Gene expression profiling of epithelial ovarian cancer reveals key genes and pathways associated with chemotherapy resistance

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ABSTRACT. The aim of this study is to analyze gene expression data to identify key genes and pathways associated with resistance to platinum-based chemotherapy in epithelial ovarian cancer (EOC) and to improve clinical treatment strategies. The gene expression data set was downloaded from Gene Expression Omnibus and included 12 chemotherapy-resistant EOC samples and 16 chemotherapy-sensitive EOC samples. A differential analysis was performed to screen out differentially expressed genes (DEGs). A functional enrichment analysis was conducted for the DEGs using the database for annotation, visualization, and integration discovery. A protein-protein interaction (PPI) network was constructed with information from the human protein reference database. Pathway-pathway interactions were determined with a test based on the hypergeometric distribution. A total of 1564 DEGs were identified in chemotherapy-sensitive EOC, including 654 upregulated genes and 910 downregulated genes. The top three upregulated genes were HIST1H3G, AKT3, and RTN3, while the top
three downregulated genes were NBLA00301, TRIM62, and EPHA5. A Gene Ontology enrichment analysis showed that cell adhesion, biological adhesion, and intracellular signaling cascades were significantly enriched in the DEGs. A KEGG pathway enrichment analysis revealed that the calcium, mitogen-activated protein kinase, and B cell receptor signaling pathways were significantly over-represented in the DEGs. A PPI network containing 101 interactions was acquired. The top three hub genes were RAC1, CAV1, and BCL2. Five modules were identified from the PPI network. Taken together, these findings could advance the understanding of the molecular mechanisms underlying intrinsic chemotherapy resistance in EOC.

Key words: Epithelial ovarian cancer; Chemotherapy resistance; Differentially expressed genes; Functional enrichment analysis; Protein-protein interaction network; Module