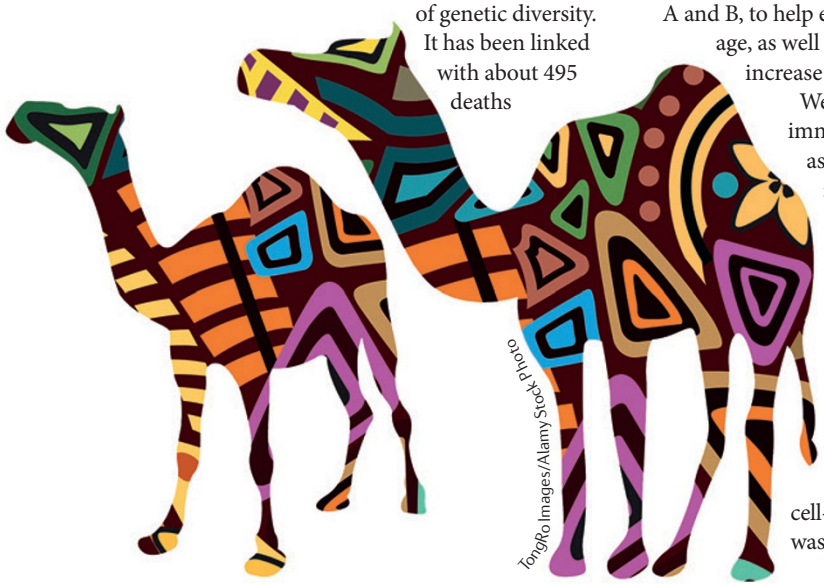
INFECTIOUS DISEASES

Vaccine for Middle East respiratory syndrome

Infection with Middle East respiratory syndrome coronavirus (MERS-CoV) is associated with severe morbidity and mortality, and is not treatable with currently available antiviral therapies. A recent study has shown that a DNA vaccine that targets the spike (S) protein of MERS-CoV is protective against infection in animal models including nonhuman primates and could be useful for the development of preventive strategies in regions affected by the virus.

MERS-CoV is an emerging coronavirus that is distinct from the severe acute respiratory syndrome (SARS)-CoV and shows high levels of genetic diversity. It has been linked with about 495 deaths in the Arabian Peninsula, Europe and the United States, and human-to-human transmission has been documented. The syndrome presents as an acute lower respiratory tract infection that can cause severe pneumonia.



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For the current study, Muthumani *et al.* focused on the S protein of CoV, which is the main envelope protein on the surface of the virus. To generate the consensus sequence for the vaccine, the team analysed the S protein genomic sequences contained in the GenBank database of the US National Institutes of Health. The construct design included sequences from CoV clades A and B, to help ensure broad coverage, as well as modifications to increase *in vivo* expression. Western blotting and immunofluorescence assays confirmed *in vitro* expression of S protein by 293T cells transfected with the MERS vaccine plasmid. In mice that were injected intramuscularly with the vaccine three times at 2-week intervals, cell-mediated immunity was elevated 1 week later. $CD4^+$ and $CD8^+$ T cells from immunized mice secreted more interferon-γ, interleukin-2 and tumour necrosis factor than did cells from vehicle-treated mice, as measured by flow cytometry. Analysis of serum samples before and after immunization revealed that the vaccine induced production of S protein-specific neutralizing antibodies.

Rhesus macaques showed similarly encouraging cellular and humoral responses to vaccination. Importantly, sera from immunized macaques showed neutralizing activity against S protein from various isolates across both MERS-CoV clades, suggesting that the vaccine could prevent immune escape by genetic variation of the pathogen and thereby provide broad protection. Immunization also protected the macaques from respiratory pathology, such as alveolar oedema and infiltration of inflammatory cells, caused by MERS-CoV challenge 4 weeks after treatment.

Camels are thought to represent a reservoir of MERS-CoV in the Middle East and to be a route of transmission to humans. In the current study, Muthumani *et al.* show that their DNA vaccine can also induce neutralizing antibodies in camels, suggesting applicability to multipart preventive strategies.

Katie Kingwell

ORIGINAL RESEARCH PAPER
Muthumani, K. *et al.* A synthetic consensus anti-spike protein DNA vaccine induces protective immunity against Middle East respiratory syndrome coronavirus in nonhuman primates. *Sci. Transl Med.* **7**, 301ra132 (2015)