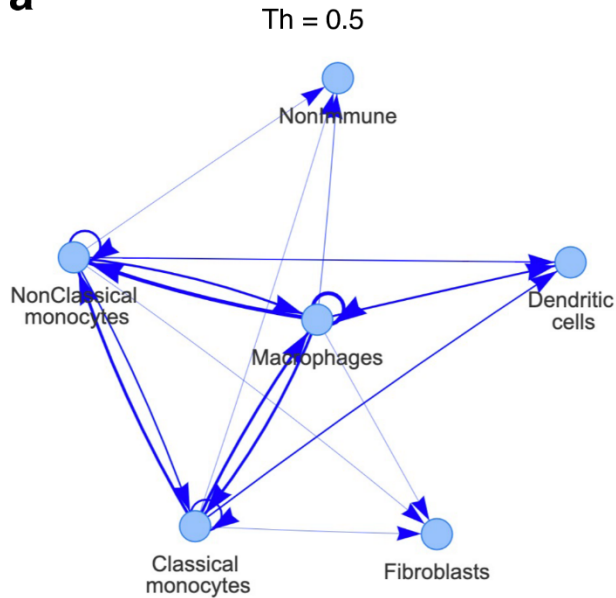


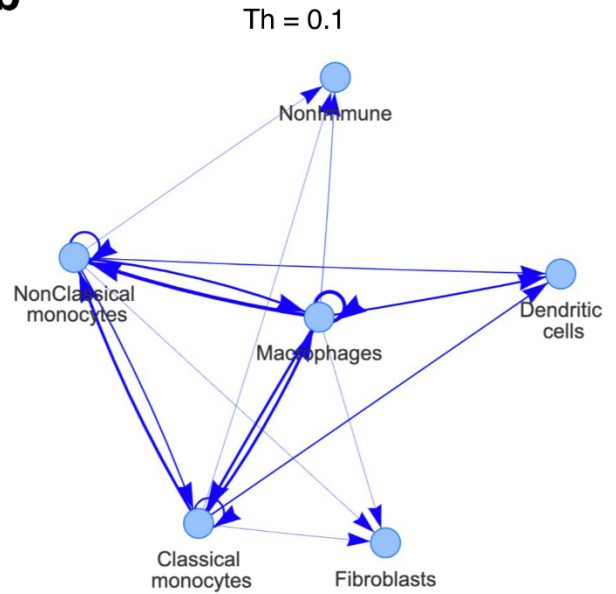
Supplementary Material

DiSiR interaction graphs for S100A8/A9 (calprotectin) pathway
across different thresholds

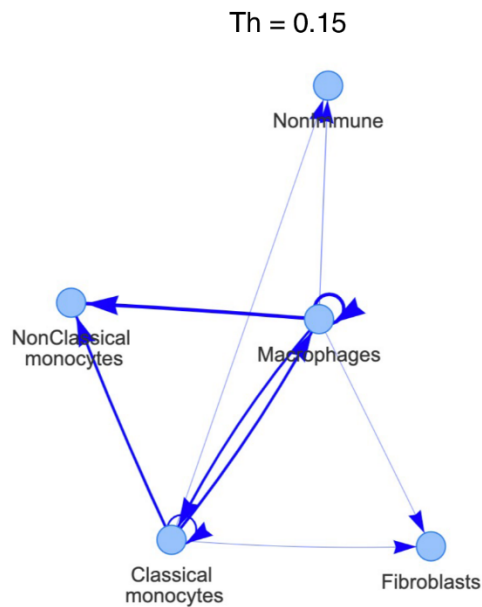
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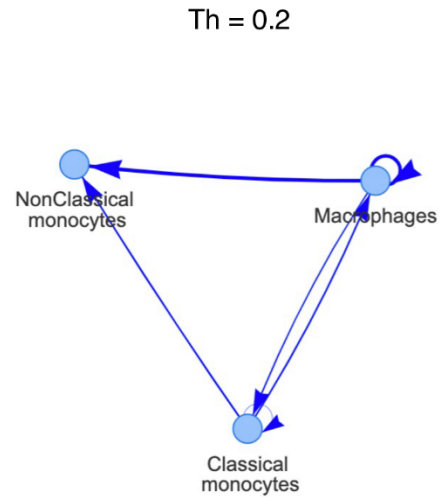
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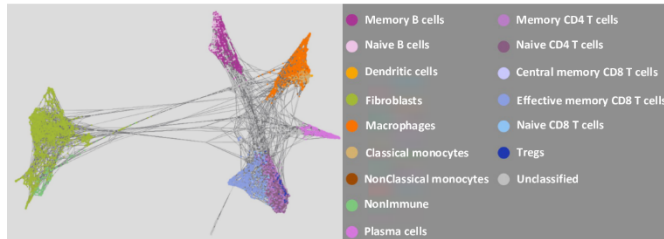
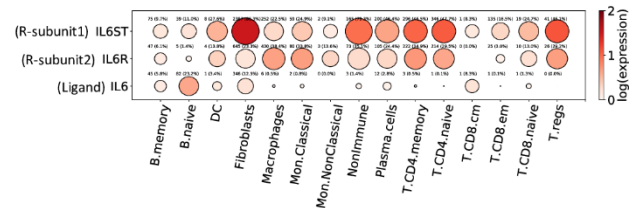
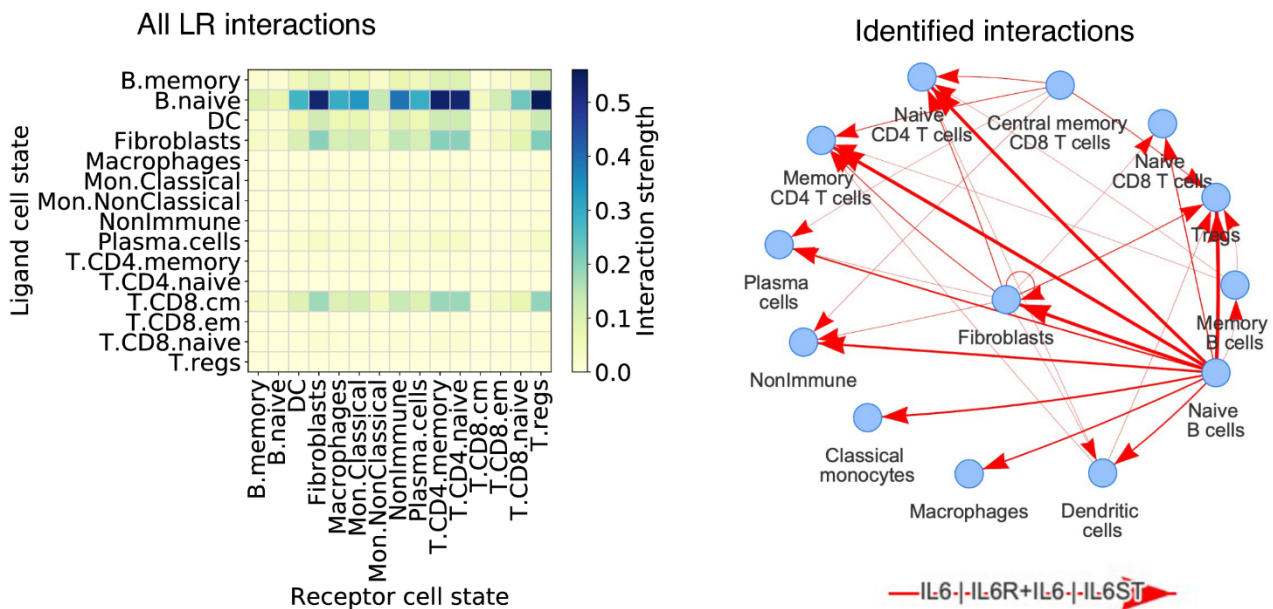
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d

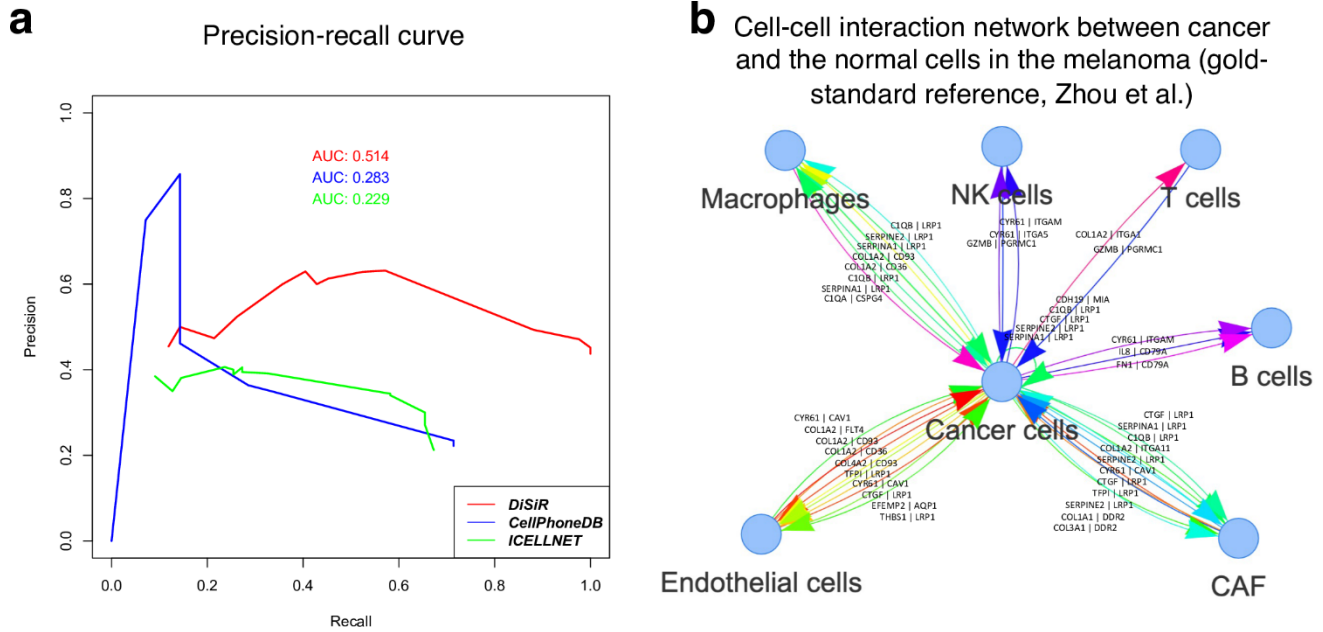


S1 Fig. DiSiR interaction graphs for S100A8/A9 (calprotectin) pathway in RA data across different thresholds: (a) $Th = 0.05$, (b) $Th = 0.1$, (c) $Th = 0.15$ and (d) $Th = 0.2$.

a RA Synovium scRNA-seq data**b** Ligand and multi-subunit receptor expressions per cell type**c** DiSiR results for IL6 pathway analysis applied on RA Synovium scRNA-seq data**S2 Fig. Analysis of IL6 signaling pathways at cell type level from RA Synovium scRNA-seq**

data. (a) UMAP representation of RA Synovium scRNA-seq data and corresponding cell type label assigned to each cell. **(b)** Circle plot illustrating max-normalized average expressions of calprotectin signaling pathway components including ligand ILR and receptor subunits, IL6R and IL6ST, per cell type (color of the circles) and fraction of cells expressing them within its corresponding cell type (size of the circles). **(c)** Left side figure is the heatmap depicting all cell-cell communication through IL6|IL6R + IL6|IL6ST interactions (when both interactions are presented). The colormap shows the strength of interaction between two cell types. The right side graph shows the significant IL6-IL6R

and IL6- IL6ST interactions between different cell types identified by DiSiR. The thickness of the graph edges corresponds to the interaction strength.



S3 Fig. Technical assessment of DiSiR using a gold-standard melanoma cellular network based on precision-recall curve. (a) Recall and precision, across different threshold values, are defined in relation to positive and negative groups for DiSiR, CellPhoneDB and ICELLNET (AUC, area under the curve). Best precision in DiSiR is obtained for $Th = 0$ (optimal threshold value) **(b)** Cell-cell interaction network between cancer and normal cells in the melanoma (our gold-standard reference) extracted in [26].