

PANEL OF POTENTIAL BIOMARKERS AND KEY MOLECULAR PATHWAYS IN CERVICAL CANCER

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Introduction: Cervical cancer remains a leading cause of cancer-related morbidity and mortality worldwide, underscoring the urgent need for robust biomarkers to improve diagnosis, prognosis, and therapeutic decision-making. **Objectives:** To identify and prioritize a panel of potential biomarkers and biological pathways in cervical cancer tissue samples including Tumor (TU), Peritumor (PTT), and Non-Cancer (NC) regions. **Methods:** The institutional ethics committee approved the study under the protocol number CAAE: 79292824.0.0000.5634. The samples were sequenced on an Illumina NextSeq 500 platform using mRNA-seq. RNA-seq data processing was performed using the nf-core/rnaseq v3.1.4 pipeline. Differential gene expression analysis (DESeq2 package in R, adjusted p-value < 0.05 and abs(log₂FoldChange) > 1), ROC curve (AUC ≥ 0.9), and clinical annotation via the OncoKB database were integrated to identify and prioritize clinically relevant biomarkers. Additionally, the parameter 'baseMean' was used to apply an additional filtering step where genes falling at or above the first quartile of the 'BaseMean' distribution for each condition's median were included. Minimum 'BaseMean' values for TU-PTT, TU-NC, and PTT-NC conditions were 4.48, 8.59, and 7.13 respectively. Functional enrichment analyses using Gene Ontology and KEGG pathways (FDR < 0.05) were performed to elucidate biological processes and pathways associated with these biomarkers. **Results:** A panel of 40 potential biomarkers were identified and categorized as 18 oncogenes, 21 tumor suppressor genes, and 9 actionable genes. Biomarkers were unique to TU-PTT and TU-NC comparisons, with no candidates identified in PTT-NC. Distinct pathways were enriched by unique biomarkers in each condition: cysteine and methionine metabolism, TGF-beta signaling, and viral infection pathways (TU-PTT); and pancreatic cancer, breast cancer, melanoma, and central carbon metabolism pathways (TU-NC). Common biomarkers between TU-PTT and TU NC, FANCA and BRCA1, were associated with key DNA repair-related pathways, including Fanconi anemia (FA), homologous recombination (HR), and platinum drug resistance. Genes within the FA and HR pathways, such as *BRIP1*, *RAD51C*, *XRCC2*, and *RAD54L*, were consistently overexpressed, indicating dysregulated DNA repair mechanisms in cervical tumors. **Conclusion:** Our study identified a panel of clinically relevant biomarkers and molecular signatures distinguishing tumor and non-cancerous cervical tissues (PTT, and NC). Key DNA repair-associated genes, emerged as promising candidates for diagnostic, prognostic, and therapeutic applications in cervical cancer.

These findings provide a foundation for biomarker-driven strategies to improve clinical management, warranting validation in larger patient cohorts.

Keywords: cervical cancer; OncoKB; biomarkers; pathways; homologous recombination; Fanconi anemia