Spatial Proteomics and Transcriptomics using GeoMx Digital Spatial Profiling

M. Eyres and G. Marshall: Medicines Discovery Catapult, Alderley Park, Cheshire, SK10 4ZF, UK.

md.catapult.org.uk

1 Digital Spatial Profiling

Traditional analysis of FFPE tissue is often hampered by either low throughput (IHC, IF) or destruction of spatial information (RNA-seq, nCounter). The NanoString GeoMx Digital Spatial Profiler (DSP) allows for both of these aspects to be maintained by remaining high plex (up to 80-plex proteomics and whole genome transcriptomics) while still maintaining spatial complexity using only a single 5µm tissue section.

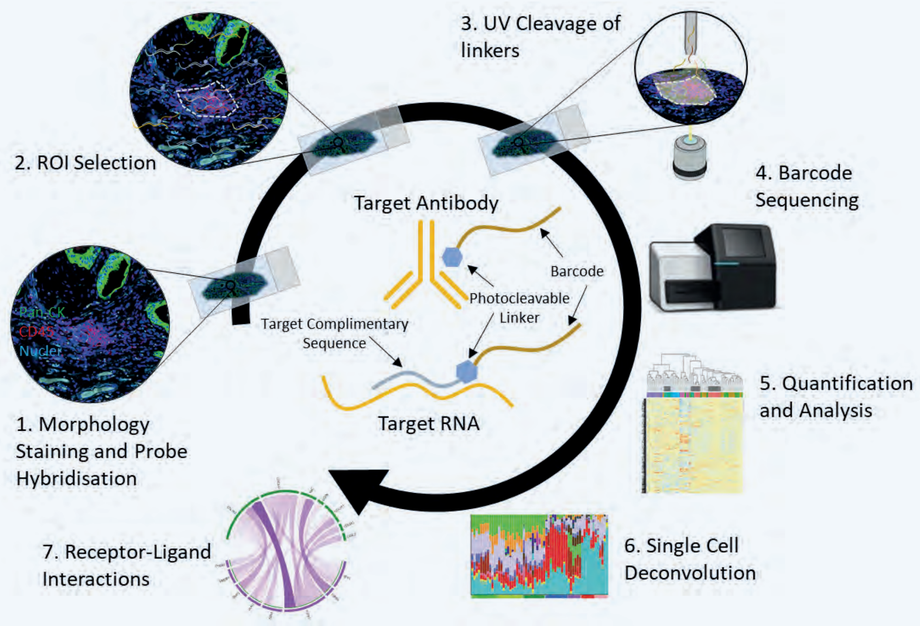

Figure 1: DSP experimental setup. The panel is incubated on FFPE tissue sections. Regions of interest (ROIs) are selected and exposed to UV light. Cleaved barcodes are then collected and sequenced.

2 High-Plex Spatial Proteomics

DSP Proteomics assays use a panel of 20-80 different antibodies focussed on a specific field of interest. For each region of interest (ROI) selected, a quantitative count for each marker in the panel is determined.

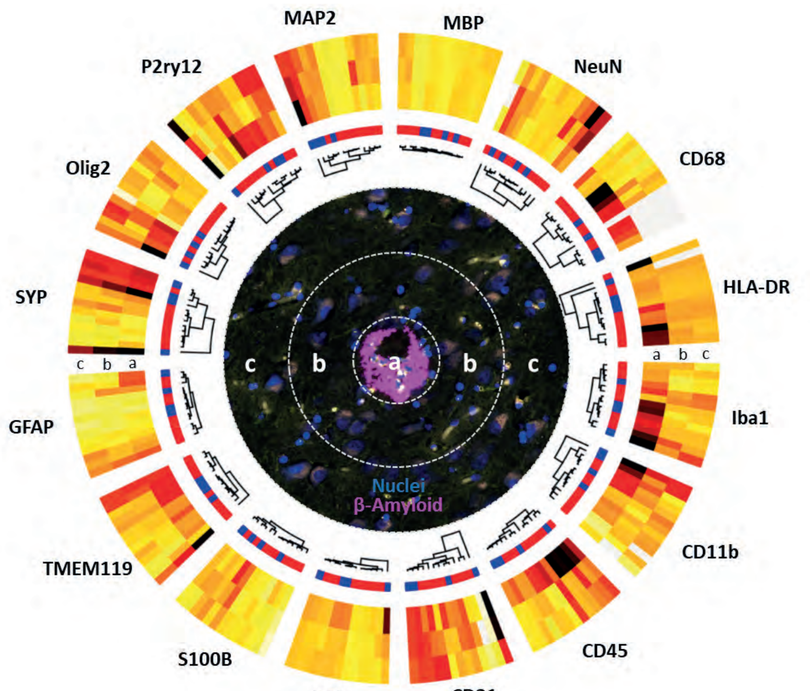

Figure 2: Spatial proteomics in sections of brain from Alzheimer's patients'. ROIs were selected around plaque regions. The inner row of each heatmap corresponds to the central ROI within the plaque region.

3 Spatial Transcriptomics

RNA assays can cover a set of cancer specific genes (~1,600 RNAs) or the whole transcriptome (~18,000 RNAs). The DSP is non-destructive so tissue sections can still be used for downstream histological analysis such as H&E.

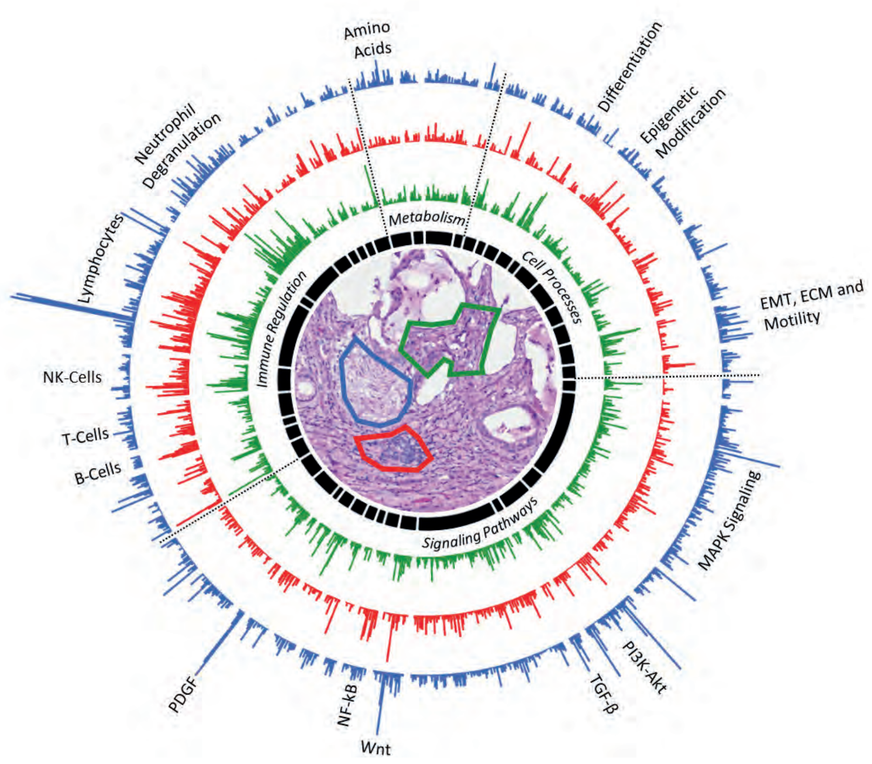

Figure 3: 1,600-plex Spatial transcriptomics in human lung tissue. ROIs were selected at **alveolar**, **immune** and **fibrotic** regions. The circular plot shows the average change in counts in each region. Each gene is ordered into its respective signalling pathway, cell type or cell process.

4 Downstream Analysis

Downstream analysis of transcriptomic data includes spatial deconvolution of individual cell types using single cell RNA-seq datasets and prediction of Receptor-Ligand interactions.

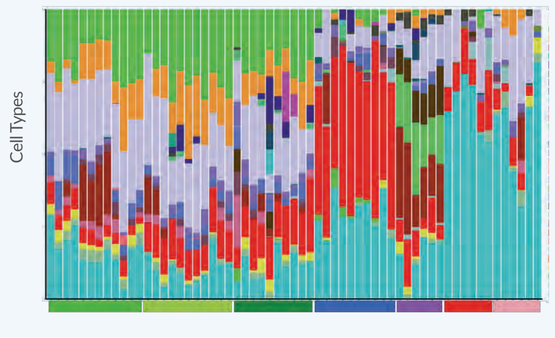

Figure 4: Spatial deconvolution of cell types within ROIs from human lung tissue using publicly available single-cell RNA-seq datasets. Abundance of each cell type is determined in each ROI.

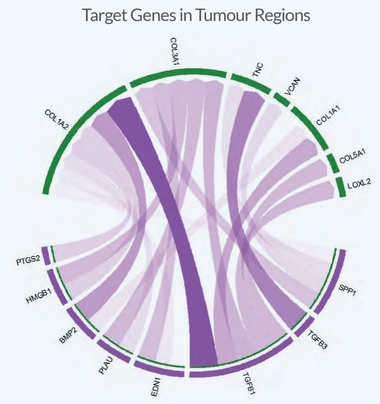

Figure 5: Predicting Receptor-Ligand interaction between adjacent regions. Ligand-Receptor pairs that are expressed in sender and receiver regions can be determined, as well as which of these interactions could induce the expression of a set of target genes in the receiver regions.

Digital spatial profiling represents a technological leap forward; enabling investigation of high-plex, quantitative, spatial proteomics and transcriptomics using FFPE tissues.

Innovate UK