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Identification of overlooked genes in DEG analysis by integrating metabolic network topology analysis

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Most of the gene expression studies reveal differentially expressed genes (DEG) followed with gene set enrichment analysis (GSEA). Although this approach is practical for reducing the number of targets to engage, it is very much prone to overlook important targets. This is because the enrichment analysis ignores the metabolic pathway topology. A single gene in DEG list that is involved in very crucial reaction will not be identified as "enriched" if there are more than few genes are found in same pathway with this candidate gene. Thus, metabolic network topology should be strongly integrated with DEG analysis to uncover genes from a given DEG list which affect critical points in metabolic network. In our study, we parsed and merged available pathway and reaction data to construct whole human metabolic network. Then, by graph theory algorithms, identified critical nodes in whole network, perturbation of which would impact the whole network. To pinpoint overlooked targets in already published or calculated DEG lists, we gathered available DEG lists and expression data and mapped resulting DEG to metabolic network. Our approach could recover previously undetected important genes. As a result, the veil called "enriched gene" is lifted so that not enriched but critically important genes are exposed.

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