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Leading by example

As Chulalongkorn University's mRNA-based ChulaCov 19 vaccine begins human testing, a quick return to normalcy is on the cards

PUBLISHED : 15 JUN 2021 AT 04:00

NEWSPAPER SECTION: LIFE WRITER: PATTARAWADEE SAENGMANEE

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| Prof Kiat Ruxrungtham from the Center of Excellence in Vaccine Research Center and Development. Photo courtesy of Chulalongkorn Hospital

As many countries are being devastated by shortages of Covid-19 vaccines, Chulalongkorn University is giving Thailand a new lease of life with its ChulaCov 19 vaccine, which began phase one of human clinical trials yesterday.

The project is a joint venture between Prof Kiat Ruxrungtham from the Center of Excellence in Vaccine Research Center and Development (ChulaVRC) and Professor Drew Weissman from the University of Pennsylvania. The vaccine will use mRNA technology to trigger an immune response against Covid-19, similar to the Pfizer-BioNTech and Moderna shots.

With a goal of supplying vaccines to the nation and Southeast Asian neighbours, this project has the potential to transform Thailand into a new player in the world of pharmaceuticals as well as bring attention to its domestic medical research scene.

"With over a decade of expertise, ChulaVRC has adopted different technologies to develop DNA, protein-based and virus-like particle vaccines for cancer, dengue fever, leptospirosis and HIV. Four years ago, we recognised the potential of mRNA technology and invited Professor Drew Weissman -- one of the pioneers of mRNA technology -- to join our annual forum. In 2019, we teamed up with Professor Weissman to develop mRNA vaccines for allergies," said Kiat.

"Initially, we intended to develop mRNA vaccines for dengue, however, the country has been hit hard by Covid-19, so we have redirected our efforts to develop a Covid-19 vaccine."

The benefit of mRNA vaccines is that they can be made rapidly. The research team spent just one month designing the prototype of ChulaCov 19 and later worked with a biotechnology company in California to produce the first batch. Between March and July last year, ChulaVRC conducted animal tests and the results showed that the vaccine could produce more than 50,000 titres of neutralising antibodies in mice and 5,000 titres in monkeys that could block the virus from entering cells. A titre is a medical expression of antibody concentration.

"Currently, mRNA vaccines can induce antibodies in average from 300 titres to more than 1,000 titres. These may be the key reason why mRNA vaccines can cross protect new variants than other vaccine platform," Kiat said.

"Before moving to clinical trials, we have to confirm in transgenic mice viral challenge model when mice vaccinated with 1µg dose of the ChulaCov 19 mRNA vaccine, compared to the control group, could completely prevent the Covid-19 symptom and block the Covid-19 virus from spreading to the bloodstream and had reduced the virus levels in the nose and lungs."

For human clinical trials, the priority is safety. The first phase will include 72 volunteers between 18 and 75 to learn how many doses will be required while the second phase will test efficacy in 5,000 people. The ChulaVRC vaccine project includes collaboration with colleagues in Malaysia and Singapore to compare blood samples from people who received the Pfizer shots and samples from Thai volunteers to examine the difference in immune response between the first and second doses.

"We will also send our vaccine to an international lab approved by the World Health Organization [WHO] for testing to ensure the second phase goes smoothly. At the moment, the WHO and National Insurance Services are

attempting to determine by how much should the vaccine increase immune systems to prevent Covid-19. This will help speed up the process and possibly avoid the need for a third phase of testing. For instance, if a vaccine for influenza can raise immunity by 40 IU, a third phase is unnecessary," Kiat said.

Regarding concerns about side effects, Kiat indicated that muscle pain and fever are good signs that the vaccine is stimulating the immune system properly. Individuals have various sensitivities based on their genes and between one to five people in a million may experience severe allergic reactions regardless of if they get vaccines based on inactivated, viral vector or mRNA technology.

"As more evidences support the emerging of viral variants that escaping vaccine efficacy, the "Beta" and "Delta" variants in particular, thus at ChulaVRC we are also working on the next-generation vaccines against these resistant viruses," Kiat said.

While many leading pharmaceutical companies have developed vaccines to contain the Covid-19 pandemic, the Thai government, Chulalongkorn University, King Chulalongkorn Memorial Hospital, the private sector and the general public have contributed more than 300 million baht to the ChulaCov 19 vaccine project.

ChulaVRC is also working with Bangkok-based BioNet-Asia to produce a second generation of the vaccine -- to protect against the Beta variant -- which will be given as a third booster shot next year for people who have already received the Oxford-AstraZeneca and Sinovac vaccines.

"We expect all second-generation vaccines to be manufactured in Thailand, which has a production capability of more than 10 million doses a year. This month, they will be tested in mice and if successful, it means our vaccine can also protect against the Delta and Gamma variants," Kiat said.

"It's good that we have mRNA technology. However, Baiya Phytopharm can also produce Covid-19 plant-based vaccines, the Government Pharmaceutical Organization has made inactivated vaccines, and Siam Bioscience has adopted viral-vector technology from AstraZeneca and Oxford University. Thailand has integrated all the technology it has available, allowing the government and private sector to engage in global trade negotiations.

"We don't expect money but instead to make Thailand and its neighbours safe. We want to provide them with vaccines also and this is the solution for economic recovery. Israel, which has inoculated 90% of its population, provides a good example of what recovery looks like. Without needing a vaccine passport, people there can go to the movies or hang out at a club. If there isn't another Covid-19 outbreak in three to six months, it's also possible that we'll be able to resume our usual lives."

Interestingly, the vaccine is more thermostable which means ChulaCov 19 is stable at 2-8 °C for up to 3 months, and at 25 °C for up to 2 weeks. This will solve the concern on logistic transportation.

"Thailand can learn a lesson from the Covid-19 crisis. It should enable academic research to enter the industry. We should have a mechanism in place to support and develop our own technology. We should join hands with researchers both universities and the private sector as well as world-class experts and biotech companies. We would like to see the government invest in this area so that Thailand can compete at the global stage," he said.

Besides the ChulaCov 19 vaccine, the research centre is also working on cancer and allergy vaccines, which will begin human trials in the middle of next year.



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