99 SPATIAL INSIGHTS INTO TUMOR IMMUNE EVASION ILLUMINATED WITH THE COSMX™ SPATIAL MOLECULAR IMAGER PLATFORM

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Background Patient response to immunotherapy has been revolutionary but remains limited due to the inability to convert excluded or cold tumors into ones which would be permissive to therapeutic intervention. To treat patients that evade immune therapy, comprehensive understanding of their tumor microenvironment (TME) is needed. To date, most profiling efforts have lacked the ability to capture high-plex 'omics data while retaining the spatial architecture of the TME. We developed the CosMx™ Spatial Molecular Imager for analyzing formalin-fixed paraffin-embedded (FFPE) or fresh-frozen (FF) tissue and capturing the expression of over 1000 RNA targets simultaneously with subcellular resolution from a single histopathology slide.

Methods We profiled a cohort of 10 patient samples with CosMx using the Human Universal Cell Characterization Panel across a range of solid tumors. This cohort represents a diverse array of patients which include both infiltrated and excluded tumors. We included technical replicates for 5 of the samples to better understand reproducibility of the assay. We were able to characterize over 1.8 million cells, and detected on average over 80% of the panel per patient and assigning more than 95% of the transcripts profiled to unique cells across these samples.

Results We were able to robustly identify more than 20 cell types by integrating our data with previous single-cell sequencing projects from the human cell atlas. We demonstrate robust delineation of critical immune cell populations from across lymphoid and myeloid lineages, as well as stromal cell populations, including cell types frequently missed using dissociated cell sequencing, such as vascular endothelium associated with immune cell migration into the tumor bed. We leveraged 450 + genes from our panel dedicated to cell lineage, cell-cell interaction, and ligand-receptor signaling to identify unique interactions happening at different scales between the tumor and the TME. These include evidence of direct inhibition of T-cell function through the PDL1 axis between tumor, and tumor intrinsic and extrinsic interactions that mediate tissue architecture and T-cell exclusion.

Conclusions The CosMx platform for profiling tissue allows for robust resolution of critical immunogenic signaling cascades and cellular interactions that are necessary to truly understand the tumor architecture. By maintaining the tissue structure, we can directly measure cellular interactions and capture cells commonly missed during dissociative studies. With this new platform, we are better poised than ever to truly understand the molecular mechanisms which drive tumor response to intervention.

FOR RESEARCH USE ONLY Not for use in diagnostic procedures.

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0099