($p = 0.038$) and NFkB1 ($p < 0.001$). NFkB DNA-binding data for 4 out of 5 NFkB family members correlated well with the number of stained nuclei: RelA ($R_s = 0.481$; $p = 0.050$), RelB ($R_s = 0.707$; $p = 0.001$), NFkB1 ($R_s = 0.767$; $p = 0.001$) and NFkB2 ($R_s = 0.440$; $p = 0.058$). Transcriptionally active NFkB dimers were found in 17/44 IBC specimens compared to 2/45 nIBC specimens ($p < 0.001$). Within the group of breast tumours with transcriptionally active NFkB, the expression of 7/8 NFkB target genes was significantly elevated compared to the group of breast tumours without transcriptionally active NFkB. The presence of transcriptionally active NFkB dimers was significantly elevated in Estrogen Receptor (ER) negative breast tumours: 16/49 ER- tumours with transcriptionally active NFkB compared to 3/41 ER+ tumours with transcriptionally active NFkB ($p = 0.004$). In this context, ER alpha gene expression data anti-correlated significantly with gene expression data for 7/8 NFkB target genes, and gene expression data for 7/8 NFkB target genes were significantly elevated in ER- breast tumours.

Conclusion: In conclusion, we demonstrated that the NFkB pathway is activated more often in IBC compared to nIBC. Our data suggest a potential cross-talk between the NFkB and ER signalling pathways in breast cancer, potentially contributing to the IBC phenotype.

306 Poster

The role of aromatase and 17-beta-hydroxysteroid dehydrogenase type 1 mRNA expression in predicting the clinical outcome in human breast cancer

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Introduction: There is a substantial evidence that breast cancer tissue contains all the enzymes responsible for the local biosynthesis of estrogens from circulating precursors. The aromatase enzyme complex is responsible for the conversion of C19 androgens to oestrogens. Also, 17-beta-hydroxysteroid dehydrogenase (17-beta-HSD) type 1 catalyzes the interconversion of estrone to the biologically more potent estradiol. It is well established that increased exposure to local estrogens in postmenopausal women is an important risk factor in the genesis and growth of breast cancer.

The aim of this study was to look at the correlation between aromatase and 17-beta HSD type 1 mRNA expression and clinico-pathological parameters in human breast cancer.

Methods: 127 tumour tissues and 33 normal tissues were analyzed. The levels of transcription of Aromatase and 17-beta HSD type 1 were determined using real-time quantitative PCR. The mRNA expression was normalized against CK19. Levels of expression were analyzed against tumour's stage, grade, nodal status, local relapse, distant metastasis and survival over 10 years follow up period. In addition, the levels were analyzed against estrogen hormone receptors status.

Results: Overall, high expression of aromatase and 17-beta HSD type 1 were correlated with poor survival ($p = 0.0105$ and 0.0182) respectively.

Increased levels of aromatase mRNA expression were positively correlated with progression of the disease as levels were significantly higher in samples of patients who had distant metastasis and local recurrence and/or died of breast related causes when comparing to those who were disease free for > 10 years ($p = 0.0015$). Furthermore, levels of aromatase mRNA expression in patients who died from breast cancer were significantly higher than normal breast tissue ($p = 0.0016$)

We also observed higher levels of aromatase mRNA in tumour samples compared to normal breast tissue. However, the difference did not reach a statistical significance.

There was no correlation between expression level of aromatase and tumour stage, lymph node status and tumour grade. Nonetheless, higher levels were observed in grade 1 tumours compared to normal tissue ($p = 0.01$)

No significant difference in expression of 17-beta HSD type 1 between normal and cancerous tissues was seen. We also noticed an increase in levels correlating with tumour grade. This correlation was statistically significant when we compared grade 1 with grade 2 and grade 1 with grade3 ($p = 0.0031$ and 0.0251 respectively)

Finally, a trend toward increased expression of aromatase is associated with ER + ($p = 0.06$) this trend was not observed in 17 beta HSD Type 1.

Conclusion: Our results suggest that higher levels of enzymes responsible for the local biosynthesis of estrogens in breast cancer patients especially aromatase carries poor outcome. This finding supports the idea that reduction of local estrogen production may improve the outcome of breast cancer in postmenopausal women and aromatase inhibitors would be an ideal modality of treatment.

307 Poster

Over-expression of activated c-Src in ductal carcinoma in situ predicts disease recurrence at 5 years and correlates with her2 positivity, high tumour grade, comedo histologic type and high proliferation

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Introduction: The oncoprotein Src kinase is downstream of receptor tyrosine kinases HER1 and HER2, and is upregulated in early stages of breast cancer. In vitro and in vivo studies have suggested that increased c-Src activity may promote breast tumour growth and metastasis. Few studies have investigated the expression of activated c-Src in breast cancer subtypes.

Aim: To evaluate the expression of activated c-Src in pure DCIS and invasive breast carcinoma and determine if the level of activated c-Src correlates with clinicopathological factors and predicts tumour recurrence.

Methods: Immunohistochemical expression of activated c-Src was evaluated in 129 women (median age 55 years) with 'pure' DCIS and 43 women with invasive breast carcinoma (median age 53 years) who underwent surgery at one unit. The median follow-up in the DCIS group was 60 months (range 10–155 months) and 65 months in the invasive breast carcinoma group. The level of activated c-Src was scored as 1(low), 2(medium) and 3(high). Estrogen receptor status (ER), HER1, HER2, and Ki67 levels were also measured by immunohistochemistry. In univariate analysis, the log rank test was used evaluate activated c-Src and recurrence-free survival.

Results: See the table.

DCIS characteristics	Level of activated c-Src			p value
	1 (low)	2 (medium)	3 (high)	
Tumour grade (n = 129)				**<0.0005**
Low	6	3	0	
Intermediate	14	20	6	
High	9	26	45	
Histological type n = 123				**<0.0005**
Comedo	2	13	13	
Mixed	7	20	28	
Non-comedo	17	17	6	
HER2 status (n = 114)				**0.002**
Negative (≤1)	13	17	6	
Positive (≥2)	13	26	39	
Ki67 Level (n = 126)				
Mean rank	51.5	59.0	74.9	0.013

In DCIS, but not invasive breast carcinoma, high levels of activated c-Src correlated with HER2 positivity, higher tumour grade, and comedo type DCIS with a high epithelial proliferation (measured by Ki67), but not tumour size, ER status and HER1 expression. Over-expression of activated c-Src was associated with an overall lower recurrence-free survival at 5 years ($p = 0.026$ Log rank). There was a trend towards higher proliferation and activated c-Src in the invasive breast tumours.

Conclusion: Activated Src kinase in DCIS predicts outcome at 5 years and is associated with HER2 positivity, high nuclear grade, comedo-type histology and a high proliferation. Activated c-Src may be important in the early stages of breast tumour development, but in later stages of breast disease, additional molecular events independent of c-Src activation might contribute to further disease progression. Targeting c-Src with intracellular small molecule inhibitors may be therapeutically useful.