Interleukin (IL)-11 is involved in the functional liaison between breast tumor cells and the surrounding stroma

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Current advances in molecular profiling methodologies and the accessibility to multi-omics datasets are paving the way toward a better understanding of heterogeneous diseases, including breast cancer (BC). In this regard, we sought to uncover the transcriptional changes triggered by estrogen and insulin in a primary BC cell line (BCAHC-1), which expresses the 46kDa isoform of the estrogen receptor (ER)α and the insulin receptor, as we previously ascertained.

Raw data from RNA sequencing of BCAHC-1 cells were processed by the Bcl2Fastq 2.20 version of the Illumina pipeline, while in silico analyses were performed in R Studio using the TCGA dataset. Real-time PCR, immunoblotting, ELISA and chromatin immunoprecipitation experiments were used to identify the molecular events triggered by estrogen and insulin in BCAHC-1 cells and cancer-associated fibroblasts (CAFs). Furthermore, migration and invasion assays allowed us to ascertain the mechanisms triggering these biological responses upon the aforementioned hormone treatments.

First, we determined that 17β-estradiol (E2) and insulin stimulate a peculiar IL-11 expression and secretion in BCAHC-1 cells. Thereafter, bioinformatics analyses confirmed the up-regulation of IL-11 in ER-positive BCs respect to adjacent normal tissues and its association with worse survival. Next, the involvement of IL-11 in pro-metastatic transduction signaling by pathway enrichment analyses was established. Worthy, we found that the secretion of IL-11 by BCAHC-1 cells prompts an invasive phenotype of CAFs through the up-regulation of genes belonging to the extracellular matrix organization pathway, namely the intercellular adhesion molecule 1 and integrin alpha 5.

Overall, our findings indicate that IL-11 secretion by BC cells may elicit a paracrine action on the surrounding stroma toward invasive properties, suggesting that IL-11 could be considered as a valuable target in comprehensive treatments of ER-positive BC patients.