COVID-19 in vitro studies: Use the right cell line

In vitro studies during the early stages of the COVID-19 pandemic demonstrated an inhibitory effect of (hydroxy)chloroquine on SARS-CoV-2 entry into host cells (using human cell lines). Based on such results and the anti-viral effect (hydroxy)chloroquine has against other viruses such as Zika and Dengue viruses, (hydroxy)chloroquine was tested as a potential treatment for COVID-19. Despite, studies suggesting a potential beneficial effect of (hydroxy)chloroquine against COVID-19, targeted update of (hydroxy)chloroquine use available on the WHO webpage concludes that:

“The current evidence on the efficacy and safety of hydroxychloroquine for the treatment of COVID-19 is limited and of very low certainty.”

Source: Hoffmann et al., 2020

A recent article by Hoffman et al., aimed to determine if (hydroxy)chloroquine does inhibit SARS-CoV-2 infection in vitro using TMPRSS2-expressing cell lines. TMPRSS2 is a human cellular protease that SARS-CoV-2 uses to facilitate viral entry into host cells. Hoffman et al., demonstrated that (hydroxy)chloroquine inhibited viral entry in Vero (kidney-derived) cell-lines that did not express TMPRSS2, but had no inhibitory effect on Vero cells-lines that expressed TMPRSS2. Additionally, (hydroxy)chloroquine had limited effect on SARS-CoV-2 entry into TMPRSS2-expressing lung cell-lines. Thus providing sufficient evidence as to why (hydroxy)chloroquine may not have had an effect against COVID-19 in humans.
Results presented by Hoffmann et al., emphasise the need for performing *in vitro* studies that mimic necessary aspects of the human microenvironment, including expression of proteins that are necessary for viral entry.

Hoffman *et al.*, 2020. **Chloroquine does not inhibit infection of human lung cells with SARS-CoV-2.** *Nature*

*Summary by Cheleka Mpande*