# NETWORK BASED APPROACHES REVEAL CELL SUBTYPE SPECIFIC ROLES OF ASTROCYTES AND OLIGODENDROCYTES DURING ALZHEIMER'S DISEASE

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Although, Alzheimer's disease seems to be neuron-based-disorder, contribution of glial cells to AD pathology is undeniable [1,2]. Investigation of transcriptomic changes on glial cells during AD is important since glial cells have many functions like synapse organization, BBB maintenance. Further investigations based on single-nuclei RNA-seq studies have revealed that astrocytes and oligodendrocytes have certain cell-subtypes, and those cell-subtypes have different expression profiles during AD [3]. In our study, protein-protein-interaction (PPI) networks were used to infer neuroprotective/neurotoxic impacts of the gene expression changes observed in astrocyte and oligodendrocyte cell subtypes during AD by using a snRNA-seq dataset that became recently available [3]. Its major difference from other snRNA-seq studies in literature for AD is the enrichment of astrocyte cells, leading to about 10-fold more captured astrocytic nuclei per donor in the dataset. KeyPathwayMiner was used to map each subtype of the cell types on PPI network, leading to identification of subnetworks enriched with differentially expressed genes [4]. Comparative analysis of the subnetworks revealed functional roles of the individual astrocyte and oligodendrocyte cell-subtypes. Detection of cell-subtypes in bulk transcriptome data by using deconvolution algorithms is another focus of our study. Deconvolution algorithms can predict cell-type specific expression values from bulk transcriptome datasets. Using MIND [5] algorithm, a comprehensive bulk AD transcriptomic dataset [6] covering 403 patients and 164 control samples was processed to predict cell type-specific expressions in the dataset, which was further subjected to clustering algorithms to predict subtypes in the cell types. PPI based subnetwork identification was also applied to those cell types. Characterization of single-cell based and deconvolution-based cell-subtype specific subnetworks through functional enrichment analysis shows that improved deconvolution algorithms are needed to better capture molecular alterations in cell types in response to AD. This study was financially supported through a grant by TUBITAK (Project Code: 120S824).

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