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MicroRNA-205 suppresses the oral carcinoma oncogenic activity via down-regulation of Axin-2 in KB human oral cancer cell

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Abstract MicroRNA (miRNA) is a small noncoding RNA molecule, 19–25 nucleotides in length, which regulates several pathways including cell development, cell proliferation, carcinogenesis, apoptosis, etc. In this study, the over-expression of microRNA-205 (miR-205) increased the number of apoptotic cells by at least 4 times compared to the control. In addition, over-expressed miRNA in KB oral cancer cells triggered apoptosis via the caspase cascade, including the cleavage of caspase-9, caspase-7, caspase-3, and PARP. Flow cytometry showed that apoptotic cell death was increased significantly by 35.33 % in KB oral cancer cells with over-expressed miR-205 compared to the control. The microarray data showed that axis inhibitor protein 2 (Axin2) was down-regulated in KB oral cancer cells transfected with miR-205. In addition, Axin2 was down-regulated by approximately 50 % by over-expressed miR-205 at both the mRNA and protein levels. Interestingly, Axin2 was up-regulated in KB oral cancer compared to human normal oral keratinocytes. Furthermore, the cell cytotoxicity and apoptotic population of KB oral cancer cells were increased significantly after Axin2 siRNA transfection. These results suggest that Axin2 is might be as potential oncogene in KB oral cancer cells. The luciferase assay showed that over-expressed miR-205 in KB oral cancer cells suppressed AXIN2 expression through an interaction with its own binding site at AXIN2 3′UTR (64–92). These results suggest that miR-205 is a novel anti-oncogenic miRNA in KB oral cancer cells, and may have potential applications in oral cancer therapy.

Keywords MicroRNA (miRNA) · AXIN-2 · Oral carcinoma · Oncogenic activity · Apoptosis

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Introduction

Oral cancer is one of major worldwide public health problems that affect any part of the oral cavity, such as the lips, tongue, mouth, and throat. Although pathophysiological studies associated with the development of oral cancer have shown that environmental factors, such as smoking, alcohol, betel quid, etc., can act as critical carcinogens, the etiology of oral cancer is largely unknown. Moreover, 40,000 patients with oral cancer will be newly diagnosed with oral or pharyngeal cancer per year in United Sates alone and only approximately 57 % of those will be alive in 5 years. Therefore, many studies are underway to develop an effective clinical treatment for oral cancer.

MicroRNA (miRNA) has the potential to provide clinically relevant information regarding the prognosis and potential response to chemotherapy in patients with a range of diseases. miRNA composed of 15–22 nucleotides are non-coding RNA molecules that act as critical regulators of gene expression at the post-transcriptional level via an interaction with the 3′-untranslated region (3′-UTR) of the target genes. Therefore, miRNA can affect a number of cellular functions, including development, differentiation,

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