World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:16, No:02, 2022

Incorporating Spatial Transcriptome Data into Ligand-Receptor Analyses to Discover Regional Activation in Cells

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Abstract : Interactions between receptors and ligands are crucial for many essential biological processes, including neurotransmission and metabolism. Ligand-receptor analyses that examine cell behavior and interactions often utilize cell type-specific RNA expressions from single-cell RNA sequencing (scRNA-seq) data. Using CellPhoneDB, a public repository consisting of ligands, receptors, and ligand-receptor interactions, the cell-cell interactions were explored in a specific scRNA-seq dataset from kidney tissue and portrayed the results with dot plots and heat maps. Depending on the type of cell, each ligand-receptor pair was aligned with the interacting cell type and calculated the positori probabilities of these associations, with corresponding P values reflecting average expression values between the triads and their significance. Using single-cell data (sample kidney cell references), genes in the dataset were cross-referenced with ones in the existing CellPhoneDB dataset. For example, a gene such as Pleiotrophin (PTN) present in the single-cell data also needed to be present in the CellPhoneDB dataset. Using the single-cell transcriptomics data via slide-seq and reference data, the CellPhoneDB program defines cell types and plots them in different formats, with the two main ones being dot plots and heat map plots. The dot plot displays derived measures of the cell to cell interaction scores and p values. For the dot plot, each row shows a ligand-receptor pair, and each column shows the two interacting cell types. CellPhoneDB defines interactions and interaction levels from the gene expression level, so since the p-value is on a -log10 scale, the larger dots represent more significant interactions. By performing an interaction analysis, a significant interaction was discovered for myeloid and T-cell ligand-receptor pairs, including those between Secreted Phosphoprotein 1 (SPP1) and Fibronectin 1 (FN1), which is consistent with previous findings. It was proposed that an effective protocol would involve a filtration step where cell types would be filtered out, depending on which ligand-receptor pair is activated in that part of the tissue, as well as the incorporation of the CellPhoneDB data in a streamlined workflow pipeline. The filtration step would be in the form of a Python script that expedites the manual process necessary for dataset filtration. Being in Python allows it to be integrated with the CellPhoneDB dataset for future workflow analysis. The manual process involves filtering cell types based on what ligand/receptor pair is activated in kidney cells. One limitation of this would be the fact that some pairings are activated in multiple cells at a time, so the manual manipulation of the data is reflected prior to analysis. Using the filtration script, accurate sorting is incorporated into the CellPhoneDB database rather than waiting until the output is produced and then subsequently applying spatial data. It was envisioned that this would reveal wherein the cell various ligands and receptors are interacting with different cell types, allowing for easier identification of which cells are being impacted and why, for the purpose of disease treatment. The hope is this new computational method utilizing spatially explicit ligand-receptor association data can be used to uncover previously unknown specific interactions within kidney tissue.

Keywords : bioinformatics, Ligands, kidney tissue, receptors, spatial transcriptome
Conference Title : ICBBE 2022 : International Conference on Bioinformatics and Biological Engineering
Conference Location : London, United Kingdom
Conference Dates : February 15-16, 2022