Biomarkers in breast cancer

EXPRESSION OF PHOSPHORYLATED PROTEINS FROM PI3-KINASE AND MAP-KINASE SIGNALING PATHWAYS IN INFILTRATING BREAST CANCER: RELATION WITH HISTOPATHOLOGIC AND MOLECULAR SUBTYPES

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Background: Activation of PI3-kinase (PI3K) and MAP kinase (MAPK) signaling pathways proteins have major implication in molecular oncogenesis and sensitivity of breast cancers to targeted therapy. The present study reports the investigation of the expression of PI3K and MAPK signaling pathway in frozen clinical specimens of breast carcinomas using multiplex bead immuno-analysis for phosphorylated-protein expression.

Methods: The expression of phosphorylated-AKT (p-AKT), p-GSK3β, p-S6 kinase, p-MEK1, p-ERK1/2 as well as total and p-P38MAPK was semi-quantitatively assessed using multiplex bead immuno-assay (Chergui et al, Clin Chem, 2009). The results were compared according to the histopathologic (SBR grade) or molecular subtypes: estrogen receptor (ER) positive, HER2 positive (3+ in IHC or FISH/CISH +) and triple negative i.e. ER, PR and HER2 negative (TN) using Wilcoxon test.

Results: Frozen specimens taken at diagnosis from 46 patients (mean age 56.3 years, range 28-91) with infiltrating breast cancer (mean tumor size 3 cm, range 0.6-10) were analyzed retrospectively. Eleven were SBR3, 35 SBR2. Twenty-nine were ER +; 10 were HER2 +; 10 were TN tumors. All specimens (15 mg total weight) were validated by HES slide examination by a pathologist to ensure a tumor content >50%. The analyses were performed in triplicate from total protein extracts adjusted at 250 µg/ml. The results were analyzed as mean fluorescence value relative to internal tumor extract standard. Significant differences in the expression of phosphorylated-protein were observed for ERK1/2 in SBR3 tumors and for AKT in HER2+ tumors. No significant difference was evidenced for MEK1, GSK3β and S6K in any other comparisons. Additionally, total-P38MAPK was differently expressed in ER +, as well as in TN tumors. No difference in phosphorylated-P38MAPK expression was observed in any case.

Conclusion: These results validate the use of multiplex bead immuno-analysis for determination of phosphorylated signaling proteins in clinical breast cancer specimens and warrant its prospective evaluation for identification of molecular diagnosis and/or response predictive biomarkers to targeted therapies.

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