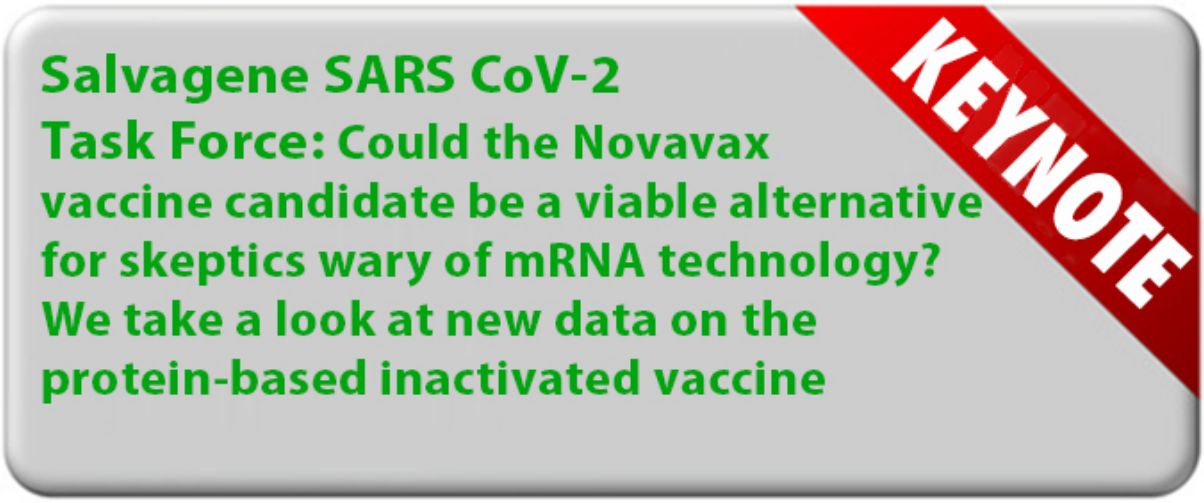
Salvagene GROUP

Business Unit: SARS-CoV-2 Task Force
Keynote: #97

October 2021



Many people who are skeptical of mRNA technology have been waiting for a conventional vaccine against coronavirus to come along. "Classic" vaccines are traditionally based on proteins. However, the one formulated by Novavax has a major disadvantage, specifically its ability to provide long-term protection against virus variants.

On 10th October, scientists presented the results of a Phase 3 trial involving almost 30,000 adults resident in the USA and Mexico. In the preprint, they report an efficacy of 90.4 percent against symptomatic infection with SARS-CoV-2. In September, the New England Journal of Medicine published results from a trial involving 15,000 volunteers in the UK which came to the same conclusion. Both studies were conducted before the Delta variant became the dominant form of the virus. It was observed that the direct side-effects of vaccination in the Phase 3 study were less noticeable with the

Novavax candidate than with the mRNA vaccines. Novavax is also injected in two doses.

Among the manufacturers of protein-based vaccines, the US pharmaceuticals giant is the furthest along in the approval process; its application has been running in the EU rolling review process since February of this year. The EU Commission has secured 200 million doses in anticipation of approval. Novavax plans to submit an application for approval of its vaccine in the USA this year. This was the state of play as of 15th October 2021. On closer inspection, however, the Novavax vaccine is somewhat less than conventional. The company itself makes reference to "innovative proprietary recombinant nanoparticle technology." Although NVX-CoV2373 is a "killed" (i.e. inactivated) vaccine and is thus consistent with an established vaccination principle, it has also been given a new type of adjuvant to boost its effectiveness. This is based on a saponin extract obtained from the soap bark tree native to Chile. It is significant that the COVID-19 vaccines approved so far do not contain an active adjuvant.

The vaccine is produced in insect cell cultures, with up to 14 SARS-CoV-2 spike proteins being combined to form a nanoparticle which, for the immune system, resembles the virus itself. But the nanoparticle does not contain any genetic material – which is not only an advantage, but also a problem. This is because RNA or DNA content strengthens the immune response. This is part of the natural defense against infection, because regular pathogens also contain genetic material.

The adjuvant of the protein-based Novavax vaccine is apparently very effective, as indicated by the high efficacy in the studies. However, it cannot solve one problem of protein vaccines: they neither penetrate body cells nor do the multiply there. This means that the stimulation of the second arm of our immune system – the cellular immune defense – does not take place.

Vaccination can initiate a cellular immune defense response (T-killer cells, memory cells) as long as the vaccine enters body cells, something that Vector and mRNA vaccines are capable of. With protein-based vaccines, on the other hand, the cytotoxic T-cells are only marginally stimulated, with the main thrust coming in the form of antibody response. This makes it easier for the virus to become resistant to these vaccines because the immune response is not as broad.

This may also explain the results of a phase 3 trial in South Africa, where the efficacy of the Novavax vaccine NVX-CoV2373 against symptomatic SARS-CoV-2 infections was only around 50 per cent – possibly because of the local dominance of SARS-Cov-2 Beta which is the most efficient variant at evading neutralizing antibodies.

There are still some gaps in our knowledge about the various Covid-19 protein-based vaccines on the horizon. Furthermore, Novavax currently seems to be having problems with its manufacturing process. It is not yet clear if and when approval will be granted, but we will continue to monitor developments. We expect more news on this front in early 2022. Also on our radar is the vaccine from the French-Austrian company Valneva. They too have recently published the results of a Phase 3 trial of their inactivated vaccine VLA2001 and are likely to submit an application for marketing authorization soon.

By contrast, we already have extensive knowledge about mRNA vaccines. They are safe and have the best efficacy rate. In our opinion, there is no good reason to wait for future marketing authorizations before getting vaccinated.

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