Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor

Perspective on oral exfoliative cytology and COVID-19

WHO has declared novel coronavirus infection (COVID-19) as pandemic diseases due to the spread of the infection across the globe [1]. It is an extremely infective disease characterized by high morbidity and mortality rate [2]. The development of vaccines and drugs is still in the stages of infancy and hence, the best strategy to limit this deadly infection is social distancing, contact tracing and vigorous testing to identify and quarantine the positive cases.

Asymptomatic carrier cases are the major concern for the spread of infection in the community. According to one study, the estimated asymptomatic proportion was 17.9% (95% credible interval (CrI): 15.5–20.2%) [3] and there is a possibility that such patients might not visit the healthcare center for the testing. Moreover, limited financial resources, infrastructure and human resources make it impossible to test every suspected case [4]. These major limitations could exaggerate the spread of infection and hence needs urgent attention.

Angiotensin-converting enzyme II (ACE2) receptor has been identified as the attachment domain for the spike receptor of COVID-19 virus [5]. Once infection enters the host cell, virus replication and shedding lead to relevant clinical manifestations. Intriguingly, attachment of spike receptor also causes depletion of ACE2 receptors, which further leads to various morbidities [6]. Thus, due to changes in the expression, ACE2 expression can be exploited for detection or screening of COVID-19 infection.

Intriguingly, ACE2 receptors have been identified on the stratified squamous epithelium of normal oral mucosal [7]. Literature also supports that oral cavity as one of the routs for the entry of COVID 19 [8]. Thus, oral epithelial cells are the potential targets for initiation and progression of the COVID-19 infection. Exfoliative cytology and brush biopsy is routinely used in oral pathology practice for obtaining oral epithelial cells for investigation. With both the technique, it is possible to retrieve cells from the deeper basilar and supra-basilar location. Thus, it is conceivable to easily retrieve COVID-19 positive epithelial cells from positive patients. This knowledge can be exploited for early detection of infection as well as and development of a suitable disease model.

Exfoliative cytology as COVID-19 detection/screening tool

Apart from the routine staining investigative techniques, immunohistochemistry can be employed on exfoliated cells to identify and quantify various proteins [9]. Protein structures are better preserved in exfoliated cells as compared to formalin-fixed paraffin-embedded tissues. Hence, better sensitivity and specificity can be achieved on exfoliative cytology immunohistochemistry. Immunohistochemistry compatible anti-ACE2 antibodies are easily available with the reputed biotechnology companies. And thus, identification and quantification of the ACE2 receptor on exfoliated cells using immunohistochemistry could be an efficient tool for the identification of asymptomatic cases. Since this technique is less time consuming, economical and easily performed, it can be used for screening populations. Exfoliative cytology samples can also be used for other investigative techniques such as reverse transcription PCR, Western blot analysis, and immunofluorescence. These can be used to further authenticate the proposed premise and reliability of exfoliative cytology as detection and screening tool

Development of COVID-19 disease model

Due to the presence of ACE2 receptors, oral epithelial cells are a potential target for COVID-19 infection. Infected oral epithelial cells are effortlessly obtained from the oral cavity using exfoliative cytology. This is the aptest sample for the generation of the cell-based COVID-19 disease model. Both primary and secondary COVID-19 cell lines can be developed for a more in-depth study of various signaling pathways related to upstream and downstream regulators of ACE2. Moreover, COVID-19 related genomic, epigenomic, proteomics and metabolomics alterations in the host cell can also be studied which will help in better understanding the pathogenesis. This disease model could be employed for future vaccine and drug development against COVID-19.

In conclusion, due existence of ACE2 receptors, oral epithelial cells are a potential target for the COVID-19 virus. Exfoliative cytology is technically less demanding and can be used for retrieving epithelial cells from COVID-19 patients. These positive cells can be exploited for early detection or screening of cases based on the differential expression of the ACE2 receptor using simple immunohistochemistry. Moreover, by using exfoliated cells most suitable disease model in the form of primary or secondary cell lines can be developed for future vaccine and drug development against COVID-19.

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Declaration of Competing Interest

None declared.

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