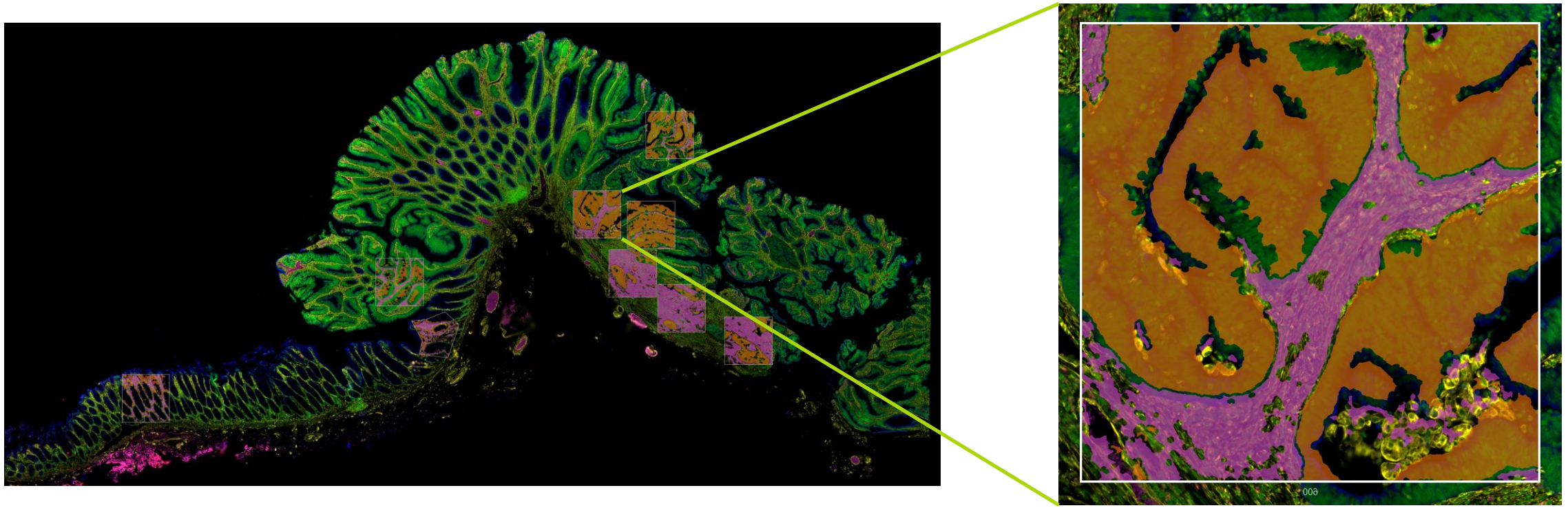
Digital spatial profiling reveals molecular and immunological hallmarks of colorectal cancer tumourigenesis

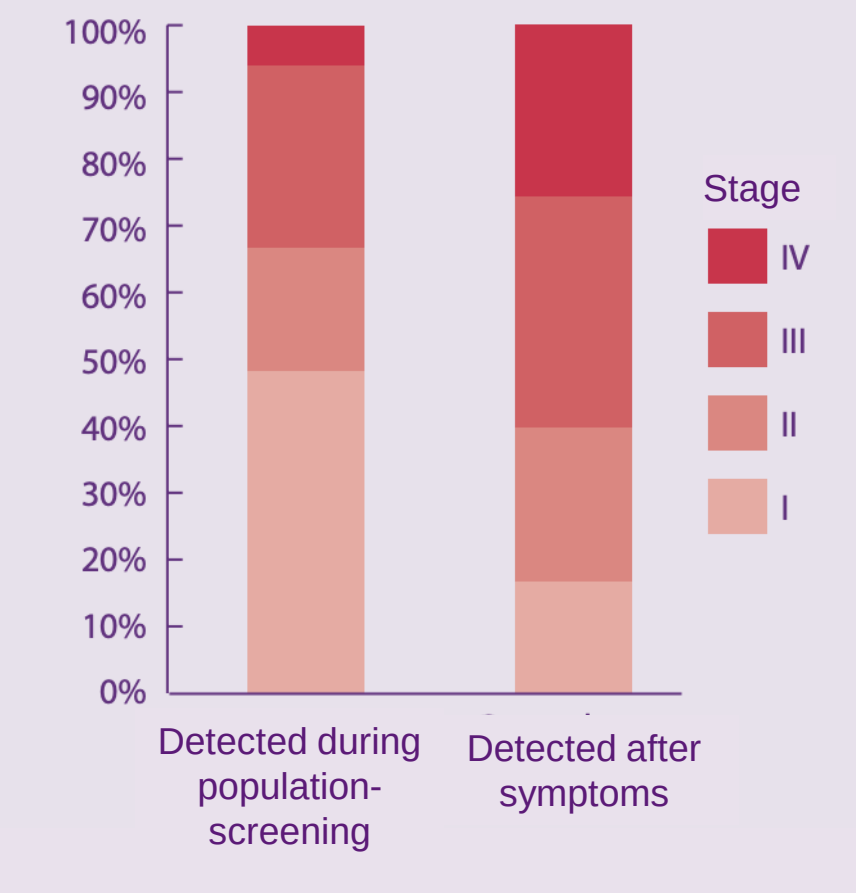
X-omics Festival 2023

Monday April 17th



Jessica Roelands
Department of Pathology, Leiden University Medical Center
Cancer Immunogenomics Lab

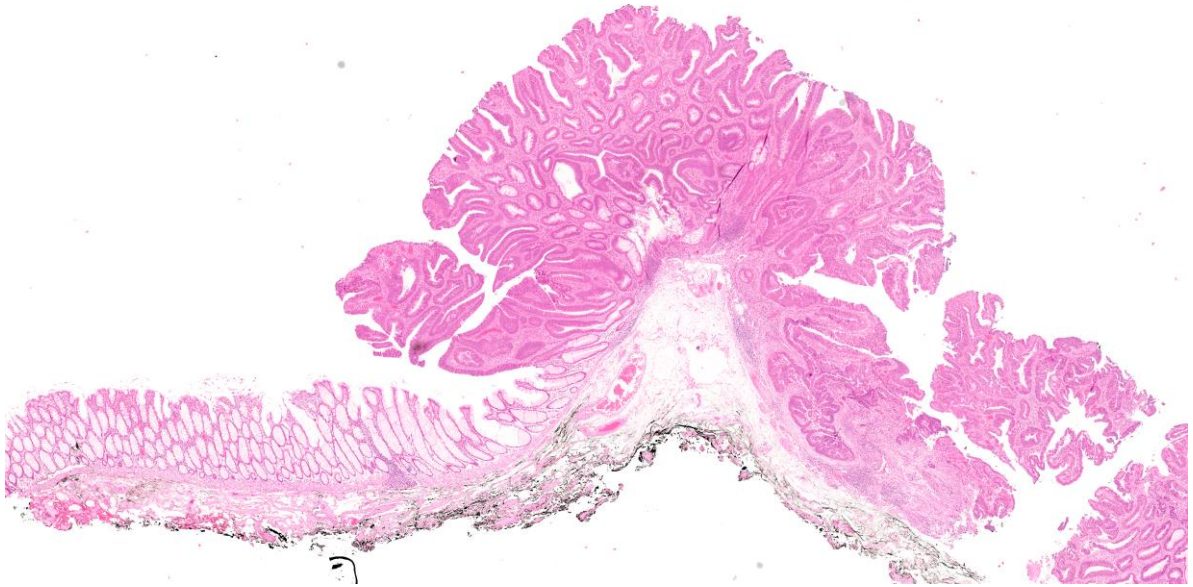
Early interception of CRC by population screening



From report RIVM (Dutch National Institute for Public Health and the Environment) on colorectal cancer screening program (2014-2017).

- Increase of diagnosis of early stage CRC as a consequence of population screening
- This development necessitates a better understanding of the biological and clinical behavior of early-stage CRC

Endoscopic submucosal dissection (ESD)

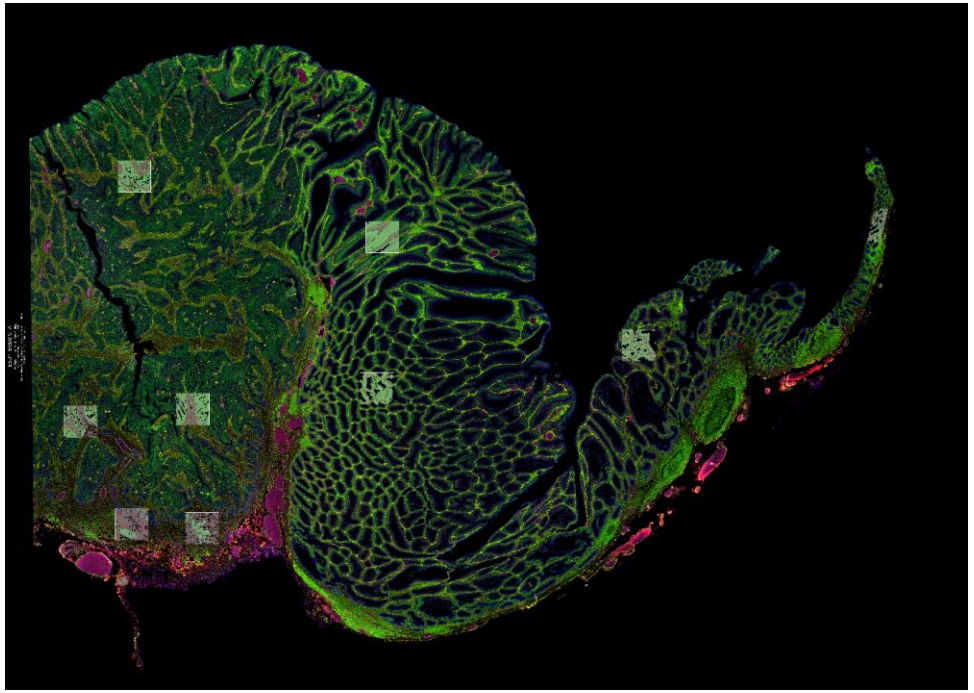


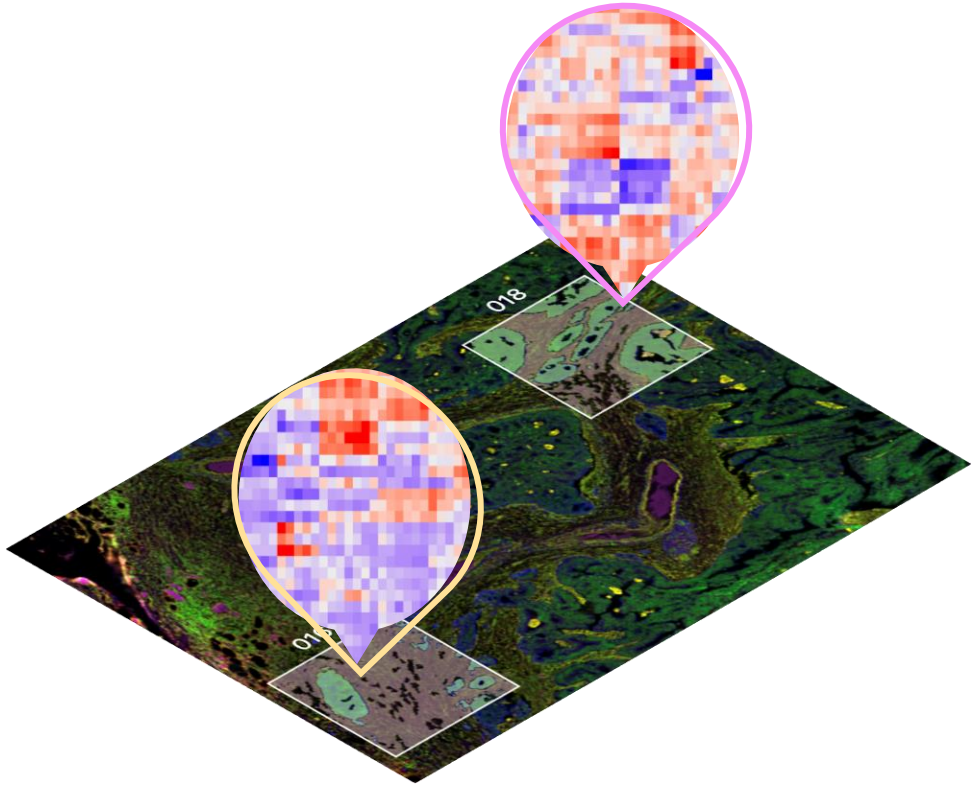
ESD- T1 colorectal cancer

- ESDs as a model to better understand colorectal tumorigenesis
- Opportunity to define biomarkers that are specifically relevant in these early stage tumors

Department of Gastroenterology and Hepatology, LUMC

Digital Spatial Profiling- GeoMx



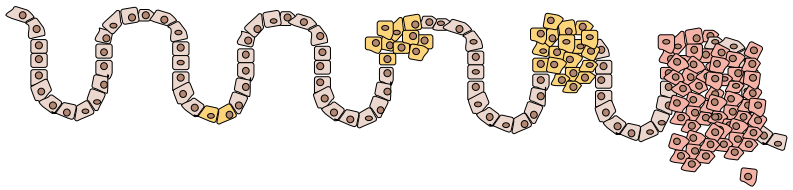


- Spatial transcriptomics to capture the expression of many genes simultaneously in specific locations within tissues

- pT1 CRC samples are particularly useful for these spatial approaches as they contain different histologies within the same lesion

GeoMx- Workflow

① Selection regions of interest

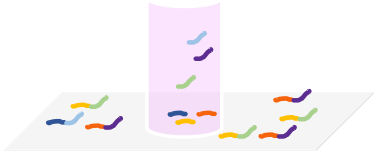


Normal | Transition | Low grade dysplasia | High grade dysplasia | Cancer

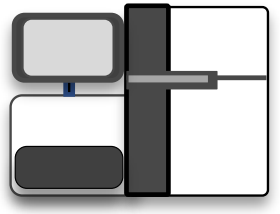
② Segmentation

Whole tissue | Epithelium | Stroma

③ Spatial gene expression profiling



UV-cleave & collect

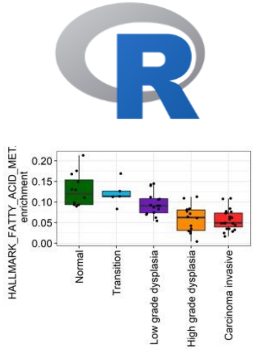


Count

④ Data processing and analysis

QC & normalization

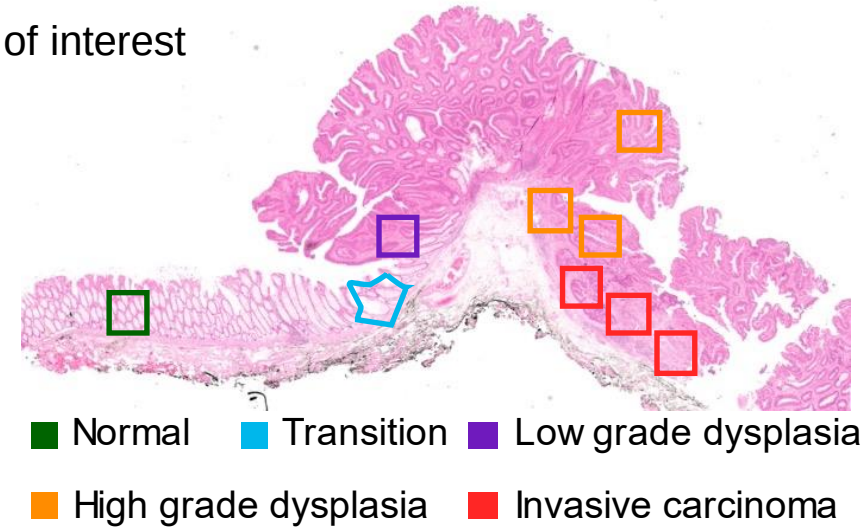
Export



‘For Research Use Only. Not for use in diagnostic procedures’

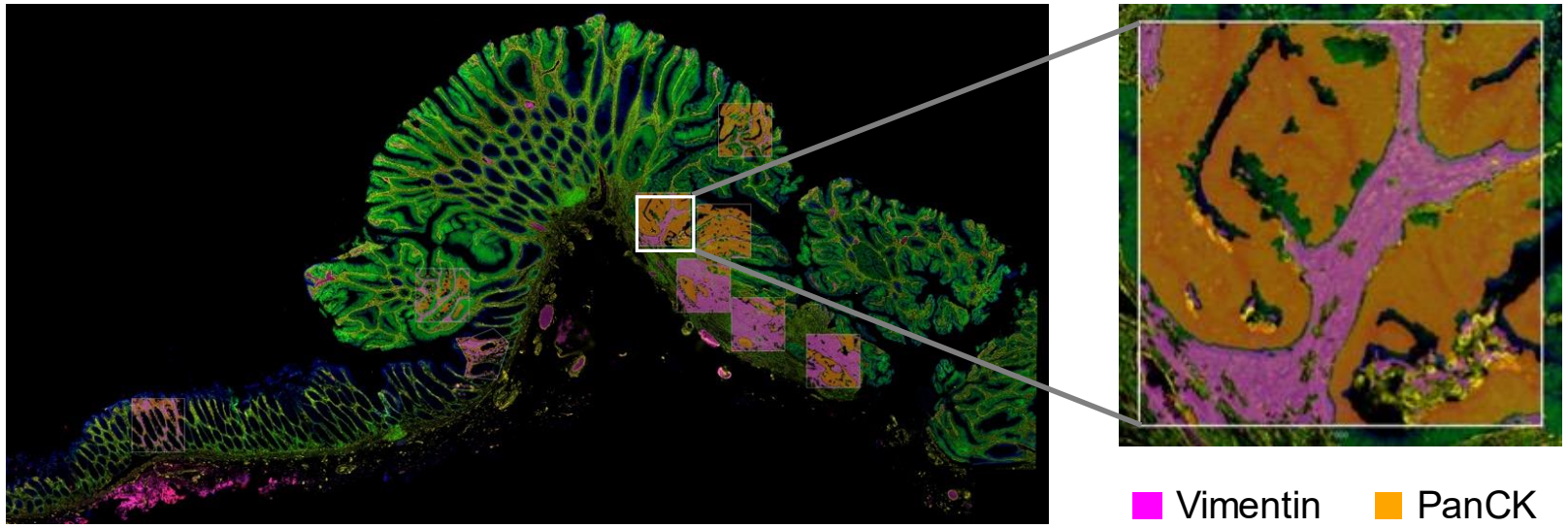
Areas of illumination

① Selection regions of interest



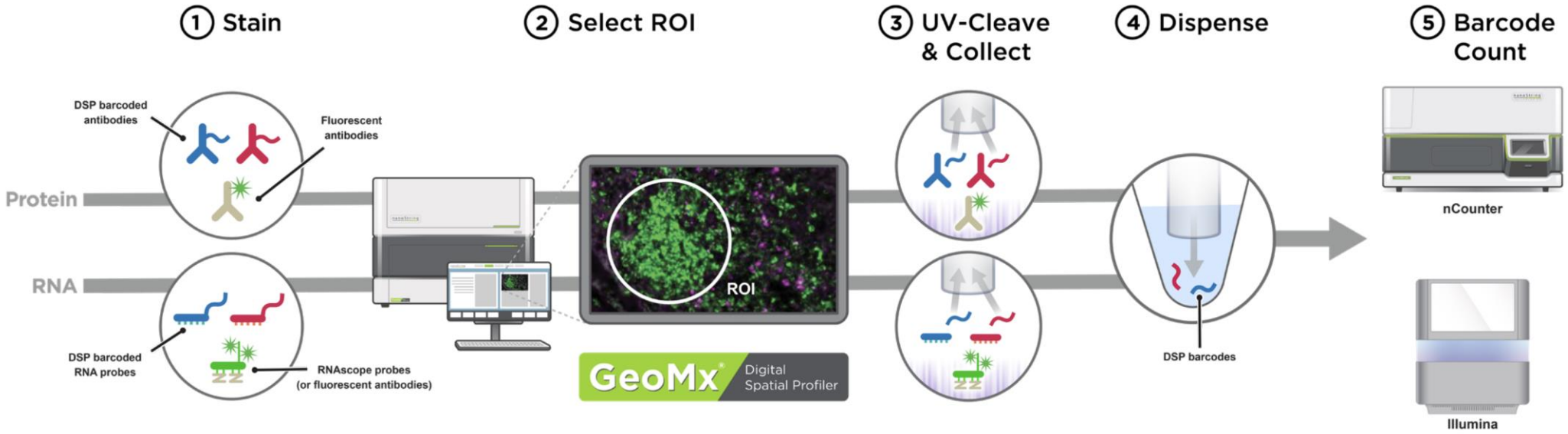
- 8 Endoscopic Submucosal Dissections (ESD)
- 9 regions of interest (ROIs) per ESD
- 2 Segments per ROI
  - PanCK+ (epithelium)
  - Vimentin+ (stroma)

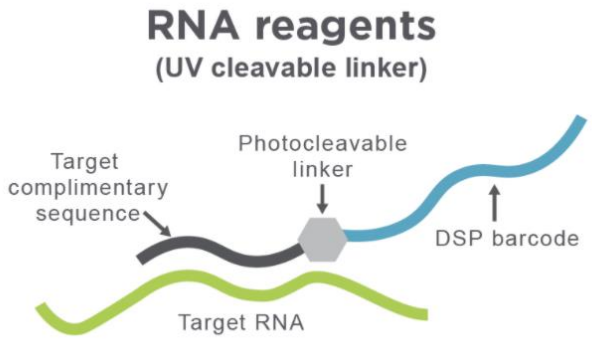
② Segmentation



GeoMx DSP technology

③ Spatial gene expression profiling





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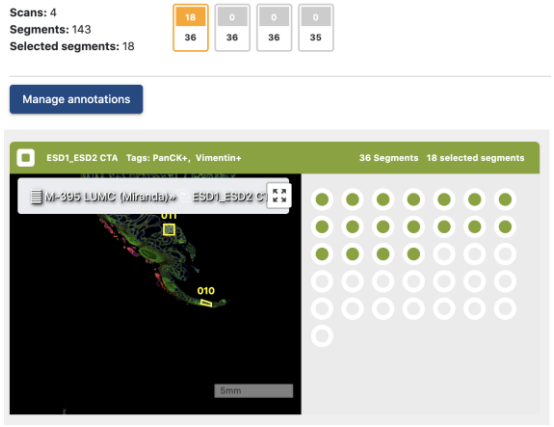
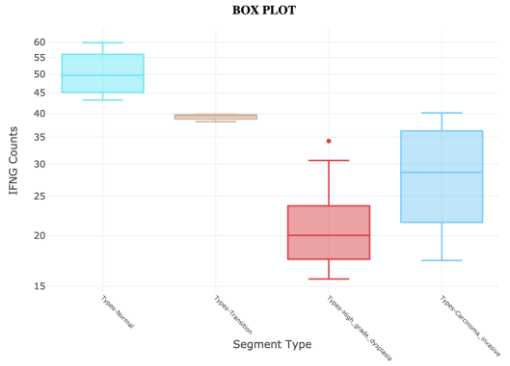
Data analysis and processing

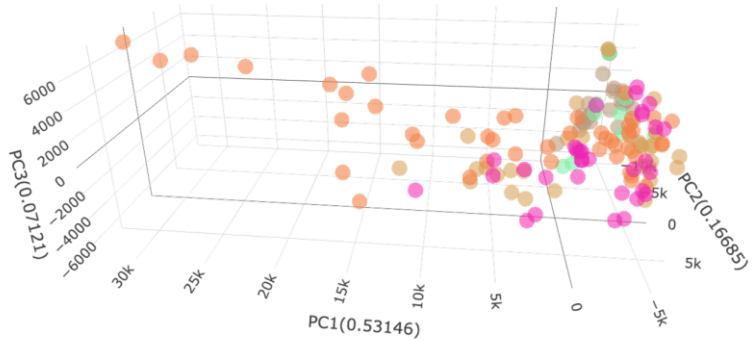
④ Data processing and analysis

DSP Analysis Suite for initial QC..

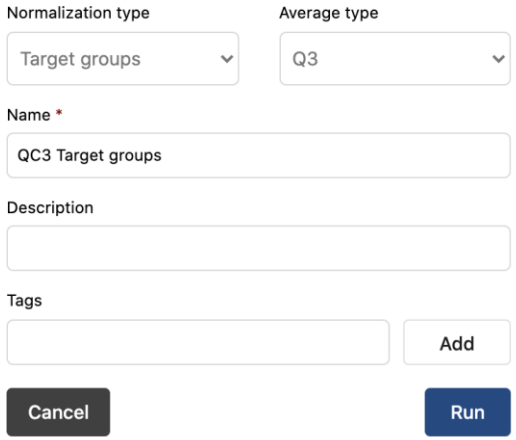


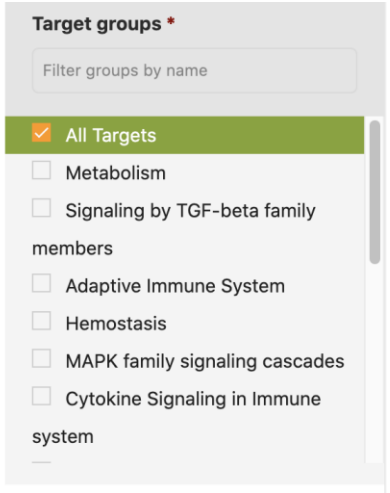
Data exploration…



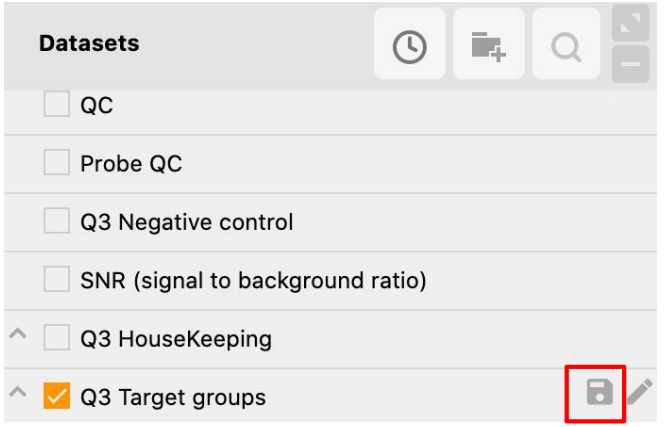


Normalization…

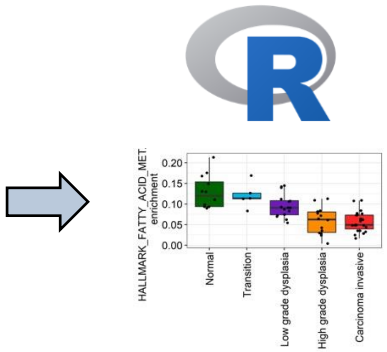




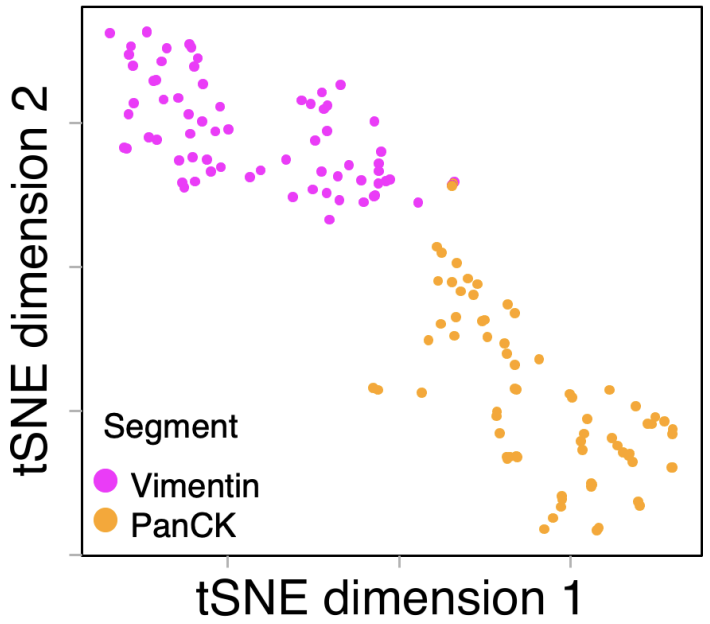
.. & export for downstream analysis in R



Save dataset



Dimension reduction by tSNE



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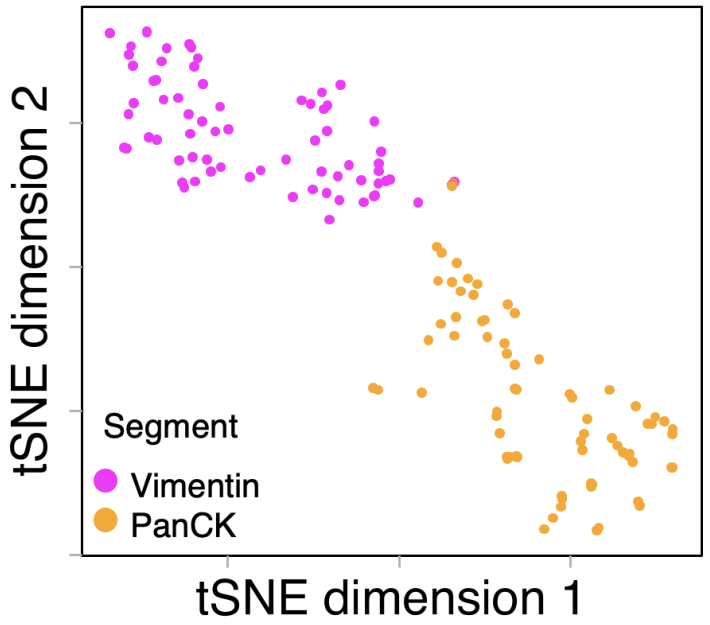
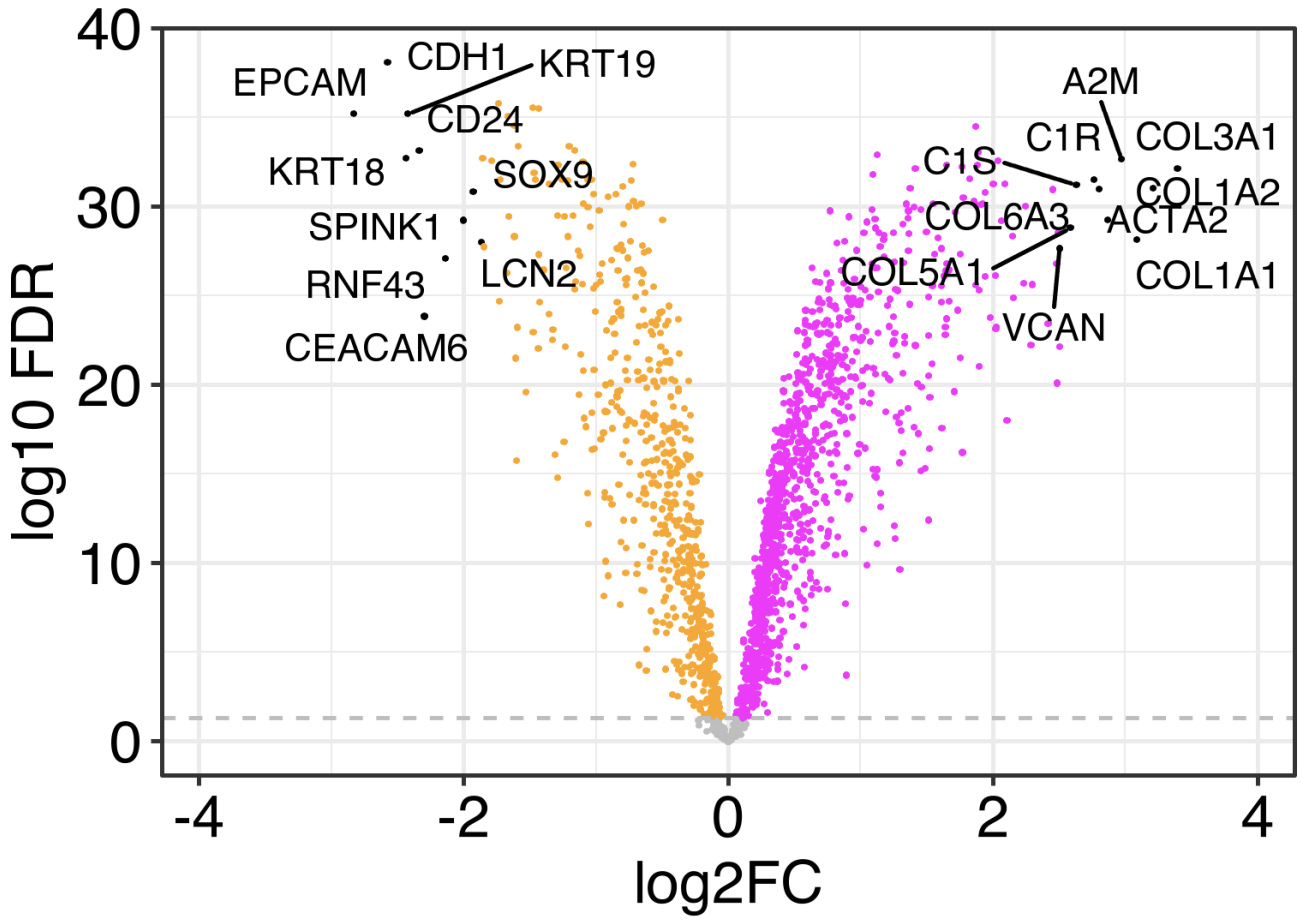
Dimension reduction by tSNE





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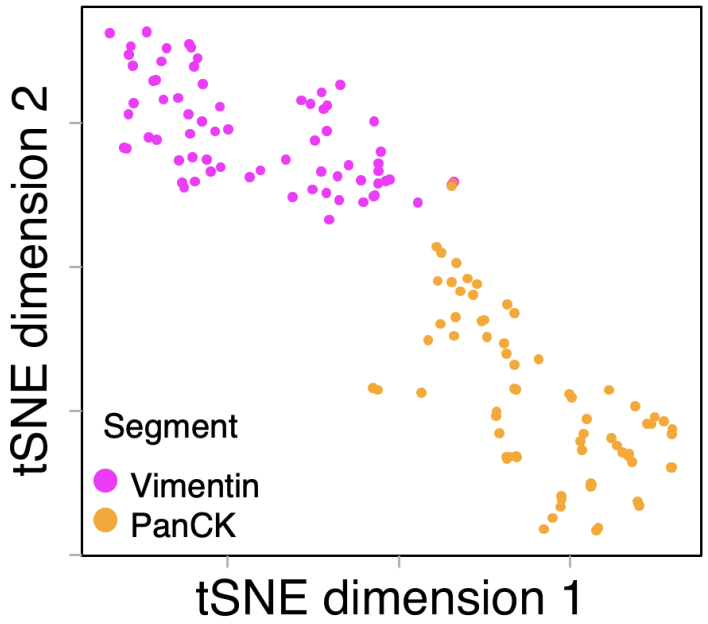
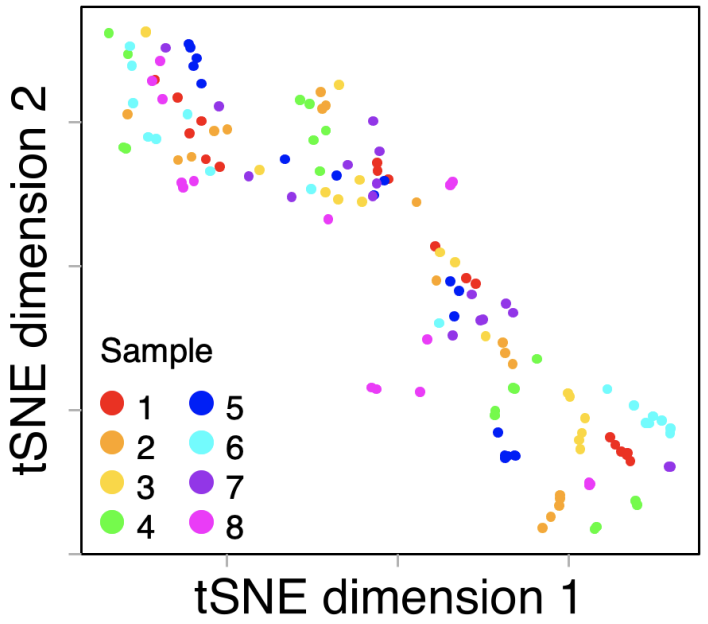
Dimension reduction by tSNE

Clear segregation of AOIs by segment



Annotation by sample ID



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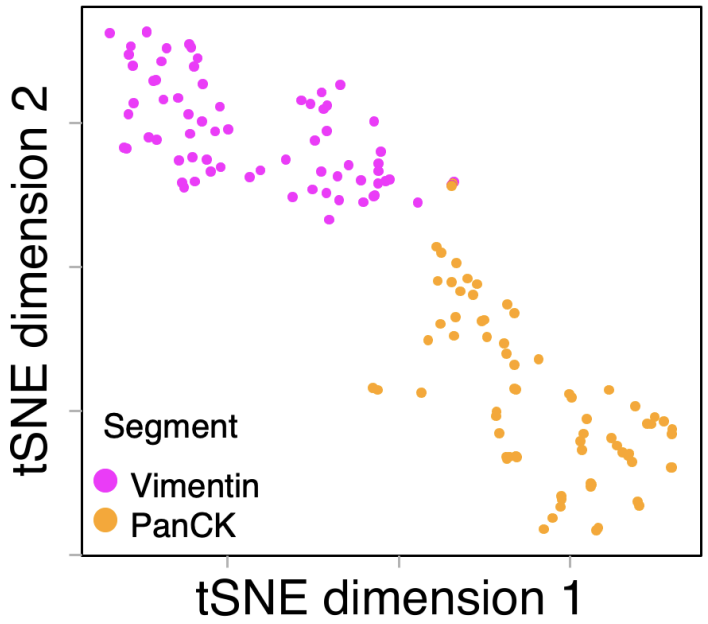
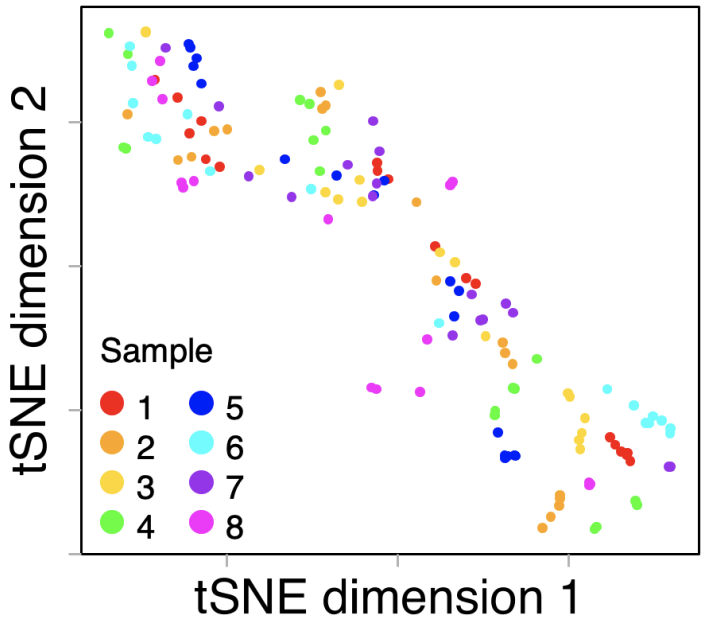
Dimension reduction by tSNE

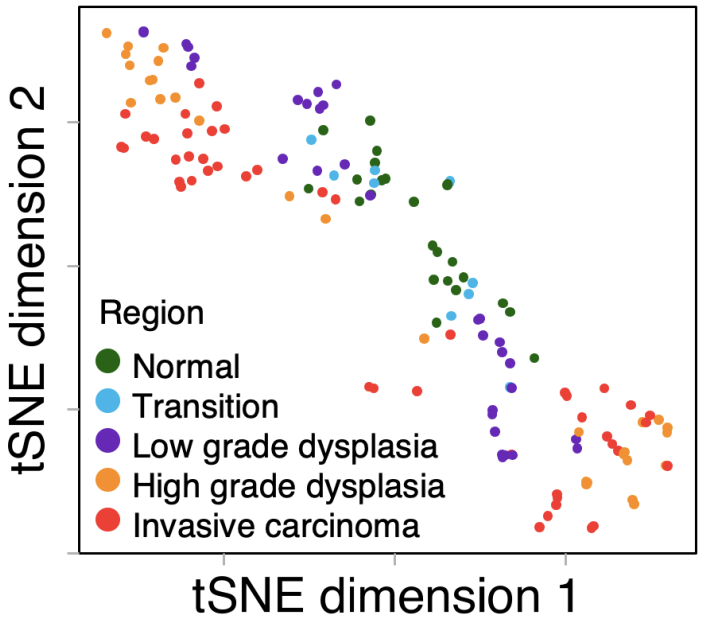
Clear segregation of AOIs by segment



Annotation by sample ID



Within segment, separation of AOIs by Region



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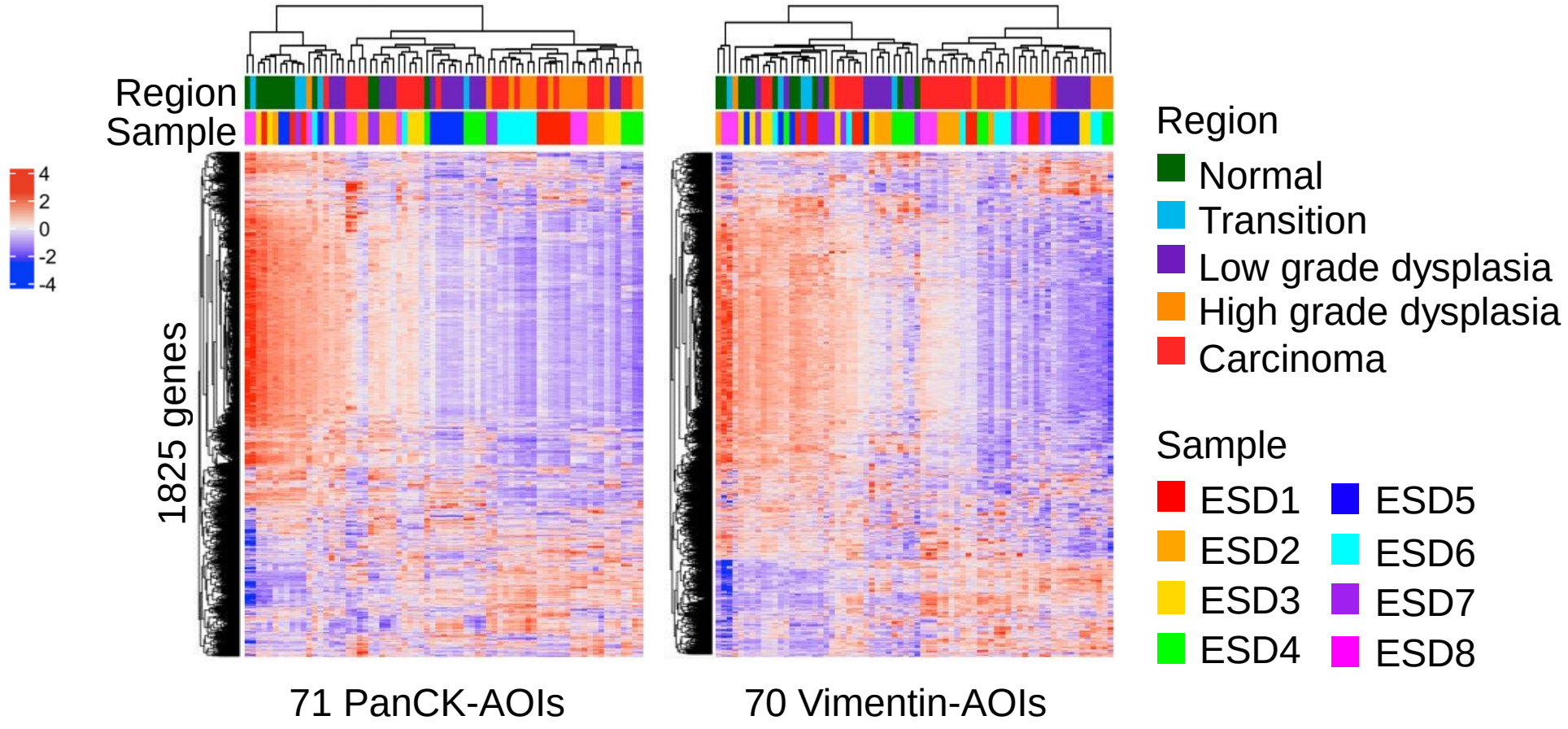
Differential gene expression by histology



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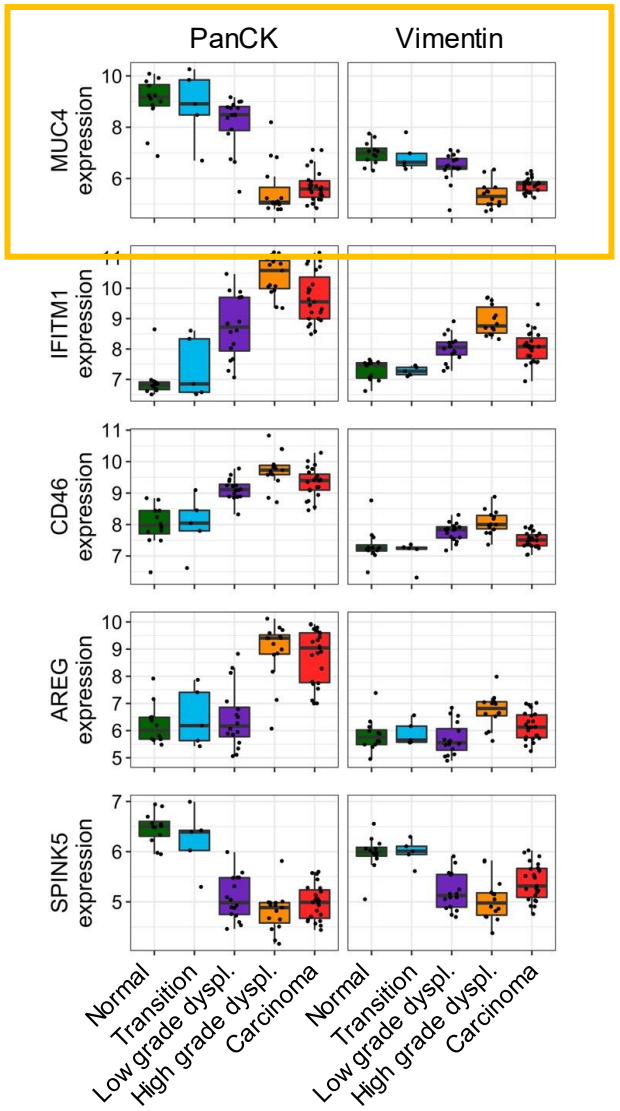
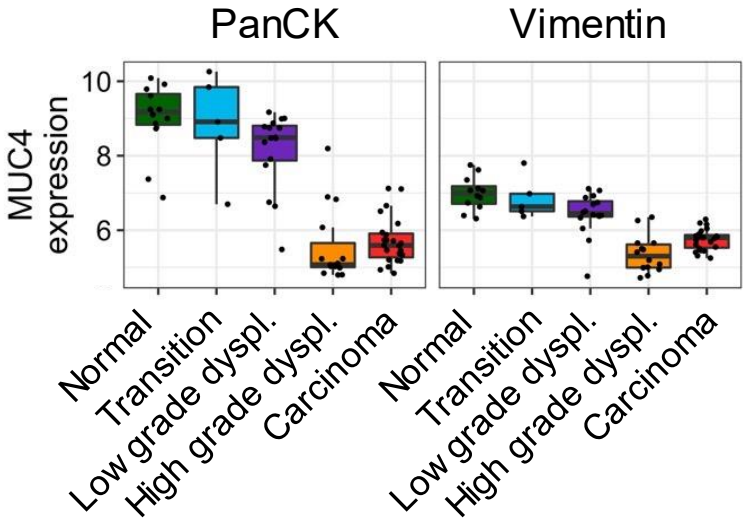
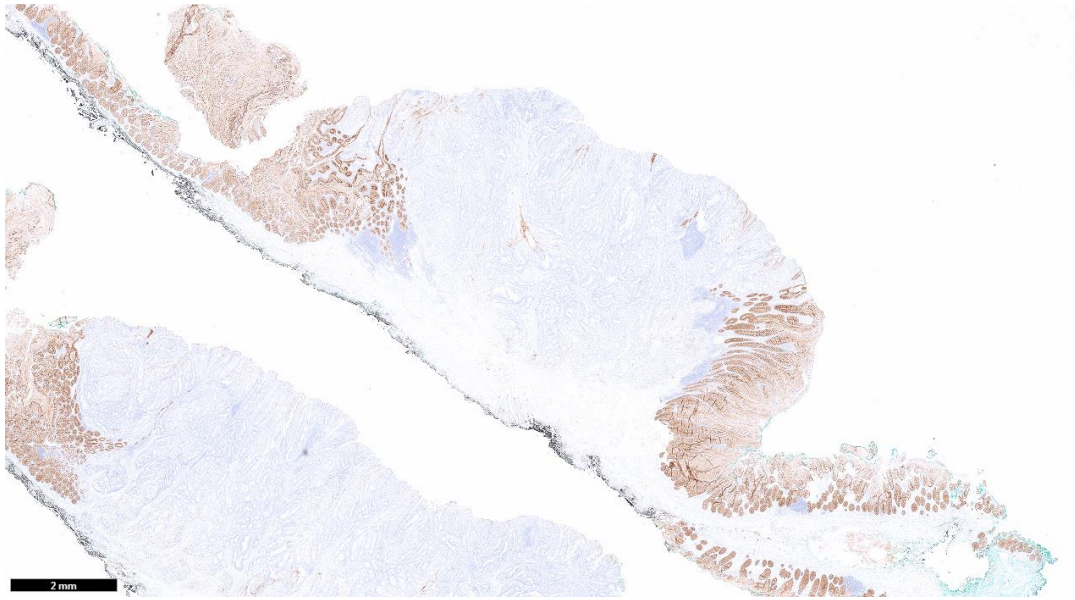
Differentially expressed genes during step-wise progression of CRC

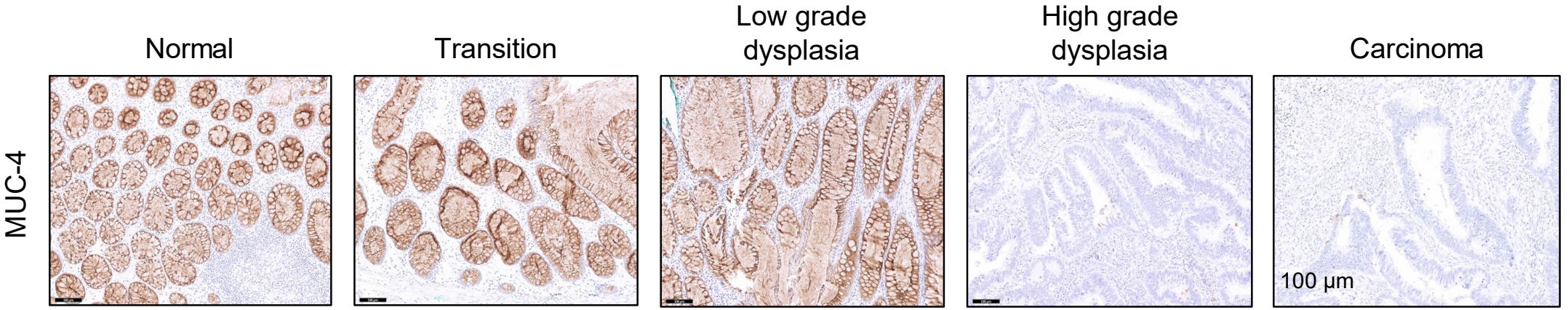
DEGs in epithelium



MUC-4 expression during step-wise progression to cancer

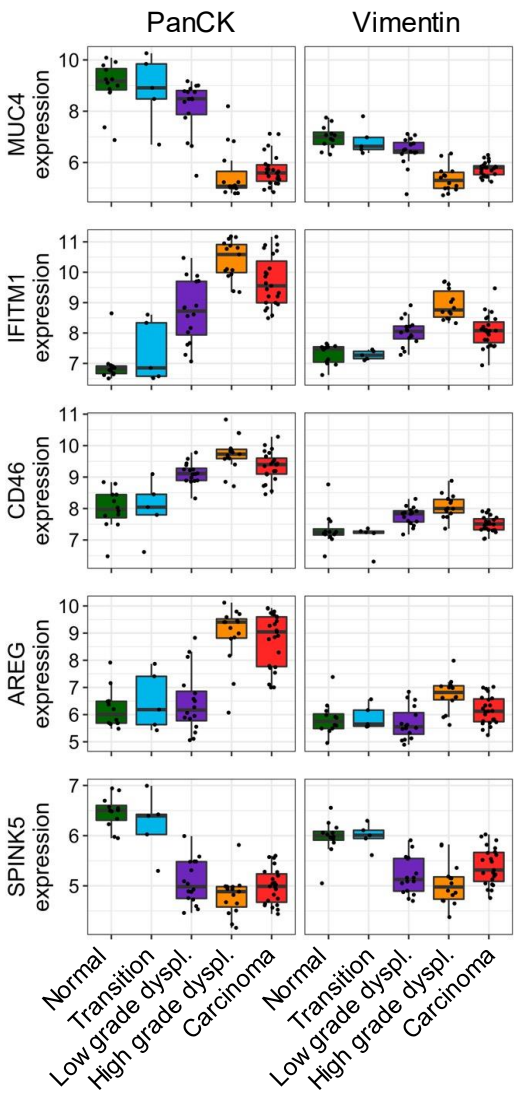




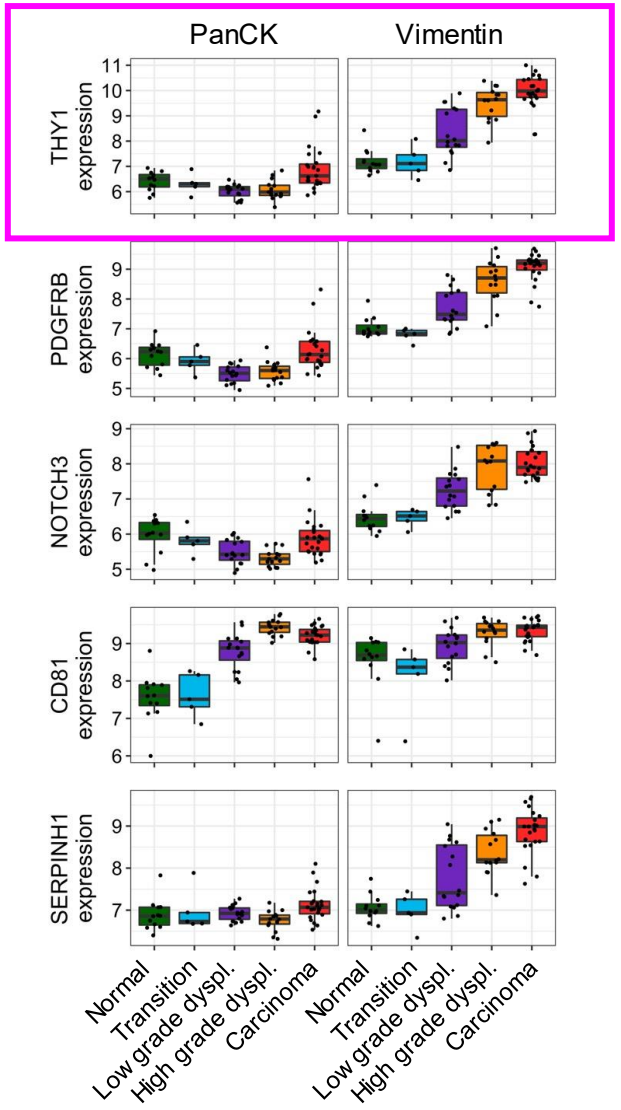


Differentially expressed genes during step-wise progression of CRC

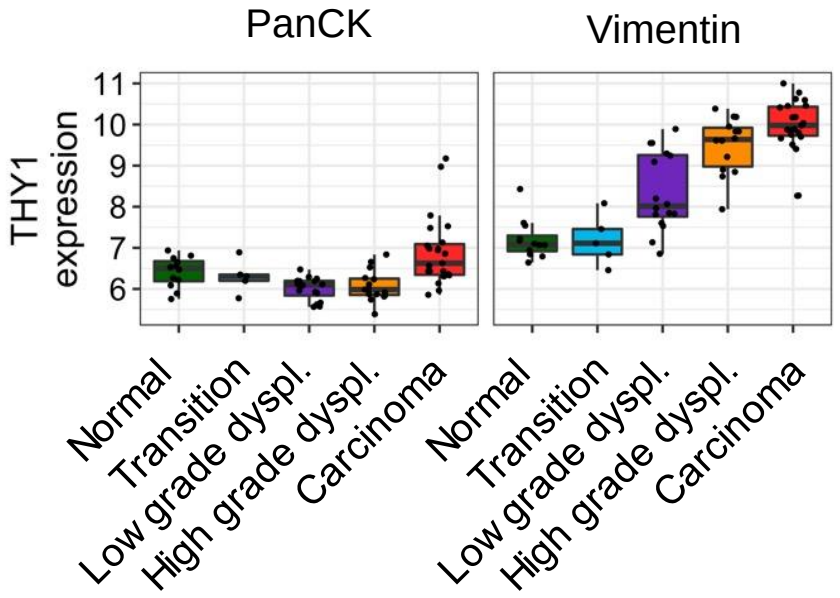
DEGs in epithelium

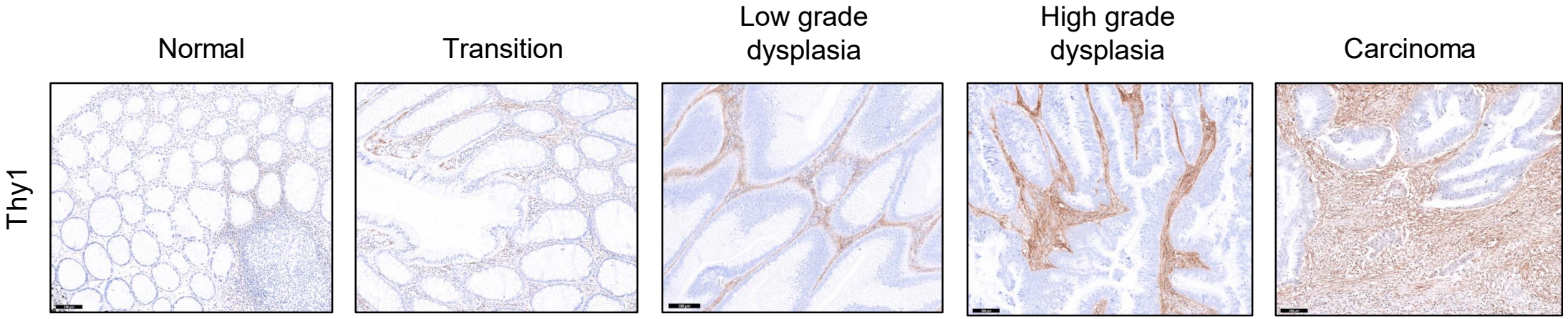


DEGs in stroma

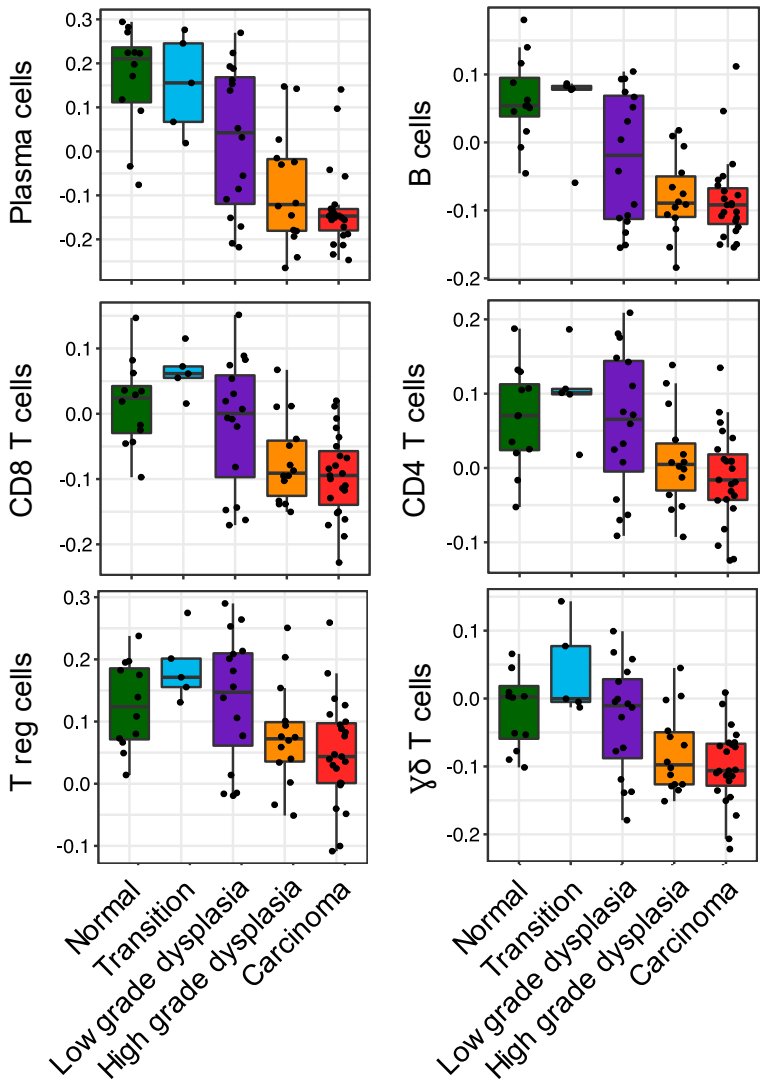


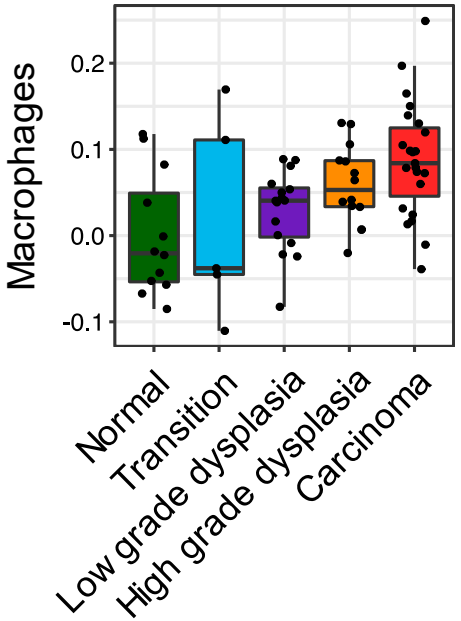
THY1 expression during step-wise progression to cancer

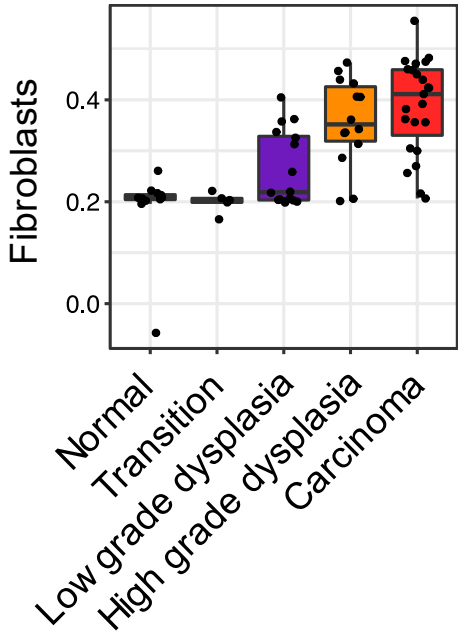


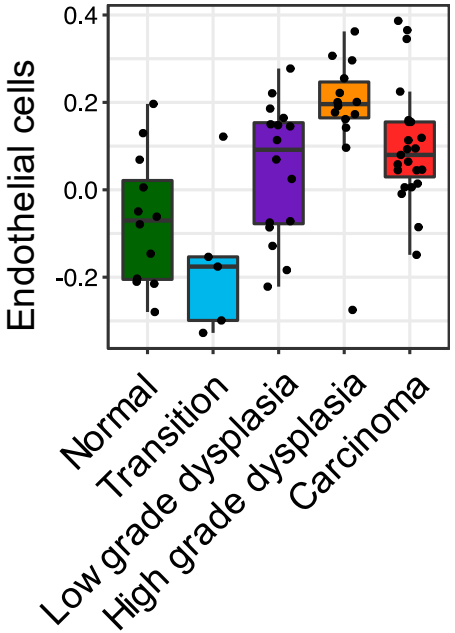


Immune Cell Deconvolution to estimate immune cell abundance









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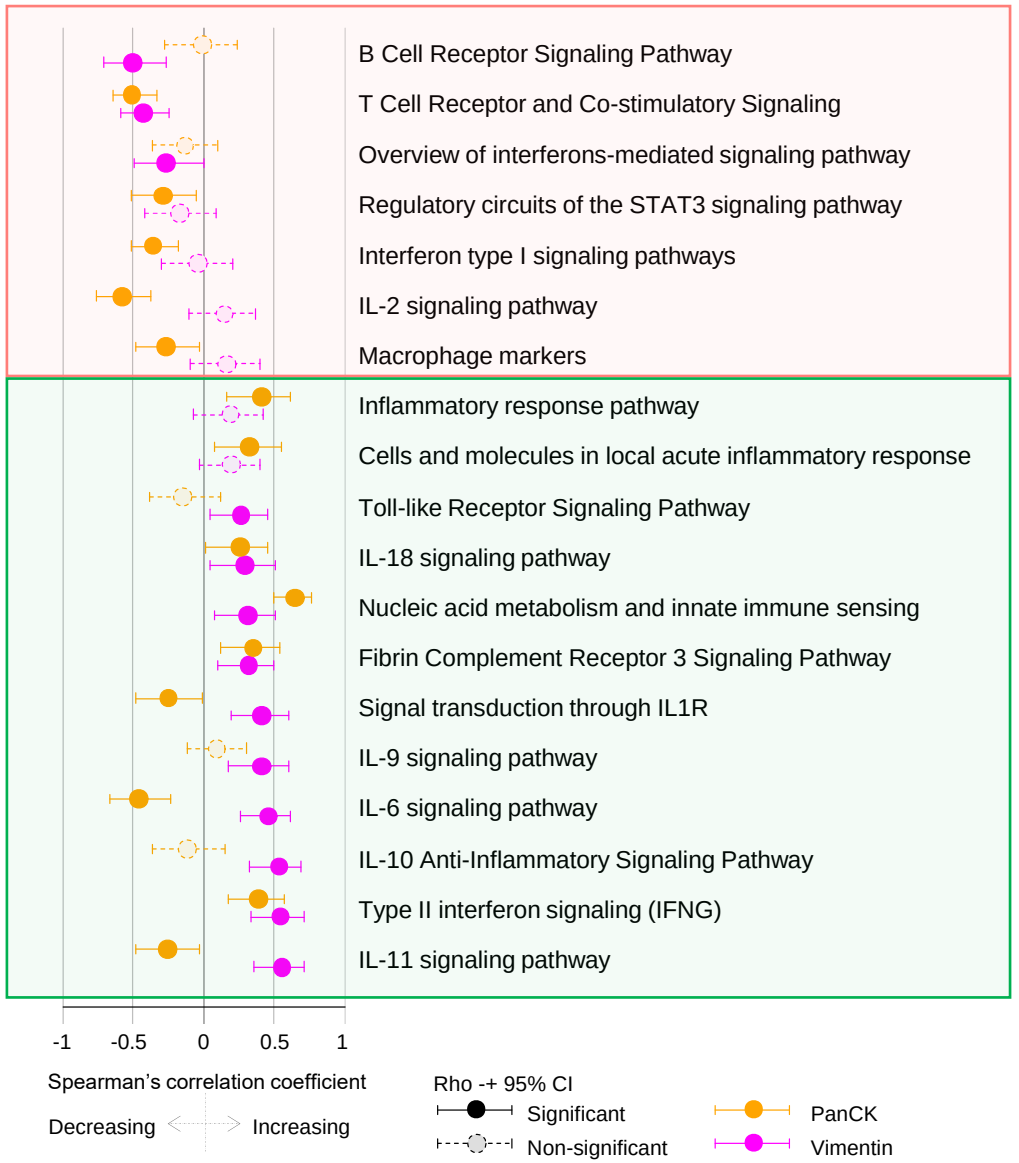
Alterations in immune-related pathway

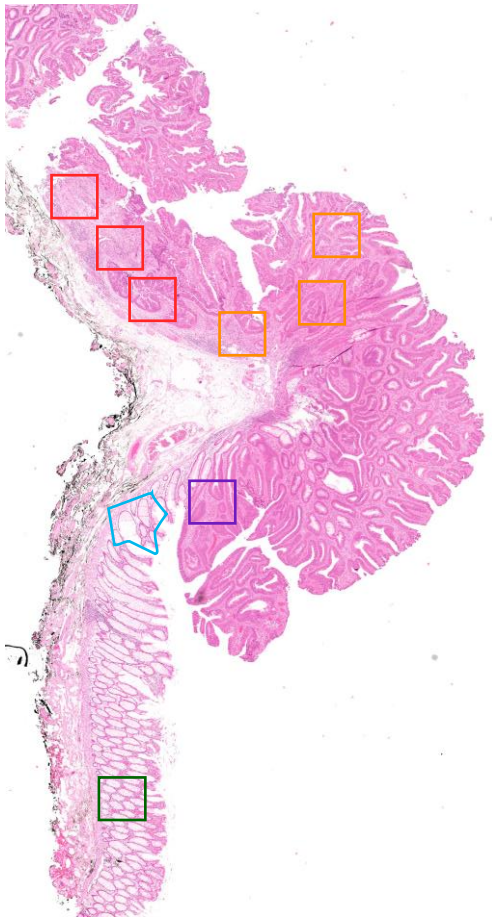


Decreasing from normal to tumor

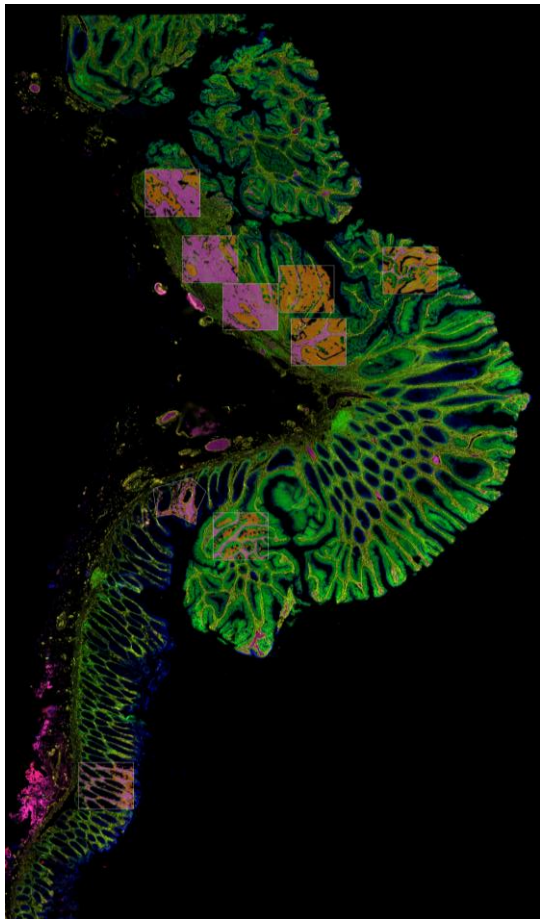
Increasing from normal to tumor

Imaging Mass Cytometry for deep characterization of the TME

H&E



GeoMx-DSP



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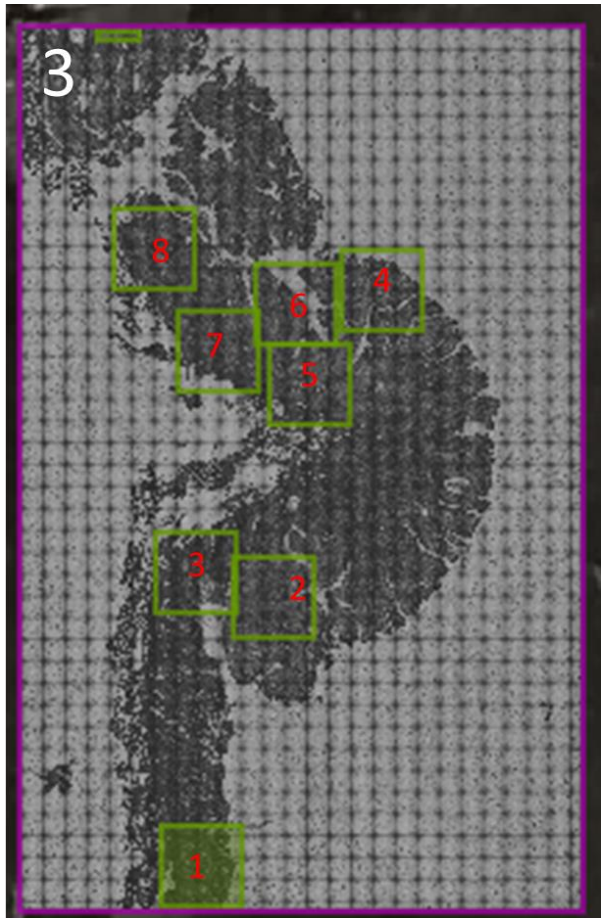
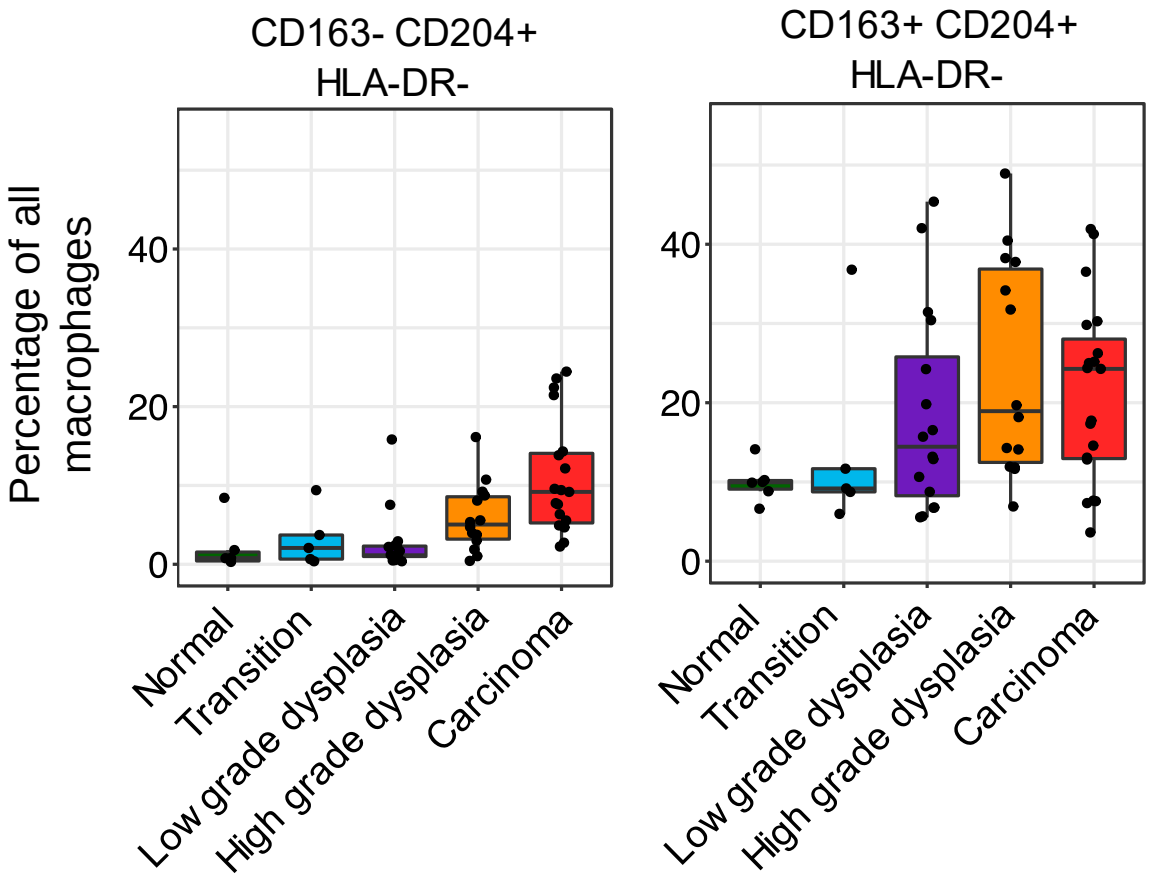


Consecutive sections of tissue for comprehensive investigation of the tumor immune microenvironment

Specific macrophages subsets increase during CRC tumorigenesis



CD204+ and HLA-DR- macrophages increase from normal tissue to cancer

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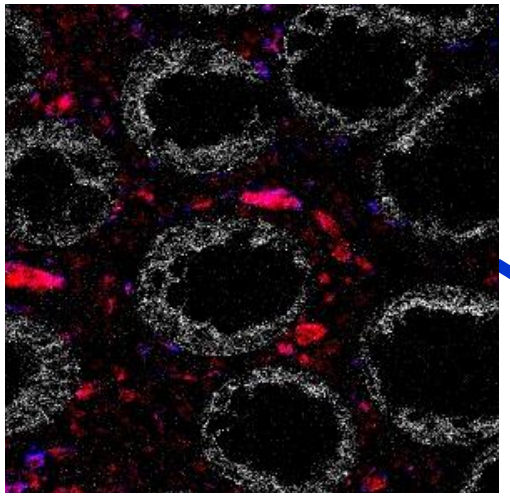
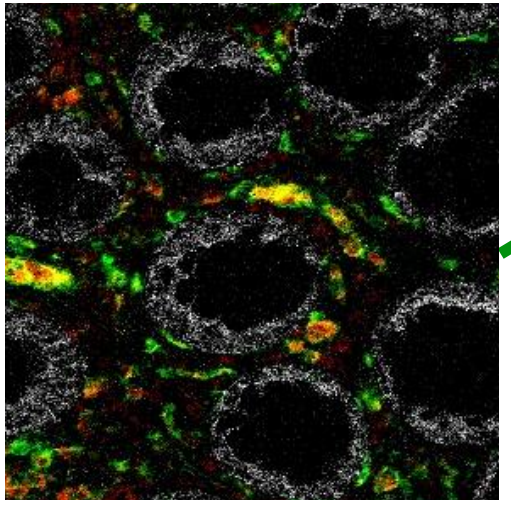
Macrophages in stroma of normal colon tissue

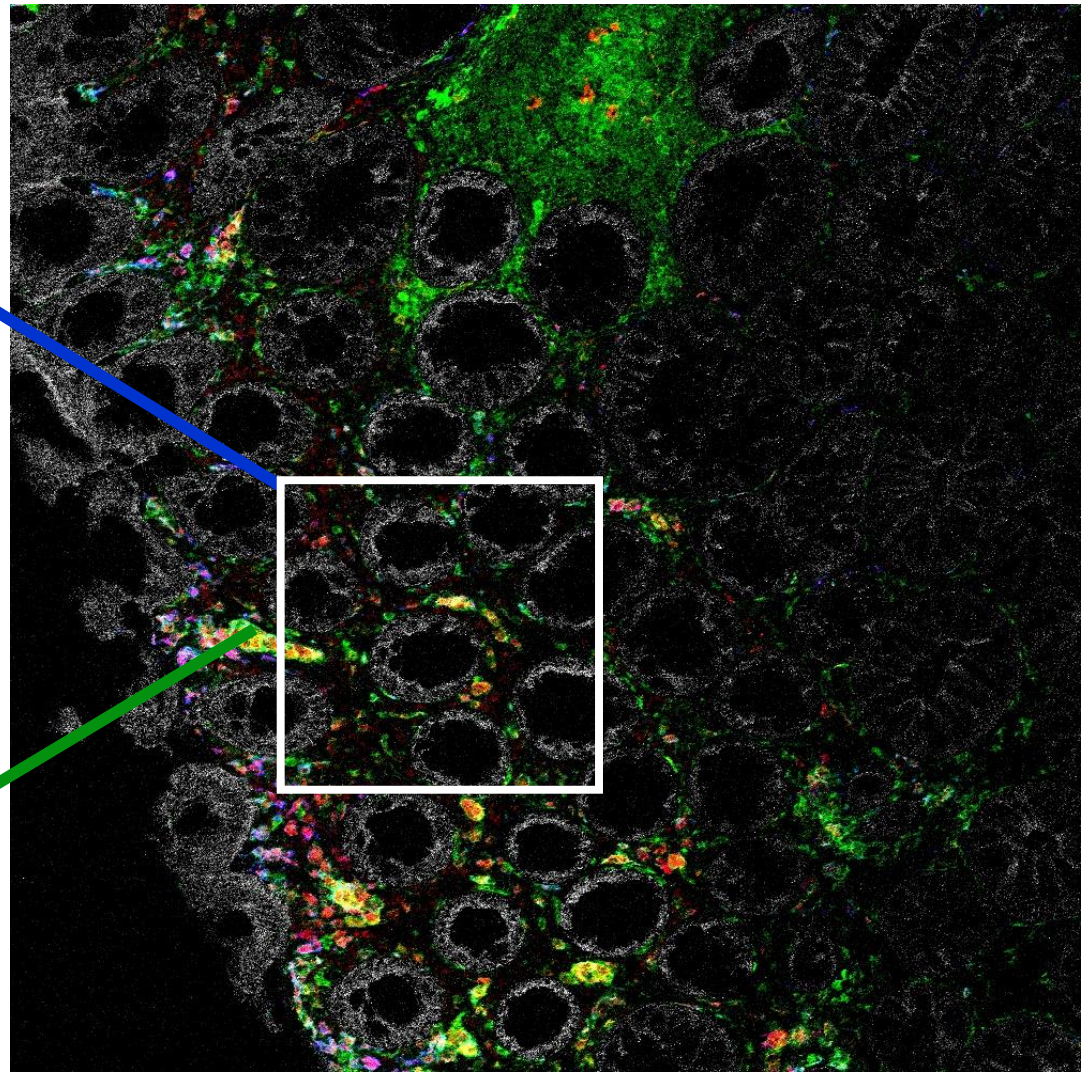
Inset CD68 CD204



Inset CD68 HLA-DR



CD68 CD204 HLA-DR



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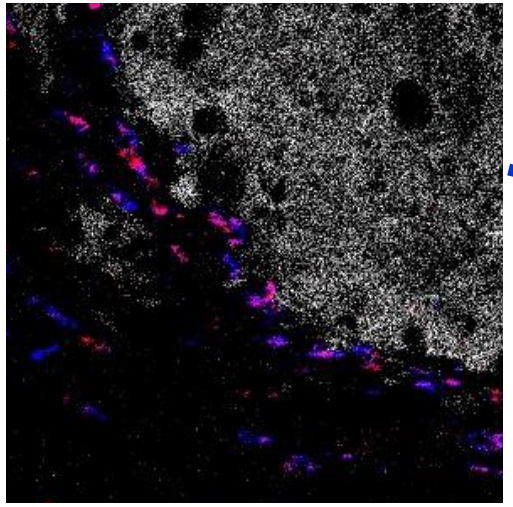
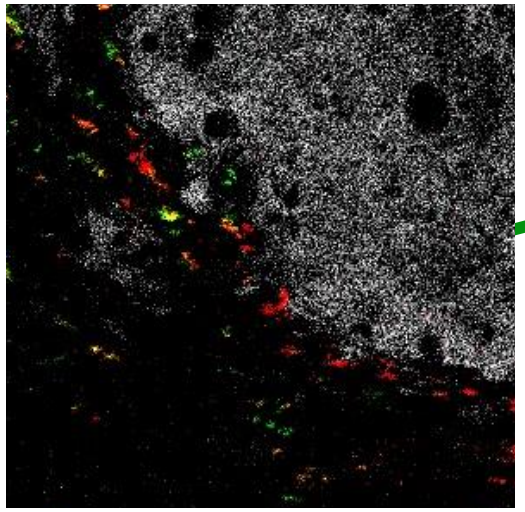
Macrophages in tumor stroma

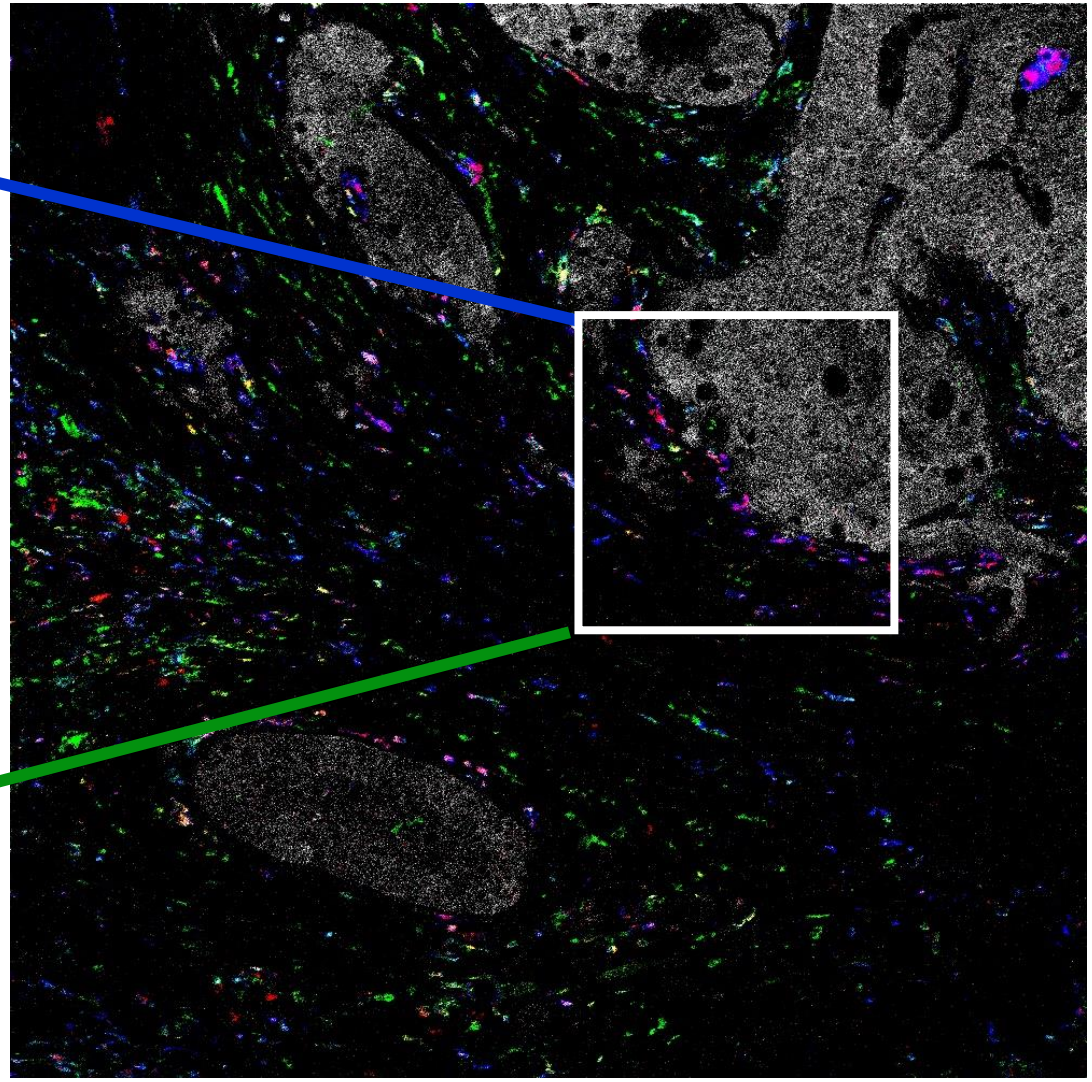
Inset CD68 CD204



Inset CD68 HLA-DR



CD68 CD204 HLA-DR



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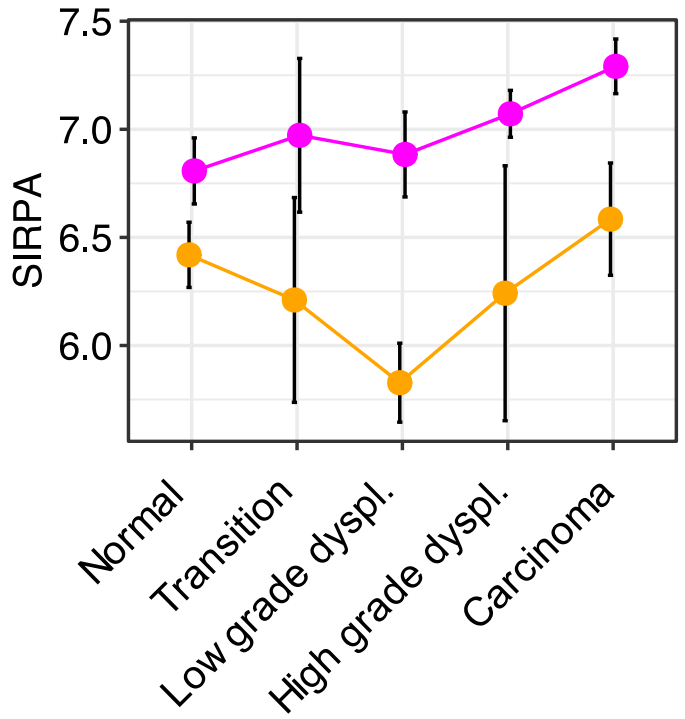
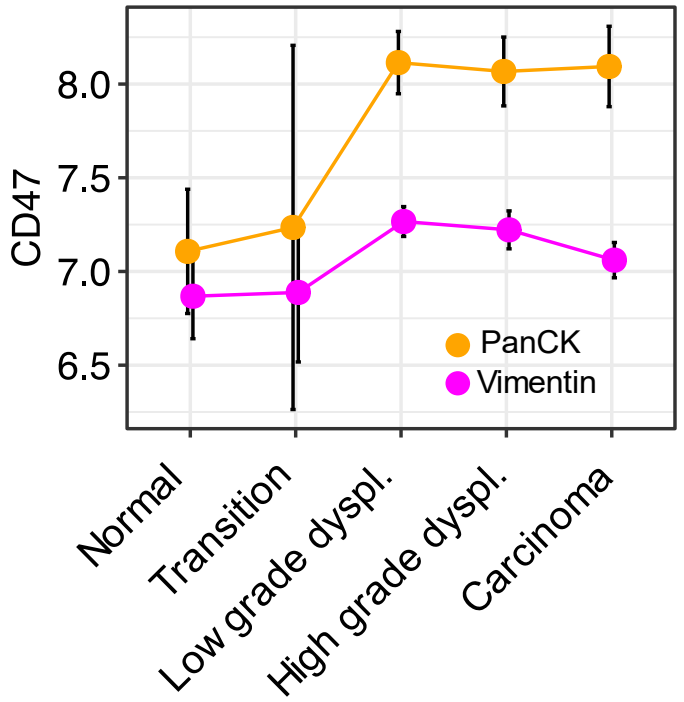
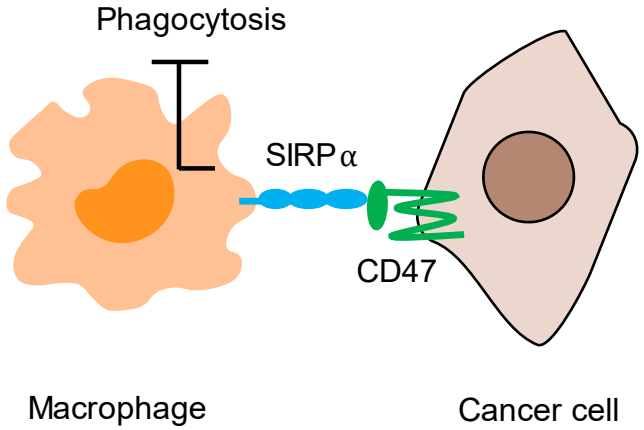
SIRPα-CD47 axis during tumorigenesis







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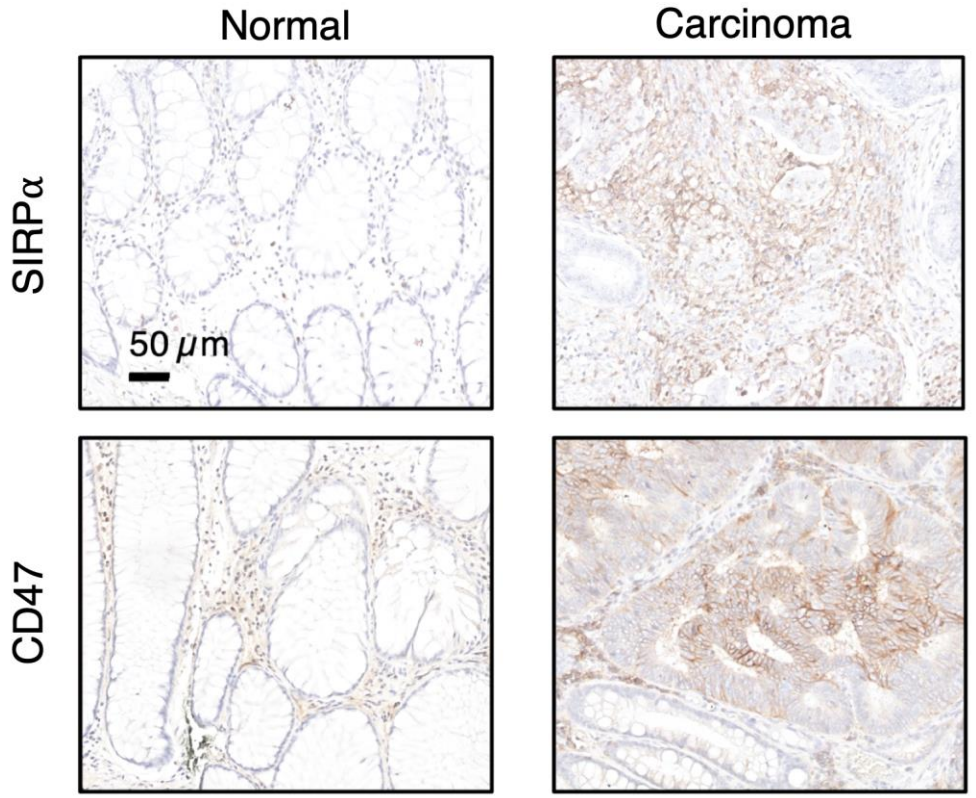
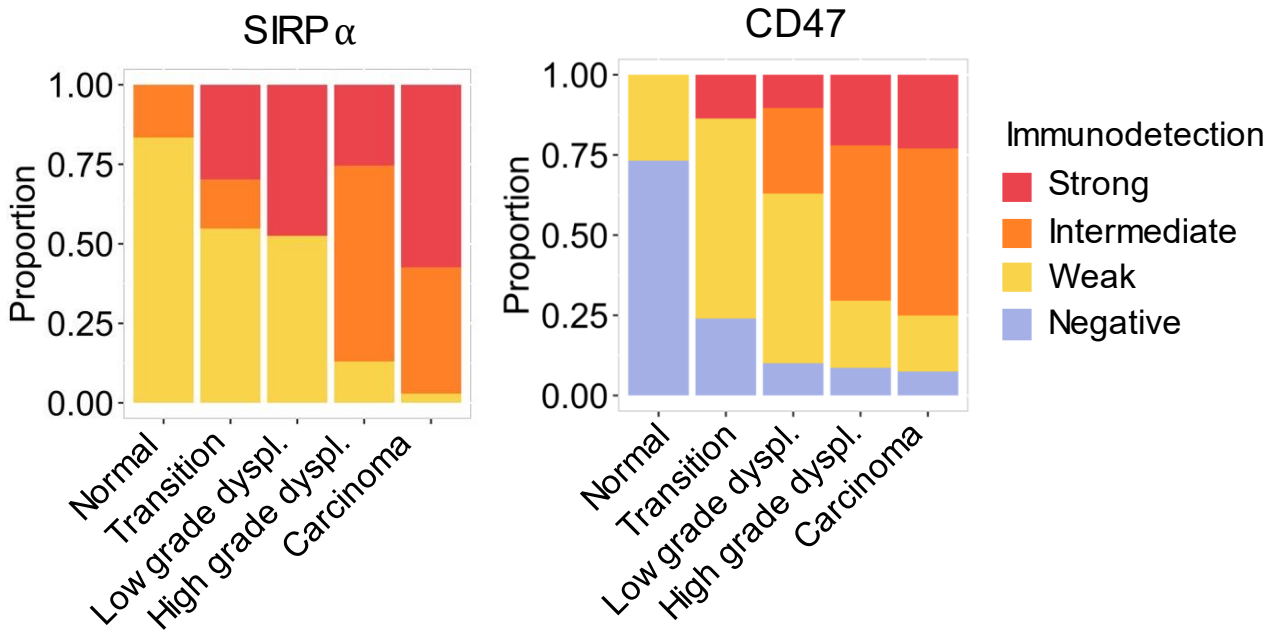
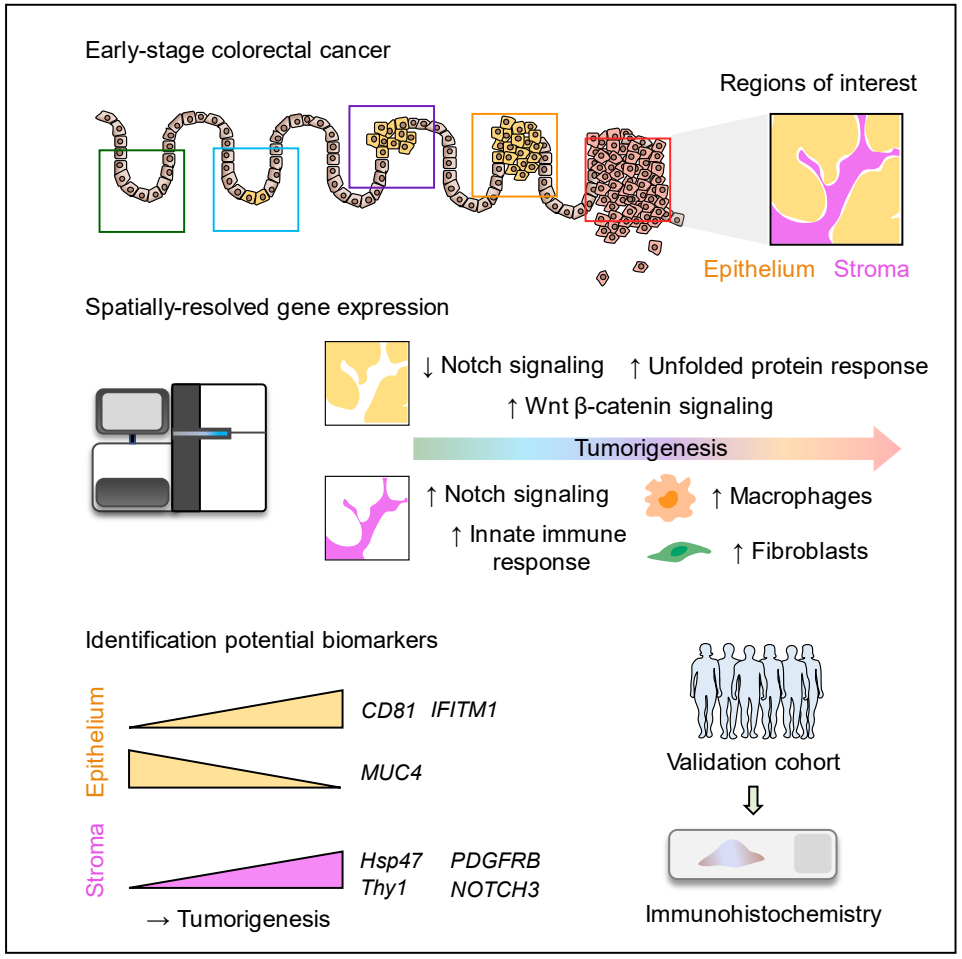
SIRPα-CD47 during step-wise progression of CRC





- Stromal SIRPα expression increases from normal to carcinoma tissue
- Epithelial CD47 expression increases from normal to carcinoma tissue

Data available for further exploration!



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GeoMx Digital Spatial Profiling gene expression data corresponding to manuscript **"Transcriptomic and immunophenotypic profiling reveals molecular and immunological hallmarks of colorectal cancer tumorigenesis"**.

CATEGORIES

- Tumour immunology
- Oncology and carcinogenesis not elsewhere classified

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