immunohistochemistry. Paraffin sections were stained with hematoxylin and eosin (H&E) or Ki67 according to standard methods. For immunohistochemistry, cryosections were stained overnight at 4°C with fluorescent antibodies.

Results H&E images confirmed that transgenic *Apc*^{1322T}mice lacking IL-25 had smaller tumours and showed less dysplasia than *Apc*^{1322T} mice with normal IL-25 expression. Ki67 staining showed that tumours express higher Ki67 levels than adjacent normal intestinal tissue. The tumour-associated tertiary lymphoid structures (TATLS) of *Apc*^{1322T} mice lacking IL-25 appeared larger, indicating a more robust anti-tumour immune response.

Likewise, *Apc*^{1322T}mice lacking ILC2s had smaller, less dysplastic tumours. TATLS in these mice were bigger than mice with ILC2s but smaller than *Apc*^{1322T} mice lacking IL-25, indicating that IL-25 may act via additional protumourigenic cell types.

Immunohistochemistry confirmed the presence of ILC2s, as well as MDSCs the tumours of *Apc*^{1322T}mice, suggesting that these cells create an immunosuppressive niche.

Conclusions This pilot study confirms that genetic ablation of either IL-25 or ILC2s promotes anti-tumour immune reactions and decreases tumour size, correlating with reduced intestinal tumour proliferative capacity and dysplasia. Mice lacking IL-25 or ILC2s had larger TATLS, which are known to be associated with improved prognosis in patients. This study, along with previous data, highlights the potential therapeutic benefit of targeting the IL-25-ILC2 axis for colorectal cancer. Further studies are required to bring this from bench to bedside.

REFERENCE

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Disclosure Information E. Jou: None. **R.J. Hill:** None. **J.E. Murphy:** None. **N. Rodriguez-Rodriguez:** None. **M. Ko:** None. **A.N.J. McKenzie:** None.

P02.07 INNATE IMMUNITY ATLAS OF HEPATOCELLULAR CARCINOMA UNRAVELS THE DIFFERENTIATION HIERARCHY OF MYELOID NK CELLS AND MDSCS

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10.1136/jitc-2022-ITOC9.26

Background Hepatocellular carcinoma (HCC) environmental risk factors include viral infection, alcohol abuse and the metabolic syndrome. While there is evidence that boosting the activity of tumor-specific T cells might benefit patients with HCC, the underlying liver soil (cirrhosis, NASH) renders this cancer's tumor microenvironment somewhat unique. Despite a significant therapeutic advance in the treatment of advanced HCC, ~75% of patients do not respond to immunotherapies for unclear reasons. Such a heterogeneous response highlights the need to further explore etiology- and organ-specific immunity towards improved patient stratification and the development of new combination therapies.

Materials and Methods With the objective to characterize the innate immunity landscapes of HCC, we employed droplet-based 3' scRNA-seq of CD45$^+$ panTCRαβ$^-$ CD19$^-$ cells, freshly isolated from tumors or adjacent non-tumoral livers of 10 HCC patients. In parallel, we used spatial transcriptomics (10x Genomics, Visium platform) to localize identified cell populations with respect to tumor and tissue features. Functional validation was carried in *ex vivo* co-culture experimentsusing patient-derived cells and *in vivo* using mouse models.

Results We present the most comprehensive atlas to date of hepatic innate immunity cells (~100,000 single cell transcriptomes). Besides describing the remarkable diversity of innate immunity cell states, our study identified and functionally characterized previously unexplored subsets of cytotoxic cells with myeloid features (myeNK) and novel myeloid-derived suppressor cell (MDSC) differentiation states. We computed signaling entropy at the single-cell level to characterize the differentiation hierarchy of these poorly annotated cells and show that myeNK cells are highly differentiated and exhibit potent lytic activity against cancer cells. Our analysis also distinguished three main MDSC lineages, a granulocytic (G-MDSC), a monocytic (M-MDSC) and an 'immature' subset with TAM-like features. This latter lineage presents the highest entropy and is the most immunosuppressive. Finally, we identify a discriminatory expression of the inflammatory receptor TREM-1 on MDSCs, particularly in NASH setting, and unravel this receptor as a potential therapeutic target in HCC.

Conclusions Our data support the stratification of patients according to etiology to define optimal therapeutic regimens and identify TREM1^{high} MDSC as deleterious effectors of HCC.

Disclosure Information J. Giraud: None. **D. Chalopin:** None. **E. Ramel:** None. **M. Derieppe:** None. **T. Boyer:** None. **N. Larmonier:** None. **O. Adotevi:** None. **J. Blanc:** None. **L. Chiche:** None. **B. Le Bail:** None. **M. Nikolski:** None. **M. Saleh:** None.

P02.08 THE ROLE OF THE INFLAMMASOME IN THE SPATIOTEMPORAL EVOLUTION OF THE IMMUNE CELL LANDSCAPE IN POST-RESECTION GLIOBLASTOMA

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10.1136/jitc-2022-ITOC9.27

Background Glioblastomas (GB) are the most severe and deadliest brain tumors in adults. Survival is estimated < 15 months after diagnosis and with a relapse rate > 95%. The current standard-of-care involves surgery, when possible, and radiotherapy coupled with chemotherapy. Two characteristics might underlie the high relapse rate in GB: 1) the infiltrative capacity of tumor cells that spread out of the hypoxic and acidic tumor core, and 2) the unique composition of the tumor immune microenvironment (TME) that is sparce in T lymphocytes and natural killer (NK) cells but dominated by glioma-associated macrophages (GAMs). Although surgery is a standard treatment in GB, it fails to remove infiltrative tumor cells and causes an inflammatory and immunosuppressive trauma that might promote GB recurrence by altering the TME. However, the post-resection diversity of immune cells