Khiali et al., *BioImpacts*, 2022, 12(3), 291-292
doi: 10.34172/bi.2022.23266
http://bi.tbzmed.ac.ir/

# SARS-CoV-2 and probable lung cancer risk

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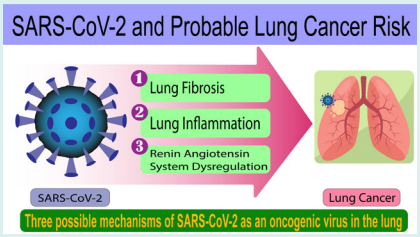
**Article Info**

***Article Type:***
Perspective

***Article History:***
Received: 25 July 2020
Revised: 14 Oct. 2020
Accepted: 2 Nov. 2020
ePublished: 26 Mar. 2022

**Abstract**




The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a global crisis with a growing number of mortalities and morbidities worldwide. Despite performing numerous researches, there are still considerable unrevealed details regarding the long-term complications and post-infection immunity of the coronavirus disease 2019 (COVID-19). Based on pathophysiological features, SARS-CoV-2 may act similarly as an oncovirus in the lung. This letter summarized three possible oncogenic mechanisms of SARS-CoV-2 that may be associated with lung cancer development.

***Keywords:*** COVID-19, SARS-CoV-2, Oncovirus, Lung cancer, Lung fibrosis

As of 14 October 2020, globally, more than 38 million cases of coronavirus disease 2019 (COVID-19) have been confirmed with about 1.1 million deaths. One of the main concerns about COVID-19 is long-term complications.[1] In this paper, we aimed to discuss three possible mechanisms of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as an oncogenic virus in the lung at a glance.

First, long-term lung complications have been reported following infection with SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV).[2-4] A 15-year follow-up of 71 patients with SARS-CoV infection showed chronic involvement of lung tissues with interstitial abnormalities.[2] Das et al, in a study of 36 patients recovered from MERS-CoV infection with a median follow-up of 43 days (ranged from 32-320 days), showed radiographic findings indicating pulmonary fibrosis in about one-third of the patients.[3] Recently, Spagnolo et al presumed pulmonary fibrosis as a long-term complication of COVID-19.[4] Moreover, a lot of evidence has shown a direct link between pulmonary fibrosis and lung cancer due to the common cellular and molecular pathways.[5-7] Accordingly, pulmonary fibrosis is a risk factor for developing lung cancer, and the prevalence of lung cancer in patients with idiopathic pulmonary fibrosis ranges from 2.7% to 48%.[7]

Second, COVID-19 hyper-inflammation and cytokine storm-induced pathologic changes should be considered. The pro-inflammatory cytokines such as interleukin 1 (IL-1), IL-6, and tumor necrosis factor-α (TNF-α) play crucial roles in COVID-19 related hyper-inflammation pathogenesis. Also, these cytokines are involved in the tumor promotion and cell transformation of lung cancer pathogenesis.[8,9] Hyper-inflammation is a critical response by the host from the first stages of cancer development.[9-11] Besides, chronic inflammation has a critical function in tumorigenesis and provides an ideal environment for carcinogenesis.[11]

Third, similar to patients suffering from non-small cell lung carcinoma (NSCLC), a down-regulation of angiotensin-converting enzyme 2 (ACE2) occurs after COVID-19 ensuing. The *ACE2* gene has been confirmed as the functional receptor for SARS-CoV-2 infection with a crucial role in virus entry into the target cell. It degrades angiotensin II (Ang II) and generates angiotensin (1-7).[12,13] Considerable evidence indicated that the renin-angiotensin system (RAS) components including ACE2, Ang (1-7), and Ang II play a key role in malignancies from the early stages. Low levels of ACE2 expression have been demonstrated as an indicator of malignancies and poor prognostic cancers. ACE2 has an inhibitory effect on cancer cell proliferation, metastasis, invasion,

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## Study Highlights

**What is the current knowledge?**

√ Data regarding follow-up of recovered cases and post-infection immunity is rare.

√ Viruses account for about one-fifth of human cancer cases.

**What is new here?**

√ SARS-CoV-2 infection could trigger lung cancer with three possible mechanisms, including pulmonary fibrosis, pulmonary inflammation, and ACE-2 downregulation.

migration, and angiogenesis, especially in NSCLC. Additionally, Ang (1-7) reduces the lung cancer cell proliferation and angiogenesis. [12,14,15] On the contrary, angiotensin II/ angiotensin II type I receptor (AT1R) axis has a regulatory effect on almost every feature of cancer, including angiogenesis, cell proliferation, dissemination, desmoplasia, tumor growth, cancer-related inflammation induction and immunosuppressive milieu formation, and tumor progression.[14, 15]

We hypothesized that SARS-CoV-2 infection could be a trigger for lung cancer. Given the large number of infected individuals and lack of data about recovered cases and post-infection immunity,[16] even a weak association of SARS-CoV-2 infection with lung cancer, the burden of disease in large population would be considerable and therefore it should be considered in public health policy and evaluated in future studies.

**Funding sources**
None to be declared.

**Ethical statement**
There is none to be declared.

**Competing interests**
None.

**Authors' contribution**
All authors are equally contributed to the paper.

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