Title: Biomimetic Nanoparticles for Targeted Therapy in Pulmonary Fibrosis

Abstract:

Pulmonary drug delivery demands advanced systems that offer biocompatibility, lung-specific targeting, and effective therapeutic outcomes. Dipalmitoylphosphatidylcholine (DPPC), the primary phospholipid component of native lung surfactant (LS), is an ideal building block for biomimetic nanoparticles due to its regulatory acceptance, structural simplicity, and compatibility with the pulmonary environment. In this study, we developed two types of biomimetic nanoparticles based on DPPC for the encapsulation and pulmonary delivery of different antifibrotic molecules. Both formulations demonstrated efficient lung biodistribution, prolonged retention for sustained drug release, and strong antifibrotic effects in vitro and in vivo.

First, we produced DPPC-based liposomes for the encapsulation of pirfenidone and investigated the role of polyethylene glycol (PEG) coating in enhancing nano-biointeractions and therapeutic efficacy. We evaluated the impact of PEGylation on surfactant protein corona formation, mucus penetration, cellular uptake, biodistribution, and antifibrotic activity using the bleomycin-induced mouse model of pulmonary fibrosis. These studies provided important insights into how PEGylation affects nanomedicine performance in the context of fibrotic lung disease.

To further harness the native bioactivity of lung surfactants, we synthesized LS-derived nanoparticles (LSNP) using microfluidic technology. This method enabled precise control over particle size (~150 nm), polydispersity, and encapsulation of both imaging agents and therapeutics. LSNP exhibited enhanced cellular uptake compared to both synthetic lipid nanoparticles (LNPs) and unmodified LS. When loaded with nintedanib, LSNP significantly inhibited myofibroblast differentiation, reduced inflammation, and suppressed extracellular matrix deposition in the bleomycin-induced pulmonary fibrosis model. Additionally, Gd(III)-labeled LSNP served as effective T1 MRI contrast agents, allowing non-invasive tracking of lung distribution, with over 85% of the dose retained in the lungs for more than six days, as confirmed by ICP-MS.

Together, these two biomimetic nanoparticle platforms offer complementary advantages for pulmonary drug delivery in the treatment of pulmonary fibrosis.

Short bio:

Dr. Susana Carregal Romero is an Ikerbasque Fellow and Ramón y Cajal researcher at CIC biomaGUNE, where she leads a multidisciplinary team focused on the development of nanomaterials for biomedical applications. Her work lies at the intersection of drug delivery, molecular imaging, and catalysis, with a strong emphasis on exploiting the unique properties of nanoparticles, such as catalytic activity, magnetism, and plasmonics, that emerge at the nanoscale.

Her early research focused on the role of nanoparticle morphology in catalysis. She later expanded into biomedical nanotechnology, developing mRNA-loaded nanoparticles and responsive delivery systems triggered by environmental stimuli like pH, light, or magnetic fields. This work laid the foundation for intracellular catalysis approaches and advanced drug delivery strategies.

Since 2022, she has independently led research projects supported by national and regional funding, focusing on multifunctional nanoparticles for cancer theranostics, lung-targeted drug delivery, and molecular imaging. Her team also investigates nano–bio interactions and develops biomimetic systems to understand cellular processes.

She co-leads a research group within the Spanish biomedical network CIBERES and actively contributes to research initiatives on pulmonary fibrosis.