

[BIOINFO 2024]

Enhancing Disease Prediction by Augmenting the Human Interactome with Cell-Type-Specific Co-Expression Networks from Single-Cell Atlas Data

Euijeong Sung¹, Junha Cha¹, Seungbyn Baek¹ and Insuk Lee^{1,*}

¹*Department of Biotechnology, Yonsei University*

*Corresponding author: insuklee@yonsei.ac.kr

Gene co-expression network inference from bulk tissue samples often misses cell-type-specific interactions, which can be detected through single-cell gene expression data. However, the noise and sparsity of single-cell data challenge the inference of these networks. We developed scNET, a framework for integrative cell-type-specific co-expression network inference from single-cell transcriptome data, demonstrating its utility in augmenting the human interactome for more accurate disease gene prediction. We address the limitations in *de novo* network inference from single-cell expression data through dropout imputation, metacells formation, and data transformation. Employing this data preprocessing pipeline, we inferred cell-type-specific co-expression links from single-cell atlas data, covering various cell types and tissues, and integrated over 850K of these inferred links into a preexisting human interactome, HumanNet, resulting in HumanNet-plus. This integration notably enhanced accuracy of network-based disease gene prediction. These findings suggest that with proper data preprocessing, network inference from single-cell gene expression data can be highly effective, potentially enriching the human interactome and advancing the field of network medicine.