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Editorial

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Is Salivary Exosome the Answer to Early Detection of Oral Cancer?

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The presence of exosomes in almost all bodily fluids including saliva[1] represents a promising surrogate approach to investigate tumour markers. This has important clinical implications for developing non-invasive salivary diagnostics and therapeutics.[2] Human saliva is an ideal fluid for developing non-invasive diagnostics and salivary biomarkers have been demonstrated in clinical studies showing promising diagnostic potentials but lacking in sensitivity mostly due to complexity of saliva.[2,3] Hence, this led to the emerging interests on exosomes which are membrane-bound extracellular vesicles carrying specific membrane proteins with numerous types of nucleic acids[4] and protein cargos,[2,5,6] well protected from degradation by extracellular enzymes. Their size (50-150 nm diameter) is an advantage for purification and reducing the overall complexity of saliva.[2] Most of the salivary exosome studies to date have been restricted to characterization of normal healthy samples.[2] Emerging studies began looking at biochemical properties of disease-derived saliva exosomes.[2,5,6] So, it seems no brainer that salivary exosome serves as the perfect target for finding a biomarker that could enable early oral cancer detection by means of a simple saliva test.

As oral cancer itself is a complex heterogeneous disease, a number of factors should be considered when investigating oral cancer exosomes in saliva. Site of tumour may have profound impact on the route where cancer exosomes enter. For example, comparing a patient with tonsillar tumour whereby its cancer exosomes may not be detectable in the patient's saliva compared to a patient with buccal or tongue tumour. Given the anatomical complexity of the oral compartment, coupled with presumably very low abundance of cancer exosomes at early stages of tumour development, and in a chemically fluctuating salivary environment, the challenges researchers are facing would be analogy to detecting an individual's cells in the sewage system.

The main challenge remains in finding a cancer specific marker(s) that represents early development of oral cancer. Many studies are restricted to comparing normal and clinically visible tumour samples which led to the identification of cancer markers that are not representative and/or detectable at early stages of tumour development. Nevertheless, a recent study has shown a promising outlook if one could identify a cancer exosome-specific marker. The group demonstrated that pancreatic tumour secretes unique cancer exosomes carrying Glypican-1 (GPC1) into the bloodstream which could be used as a biomarker for detecting early pancreatic cancer in patients.[7] However, oral cancer is a highly complex, multi-staged, multi-factorial and highly heterogeneous disease, it is unlikely that it could be represented by a single biomarker throughout tumourigenesis.[8,9] The future of early oral cancer detection studies may lie in longitudinal sampling of individuals (ideally from conception!) to provide comprehensive and progressive clinical record and biological data in the hope to identify a predictive signature(s) indicative of oral cancer development. As for the question whether oral cancer exosomes could be the answer for early oral cancer detection, the answer may lie in the identification of a unique early oral cancer-specific exosomal marker, if there is one.

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