

Integrated Network and Regulatory Motif Analysis Identifies Key Hub Genes in High-Grade Ovarian Cancer

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Background and Objectives: High-grade ovarian cancer is characterized by extensive transcriptional dysregulation, genomic instability, and aberrant control of cell proliferation. Identification of central molecular regulators may improve understanding of disease biology and reveal candidate biomarkers or therapeutic targets. This study aimed to identify key hub genes, functional modules, and regulatory motifs associated with ovarian tumorigenesis using an integrated bioinformatics approach.

Methods: The transcriptomic dataset GSE26712, comprising 185 primary late-stage high-grade ovarian tumors and 10 normal ovarian surface epithelium samples, was re-analyzed using GEO2R. Differentially expressed genes were mapped to a protein-protein interaction network using STRING and Cytoscape. Hub genes were prioritized using the CytoHubba plugin across four algorithms: Maximal Clique Centrality, Density of Maximum Neighborhood Component, Maximum Neighborhood Component, and Degree. Functional network modules were detected using ClusterONE, while promoter motif discovery and functional annotation were performed using MEME, Tomtom, and GOMo.

Results: Differential expression profiling indicated prominent activation of cell-cycle, DNA-replication, chromosome-segregation, and mitotic regulatory programs. Network analysis highlighted a core hub set including CDK1, TOP2A, CDC20, CCNB2, BIRC5, UBE2C, BUB1, NCAPG, RRM2, KIF2C, CENPA, and MELK. ClusterONE revealed densely interconnected modules predominantly associated with mitotic regulation and chromosomal organization. Regulatory motif analysis suggested enrichment of E2F-, FOXM1-, and NF-Y-associated regulatory elements, consistent with coordinated activation of proliferative transcriptional programs.



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Conclusion: Integrated network and regulatory analysis identified a cell-cycle-centered hub signature potentially contributing to high-grade ovarian cancer progression. These genes and regulatory motifs represent candidate molecular biomarkers and potential targets for further experimental and therapeutic investigation.