqueous One solution cell proliferation assay kit (Promega) with or without androstenedione.

Results: RORα transfection significantly augmented the aromatase mRNA levels, particularly those containing exon I.4. The endogenous aromatase activity was augmented by increasing the amount of RORα in a dose-dependent manner. Moreover, in the presence of androstenedione, which is converted to estrone by aromatase, the cell proliferation was stimulated by RORα in MCF7. Without androstenedione, the proliferation was not stimulated by RORα.

Conclusion: These results indicate that the expression of aromatase and endogenous aromatase activity are partly regulated by RORα, which may accelerate the conversion of androstenedione to estrone, leading to the proliferation of ER-positive breast cancer cells. Thus, RORα may be one of the critical factors for prognosis of breast cancer.

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Inhibin A is downregulated during chemotherapy in patients with breast cancer

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Introduction: Inhibins are dimeric glycoproteins, composed of an alpha-subunit (INH-α) and one of two possible beta-subunits (βA or βB), with substantial roles in human reproduction and in endocrine-responsive tumours. Aims of this study were to determine the serological measurement of Inhibin A (α-βA) in breast cancer patients during chemotherapy.

Material and Methods: A series of 28 breast cancer patients who underwent standardized chemotherapy (3 × FEC and 3 × Docetaxel) were prospectively evaluated before chemotherapeutic treatment as well as after chemotherapy and two years after chemotherapy for the serological expression of Inhibin A. For serological analysis the Ultrasensitive Inhibin A ELISA (DSL − U.S.A.) was used according to manufactures instruction. For statistical analysis the Wilcoxon rang sum test was used for paired samples. Statistical significance was assumed at $p < 0.05$.

Results: The concentration of Inhibin A showed a significant decrease between data obtained before chemotherapy and after chemotherapy ($p < 0.005$) and two-year follow up ($p < 0.001$). Interestingly, there were no obtained differences between the four-week and two-year follow up ($p = 0.744$).

Conclusion: Therefore, chemotherapy decreases significantly the Inhibin A concentration during chemotherapy. This might reflect a suppression of ovarian function and might be a marker for chemotherapy-induced amenorrhoea. Moreover, it has been suggested that Inhibin A might be a tumour marker for breast cancer, and therefore a sudden increase of its concentration might be indicative of breast cancer recurrence.