

MicroRNAs : A key player in oral tumors pathogenesis

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Abstract

Oral tumors are one of main tumors which could be related with serious health problems worldwide. It has been indicated that several cellular and molecular pathways including genetics and epigenetics mechanisms (e.g. chromosomal alterations, and microRNA) could be anticipated in oral tumors pathogenesis. The recognition of these pathways is found as key steps for better treatment of oral tumor patients. MicroRNAs (miRNAs) are one of important molecules which could be involved in various physiological processes in oral tumors. These molecules are known as short non coding RNAs which are associated with initiation and progression of various diseases such as oral tumors. Multiple lines of evidence showed that various miRNAs (i.e. miR-9, miR-7, miR-21, miR-31, miR-15a and miR-16-1) via targeting various cellular and molecular pathways such as epidermal growth factor receptor (EGFR), MAPK, Akt, ERK, Jak/STAT, and PTEN could be involved in oral tumors pathogenesis. Here, we summarized various miRNAs which have critical roles in oral tumors pathogenesis. Moreover, we highlighted the utilization of various miRNAs as diagnostic and therapeutic biomarkers for patients with oral tumors.

Biology functions and stability of miRNAs

MiRNAs are small non-coding RNAs which the average length of them is 21-22 nucleotides. It has been showed that miRNA processed from a hairpin precursor(1). At first step, MiRNAs originate from *pri-miRNA* (pri-miRNAs). RNA polymerase II and some transcription factors could regulate this process. Ribonuclease III (Drosha) and its cofactors (PACT and TRBP) could cleavage pri-miRNAs in cytoplasm and provide a duplex miRNA with 21-22 nucleotides in length. After dissociated double strands of miRNA, one of strands could incorporate into the RISC (RNA-induced silencing complex) or RITS (RNA-induced transcriptional silencing). Single strand of miRNA present in the RISC or RITS are able to provide a target for various mRNAs and can inhibit their translation *via* cleavage and degrading of them (1)(Figure 1).

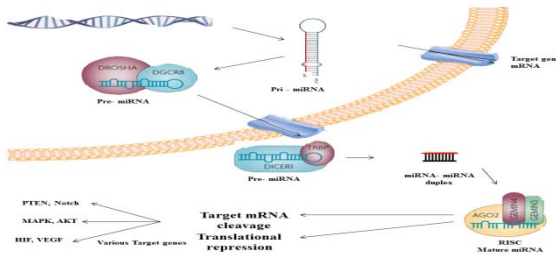


Figure 1. A scheme of miRNA biogenesis and its cellular targets

Molecular pathways involved in oral tumors

It has been showed that there are a various types of oral tumors such as **squamous cell carcinoma** (accounted for more than 90 percent of oral cancers), **verrucous carcinoma**, **lymphomas**, fibroma, keratoacanthoma, and odontogenic tumors which could be associated with cancerous conditions in infants and adults (3). Oral tumors are multifactorial diseases which a variety of genetical and environmental factors could be involved in pathogenesis of them (3).

A large number studies indicated that a various genetical factors including oncogenes, tumor suppressors, epigenetic mechanisms, and chromosomal abnormalities could critical roles in initiation and progression of oral tumors in infants and adults (3). Identification of them may provide better understanding of biology pathways involved in oral tumors and could contribute to using of better therapeutic platforms for patients with oral tumors (3). Here, we mention a variety of oncogenes; tumor suppressor genes and chromosomal abnormalities which could be associated with initiation and progression of oral tumors (Figure 2).

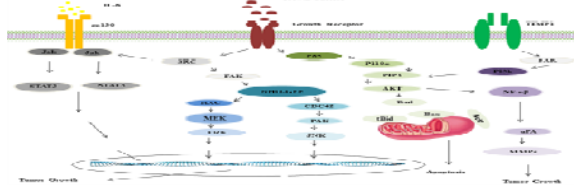


Figure 2. Various cellular and molecular pathways involved in oral tumors

MicroRNAs AND Oral tumors

MicroRNAs (miRNAs) are small non-coding RNAs which are involved in a variety of cellular and molecular pathways (2). A large number studies indicated that deregulation of miRNAs are associated with various types of diseases such as stroke, cardiovascular diseases, inflammatory diseases and cancer (3). Many studies indicated that deregulation of a variety of miRNAs such as miR-9, miR-7, miR-21, and miR-31 could be involved in pathogenesis of oral tumors (4). Hence, it seems that these molecules could be used as diagnostic, prognostic and therapeutic biomarkers for various types of tumor such as oral tumors (4).

In a study, Diniz et al., indicated that miR-15a and miR-16-1 could affect on expression of Bcl2 in keratocystic odontogenic tumors (KOTs) (5). Their results showed that there were up regulation of miR-15a and miR-16-1 in the KOTs samples than healthy subjects. Up regulation of miR-15a miR-16-1 could lead to decreasing of Bcl2 expression in the human KCOT-1 cell line. Hence, miR-15a and miR-16-1 exert their effects via targeting Bcl2. These results indicated that miR-15a and miR-16-1 could be used as diagnostic and therapeutic biomarkers in KOTs therapy (3) (Table 1).

Table 1. Various microRNAs involved in oral tumors

Type of tumors	Biomarker	Expression	Diagnosis methods
Schwannomas	miR-7	Down regulation	IHC, qRT-PCR
Eosinophilic Granuloma	OKT6	Up regulation	IHC
	S-100	Up regulation	IHC
Langerhans Cell Histiocytosis	CD1a	Up regulation	IHC
	S100	Up regulation	IHC
Squamous Cell Carcinomas	miR-9	Up regulation	qRT-PCR
	miR-7	Down regulation	qRT-PCR
	miR-21	Down regulation	qRT-PCR
	miR-31	Up regulation	qRT-PCR

Conclusion

Oral tumors are one of important public health problems worldwide. Identification of cellular and molecular pathways involved in oral tumors could contribute to better understanding oral tumors behavior and led to create and design new therapeutic approaches. Many studies indicated that deregulation of a variety of miRNAs such as miR-9, miR-7, miR-21, and miR-31 could be involved in pathogenesis of oral tumors. Hence, it seems that these molecules could be used as diagnostic, prognostic and therapeutic biomarkers for various types of tumor such as oral tumors .

References

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