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One of the main immunosuppressive mechanisms by which cancer avoids eradication by the immune system is the expression of PD-L1, the ligand for T-cell inhibitory receptor PD-1. PD-1 activation by PD-L1 leads to CD4+/CD8+ lymphocyte exhaustion, which is at the focal point of today's cancer immune therapies. However, little is known about which other immunosuppression mechanisms are triggered by tumor-intrinsic PD-L1 expression.
To genetically address tumor-immune system interactions in a triple negative breast cancer (TNBC) model, we developed a CRISPR/Cas9 expressing TNBC-like EO771 cell line platform. Using flow cytometry, we characterized the immune response associated with the progression of EO771 tumors, which resembled immunosuppression signatures associated with poor prognosis in TNBC patients: an increase in pro-tumoral M2 macrophage polarization, a decrease in MHCII+ Antigen Presenting Cells (APCs) and a marked increase of T-cell exhaustion.
To test the role of tumoral PD-L1 in tumor-mediated immune escape, we generated PD-L1 KO EO771 cell lines. Using CRISPR/Cas9 edited EO771 lines KO for PD-L1, we found that tumor intrinsic PD-L1 expression is required for tumor growth. Interestingly, we also found that PD-L1 expressed by the tumor cell exerts a general impact over the tumoral immune infiltrate composition: a) it is required for the differentiation of M2 macrophages and for the enrichment of myeloid derived suppressor cells and b) in the T-cell compartment, unexpectedly, tumoral PD-L1 is needed to exhaustion of effector CD4+ but not cytotoxic CD8+ cells.
All together, these data suggests that tumor-intrinsic PD-L1 plays a key role on TNBC tumor growth by triggering different immunosuppressive mechanisms in the tumor immune landscape. Using this editable EO771 model platform, we will be able to massively test tumoral PD-L1 synthetic interactions to identify candidate genetic targets to overcome PD-1/PD-L1 resistance in TNBC.

230. (427) **B16F10-OVA TUMOR-BEARING MICE INJECTED VIA INTRAPERITONEAL REPRESENT AN EXCELLENT MODEL TO STUDY TUMOR-INFILTRATING B CELLS**

Brunotto V[1], Abrate C[1], Gazzoni Y[1], Bossio S[1], Almada L[1], Gruppi A[1], Acosta Rodriguez E V[1], Montes CL[1].
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Previous works demonstrate that CD8+ tumor-infiltrating T cells play a pivotal role in the anti-tumor response. However, the role of B cells is not completely elucidated. In this work, we evaluate tumor-infiltrating (TI) lymphocytes in two different murine melanoma models focalizing the study in the B cell population. C57BL/6 mice were injected subcutaneously (sc) or intraperitoneally (ip) with $4x10^5$ B16F10-OVA tumor cells and on day 14, tumors and spleen were collected. By Flow cytometry, we observed, that compared to mice injected sc, ip-injected mice show higher frequency of TI-CD45+ cells (p=0.03) but no differences in the % of TI-CD8+ T cells or CD8+ exhausted T cells (TIM-3+PD-1+). While there are no differences in Tregs frequency, TI-CD4+ conventional T cells are more frequent in ip-injected mice (p=0,01), moreover the % of TI-CD19+ cells is significantly increased in these mice compared to sc-injected mice (p≤0.0001). Surprisingly, in tumor microenvironment of the ip-injected mice, we detected a high % of B cells (43.4±6.0) exhibiting naïve phenotype and a significant frequency of plasmablast (19.8±8.8). A high frequency of plasmablast express the activation marker CD69 (89.2 ±3.5) and the ecto-enzyme CD39 (60.2 ±23.1). The B cell compartment is different in the spleen from ip-injected mice. Indeed, while the % of naïve B cells is similar (42.4±4.9), the frequency of the plasmablast is significantly lower (4.2±1.0). Additionally, we observed that the frequency of CD69-expressing plasmablast reach a value of 19.6±9.8 while the % of $CD39^{high}$-expressing plasmablast is only 8.4±2.0.
Taken together these results demonstrated that ip- tumor injected mice represent an excellent model for the study of TI- B cell compartment. Future studies will be perform to understand the role of the TI-plasmablast expressing an activation marker and CD39 in the immune response against tumors.

231. (447) **CHARACTERIZATION OF TUMOR INFILTRATING NK CELLS (TINK) AND TYPE 1 INNATE LYMPHOID CELLS (ILC1) IN BREAST CANCER**

María Cecilia Santilli, María Victoria Regge, Mariana Gantov, Adrián Friedrich, Jessica Mariel Sierra, Florencia Secchiari, Aldana Trotta, Natalia Rubinsztain, Belén Candela Lozada Montanari, Mercedes Beatriz Fuertes, Norberto Walter Zwirner, Carolina Inés Domaica,
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ILC1 and NK cells share several phenotypic and functional characteristics and display plasticity because they can interconvert one into another in a context-dependent manner. Indeed, TGF-β-driven conversion of TINK into intermediate populations of ILC1 (intILC1) and ILC1 has been proposed as a tumor immune escape mechanism. However, the role of ILC1 in antitumor immunity remains ill-explored. Thus, the aim of this work was to investigate TINK and ILC1 in the tumor microenvironment (TME) using the 4T1 triple-negative breast cancer mouse model. BALB/c mice were injected with $3x10^4$ 4T1 cells and after 19 days, mice were euthanized and cell suspensions of tumor, draining lymph nodes, spleen, lungs, and liver were obtained to study NK cells, intILC1 and ILC1 by flow cytometry. Tissues from healthy mice were also obtained. ILC1 and intILC1 were present in tumor and lung, but were absent in spleen and lymph nodes, while only ILC1 were found in liver from both groups of mice. A higher frequency of intILC1 than of ILC1 ($p<0.01$) was observed in the TME. In lung, where 4T1 metastasizes, higher frequencies of ILC1 were observed in 4T1 tumor-bearing mice than in healthy animals ($p<0.05$). Like TINK, both cell types expressed the activating receptor NKG2D in the TME, while 4T1 cells expresses NKG2D ligands. NKG2D expression was higher in ILC1 and intILC1 present in the TME than in liver ($p<0.05$) and lungs ($p<0.05$) either from tumor-bearing or healthy mice. Also, intILC1 and ILC1 from tumor-bearing mice or from healthy mice expressed CD69, supporting their sentinel-like tissue resident characteristics. Moreover, within the TME, ILC1 exhibited higher expression of Ly6C (associated with ILC1 activation) than in the liver of tumor-bearing mice ($p<0.01$) and such expression was higher in ILC1 than in intILC1 ($p<0.05$) and TINK ($p<0.01$). We conclude that the TME contains ILC1 that display an activated phenotype, which suggests that they might be involved in tumor immunoediting.

232. (449) **ANTI-CTLA-4 TREATMENT PROMOTE THE EXPANSION OF CD39+ CONVENTIONAL CD4+ T CELLS**

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Previously we demonstrated that tumors from different experimental mice models are infiltrated with $FOXP3^-$ CD4+ cells (Tconv) expressing CD39. CD39 is an unequivocal marker CD8+ of exhaustion. Tumor infiltrating (TI) CD39+Tconv cells represent an heterogeneous population with features of exhaustion. Transcriptional profiling of