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Identification of key breast cancer phenotypes

A. Green[1], J.M. Garibaldi[2], D. Soria[2], F. Ambrogi[3], D.G. Powe[4], G. Ball[5], P.J.G. Lisboa[6], P. Boracchi[3], E. Biganzoli[3], I.O. Ellis[1]. *[1]University of Nottingham, School of Molecular Sciences, Nottingham, United Kingdom; [2]University of Nottingham, School of Computer Science, Nottingham, United Kingdom; [3]University of Milan, Institute of Medical Statistics and Biometry, Milan, Italy; [4]Nottingham University Hospitals, Histopathology, Nottingham, United Kingdom; [5]Nottingham Trent University, School of Biomedical and Natural Sciences, Nottingham, United Kingdom; [6]Liverpool John Moores University, School of Computing and Mathematical Sciences, Liverpool, United Kingdom*

Background: Breast cancer is a heterogeneous disease, of which several forms have been identified on the basis of their gene expression characteristics. However, translation of this molecular genetic approach into routine clinical practice remains elusive or prohibitively expensive. We have previously demonstrated that protein expression characteristics can be used to identify comparable classes. In this study, we extend this approach and further define the key criteria for class membership.

Material and Methods: Expression of twenty-five proteins, with known relevance to breast cancer, have been assessed in a series of 1,076 patients. This large data set has been examined by four alternative data clustering techniques [Hierarchical, K-means (KM), Partitioning around medoids (PAM), Adaptive resonance theory (ART)]. Concordance between techniques was used to elucidate 'core classes' of patients which could be well characterised.

Results: A total of 663 (62%) of the 1076 patients were assigned to six core classes, while 413 (38%) patients were of indeterminate or mixed class. Three core classes correspond to well known clinical phenotypes (luminal A, luminal B and HER2). Two classes correspond to the well known basal phenotype, but exhibit a novel differentiation into two sub-groups. The last class appears to characterise a novel luminal subgroup.

Conclusions: Key clinical phenotypes of breast cancer can be identified using standard, widely available immunocytochemistry technology. The main luminal and basal breast cancer phenotypes appear to be heterogeneous, containing distinct sub-groups. The six clinical phenotypes determined in this study are a new luminal group, luminal N, the new basal sub-groups, basal p53 altered and basal p53 normal, as well as the previously well-established luminal A, luminal B and HER2 groups.

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High expression of p130Cas/BCAR1 significantly associated with early relapse in hormone receptor positive, axillary node positive breast cancer patients

S. Lee[1], Y.S. Lee[1], S. Kwon[1], S.Y. Kong[1], B. Kwon[1], Y. Kwon[1], K.H. Min[1], H.S. Kang[1], J. Ro[1], E.S. Lee[1]. *[1]National Cancer Center, Center for Breast Cancer, Goyang, Korea*

Background: Tamoxifen is a still major drug to reduce the risk of recurrence and to prolong the survival of receptor positive breast cancer patients. Even if most patients benefit from tamoxifen, many tumors become resistant. The adhesion-associated molecule p130Cas/BCAR1 is known to promote resistance to tamoxifen. We have studied the expression of mRNA and protein by RT-PCR and immunohistochemical (IHC) staining about BCAR1 and correlation with early relapse in node positive, hormone positive breast cancer patients.

Materials and Methods: We have conducted this study in both retrospective and prospective ways. Retrospectively collected 87 tumors, 61 tumors from disease free patients more than 2 years of tamoxifen and 26 tumors from who showed recurrence within 2 years, were analyzed by IHC expression of EGFR1, Her-2/neu, p53 and BCAR1. BCAR1 was the only one significantly related with early relapse (Odds ratio:4.08, p = 0.0056). Then, prospective study was designed with consecutive 190 node positive, hormone positive breast cancer patients from October 2001 through December 2005. All patients received standard operations, adjuvant or neo-adjuvant chemotherapy, with or without radiation therapy and followed by tamoxifen therapy. The expression of BCAR1 mRNA was checked by semi-quantitative RT-PCR in peripheral blood sample and evaluated with protein expression by IHC staining of primary tumor. We also analyzed correlation between the expression of BCAR1 and clinicopathologic parameters and early relapse.

Results: Mean follow up time was 32 months and 16 recurrences developed. The expression of BCAR1 mRNA in peripheral blood and IHC staining of primary tumor was significantly correlated (p = 0.044). The patients who had higher expression of BCAR1 mRNA showed poorer outcome of disease-free survival (p = 0.0001) than those of non-detectable or weak expression. The patients who had strongly positive estrogen receptor and weak expression of BCAR1 mRNA showed the best outcome of disease-free survival (p = 0.0001) in multivariate analysis.

Conclusions: High expression of p130Cas/BCAR1 significantly associated with early relapse in hormone receptor positive, axillary node positive breast cancer patients.

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Clinicopathologic characteristics of triple negative breast cancer in early stages

J. Ahn[1], S. Kang[1], K. Kwun[1]. *[1]Dongsan Medical center Keimyung University, General Surgery, Daegu, Korea*

Background: Triple negative breast cancer (estrogen receptor-negative, progesterone receptor-negative, and c-erb B2 receptor-negative) is associated with high risk of recurrence and poor clinical outcome. Clinicopathologic characteristics of triple negative breast cancer is important to prediction of prognosis and decision of treatment guideline. We investigated the characteristics of triple negative breast cancer in early stages.

Materials and Methods: We reviewed the records of 821 early stage (stage I and II) breast cancer patients who treated at our hospital from 1995 to 2005. We examined difference between triple negative group compared with non triple negative group in relation to clinicopathologic characteristics.

Results: Of 821 early stage breast cancer patients, 200 cases (24.4%) were of triple negative group. The mean age of triple negative group was 47.9 and non triple negative group was 48.9. Both histologic grade and nuclear grade of triple negative group were significantly higher than those of non triple negative group (p = 0.000). Large tumors (T2 and T3) in triple negative group were significantly more than those in non triple negative group (p = 0.042), but there was no significant difference in lymph node involvement between two groups (p = 0.933). As of May 2007, with a median follow-up time of 50 months, there have been 50 local recurrences, 98 distant metastases, and 65 deaths. There were significant high rates of local recurrence (n = 21, 10.5%) and death (n = 25, 12.8%) in triple negative group (p = 0.006, p = 0.010 respectively).

Conclusions: Patients classified as triple negative breast cancer have poor pathologic findings and prognoses. Careful treatment and follow-up is important to triple negative breast cancer in early stages and further investigation is necessary to triple negative breast cancer.

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HER-2 overexpression does not decrease survival of breast cancer patients with brain metastases

K. Krzemieniecki[1], E. Pluta[1]. *[1]CO Instytut Onkologii, Head and Neck Cancer, Krakow, Poland*

Background: HER-2 positivity is an increasingly recognized risk factor for development of brain metastases (BM). Approximately 10−30% with HER-2 overexpression will present BM, according to recent studies. There are not enough sufficient data on correlation between HER-2 positivity and survival of patients presenting BM. Overall survival and post-radiotherapy survival were analyzed in presented study.

Material and Method: HER-2 overexpression reported in 35% of cases between 31 breast cancer patients treated recently with radiotherapy due to BM in Krakow Cancer Institute. Whole-brain radiotherapy technique with total dose ranging from 20 to 40 Gy was used.

Results: No significant differences in overall survival (p = 0.1138) and post-radiotherapy survival (p = 0.3279) were detected between HER-2 positive (60 months and respectively 7.1 months) and negative groups (45 months and respectively 6.1 months).

Conclusion: HER-2 positivity is a known risk factor for BM development in breast cancer patients but does not affect survival among patients with detected and irradiated BM.

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Proliferation rate, microvessel density, expressions of HER-2, hormone receptors and P53 protein as predictors of tumour response to adjuvant anthracycline treatment in breast cancer patients

B. Biesaga[1], J. Niemiec[1], Z. Ziobro[2], J. Wysocka[3], A. Kruczak[3]. *[1]Maria Curie Sklodowska Institute, Dept. of Radiation Biology, Krakow, Poland; [2]Maria Curie Sklodowska Institute, Dept. of Medical Oncology, Krakow, Poland; [3]Maria Curie Sklodowska Institute, Dept. of Pathology, Krakow, Poland*

Background: Among breast cancer (T1−T2, N1−N2, M0) patients treated radically with surgery and adjuvant chemotherapy based on anthracyclines, in about 60% of woman local recurrence is observed. These differences in treatment outcome indicate the need to identify biological markers of