Science and Technology Facilities Council

Understanding the enhanced mRNA functional delivery of lipid nanoparticles formulated using a high-throughput platform

Biopharmaceutical company, AstraZeneca, recently developed an automated technique to generate lipid nanoparticles for mRNA delivery and used neutron scattering to investigate how it compared to standard production methods.

Challenge

Lipid nanoparticle (LNP) encapsulation is one of the most successful non-viral delivery technologies to shield mRNA from degradation.

To accelerate the study of LNPs, a team from AstraZeneca developed an automated high-throughput platform to generate and screen LNPs for mRNA delivery. The team wanted to evaluate the mechanistic and physiochemical properties of LNPs prepared using the automated process, to understand their enhanced mRNA functional delivery compared to those produced by a standard microfluidic mixing platform.

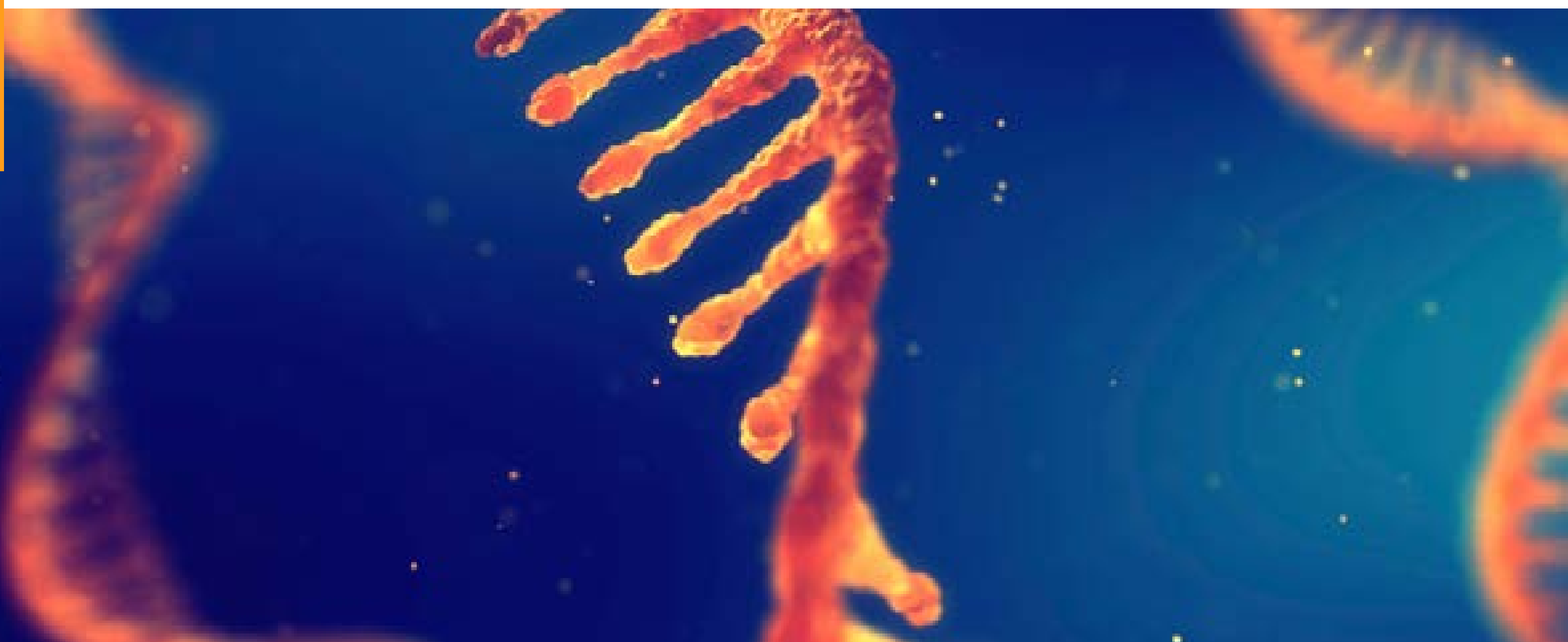
Solution

The AstraZeneca team exploited the complementarity of small-angle neutron scattering (SANS) and small-angle X-ray scattering (SAXS) to compare the internal structure of LNPs generated using the new automated process versus those generated by the standard process.

Benefits

The studies revealed that LNPs produced using the automated system were larger, had a higher mRNA loading, a more hydrophobic surface, and more hemolytic and beneficial cellular uptake pathways. As a result, LNPs made using the new automated platform were 4.5 times more effective than those made via the standard protocol.
Crucially, the findings have provided valuable insight to accelerate research and development of mRNA therapeutics.

> **“We deeply appreciate the support from ISIS facility and scientists for the neutron beam time and the valuable knowledge which help us unveil the internal and surface property of the mRNA LNP nanoparticles.”**
>
> Lili Cui, Senior Scientist Formulation Advanced Drug Delivery, AstraZeneca



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ISIS Neutron and Muon Source

ISIS Neutron and Muon Source has successful collaborations with many different industries, delivering insights to develop new and improved materials and processes.

Why use neutrons?

Study structure

Neutron wavelengths are comparable to the spacings of atoms and molecules.

Study dynamics

Neutron energies are comparable to the time scales of molecular diffusion, vibrations and rotations.

Study magnetism

The neutron's magnetic moment can be used to study the microscopic magnetic properties of materials.

Penetration power

Neutrons can penetrate deep into matter (including many different metals) enabling the study of large samples – even within complex sample environments.

Non-destructive

As a non-destructive, non-invasive probe, neutrons are suitable for the characterisation of delicate and precious samples.

Versatile sample environments

Sophisticated sample environments enable measurements under operating conditions – including extreme temperatures and pressures.

Sensitivity to light elements

The neutron scattering power of nuclei varies in a random manner such that lighter atoms (e.g. H, Li) can be studied in the presence of heavier ones.

Isotopic contrast

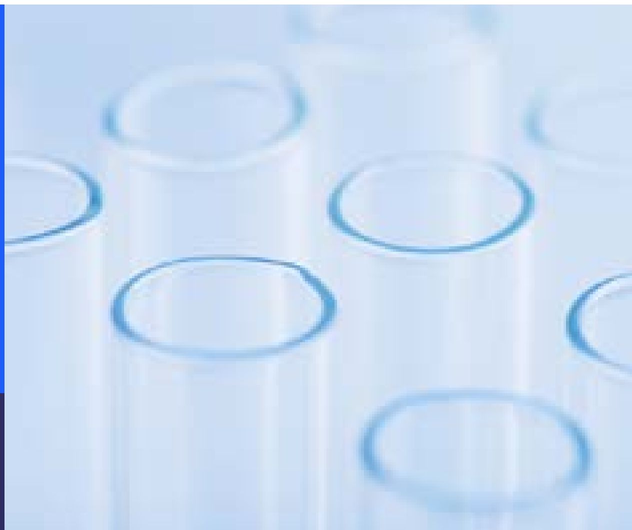
Neutrons are sensitive to different isotopes of the same element, so isotopic substitution (e.g. H/D) can be used to highlight specific structural features.

Complementarity

Neutron scattering is highly complementary to other techniques, such as X-ray scattering, electron microscopy, magnetic resonance and computational methods.

How to work with ISIS

ISIS offers industrial users access to advanced analytical techniques and expert scientific and technical support for materials characterisation. Access options include proprietary use, academic partnerships, grant funded access, and the Industrial Collaborative Research and Development (ICRD) program.



For more information, email ISISindustry@stfc.ac.uk to discuss the most suitable method to solve your challenge.