In-vivo models to assess co-infection of SARS-CoV-2 and Influenza virus

Background

It is foreseeable that individuals may experience simultaneous or sequential exposure to SARS-CoV-2 and seasonal influenza virus in the near future.

The recorded incidence of co-infections of respiratory viruses is relatively low, and, it is possible that co-infection will have little impact on the course of disease in the majority of cases; however, there is potential for exacerbation of disease in some individuals.

Of note, in historical studies of influenza challenge in the ferret model performed at PHE Porton Down, deep sequencing of nasal wash samples has revealed the presence of naturally occurring alpha coronaviruses. There was no significant exacerbation of disease observed in these studies.

Animal models

The ferret is commonly used to study the pathogenesis of clinical isolates for seasonal influenza viruses with an array of reliable endpoints that include, upper respiratory tract (URT) virus shedding, weight and temperature change, and for some strains (H1N1) mild lung pathology.

In general, this is a non-fatal, mild challenge model.

PHE has recently characterised the ferret as a model for SARS-CoV-2 infection with endpoints of URT virus shedding and mild transient lung pathology.

As both viruses are able to infect URT and LRT tissues a co-infection study using the ferret model makes practical sense.

Proposal

As it is not sensible to assume that any particular ordering of infections would be most likely to occur should seasonal influenza and SARS-CoV2 be coincidentally circulating in the human population we suggest that it would be prudent to perform sequential challenge studies for both virus combinations with controls for both viruses. That is:

1. Infect IN 1m SARS-CoV-2 day 0. Day 2 challenge IN H1N1 (1 ml for immediate access to lungs). Cull Day 6-8[1]. Endpoints; weight/temp/symptoms URT virus shedding and lung pathology
2. Infect IN 1ml H1N1 day 0. Day 2 challenge SARS-CoV-2 IN 1ml volume. Day 6-8. Endpoints; weight/temp/symptoms URT virus shedding and lung pathology
3. SARS-CoV-2 only IN challenge control
4. H1N1 only IN challenge control

[1] The timing of the challenges is related to the transient nature of the virus infections in the URT and the ability to decipher impact on lung pathology.