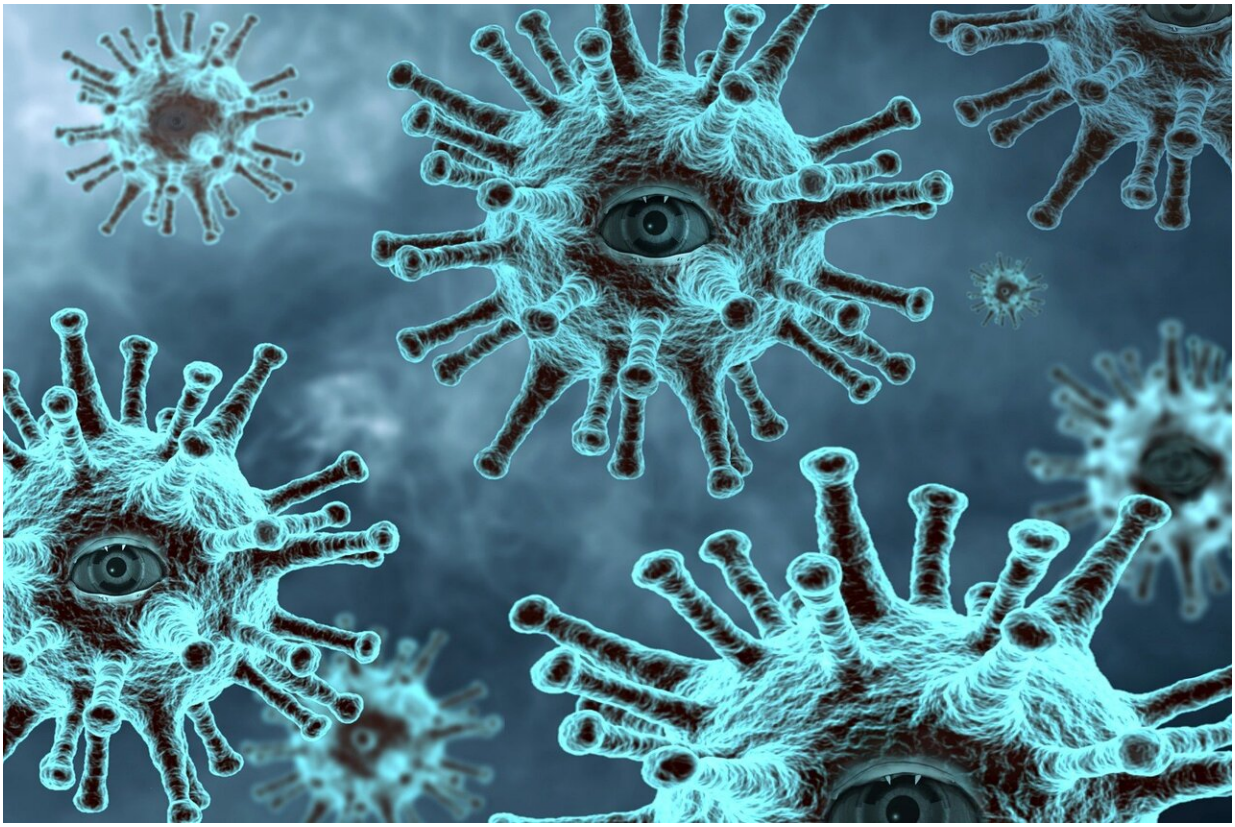
New approach against COVID-19

March 26 2021, by Gunnar Bartsch



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If Professor Thomas Rudel and the biopharmaceutical company Aeterna Zentaris GmbH have their way, there could possibly be significant enhancement in the fight against the global Corona pandemic in the future: a vaccination that is not administered by syringe, but in the form of a capsule that can simply be swallowed. Preclinical development,

which should pave the way for the first clinical trials in humans, has already begun.

Thomas Rudel holds the Chair of Microbiology at the Julius Maximilian University of Würzburg (JMU). A good year ago, he came up with the idea for oral vaccination. His approach: "We use an approach that has already been in use for many years, millions of times over, as protection against typhoid infection." The oral typhoid vaccine is based on a special strain of bacteria, Salmonella Typhi Ty21a.

Potentially strong immune response

Rudel and the scientists in his laboratory are now also working with the same bacterial strain. However, with a significant modification: "We have programmed the bacteria to produce SARS-CoV-2 antigens," explains the microbiologist. Protected in a capsule from the attack of gastric acid, the bacteria are supposed to unfold their effect in the human small intestine after passing through the stomach. The scientific approach assumes that the bacteria can present the antigens to the immune system there.

"Special cells in the intestinal wall are supposed to ensure that bacteria and the antigens are taken up by immune cells and transported further into lymphoid tissue," says Rudel. There, they could in turn activate other cells of the immune system—so-called B cells and T cells—and initiate an immune response. Rudel hopes that, if successful, this immune response will be so strong that all of the human mucous membranes will be put on alert, and as a result coronaviruses will already be prevented from entering the body there.

Built-in safety anchor

There is a simple reason why the bacteria developed by Rudel's team should produce not one but two antigens: as has been shown in recent months, SARS-CoV-2 mutates frequently. This could have the consequence that one antigen is only weakly effective if the virus should have changed accordingly. The second antigen could therefore serve as a "safety anchor": It is based on a gene that has been shown to mutate only rarely.

Comparatively cheap to produce, easy to administer and relatively stable even at normal temperatures: these are a few advantageous properties that such a novel vaccine could possess when it reaches market maturity. If successful, this would also make it attractive for use in countries where it is difficult to ensure a cold chain with temperatures as low as minus 70 °C without interruption.

Experience from previous vaccine development

Thomas Rudel and his team are developing the vaccine strains with financial support from Aeterna Zentaris GmbH and will complete preclinical work; after successful completion of the preclinical work, the pharmaceutical company would be responsible for the subsequent clinical trials. Rudel is confident that the necessary approvals could be obtained relatively quickly. A few years ago, Aeterna Zentaris had already worked with a similar procedure on a prostate cancer vaccine that was about to enter clinical trials and had been approved by the authorities for clinical testing. The team can now build on this experience.

Despite all the euphoria, Rudel warns that there is no guarantee that an oral vaccine against Covid-19 will soon be available in pharmacies. After all, many active substances have failed even at a late stage of development because they were not sufficiently effective or showed unexpected and undesirable effects. This risk always exists. Rudel is all

the more eager to wait for the coming months.

Provided by University of Würzburg