1726P - INVESTIGATING ADIPOCYTES-TUMOR CELLS INTERACTION AND ITS EFFECT ON DISEASE PROGRESSION IN LOBULAR BREAST CANCER WITH SPATIAL TRANSCRIPTOMICS

**BACKGROUND**

- Invasive lobular breast cancer (ILC) represents around 15% of all invasive breast cancers (BC).
- Characterized by late relapse.
- Loss of cell adhesion and typical "single file" pattern of the cells.
- Often frequent mutation of CDH1, PTEN and AKT.

**Objectives**

- To characterize the spatial transcriptomic heterogeneity of lobular ILC, including tumor microenvironment.
- To investigate whether spatial transcriptomics may improve the prediction of the risk of recurrence in lobular breast cancer.

**Hypothesis**

- A higher amount and a different morphology of fat tissue has been observed in samples coming from patients who relapsed.
- Higher levels of genes related to immune system are observed in relapse samples.

**Methods**

- Spatial transcriptomics
- Histo-morphological annotation of IHC data relative to ST samples
- Image co-localisation analyses
- Gene expression signature identification via DGE

**Results**

- Spatial transcriptomics (ST – Fig. 2) was performed on 43 ILC primary tumor samples (HR+, HER2-) coming from patients with long-term follow-up (Table 1).
- TCGA and METABRIC (HR+, HER2-) lobular bulk RNA-seq were used as validation sets.
- Annotation of the IHC slides (Fig. 3) allowed us to observe a higher amount of contacts at the pixel level between adipocytes and tumor in relapse samples (Fig. 4, p<0.001).
- A 27 gene expression signature was obtained through differential gene expression (DGE) analysis between adipocytes-tumor contact area in relapse vs non-relapse samples (Fig. 5a).
- In METABRIC and TCGA, higher levels of the signature were observed in samples carrying PIK3CA mutation (Fig. 5b, p<0.01) and METABRIC.
- In METABRIC and TCGA, higher levels of the signature correlates with poor prognosis for OS, DSS, DMFS, EFS, also when correcting for clinical variables and immune-proliferation related signatures (HA curves for OS and DSS in METABRIC in Fig. 4c and d respectively).

**Conclusions**

- In tumor cell lines (PharmacokIT, Gray dataset) higher levels of our signature were associated to greater sensitivity to chemotherapeutic agents (such as Etoposide and Cisplatinum) and PI3K pathway-targeting agents (Fig. 5c).

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