Vaccine candidate protects against COVID-19 and yellow fever

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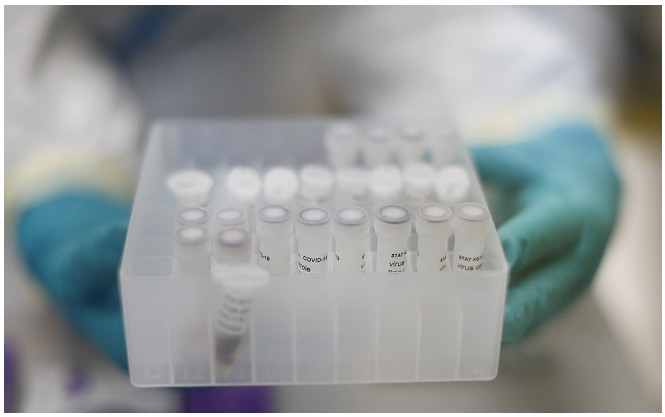


A lab worker holds frozen virus samples at the KU Leuven Rega Institute. Credit: Layla Aerts for KU Leuven

Virologists at the Rega Institute at KU Leuven (Belgium) have developed a vaccine candidate against Covid-19 based on the yellow fever vaccine, which as a result also works against yellow fever. Results published today in *Nature* show that the vaccine protects hamsters from infection with the SARS-CoV-2 coronavirus after a single dose. The vaccine is also effective in monkeys. The team is currently preparing for clinical trials.

To engineer their vaccine, tentatively named RegaVax, the team led by Professor Johan Neyts and Kai Dallmeier inserted the genetic code of the SARS-CoV-2 spikes into the genetic code of the yellow fever vaccine. The researchers tested the vaccine in healthy hamsters and monkeys. Another group of the animals received a placebo.

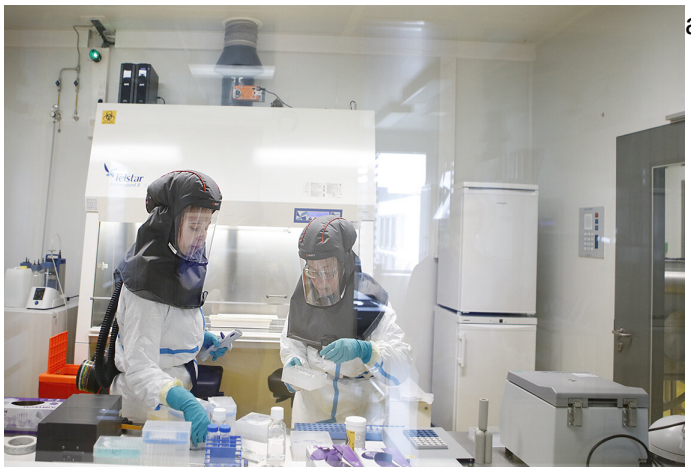
The researchers first vaccinated the hamsters and then dripped the virus into their noses. Ten days after a single vaccine dose, most of the hamsters were protected against the virus. Three weeks after vaccination, all hamsters were protected. "They also didn't develop any lung infections. The lungs of the hamsters in the control groups, by contrast, showed clear signs of infection and disease," Neyts explains.

The team also tested the vaccine in monkeys. "In some of the monkeys, we observed neutralizing antibodies already seven days after vaccination. After fourteen days, high titers of neutralizing antibodies were measured in all animals. This is very fast. Moreover, in the vaccinated animals, the virus was completely or nearly completely gone from their throats."

Long-lasting immunity

"Ours is the only vaccine currently in development against Covid-19 that also protects against yellow fever," explains professor Neyts. Previously, the Rega team used the yellow fever vaccine as the foundation for vaccine candidates against Zika, Ebola, and rabies. "The effectiveness and safety of the yellow fever vaccine, which has been in use for 80 years, is well-established. More than 500 million people have already received this vaccine. One dose offers fast protection against yellow fever that in nearly all cases lasts for life."

"A vaccine that works against Covid-19 and yellow fever could offer an important contribution to the WHO's campaign to eradicate yellow fever by 2026," Neyts continues. "Especially now that we know there are mosquito species present in Asia that can transmit the yellow fever virus."



Lab workers work on infected tissue at the KU Leuven Rega Institute. Credit: Layla Aerts for KU Leuven

RegaVax works after one dose, unlike many of the front-runners in the race today, which require a repeat vaccination after one month. "This has important logistical implications, in particular for countries with a less advanced medical system," explains professor Neyts. "Additionally, we expect that the vaccine will offer long-lasting immunity to Covid-19. It could therefore be an ideal candidate for repeat vaccinations when immunity decreases in people who have received one of the first-generation vaccines."

Finally, the vaccine can be stored at 2-8 °C, while some vaccines require a cold chain with temperatures down to -70 °C. That's already challenging in the Western world, but it may be nearly impossible to vaccinate large populations in remote tropical and subtropical regions," Neyts explains.

"An inexpensive, single-dose vaccine that rapidly protects against infection, that can be stored and transported at fridge temperature, and that may, like the yellow fever vaccine on which it is based, result in long-lasting immunity, provides an important and much-needed diversification of the Covid-19 vaccine landscape," Neyts concludes.

His team is now preparing for clinical trials next year and has joined forces with a specialized and accredited company that will produce the vaccine candidate for testing in humans.

New technique

RegaVax is a vector vaccine: it uses the genetic code of the yellow fever vaccine virus as a carrier (or vector) for the genetic code of the coronavirus spikes. "When working with a related virus, such as the Zika virus, pieces of the genetic code of the yellow fever vaccine virus are swapped with a similar piece of the code of the targeted virus. Using this strategy the team recently developed a Zika vaccine candidate. However, since SARS-CoV-2 is unrelated to yellow fever, a new technology had to be developed to insert an entirely unrelated genetic sequence in the yellow fever vaccine backbone. This concerns an important innovation in the vaccine field."

Virus inhibitors

"Mind you: vaccines are not a solution for people who are already ill. That is why we are also developing a cure to help Covid-19 patients," Neyts concludes. "We recently published on the protective activity of the Japanese flu drug favipiravir in hamsters. We have identified some other existing medicines or combinations thereof that inhibit the virus. We are now first exploring their effect in infected hamsters. At the same time, we aim to develop new and powerful virus inhibitors against SARS-CoV-2. For this purpose, we have already tested more than 1.6 million molecules in our fully automated high biosafety laboratory. We're looking for a needle in a haystack."

More information: Lorena Sanchez-Felipe et al, A single-dose live-attenuated YF17D-vectored SARS-CoV-2 vaccine candidate, *Nature* (2020). DOI: 10.1038/s41586-020-3035-9

Provided by KU Leuven