Functional nanomaterials based on drug–lipid–ligands as targeted delivery systems for anticancer agents in lung adenocarcinoma

One of the biggest challenges in cancer treatment today is that most chemotherapy drugs don't discriminate between cancer cells and healthy cells. As a result, patients often suffer from severe side effects, while the drugs may not reach the tumour effectively. This project aims to develop a smart drug delivery system based on tiny, targeted particles that can carry the drug directly into lung cancer cells, where the drug will be released. The project focuses on a specific type of lung cancer called lung adenocarcinoma (LUAD), which is not only the most common form of lung cancer but also the deadliest. Globally, lung cancer is the most frequently diagnosed cancer and the leading cause of cancer-related deaths. This alarming statistic drives the urgent need for better, more precise treatments.

To meet this challenge, the research will focus on designing specialised nanomaterials—very small molecules that combine three important parts:

- a targeting unit (in this case, a sugar called mannose) that guides the nanoparticle to lung cancer cells,
- a lipid matrix, which helps the nanoparticles form stable structures and stays intact as they travel through the bloodstream,
- a linker, responsible for specific release,
- a chemotherapeutic agent, such as etoposide, gemcitabine, or crizotinib, which will only be released once the nanoparticle enters the cancer cell.

Why mannose? Certain lung cancer cells display a protein called CD206 on their surface, which binds specifically to mannose. This means that mannose can act like a homing signal, helping the drug-loaded particles find and enter the tumour cells, leaving healthy cells intact. What makes this approach unique is the way the drug is attached to the nanoparticle. Instead of simply embedding the drug in the particle (as is often done), the drug will be chemically linked in a way that keeps it inactive during circulation. Once the nanoparticle reaches the acidic environment inside the cancer cell's lysosomes, the drug will be released. This approach will prevent the drug from leaking out too early from the particle and harming other tissues. The idea of the smart drug delivery is presented in **Fig. 1.**

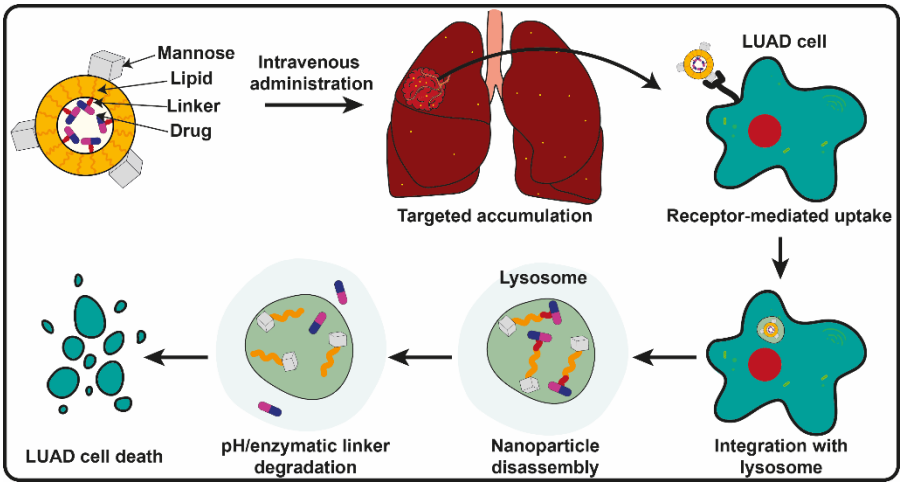

*Fig. 1. D*iagram showing the idea of the drug delivery system.

To carry out this plan, the researchers will follow three main steps:

Chemical Design and Characterisation: Scientists will chemically modify the nanomaterials, protecting and modifying key parts of the molecule to ensure stability and functionality. These materials will be carefully analysed to confirm that their structures are correct using techniques like NMR and mass spectrometry.

Nanoparticle Formation: The materials will be assembled into nanoparticles using established lab methods. Researchers will compare these new particles with standard nanoparticles that contain physically encapsulated drugs and also with particles without any drug inside. They will measure the size, shape, drug release profile, and how stable the particles are under different conditions, such as changes in temperature, pH, and exposure to enzymes.

Biological Testing: Finally, the new drug delivery systems will be tested in a variety of lab procedures. This includes studying how the particles interact with cell membranes, how toxic they are to lung cancer cells and healthy cells, how efficiently they are taken up by cells, and where they go inside the cell. Tests will also be done using zebrafish, a well-established model for studying toxicity and behaviour in living organisms.

The project's expected results are twofold. First, it will show whether it is possible to create lipid-based nanomaterials that carry both a targeting agent and a drug in a chemically linked, stable form. Second, it will determine whether this new delivery system is better than existing approaches in treating LUAD, by being more effective against cancer cells while reducing side effects to the other parts of the body.

If successful, this work could lead to a new generation of individualised chemotherapeutic approaches, offering safer and more efficient care for lung cancer patients.