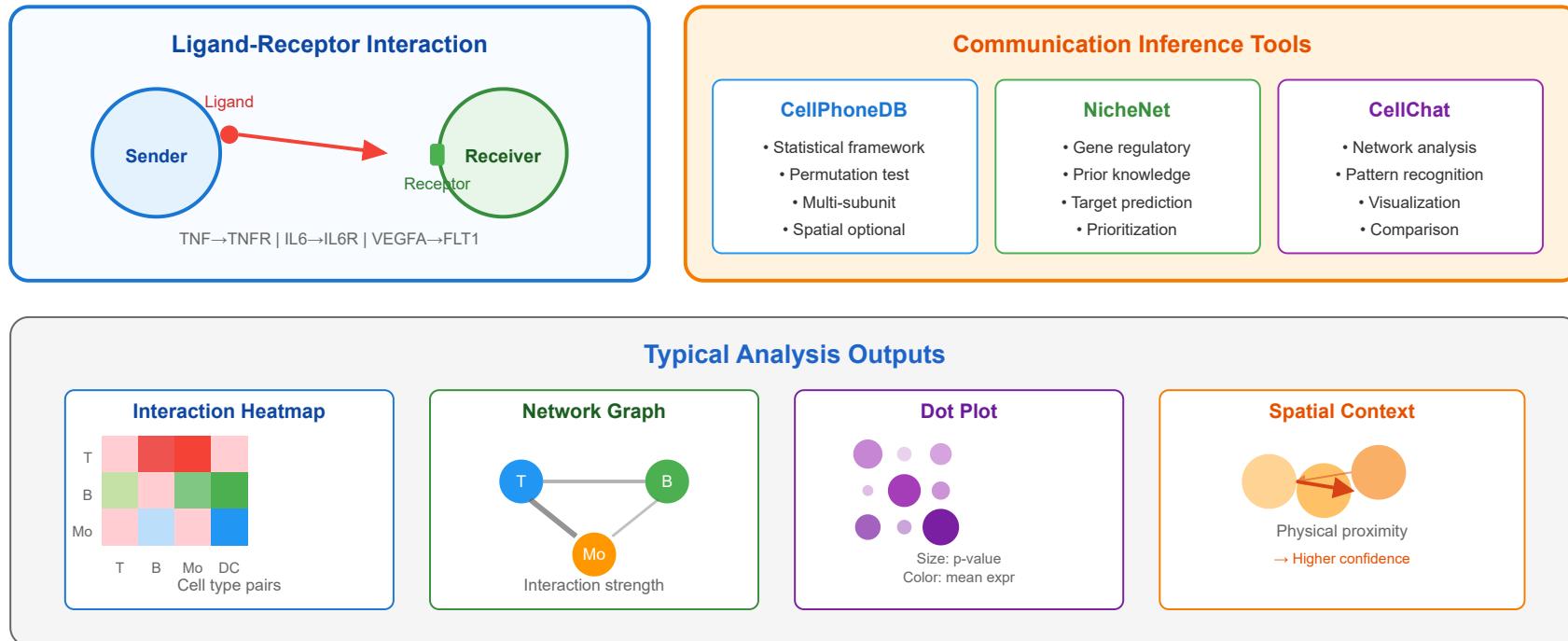


Cell-Cell Communication

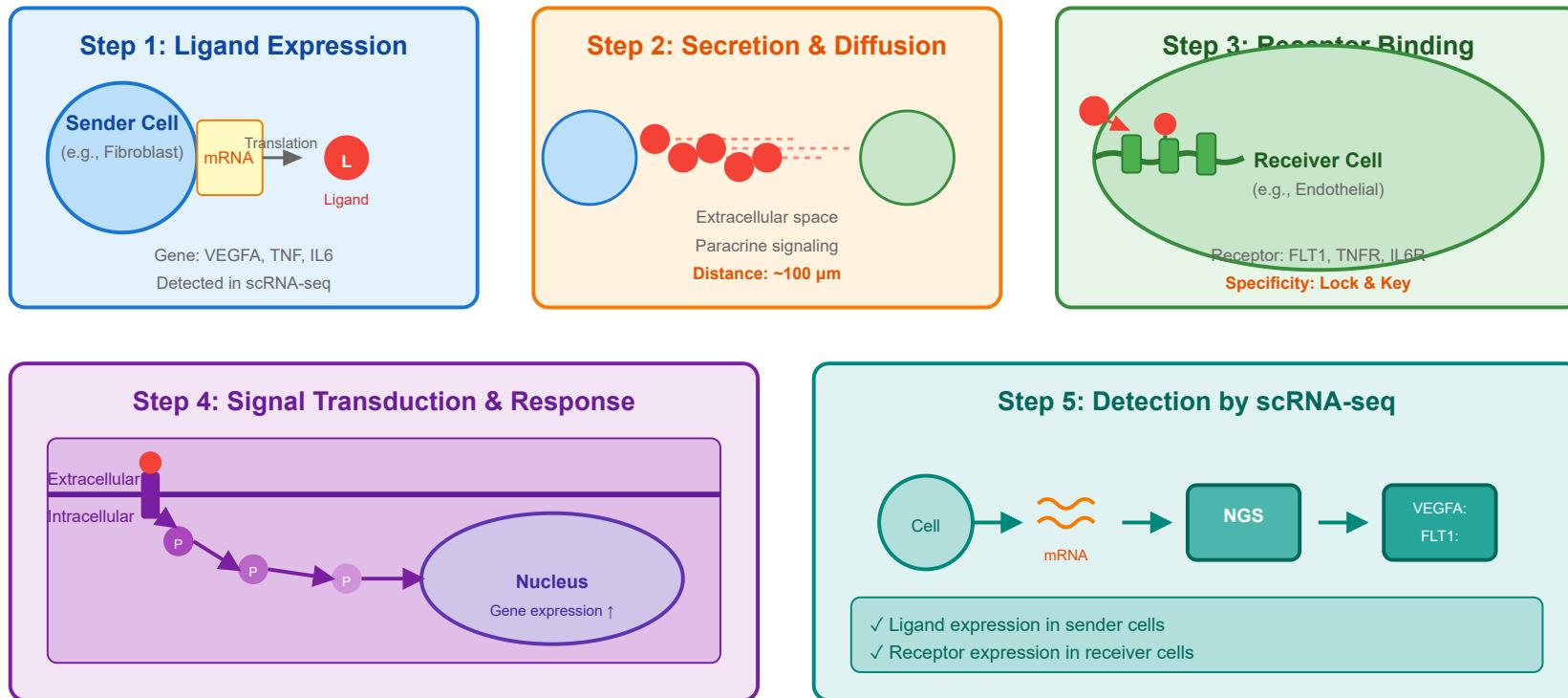
Inferring Cell-Cell Interactions from scRNA-seq



Infer cellular communication from expression patterns

Detailed Mechanism of Ligand-Receptor Interaction

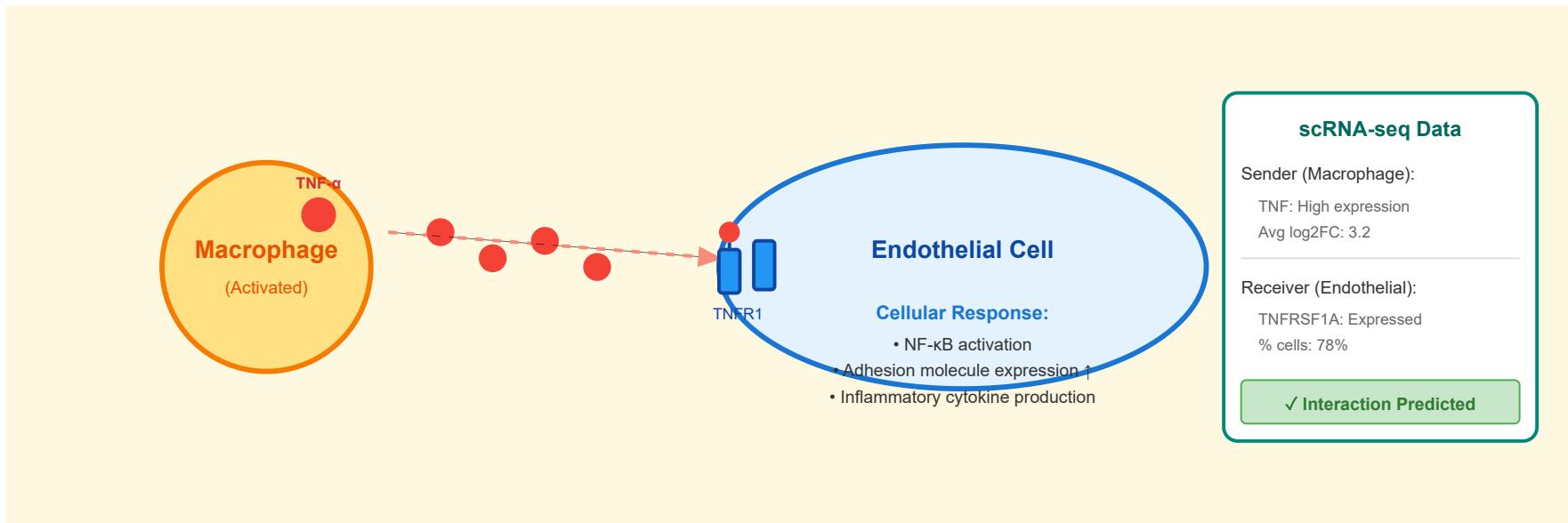
Step-by-Step Communication Process



From gene expression to cellular response: A complete signaling cascade

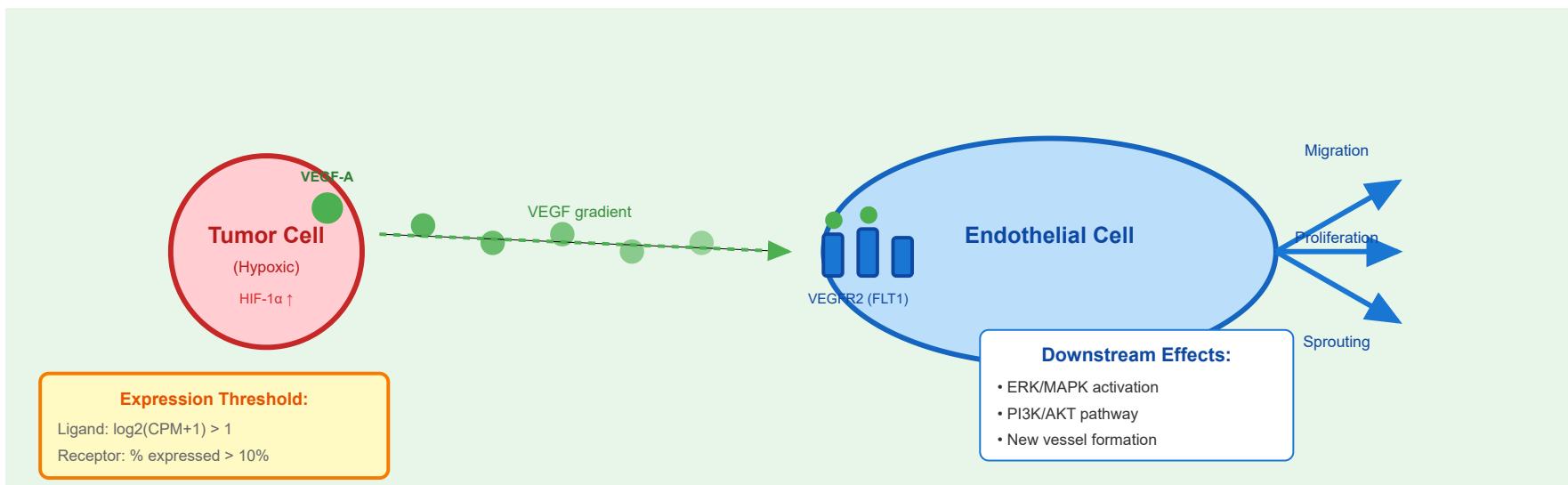
Real-World Examples of Cell-Cell Communication

Example 1: Immune Response - TNF Signaling



Biological Context: During inflammation, activated macrophages secrete TNF- α , which binds to TNFR1 on endothelial cells. This triggers the expression of adhesion molecules (ICAM-1, VCAM-1), facilitating leukocyte recruitment to inflamed tissues. This is a classic example of paracrine signaling in immune responses.

Example 2: Angiogenesis - VEGF Signaling

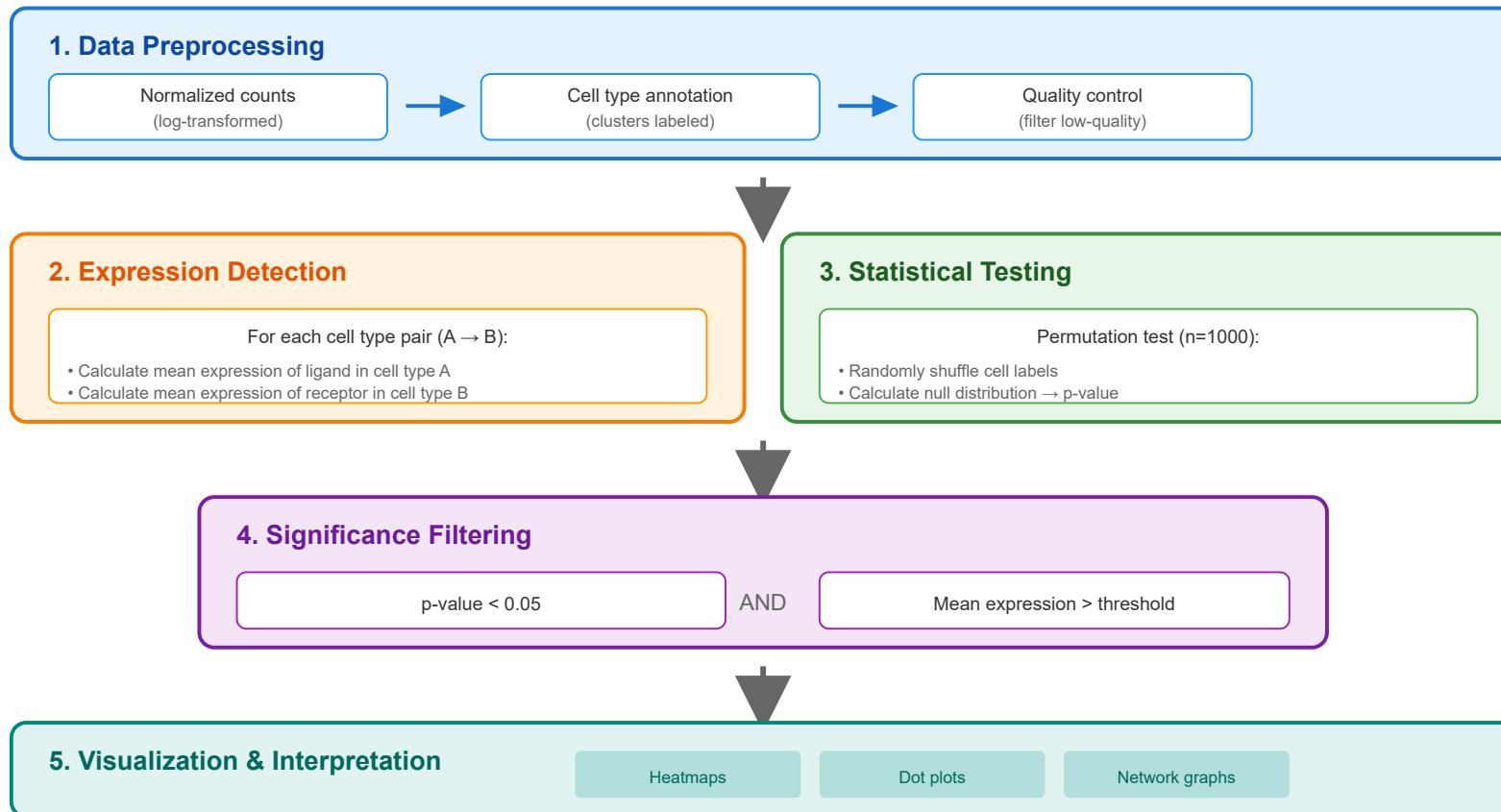


Biological Context: In hypoxic tumor microenvironments, tumor cells upregulate VEGF-A through HIF-1 α . VEGF-A binds to VEGFR2 (KDR/FLK1) on endothelial cells, promoting angiogenesis. scRNA-seq can detect this interaction and help identify pro-angiogenic cell populations, making it valuable for cancer research and anti-angiogenic therapy development.

Computational Analysis Workflow

Step-by-Step Analysis Pipeline

CellPhoneDB Analysis Pipeline



Key Parameters

- **Expression threshold:** Minimum expression level (e.g., $\log_2(\text{CPM}+1) > 0.1$)
- **Percentage threshold:** Min % of cells expressing (e.g., >10%)
- **p-value cutoff:** Significance level (typically 0.05)
- **Permutations:** Number of randomizations (usually 1000)

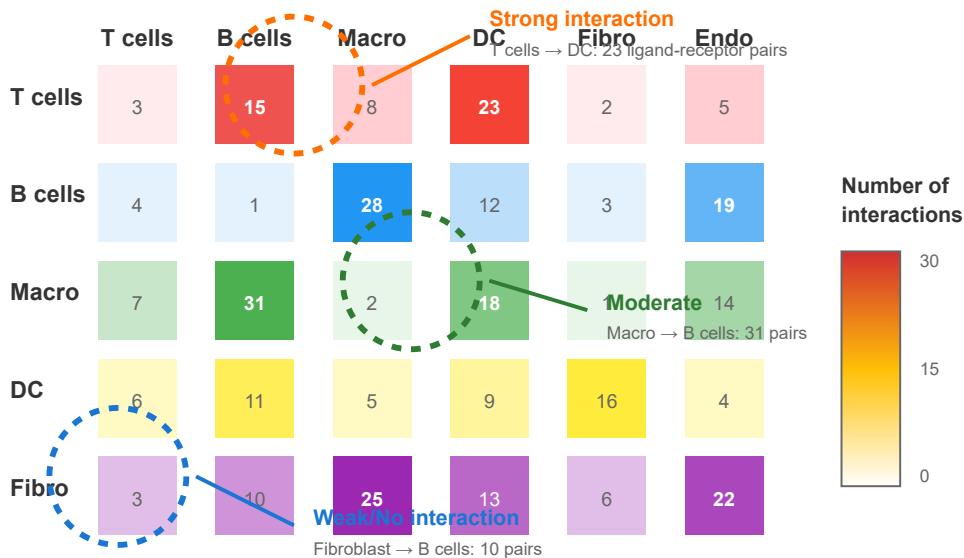
Output Interpretation

- **Mean values:** Average expression of ligand and receptor
- **p-value:** Statistical significance of interaction
- **Interaction score:** Combined metric of expression and significance
- **Specificity:** How unique the interaction is to cell type pair

Interpreting Analysis Results

Understanding Heatmap Outputs

Example: Interaction Heatmap



Key Interpretation Points:

- Diagonal patterns:** Autocrine signaling (cells talking to themselves)
- Off-diagonal hotspots:** Strong paracrine interactions between different cell types
- Asymmetry:** Direction matters – A→B may differ from B→A (different ligands/receptors)
- Biological validation:** Always validate computationally predicted interactions with literature or experiments
- Spatial context:** Physical proximity increases confidence in predicted interactions

Common Pitfalls to Avoid:

- Don't assume all significant interactions are biologically relevant
- Consider expression thresholds carefully – too low leads to false positives
- Check for batch effects that might create artificial cell-cell communication signals

- Remember that correlation doesn't imply causation – experimental validation is essential