Seminar in Medical Microbiology

Title: Comprehensive circular RNA expression profile and their roles in cervical cancer

Student: Miss Juthamas Subin **ID:** 665070019-3

Advisor: Assist. Prof. Dr. Sirinart Aromseree

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Abstract

Cervical cancer (CC) is a major cause of cancer-related mortality in women, mainly cause by HR-HPV persistent infection. Squamous cell carcinoma (SCC) and adenocarcinoma (ADC) are two major histological variants of cervical malignant tumors. Circular RNAs (circRNAs) are noncoding RNAs with stable structures and tissue-specific expression. Several studies revealed that circRNA dysregulation is closely related to the progression of tumors.

RNA sequencing analysis from three pairs of CC tissue and adjacent normal tissue (ANT) from HPV-16 positive patients with SCC, ADC or ASC revealed a total of 11,685 annotated circRNAs. There were 42 upregulated and 98 downregulated circRNAs. Two-hundred and fifteen circRNAs were upregulated in SCC but downregulated circRNAs in ADC, while 50 circRNAs displayed the opposite trend. Functional enrichment analysis based on different expressions of circRNAs found that in all the three pathologic variants of CC was the ‘‘ubiquitin-mediated proteolysis’’ pathway. The competing endogenous RNA (ceRNA) network was constructed. This study provides new insights into the process of tumor differentiation mediated by HPV [1].

CircRNAs related to CC were screened through the Gene Expression Omnibus (GEO) datasets number GSE102686 and GSE113696. Circ_0087429 was significantly downregulated in CC tissues and cells. In addition, circ_0087429 significantly inhibited the proliferation, migration, invasion, and angiogenesis of CC *in vitro* and tumor growth and metastasis *in vivo*. Osteoglycin (OGN), a type SLRPs, functions involve in various biological processes and its significantly downregulated in CC tissues and cells. Circ_0087429 upregulated the expression of OGN by competitively binding with miR-5003-3p, thereby reversing EMT and inhibiting the progression of CC. EIF4A3 inhibited circ_0087429 expression by binding to its flanking regions. Collectively, these findings provide a new potential target for the treatment of CC [2].

In summary, the distinctive expression profile and the roles of circRNAs can be used as biomarkers for diagnosis and treatment outcomes of CC.

References

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2. Yang, M., Hu, H., Wu, S., Ding, J., Yin, B., Huang, B., Li, F., Guo, X., Han, L.: EIF4A3-regulated circ_0087429 can reverse EMT and inhibit the progression of cervical cancer via miR-5003-3p-dependent upregulation of OGN expression. Journal of Experimental and Clinical Cancer Research. 41, (2022). https://doi.org/10.1186/s13046-022-02368-