

Epithelium-stroma reciprocal influence in breast cancer. Focus on plasma membrane features related to cell migratory/invasive ability

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Interactions occurring between malignant cells and stromal microenvironment greatly influence progression of breast cancer. In a previous study, we co-cultured mammary cancer cells exhibiting different degrees of metastatic potential (MDA-MB-231>MCF-7) with fibroblasts isolated from breast healthy skin (normal fibroblasts, NFs) or breast tumor stroma (cancer-associated fibroblasts, CAFs). In this system, we demonstrated the influence exerted in particular by CAFs on malignant cells, leading to the acquisition of a more aggressive/invasive phenotype (i.e. reduced adhesion, epithelial-mesenchymal transition, enhanced plasma membrane fluidity and migration velocity/directness).

In the present study, we evaluated the reciprocal effect of breast tumor cells and fibroblasts in co-culture on the expression of the main enzyme regulating the fatty acids membrane composition, Stearoyl-CoA desaturase 1 (SCD1). Abnormally high levels of SCD1 have been reported in different cancers and transformed cells and the enzyme has been recently raised to the role of key regulator of cell growth, programmed cell death and carcinogenesis. In our experience, Western blot analysis demonstrated a strong increase in SCD1 expression in both MCF-7 and MDA-MB-231 cells, resulting from their interaction with CAFs and, at a lesser extent, with NFs. High levels of SCD1 were also observed in both NFs and CAFs when co-cultured with MCF-7 cells. MDA-MB-231 cells more slightly up-regulated the enzyme expression in NFs or even induced a certain inhibition in CAFs.

The fibroblast-triggered up-regulation of SCD1 in cancer cells could reasonably be considered the molecular event underlying the increase of membrane fluidity, previously observed in tumor cells co-cultured with NFs and, notably, with CAFs. This change might downstream promote the previously described increase in tumor cell motility.

Keywords: Breast cancer cells, fibroblasts, membrane fluidity, Stearoyl-CoA desaturase 1.