

MERS vaccines advance, but will humans or camels get the job?

A newly identified illness first found in Saudi Arabia in 2012 has since claimed at least 554 lives, including 36 deaths confirmed by the World Health Organization in an outbreak that began in South Korea in May of this year. The disease, known as Middle East respiratory syndrome (MERS) is caused by a type of coronavirus, one of a large family of viruses that includes those responsible for severe acute respiratory syndrome (SARS) and the common cold. “Although it has been three years since the emergence of MERS in humans was recognized, the global community remains within the grip of this emerging infectious disease,” the WHO wrote in a statement issued on 3 September.

It is not just humans who are infected. Last month, Saudi Arabia’s Ministry of Agriculture announced that as many as 7,700 of the country’s camels—around 3% of the 233,000 camels that it says reside there—are infected with the MERS coronavirus. In parts of the Middle East, however, the infection rate is above 95%, according to tests that can detect antibodies generated against the MERS virus (*Emerg. Infect. Dis.* 20, 552–559, 2014).

Infected camels seem to be able to transmit the pathogen to humans (*Emerg. Infect. Dis.* 20, 1999–2005, 2014). “Dromedary camels are the source, and you see continuous introduction from that source in the human population,” says Vincent Munster, chief of the Montana-based Virus Ecology Unit, part of the US National Institute of Allergy and Infectious Diseases’ Laboratory of Virology. Given that camels are a source of infection, Munster says, efforts should focus on minimizing the spread of the virus in these animals. Now that scientists have made strides toward vaccine development against the virus, the question is whether immunization programs should focus on inoculating humans or camels.

Shots at success

Vaccines for MERS have not yet reached human trials, but early stage research has offered signs of promise in animal studies. In May, scientists reported that modifying a vaccinia Ankara virus to produce a spike glycoprotein found in the MERS coronavirus could induce mice to produce antibodies that fight MERS. The modified virus also protected rodents from infection with the pathogen (*J. Virol.* 89, 8651–8656, 2015). Two months later, another group elicited MERS coronavirus–neutralizing antibodies in both mice and rhesus macaques by first administering an immunization that incorporated a DNA plasmid vector expressing



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Worth a shot? Camels may get vaccinated.

the full-length spike protein of the virus, and then following it with a booster consisting of the S1 subunit of that protein (*Nat. Commun.* 6, 7712, 2015).

In August, a different team offered evidence that a synthetic DNA vaccine encoding the MERS spike protein showed promise in mice, rhesus macaques and, crucially, camels (*Sci. Transl. Med.* 7, 301ra132, 2015). Although the study included only three camels, all of them had some antibodies against the spike protein when examined 11 weeks after immunization, and two showed robust levels of neutralizing antibodies after vaccination. Ideally, research will produce MERS vaccines for humans as well as camels, says David B. Weiner, one of the study’s authors and a molecular immunologist at the University of Pennsylvania’s Perelman School of Medicine in Philadelphia. “Camels—particularly juvenile camels—represent an important part of the transmission cycle, so vaccination in this population could play an important role in breaking the human transmission cycle,” Weiner says. “However,” he adds, “it’s also important to have an effective human vaccine to protect persons in the case of outbreaks.”

But with limited resources, scientists are weighing whether to prioritize vaccine development in camels or humans. One thing that camels have going for them is the likely easier drug approval path. There are looser safety standards for livestock vaccines than for those given to humans, generally speaking. “It’s easier regulatory-wise to make an animal vaccine than a human vaccine,” explains Matthew Frieman, an immunologist at the University of Maryland School of Medicine.

Frieman adds that whereas in outbreaks of other diseases, animals that harbor dangerous virus are culled on a massive scale, this is unlikely to happen to camels. Countries such as Saudi Arabia use camels for everything from transportation to milk and meat. The animals have religious significance, and are worth many thousands of dollars. “They are not going to kill all the camels,” Frieman says. “They rely on them too much.” The value that the Saudi society ascribes to these animals was evident, for example, in a social media campaign last year, in which people made videos of themselves kissing camels—a way of protesting restrictions the Saudi government had put forth asking people to wear masks around the animals.

Vulnerable populations

Vaccinating humans for MERS will not be straightforward. Munster notes that many of the people who are most vulnerable to MERS have compromised immune systems or are already sick, making them poor candidates to receive a vaccine.

But there are also reasons to prioritize a human vaccine. Studies have suggested that human-to-human transmission of the virus can take place in hospital settings, and the virus may mutate in a way that causes it to become more infectious as it passes between people. “The data so far—which is remarkably limited—is that it is not mutating to become more infectious in humans. But it’s probably only a matter of time before that happens,” Frieman says.

Markus Maeurer, an immunologist at the Karolinska University Hospital in Sweden, agrees that a human vaccine is a tool we should develop as a precautionary measure, in case the virus becomes more easily transmissible and virulent in humans. “We always have to expect the unexpected,” he says. Maeurer adds that it may be simpler to characterize the subtleties of the human response to vaccines in development because scientists have more methods available to analyze the human immune response than to study that of camels. Researchers also speculate that there might be greater future financial incentives to getting a human vaccine approved.

For now, scientists say that it’s unclear whether the first successful MERS vaccine will target humans or camels. “I think it’s an important question for how this will work,” Frieman says. “It’s come up a lot.”

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