Developing and delivering mRNA lipid nanoparticle therapeutics

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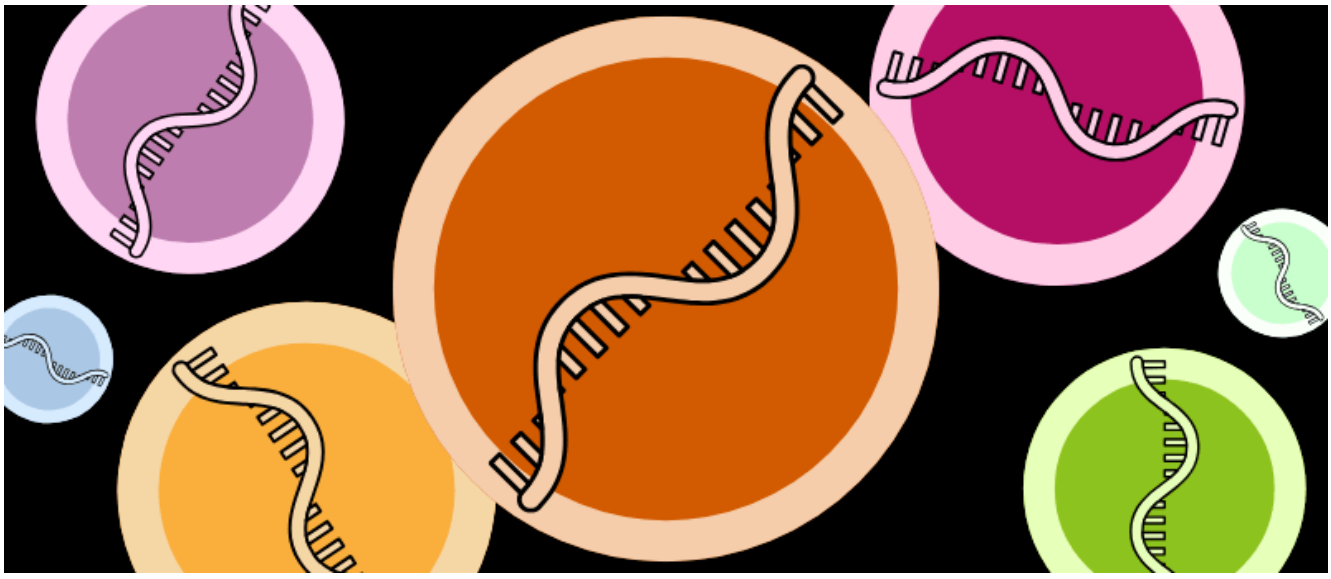

Örn Almarsson is the Co-Founder and CEO of a startup biopharma company called Axelyf (Hafnarfjörður, Iceland & MA, USA) that is developing lipid technologies to safely and efficiently deliver mRNA therapeutics. Örn previously worked for companies like Merck (PA, USA) and Moderna (MA, USA), where he and his team developed therapeutic delivery systems for mRNA, before co-founding Axelyf.

At ELRIG Research & Innovation (10–11 March 2025; London, UK), Örn spoke about mRNA lipid nanoparticle technology for delivering therapeutics in the future. In his talk, he demonstrated that there are ways to deliver therapeutics that produce large proteins like antibodies from mRNA templates. We caught up with Örn to learn more about mRNA therapeutics and lipid delivery systems, as well as what we can expect from these therapeutics in the future.

What are mRNA lipid nanoparticles (LNPs)?

The easiest way to describe them is that they are multicomponent lipid assemblies that have mRNA within them. They are approximately the size of a virus, but they're composed of lipid components that sometimes cause the particles to look like lipoprotein particles, which are naturally found in the bloodstream. Because of this, mRNA LNPs are sometimes mistaken for native lipid particles, so they end up in the liver, which is often the delivery target tissue. However, we're also working on how to deliver these particles to other tissues.

What are the delivery challenges associated with mRNA therapeutics and how is Axelyf addressing these challenges?

If you set aside cost, which is a continuous improvement opportunity in every industry, the challenges we see revolve around stability, side effects and therapeutic targeting of the biologic products. The world and all its various geographies are not optimally served if your biologic products are not sufficiently stable to be shipped and used everywhere. mRNA therapeutics require a cold chain to remain stable, which poses an issue for some medical infrastructures. Many groups are working on thermal stability, and Axelyf is determined to do a good job managing the issues that eventually cause loss of shelf life. That said, many RNAs such as mRNA have chemical instability that is inherent and it takes a lot of engineering to mitigate this instability.

Another major challenge besides stability is the inflammatory response that can accompany the delivery of mRNA therapeutics, especially when using lipid delivery systems. If we're trying to treat someone with an autoimmune disease or an inflammatory condition, we don't want to give them something that has a delivery component that causes inflammation. We are looking at the combination of potency enhancement (meaning that we can use less of the material to get the same effect in biology) and the immunostimulatory signals from delivery to develop the optimum delivery approach for each purpose.

Finally, the third main challenge with delivering mRNA therapeutics via lipid particles is tissue distribution and addressing how to get therapeutics into certain organs. This is a tall task for lipid systems, but progress is being made on surface modifications that allow for both longer circulation and less recognition by the liver, so the packages can be delivered outside the liver. Axelyf has significant interest in this and a collaboration in Ireland on the topic, and there are many other companies in this space, which offer great expansion opportunities for nanoparticles to deliver RNAs to many parts of the body.

What techniques are used to develop mRNA therapeutics as well as mRNA LNPs?

mRNA therapeutic development is based on nucleic acid sequence knowledge that can be designed and developed. It starts with a DNA plasmid template that has the information that you can then transcribe into your mRNA. Once you have your mRNA in solution, you can encapsulate it inside an LNP that you have designed in a micromixing process with the mRNA and lipid components, producing a sterile, injectable product.

What impact will mRNA LNPs have on therapeutics development in the future?

They're already having an impact and will continue to have an impact because LNPs provide a very useful and adaptable way to deliver nucleic acid therapeutics. We will be seeing many examples of successes in therapy over the coming years – for example, the use of mRNA LNP technology to accomplish precise and safe gene editing in humans. Such therapy can radically change the course of someone's life for the better. The mRNA approach is perfect for this purpose because it creates the editing system in a transient way, in the right cells and the right spots in the genome – like fixing a typo in a large computer program. The mRNA LNP technology has these types of transformative

possibilities. The particles to deliver RNA will continue to be modified in various ways to become more potent, versatile for targeting different tissues, safe and commercialized.

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