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Subcellular imaging in murine models of metastatic colorectal cancer using a whole transcriptome Spatial Molecular Imaging panel (22,000-plex)

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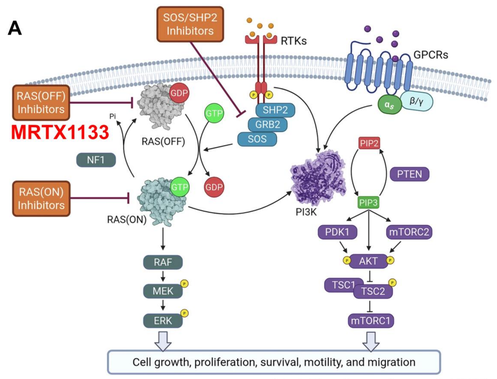
Introduction

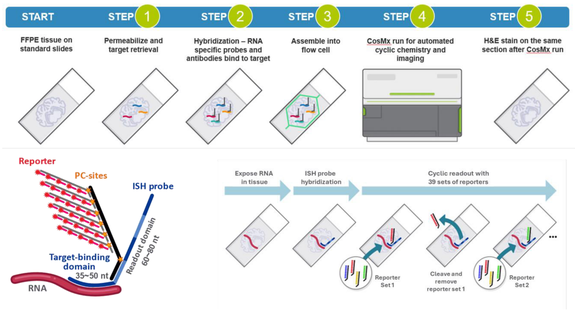
Colorectal cancer is the second leading cause of cancer death in the Western world, and metastatic disease drives most mortality, with only about 5% five-year survival in late-stage patients. KRAS mutations, present in roughly 40% of CRC cases, contribute to resistance to EGFR-targeted therapies and chemotherapy, and KRAS inhibitors have shown more limited benefit in CRC than in cancers like NSCLC due to pathway reactivation and tumor plasticity. Better understanding of treatment response at single-cell and spatial resolution, especially tumor–immune interactions, is therefore critical. To address the lack of high-plex, subcellular spatial tools in mouse models, we developed a mouse Whole Transcriptome assay covering over 22,000 targets for comprehensive spatial profiling and future multiomic studies.

Method

Orthotopic metastatic CRC mouse model treated with either vehicle or KRAS-G12D inhibitor MRTX1133



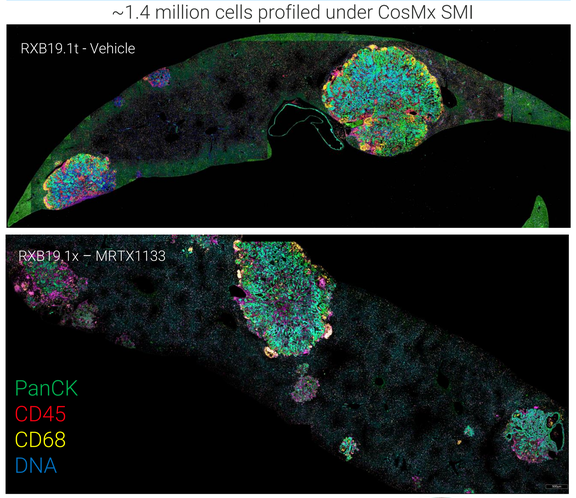
SMI profiling using CosMx Mouse Whole Transcriptome Assay (22,000 plex)

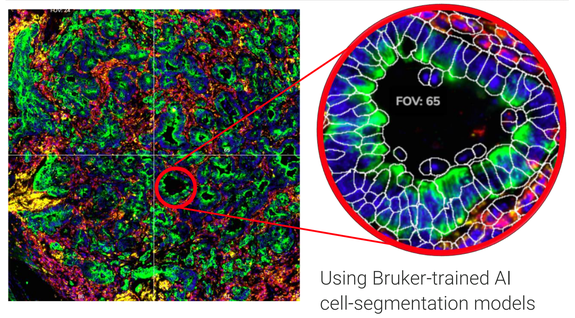


Results

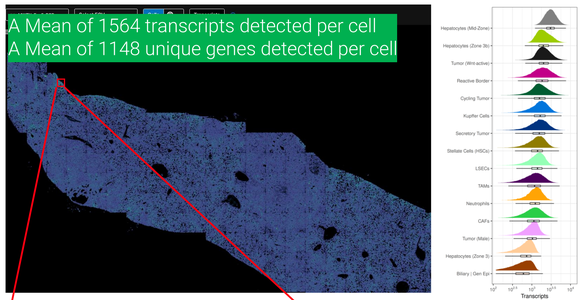
COSMX MOUSE WHOLE TRANSCRIPTOME ASSAY

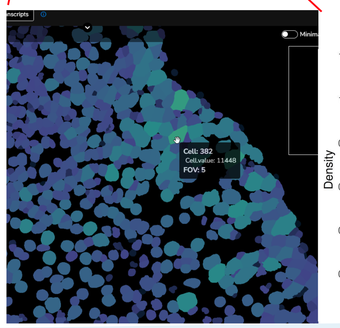
~1.4 million cells profiled under CosMx SMI



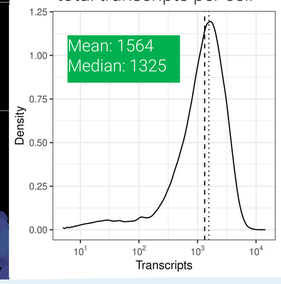


Using Bruker-trained AI cell-segmentation models

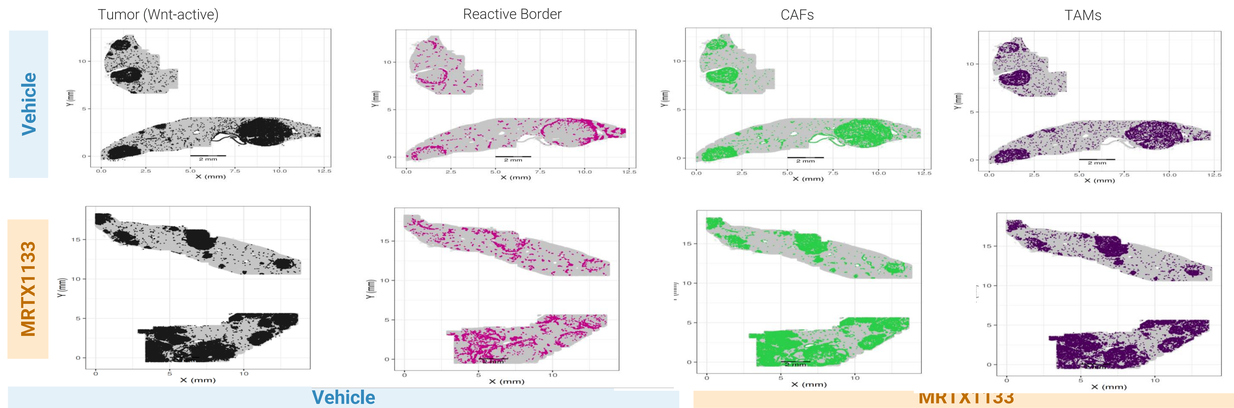




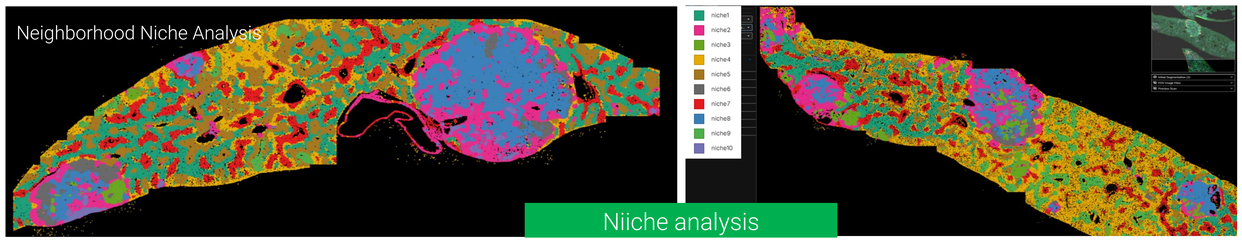
Single-cell distribution of total transcripts per cell

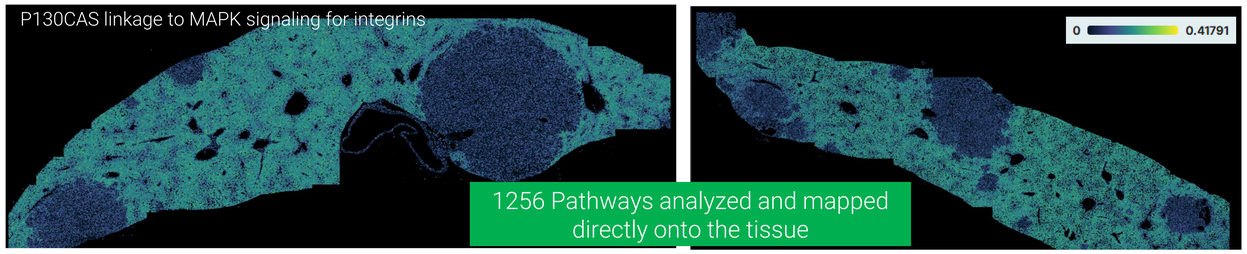


CELL CLUSTERING, NEIGHBORHOOD AND PATHWAY ANALYSIS

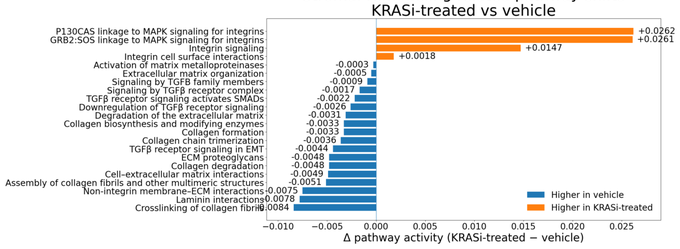


Vehicle — MRTX1133





Stromal-remodeling related pathway shifts KRASi-treated vs vehicle



Conclusion

CosMx WTX spatial profiling of Mouse CRC liver metastases provides whole-transcriptome single-cell data across entire tissue. Cell clustering, neighborhood analysis and pathway analysis suggested stromal remodeling as an early feature of the treatment response.