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.

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COVID-19 vaccination in animals: A strategy for combating the global outbreak

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Dear Editor,

The transmission of viruses among different species has caused great loss to public health and global economy in the past several decades. According to data from the United States Agency for International Development, nearly 75% of emerging or re-emerging infectious diseases in the last century have originated from animals, such as human immunodeficiency virus, Ebola virus, H5N1 avian influenza virus, and H1N1 swine influenza virus (USAID, https://www.usaid.gov/news-information/fact-sheets/emerging-pandemic-threats-program). Strikingly, all pathogenic human coronaviruses (hCoVs) have originated from animals [1–3] (Fig. 1). Since the coronavirus disease 2019 (COVID-19) pandemic, scientists have considered the impact of the SARS-CoV-2 virus on pets, livestock, and wild animals. Recent studies have shown that various animals can be infected with severe acute respiratory syndrome CoV-2 (SARS-CoV-2) [4]. Animals infected under experimental conditions include cats, ferrets, hamsters, non-human primates, minks, tree shrews, fruit bats, and rabbits, indicating that these species are susceptible to SARS-CoV-2 infection [5,6].

Many natural infections have also occurred in animals [7]. SARS-CoV-2 RNA has been detected in dogs in the United States and Hong Kong [8,9]. Cats have tested positive for infection via reverse transcription-polymerase chain reaction in the Netherlands, France, Hong Kong, Belgium, Spain, and the United States. In addition, SARS-CoV-2 has been detected in tigers and lions in a zoo in New York [10,11]. SARS-COV-2 antibodies have been detected in the sera of cats in Italy, the Netherlands, and Wuhan, China. SARS-CoV-2 mutations in mink infections have been discovered in Denmark, the Netherlands, the United States, and Spain. Mink farms in the Netherlands have reported human-to-mink and mink-to-human transmission, which poses a high risk of cross-species transmission of SARS-CoV-2 [1–3,5]. Animal-to-human transmission of SARS-CoV-2 was also reported in Hong Kong, wherein the SARS-CoV-2 Delta variant (AY. 127) was transmitted from pet hamsters to humans [12]. The discussion on wildlife infection may lead to disputes regarding evacuation. Pet infection may lead to animal-to-animal or animal-to-human transmission, increasing the possibility of cross-species transmission of the virus and virus mutations. The intermediate host of SARS-CoV-2 is still unclear; based on mutations in the virus, once a certain animal becomes a mixing vessel, the resulting infection may become uncontrollable and unpredictable. In view of the prolonged COVID-19 pandemic, the range of susceptible animals may continue to expand, coupled with the fact that animals themselves can be infected with specific coronaviruses, which increases the possibility of animals serving as mixing vessels to promote viral mutation. Globally, apart from clinical trials on COVID-19 vaccines for minks and cats in Russia [13], research and development on SARS-CoV-2 vaccines for animals are rare. Therefore, to prevent animals from becoming mixing vessels for the virus, it is important to develop animal-oriented vaccines against SARS-CoV-2 [14].

Newcastle disease virus (NDV) is a fast-replicating virus prevalent in all avian species. It causes severe contagious disease in chickens and is a natural host range-restricted virus in other species, in which NDV infection does not cause any disease symptoms [15]. NDV strains vary widely in virulence. Naturally occurring low-virulence NDV strains, such as LaSota and B1, are widely used as live attenuated vaccines in the poultry industry and other animal vaccines; thus, they represent ideal vector candidates for development of animal vaccines against SARS-CoV-2 [15,16]. Warner et al. [17] have engineered recombinant Newcastle disease virus (NDV) vectors expressing the full-length SARS-CoV-2 spike protein (NDV-FLS). They used NDV-FLS for immunization of Syrian hamsters that showed a robust SARS-CoV-2-neutralizing antibody response, suggesting that NDV-vectored vaccines represent a viable option for protection against COVID-19.

The vaccination of susceptible animal species, such as cats, minks, deer, and great apes (Table 1), is essential for public health, and the successful elimination of SARS-CoV-2 will only be possible by controlling transmission in all susceptible animal species. Eliminating the spread of the virus between animals will not only help prevent re-emergence of viruses in humans but also prevent emergence of novel variants such as the SARS-CoV-2 mink variant at the human-animal interface, facilitating successful prevention and control of the

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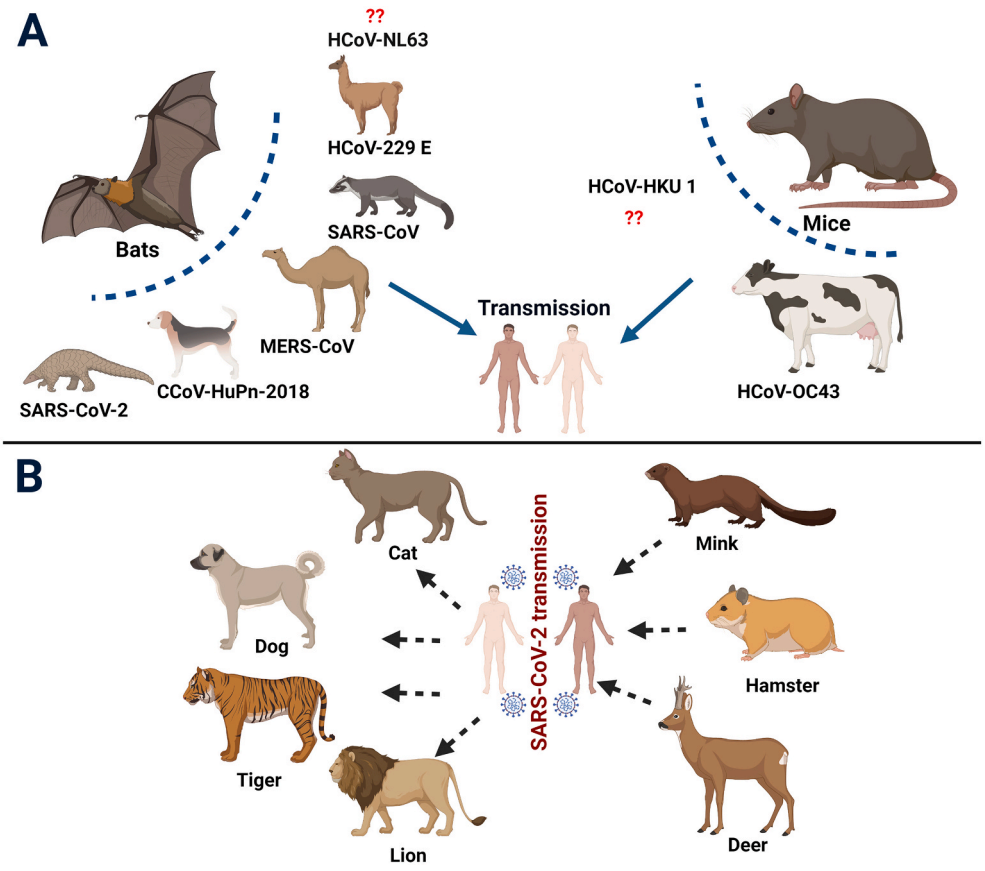

Fig. 1. A. The figure represents the coronaviruses able to infect humans from animals. Bats and mice are the origins of most CoVs infecting humans. These viruses transmit to humans through intermediate hosts; unidentified (e.g. HCoV-NL63 and HCoV-HKU1) and identified (e.g. camel for MERS and civet cats for SARS-CoV). B. The figure shows examples of the reported SARS-CoV-2 transmission from human to animal and vice versa.

Table 1
Examples of animal COVID-19 vaccines used in domestic and wild animals.

Animal vaccine	Description	Target animals
Carnivac-Cov (inactivated vaccine) March 2021	The first COVID-19 vaccine for animals developed by Russia have been shown to elicit robust responses in animals vulnerable to SARS-CoV-2 infection such as dogs, cats, foxes, and minks. It contains an inactivated SARS-CoV-2 virus strain. Vaccination with Carnivac-Cov induced immunity that lasted for at least six months after the vaccination	Dogs, cats, foxes, and minks
LinearDNA™ COVID-19 vaccine	LinearDNA™ ("linDNA") vaccine encoding the RBD domain of SARS-CoV-2. linDNA developed through a joint effort between Applied DNA Sciences (United States) and EvviVax (Italy). Clinical trials showed that the vaccine is safe and immunogenic and support the development of vaccines for preventing viral spread in susceptible species, especially those in close contact with humans. Recently, a linearDNA vaccine was successfully elicited neutralizing antibodies and cellular immunity against SARS-CoV-2. LineaRx announced the successful expression *in vitro* of its linDNA SARS-CoV-2 vaccine candidate encapsulated within lipid nanoparticles (LNP). The linDNA-LNP vaccine will be used in upcoming *in vivo* animal studies to assess the performance of linDNA-LNP vaccines and will inform the final design of the Company's lead veterinary asset, a linDNA-LNP canine lymphoma vaccine candidate.	Domestic cats (Now is reported to be focused on inoculating mink instead)
Zoetis vaccine July 2021	The captive orangutans and bonobos at the San Diego Zoo in the United States of America became the first non-human primates to receive an experimental COVID-19 vaccine developed specifically for animals by the veterinary pharmaceutical company Zoetis. It has been authorized for experimental use on a case-by-case basis by the United States Department of Agriculture (USDA).	Dogs and cats, minks
Ancovax June 2022	India's first COVID-19 vaccine for animals. It contains an inactivated SARS-CoV-2 (Delta) antigen capable of neutralizing both Delta and Omicron variants	Dogs, lions, leopards, mice, and rabbits

pandemic. Trials for designing and developing an oral vaccine applied to a foodstuff favored by the target species and distributed in places where animals are likely to consume it could be a promising strategy.

Ethical approval

This article does not require any human/animal subjects to acquire such approval.

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Author contribution

Om Prakash Choudhary: Conceptualization, Data Curation, Writing - Original Draft, Writing - review & editing. **Priyanka**: Conceptualization, Writing - Original Draft, Writing - review & editing. **AbdulRahman A. Saied:** Data Curation, Writing - Original Draft, Writing - review & editing. All authors critically reviewed and approved the final version of the manuscript.

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Guarantor

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Data statement

The data in this correspondence article is not sensitive in nature and is accessible in the public domain. The data is therefore available and not of a confidential nature.

Declaration of competing interest

All authors report no conflicts of interest relevant to this article.

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