Characterization by Mass Spectrometry of the lipid metabolism in the different molecular breast cancer subtypes

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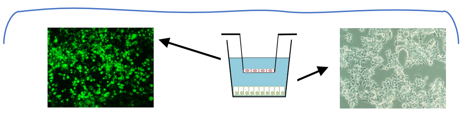
BACKGROUND AND AIM

Although early diagnosed breast cancers usually have a good clinical outcome, most breast cancers also have a high probability for progression to metastasis, which is associated with poor prognosis and the main cause of breast cancer death. Adipose tissue, considered previously as an energy storage organ, plays an important role in cancer progression. Our aim is to understand how adipose tissue could modulate the tumor by the communication between BC cells and the adipocytes. Therefore, different molecular subtypes of BC exist and its crucial to understand the behaviour in this process in each one to achieve a personalize medicine.

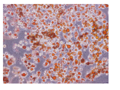
METHODS

COCULTURE



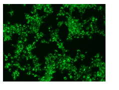
ADIPOCYTES   BC CELLS

OIL RED



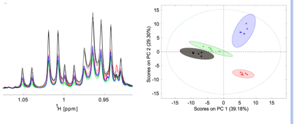
ADIPOCYTES

PA STAIN TRACKING



BC CELLS

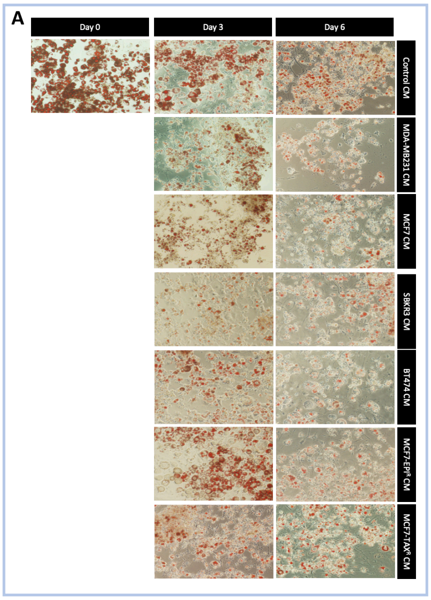
MNR AND PCA ANALYSIS



BC CELLS

RESULTS

BCC AND ADIPOCYTES COCULTURE INCREASES THE LIPID TRANSFER FROM ADIPCOYTES TO TUMOR CELLS



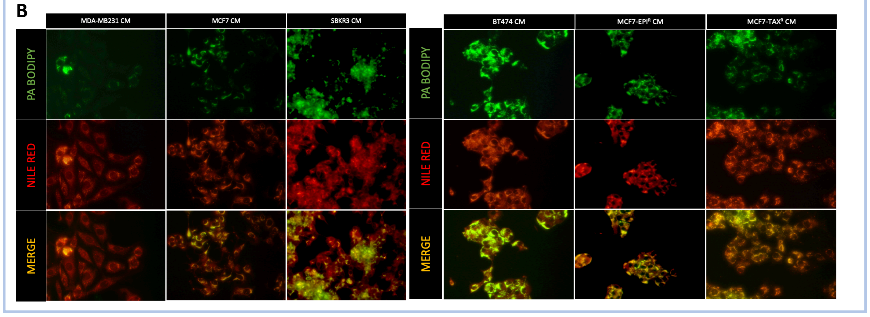
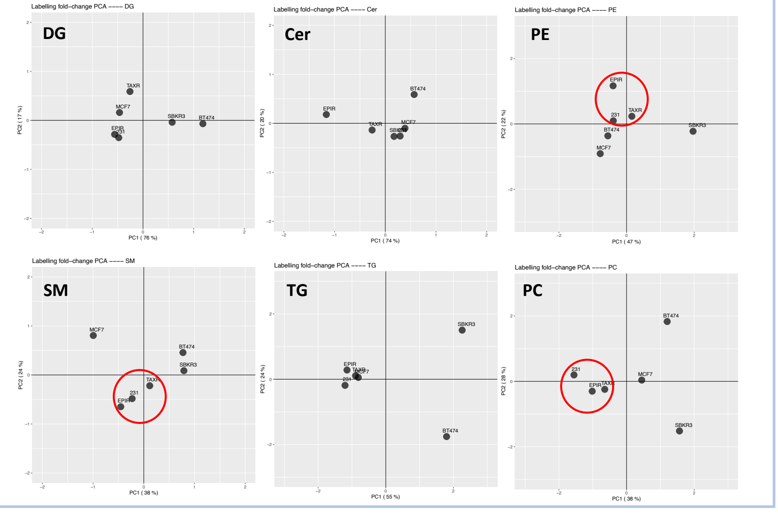


Fig1. Coculture between BC and mature adipocytes increases the lipid transfer form adipocytes to tumor cells. An Oil red staining for mature adipocytes at different time point after coculture with different BC cell lines (MDA-MB 231, MCF7, SBKR3, BT474, MCF7-EPIR and MCF7-TAXR). (**A**) We could observe that those adipocytes cocultured with BCC suffer a higher loss of lipid droplets compared to those adipocytes cultured in Control media. Oil red staining was extract and measured. We observed significant differences at both time points. One-way ANOVA. $p<0,05$ was considered significant. (**B**) Later, during preadipocytes differentiation Palmitic- acid labeled with BODIPY was added. Then matured labeled adipocytes were cocultured with different BC cell lines and after 24 hours cells were analyzed under a fluorescent microscope. We could observe that Palmitic acid form mature adipocytes was been incorporated into the different BC cell lines and it colocalize with the neutral and polar lipids within the cells.

BCC LINES HAVE A DIFFERENT AND SPECIFIC LIPID PATTERN IN THE PALMITIC TRANSFORMATION AFTER THE COCULTURE WITH ADIPOCYTES. THEREFORE, RESISTANT CELLS LIPID PATTERN DIFFERS FORM THEIR SENSITIVE CELL LINE AND ARE CLOSELY TO TNBC CELL LINE PATTERN

Fig2. BCC lines have a different and specific lipid pattern in the palmitic transformation after the coculture with adipocytes. therefore, resistant cells lipid pattern differs form their sensitive cell line and are closely to TNBC cell line pattern. Labeled C Palmitic acid was added during adipocytes differentiation. Then, they were cocultured with different BCC lines and samples were pass through Magnetic Nuclear Resonance (MNR). We could observe that the labeled carbon form PA was present In different new lipidic families, suggesting that PA had been transferred form adipocytes to the BCC and it had been transformed in different lipidic families.
We have observed that for these lipidic families the pattern of transformation was different in the BCC lines analysed.
Surprisingly, MCF7 resistant to Paclitaxel (TAXR) and Doxorubicin (EPIR) cell lines had a pattern more similar to the TNBC. Transformation of PA into Phosphatidylcholines, phosphoethanolamine and Sphingomyelins was more similar between resistant cells and TNBC than the sensitive and resistant cells.



DISCUSSION AND CONCLUSION

BC treatment as well as many other cancer types need to be understood and analyzed one by one until a personalized medicine will be reached. Crosstalk between BCC and adipose tissue is crucial for cancer progression and dissemination. Understanding the way that different BC molecular subtypes stablish this contact with mature adipocytes and how they can transfer specific lipids into their cytoplasm is essential for a future specific treatment. In the same way, understanding why each BC molecular subtype has a specific lipidic pattern can be later extrapolate to a specific treatment and to improve a personalize medicine in BC patients.