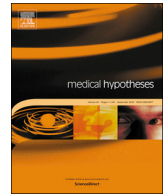




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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.



## Covid-19, TMPRSS2, and whether androgen regulation affects pandemic virus gender incidence and age distribution of disease



The likely reason that Covid19 has male predominance is that it appears to be an androgen driven pathogen. SARS-COV2, coronavirus spike protein undergoes proteolytic activation by Transmembrane Serine Protease 2 (TMPRSS2), to enable SARS-COV-2 to utilize the ACE2 receptor for cellular entry [1].

TMPRSS2 is highly expressed primarily in prostate epithelium, high-grade prostate cancers and is androgen regulated [2].

Androgen regulation may explain the paucity of cases of Covid19 in preadolescents, since they don't have the androgens to prime the TMPRSS2 cell surface protease.

Covid19 has affected men, smokers and the elderly more than other groups.

Smoking appears to increase the ratio of androgens to estrogen, which may prime the TMPRSS2 cell surface protease [3].

Possibly, benign prostatic hypertrophy being more common in elderly men, may contribute to increased TMPRSS2 as well, leading to increased severity of viral infection in the older age group.

Inhibitors of TMPRSS2 include bromohexine [2] and Camostat [1].

Inhibiting androgens could also be another approach to managing the Covid19 virus.

TMPRSS2 is also a host cell factor necessary for viral spread of H1N1 and H3N2 influenza A viruses, indicating a similar phenomena may occur with other pandemic viruses, since male predominance has been observed in pandemic influenza A [4].

No Grant Support.

### 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.2020.109773>.

### References

- [1] Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrier T, Erichsen S. et al. SARS-COV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell* [Online ahead of print].
- [2] Lucas JM, Heinlein T Kim, Hernandez SA, Malik MS, True LD, et al. The androgen-regulated protease TMPRSS2 activates a proteolytic cascade involving components of the tumor microenvironment and promotes prostate cancer metastasis. *Cancer Discov* 2014;4(11):1310–25.
- [3] Cochran CJ, Gallicchio L, Miller SR, Zacur H, Flaws JA. Cigarette smoking, androgen levels, and hot flashes in midlife women. *Obstet Gynecol.* 2008;112(5):1037–44. <https://doi.org/10.1097/AOG.0b013e318189a8e2>.
- [4] Hatesuer B, Bertram S, Mehnert N, Bahgat M, Nelson PS, Pohlman S, et al. Tmprss2 is essential for influenza H1N1 virus pathogenesis in mice. *Plos Pathog* 2013;9(12):e1003774 <https://doi.org/10.1371/Journal.ppat.1003774>. Published online 2013 Dec 5.

Steven R. Brenner  
8300 Delmar, Apt. 406, University City, MO 63124, USA  
E-mail address: [SBren20979@aol.com](mailto:SBren20979@aol.com).