Materials and Methods: CGH is a technique by which we can detect amplifications or deletions in the genome in a single hybridisation experiment. DNA was extracted from both MCF-7 and CL-9. The CGH assay was performed using: MCF-7 DNA - normal placental DNA, b) CL-9 DNA - normal placental DNA, c) MCF-7 DNA - CL-9 DNA. Images were captured with a CCD camera and analysed. Metaphases were prepared from the cell lines and analysed by cytogenetics and also by chromosomal painting.

Results: CGH analysis for the tamoxifen sensitive and resistant clone showed many areas of concordance but important differences were seen in amplification of chromosomes 2p16.3-23.2, 2q21-34, 3p12.3-14.1, 3p22-26, 3q, 12q13.2-22, 13q12-14, 17q21.3-23, 20q11.2-13.1 and 21q11.2-21 as well as the deletion of chromosomes 6p21.1, 6p23-25, 7q11.1-31, 7q35-36, 11p15, 11q24, 13q33, 17p, 18q12-21.1, 19p, 19q13.3, 22q13.1-13.2. These findings were confirmed by cytogenetics and chromosomal painting.

Discussion and Conclusions: Transformation from a tamoxifen sensitive to a resistant phenotype could be explained by changes at the molecular level. Definite alterations in the genetic profile were seen in the tamoxifen resistant cell line involving regions harbouring potential genes e.g. *TGF-β* at 19q13.3, *MDM-2* at 12q14.3-15. These may be involved in the development of tamoxifen resistance and need further evaluation. This study has shown that the development of tamoxifen resistance is associated with changes at the chromosomal level.

O-86. COMPARISON OF OESTROGEN RECEPTOR α AND β mRNA AND PROTEIN IN MALIGNANT AND NON-MALIGNANT BREAST

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The identification of a second oestrogen receptor (ER), ERβ, has resulted in interest in its role in the response of breast cancers to endocrine therapy. In this study we have studied ERβ mRNA and protein in malignant and non-malignant breast and compared it to ERα to define its significance in breast cancer.

62 cancers (38 with adjacent normal), 32 normal tissues and 8 benign lesions were studied using RT-nested PCR for mRNA expression and immunohistochemistry for protein expression. The identity of expressed sequences was confirmed by automated sequencing. 41/62 tumours (66%) expressed wt ERβ mRNA in comparison to 90% for wt ERα and 8 only expressed an exon 5-deleted variant. All but one cancer expressed either ERα or ERβ alone or both genes (34 cases). Surrounds showed similar expression to the corresponding tumours and all 8 benign lesions expressed wt ERα and 7 expressed ERβ. For the carcinomas weak/moderate staining for ERβ protein was detected in 1–25% of tumour cells in 3 of 4 Grade I, 8/27 grade II and 7/29 grade 3 cases. ERα protein was detected in 70% and showed a significant association with grade. Non-involved, normal and benign tissues showed moderate to strong staining of 10–75% of both myoepithelial and epithelial cells. For the 32 normal tissues examined, there was no relation ship to menstrual cycle phase. For surrounds, 13 premenopausal cases showed similar staining to the normal controls, whereas the postmenopausal group (16 cases) showed significantly more expression of ERβ in the ducts ($p = 0.002$, Kruskal Wallis).

In comparison to ERα there is loss of ERβ in breast carcinomas but there is still a weak association with better grade.

O-87. TAMOXIFEN AND ARIMIDEX DO NOT INHIBIT ANGIOGENESIS IN VITRO

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Angiogenesis is vital for tumour growth and metastases and has been identified as an independent prognostic factor for recurrence in breast cancer. The aim of this study was to examine the anti-angiogenic properties of endocrine therapies, Tamoxifen and Arimidex using a human *in vitro* model of angiogenesis.

In this model human endothelial cells are co-cultured with human fibroblasts in a specially designed medium (TCS CellWorks Ltd., UK). The effects on tubule formation of Tamoxifen (0.5 μM, 1.0 μM), Arimidex (0.1 μM and 0.05 μM) and Suramin, a known anti-angiogenic agent, were assessed following staining with CD31 monoclonal antibody in six separate plates.

Results: Tamoxifen and Arimidex do not inhibit tubule formation as compared to the control ($p > 0.05$). Tamoxifen (0.5 μM) shows a 12% and 16% increase in total tubule length alone, and in combination with Arimidex (0.05 μM), respectively. This pro-angiogenic effect did not reach statistical significance. Culture with suramin resulted in significant inhibition of total tubule length as compared to the control and all drug doses ($P < 0.001$).

Control	Tamoxifen		Arimidex		Suramin
	1 μM	0.5 μM	0.1 μM	0.05 μM	
935.8 (145)	895.6 (128.3)	1055.1 (139.3)	819.7 (178.5)	925.1 (158.2)	336.7 $(132)_{6)}$

*tubule length shown in mm; Data = Mean (Standard Deviation), Stats = ANOVA and Tukey HSD tests

Conclusion: This model shows that neither Tamoxifen, nor Arimidex have an anti-angiogenic effect on endothelial cell tubule formation, in contrast to previous *in vitro* studies.

O-88. SERUM AND TISSUE CerbB-2 ANTIGEN LEVELS PREDICTS OUTCOME AND RESPONSE TO HORMONAL THERAPY OF BONE METASTATIC BREAST CANCER

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Bone metastases are considered oestrogen receptor positive and