

# Estrogen promote angiogenesis and metastasis in breast cancer

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## Background

Estrogen are well known stimulators of angiogenesis and mediate their effects through their receptors, estrogen receptors  $\alpha$  and  $\beta$  (ESR $\alpha$  and ESR $\beta$  respectively). The aim of this study was to investigate whether or not estrogen, apart from angiogenesis, promote also metastasis.

Two pro-angiogenic factors were quantified, Fibroblast Growth Factor Receptor (FGFR) and CD31, and c-Met as metastatic marker. FGFs promote endothelial cell proliferation and their organization into vessels. CD31 (also known as PECAM-1, Platelet Endothelial Cell Adhesion Molecule) is an endothelial marker and plays a key role in tissue regeneration. On the other hand, c-Met is a proto-oncogene which encodes the Hepatocyte Growth Factor Receptor (HGFR). Abnormal MET activation in cancer triggers tumor growth, formation of new vessels and metastasis.

## Materials and methods

RNA was extracted from 30 different breast cancer patients' cells with TRIzol reagent. cDNA synthesis and real time PCR followed and were carried out with First Strand cDNA synthesis and Maxima SYBR Green qPCR Master Mix respectively.

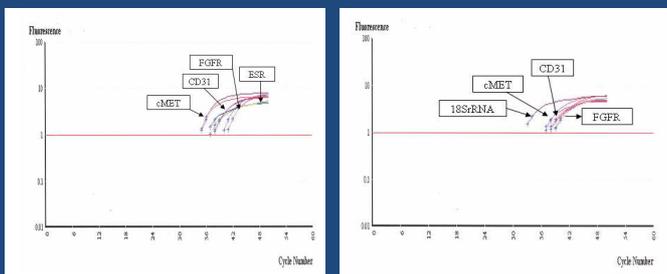


Figure 1. Real Time PCR diagrams for FGFR, CD31, cMet genes in ESR -ve (left diagram) and ESR +ve (right diagram) patients.

	FGFR	CD31	cMET
ESR +ve	39.67	36.76	35.28
ESR -ve	35.7	33.66	31.49
$\Delta$ Ct (Ct target gene-Ct reference gene)	3.97	3.1	3.79
$\Delta\Delta$ Ct (Ct for 18SrRNA=22.66 and 22.92 for ESR +ve and -ve respectively)	4.23	3.36	4.05

Table.  $\Delta$ Ct and  $\Delta\Delta$ Ct of FGFR, CD31, cMet genes among ESR +ve and ESR -ve patients.

## Results

The results showed increased expression of not only the pro-angiogenic factors, FGFR and CD31, but of the c-Met also. Specifically, the resulting Cts from the Real Time PCR for FGFR, CD31 and c-Met genes, for the 30 patients, showed that all markers have a higher expression in ESR +ve patients (about  $10^4$ ,  $10^3$  and  $10^{3.5}$  times respectively) than the ESR negative control patients. The table presents the  $\Delta$ Cts indicative of one sample.

Such evidence suggest that estrogen except angiogenesis, as we have proved in a previous study, promote and metastasis of the tumor cells to other organs too.

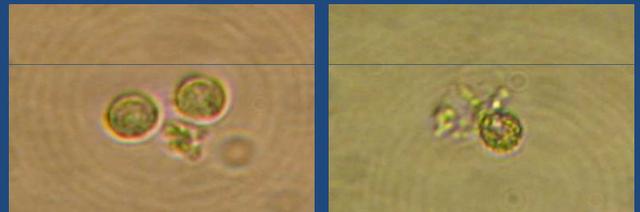


Figure 2. Circulating tumor cells from a stage III Breast cancer patient.

## Conclusion

The proof that estrogen not only promote angiogenesis but metastasis too is significant. Many of the pro-angiogenic factors are potent therapeutic targets in cancer research. This study suggests that metastatic markers, such as c-Met, should also be considered as an area of investigation in cancer research.

## References

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