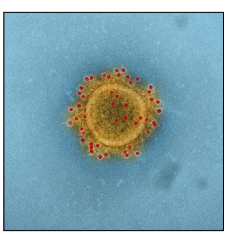
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Two Middle East respiratory syndrome vaccines: first step for other coronavirus vaccines?



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Since the outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002, the emergence and expansion of endemic and epidemic coronaviruses has been accelerating on a scale not seen for any other group of viruses with pandemic potential. In the past two decades alone, five new human coronaviruses have been discovered, three of which are highly pathogenic.[1,2] The coronavirus disease 2019 (COVID-19) pandemic is just the latest example of the danger posed by zoonotic diseases, foreshadowed by the regional, but unabated, emergence of Middle East respiratory syndrome coronavirus (MERS-CoV).[3] In recognition of its intrinsic threat to public health and as a prototypical member of the family Coronaviridae, WHO, in 2015, prioritised MERS-CoV as a pathogen to which increased resources should be dedicated for countermeasure research and development. The newly established Coalition for Epidemic Preparedness Innovations followed suit with investments in the development of candidate MERS-CoV vaccines.[4] In subsequent years, three vaccine candidates have completed initial clinical evaluation and are now ready for advanced testing.[5-9]

For more on the **report by WHO** see https://www.who.int/blueprint/about/r_d_blueprint_plan_of_action.pdf

In *The Lancet Infectious Diseases*, two groups[8,9] report results from phase 1 clinical trials of non-replicating viral vector MERS-CoV vaccines. Pedro Folegatti and colleagues[8] summarise the safety and immunogenicity of a chimpanzee adenovirus-vectored vaccine, ChAdOx1 MERS, and Till Koch and colleagues[9] do the same for a poxvirus-vectored vaccine, MVA-MERS-S. The two vaccines demonstrated tolerable safety profiles (no vaccine-related serious adverse events were reported for either vaccine) and induced humoral and cellular immune responses at peak, post-vaccination timepoints. ChAdOx1 MERS was administered as a single injection, whereas MVA-MERS-S was given as a two-dose regimen, with a 28-day interval between doses. Both products were tested in a dose-escalating design. Although the frequency and severity of adverse events were proportional to vaccine dose in both studies, only higher doses of ChAdOx1 MERS improved immunogenicity. A single dose of ChAdOx1 MERS also showed an earlier ascent and slower decay of antibody-mediated and cell-mediated immunity than two doses of MVA-MERS-S. While noting that binding antibody levels are reported differently between these studies, a single dose of ChAdOx1 MERS vaccine induced detectable antibody titres at day 180 (in 18 [75%] of 24 participants) and day 364 (13 [68%] of 19 participants) after vaccination, whereas with MVA-MERS-S only three (14%) of 22 vaccine recipients had detectable antibody titres at day 180.

For more on **vaccine candidates** see https://brightoncollaboration.us/brighton-collaboration-cepi-covid-19-web-conference/

Differences in the magnitude, kinetics, and character of the elicited immune responses raise common concerns for the development pathway of outbreak vaccines against MERS-CoV and, more acutely, SARS coronavirus 2 (SARS-CoV-2). Interrogation of the humoral and cellular immune profiles of the vaccine candidates highlights the first point: what immune responses do coronavirus vaccines need to elicit to confer protection against infection or severe disease? Although the question is applicable to many viruses, the answer to this question has been elusive among coronaviruses.[10,11] Without previous identification of a potential correlate of protection, it becomes difficult to ascertain the relevance of immunogenicity outputs. Second, there remains a lack of consensus on the methodology by which immunogenicity outputs are measured.[12] Although the two trials report similar assessments of humoral responses—binding antibody, wild-type MERS virus, and pseudovirus neutralisation assays—it is difficult to know how these individual results compare between studies. Koch and colleagues[9] found a strong correlation between binding and neutralising antibody titres (Spearman's correlation r=0·86 [95% CI 0·6960–0·9427], p=0·0001), whereas Folegatti and colleagues[8] did not (Spearman's r=0·28, p=0·175). Does this represent an immunologically relevant difference between vaccine-induced responses or a methodological difference between laboratories? Finally, some animal studies suggest that certain SARS-CoV and MERS-CoV vaccines might, upon viral challenge, be associated with eosinophilic pulmonary infiltrates. This finding underscores the importance of factoring safety into the design, monitoring, and long-term follow-up of coronavirus vaccine trials—something that cannot be fully addressed in the two early-stage MERS vaccine trials herein, but which will undoubtedly be considered in future efficacy trials.

The experience with SARS and the emergence of MERS, particularly during the outbreaks of 2014–15 in the Arabian and Korean peninsulas, were harbingers of the consequences of COVID-19, and similar pathogens, on all sectors of society—not only in overall morbidity and mortality, but also in the capacity to level economies and disrupt social order.[13] If MERS has been eclipsed by its pandemic cousin, then the lessons learned have prepared the global vaccine research and development community for moving coronavirus vaccines forward at an accelerated pace, such that first-in-human COVID-19 vaccine trials are moving on unprecedented, shortened timelines. To stay ahead of these increasingly frequent outbreaks, the field must maintain momentum in advancing rapid, scalable, and translatable vaccine strategies, not only for MERS-CoV, but even more urgently for SARS-CoV-2 and, ultimately, the next novel coronavirus that leaps from its animal host to humans.

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Balanced immunity is key for a successful dengue vaccine

The search for an efficacious dengue vaccine continues and The Butantan Institute (Sao Paulo, Brazil)—the largest producer of immunobiological products in both Brazil and Latin America overall—is in the process of developing a vaccine that harnesses a balanced humoral and cellular immunological response to provide enhanced and equal protection against the four dengue virus (DENV) serotypes (DENV-1–4).

Dengue remains the most common arbovirus infection in the world, causing between 50 and 100 million clinical cases and an estimated 9000–20 000 deaths per year.[1] The steady increase in dengue incidence is concerning, with cases doubling every decade since 1990, highlighting the need for more efficient control strategies. Vaccines are considered one of the most successful contributors to global health[2] due to their success in disease eradication; thus, vaccination is considered the best approach to halt the expansion of dengue.

Major milestones in dengue vaccine development have been achieved since the first efficacy vaccine assessment by Albert Sabin in 1945 in New Jersey.[3] At present, one licensed vaccine CYD-TDV (Dengvaxia; Sanofi Pasteur, Lyon, France) is available and two vaccines are in large global phase 3 trials, with the essential requirement for such vaccines to provide equal protection against all four dengue serotypes while preventing antibody-dependent enhancement. Variable efficacy against some dengue serotypes and risk of antibody-dependent enhancement in subgroups of vaccine recipients continue to be a concern with leading vaccine candidates.[4,5]

Esper Kallas and colleagues[6] report safety and immunogenicity results from a phase 2 trial of the live-attenuated dengue vaccine Butantan-DV tested in

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