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Protein-protein interaction network analysis for breast cancer biomarker identification using Cytoscape software

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Breast cancer is a heterogeneous disease and the leading cause of mortality among women worldwide. Early diagnosis is a key to eradication of breast cancer. In this study, protein-protein interaction network analysis distinguished the most significant genes involved in cancer progression that may act as potential biomarkers in the early detection of breast cancer. 200 proteins related to breast cancer were retrieved from the STRING database and analyzed by Cytoscape 3.8.2. The significant clusters were obtained from Molecular Complex Detection (MCODE). Hub gene analysis using Degree, Edge Percolated Component (EPC), Maximum Neighborhood Component (MNC) and Bottleneck calculation methods ranked the top ten significant genes through CytoHubba. Further, crucial genes based on the analysis of seed proteins and hub genes were determined and enriched by ClueGo v2.5.8 via gene ontology and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways. Eight significant genes were identified. Consequently, tumor protein p53 (TP53), MYC, estrogen receptor-1 (ESR1) and AKT serine/threonine kinase-1 (AKT1) were identified as significant hub genes, whereas caspase-8 (CASP8), breast cancer gene-2 (BRCA2), poly (ADP-ribose) polymerase-1 (PARP1) and NIMA related kinase-10 (NEK10), were distinguished as seed proteins. ClueGo output revealed four main functions: response to gamma radiation, regulation of mitochondrial membrane potential, endometrial cancer and central carbon metabolism in cancer. Crucial genes identified in this study offer a potential biomarker panel for breast cancer. Further investigation and validation of these genes is required to assess the true potential of these genes to serve as early markers of breast cancer.

Keywords: MCODE, CytoHubba, ClueGo, Hub genes, Bottleneck, Seed proteins

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