IJAE
Vol. 119, n. 1 (Supplement): 10, 2014
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Breast cancer-associated fibroblasts promote tumor cell migration: crucial role of Stearoyl CoA Desaturase1 and paracrine signalings

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The key role played by the stroma in breast cancer development and progression has been widely recognized.

Recently, we reported that the cross-talk between epithelial and stromal cells affects structural and functional features correlated with the invasive phenotype of breast cancer cells by co-culturing mammary cancer cells with different 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) [1].

This study was designed to deepen the knowledge of the role played notably by CAFs in promoting breast tumor cell migratory skill through the analysis of the expression/activity of downstream potential target molecules and of the contribution of paracrine signalings.

Thus, we investigated the influence of fibroblasts on the expression of Stearoyl-CoA desaturase 1 (SCD1), the main enzyme regulating membrane fluidity, as well as on the level and activity of its transcription factor, SREBP1, in breast cancer cells. The ability of CAFs to promote a 2-3 fold increase in SCD1 mRNA and protein expression as well as an induction of SREBP1 DNA binding activity has been shown in the two cancer cell lines. Both siRNA-mediated and pharmacological inhibition of SCD1 impaired tumor cells migration. To clarify the possible role of tumor-stroma paracrine interaction in the previously reported improvement of cancer cell migratory ability, cocultures were set up in presence of neutralizing antibodies against hepatocyte growth factor, transforming growth factor-β or basic fibroblast growth factor. Cell tracking analysis demonstrated that the CAF-mediated increase in tumor cell migration speed was reduced or abolished by neutralizing the above soluble factors.

These results provide new insights in understanding the role of CAFs in promoting tumor cell invasiveness and may help to devise new targeted therapeutic approaches.

References

[1] Angelucci et al. (2012), PLoS One 7: e50804.