of effective chemotherapeutic drugs are available, it is difficult to predict which combination of drugs shows clinical benefit in the individual patient. Clearly, molecular markers are needed that can predict therapy efficacy.
Our goal is to identify protein markers that can predict resistance to anthracycline-based chemotherapy in breast cancer patients using a **comparative proteomics approach**.
Materials and Methods: Snap frozen primary breast tumour tissues (n = 34) were used from patients treated with first line anthracycline-based chemotherapy for recurrent disease. 23 patients responded to treatment (objective response, OR), 15 were resistant (progressive disease, PD). From each tumour tissue, 10 mm cryosections were subjected to laser capture microdissection. Per tissue, ~4,000 epithelial tumour were collected, tryptic digests were prepared, and measured by MALDI-FTICR mass spectrometry (MS). Comparative peptide profiling performed for the identification of differentially abundant proteins, which were subsequently associated with clinical parameters.
Results: A total of 165 differential peptides were identified ($p < 0.05$), of which 16 had a $p < 0.01$. Of the latter peptides, 1 was higher in OR, 11 were higher in PD, and 4 were uniquely present in PD. Through targeted MS/MS, amino acid sequence of 10 peptides was revealed. 10 out of 16 peptides associated with progression free survival upon first line FEC/FAC treatment. Using step-down analysis, a 2 peptide predictor (representing NONO and RPS2A proteins) was built. The predictor had a strong correlation with therapy resistance ($X^2 = 14.8$, $p < 0.0001$), HR = 7.0, [95% CI: 2.4–20.3], $p < 0.0001$.
Conclusion: A 2-peptide predictor was identified for 1st line chemotherapy resistance in breast cancer. Further validation in independent samples is needed to determine clinical relevance.

5083 POSTER

The Predictive and Prognostic Significance of PTEN, P27 and PI3K Expression in HER2 Overexpressing Metastatic Breast Cancer

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Background: In this study we aimed to investigate the predictive and prognostic significance of PTEN, PI3K and p27 expression which are components of the PI3K/Akt signaling pathway in HER2 positive metastatic breast cancer.
Material and Methods: Twenty-five patients who carried a diagnosis of metastatic HER2 positive breast carcinoma and who have received trastuzumab-based therapy as first-line treatment were recruited for the study group. All of the patients breast tissue samples were evaluated for PTEN, PI3K and p27 expression by immunohistochemistry and their correlations with tumour characteristics, response to treatment, time to progression (TTP), time to recurrence (TTR) and overall survival (OS).
Results: In 76% (n = 19) of the patient group PTEN expression and in 80% (n = 20) p27 expression was found to be negative. In 24 subjects (96%) PI3K expression was reported as positive. When the group of patients who respond to trastuzumab treatment was compared to the group who did not respond to treatment with trastuzumab, there was no statistically significant association found for expression of PTEN, p27 and PI3K. When the same comparison was made for tumour characteristics a significant relation was found between tumour size and PTEN, p27 and PI3K expression (p values 0.009, 0.003 and <0.001, respectively); but a statistically significant relation between expression of the above stated expression of the genes and tumour grade, lymphatic invasion, vascular invasion, and presence of distant metastasis was not found to be present. OS and TTP was significantly longer in the patient group who responded to trastuzumab based treatment compared to the group who was unresponsive to the treatment (p values 0.016 and 0.006, respectively). Although the status of PTEN, p27 and PI3K expression was not found to be significantly correlated with response to trastuzumab treatment a trend towards lower OS, TTP and TTR in patients with loss of PTEN expression which did not reach a statistical significance was observed. A similar trend for lower OS and TTR in patients whose tumour tissues did not express p27 was also found. A relation between PI3K expression and tumour characteristics with OS, TTP and TTR was not found.
Conclusions: Loss of expression of PTEN, low expression of p27 and positive PI3K expression was found to be frequent in HER2 positive breast cancer. Their frequency was higher when compared to frequency of expression in sporadic breast cancer reported in the literature. Although the small number of our study group has made statistical interpretation of the results difficult, we propose the results of our study support the view that the presence of PTEN and p27 expression in HER2 positive metastatic breast cancer predicts response to trastuzumab treatment and shortened OS. Our results indicate that PI3K/Akt signaling pathway is active in HER2 overexpressing breast cancer.

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Receptor Conversion in Breast Cancer Brain Metastases (BM)

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Background: Several studies have indicated that the phenotype of breast cancer metastases may differ from those of primary tumour (PT). However, the data on such conversion for BM is limited. We compared the immunohistochemistry (IHC) expression of ER, PgR and HER2 in BM with that in the matched PT in 96 breast cancer patients (pts) who underwent excision of BM.
Methods: Pt characteristics (after exclusion of missing data): mean age at brain surgery: 52 years (29−83 years); 84% ductal carcinoma, 58% grade 3, 41% ER+, 30% PgR+ (⩾10% tumour cells with nuclear staining), 44% HER2+ (IHC 3+ or FISH+), 32% triple-negative (TN). 95% of pts underwent breast cancer surgery, preceded in 40% by systemic therapy. Prior to brain surgery 96% and 42% of pts, respectively, received chemotherapy or endocrine therapy as (neo)adjuvant or palliative treatment, and 77% of HER2+ pts received trastuzumab. The median time from breast cancer diagnosis to brain surgery was 29 months (range: 0 to 166 months). 67% of pts had single BM and 24% had 1−3 lesions. The most common site of BM was cerebellum and parietal lobe. 64% of pts had controlled extracranial disease at brain surgery and 87% had Karnofsky PS ⩾ 70%. After brain surgery 83% of pts received radiotherapy, 57% chemotherapy, 21% endocrine therapy and 27% anti-HER2 therapy.
Results: ER and PgR conversed to negative in 47% and 59% of pts, respectively, and to positive in 19% and 13% (Table). The respective conversions for HER2 were 8% and 13%. Of the 31 TN cancers 8 (26%) gained ER or PgR and 2 (7%) HER2. The percentage of hormone receptor (HR) positive tumours was lower in BM than in PT (ER: 33% vs 41%; PgR: 22% vs 30%, respectively), whereas it was similar for HER2+ (44% vs 47%) and TN cancers (32% vs 34%). HER2 loss in BM occurred in only 8% of pts who received trastuzumab. The median overall survival from brain surgery in the entire group was 13.4 months (16.1, 12.2 and 15.7 months for ER/PgR+, TN and HER2 in BM, respectively; all HER2+ pts were assigned to HER2+ group, irrespective of HR expression). There was no apparent prognostic impact of any receptor conversion.
Conclusions: Receptor conversion is a common event in breast cancer BM. Predominant conversion includes the loss of HRs, whereas HER2 and TN phenotypes are more stable. Trastuzumab therapy does not impact HER2 expression in BM.

Receptor	Total	pos-neg (%)	neg-pos (%)
ER	95	18/38 (47%)	11/57 (19%)
PgR	94	16/27 (59%)	9/67 (13%)
HER2	92	3/40 (8%)	7/52 (13%)

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New Curcumin Analogue RL-66 Has Promising Anti-breast Cancer and Antiangiogenic Activity

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Previously we reported that the new curcumin analogue RL-66 had promising cytotoxicity in various estrogen receptor (ER) negative breast cancer cells. Therefore, we further explored the anticancer potential of RL-66 in MDA-MB-468 human breast cancer cells. Cell cycle distribution and apoptosis induction were assessed by flow cytometry and protein expression was analyzed by Western blotting. Furthermore, the effect of RL-66 on tumour growth was examined in MDA-MB-468 mouse xenograft