A New Oral Vaccine Tablet Could Reshape Infectious Disease Prevention

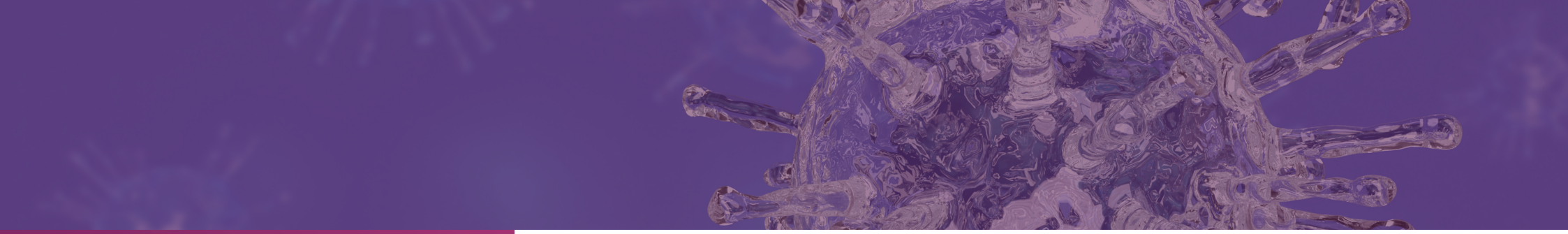
Dr Becca Flitter
Dr Sean Tucker
Dr Molly Braun

SEPTEMBER 2024

doi.org/10.33548/SCIENTIA1074

MEDICAL &
HEALTH SCIENCES

Scientia



A New Oral Vaccine Tablet Could Reshape Infectious Disease Prevention

Scientists are developing next-generation vaccines that improve protective immunity and address many of the challenges associated with administering traditional injected vaccines. Dr Sean Tucker and a team from Vaxart have developed an oral temperature-stable tablet vaccine platform that can be modified for a variety of pathogens. This vaccine tablet has a range of benefits: it can be self-administered, distributed easily without requiring ultra-low temperatures, and generates a strong immune response at barrier surfaces such as the gut, nose, and throat – the common entry points for pathogens.

Vaccines: A Vital Public Health Intervention

Vaccines are one of the most important public health interventions available. The World Health Organization estimates that over the last 50 years, 154 million lives have been saved by vaccines – this equates to an incredible six lives every hour for each of those 50 years.

Vaccines work by training our immune system to recognise and fight viruses and bacteria without actually exposing us to the disease-causing pathogens. Vaccines predominantly work by delivering parts of the pathogen to your body's immune system. These pieces of pathogens, known as antigens, are unique to each microorganism. Following vaccination, the immune system not only learns how to destroy these pathogens but also remembers how to respond if we later encounter the same pathogen again. The human body possesses immune cells that protect against diseases located in the circulation and at barrier surfaces such as our gut and respiratory tract. It is these specialized immune cells that are trained by vaccines to remember specific antigens and prevent your body from becoming infected when you are exposed to pathogens.

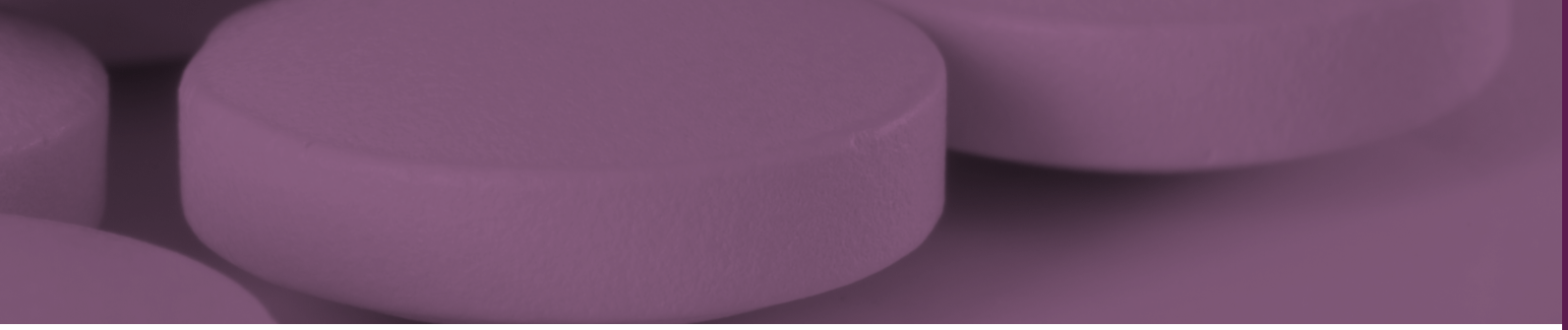
Getting a vaccine doesn't just protect the individual but also benefits the community. When a significant portion of the population is vaccinated against a disease, it is harder for the pathogen to circulate. Importantly, this protects people who aren't able to have the vaccine themselves, such as young children or people with underlying health conditions. Inefficient distribution, temperature requirements, and vaccine hesitancy, all continue to impede efforts to increase vaccination rates. Therefore, new vaccines that are easy to distribute could help alleviate these barriers and increase immunization rates.

Limitations with Traditional Vaccines

While existing vaccines have been critical major advances in public health around the globe, limitations remain, including speed of distribution, lack of healthcare infrastructure, and vaccine hesitancy. Traditional vaccines can take a long time to develop and manufacture, especially those for novel pathogens or new strains of existing ones. Most vaccines need to be kept at very cold temperatures for them to be effective, leading to additional problems with logistics and accessibility in remote or developing areas.

The majority of vaccines are given as needle-based injections, which require administration by a trained healthcare professional. This can be logistically challenging and requires an effective healthcare infrastructure to distribute. Another drawback is injectable vaccines need efficient sharps and biohazardous waste disposal streams and can produce significant medical waste. Further, the use of needles contributes to vaccine hesitancy, with research showing that a fear of needles is listed as a reason for people turning down vaccines.

Lastly, it is worth noting that administering vaccines via injection results in immunity primarily in the bloodstream rather than creating protective responses at barrier surfaces, which are common entry points for pathogens. To address these concerns, scientists at Vaxart have developed a new generation of vaccines that are easy to distribute, can be administered without the use of needles, can be transported without low-temperature requirements, and produce immune responses in multiple places in the human body.



Designing a Novel Vaccine Tablet

Dr Sean Tucker and a team of researchers at Vaxart in South San Francisco, USA, have developed a novel way of giving vaccines as tablets instead of injections. This oral vaccine tablet delivery system contains a modified harmless virus that cannot replicate and contains a pathogen-specific antigen. The tablet also has a natural small molecular adjuvant, used to generate a stronger and longer-lasting immune response to the antigen presented to the body. After swallowing the tablet, the immune cells of the human body activate and produce an immune response to the specific pathogen.

The Vaxart oral tablet vaccine has many benefits compared to traditional injected vaccines. The team can quickly modify and adapt the antigens that are incorporated into the tablet. This flexibility allows for the rapid development of new vaccines and is likely to be vital in outbreak situations with new strains or emerging pathogens. As administration is via an oral tablet, there is no need for needles or trained healthcare professionals to deliver the vaccines. The tablet is also stable at room temperature for extended periods. These factors help make the Vaxart system accessible to populations around the world without the logistical challenges seen with traditional injection-delivered vaccines that require strict cold storage. Another advantage of the oral tablet system is the lack of adverse effects. Whilst it is common to have injection site soreness, fatigue and fever after receiving a traditional vaccine injection, this tablet vaccine platform has a favourable safety profile and effectively avoids many of these side effects.

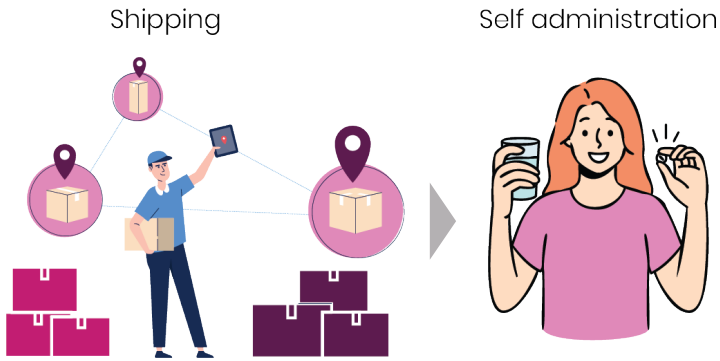
One of the key advantages of this oral vaccine platform is the location where the vaccine is delivered and initiates an immune response. Vaxart's oral vaccine is delivered into the body through the gut rather than injected into the muscle. Administration of the antigens at a barrier surface allows the tablet system to enhance the immune response in mucosal areas (such as the gut and respiratory tract) where pathogens typically enter the body. Rigorous clinical trials have also been completed to further understand the safety and efficacy of this tablet vaccine platform against flu, COVID-19, and norovirus infectious diseases. These trials have provided additional evidence for the mechanisms behind the strong mucosal immune response offered by Vaxart's technology.

Ensuring a Strong Frontline Defence

Mucosal immunity refers to the immune defence system at the body's barrier surfaces, such as the lining of the nose, throat, lungs, and intestines, where many pathogens enter the body. At these mucosal surfaces, specialized immune cells produce antibodies that help stop pathogens at these entry points, protecting the individual from infection. By designing vaccines that produce mucosal immunity, Vaxart's tablet vaccine provides another layer of protection where pathogens first enter the body, offering a strong frontline defence against infections.

A key molecule produced by the immune system at mucosal surfaces is immunoglobin A (IgA). This special type of antibody binds to invading pathogens and prevents them from attaching to our cells and moving into the body. There are two main forms of IgA – monomeric IgA, which is found in the blood, and dimeric or secretory IgA (sIgA), which is found in our mucosal surfaces and can bind to more than one pathogen particle at once, further reducing the risk of pathogen entry. The Vaxart oral tablet vaccine generates both strong monomeric IgA in the blood and dimeric sIgA at mucosal surfaces, protecting the body in multiple ways.

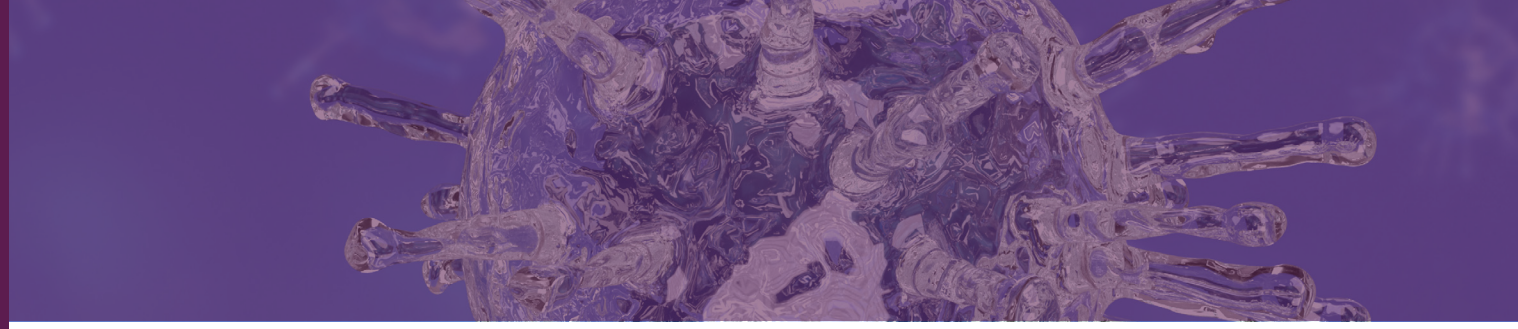
> Getting a vaccine doesn't just protect the individual but also benefits the community. When a significant portion of the population is vaccinated against a disease, it is harder for the pathogen to circulate.

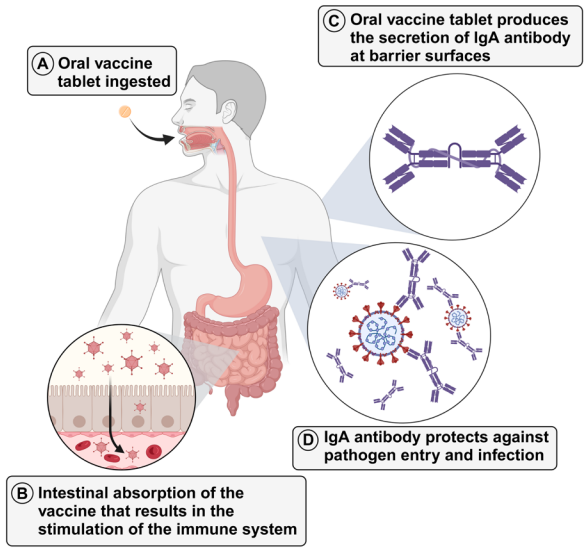


Λ Oral vaccination administration is fast and efficient.

“

The Vaxart oral tablet vaccine has many benefits compared to traditional injected vaccines. The team can quickly modify and adapt the antigens that are incorporated into the tablet. This flexibility allows for the rapid development of new vaccines and is likely to be vital in outbreak situations with new strains or emerging pathogens.





Quick overview of how oral vaccination works.

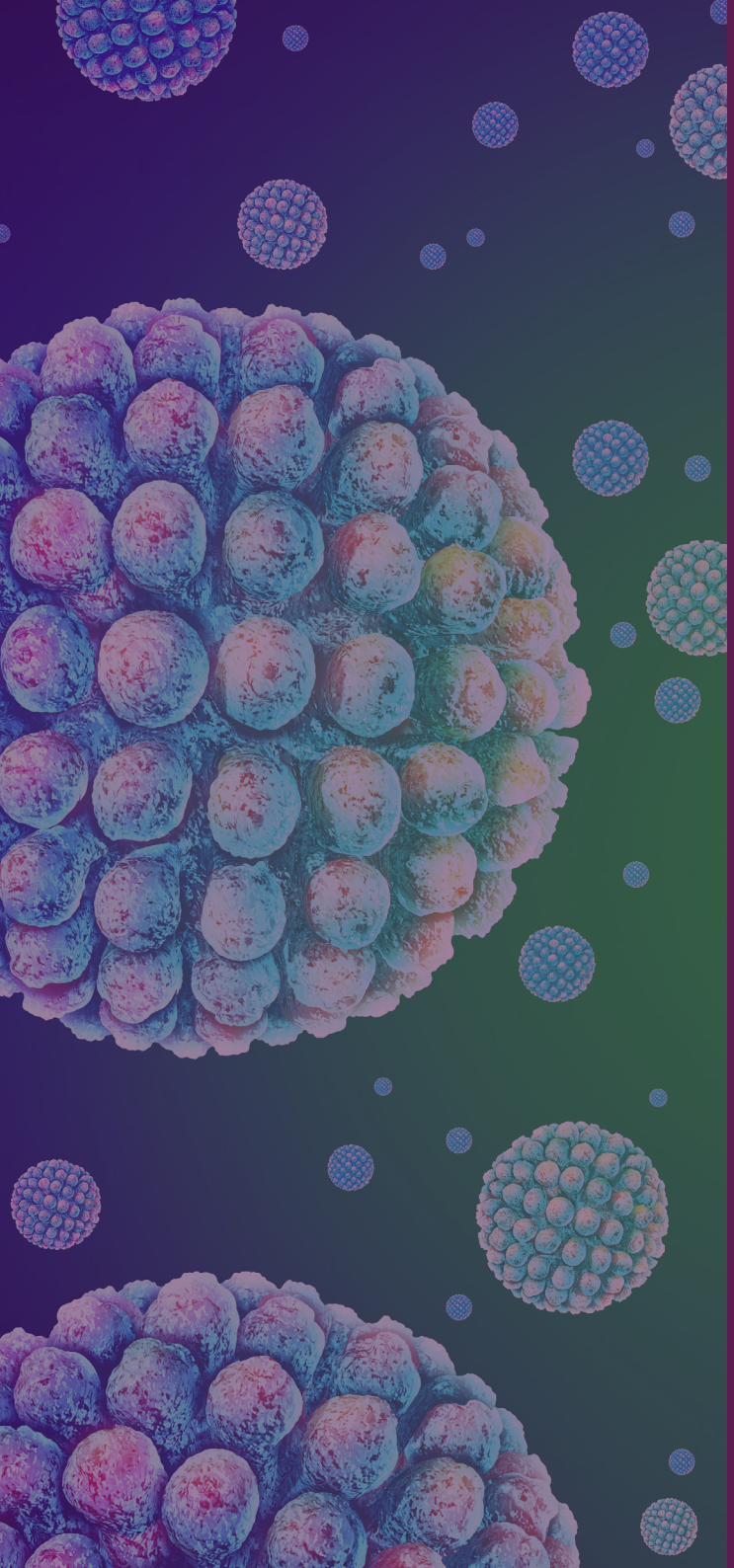
New Promise for Preventing Viral Diseases

Norovirus is a leading cause of gastroenteritis and foodborne illness around the world. This virus infects the mucosal tissues in the gut, and there is currently no effective vaccine to protect against the illness. In a clinical trial, the Vaxart norovirus tablet vaccine delivered to the small intestine generated IgA immune responses against the virus in both the gut and saliva. This study provided the first evidence that this vaccine tablet delivered to the gut produced biological communication that produced immune responses at distant mucosal sites. It also highlighted the potential value of the Vaxart vaccine platform, which produced significant IgA responses against norovirus at multiple barrier surfaces, showing this vaccine may protect against pathogen entry.

Influenza vaccines are routinely given every year to millions of people, requiring care from healthcare professionals and maintaining extended cold chain (temperature) logistics. There are currently no licensed oral influenza vaccines. A clinical trial using Vaxart's oral vaccine tablet technology expressing an influenza antigen showed that vaccinated individuals produced robust IgA immune responses in the blood and on mucosal surfaces. This clinical trial also showed the vaccine tablet was equally effective at preventing influenza infection compared to the licensed injectable vaccine. These data may be the first step towards a new effective oral influenza vaccine that could be easily distributed.

Vaxart has also developed a COVID-19 vaccine. In a preclinical animal study, immunized animals were less likely to transmit the SARS-CoV-2 virus to non-vaccinated animals, demonstrating that this technology could reduce the spread of the virus. This vaccine is currently being evaluated in humans, and it is the first COVID-19 oral vaccine tablet to reach phase 2 clinical trials. Excitingly, Vaxart has recently been awarded significant funding from the US Government to conduct a COVID-19 clinical trial in 10,000 participants. Multiple clinical studies have shown that SARS-CoV-2 injected vaccines generate poor mucosal immunity. In the upcoming COVID-19 clinical trial, the Vaxart team aims to show their oral tablet technology has the capacity to produce protective secretory IgA at multiple mucosal surfaces and reduce infection. If successful, this vaccine approach will also be evaluated for its ability to reduce person-to-person SARS-CoV-2 transmission.

It is clear that the Vaxart oral vaccine shows exciting promise for preventing viral infection and reducing transmission, a much-needed intervention in the aftermath of COVID-19. Oral vaccine tablet delivery provides many improvements upon traditional injectable vaccines. Vaccine tablets will be easier to distribute, are temperature stable, and hopefully diminish vaccine hesitancy due to needle phobia. However, most importantly, this oral table vaccine approach stimulates mucosal immunity, enhancing immune protection at barrier surfaces and blocking viral entry into the body. Vaxart's revolutionary tablet vaccine platform has the potential to revolutionize the way the world gets vaccinated – a pill that (re)moves the needle.



MEET THE RESEARCHERS



Dr Becca Flitter, Dr Sean Tucker, Dr Molly Braun, Vaxart, San Francisco, CA94080, USA

Dr Sean Tucker iis the Chief Scientific Officer and founder of Vaxart. Dr Tucker received an MS in Chemical Engineering from the University of California, Berkeley and a PhD in Immunology from the University of Washington. His research and clinical interests are dedicated to novel ways to deliver vaccines that protect against mucosal infections and decrease pathogen transmission.

Dr Becca Flitter is the Associate Director of Immunology at Vaxart in San Francisco where she leads a team that studies oral vaccination in preclinical and clinical studies. Dr Flitter received her PhD from the University of Pittsburgh School of Medicine and a Master's in Public Health from the University of California, Berkeley. Her research expertise lies in mucosal immunology and host-pathogen interactions.

Dr Molly Braun was awarded a PhD in Microbiology from the Boston University School of Medicine. During her doctoral and postdoctoral studies, she worked with pharmaceutical companies to investigate antiviral mechanisms and studied immune responses to infection. Dr. Braun is now a Senior Scientist at Vaxart, where she uses her expertise to examine antibody and T cell responses after vaccination.

CONTACT

bflitter@vaxart.com, stucker@vaxart.com, mbraun@vaxart.com

https://vaxart.com/

https://www.linkedin.com/company/vaxart/mycompany/

VAXART

FUNDING

Gates Foundation

Biomedical Advanced Research and Development Authority

FURTHER READING

SN Tedjakusuma, CA Lester, ED Neuhaus, *et al.*, A Next-Generation Adenoviral Vaccine Elicits Mucosal and Systemic Immunogenicity and Reduces Viral Shedding after SARS-CoV-2 Challenge in Nonhuman Primates, *Vaccines*, 2024, 12, 132. DOI: https://doi.org/10.3390/vaccines12020132

BA Flitter, MR Braun, SN Tucker, Drop the Needle; A Temperature Stable Oral Tablet Vaccine Is Protective against Respiratory Viral Pathogens, *Vaccines*, 2022, 10, 593. DOI: https://doi.org/10.3390/vaccines10040593

SN Langel, S Johnson, CI Martinez, *et al.*, Adenovirus type 5 SARS-CoV-2 vaccines delivered orally or intranasally reduced disease severity and transmission in a hamster model, *Science Translational Medicine*, 2022, 14(658), eabn6868. DOI: https://doi.org/10.1126/scitranslmed.abn6868

D Liebowitz, K Gottlieb, NS Kolhatkar *et al.*, Efficacy, immunogenicity, and safety of an oral influenza vaccine: a placebo-controlled and active-controlled phase 2 human challenge study, *The Lancet Infectious Diseases*, 2020, 20(4), 435–444. DOI: https://doi.org/10.1016/S1473-3099(19)30584-5

L Kim, D Liebowitz, K Lin, *et al.*, Safety and immunogenicity of an oral tablet norovirus vaccine, a phase I randomized, placebo-controlled trial, ***JCI insight***, 2018, 3(13), e121077. DOI: https://doi.org/10.1172/jci.insight.121077

Find out more at **scientia.global**