

Llama antibodies have 'significant potential' as potent COVID-19 treatment

September 22 2021



Novel Coronavirus SARS-CoV-2 Transmission electron micrograph of SARS-CoV-2 virus particles, isolated from a patient. Image captured and color-enhanced at the NIAID Integrated Research Facility (IRF) in Fort Detrick, Maryland. Credit: National Institute of Allergy and Infectious Diseases, NIH

A unique type of tiny antibody produced by llamas could provide a new frontline treatment against COVID-19 that can be taken by patients as a simple nasal spray.

Research led by scientists at the Rosalind Franklin Institute has shown that nanobodies—a smaller, simple form of antibody generated by llamas and camels—can effectively target the SARS-CoV-2 virus that causes COVID-19.

They found that short chains of the molecules, which can be produced in large quantities in the laboratory, significantly reduced signs of the COVID-19 disease when administered to infected animal models.

The nanobodies, which bind tightly to the SARS-CoV-2 virus, neutralizing it in cell culture, could provide a cheaper and easier to use alternative to [human antibodies](#) taken from patients who have recovered from COVID-19. Human antibodies have been a key treatment for serious cases during the pandemic, but typically need to be administered by infusion through a needle in hospital.

Public Health England has described the research as having "significant potential for both the prevention and treatment of COVID-19", adding that the nanobodies "are among the most effective SARS-CoV-2 neutralizing agents we have ever tested."

"Nanobodies have a number of advantages over human antibodies," said

Professor Ray Owens, head of protein production at the Rosalind Franklin Institute and lead author of the research. "They are cheaper to produce and can be delivered directly to the airways through a nebuliser or nasal spray, so can be self-administered at home rather than needing an injection. This could have benefits in terms of ease of use by patients but it also gets the treatment directly to the site of infection in the respiratory tract."

The research team, whose findings are published in the journal *Nature Communications*, were able to generate the nanobodies by injecting a portion of the SARS-CoV-2 spike protein into a llama called Fifi, who is part of the antibody production facility at the University of Reading.

The spike protein is found on the outside of the virus and is responsible for binding to human cells so it can infect them.

Although the injections did not make Fifi sick, it triggered her immune system to fight off the virus protein by generating nanobodies against it. A small blood sample was then taken from the llama and the researchers were able to purify four nanobodies capable of binding to the COVID-19 virus.

The nanobodies were then combined together into chains of three to increase their ability to bind to the virus. These were then produced in cells in the laboratory.

The team found three nanobody chains were able to neutralize both the original variants of the COVID-19 virus and the Alpha variant that was first identified in Kent, UK. A fourth nanobody chain was able to neutralize the Beta variant first identified in South Africa.

When one of the nanobody chains—also known as a trimer—were administered to hamsters infected with SARS-CoV-2, the animals

showed a marked reduction in disease, losing far less weight after seven days than those who remained untreated. Hamsters that received the nanobody treatment also had a lower viral load in their lungs and airways after seven days than untreated animals.

"Because we can see every atom of the nanobody bound to the spike, we understand what makes these agents so special," said Professor James Naismith, Director of the Rosalind Franklin Institute, who helped lead the research.

The results are the first step towards developing a new type of treatment against COVID-19, which could prove invaluable as the pandemic continues.

"While vaccines have proven extraordinarily successful, not everyone responds to vaccination and immunity can wane in individuals at different times," said Professor Naismith. "Having medications that can treat the virus is still going to be very important, particularly as not all of the world is being vaccinated at the same speed and there remains a risk of new variants capable of bypassing vaccine immunity emerging."

If successful and approved, nanobodies could provide an important treatment around the world as they are easier to produce than human antibodies and don't need to be stored in cold storage facilities, added Professor Naismith.

The research team, which included scientists at the University of Liverpool, University of Oxford and Public Health England, now hope to obtain funding so they can conduct further research needed to prepare for clinical studies in humans.

Prof Miles Carroll, Deputy Director of the National Infection Service, Public Health England (PHE), said: "Although this research is still at an

early stage, it opens up significant possibilities for the use of effective nanobody treatments for COVID-19.

"These are among the most effective SARS-CoV-2 neutralizing agents we have ever tested at PHE. We believe the unique structure and strength of the nanobodies contribute to their significant potential for both the prevention and treatment of COVID-19 and look forward to working collaboratively to progress this work into [clinical studies](#)."

Dr. Andrew Bourne, Director of Partnerships at EPSRC, said: "Utilizing the unique properties of llamas' nanobodies, this research could lead to an important new form of treatment for COVID-19 that is cheaper to produce and easier to administer.

"It is a vivid illustration of the impact that long-term discovery research at the cutting edge of physical and life sciences, as undertaken at the Rosalind Franklin Institute, can have."

Professor James Stewart, co-author and professor of molecular virology at the University of Liverpool said: "The pre-clinical trials of the nanobodies in hamsters are extremely encouraging and suggest that they may be effective at treating COVID-19 disease as well as help prevent infection. Having therapies such as this will be important for populations that are either unvaccinated or where vaccination is inappropriate or ineffective."

The researchers, who were funded by the UK Research and Innovation's Medical Research Council and the Engineering and Physical Sciences Research Council, The EPA Cephalosporin Fund and Wellcome, also hope the nanobody technology they have developed could form a so-called 'platform technology' that can be rapidly adapted to fight other diseases.

"When a new virus emerges in the future, the generic technology we have developed could respond to that, which would be important in terms of producing new treatments as quickly as possible," said Professor Owens.

More information: A potent SARS-CoV-2 neutralising nanobody shows therapeutic efficacy in the Syrian golden hamster model of COVID-19, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-25480-z](https://doi.org/10.1038/s41467-021-25480-z)

Provided by The Rosalind Franklin Institute

Citation: Llama antibodies have 'significant potential' as potent COVID-19 treatment (2021, September 22) retrieved 4 May 2024 from <https://medicalxpress.com/news/2021-09-llama-antibodies-significant-potential-potent.html>

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