

2019-nCoV Literature Situation Report (Lit Rep) February 3, 2020

Key Takeaways

- Implications of 2019-nCoV recognition of the human cell receptor angiotensin converting enzyme II (ACE2) is a hot topic, with researchers considering everything from potential therapies to novel transmission mechanisms based on this information.
- Accurate estimates of the basic reproductive number for 2019-nCoV are difficult to calculate given the current uncertainties in the developing epidemic. A recent paper using a pooled estimate found an estimated R_o of 3.1, with likely values ranging from 2.1-5.7.

Transmission

- H Zhang, *et al* propose a potential digestive system route of transmission, based on gene expression data related to angiotensin converting enzyme II (ACE2) in human tissues from lung, esophagus, stomach, ileum, and colon. Among ACE2-expressing cells in the tissue types assessed, ACE2 expression was found to be highest in the ileum and colon.
- ACE2 appears to be important in cellular mechanisms of infection by 2019-nCoV and other coronaviruses (e.g., SARS). Patients with 2019-nCov can have GI symptoms. Fecal transmission of SARS CoV was a neglected risk during the SARS epidemic.
- Epidemiologic support for the potential role in transmission is not provided. Zhang H, et al. (Jan 31, 2020). The digestive system is a potential route of 2019-nCov infection: a bioinformatics analysis based on single-cell transcriptomes. Pre-Print. https://www.biorxiv.org/content/10.1101/2020.01.30.927806v1

Modelling and Prediction

- SW Park, *et al.* assess preliminary basic reproductive number (R₀) estimates in several reported modeling approaches. They identify improved information on generation interval (time from when an individual is infected to when they infect another individual) as a key parameter to improve R₀ estimates.
- The pooled estimate of R₀ constructed using their defined approach is 3.1, with a 95% confidence interval of 2.1-5.7. This wide confidence interval likely reflect uncertainties in the currently available epidemic information.

Park SW, et al. (Feb 2, 2020). Reconciling early-outbreak preliminary estimates of the baseline reproductive number and its uncertainty: a new framework and applications to the novel coronavirus (2019-nCoV) outbreak. Pre-Print. https://www.medrxiv.org/content/10.1101/2020.01.30.20019877v2

Origins, Reservoir, and Virus Background

- M Hoffman, *et al.* found that 2019-nCoV uses the same receptor, ACE2, used by SARS viruses to invade host cells; and that another cellular protease may be part of the process, presenting another potential target for therapy. They also consider how similarities with SARS may translate to 2019-nCoV transmission and pathogenicity.
- Sera from a convalescent SARS patient partially inhibited 2019-nCov entry into target cells *in vitro*.
- Extrapulmonary SARS-CoV spread in ACE2-expressin tissues was observed, and should be assessed for 2019-nCoV. The role of an additional protein (TMPRSS2) in 2019n-CoV entry may affect these comparisons.

Hoffman M, et al. (31 Jan, 2020). The novel coronavirus 2019 (2019-nCoV) uses the SARS-1 coronavirus receptor ACE2 and the cellular protease TMPRSS2 for entry into target cells. Pre-Print. https://www.biorxiv.org/content/10.1101/2020.01.31.929042v1

Clinical Characteristics

- This article provides additional information on a father-son pair from Vietnam, reported earlier
- The father was a 65 year-old with a history of hypertension, type 2 diabetes, coronary heart disease, and lung cancer.
 - *o* He became ill with fever on 17 January, 2020, and was admitted to hospital through the ED on 22 January. His condition was improving on and after 26 January.
 - *o* He tested positive (RT-PCR) for 2019-nCoV from a throat swab.
 - *o* Chest x-ray showed left lung upper lobe infiltrate, which progressed for a few days and started to resolve in hospital
 - *o* He was treated empirically with antivirals and broad-spectrum antibiotics (unspecified); and on supplemental oxygen due to increasing hypoxia and dyspnea.
- The son was an otherwise-healthy 27 year old with dry cough, fever, loose stools, and vomiting before admission, starting on 20 January (estimated incubation period, 3 days).
 - *o* He presented at the hospital on the same day as his father (22 Jan) and had normal chest x-ray and labs. He was listed as stable from 23 January on.
 - He also tested positive (RT-PCR) for 2019-nCoV from a throat swab.
 Phan LT, et al. (2020). Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. NEJM. DOI: 10.1056/NEJMc2001272

In addition to the articles described here, there are several editorials, commentaries, and technical (e.g., drug trial) papers available to view via the <u>2019-nCoV SharePoint site</u> along with previous Lit Reps.