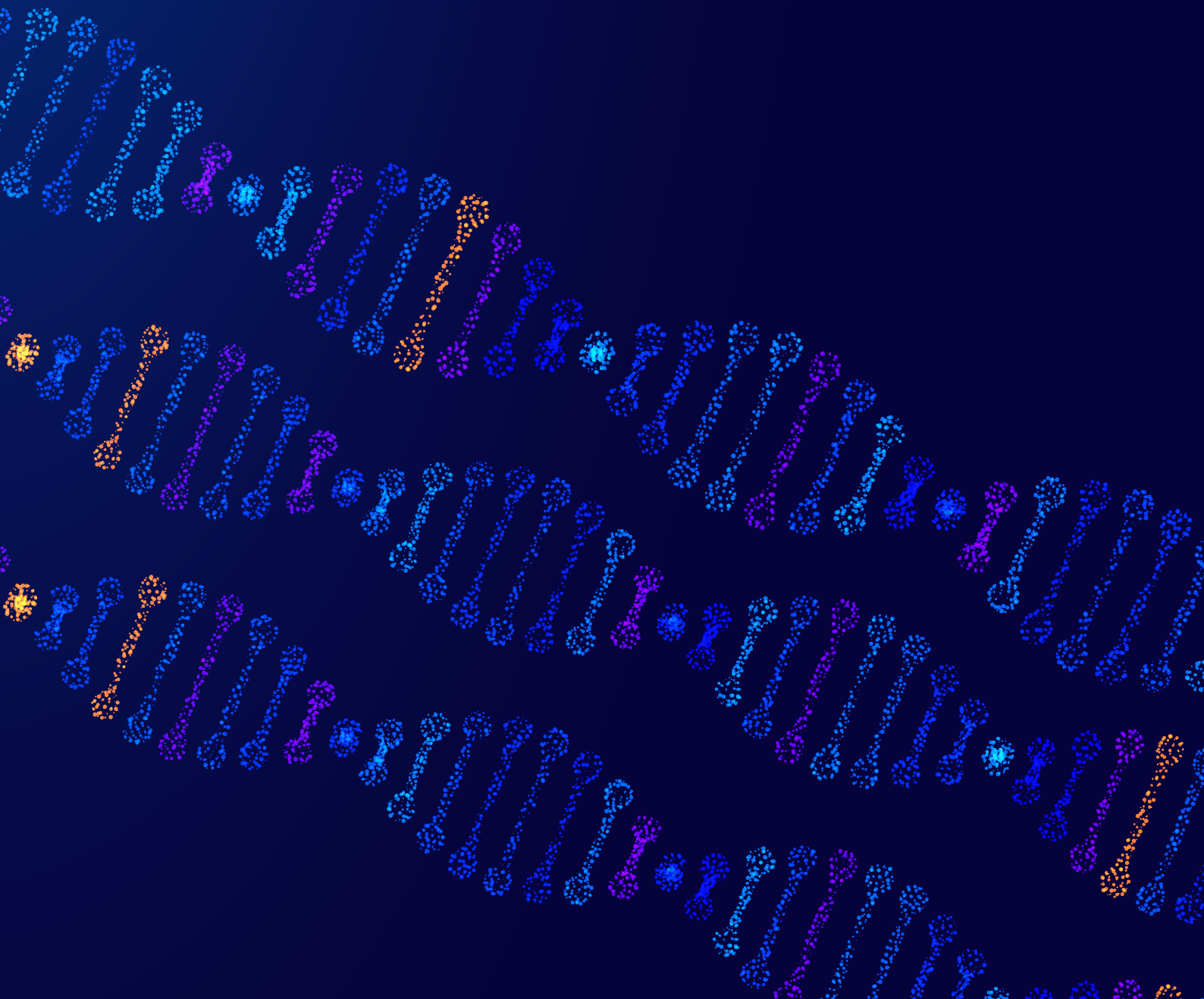
excelra

Advanced Target Profiling in Cancer

A Spatial and Single-Cell Transcriptomics Approach

CASE STUDY



CLIENT'S CHALLENGE AND GOAL

The main aim of the project was to perform Target profiling in cancer samples using relevant spatial transcriptomics and scRNA-seq datasets to understand the potential impact of their Target of interest in the tumor microenvironment (TME). The objective started with mining of the appropriate datasets from public sources across the selected cancer types and then analyze them to understand the potential impact of the target onto neighbouring cells in selected human cancers. Here, the spatial transcriptomics came very handy as it allowed us to perform the comparitive study even between different regions of interests due to high/low target gene expression.

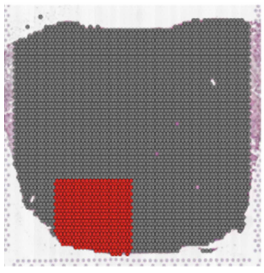
OUR CLIENT

A biotech company developing innovative immunotherapies for cancer patients

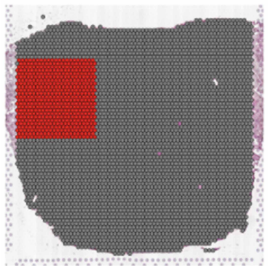
OUR APPROACH

It all started with identifying relevant single cell as well as spatial omics datasets for the given cancer sub-types having sample count enough to provide statistically significant results. Cell annotation of scRNA-seq datasets were completed, we performed correlation analysis of cell type abundances with the gene expression of a target to identify statistically significant correlations across contexts. Correlation analysis revealed if the association of target gene expression was correlated with the immune cell abundances in the TME or not. Increased correlation of target expression with immune cell abundances indicate potential association of that gene in TME processes and remodeling.

To understand the impact of a target on gene expression of neighboring cells, we utilized an ROI (Region of interest) approach to perform within-ROI and across-ROI comparisons involving spatial transcriptomics datasets. Within ROI approach included comparing high-target versus low-target gene expression within a selected ROI for all the cell-types across every tissue slice. For across-ROI comparisons, we selected an ROI with high-target expression and compared that with low-target expressing ROI region across cell-types of every tissue slice. These comparisons yielded DEGs for every cell-type within and across the ROI regions for every cancer or control tissue slice. We compared the within-ROI and across-ROI results to identify DEGs obtained with both approaches. Such comparative analysis helped us understand the effect of Target on the neighbouring cells within TME at the cell type as well as Molecular signature level. Finally, we further classified the DEGs obtained from within-ROI and across-ROI comparisons to identify differentially expressed cytokines within metadata groupings.



Highlights
- Group 1
- Unselected

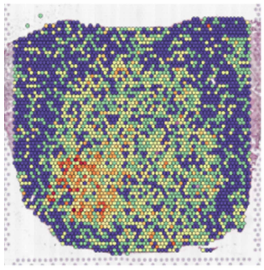


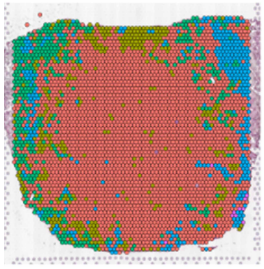
Highlights
- Group 1
- Unselected

High expression ROI

ROI-level comparison
Within ROI and across ROI comparisons (high vs. low) were carried out to understand the effect of target gene expression in every cell-type on neighbouring cells

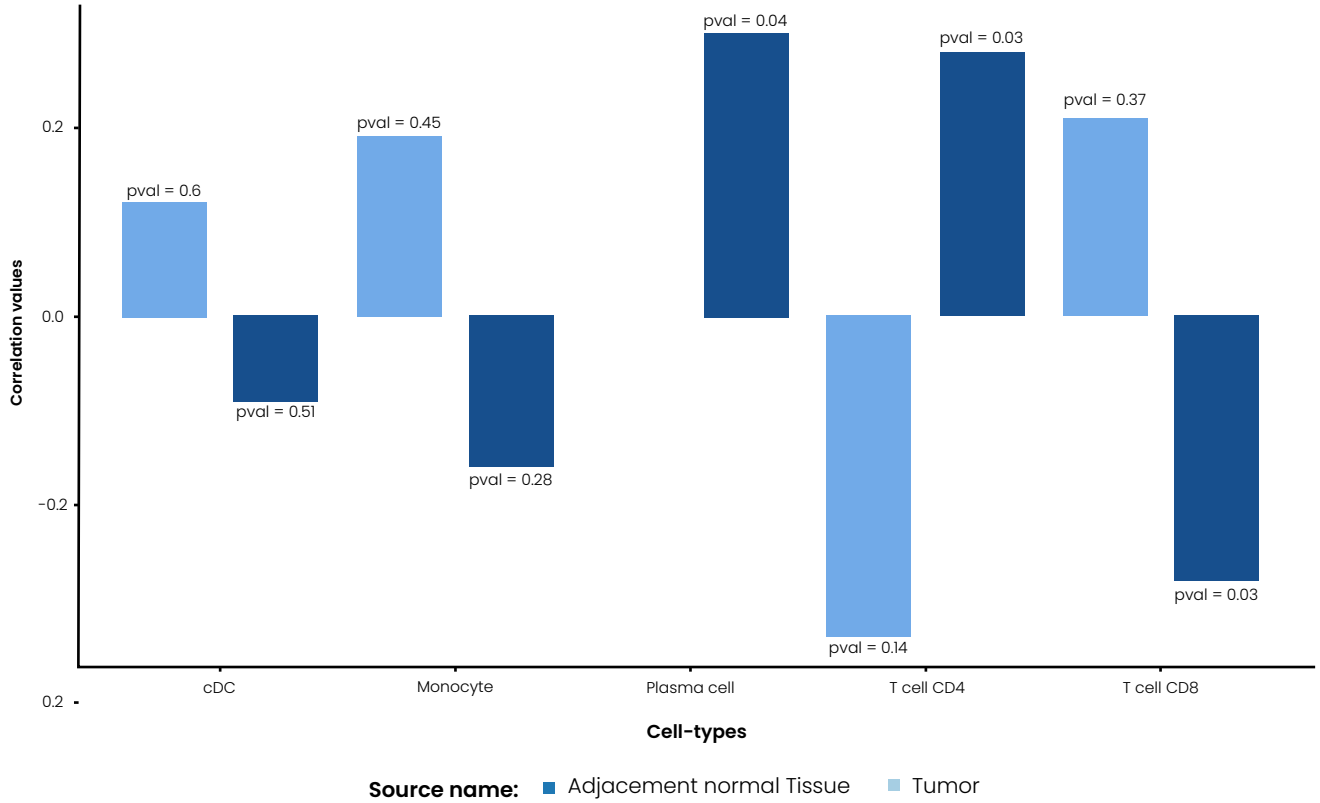
Gene1



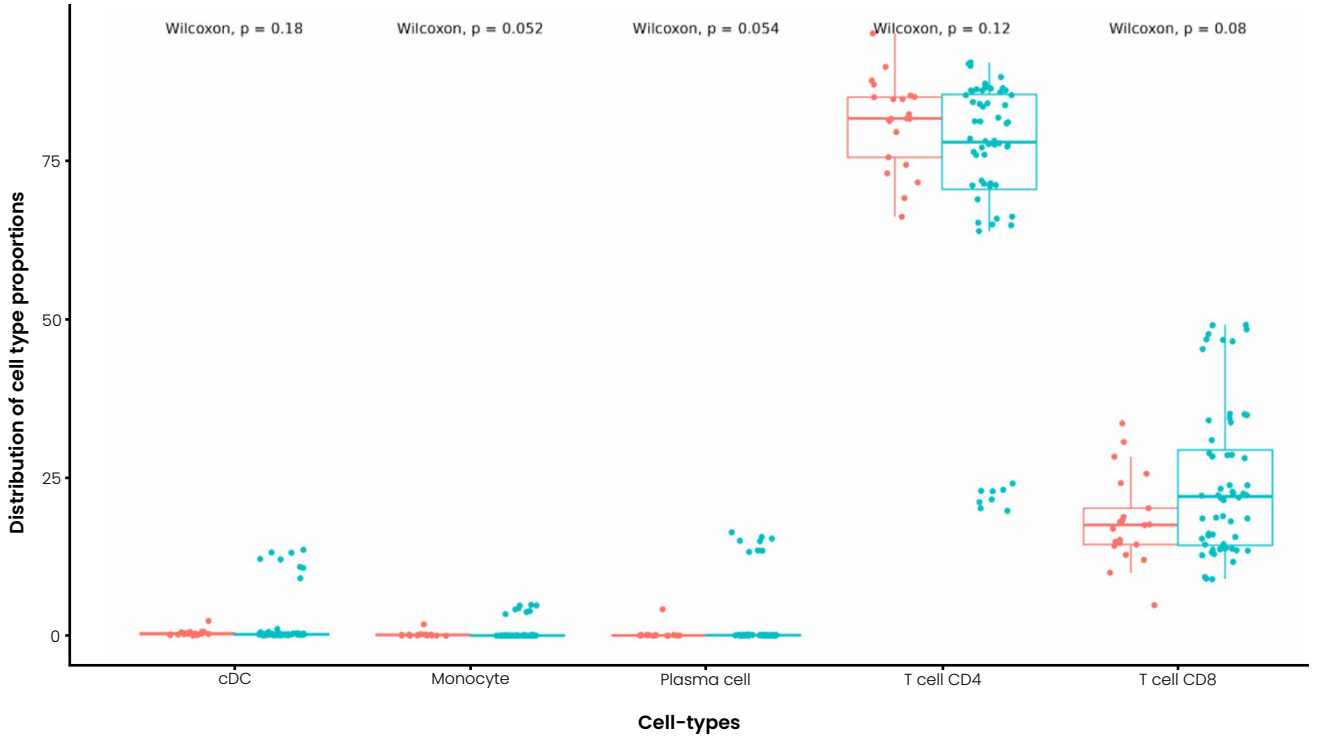


Ident
- Epithelial cells
- Myeloid cells
- Endothelial cells
- Fibroblasts
- B cells

Correlation of target gene expression with cell-type abundances across normal and tumor



Distribution of cell type proportions across samples



OUR SOLUTION

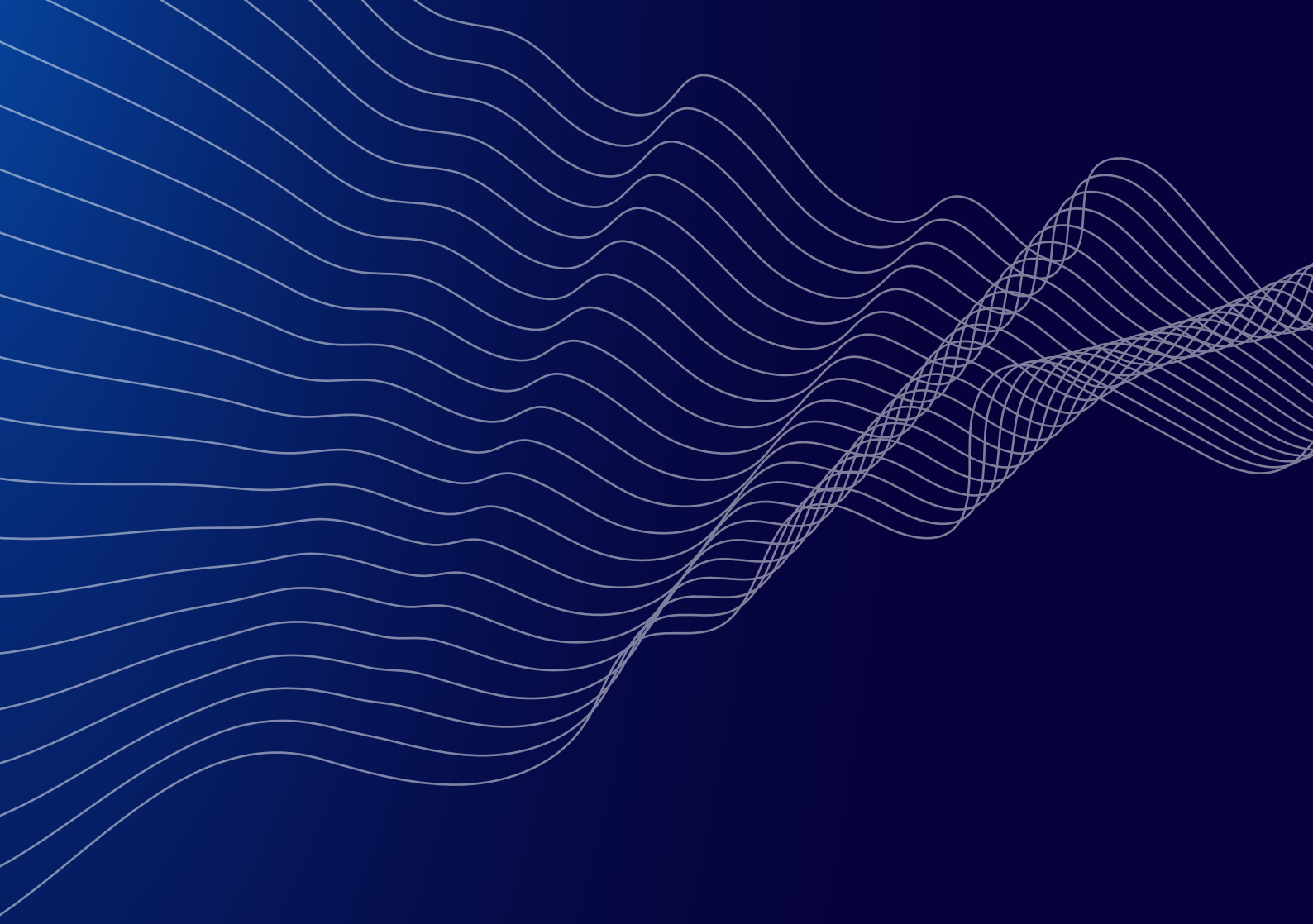
The client engaged Excelra to perform analysis of publicly available spatial and scRNA-seq datasets. For this, Excelra first mined available scRNA-seq and spatial transcriptomics datasets and performed metadata curation for the selected datasets. Then, Excelra performed the basic processing of these datasets using the in-house workflows and identified the cell-type(s) where the gene expression of the target was the highest. The client also made use of our product Single Cell Browser to further explore the processed scRNA-seq datasets.

Spatial transcriptomics offers an unbiased way to obtain gene expression information at cellular resolution in the tissue context. Despite the unavailability of knockdown/ knockout cellular models available for the target, we used a novel ROI approach to characterize the role of the target in the spatial transcriptomics datasets across contexts. These comparisons yielded common and specific transcriptomics features consistent across different control and cancer tissue sections.

CONCLUSION

We included a novel approach using ROI to understand the role of the target even without the availability of knockout/knockdown cellular models. Through an indirect approach, we obtained the gene and cytokine expression differences between high-target and low-target ROIs as well as within ROIs across multiple cancer contexts.

In summary, spatial transcriptomics allows us to understand the impact of potential targets in space.



Where data means more

excelra

SAN FRANCISCO • BOSTON • LONDON • GHENT/GENT • UTRECHT • HYDERABAD

Connect with our experts: marketing@excelra.com

www.excelra.com