SARS virus infection of cats and ferrets

There is now a choice of animal models for testing therapies against the human virus.

The reservoir of the coronavirus isolated from patients with severe acute respiratory syndrome (SARS)[1,2] is still unknown, but is suspected to have been a wild animal species. Here we show that ferrets (*Mustela furo*) and domestic cats (*Felis domesticus)* are susceptible to infection by SARS coronavirus (SCV) and that they can efficiently transmit the virus to previously uninfected animals that are housed with them. The observation that these two distantly related carnivores can so easily be infected with the virus indicates that the reservoir for this pathogen may involve a range of animal species.

Serological and virological studies have indicated that Chinese ferret badgers (*Melogale moschata*), masked palm civets (*Paguma larvata*) and raccoon dogs (*Nyctereutes procyonoides*) can be infected with a virus that is very similar to SCV (ref. 3). Domestic cats living in the Amoy Gardens apartment block in Hong Kong, where more than 100 residents contracted SARS last year, were also found to be infected with SCV.

To test the susceptibility of domestic cats and ferrets to SCV infection, we inoculated them intratracheally with 10^6 median tissue-culture infectious dose units ($TCID_{50}$), which we obtained from patient 5688 (who died from SARS) and then passaged four times on Vero 118 cells[4,5] *in vitro*. We then took nasal, pharyngeal and rectal swabs from the animals on different days post-infection (p.i.). Four animals from each group were killed at 4 days p.i. and were necropsied according to a standard protocol[4,5].

No clinical signs were seen in SCV-inoculated cats, whereas three out of six ferrets became lethargic from days 2–4 p.i. and one of these ferrets died 4 days p.i. All cats (Fig. 1a) and ferrets (Fig. 1b) shed SCV from the pharynx, starting at 2 days p.i. and continuing until days 10 and 14, respectively, as demonstrated by polymerase chain reaction with reverse transcription (RT–PCR)[5]. The virus was isolated[4,5] from all pharyngeal swabs taken on days 2–8 p.i. and from nasal swabs taken from two cats on days 4 and 6 p.i. SCV was not detected in nasal swabs from ferrets or in rectal swabs from cats or ferrets.

Infection of the respiratory tract was evident in all animals tested: SCV was isolated from the trachea and lungs (see supplementary information). Quantification of the viral titres in lung homogenates revealed relatively low SCV titres (geometric mean ± s.d.) in the lungs of SCV-inoculated cats ($1 \times 10^3 \pm 0.51$ $TCID_{50}$ ml^{-1}) compared with those in ferrets ($1 \times 10^6 \pm 0.70$ $TCID_{50}$ ml^{-1}). Histologically, SCV infection was associated with pulmonary lesions similar to those seen in SCV-infected macaques[4,5], except that they were milder, particularly in SCV-infected cats, and did not feature syncytia.

In the gastrointestinal and urinary tracts, SCV was detected by RT–PCR (see supplementary information). Follow-up of the remaining SCV-inoculated animals ($n = 2$ per group) revealed that they had all seroconverted[5] by 28 days p.i. (neutralizing antibody titres of 40–320). Two attempts to infect suckling mice through intracerebral inoculation failed.

Non-inoculated cats (Fig. 1c; $n = 2$) and ferrets (Fig. 1d; $n = 2$) that were housed with the inoculated cats and ferrets, respectively, became infected with SCV: viral titres gradually increased from 2 days p.i. onwards, peaking at days 6–8 p.i. Neither of the cats showed clinical signs of infection, but both had seroconverted by day 28 (they had virus-neutralizing antibody titres of 40 and 160, respectively). Both ferrets were lethargic and developed conjunctivitis; they died on days 16 and 21 p.i. We established by pathological examination that the main lesions in both animals were marked hepatic lipidosis and emaciation. There was no evidence that either of these animals died from SCV-associated pneumonia, although SCV was isolated from post-mortem lung specimens of one animal.

Our results show that ferrets and domestic cats are susceptible to experimental infection by SCV, and that the virus is efficiently transmitted to animals living with them. These species might therefore be useful as animal models to test antiviral drugs or vaccine candidates against SARS.

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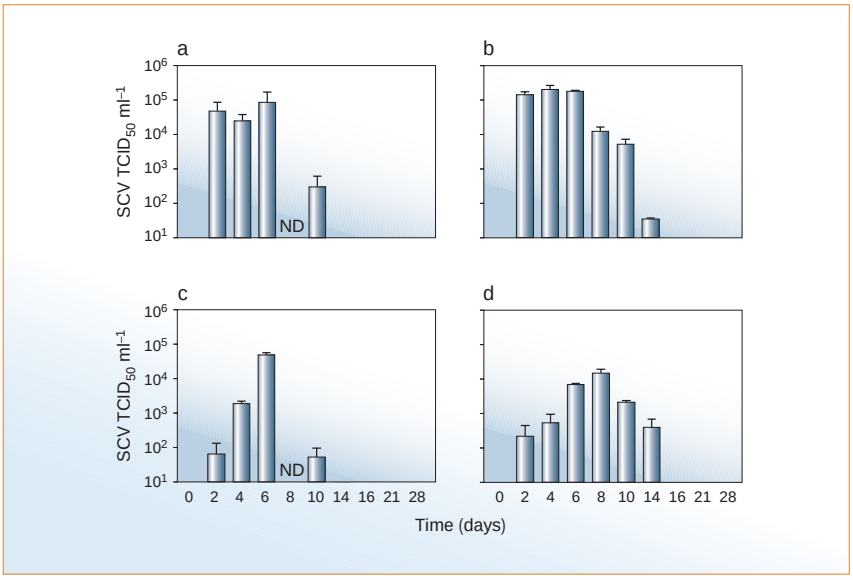

Figure 1 Daily excretion of SARS coronavirus (SCV) in ferrets and domestic cats after inoculation with the virus or exposure to infected animals. **a, b,** SCV titres per ml from cats (**a**) and ferrets (**b**) ($n = 6$ of each) that had been inoculated with SCV through the respiratory route. Four animals from each group were killed on the fourth day after infection, and two were kept until day 28. **c, d,** SCV titres from non-inoculated cats (**c**) and ferrets (**d**) ($n = 2$ of each) that had been housed with inoculated cats and ferrets, respectively. SCV excretion was quantified in pharyngeal swabs by using reverse transcription with the polymerase chain reaction, and was compared to a titrated SCV standard. ND, not determined.