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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First clinical trial of a MERS coronavirus DNA vaccine

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See Articles page 1013

Middle East respiratory syndrome (MERS) coronavirus is an emerging pathogen with pandemic potential that continues to cause sporadic human disease 7 years after the first case in a human was detected in 2012.[1] Zoonotic transmission with consequent risk of human epidemics will probably continue into the future, given that MERS coronavirus appears to be highly endemic among dromedary camels from geographically widespread areas of the Middle East and Africa.[2] In light of this potential threat to global public health, WHO along with the Coalition for Epidemic Preparedness Innovations have prioritised research and development of countermeasures against MERS coronavirus,[3,4] and WHO has developed a target product profile for both preventive and reactive use of MERS coronavirus vaccines.[5]

In *The Lancet Infectious Diseases*, Kayvon Modjarrad and colleagues[6] report results from their phase 1, open-label, dose-ranging study of GLS-5300, the first DNA vaccine candidate against MERS coronavirus to enter clinical trials. In the study, 75 adults aged 18–50 years at one site in the USA were enrolled sequentially using a dose-escalation protocol to receive 0·67 mg, 2 mg, or 6 mg GLS-5300 intramuscular injection at baseline, week 4, and week 12 followed immediately by co-localised intramuscular electroporation. The primary outcome of the study was safety, assessed during the vaccination period up to 48 weeks after dose 3.

There were no vaccine-associated serious adverse events. The most common adverse events were injection-site reactions (in 93% of participants), the most common solicited symptom was administration-site pain (92%), and the most common unsolicited adverse events were infections (36%). Seroconversion measured by MERS coronavirus spike glycoprotein subunit 1 (S1)-ELISA was detected in 66% and 86% of participants after the first and second injections, respectively, and in 79% at week 60. Neutralising antibodies were detected in 27 (43%) of 63 participants at week 14, 25 (39%) of 65 at week 24, and two (3%) of 66 at week 60. MERS coronavirus S-specific IFNγ-ELISPOT responses were detected in 47 (71%) of 66 participants after the second injection and in 44 (76%) of 58 after the third vaccination.

No licensed MERS coronavirus vaccine is currently available, and substantial challenges exist to the development of such a vaccine. These include: (1) available animal models (eg, transduced mice, and transgenic mice, rabbits, rhesus macaques, marmosets, alpacas, and camels) might not mimic human disease;[7] (2) an immune correlate of protection has not been defined, and the protective immune response in natural infection is poorly understood, although both humoral and cellular responses are probably necessary for viral clearance;[8] (3) there is a theoretical risk of immune enhancement during MERS coronavirus infection after vaccination, possibly leading to immunopathological pulmonary eosinophilic infiltration;[9] (4) demonstration of efficacy in the field will probably not be possible, necessitating alternative regulatory pathways for licensure; and (5) if MERS shifts from a pattern of sporadic outbreaks to pandemic spread, it is not known whether vaccines based on current MERS coronavirus isolates will offer protection against pandemic strains.

The results of Modjarrad and colleagues' study illustrate the challenges and promise in developing a vaccine against a novel pathogen with episodic outbreaks and little available knowledge. Despite preclinical demonstration of protection by GLS-5300

against radiological and histopathological pneumonia after MERS coronavirus challenge in rhesus macaques,[10] it remains difficult to interpret the relevance of the immunogenicity parameters that were assessed in humans in the phase 1 trial given our poor understanding of protective natural immune responses. Modjarrad and colleagues sought to bridge this gap in a post-hoc analysis by obtaining samples from ten individuals who had recovered from natural MERS coronavirus infection during the 2015 outbreak in South Korea (convalescent serum and peripheral blood mononuclear cell samples were obtained at a mean of 19·8 months [SD 0·7] after the original MERS diagnosis). Anti-S1 and neutralising antibody titres following natural infection were significantly higher than vaccine-induced responses in the acute phase, but were not different to vaccine in late convalescent samples and at similar post-vaccination timepoints.

Given the differences between S1-ELISA and neutralising antibody responses to GLS-5300, the comparison of post-natural infection versus post-vaccination responses will have an important role in the development of vaccines against sporadically occurring pathogens such as MERS coronavirus. Despite many challenges for development, the platform technologies on which vaccines such as GLS-5300 are based hold promise against novel pathogen threats because of the rapidity with which they can be formulated and manufactured; four MERS coronavirus vaccine candidates that have started phase 1 trials are based on different platform technologies.[6] Completion of the phase 1 trial of GLS-5300 represents an incremental but important step in the development of vaccines against emerging viral global threats.

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I-KY and JHK's institution is collaborating with GeneOne Life Science on a Middle East respiratory syndrome coronavirus vaccine trial in South Korea.

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Use of reverse genetics to inform Ebola outbreak responses

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See **Articles** page 1023

For **Ebola virus sequence information obtained from the Democratic Republic of the Congo outbreaks** see http://virological.org/t/drc-2018-viral-genome-characterization/230

Since 1976, Ebola viruses have caused sporadic outbreaks and epidemics throughout central and west Africa. In recent years, the size and duration of these outbreaks has grown exponentially, as exemplified by over 28 000 cases with more than 11 000 deaths in the 2013–16 west African epidemic. An ongoing outbreak in the Ituri and North Kivu provinces of the Democratic Republic of the Congo, began in July 2018 and has spilled over to Uganda, resulting in 2181 cases and 1459 deaths (as of June 17, 2019).[1,2] By contrast, previous outbreaks never reached more than a few hundred cases and were generally short-lived, likely because of their emergence in relatively isolated locations. Factors leading to the scale and duration of the 2013–16 west African epidemic included, but were not limited to, a highly mobile society, inadequate public health infrastructure, and absence of an approved vaccine. Many important advances in the understanding of Ebola virus infection and recovery were made during this outbreak, which contributed to the refinement of medical countermeasures including vaccines, therapeutics, and diagnostics.

The development of reverse genetics systems (ie, techniques for the generation of infectious