Chemical exposome, microenvironment & breast cancer aggressiveness

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Breast cancer (BC) is a major public health concern, and its prognosis is very poor once metastasis occurs. The tumor microenvironment and chemical pollution have been suggested recently to contribute, independently, to the development of metastatic cells. The BC microenvironment consists, in part, of adipocytes and preadipocytes in which persistent organic pollutants (POPs) can be stored. We conducted an exploratory case-control study in which the concentrations of 49 persistent organic pollutants (POPs) were measured in both adipose tissue (AT) and serum samples from BC patients, with or without lymph node metastasis. The concentrations of several POPs in AT were positively associated with the risk of lymph node metastasis and the tumor size. We then developed a co-culture model using BC MCF-7 cells or MDA-MB-231 cells together with hMADS preadipocytes to investigate the contribution of the microenvironment and 2,3,7,8-tetrachlorodibenzo-p-dioxin TCDD, one of the identified POPs. Global differences were characterized using a high-throughput proteomic assay. Subsequently we measured the BC stem cell-like activity, analyzed the cell morphology, and used a zebrafish larvae model to study the metastatic potential of the BC cells. We found that coexposure to TCDD and preadipocytes modified BC cell properties; moreover, it induced the expression of ALDH1A3, a cancer stem cell marker, and the appearance of giant cancer cells with cell-in-cell structures (CICs), which are associated with malignant metastatic progression, that we demonstrated in vivo. The results of our study using BC cell lines co-cultured with preadipocytes and a POP and an in vivo zebrafish model of metastasis suggest that the interactions between BC cells and their microenvironment could affect their invasive or metastatic potential.