Seminar in Medical Microbiology

Title: Circular RNA Dysregulation in Cervical Cancer: Emerging Targets for Therapeutic Intervention

Student: Miss Juthamas Subin **Student ID:** 687070025-4

Advisor: Assist. Prof. Dr. Sirinart Aromseree

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Abstract

Cervical cancer (CC), primarily driven by persistent infection with high-risk human papillomavirus (HR-HPV), remains the fourth leading cause of cancer-related mortality among women worldwide. In recent years, circular RNAs (circRNAs) have emerged as important regulators in cancer biology, including CC; however, the functions of many newly identified circRNAs remain poorly understood.

Using circRNA sequencing of clinical specimens from five CC tissues and five matched adjacent normal tissues, circSTX6 was identified as the most significantly upregulated circRNA in CC. Functional assays demonstrated that circSTX6 overexpression enhanced CC cell proliferation, migration, invasion, and tumour growth, whereas circSTX6 knockdown reversed these effects. Mechanistically, circSTX6 was shown to bind and stabilize the transcription factor SPI1, leading to increased IL6 transcription and activation of the JAK2/STAT3 signaling pathway. Furthermore, METTL3-mediated N6-methyladenosine (m6A) modification stabilized circSTX6 via YTHDC1 recognition, forming a positive feedback loop among METTL3, circSTX6, and SPI1. These findings highlight circSTX6 as a potential molecular therapeutic target in CC. (Han et al. 2025)

The effects of the serine/arginine-rich splicing factor 3 (SRSF3) inhibitor, theophylline, were evaluated in SiHa and C33A CC cell lines using cell cycle analysis by fluorescence-activated cell sorting (FACS) and apoptosis assessment by Annexin V/propidium iodide (PI) staining. Theophylline induced S-phase arrest in SiHa cells and G2/M phase arrest in C33A cells, accompanied by significant cytotoxic effects. CircRNA_400029 and hsa_circ_0001038 were identified as upregulated in CC, and bioinformatic analyses revealed their interactions with the tumour-suppressive miRNAs miR-16-5p and miR-205-5p, respectively. Construction of a competing endogenous RNA (ceRNA) network and KEGG pathway analysis further identified key signaling pathways involved in CC progression and identified SRSF3 as a potential regulator within these putative pathways. These findings suggest that theophylline exerts cytotoxic effects in CC cells and may be repurposed as a potential theragnostic agent for CC. (Nyalambisa, A et al., 2025)

In summary, accumulating evidence indicates that dysregulated circRNAs play critical roles in CC progression and may serve as promising targets for the development of novel therapeutic strategies.

References

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