EDITORIAL

The SARS-CoV-2 Virus could Downregulate Dual Specificity Phosphatase-1 Expression in Oral Cancer: A Plausible Hypothesis that could Explain Oral Cancer Progression in the COVID-19 Pandemic and Post-pandemic Situation

Rajeswari Ramesh[1], Pearlcid Siroraj[2], Saranya Varadarajan[3], Thodur Madapusi Balaji[4], Shankargouda Patil[5]

Abstract

This study explores the downregulation of Dual Specificity Phosphatase-1 (DUSP-1) expression in oral cancer progression during the pandemic and post-pandemic situations.

Keywords: COVID-19, Dual specificity phosphatase-1, Oral cancer, SARS-CoV-2.

The Journal of Contemporary Dental Practice (2022): 10.5005/jp-journals-10024-3334

The SARS-CoV-2 virus has been implicated as the causative organism for the COVID-19 illness that has been doing the rounds affecting the entire human rac.[1] This disease was upgraded as a pandemic by the World Health Organization in 2020.[2] Ever since then, many preventive measures such as the imposition of lockdowns, social distancing protocols, wearing of masks, and vaccination procedures have been devised and implemented at a global level to prevent the spread of the disease. It is known that the COVID-19 illness predominantly spreads through droplet infection and causes severe respiratory distress and pneumonia in some afflicted individuals requiring hospitalization and respiratory support.[3]

It is noteworthy that the SARS-CoV-2 virus enters the human system through certain portals, of which the oral cavity is significant.[1] The expression of ACE-2, the receptor for SARS-CoV-2 virus spike glycoprotein has been demonstrated in the oral cavity.[4] Moreover, there is also evidence linking oral diseases such as oral cancer and periodontal disease to increased risk of viral entry through various molecular mechanisms.[5] About oral cancer, it has been suggested that upregulation of certain mediators such as furin, cathepsin,[5] and EMMPRIN[6] make cancerous tissues more vulnerable to SARS-CoV-2 entry. In this connection, we suggest the importance and possible role that could be played by DUSP-1 that has not previously been explored.

Dual Specificity Phosphatase-1, also called MAPK phosphatase-1 (MKP-1), is an endogenous inhibitor of the MAPK pathway and affords anti-inflammatory effects by dephosphorylating of p38 MAPKs, switching off the pathway.[7] This in turn has several effects such as inhibition of inflammation, anaphylaxis, and tissue destruction.[8] It is noteworthy that DUSP-1 expression is downregulated in cancer progression as demonstrated in animal and human models.[9,10] Interestingly, the recent research has also shown that the SARS-CoV-2 virus could also attenuate DUSP-1 expression.[11] Vital data from an *in silico*, nasopharyngeal swab, and culture-based study from human subjects have demonstrated the inhibitory effect of the SARS-CoV-2 virus on DUSP-1 expression.[11] In the oral cancer scenario, this finding could have several implications as we list hereafter.

[1]Department of Oral and Maxillofacial Pathology, Siroraj Hospital, Thoothukudi, Tamil Nadu, India

[2]Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India

[3]Department of Oral Pathology and Microbiology, Sri Venkateswara Dental College and Hospital, Chennai, Tamil Nadu, India

[4]Tagore Dental College and Hospital, Chennai, Tamil Nadu, India

[5]Department of Maxillofacial Surgery and Diagnostic Sciences, Division of Oral Pathology, Jazan University, Jazan, Saudi Arabia

Corresponding Author: Shankargouda Patil, Department of Maxillofacial Surgery and Diagnostic Sciences, Division of Oral Pathology, Jazan University, Jazan, Saudi Arabia, Phone: +96 6507633755, e-mail: dr.ravipatil@gmail.com

How to cite this article: Ramesh R, Siroraj P, Varadarajan S, *et al*. The SARS-CoV-2 Virus could Downregulate Dual Specificity Phosphatase-1 Expression in Oral Cancer: A Plausible Hypothesis that could Explain Oral Cancer Progression in the COVID-19 Pandemic and Post-pandemic Situation. J Contemp Dent Pract 2022;23(10):963–964.

Source of support: Nil

Conflict of interest: None

It is already proposed that oral cancer patients could be at increased risk for SARS-CoV-2 based on the overexpression of certain markers as previously explained. Now comes a situation where, after the SARS-CoV-2 infection, there could be increased rates of oral cancer progression in the COVID-19 affected patients mediated through DUSP-1 downregulation caused by the SARS-CoV-2 virus. This finding if proven would have large implications in understanding the progression of oral cancer in the current scenario. We have previously demonstrated the implications of lockdown protocols on cancer patient inflow rates in a tertiary cancer care center in India.[12] We at this point reiterate that the SARS-CoV-2 infection has caused multiple impacts which have still not been researched and explored. These impacts could have profound disastrous effects even after the pandemic situation ends. We suggest that clinical studies

to understand oral cancer progression in the pandemic situation in SARS-CoV-2 affected oral cancer patients are required to understand if the deadly virus has enhanced cancer progression through molecular mechanisms such as DUSP-1 inhibition. If fruitful results are obtained from such clinical studies, it should become a clinical mandate to recall and review all cancer patients for progression and metastasis in the post-pandemic situation considering that many cancer patients could have been affected by both symptomatic and asymptomatic forms of SARS-CoV-2 infection and would have been unable to visit hospitals during the lockdown period.

References

1. Herrera D, Serrano J, Roldán S, et al. Is the oral cavity relevant in SARS-CoV-2 pandemic? Clin Oral Investig 2020;24(8):2925–2930. DOI: 10.1007/s00784-020-03413-2.
2. Zhou P, Yang X-L, Wang X-G, et al. Addendum: a pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;588(7836):E6–E6. DOI: 10.1038/s41586-020-2951-z.
3. Thevarajan I, Buising KL, Cowie BC. Clinical presentation and management of COVID-19. Med J Aust 2020;213(3):134–139. DOI: 10.5694/mja2.50698.
4. Xu H, Zhong L, Deng J, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int J Oral Sci 2020;12(1):8. DOI: 10.1038/s41368-020-0074-x.
5. Madapusi Balaji T, Varadarajan S, Rao USV, et al. Oral cancer and periodontal disease increase the risk of COVID 19? A mechanism mediated through furin and cathepsin overexpression. Med Hypotheses 2020;144:109936. DOI: 10.1016/j.mehy.2020.109936.
6. Varadarajan S, Balaji TM, Sarode SC, et al. EMMPRIN/BASIGIN as a biological modulator of oral cancer and COVID-19 interaction: Novel propositions. Med Hypotheses 2020;143:110089. DOI: 10.1016/j.mehy.2020.110089.
7. Caunt CJ, Keyse SM. No TiDual-specificity MAP kinase phosphatases (MKPs) Shaping the outcome of MAP kinase signalling. FEBS J 2013;280(2):489–504. DOI: 10.1111/j.1742-4658.2012.08716.x.
8. Korhonen R, Turpeinen T, Taimi V, et al. Attenuation of the acute inflammatory response by dual specificity phosphatase 1 by inhibition of p38 MAP kinase. Mol Immunol 2011;48(15–16):2059–2068. DOI: 10.1016/j.molimm.2011.06.439.
9. Zhang X, Hyer JM, Yu H, et al. No DUSP1 phosphatase regulates the proinflammatory milieu in head and neck squamous cell carcinoma. Cancer Res 2014;74(24):7191–7197. DOI: 10.1158/0008-5472.CAN-14-1379.
10. Shen J, Zhang Y, Yu H, et al. Role of DUSP1/MKP1 in tumorigenesis, tumor progression and therapy. Cancer Med 2016;5(8):2061–2068. DOI: 10.1002/cam4.
11. Saheb Sharif–Askari F, Saheb Sharif–Askari N, Goel S, et al. SARS-CoV-2 attenuates corticosteroid sensitivity by suppressing DUSP1 expression and activating p38 MAPK pathway. Eur J Pharmacol 2021;908:174374. DOI: 10.1016/j.ejphar.2021.174374.
12. Dillibabu T, Varadarajan S, Balaji TM, et al. COVID-19 pandemic and lock-down protocols: Impact in an indian tertiary cancer center. Oral Oncol 2022;124:105484. DOI: 10.1016/j.oraloncology.2021.105484.