Abstract #81

The association between melanoma liver metastases (mets) and the systemic anti-tumor immune profile

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Background

- A majority of patients with advanced melanoma will present with innate or acquired resistance during treatment with immune checkpoint inhibitors (ICI)[1]
- Patients with melanoma liver mets have significantly reduced response and overall survival rates when treated with ICI compared to patients without liver mets[2,3]
- To date, there has been limited information assessing the impacts of the presence of liver mets on the systemic immune response

Aim

- To analyze circulating and local tumour (non-liver) immune profiles of melanoma patients with versus without concurrent liver mets to elucidate the factors behind why patients with liver mets have worse outcomes overall

Methods

Cohort 1

- Pre-treatment PBMCs from 37 patients with advanced melanoma were profiled using mass cytometry (CyTOF) spanning 46 markers.
- Expression of specific immune cells and clusters were compared between those with (n=8) versus without (n=29) liver mets

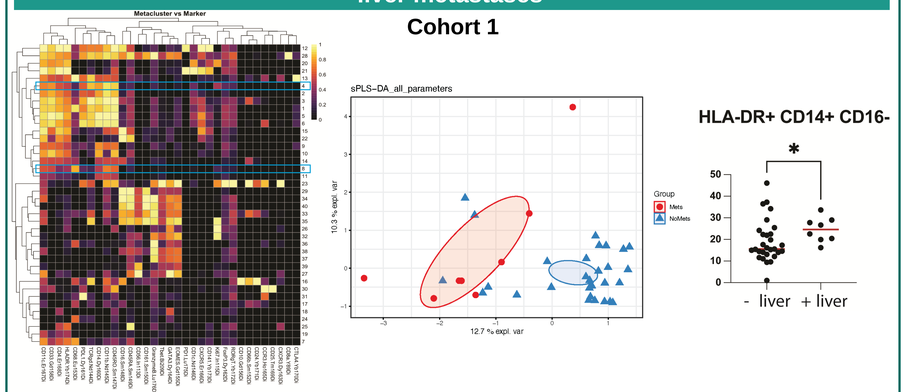
Cohort 2

- 93 FFPE melanoma biopsies comprised of lymph node, subcutaneous and brain metastases from untreated metastatic melanoma patients were identified and used for opal multiple IHC (mIHC):
  - *mIHC panels:* (1) CD3, Tim3, CD103, PD1, FoxP3, Sox10; (2) CD68, CD14, CD16, PD-L1, Sox10
  - *Analysis:* Immune cell densities and cell proportions were compared between patients with (n=40) versus without (n=53) liver mets at the time of biopsy

Results

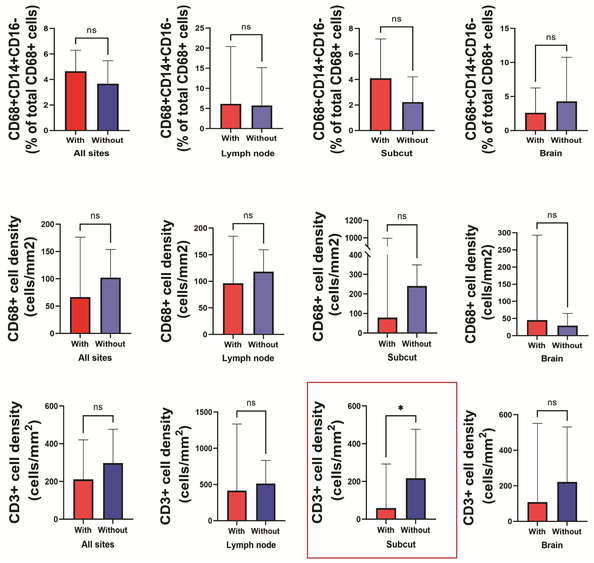
Patients with liver metastases have an increased proportion of circulating classical monocytes (HLA-DR+CD14+CD16-) compared to patients without liver metastases

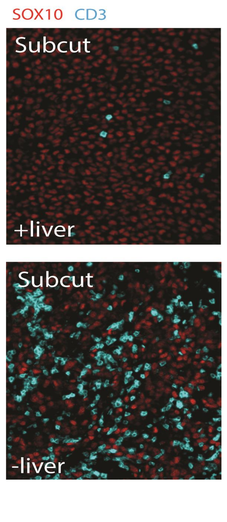
Cohort 1



Patients with concurrent liver metastases had increased CD3+ T cell density in subcut metastases compared to patients without liver metastases

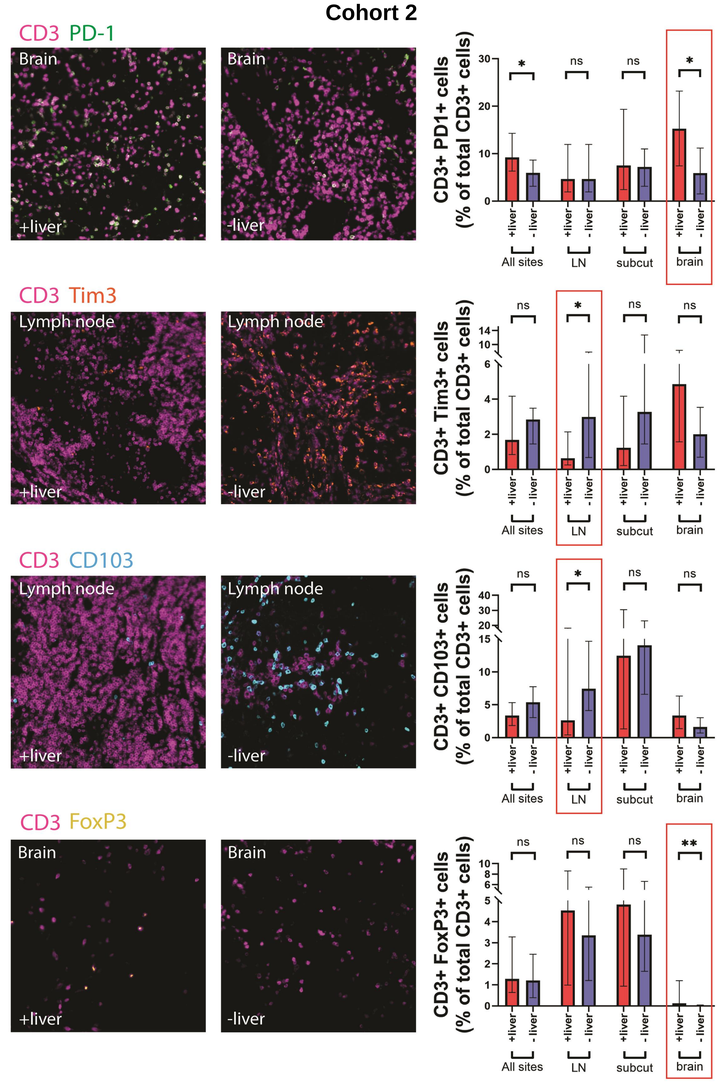
Cohort 2





Patients with concurrent liver metastases had a reduced proportion of CD3+T cells expressing Tim3 and CD103 in LN metastases compared to patients without liver metastases

Cohort 2



Conclusions

- Patient with liver metastases have an increased proportion of HLA-DR+CD14+CD16- cells (classical monocytes) in peripheral blood
- In non-liver tumor biopsies, the presence of concurrent liver metastases is associated with differences in T cell (but not myeloid cell) populations
- The presence of liver metastases may have a specific impact on immune populations at different metastatic sites. This highlights the need for further validation and investigation into the mechanisms by which the presence of liver metastases may exert this effect

References

1. Gide, T *et al.* CCR, 2018
2. Pires da Silva *et al.* JCO 2021
3. Pires da Silva *et al.* Cancers, 2020

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