Human cell-type-specific network atlas (hcNETLAS) for connecting links from genes to cells to diseases

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Abstract

The heterogeneity of human cells stems from intricate gene interactions as well as differential gene expression. Network analysis leveraging single-cell RNA sequencing data provides a powerful framework to decode these complex biological interactions within a cellular context. Here, we introduce the human cell-type-specific network atlas (hcNETLAS), a comprehensive database of 198 cell-type-specific gene networks from 61 cell types across 25 tissues. Through the provision of biologically relevant genetic interplay, hcNETLAS revealed its potency in characterizing tissue- and cell-type-specific immunology. Moreover, hcNETLAS networks serve as valuable references for disease analyses at the cellular level. We delineate three hcNETLAS analysis pipelines that elucidate potential disease markers, identify pivotal cell types, and unveil modular functional characteristics of disease networks. Demonstrating in lung cancer, systemic lupus erythematosus (SLE), and Alzheimer's disease (AD), hcNETLAS unearths significant associations between phenotypes and interactomes. All the network databases and our disease analysis pipelines are freely accessible on GitHub (https://github.com/netbiolab/hcNETLAS). This novel network atlas promises in decoding cellular heterogeneity, enhancing our understanding of disease mechanisms, and potentially offering novel insights for diagnostics and therapeutics.

Keywords: network biology, cell-type-specific network, single-cell transcriptome, disease markers