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.

SARS-CoV-2 infection in conjunctival tissue

Authors' reply

We thank Yu-Chi Liu and colleagues for their correspondence on our study[1] on the tropism of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in ex-vivo cultures of human ocular and respiratory tissues, in which they highlight three key points. The first point involves the dynamic nature and antimicrobial properties of the tear film, and the challenge of mimicking these properties in model systems. With regards to the antiviral effects of tear fluid, it is relevant to note that other enveloped viruses (eg, herpes simplex virus type 1 [HSV-1][2] and the H7N7 avian influenza A virus[3]) and non-enveloped viruses (eg, enteroviruses and adenoviruses)[4] can effectively infect the conjunctiva (leading to conjunctivitis), and that the comparative replication of HSV-1[5] and pandemic H1N1 influenza viruses[6] has also been shown in ex-vivo explant cultures of human ocular tissue, even in the presence of the same antiviral and viral clearance mechanisms. As the authors themselves note, conjunctivitis has been reported in patients with SARS-CoV-2, with a prevalence ranging from 0·9% to 31·6%. The fact that the number of conjunctival samples positive for SARS-CoV-2 RNA has been low does not preclude the possibility that conjunctival infection could indeed occur, and our study[1] supports such a possibility. The most notable finding in our study was that SARS-CoV-2 replicated in and infected ex-vivo human conjunctival explant cultures more extensively than SARS-CoV under the same standardised experimental settings.[1]

Regarding the second point about the apparent absence of angiotensin-converting enzyme 2 (ACE2) receptors on the conjunctival tissue, we provide clear evidence of virus infection in ex-vivo conjunctival tissue.[1] We argue that the apparent absence of ACE2 receptors on the conjunctival mucosa needs to re-investigated, and if this receptor is confirmed to be absent, then alternative receptors for the virus need to be sought.

With regards to the third point about the immunohistochemistry findings, the viral antigen-positive cells were, in our view, mainly the epithelial cells on the surface and not the stromal cells, as assessed by a clinical pathologist and an ophthalmology specialist. Nevertheless, a logical next step for the follow-up study would be to analyse the conjunctiva tissues at multiple timepoints to understand how the virus enters the conjunctiva and proliferates, although this will highly depend on the availability of conjunctival tissue.

In summary, our finding that the replication of SARS-CoV-2 is higher than SARS-CoV in a physiologically relevant human conjunctival explant culture model, prompts further awareness and research into this route of transmission, which has been documented clinically.

We declare no competing interests.

*Kenrie PY Hui, Malik Peiris, JM Nicholls, *Michael CW Chan*
mchan@hku.hk

School of Public Health (KPYH, MP, MCWC) and Department of Pathology (JMN), Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Special Administrative Region of Hong Kong, China

1 Hui KP, Cheung M, Perera R, et al. Tropism, replication competence, and innate immune responses of the coronavirus SARS-CoV-2 in human respiratory tract and conjunctiva: an analysis in ex-vivo and in-vitro cultures. *Lancet Respir Med* 2020; **8:** 687–95.

2 Kaye S, Choudhary A. Herpes simplex keratitis. *Prog Retin Eye Res* 2006; **25:** 355–80.

3 Fouchier RA, Schneeberger PM, Rozendaal FW, et al. Avian influenza A virus (H7N7) associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. *Proc Natl Acad Sci USA* 2004; **101:** 1356–61.

4 Jhanji V, Chan TC, Li EY, Agarwal K, Vajpayee RB. Adenoviral keratoconjunctivitis. *Surv Ophthalmol* 2015; **60:** 435–43.

5 Alekseev O, Tran AH, Azizkhan-Clifford J. Ex vivo organotypic corneal model of acute epithelial herpes simplex virus type I infection. *J Vis Exp* 2012; e3631.

6 Chan MC, Chan RW, Yu WC, et al. Tropism and innate host responses of the 2009 pandemic H1N1 influenza virus in ex vivo and in vitro cultures of human conjunctiva and respiratory tract. *Am J Pathol* 2010; **176:** 1828–40.