FABP4 AND FABP5 PLAY AN IMPORTANT ROLE IN BREAST CANCER PROGESSION

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BACKGROUND AND AIM

Breast cancer is the most common cancer among women in developed countries and the second leading cause of all cancer-related deaths. Adipose tissue has gained importance in the pathogenesis of many metabolic diseases, particularly cancer. Tumor microenvironment plays an important role in cancer progression. Adipose tissue has been described as an endocrine tissue which can produce and release a high number of factors and components that are able to modify the transcriptome, proteome, metabolism as well as the behavior of breast cancer cells.

Our objective is to understand how the adipose tissue secretome, could modify breast cancer characteristics and potentiate the different cancer hallmarks. For this reason, we cultured BC cell line MCF7 with adipocyte CM and we tested for different cancer hallmarks such as proliferation, survival, migration and invasiveness.

ADIPOCYTE CM INCREASES BC LIPID UPTAKE AND DIFFERENT FATBP TRANSCRIPTS AND PROTEIN

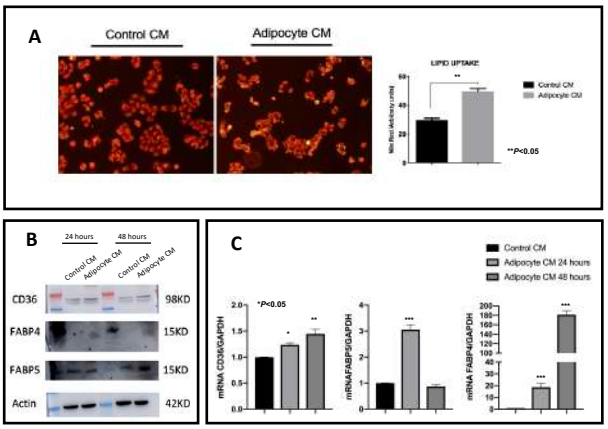

Fig1. Adipocyte cm increases BC lipid uptake and different FATBP transcripts and protein. (**A**) Adipocyte CM increases lipid uptake in BC. (**B**) Adipocyte CM increases the protein and mRNA transcripts (**C**) levels of CD36, FABP4 and FABP5 in BC cell line MCF7. p<0,05 was statistically significant. T-Student.

ADIPOCYTE CM ENHANCES DIFFERENT CANCER HALLMARKS

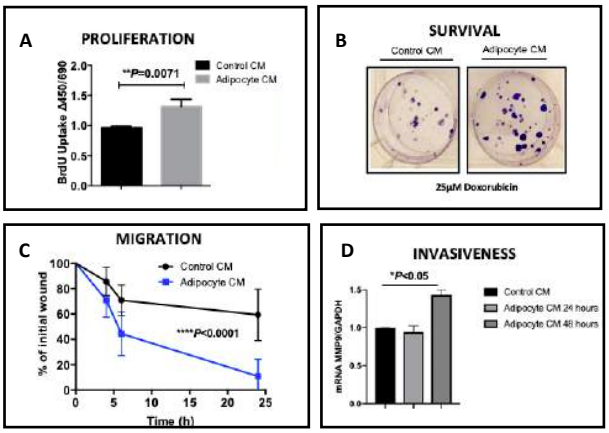

Fig2. Adipocyte CM enhances different cancer hallmarks in BC. Adipocyte CM enhances proliferation (**A**) in MCF7 cell line, as well as its capability to survive to Doxorubicin (**B**), increasing the formation of colonies. It also enhances the migration ability after a wound scratch (**C**). Therefore, adipocyte CM increases the mRNA of MMP9 in MCF7 cells (**D**), a clear sign of an increase of the invasiveness and EMC remodeling in cancer. <0,05 was statistically significant. T-Student.

FABP4 AND FABP5 INHIBITION DECREASES PARTIALLY LIPID UPTAKE AND FATBP TRANSCRIPTS

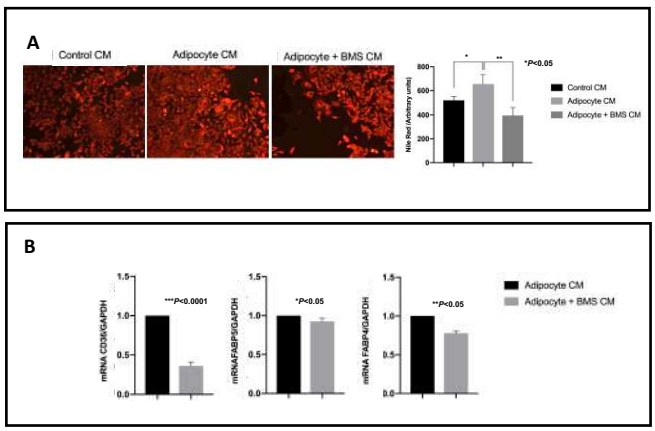

Fig3. FABP4 and FABP5 inhibition decreases partially lipid uptake and FABP transcripts. BMS309403 reduces the lipid uptake in MCF7 cell line that previously have increased adipocyte CM. It also reduces the mRNA of the FATBP CD36, FABP4 and FABP5 in tumor cells. <0,05 was statistically significant. T-Student.

FABP4 AND FABP5 INHIBITION DECREASES PARTIALLY CANCER HALLMARKS EFFECTS OF ADIPOCYTE CM

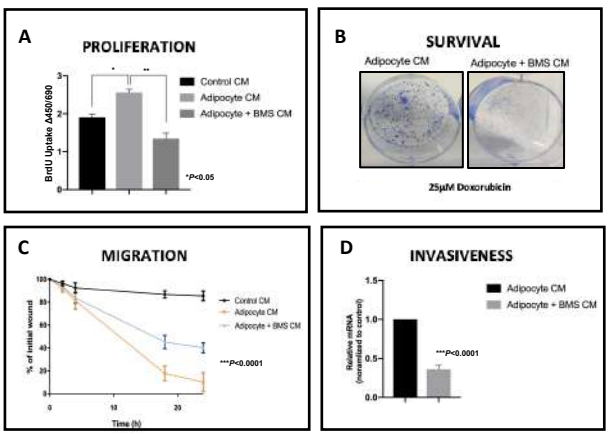

Fig2. FABP4 and FABP5 inhibition decreases partially cancer hallmarks effects of adipocyte CM BMS309403 reduces the proliferation rate of tumor cells, the ability of colonies formation after Doxorubicin addition, the migration capability after wound scratch and MMP9 mRNA levels in MCF7 cells. <0,05 was statistically significant. T-Student.

DISCUSSION AND CONCLUSION

Adipocyte conditioned media is able to enhance several cancer hallmarks such as survival or proliferation. Adipocyte media is able to increase wound healing Luminal A breast cancer cell line increasing their migratory ability. MMP9 mRNA levels are increased by adipocyte conditioned media that might confine an invasive behavior that leads to metastasize surrounding tissues.

We have also observed an increase in the fatty acid transporters FABP4 FABP5 and CD36 protein amount and mRNA levels which may assist in lipid transfer from adipocytes to tumor cells. FABP4 and FABP5 are key fatty acid transporters and different studies have correlated an increase of these fatty acid transporters with a worst prognosis. Inhibition of these proteins in mature adipocytes reduces significative the cancer hallmarks mentioned above and the lipid uptake in BC Luminal A. This throws to the conclusion that these proteins leads partially to a rise of cancer progression becoming an interesting target in cancer treatment.