Circular RNAs in head and neck cancer diagnosis and potential molecular targeting

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Abstract

Circular RNAs (circRNAs) are a class of non-coding RNAs which is being explored recently. CircRNAs are highly conserved across species and exhibit tissue/developmental stage-specific expression. circRNAs are more stable than linear mRNAs and lack a 5′-terminal cap and 3′-terminal poly A tail. CircRNAs modulate gene expression at the transcriptional and post-transcriptional levels. circRNAs play different functional roles in hallmark cancer events both as oncogens and tumor suppressors including regulation of angiogenesis, induction of metastasis and invasion, evading cell death. Here, we outlined the molecular mechanisms of circRNA function to regulate the molecular events in cancer. We also reviewed the current knowledge and recent finding regarding the association of circRNA with head and neck cancer. We briefly discussed the potential of circRNA as diagnostic biomarkers as well as the possibility for therapeutic targeting.

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Figure 1. Biogenesis and functions of circular RNA
advanced clinical stage showed higher levels of hsa_circRNA_100855 expression [7]. The hsa_circRNA_104912 level was significantly lower in laryngeal squamous cell carcinoma than in corresponding adjacent non-neoplastic tissues [7]. Patients with T3-4 stage, neck nodal metastasis, poor differentiation or advanced clinical stage had a lower hsa_circRNA_104912 expression [7].

In another study, Verduci et al. [8], using a sample consisted of 115 head and neck squamous cell carcinoma patients, reported that circPVT1 is over-expressed in tumors compared to matched non-tumoral tissues [8]. The overexpression was mainly related to TP53 mutation status and was related to a more malignant phenotype. Mechanistically, the circPVT1 expression is transcriptionally increased by the mut-p53/YAP/TEAD complex [8]. circPVT1 modulated the gene involved in cell proliferation [8]. Xia et al. [9] reported overexpression of hsa_circ_0067934 in esophageal cancer cells compared to the adjacent noncancerous tissue samples. The expression levels were related to poor tumor differentiation and late tumor staging and higher involvement of lymph nodes [9].

In conclusion, emerging evidence indicates that circRNAs function as important drivers of cancer. However, this line of research is still emerging. Future studies should focus on mechanistic characterization and causal association of circRNAs in tumorigenesis in head and neck cancer. Parallel with mechanistic studies, well-controlled clinical studies are needed to assess the utility of circRNAs for diagnosis and therapeutic purposes. Based on the recent reports, circRNAs can be as potentially promising candidates not only as a biomarker for cancer diagnosis but also a potential monitoring and therapeutic targets.

Various circular RNAs (circRNAs) can be generated from a same genomic locus. circRNAs are formed by non-canonical splicing process. circRNAs consist of one or more exons and can also have unspliced intronic sequences. Colored bars (exons) black lines (introns). In recent years various roles of circRNAs in cellular processes is arising such as miRNA sponge, RBP sponge, regulator of mRNA expression and translation, protein scaffolding and as delivery vehicles for miRNA-Ago complex or RBP proteins.

**Author contributions**

FMH and SB both contributed equally to drafting the work. Both authors contributed to concept, writing, and final approval.

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