Protein profiling of the blood-brain barrier through publicly available omics data

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ABSTRACT

Multiomics data generated through various experiments and uploaded to public repositories have the potential to help researchers in understanding differentially expressed genes in different tissues. One such example is the blood-brain barrier (BBB), for which drug development is a problem because most therapeutic molecules cannot cross the BBB. Among the cell types that form the BBB, endothelial cells are the most important and functional members of the BBB [1], which prevent the entry of most molecules from the blood into the brain [2]. Therefore, it is becoming increasingly important to determine the molecular characterization of the BBB in order to find receptors that are specifically expressed in the brain endothelial cells and could be potential drug targets. To this end, we compiled bulk RNA-Seq data from 309 healthy samples from 68 studies and 16 tissues, one of them being the brain microvascular endothelial cells (BMECs). We then developed a highly adaptive transcriptomics analysis framework for pairwise differential expression tests between tissues (15 such comparisons, each of the form “BMEC vs {Tissue}”.), and pooled these comparisons, taking into account fold change and significance for each protein-coding gene tested. Our framework allowed us to extend our analyses to many different configurations (with/without stem cell derived BMEC samples, etc.), which enabled us to not only identify specific genes that were compliant with literature, but also to address the transcriptomic differences between different sources of BMECs (fresh tissue, stem cell derived, etc.). We hope to make the results available through a user-friendly interface where they can be explored with greater flexibility, and expand on what we already have along with the integration of available proteomics data on BMECs to create an “ensemble gene prioritization network” that will facilitate downstream analysis of drug targets in laboratory settings.

References

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