

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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

ELSEVIER

Contents lists available at ScienceDirect

Medical Hypotheses

journal homepage: www.elsevier.com/locate/mehy



2019-nCoV-SARS-CoV-2 (COVID-19) infection: Cruciality of Furin and relevance with cancer



SARS-CoV-2 (covid-19), which emerged from Wuhan, China became a pandemic in the world. Day by day, the number of new cases and deaths in most of the European countries and the United States are increasing as it is decreasing in China [1].

This virus has some similarities and dissimilarities from other coronaviruses. The most divergent one is the Spike (S) protein of the virus which has a furin-like cleavage site and it is cleaved by proteases during virion biosynthesis, as well as during entry into target cells. It is called as "spiky invader" because it has a role in the attachment of the virus to the host cell receptor ACE2, especially the lung alveolar epithelial cells [2]. It is crucial to define the protease cleavage specificity of viruses that impact human or animal health. The proprotein convertase furin is found to facilitate tumour formation and progression [3]. Furin's tissue distribution is ubiquitous and its expression has been confirmed in a large spectrum of cancers, such as lung, head and neck, colon and gynecologic cancers and sarcomas [3]. Furin is thougt to be a pro-oncogenic driver in KRAS and BRAF mutant colorectal cancer [4]. Aberrant expression or activity of furin may result in a variety of disorders such as diabetes, cancer and coronaviruses exploit furin for the activation of their glycoproteins [5]. Since furin is highly expressed in lungs, an enveloped virus that infects the respiratory tract may successfully exploit this convertase to activate its surface glycoprotein [2].

In a same manner, retrovirus's envelope glycoproteins are cleaved by furin and other proprotein convertases (PC). It was also demonstrated that HIV infection induces the expression of some proteins which restrict the trafficking of furin to the golgi where the PC remains inactive [6]. Like HIV virus; this new virus could be carcinogenic.

Interestingly, serum furin levels were found to be lower in patients with HT in the Chinese population [7] and it is also linked with obesity in the same population [8]. Diabetes, hypertension and ischemic heart diseases were the most common comorbidities associated with Covid-19 in the Chinese and Italian population [9,10]. But the fatality rates differ in these two countries [9,10]. These findings make us think that there could be a relationship between furin activities of different populations and the different clinical scenarios of the 2019-nCoV infection

Declaration of Competing Interest

The authors declare that they have no known competing financial

interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mehy.2020.109770.

References

- COVID-19, a pandemic or not? Lancet Infect Dis 2020 Mar 13. pii: S1473-3099(20) 30180-8. doi: 10.1016/S1473-3099(20)30180-8. [Epub ahead of print].
- [2] Coutard B, Valle C, de Lamballerie X, Canard B, Seidah NG, Decroly E. The spike glycoprotein of the new coronavirus 2019-nCoV contains a furin-like cleavage site absent in CoV of the same clade. Antiviral Res 2020;176:104742.
- [3] Jaaks P, Bernasconi M. The proprotein convertase furin in tumour progression. Int J Cancer 2017;141(4):654–63.
- [4] He Z, Thorrez L, Siegfried G, Meulemans S, Evrard S, Tejpar S, et al. The proprotein convertase furin is a pro-oncogenic driver in KRAS and BRAF driven colorectal cancer. Oncogene 2020 Mar 6. doi: 10.1038/s41388-020-1238-z. [Epub ahead of print].
- [5] Braun E, Sauter D. Furin-mediated protein processing in infectious diseases and cancer. Clin Transl Immunol 2019;8(8):e1073.
- [6] Izaguirre G. The Proteolytic Regulation of Virus Cell Entry by Furin and Other Proprotein Convertases. Viruses 2019;11(9):E837.
- [7] He Y, Ren L, Zhang Q, Zhang M, Shi J, Hu W, et al. Serum furin as a biomarker of high blood pressure: findings from a longitudinal study in Chinese adults. Hypertens Res 2019:42(11):1808–15.
- [8] He Y, Ren L, Zhang Q, Zhang M, Shi J, Hu W, et al. Deficient serum furin predicts risk of abdominal obesity: findings from a prospective cohort of Chinese adults. Postgrad Med J 2020 Feb 29. pii: postgradmedj-2019-137422. doi: 10.1136/postgradmedj-2019-137422. [Epub ahead of print].
- [9] Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020 Mar 13. doi: 10.1001/jamainternmed.2020.0994. [Epub ahead of print].
- [10] Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA 2020 Mar 23. doi: 10.1001/jama. 2020.4683. [Epub ahead of print].

Cigdem Usul Afsar Balıkesir University Medical Faculty, Department of Internal Medicine and Medical Oncology, Balıkesir, Turkey