EDITORIAL | prostate cancer

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COVID-19 and Prostate Cancer, Can Two Negatives Equal a Positive?

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Abstract

This is a letter to the editor on the discussion on COVID-19 and prostate cancer.

Letter to the editor

Prostate cancer is the second leading cause of cancer-related deaths among men in the United States, and one in eight men will be diagnosed with the disease in their lifetime. In 2022, 34,500 American men are estimated to have died of prostate cancer. Current treatment of prostate cancer often involves surgery, radiation, and hormonal therapy [1].

Immunotherapy plays a critical role in many cancer treatments including melanoma, bladder cancer and prostate cancer [1, 2]. Several immunotherapies have been approved by the US FDA for the treatment of melanoma. For bladder cancer, six immunotherapeutic drugs have been approved for clinical use and the BCG vaccine is one of them [2]. The BCG vaccine has been successfully used as an effective treatment for superficial bladder cancer. In fact, its anti-tumor effect is directly associated with an increase immune response of the host and its direct effect on cancer cells [3]. Interestingly, only one immunotherapy has been approved for use in prostate cancer and it is the vaccine called Sipuleucel-T, which is also known as Provenge. This vaccine was found to reduce the risk of death from prostate cancer by 22.5% [4].

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), is a lethal virus that may cause multiple organ system dysfunction. An outbreak of SARS-CoV-2 began in December 2019 and has infected hundreds of millions of people worldwide so far [5]. Meanwhile, this lethal virus may trigger a strong immune response in the host [6]. Thus, it would be very interesting to investigate if SARS-CoV-2 infection could enhance the host's anti-tumor immunity.

In this regard, our lab has investigated if SARS-CoV-2 spike protein has any effect on the growth of prostate cancer and we found that SARS-CoV-2 spike protein reduced the survival of prostate cancer cells. SARS-CoV-2 spike protein was also found to promote apoptosis, while decreasing the proliferation, of prostate cancer cells. The anti-proliferative effect of SARS-CoV-2 spike protein on prostate cancer cells was associated with downregulation of cyclin-dependent kinase 4. The increased apoptosis of prostate cancer cells induced by SARS-CoV-2 spike protein was associated with the upregulation of Fas ligand [7]. We further expanded our study to investigate if SARS-CoV-2 spike protein has any effect on expression of costimulatory molecules. To our surprise, it was found that SARS-CoV-2 spike protein caused a downregulation of ICAM-2 but an upregulation of ICOSL [8]. Our studies suggest that SARS-CoV-2 spike protein may not only inhibit growth of prostate cancer, but also modulate the expression levels of costimulatory molecules which are critical for immune response.

Consistent with our studies, another study, while not dealing with prostate cancer specifically, found that SARS-CoV-2 spike protein induced cell death in lung cancer cell lines [9]. Furthermore, this study showed that the size of lung cancer was reduced when SARS-CoV-2 spike protein was intranasally injected into mice with lung cancer. Thus, this study demonstrates that

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SARS-CoV-2 spike protein may be capable of inhibition of growth of lung cancer both in vitro and in vivo [9]. Moreover, SARS-CoV-2 has been recently found to possibly enhance anti-tumor response when used simultaneously with the BCG vaccine [10].

Conversely, other studies have shown that SARS-CoV-2 spike protein has induced growth in certain types of cancers such as breast cancer and lung cancer. It has been cited that spike protein from the variant of SARS-CoV-2 caused a stronger level of epithelial-mesenchymal transition (EMT) within breast tissue and EMT levels have an association with cancer resistance to apoptosis [11]. This study further revealed that the variant of SARS-CoV-2 activated transcription factor NF-κB, resulting in breast cancer survival and progression [11]. In another study, SARS-CoV-2 has additionally been shown to play an important role in breast cancer metastasis by the upregulation of Snail, a transcriptional repressor responsible for cancer progression [12]. These studies suggest SARS-CoV-2 spike protein/SARS-CoV-2 infection may favor development, growth or metastasis of cancer.

In short, the conflicting studies suggest that the relationship between SARS-CoV-2 spike protein/SARS-CoV-2 infection and prostate cancer is still a mystery. Thus, it seems too early to say the two negatives equal a positive in regard of COVID-19 and prostate cancer. More research is needed to adequately address the clinical relevance between SARS-CoV-2 spike protein/SARS-CoV-2 infection and prostate cancer. These future studies will hopefully improve prognosis of prostate cancer.

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None.

Ethical policy

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study. Approval from institutional ethical committee was taken.

Availability of data and materials

All data generated or analysed during this study are included in this publication.

Author contributions

Yujiang Fang initiated the idea. Cade C. Lewis, Aidan J. Heslin and Cole R. Formslag wrote the draft. Yujiang Fang and Wakefield made critical revision to the draft.

Competing interests

The authors declare no conflict of interest.

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