immunologic pathways was also assessed. The performance of previously identified immune signatures as the Immunologic Constant of Rejection (ICR), which captures an active Th1/cytotoxic response associated with favorable prognosis and responsiveness to immunotherapy, was also checked within each tumor subtype.

Results We found 5 main modules, in agreement with results obtained in adult solid tumors: Wound Healing, TGF-B signaling, IFN-G signaling, Macrophages and Lymphocytes (figure 1). These 5 modules clustered pediatric patients into 6 immune subtypes S1–S6 with distinct survival (S2 vs S4, p=0.0044, adjusted for cancer type), S2 cluster has the best overall survival and characterized by low enrichment of wound healing signature, high Th1, low Th2 and high expression of HLA 1 and HLA2, while the opposite holds true for cluster S4 with the worst survival and highest enrichment of wound healing signature, high Th2, and low Th1. The S6 cluster is characterized by highest enrichment of lymphocyte signature, the highest expression of immune checkpoints accompanied by elevated expression of exhaustion markers, and an unpolarized immune response with high abundance of macrophages. Additionally, pan-cancer, the upregulation of WNT-Beta catenin pathway is associated with adverse outcome and lack of T-cell infiltration. In the per-cancer analysis, ICR is associated with better survival in osteosarcoma and with worse survival in Wilms' tumors, similarly with what observed in adult kidney's cancer despite the different embryological origin.

Conclusions We demonstrated that pediatric solid cancers can be classified according to their immune disposition, unveiling unexpected similarity with adults' tumors. Immunological parameters might be explored to refine diagnostic and prognostic biomarkers and to identify potential immune responsive tumors. This is the first pan-cancer immunogenomic analysis in children.

REFERENCES

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0520

Abstracts

522 METABOLIC REQUISITES FOR T CELL PROTEIN TRANSLATION IN TUMORS
Katie Hurst, Megan Tennant*, Alex Andrews, Lee Leddy, David Neskey, Lauren Ball, Jessica Thaxton. Medical University of South Carolina, Charleston, SC, USA

Background T cells are a secretory immune subset with the capacity to control solid tumors. Protein translation is of paramount importance in CD8 T cells, controlling proliferation, stimulation and lineage fate.

Methods Herein, we used both the fluorescent analogue of methionine homopropargylglycine (HPG) incorporation assay and O-propargyl-propomycin (OPP) method which enters the A-site of the ribosome and effectively labels and terminates nascent polypeptide chains to monitor protein synthesis in mouse and human tumors. Moreover, we employed label free quantitative proteomics (LFQ), lipidomics, metabolic analysis, and in vivo animal modeling to elucidate mechanisms of protein translation in antitumor immunity.

Results We found that canonical protein synthesis is restricted in endogenous CD8 tumor infiltrating lymphocytes (TILs) by the tumor microenvironment (TME). Proteomic analysis revealed that glycoegenolysis and B-oxidation of fatty acids (FAO) were upregulated in CD8 T cells under tumor stress but these metabolic sources were unable to support translation in the TME. Further, we discovered that glucose metabolism and mammalian target of rapamycin complex 1 (mTORC1) preferentially hinder protein synthesis in CD8 TILs. These data enabled the discovery that proteasomal protein...
A SUBSET OF MATURE NEUTROPHILS CONTAINS THE STRONGEST PMN-MDSC ACTIVITY IN BLOOD AND TISSUE OF PATIENTS WITH HEAD AND NECK CANCER

Yu Si, Kirsten Bruderek, Simon Merz, Philip Jansen, Matthias Gunzer, Joachim Klode, Anthony Squire, Sven Brandau, Sven Brandau*. University Hospital Essen, Essen, Germany

Background: A high neutrophil-to-lymphocyte ratio in the circulation and high frequencies of tumor-associated neutrophils (TAN) in malignant tissue are associated with poor outcome and tumor progression in patients with cancer. It is hypothesized that immunosuppressive neutrophil activity (aka PMN-MDSC activity) contributes to this effect. In addition, this MDSC activity represents a major resistance mechanism in different types of immunotherapy. The exact cellular identity of human PMN-MDSC is still under debate. Improved immunomonitoring and functional characterization of MDSC is needed in order to exploit these cells as novel biomarkers and targets for combination immunotherapy.

Methods: In this study, we sought to identify the neutrophil subset that contained the highest T cell suppressive activity. To this end, we purified different subsets of circulating neutrophils by FACS and performed multi-parameter immunofluorescence together with digital pathology on 2-D and 3-D tumor tissue samples.

Results: We found that a population of circulating, mature, arginase 1+ neutrophils that co-purified with mononuclear cells in density gradients, most potently suppressed T cell function in multiple in vitro assays. These PMN-MDSC were also superior to monocytes MDSC in T cell suppression. Using a novel technology of tissue whole mount labelling, clearing and imaging we derived 3-D spatial maps of neutrophil – T cell interaction in human tumors. We found that T cells, which were conjugated to arginase 1+, myeloperoxidase + TAN, had significantly reduced expression of proliferation and cytotoxicity markers. In patients, frequent conjugation of T cells to those PMN-MDSC was associated with poor prognosis. In contrast to circulating PMN-MDSC, tissue PMN-MDSC expressed high amounts of LOX-1 (oxidized low density lipoprotein receptor 1) and a high intratumoral frequency of LOX-1+ PMN-MDSC was associated with poor survival.

Conclusions: We identified and characterized PMN-MDSC activity in human cancer patients. Our findings will facilitate and improve MDSC immunomonitoring and MDSC targeting in combination therapies.