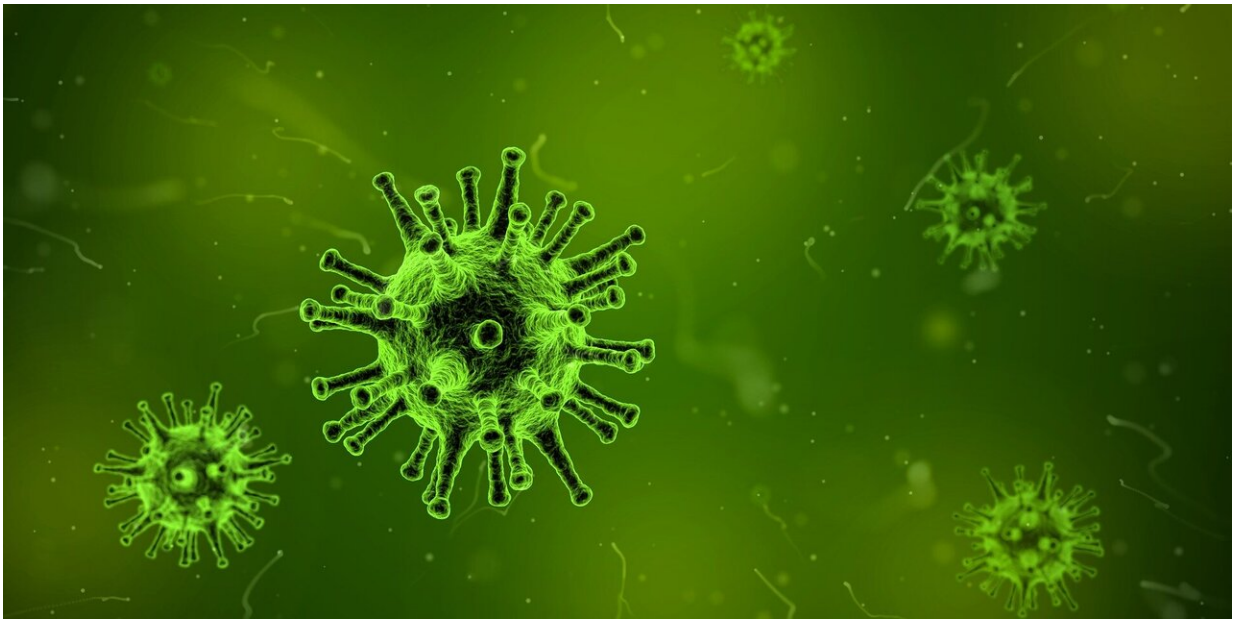
Nanotechnology delivers hepatitis B vaccine

July 12 2019



Credit: CC0 Public Domain

Brazilian and European researchers have demonstrated exactly how a nanotechnology-based compound delivers an oral vaccine against hepatitis B to the immune system. When particles containing silica and an antigen combine, even though they are different sizes, they reach the intestine without being destroyed by the acidity of the digestive system.

A compound of nanostructured SBA-15 silica and HBsAg, the hepatitis B surface antigen, was submitted to different types of X-ray imaging in European laboratories.

The nanostructured silica was developed by researchers at the University of São Paulo's Physics Institute (IF-USP) in Brazil. The antigen was created by the Butantan Institute, which is also in São Paulo. The results are published in *Scientific Reports*.

The aim of the study was to understand how a 22-nanometer-sized antigen binds to silica nanotubes with a diameter of approximately 10 nanometers and a honeycomb-like structure. One nanometer (1 nm) is a billionth of a meter. Studies carried out at USP revealed the measurements of both the antigen and the silica nanotubes using small-angle X-ray scattering (SAXS), dynamic light scattering (DLS), and transmission electron microscope.

"Despite the size difference, tests [in animals] produced an excellent immune response to the oral vaccine—as good as the injectable form or better," said Márcia Fantini, full professor at IF-USP.

X-ray and neutron imaging was coordinated by Heloisa Bordalo, a Brazilian researcher at the University of Copenhagen's Niels Bohr Institute in Denmark. In collaboration with other researchers in Denmark as well as colleagues in France, Germany, Sweden and Switzerland, Bordalo submitted the compound to small-angle X-ray scattering (SAXS), among other techniques.

The three-dimensional images obtained by these techniques showed that although the antigen did not enter the nanotubes, it was retained in 50 nm macropores between the nanotubes. This protected it from the acidity of the digestive system.

The images also enabled the researchers to determine the ideal proportion of silica and HBsAg so that the antigen did not agglomerate, hindering the dispersion of the active principle in the patient's intestine. "The oral and intranasal routes are natural modes of vaccine

administration. Nature is the best vaccination agent. However, a vaccine that contains a protein, as in this case, is destroyed by high acidity and its own proteases in passing through the stomach, so it doesn't reach the immune system, particularly the small intestine," said Osvaldo Augusto Sant"Anna, Scientific Leader at Butantan Institute and responsible for development of the HbsAg antigen.

Before proceeding to clinical trials, the team will test polymers that can be used to coat the entire structure and increase the medication's resistance to the human stomach. In animal trials, the formulation proved to be as effective as the injected vaccine, if not more so, in delivering the antigen to the intestine, where the immune system can detect it and produce antibodies against the virus.

According to the World Health Organization (WHO), approximately 257 million people currently live with hepatitis B worldwide.

Polyvaccine

Through a project supported by FAPESP, the group led by Sant"Anna, Fantini and Bordalo is now developing new antigens to add to the compound. The idea is to have at least a triple vaccine by adding other antigens against diphtheria and tetanus.

However, the formulation may evolve to become a polyvaccine that also immunizes people against whooping cough, poliomyelitis and Haemophilus influenzae type B (Hib), the bacterium that causes meningitis and pneumonia, among other diseases.

The antigens must combat the diseases without interfering with each other. "There have been very interesting results with diphtheria, and we're now going to test it for tetanus, initially in injectable form," Sant"Anna said.

More information: Martin K. Rasmussen et al, 3D visualisation of hepatitis B vaccine in the oral delivery vehicle SBA-15, *Scientific Reports* (2019). DOI: 10.1038/s41598-019-42645-5

Provided by FAPESP