recruitment of SP-1 to DNA, especially under insulin treatment, while SP-1 loading with or without insulin on DNA containing Lep-2548G/G was minimal. In contrast, nucleolin binding to Lep-2548G/A was downregulated in response to insulin, while it was not regulated on Lep-2548G/G. These results were confirmed by DNA affinity immunoprecipitation with specific Lep-2548G/A and control probes. Enhanced loading of SP-1 near Lep-2548G/A was paralleled by higher basal and insulin-induced expression of leptin mRNA in MDA-MB-231 cells.
Conclusions: The occurrence of Lep-2548G/A can enhance basal and insulin-induced leptin expression in breast cancer via SP-1- and nucleolin-dependent mechanisms.

2016 POSTER

Expression of the putative breast cancer gene BASE; relationship with microRNA-154* and estrogen receptor status

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Background: The role of micro-RNAs in the regulation of fundamental cellular processes such as proliferation, differentiation and apoptosis has advocated them as a novel molecular mechanism in the aetiology of carcinogenesis. It is estimated that 30% of human genes are regulated by micro-RNAs, many of which are cancer related. One such potential gene, BASE has been shown by in-vitro studies to be estrogen responsive and breast cancer specific. Little is known, however, about the associations or precise regulation of BASE expression in breast cancer tissues.
Aims: To quantify the expression of BASE and its putative targeting microRNA miR-154* in breast cancer tissues, and to establish potential correlations with clinicopathological variables.
Materials and Methods: Whole genome molecular profiling of gene expression and mi-RNA sequences was performed in 16 early stage, matched breast cancer specimens, to identify differentially expressed genes and micro-RNAs.
Expression of selected micro-RNAs including miR-154* were validated using RT Q PCR in a further 52 breast tumour samples. BASE was identified as a computationally predicted target of miR-154*, and its expression was also validated 52 breast tumour specimens and breast cancer cell lines. Associations between expression of BASE and miR-154* and clinico-pathological variables were examined
Results: BASE was expressed in 50% of tumour samples. A significantly higher proportion of tumours expressing BASE were estrogen receptor (ER) positive than ER negative ($p = 0.019$). BASE expression was also detected in the ER+ve cell lines but was not detected in an ER−ve cell line. MiR-154* was expressed in all breast tumour samples. The expression of miR-154* was significantly lower in ER+ve than ER−ve tumour samples ($p = 0.001$)
Conclusions: These findings suggest that the expression of both miR-154* and putative target gene BASE correlate with estrogen receptor status in breast tumours. This highlights the importance of these molecules breast cancer. Functional analysis to elucidate a possible interaction between these molecules is underway.

2017 POSTER

Prognostic value and response to chemotherapy of immunohistochemical phenotypes (IP) of 141 operable breast cancer patients (pts) included in phase III trials of adjuvant therapy

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Background: Gene expression arrays and IP studies classified breast cancer in three distinct subtypes: basal, HER2/neu and luminal that are associated with different clinical outcomes.
Methods: In 141 pts with operable breast cancer, included in phase III trials of adjuvant therapy in our center, immunohistochemical staining was performed on 3μm sections of paraffin blocks, containing tissue-arrays of tumour tissue.A basal phenotype (BP) was defined by negative estrogen receptor (ER) and progesterone receptor (PR) and positive cytokeratin (CK) 5/6 or EGFR immunoreactivity. HER2/neu phenotype as positive c-erb B2 by HercepTest™ and luminal phenotype (LP) by positive ER, PR and CK 7/8 and negative HER-2. Survival curves were calculated by the Kaplan-Meier method. The differences between survivals were estimated using the log rank test. Multivariate Cox regression analysis was used to evaluate any independent prognostic effect of the variables on disease-free survival (DFS).
Results: Complete clinical follow-up information was available for 141 pts. The median follow-up period was 52 months (range 1–103 months). During this period, 13.8% pts died from breast cancer and 27.7% pts relapsed. At the time of the primary diagnosis 10.4% of the pts had lymph node negative disease and 89.6% had positive lymph nodes. 50.8% pts received standard chemotherapy with anthracycline and taxanes, 7.7% Trastuzumab, 62.3% radiotherapy and 61% pts received hormonotherapy. Positivity for LP was 65.2%, BP 9.9% and Her-2 phenotype 8.5%. 16.3% didn't fit for any of the three subtypes. Median DFS for BP: 24 moths, for LP and Her-2 phenotypes median DFS was not reached. 5 years DFS were; BP: 19%, LP: 63% and Her-2: 56%. Kaplan-Meier survival analyses demonstrated that the presence of a detectable BP was highly significantly associated with a worse DFS compared with the presence of a LP, log rank test ($p = 0.0001$). Multivariate Cox regression analyses estimated that the prognostic effect of BP in relation to DFS was independent of lymph node, stage and tumor size, HR: 0.12 95% CI (0.05−0.2). In the group of patients who received standard-based adjuvant chemotherapy, both DFS and OS were found to be significantly shorter in the BP ($p < 0.05$).
Conclusions: We found that expression of BP was associated with poor prognostic in the context of randomized phase III trials. Standard adjuvant chemotherapy seems to be less effective in these tumours and new therapeutic approaches are indicated.

2018 POSTER

Can differences in cellular antioxidant enzyme status predispose to breast cancer in women without a recognised increased risk?

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Introduction: Up to 10% of patients with breast cancer have a known genetic defect (eg. BRCA-1, BRCA-2) but the aetiological factors in the others remain unclear. We hypothesise that impaired expression of cellular antioxidant enzymes and subsequent reduction in the ability to counter DNA damage due to oxidative stressors could be, at least in part, important in the aetiology of breast cancer.
Method: We obtained whole blood and PBMNC from women with breast cancer ($n = 20$) and from an age matched control group without known risk ($n = 20$). Erythrocyte and plasma glutathione peroxidase-1 (GPX1) activity was determined in both groups using a spectro-photometric method. Aliquots of PBMNC were used to determine gene expression of redox enzymes in untreated, fresh cells using RT-PCR. Further aliquots of PBMNCs were incubated in autologous plasma for 24 hrs and stimulated with hydrogen peroxide (1 mM) for 15 minutes to assess inducibility of the selenium-dependent antioxidant enzymes (GPX1) and (GPX4).
Results: Neither GPX1 activity in plasma or erythrocytes nor mRNA expression in fresh, non-induced PBMNC differed significantly between groups although mRNA tended to be lower in the cancer group. However, GPX4 gene expression in fresh PBMNC was significantly (30%, $p < 0.004$) reduced in the cancer group. Percentage induction of mRNA by hydrogen peroxide was similar (30−40%) for GPX1 and GPX4 in both groups but absolute GPX4 induction was lower in the cancer group due to a lower un-stimulated, starting value.
Conclusion: Breast cancer patients do appear to have a lower redox enzyme expression than non-cancer patients which would be expected to impair their ability to counter free-radical damage to DNA resulting in greater risk of genetic mutations.

2019 POSTER

The role of primary stromal cell-derived chemokines in the breast tumour microenvironment

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Background: It is well established that within the breast tumour microenvironment, neoplastic epithelial cells coexist with stromal fibroblasts. Stromal cells secrete a variety of chemokines which may potentially mediate the reciprocal interactions between breast stromal and epithelial populations. However, the specific chemokines involved and their mode of action remain to be defined.
The aim of this study was to identify factors secreted by tumour stromal cells and elucidate their potential role within the tumour microenvironment.
Methods: Human breast tumour specimens harvested at surgery were separated into epithelial and stromal fractions for culture. Tissue harvested at reduction mammoplasty served as normal controls. Chemokines secreted by the stromal populations were detected using Chemiarray™, ELISA and RQ-PCR. Transwell® inserts were used to assess migration of breast cancer epithelial cell lines (MDA-MB-231 and MCF-7) in response to primary stromal cells.