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MoBC-Net: R-Package for Distance between Modules-of-Interest and Module-Betweenness Centrality of Key Bridge Nodes

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Protein-protein interaction (PPI) network analysis of differentially expressed genes (DEGs) is a common procedure for target identification (TI). Typically, this involves identifying communities within a PPI network and narrowing down to modules of interest (MoIs) by analyzing the functions of these modules and their interconnections. However, focusing only on DEGs in network analysis may neglect the contributions of non-DEGs and the interactions between DEGs and non-DEGs. Additionally, the final step of identifying hidden targets heavily relies on expert domain knowledge and entails a labor-intensive literature review process. To address these limitations, there is a need to elucidate the relationships that context-specific DEGs, derived from specific datasets, have within a broader, knowledge-based context-free PPI network. Moreover, it is essential to identify the proteins predominantly involved in these interactions, supported by quantitative measures.

In this study, we introduce an R package named MoBC-Net. This package is designed to quantify the distance between distinct MoIs within a network and to identify key bridge nodes using a novel metric termed module-betweenness centrality (MoBC). MoBC-Net incorporates a comprehensive range of cluster distance metrics, such as shortest, closest, kernel, center, and separation distances, and evaluates their statistical significance. Additionally, the package provides tools for identifying key bridge nodes along frequently traveled pathways connecting the MoIs and quantifies their contributions through MoBC values. In experimental results, we applied MoBC-Net to the Cancer Genome Atlas Breast Invasive Carcinoma (TCGA-BRCA) dataset. The results demonstrate that MoBC-Net enhances the interpretation of biological significance by allowing researchers to efficiently focus on areas of interest within a network, based on the significance of inter-cluster connections and the identification of key bridge nodes.