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Role of Stearoyl-CoA Desaturase 1 and 5 in breast cancer cell migration and survival

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We previously reported that a major component of breast tumor stroma, the "cancer-associated fibroblasts" (CAFs), induced epithelial-mesenchymal transition and an increase in cell membrane fluidity as well as in migration speed and directness in poorly (MCF-7) and highly invasive (MDA-MB-231) breast cancer cells. We next investigated the mechanisms responsible for the CAF-promoted tumor cell migration demonstrating the crucial role of Stearoyl-CoA desaturase 1 (SCD1), one of the main enzyme regulating membrane fluidity. We found SCD1 to be upregulated in tumor cells co-cultured with CAFs and that its inhibition (pharmacological or siRNA-based) impaired both intrinsic and CAF-driven tumor cell migration. In the present study, we deepen the understanding of the mechanisms involved in the SCD1-based modulation of tumor cell migration, as well as the possible role of the other human SCD isoform, SCD5. Thus, in the two above mentioned cell lines we studied whether the inhibitory effect produced on cell migration by SCD1 depletion was due to the deficiency of oleic acid (OA), the main SCD1 enzymatic product. By a wound healing assay, we found that the addition of OA nullified the inhibitory effects produced on tumor cell migration by the SCD1 inhibition in both the cell lines while SCD5 appeared not to be involved in the regulation of their motility but it was upregulated in MCF-7 cells co-cultured with CAFs. Because of the high number of detached MCF-7 cells silenced for SCD5, we investigated the role of the desaturase on tumor cell survival and an induction of necrosis was found. Consistently with the promotion of tumor cell migration, CAFs have also been found to induce the activated form of the hepatocyte growth factor receptor, p-MET, in the two cell lines.

These results provide further insights in understanding the role of SCD1 in both intrinsic and CAF-stimulated mammary tumor cell migration. Moreover, our data seem to suggest the ability of CAFs to promote the maintenance of tumor cell survival by the induction of SCD5 levels.

Keywords

Breast cancer cells, cancer-associated fibroblasts, SCD1, SCD5, cell migration, cell survival