

## Breast cancer stroma influences the migratory behaviour of epithelial malignant cells: the role of secreted hepatocyte growth factor

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In breast tumor, interactions occurring between malignant cells and stromal microenvironment heavily influence various aspects of cancer biology. We recently reported that this cross-talk affects structural and functional features correlated with the invasive phenotype of breast cancer cells by co-culturing mammary cancer cells exhibiting different degrees of metastatic potential (MDA-MB-231>MCF-7) with fibroblasts, particularly those isolated from breast tumor stroma (cancer-associated fibroblasts, CAFs).

In the present study, we aimed to elucidate some aspects of the epithelium-stroma interaction, related to two linked CAF-triggered effects we previously described: a) increase in cancer cell plasma membrane fluidity; b) increase in speed and directness of cancer cell migration.

Thus, we tested the effect of fibroblast/breast cancer cell co-culturing on the expression of Stearoyl-CoA desaturase 1 (SCD1), the main enzyme regulating the fatty acid membrane composition whose up-regulation has been reported in different cancer cells, generally leading to loosely packed membranes. Western blot analysis revealed a dramatic CAF-promoted increase in SCD1 expression in both MCF-7 and MDA-MB-231 cells. Quantitative real-time PCR demonstrated similar variations in the SCD1 transcript levels.

With the aim of clarifying the possible role of soluble factors in the CAF-induced increase in speed and directness of cancer cell migration, we performed co-culture assays in presence of a neutralizing antibody against hepatocyte growth factor (HGF) which is released by CAFs and notoriously affects cancer cell motility. We demonstrated that speed and directness increases were strongly reduced or completely abolished by the addition of the anti-HGF neutralizing antibody to the culture medium.

These results provide new insights in understanding the role of CAFs, the main host stromal component of breast cancer, in promoting the tumor cell invasive attitude and may help in defining further promising therapeutic targets.

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### Key words

Breast cancer cells, cancer-associated fibroblasts, migration, SCD1, hepatocyte growth factor.