Letter to the Editor

Significance of Non-Coding RNAs in Oral Cancer: From Biomarkers to Therapeutic Targets

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Dear Editor,

Oral squamous cell carcinoma (OSCC) is a group of very aggressive cancers that are diverse in terms of their etiology, clinical presentation, and molecular makeup. Although the processes behind the development of OSCC are poorly understood, the majority of OSCCs are linked to alcohol and tobacco use, operating both alone and in concert. This shows that the environment plays a significant role in carcinogenesis.[1] The standard chemotherapy regimen for oral cancer consists of paclitaxel, 5-fluorouracil (5-FU), and cisplatin (CDDP) either separately or in combination.[2] High-throughput genome sequencing has revealed that over 90% of the human genome consists of non-coding RNA transcripts, which do not code for proteins but play an important role in gene regulation.[3]

According to high-throughput genome sequencing, more than 90% of the human genome encodes non-coding transcripts, which do not code for proteins.[4] Non-coding RNAs, such as microRNAs (miRNAs), long non-coding RNAs (lncRNAs), circular RNAs (circRNAs), and PIWI-interacting RNAs (piRNAs), do not code for proteins but play an important role in regulating gene expression at the epigenetic, transcriptional, post-transcriptional, and translational levels (Fig. 1). In oral cancer, dysregulated ncRNA expression has been associated with tumor initiation, progression, and

resistance to treatment. For example, lncRNAs and miRNAs interact, with lncRNAs functioning as competitive endogenous RNAs (ceRNAs) to modify miRNA activity and alter mRNA expression in cancer cells.[5] LncRNAs, in particular, have received a lot of attention because of their roles in tumorigenesis, prognostic outcomes, oral cancer progression, and associated signaling pathways. These molecules have important functions in a range of physiological and pathological processes, including cancer and the complexity of gene regulation networks. Identifying and characterizing lncRNAs linked with oral cancer provides vital insights into their potential as biomarkers for early detection and targets for developing successful therapeutics, while also addressing the challenges in using ncRNAs for improved patient outcomes.[6,7] Three tumor suppressor lncRNAs (MEG3, POU3F3, and PANDAR), two metastasis-associated lncRNAs (LINC00312 and MALAT1), and six lncRNAs (CDKN2B-AS1, H19, HOTAIR, AP5M1, linc-RoR, and FALEC) are linked to cell proliferation.[8] MicroRNAs (miRNAs) have emerged as key participants in the pathogenesis of oral cancer. MicroRNAs are tiny non-coding RNA molecules that control gene expression after transcription, influencing a variety of biological and pathological processes, including cancer formation and progression. Their involvement in oral cancer emphasizes their potential as early detection biomarkers and targets for novel techniques. Research

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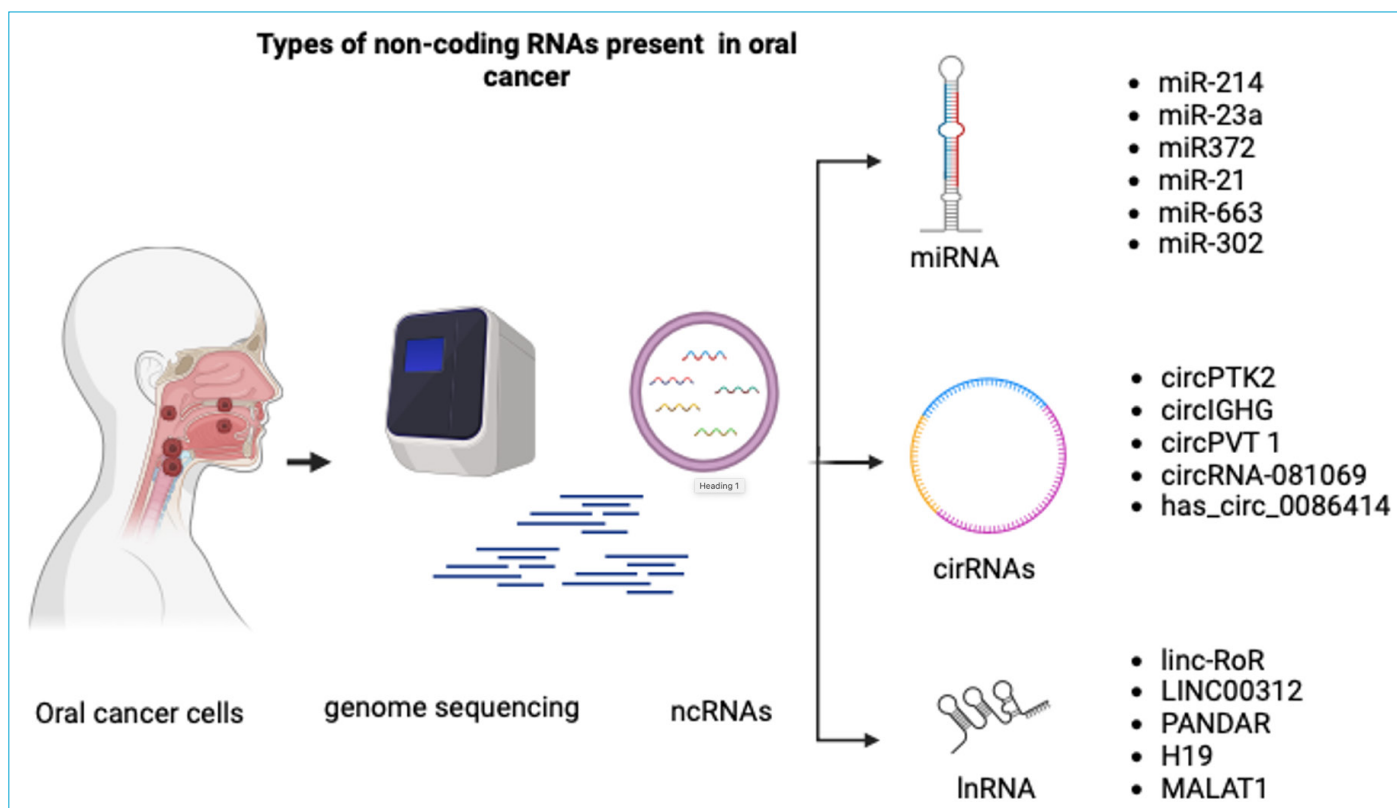**Phone:** +91-9952495300 **E-mail:** anbarasuk.sse@saveetha.com

Figure 1. Classification of non-coding RNAs in oral cancer progression.

has discovered certain miRNAs that are dysregulated in oral cancer, including overexpression of miR-150-5p, miR-548b, miR-18a, and miR-423-5p, among others, in various biological samples such as plasma, tissue, and saliva. High expression levels of miR-99a are connected to improved prognosis and longer overall survival, but overexpression of miR-183 implies a higher risk of poor outcomes. Manipulating the expression of certain miRNAs, such as miR-155-5p, miR-24-3p, and miRNA-10a, is being studied as a novel method for cancer therapy.[9] This makes miRNAs helpful for studying the molecular basis of oral cancer as well as identifying functional markers for its diagnosis, prognosis, and treatment.[10]

Circular RNAs (circRNAs) are emerging as important players in the pathogenesis and therapeutic management of oral cancer, particularly oral squamous cell carcinoma (OSCC), which is a major global health problem due to its poor survival rates. CircRNAs are distinguished by their closed-loop structure, which is extremely stable and conserved across tissues. Their dysregulation in OSCC is related to numerous clinicopathological features and prognoses, indicating their potential as biomarkers for diagnosis and treatment.[11] CircRNAs are important in oral cancer because they participate in crucial signaling networks, act as regulators, and contribute to the disease's molecular mecha-

nisms. They are recognized for their therapeutic relevance as new biomarkers because of their participation in OSCC development and their potential utility in predicting clinical outcomes and treatment responses. Stable silencing of particular circRNAs in OSCC cell lines has been found to demonstrate oncogenic activities, indicating their functional significance in cancer progression and their prospective therapeutic targets.[12] PIWI-interacting RNAs (piRNAs), along with other non-coding RNAs (ncRNAs), are critical in the progression and resistance to therapy in oral cancer. They influence many cellular processes via changes in the transcriptional, post-transcriptional, and translational alterations, and epigenetic domains. The differential expression of various ncRNAs, including piRNAs, in blood or saliva indicates their potential as diagnostic and prognostic markers, underscoring the urgent need for better knowledge and development of diagnostic and therapeutic techniques for oral cancer.[3]

The identification and characterization of ncRNAs using bioinformatics tools have revolutionized our understanding of gene expression and regulation. Bioinformatics is the application of computational tools and databases to analyze massive amounts of data generated by high-throughput sequencing technologies such as RNA sequencing (RNA-seq), which has been critical in identifying and

characterizing ncRNAs such as microRNAs (miRNAs) and long non-coding RNAs (lncRNAs). One of the first hurdles in ncRNA research is establishing whether a transcript is coding or non-coding. This entails assessing the coding potential of ncRNAs, which is confounded by their capacity to contain open reading frames (ORFs) entirely by accident. Mass spectrometry proteomics has also been employed to improve the accuracy of non-coding transcript definitions.[13] In terms of computational modeling, various novel methodologies have been developed to predict and characterize ncRNAs and their roles. Computational models have been developed to predict lncRNA secondary structures, infer miRNA subcellular localization, and comprehend circRNA-disease relationships. These models frequently incorporate multiple computational modules, such as graph convolutional networks and machine learning techniques, to predict ncRNA interactions and functions with greater precision.[14] The bioinformatics tools and databases available for ncRNA research have a wide range of functions, from predicting biological interactions to assessing their role in gene regulatory networks. These techniques are essential for generating novel interactions, which are subsequently tested empirically, resulting in a cycle of mutual enrichment between computational predictions and experimental discoveries.[15]

In oncology, oral squamous cell carcinoma (OSCC) poses a significant problem because of its aggressive nature, range of etiologies, and intricate molecular makeup. Despite their effectiveness, traditional chemotherapy regimens draw attention to the need for new therapeutic strategies. The knowledge of gene regulation has been completely transformed by the finding that non-coding RNAs (ncRNAs) account for more than 90% of the human genome. They include circRNAs, piRNAs, miRNAs, and lncRNAs, which are essential for controlling gene expression and play a complex role in the etiology of OSCC. The initiation, development, and resistance to therapy of oral cancer are all influenced by the dysregulation of non-coding RNAs (ncRNAs). The interaction between lncRNAs and miRNAs occurs in intricate regulatory networks that influence the behavior of cancer cells. The discovery of particular non-coding RNAs (ncRNAs) as biomarkers presents opportunities for tailored therapeutics and early detection. The identification and characterization of non-coding RNAs (ncRNAs) have been greatly aided by bioinformatics, which uses computer models and high-throughput sequencing methods to anticipate the relationships and roles of ncRNAs. By combining experimental and computational methods, we can better understand the functions that non-coding RNAs play in cancer and the development of new therapeutic strategies.

To conclude, the investigation of non-coding RNAs (ncRNAs) in oral squamous cell carcinoma (OSCC) offers valuable insights into the molecular mechanisms behind this highly aggressive cancer type, potentially leading to enhanced diagnostics, prognoses, and treatment options. To completely realize the promise of non-coding RNAs in the fight against oral cancer and in enhancing patient outcomes, more studies in this area are necessary.

Disclosures

Conflict of Interest: None declared.

Authorship Contributions: Concept – S.R., K.A.; Design – K.A.; Supervision – K.A.; Materials – S.R.; Literature search – S.R.; Writing – S.R., K.A.; Critical review – K.A.

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