EVALUATING DIVERSE DECONVOLUTION METHODS FOR TUMOR SPATIAL TRANSCRIPTOMIC DATASETS

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Background Spatial transcriptomics technology may improve our ability to understand the organization of tumor microenvironment (TME) and uncover the recurrent interaction patterns across diverse cell types. While naturally complementing traditional scRNA-Seq, recent popular spatial platforms (such as 10x visium) fail to achieve single-cell resolution and require deconvolution methods to calculate the underlying cell type distributions. There are dozens of spatial deconvolution methods whereas systematic benchmarks comparing the methods are lacking.

Methods Here we present a comprehensive evaluation of 3 widely-used and top-performing deconvolution methods, DeconRNASeq, CARD, Cell2location, as well as 3 label transfer methods that assign a single cell type to one spot. We benchmarked these tools in four publicly available human breast cancer datasets by measuring the correspondence (spearmanr, pearsonr and F1-score) between inferred cell type proportions and normalized expressions of canonical marker genes at each spatial spot.

Results Cell2location consistently performs best. We further showed deconvolution methods that are particular designed for spatial context (CARD, Cell2location) achieved significantly better results compared to bulk deconvolution (DeconRNASeq) and label transfer methods (ingest, Seurat, Scanorama), suggesting the explicit modeling of spatial correlations and consideration of technical artifacts between sequencing technologies are crucial. Furthermore, when pairing with clinically unmatched scRNA reference, the deconvolution performance is largely on par with the available matched reference for non-tumor cells, indicating that publicly available scRNA data can serve as reference for spatial deconvolution.

Conclusions Taken together, our study suggests that methods such as Cell2location with either matched or unmatched references will give actionable deconvolution in spatial studies in tumor tissues.