



# Identification of Key Biomarkers and Regulatory Networks in Uterine Cancer Using RNA-Seq Data from TCGA

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## ABSTRACT

**Introduction:** Uterine cancer (UC) is a leading cause of cancer-related deaths in women globally. The growing incidence of cases emphasizes the need for diagnostic and therapeutic approaches. Conventional diagnostic techniques, such as imaging and biopsy, are frequently expensive, time-consuming, and invasive, restricting their availability and effectiveness. Consequentially, there is an urgent need for more effective, non-invasive, and cost-effective approaches that may be generally adopted for the early detection and appropriate management of UC. This study aimed to identify potential biomarkers for UC diagnosis and elucidate the regulatory networks mediated by miRNAs and transcription factors (TFs) using RNA-Seq data from the Cancer Genome Atlas (TCGA).

**Methods and Materials:** RNA-Seq data for UC and standard tissue samples were obtained from the TCGA using the TCGAbiolinks package in R. The data processing involving normalization and differential expression analysis was performed using the same package. Genes identified as differentially expressed genes (DEGs) were selected based on a  $p$  less than 0.05 and a log fold change (LogFC) greater than or equal to 1. The functional importance of DEGs was investigated using gene ontology (GO) and KEGG pathway analyses. Protein-protein interaction networks and hub genes were identified using STRING and Cytoscape. miRNA-target interactions were explored with miRTarBase and miRNet, while TF-target interactions were analyzed using TRANSFAC and ChEA databases. The validation of hub genes was conducted using receiver operating characteristic (ROC) curve analysis and the GEPIA database.

**Results:** According to the analysis, 413 DEGs were identified, with 264 genes upregulated and 149 genes downregulated. The key DEGs identified were *CEACAM5*, *FLNC*, *CDKN2A*, *MMP9*, *KRT5*, *DCN*, *CNN1*, and *SFN*. The GO enrichment study revealed essential biological processes, including regulating vascular-associated smooth muscle cell proliferation (GO: 1904705) and the negative regulation of cysteine-type endopeptidase activity involved in the apoptotic process (GO: 0043154). The KEGG pathway analysis revealed significant pathways in cancer development, specifically the p53 signaling pathway and cytokine-cytokine receptor interaction. miRNA interactions highlighted hsa-mir-16-5p, hsa-mir-155-5p, hsa-let-7b-5p, hsa-mir-124-3p, and hsa-mir-941 as key regulators. TF analysis indicated significant interactions with MYC, EGR1, and SUZ12. ROC curve analysis demonstrated the diagnostic potential of the identified hub genes.

**Conclusion and Discussion:** Potential biomarkers for UC include the *CEACAM5*, *FLNC*, *CDKN2A*, *MMP9*, *KRT5*, *DCN*, *CNN1*, and *SFN* genes. The identified miRNAs and TFs have significant roles in regulating these genes, providing valuable insights into the molecular pathways that underlie UC. These findings offer promising opportunities to develop innovative diagnostic and therapeutic approaches for UC.

**Keywords:** MicroRNAs, RNA-Seq, Uterine neoplasms

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