Conclusions: Our findings suggest that miR-34a is involved in docetaxel resistance, which may act by targeting BCL2 and cyclinD1.

doi:10.1016/j.ejcsup.2010.06.055

O-55 TRANSLATIONAL LANDSCAPE OF EPITHELIAL MESENCHYMAL TRANSITION IN MOLECULAR CLASSES OF INVASIVE BREAST CANCER

Mohammed A. Aleskandarany [a], Andrew R. Green [a], Emad A. Rakha [b], Des G. Powe [b], Ian O. Ellis [a,b]. [a] *Division of Pathology, University of Nottingham, UK.* [b] *Department of Pathology, Nottingham University Hospitals, UK*

Epithelial Mesenchymal Transition (EMT), as defined by loss of epithelial characteristics and gaining a more mesenchymal-like phenotype, has been largely reported *in vivo*. However, the actual occurrence of events defining EMT is rarely fully observed *in vivo*. We aimed to explore the translational landscapes of EMT in breast cancer (BC) with relevance to potential triggering pathways and BC molecular subtypes. Clustering analysis was performed on a well-defined clinically annotated series of invasive non-lobular BC ($n = 431$) prepared as tissue microarray (TMAs). A large panel of biomarkers including cadherins, TGFβ1, PIK3CA, pAkt, cytokeratins, Erb-family members and hormone receptors, has been studied. Differential expression of EMT markers was observed between molecular BC subtypes (Luminal1 and 2, $HER2^+$, and basal-like (BLBC), where BLBC expressed lower E-cad, higher P-cad, smooth muscle actin and PIK3CA, relative to $HER2^+$ BC that expressed highest levels of N-cad, TGFβ1 and PIK3CA. Within luminal tumours subdivisions, expression levels of N-cad, TGFβ1, pAkt and PIK3CA differed considerably. N-cad contributed to cluster separation more than E-cad ($F = 13.14$ and 1.68, respectively). Moreover, E-cad/N-cad switch occurred more frequently in BLBC and $HER2^+$. Significant differences were observed between these four clusters for breast cancer-specific and disease-free survivals ($p < 0.001$).

BLBC and $HER2^+$ BC preferentially displayed EMT/cadherin switch than luminal BC, explaining their indigenous tendency for progression. In addition, EMT/cadherin switch programs in BC appear to occur synergistically with TGFβ1 and PIK3/Akt pathways activation. These data explain, at translational level, the varied clinical behaviour of BC molecular classes, thus could help developing targeted therapies against EMT-associated pathways.

doi:10.1016/j.ejcsup.2010.06.056

O-56 HIGH EXPRESSION OF SPHINGOSINE 1-PHOSPHATE RECEPTORS, $S1P_1$ AND $S1P_3$, SPHINGOSINE KINASE 1 AND ERK-1/2 IS ASSOCIATED WITH DEVELOPMENT OF TAMOXIFEN RESISTANCE IN ER POSITIVE BREAST CANCER PATIENTS

Carol Watson, Jaclyn S. Long, Clare Orange, Claire L. Tannahill, Elizabeth Mallon, Liane M. McGlynn, Susan Pyne, Nigel J. Pyne, Joanne Edwards. *University of Glasgow, UK*

Cell line studies demonstrate that sphingosine kinase 1 (SK1) and extracellular signal regulated kinase 1/2 (ERK-1/2) interact in an oestrogen receptor (ER) dependent manner to influence breast cancer cell growth and migration. A cohort of 304 ER positive breast cancer patients, were utilised to investigate the prognostic significance of SK1, sphingosine 1-phosphate receptors 1, 2 and 3 ($S1P_1$, $S1P_2$ an $S1P_3$) and ERK-1/2 expression. Expression levels of SK1, $S1P_1$, $S1P_2$ and $S1P_3$ were established by immunohistochemistry. Cytoplasmic and nuclear SK1 expression was associated with shorter time to recurrence on tamoxifen (recurrence time) ($p = 0.022$ and $p = 0.016$, respectively) and high membrane $S1P_1$ expression was also associated with shorter time to recurrence ($p = 0.008$). High cytoplasmic $S1P_1$ and $S1P_3$ expression were associated with shorter disease specific survival ($p = 0.036$ and $p = 0.019$). Those patients with tumours that expressed high levels of both cytoplasmic SK1 and ERK-1/2 had significantly shorter recurrence time than those that expressed low levels of cytoplasmic SK1 and cytoplasmic ERK-1/2 ($p = 0.00008$), with a difference in recurrence time of 10.5 years. Similarly, high cytoplasmic $S1P_1$ and cytoplasmic ERK-1/2 expression ($p = 0.004$) and high cytoplasmic $S1P_3$ expression and cytoplasmic ERK-1/2 expression ($p = 0.004$), were associated with shorter recurrence time. These results support a model in which the interaction between SK1, $S1P_1$ and/or $S1P_3$ and ERK-1/2 might drive breast cancer progression and this therefore warrants further investigation.

doi:10.1016/j.ejcsup.2010.06.057

O-57 SCREEN DETECTED DCIS IN THE EAST MIDLANDS REGION: COMPARISONS IN TREATMENT AND OUTCOME OVER TIME (1988–2003)

J.A. Reed [a], A. Murphy [a], G. Comerie [a], D.M. Sibbering [b]. [a] *East Midlands Quality Assurance (QA) Reference Centre, Nottingham, UK.* [b] *Royal Derby Hospital, Derby, UK*

A retrospective study was carried out comparing three cohorts of consecutive patients diagnosed with DCIS via the NHSBSP in the East Midlands region. Diagnostic, treatment and follow-up outcome data was collected by individual patient case notes review, and where necessary by contacting general practitioners. Kaplan–Meier survival analysis was performed using SPSS.

Histological excision margins were increasingly clear over time 88% (88/93), 91.5% (94/97) and 98% (00/03). The overall local recurrence free survival rate was identical for both earlier periods with 92% at 5 years but improved to 96.1% over 2000/03. 40–56% of all local recurrences were invasive; 13/23 (88/93), 14/26 (94/97), and 8/21 (00/03). Use of tamoxifen within the three cohorts was similar (44–46%) and made no significant difference to rates of local or contralateral recurrence free survival. Significant differences in local recurrence rates by operation type were observed (see Table 1).

Conclusion: Local recurrence rates after breast conserving surgery for screen detected DCIS have reduced over time. This is likely to be related to higher rates of non-operative diagnosis, combined with improved histological assessment (grading and

Table 1

Time period	1988–1993 (*n.* 300)	1994–1997 (*n.* 319)	2000–2003 (*n.* 547)
Non-operative diagnosis	59 (20%)	142 (45%)	439 (80%)
Treatment			
Mastectomy	134 (45%)	127 (40%)	205 (37%)
Wide local excision	123 (41%)	141 (44%)	294 (54%)
Diagnostic excision alone	43 (14%)	51 (16%)	48 (9%)
Radiotherapy (post conservation)	24 (15%)	25 (13%)	186 (54%)
Tamoxifen	139 (46%)	149 (47%)	240 (44%)
5 year LRR			
Mastectomy	2 (1.5%)	3 (2.5%)	1 (0.5%)
Wide local excision	12 (10%)	17 (12%)	19 (6.5%)
Diagnostic excision alone	9 (22%)	6 (12%)	1 (2%)

margin status), more aggressive surgery and increasing use of radiotherapy.

doi:10.1016/j.ejcsup.2010.06.058

O-58 FACTORS INFLUENCING LOCAL CONTROL IN PATIENTS UNDERGOING BREAST CONSERVATION SURGERY FOR DUCTAL CARCINOMA IN SITU

J. Mathew [a], R. Karia [a], N. Warrich [a], D. Morgan [b], A. Lee [c], I. Ellis [c], J. Robertson [a], A. Bello [a]. [a] *Division of Breast Surgery, Nottingham University Hospitals, Nottingham, UK.* [b] *Department of Oncology, Nottingham University Hospitals, Nottingham, UK.* [c] *Department of Pathology, Nottingham University Hospitals, Nottingham, UK*

Background: The aim of our study was to assess various risk factors for local recurrence (LR) in patients undergoing breast conservation surgery (BCS) for ductal carcinoma in situ (DCIS).

Materials and methods: Retrospective case note review between January 1975 and June 2008. In our hospital a margin of $\geqslant$10 mm is considered acceptable. Patients were divided into three groups based on pathological margin (<5 mm, 5–9 mm and $\geqslant$10 mm). Cox regression model for multivariate analysis of local recurrence was used with variables with significant *P* values (<0.05) in the univariate analysis carried out using SPSS version 16.

Results: Overall 239 women had BCS for DCIS during the above period. The median age was 59 years (40–86) and the median follow-up was 76 months (1–308). Pathological findings included median size of 11 mm (1–50), 75 cases with comedo necrosis and 5 patients with microinvasion (<1 mm). Overall 193 patients had grades recorded (44 low grade, 54 intermediate grade and 95 high grade).

Overall LR rate was 17% (40/239), of which 65% (26/40) were invasive recurrences. Thirty-one patients were $\leqslant$ to 50 years and 32% (10/31) developed LR compared to 14% (30/208) in those above 50 years ($P = 0.018$). Forty-three percent of patients (6/14) with <5 mm margin developed LR compared to 12% (3/25) with 5–9 mm margin and 14% (27/188) with $\geqslant$10 mm margin. Four out of 12 patients with unknown margin status developed LR. The LR rate in patients with <5 mm (6/14) margin was significantly higher compared to those with $\geqslant$5 mm (30/213) margin (P value < 0.012). Three out of 5 patients with microinvasion developed LR and it was statistically significant ($P = 0.034$) compared to those without microinvasion. On multivariate analysis age $\leqslant$50 years, <5 mm pathological margin and microinvasion were independent poor prognostic factors for local recurrence.

Conclusion: Our study shows that younger age ($\leqslant$50 years), a clear margin <5 mm and associated microinvasion are poor prognostic factors for LR in patients undergoing breast conservation surgery for DCIS.

doi:10.1016/j.ejcsup.2010.06.059

O-59 SINGLE CENTRE EXPERIENCE OF 500 PATIENTS WITH INTRA-OPERATIVE RT-PCR BREAST SENTINEL NODE ANALYSIS

V. Brown, R. Cutress, T. Simoes, A. Agrawal, M. Wise, I. Cree, C. Yiangou. *Portsmouth Breast Cancer Centre, Queen Alexandra Hospital, Portsmouth, UK*

Introduction: Tumour specific mRNA markers detected by real time reverse transcriptase-polymerase chain reaction (RT-PCR) have been used to detect breast cancer metastases in sentinel lymph nodes. We present our experience of 500 consecutive cases in a single centre.

Methods: All clinically and radiologically node negative patients who underwent sentinel node biopsy (SLNB) were included in the study over a 24-month period. SLNB was performed according to New Start guidelines. Intraoperative analysis was performed on alternate slices at 2 mm intervals, with the remaining slices sent for standard histological analysis. The GeneSearch assay (Veridex LLC, Warren, NJ) was used to detect the expression of mammaglobin (MG) and cytokeratin 19 (CK). Patients were considered SLNB positive if one or more sentinel lymph nodes were positive for either MG or CK.

Results: Sentinel lymph nodes (912) were analysed with an average of 1.8 nodes per patient. The cohort was representative