UNIVERSITI TEKNOLOGI MARA

INHIBITORY EFFECT OF 5-AZA-DC AND EXPRESSION OF MIR-129-3P IN ORL-48T

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, thereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

Oral cancer is recorded as the sixth highest malignancy globally. In Malaysia, oral cancer deaths have been reached 1,060 or 0.83% of total deaths in 2018. Current cases reported that oral cancer can be treated when detected at an early stage of the disease. However, so many cases are still detected at a late stage of disease, thus increasing the mortality rate of the patients. MicroRNAs (miRNAs) is a group of small non-coding RNAs, which plays a role in post-transcriptionally regulating gene expression, and miR-129-3p was reported affecting the cell proliferation, apoptosis, and even chemotherapy resistance in different types of cancer. Research has shown that deregulation of miRNAs in almost every type of human cancer, and the signature of miRNA expression in tumour can be potentially applied in cancer detection and prognosis. Epigenetic drugs, 5-aza-2'-deoxycytidine (5-aza-dC) function as a methylation inhibitor, also is implemented in treating cancer which possibly reverses aberrant gene expression profiles associated with different diseases. The aim of this study is to measure the inhibitory effect 5-aza-dC towards proliferation of the oral cancer cell line, ORL-48T and normal human gingival fibroblast, hGF using an in vitro model. In addition, the evaluation of miRNA-129-3p expression of treated ORL-48T and hGF with 5-aza-dC using quantitative Real-Time Polymerase Chain Reaction (RT-PCR) was also carried out in this study. Inhibitory effects of 5-aza-dC on ORL-48T and hGF proliferation was studied using 3-4,5-dimethylthiazol-2-yl-2,5 -diphenyltetrazolium bromide (MTT)-based assay. Statistical analysis revealed that treatment with 40 µM of 5-aza-dC for 72 h, and 20 µM of 5-aza-dC for 144 h had significantly decreased the viability of oral cancer cells ($p=0.03$). The expression of miR-129-3p was also found to be significant between the treated and untreated ORL-48T ($p=0.02$). However, there was no significant difference between treated and untreated hGF. Overall studies indicate that miR-129-3p was upregulated in an oral cancer cell which showed a signal of oncogenesis and potential target to detect oral cancer. These findings also suggested the inhibitive effect of 5-aza-dC towards the proliferation of ORL-48T cells. Therefore, the findings from this study would be useful for detection, prognostic, diagnostic or therapeutic targets of oral cancer and improve the survival rate of oral cancer patients in the future. Moreover, it could help in the development of effective cancer treatment by applying miR-129-3p as potential biomarker in detecting oral cancer.

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