

MicroRNA-based biomarkers for oral cancer

Sir,

Oral cancer (OC) is one of the common cancers in India and the age-adjusted incidence rates of OC in the country are higher. One of the issues concerning OC is the late diagnoses or locally advanced stage of presentation in the majority of the cases. Environmental and lifestyle factors such as tobacco chewing, alcohol consumption, poor oro-dental hygiene, and viruses like human papilloma virus are known to contribute to the development of OC. Furthermore, there are additional risk factors like consumption of betel and areca nut, which are significantly associated with cancers of the oral cavity. OC burden is one of the major health concerns in India, and with unabated use of chewable tobacco consumption in the country, this burden is expected to rise in the future.

A noncoding RNA is a functional RNA molecule that is transcribed from the DNA, but not translated into proteins. There are two types of noncoding RNAs, namely, long noncoding RNAs and microRNAs. These noncoding RNAs exert effects on several biological processes such as immune modulation, metabolic control, cell cycle, and stem cell differentiation. MicroRNAs regulate gene expression by either degrading or making the target messenger RNAs silent and thereby rendering ineffective protein synthesis required during cell proliferation or apoptosis. Some microRNAs are overexpressed, whereas some are under-expressed in cancer giving rise to signature microRNA patterns. MicroRNAs, which are overexpressed, are considered as oncogenes and are labeled as “oncomirs.”^[1] Moreover, microRNA profile is altered in the blood of cancer patients compared with that of healthy persons.^[2] Analysis of microRNA levels in human plasma and serum showed that extracellular microRNAs are stable in body fluids.^[3] Therefore, there is a need to develop noncoding microRNA biomarkers that could be used as a prognostic marker. Furthermore, noncoding RNAs in OC that can be used as a therapeutic target should also be investigated. Targeting noncoding RNAs by novel agents are known.^[4] Noncoding microRNAs possess unique properties such as their small size, fixed and known sequence, and are conserved in the cell. These features make them ideal for targeting by antisense inhibition or by replacements in case of

a down-regulated expression scenario. A simple explanation for the origin of extracellular microRNAs is that the death of cells as a consequence of disease, breach in cancerous cells onto extracellular matrix or other necrotic events result in the passive release of microRNAs in the cytoplasm, and the released microRNAs are detected in the blood and tissue fluids. In OC, the typical signature pattern of microRNAs will be present in the blood and/or saliva. The objective should be to identify a panel of highly sensitive and specific microRNAs in patients with OC. This will pave the way for the development of microRNA-based biomarkers as targets for novel therapeutic agents. Sufficient uptake in the tissue without the need of developing formulation gives targeting microRNA therapeutics an extra edge.^[5] The process from microRNA profiling to the development of targeted therapies is a long road to travel. It begins with bioinformatics prediction and microRNA profiling, followed by validation and *in vivo* studies and finally clinical trials. Identification of microRNA biomarkers in OC as prognostic markers and therapeutic targets for the treatment are the need of the hour.

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