MIST: Artificial intelligence-assisted design of experiments as a tool to streamline the development of siRNA-lipid nanoparticle therapeutics in soft mist inhalers

POPULAR SCIENCE SUMMARY OF THE PROJECT

If you or your children have ever suffered from bronchitis or pneumonia, your doctor may have prescribed medication for nebulization. You might also remember that administering the medicine took quite a while, and you had to sit impatiently by the nebulizer. Nebulization is an example of inhaled drug delivery, which involves converting a liquid medicine into a mist that the patient then inhales. This is a common route of administration for lung diseases such as asthma, pneumonia, and chronic obstructive pulmonary disease.

Did you receive a COVID-19 vaccine during the pandemic? Most of us were vaccinated with formulations in which messenger RNA (mRNA) molecules were enclosed in tiny lipid particles called lipid nanoparticles (LNPs). These vaccine solutions were administered via intramuscular injection, often followed by pain lasting for several days.

Now imagine that such a vaccine could be delivered as a mist sprayed from a modern nebulizer, a soft mist inhaler that doesn’t require electricity! Painless, quick, and convenient inhalation-based drug delivery!

The goal of our project is to develop an advanced pharmaceutical formulation for delivering small RNA molecules, specifically small interfering RNA (siRNA), enclosed in lipid nanoparticles, which will be sprayed using a soft mist inhaler. This type of inhaler ensures consistent and efficient delivery of the medication to the lungs. However, a significant challenge remains in maintaining the long-term stability of siRNA-LNPs in solution and preserving the nanoparticles during aerosolization. Therefore, we aim to develop new lipid nanoparticles using lipids whose chemical structure enhances the mechanical stability of the LNPs during aerosolization and prolong their storage stability.

RNA-based drugs are a new class of therapeutics that are set to revolutionize medicine and existing treatment methods. siRNA molecules can downregulate the expression of specific genes, offering a promising method for treating various conditions, including cancer, asthma, and diseases linked to gene overexpression. During siRNA-LNPs evaluation, we will use cellular models that mimic the structure of the human lung epithelium as well as tissue models derived from healthy lung tissues received from patients during surgical procedures.

To design the composition of new LNPs, optimize the manufacturing process, and predict their stability, we will use statistical tools such as Design of Experiments (DoE), supported by artificial intelligence-based solutions.

Our project will contribute to the advancement of modern techniques and the development of innovative pharmaceutical formulations, for example, siRNA delivered as a gentle mist through a soft mist inhaler. Our approaches will not only accelerate and improve the development of new therapies but also reduce the number of required experiments and the overall research costs. New AI-based digital tools may prove extremely useful in the development of future drugs and pharmaceutical dosage forms.