

Multi-omics spatial analysis of colon cancer tissue reveals emergence of an immunosuppressive tumor maintenance system

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Abstract

Using a combination of modalities such as sequential multiplex immunofluorescence (mIF) and spatial transcriptomics (STx) we investigated spatial distribution, phenotype, function, and gene expression profile within the colon cancer and healthy colonx tissue. Immunosuppressive cells, Treg and M2 macrophages were in the TME. Presence of other immune cells was not sufficient to prevent crypt hyperproliferation. Immune cell infiltration into the crypt was prevented by a stromal cell barrier. While immunosuppressive phenotype was observed using antibodies, a strong presence of immunosuppressive genes was not found in transcriptomic study. The latter showed gene expression signatures related to processes of DNA damage, cell death, and hypoxia in epithelial cell regions.

Multi-omics Spatial Imaging and Analysis



Antibody Panel

Checkpoint	Structural	Stromal	T cells	Autophagy & Hypoxia
PD-1	E-Cadherin	α-SMA	CD3	CA-9
PD-L1	PanCK	Podoplanin	CD4	LC3B
IDO-1	NK Cell	Neutrophil	CD8	Endothelial
VISTA	CD56		FOXP3	
ICOS	B Cell	CD177	Treg	CD31
CTLA-4		CD20	TCR delta	
TIM-3			Granzyme B	

5 um FFPE sections were prepared from stage IIA colon cancer sample of a 56-year-old individual exhibiting moderate to poorly differentiated adenocarcinoma of T3, N0 staging. The tumor was microsatellite stable (MSS) and mismatch repair proficient (pMMR). There was low tumor mutational burden.

Results and Conclusions

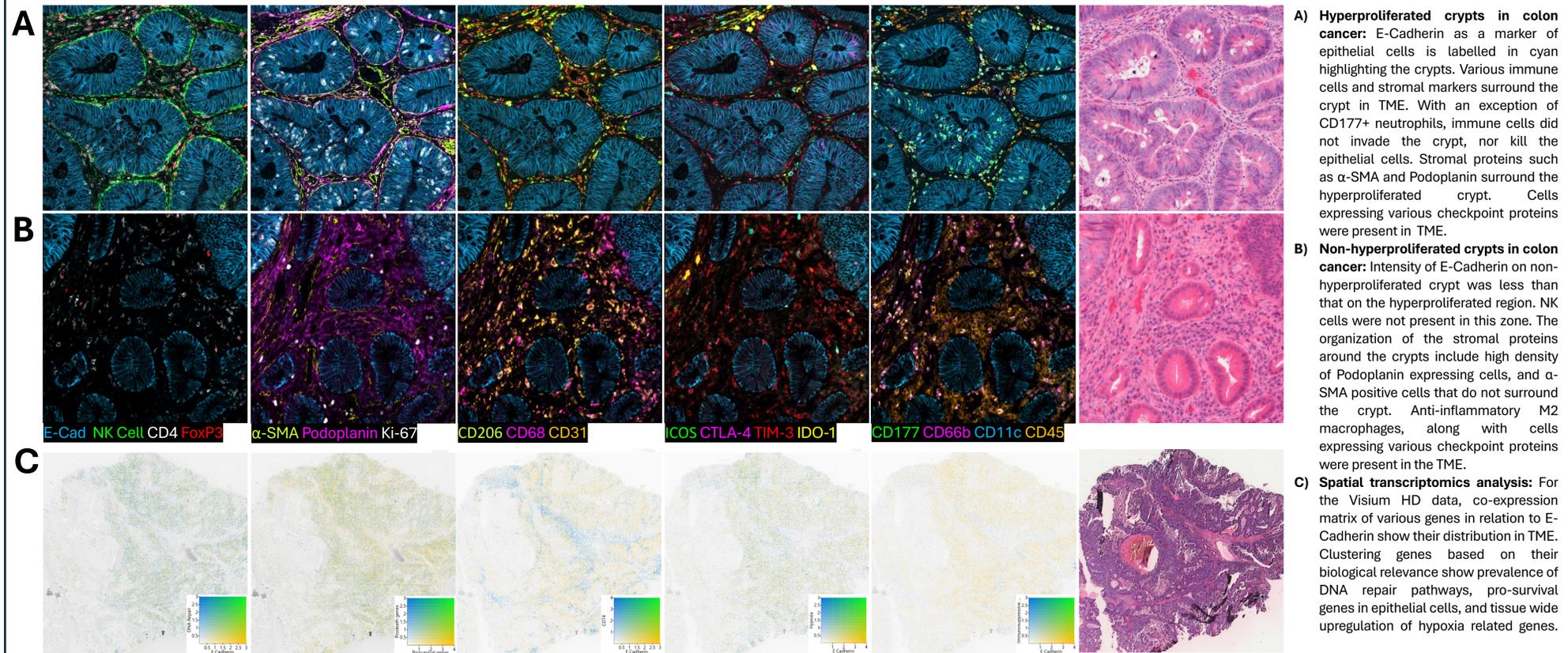


FIGURE 1 – Colon cancer sample show differentially proliferated crypts, TME diversity, immune cell evasion and gene expression signatures related to various processes using multi-omics imaging and transcriptomics

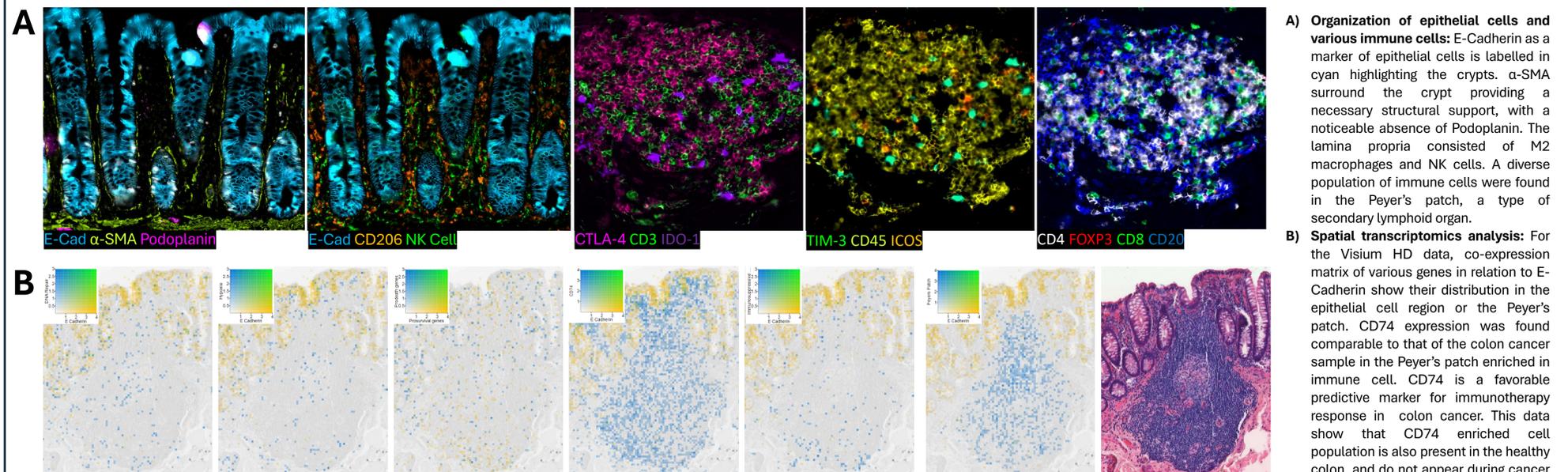


FIGURE 2 – Healthy colon sample show organization of crypts, supporting stromal cells, and a diverse immune cell population in the Peyer's patch



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