Optimising RNA Vaccines and Therapeutics

Safer RNA Vaccines and Therapeutics

Noxopharm Ltd (ASX:NOX) is an innovative Australian biotech company discovering and developing novel proprietary anti-inflammatory technologies and cancer treatments. Led by a highly experienced management team, its Sofra™ platform represents a pioneering approach to optimize mRNA vaccines and treat autoimmune and inflammatory diseases.

The Noxopharm Sofra™ technology platform is based on ultra-short oligonucleotides (oligos) with diverse applications to modulate inflammation. The lead candidate in the Sofra platform is SOF-VAC™, a novel mRNA vaccine enhancer.

Improving mRNA Vaccines

Noxopharm and its subsidiary Pharmorage, in strategic collaboration with Hudson Institute of Medical Research, have developed several preclinical 3-base oligos (3-mers) that have displayed highly potent and selective reduction of inflammation through binding to Toll-like receptors 7 and 8 (TLR7 and TLR8).

These ultra-short oligos represent a new class of drugs, and are significant due to their extremely potent anti-inflammatory activities. This activity has been demonstrated in in-vitro and in animal models.

When an mRNA vaccine is injected, the mRNA breaks down into fragments, some of which activate the TLR7 inflammation receptors. This results in overstimulation that causes inflammation known as reactogenicity. In contrast, SOF-VAC blocks TLR7 inflammation receptors, thereby reducing the reactogenicity (inflammation) caused by mRNA vaccines at its source.

SOF-VAC has a well-defined selective mechanism of action, its ability to reduce inflammation and improve vaccine safety while preserving vaccine efficacy has been demonstrated. It offers the mRNA vaccine industry the opportunity to enhance existing vaccines and to broaden the range of mRNA technologies, including mRNA therapeutics being developed for new treatments.

Hudson Institute of Medical Research and Pharmorage have recently been supported with AU$3 million in government grants. In terms of financial opportunity, the mRNA market in 2021 was US$42 billion, and is expected to grow to US$128 billion by 2030 at a compound annual growth rate of 13%.

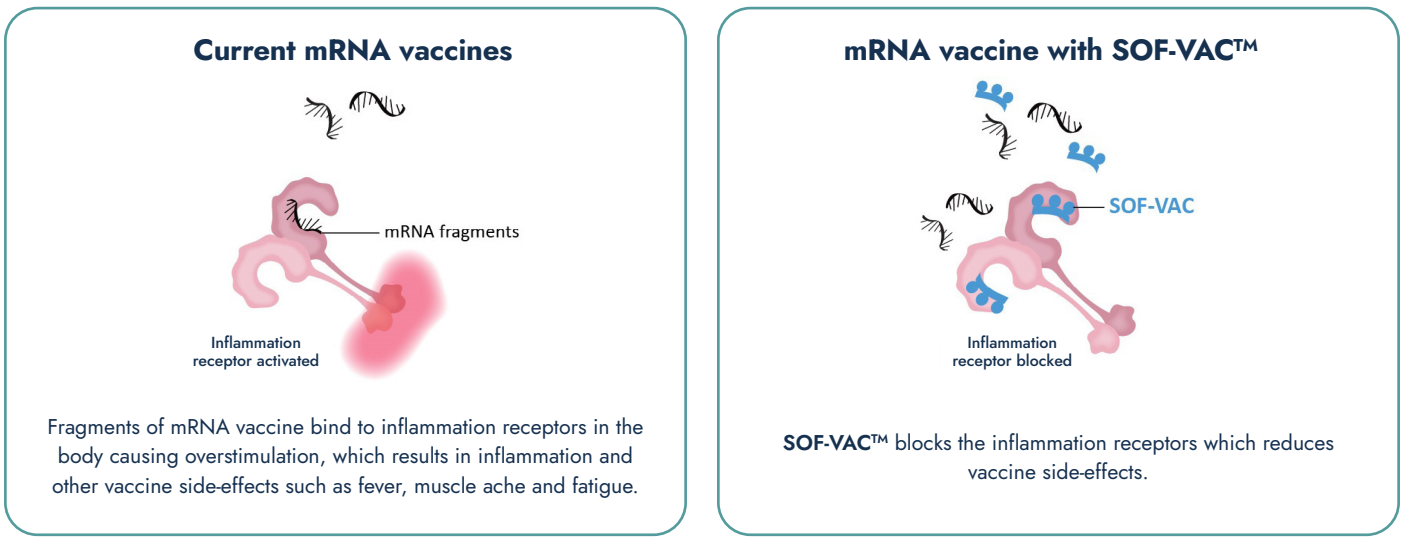


Figure 1. Working hypothesis of the action of SOF-VAC co-administered with mRNA vaccines.

In-vivo Study Results

SOF-VAC reduces mRNA-induced inflammation

To determine if SOF-VAC was effective at reducing mRNA-induced inflammation (reactogenicity) in a mouse model, inflammatory cytokine levels were measured in the blood six hours post-injection. Averaged across nine cytokines (inflammatory markers), an approximate 50% reduction (48.2%) in cytokine levels was detected (Fig. 2), including highly significant decreases ($p<0.001$) in several critical cytokines driving post-vaccine inflammation and side effects.

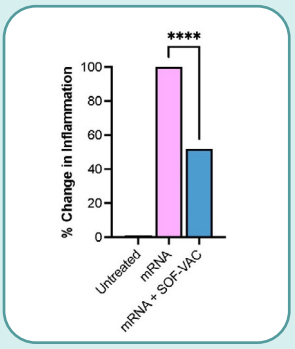


Figure 2. Compounded average percentage showing highly significant decrease in levels of nine inflammatory cytokines ($p<0.001$) detected in the blood of mice six hours post-injection with mRNA alone or mRNA co-packaged with SOF-VAC.

Full RNA effectiveness maintained in combination with SOF-VAC

To measure whether the mRNA activity was preserved in the presence of SOF-VAC, the mRNA used was translated by cells in the body to make a protein (luciferase), allowing for in-life bioluminescent detection and quantification of mRNA expression using a specialised imaging machine.

Luciferase activity in the mice at six hours post-injection showed no significant difference in protein expression between the mice that received the luciferase mRNA alone and those that received luciferase mRNA co-packaged with SOF-VAC (Fig. 3). The function, i.e., activity, of the mRNA was fully preserved, demonstrating that SOF-VAC did not reduce mRNA translation.

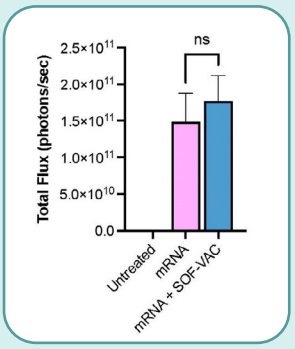
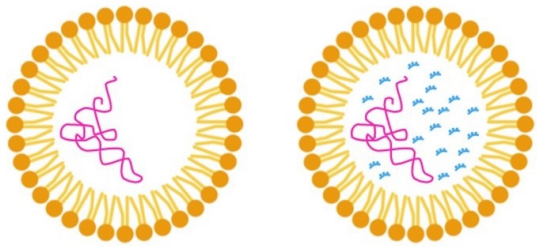


Figure 3. Measurement of mRNA expression (bioluminescence) in mice six hours post-injection with luciferase mRNA alone or mRNA co-packaged with SOF-VAC showed no significant difference.

Successful co-packaging of SOF-VAC into mRNA delivery system



Images created using BioRender

Figure 4: LNP delivery system

Lipid-based nanoparticles (LNPs) are used to deliver mRNA in vaccines currently in use.

SOF-VAC was co-packaged with mRNA inside ALC-0315 ionizable LNPs, an FDA-approved mRNA delivery system that has been successfully deployed for Pfizer/BioNTech's BNT162b2 mRNA COVID-19 vaccine.

Co-packaging of SOF-VAC with mRNA inside this delivery system did not impact the integrity and properties of the LNPs.

- **SOF-VAC reduces mRNA-induced inflammation**
- **Full RNA effectiveness maintained in combination with SOF-VAC**
- **Successful co-packaging of SOF-VAC into standard mRNA delivery system**

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