Analysis at single cell level of the heterogeneity of tumor associated macrophage in triple negative breast cancer.

Introduction
Tumor associated macrophages (TAM) represent strong regulator of immune suppression, playing an essential role in diverse phases of tumor growth and dissemination. The role of inhibitory/co-stimulatory signals on TAM and their possible implication in the modulation of the outcome of human malignancies remain to be investigated. For these reasons, we aim to dissect the true composition of TAM in human breast cancer.

Methods
Here, we analysed at RNA-single cell level the myeloid compartment enriched in triple negative breast cancer (TNBC). After mechanic and enzymatic dissociation of non-tumor (NT) and tumor (T) samples we enriched, by sorting, HLA-DR+CD11c+ myeloid cells from each counterpart, and then performed, by 10X Chromium technology, the RNA analysis at single cell level.

Results-Conclusion
The bioinformatic analysis of RNA, at single cell, demonstrated a peculiar distribution of different clusters between NT and T counterparts.
First, we observed an accumulation of “activated monocytes” in the intermediate states of differentiation, showing a peculiar signature of classical inflammatory monocyte markers like FCGR3A, SOD2, IFITM2, IFITM3, ISG15, MAFB, S100A8, S100A9, CD14 expressing also different adhesion molecule-related genes, ICAM1, PECAM1, ICAM2, suggesting a preferential accumulation at the tumor site.
We could also detect DC populations characterizing by the expression markers like CCR7, CXCR4, CD1A, CD207, AXL, CD80 and again a cluster representing DC2, showing CD1c, CLEC10A, with high expression of different HLA-DR-DQ molecules.
Accumulated at different levels, in different patients, we could also find MRC1, MSR1, TREM2, APOE, FOLR2, identified recently as TAM genes, all shared in a specific subset. Supporting the notions of pro-tumorigenic functions of these genes, the differential distribution among patients may impact the overall immune responses to cancer.
Further evaluations will be focus on the functional study of diverse populations, potentially dissecting pro- or anti-tumor roles.

Keywords : myeloid cells, macrophages, single cell, triple negative breast cancer
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