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Optimizing Lipid Nanoparticles for Targeted Intracellular Delivery in Aceruloplasminemia Treatment

Modestas Mažerimas [1], Eimina Dirvelyte [2], Urte Neniškyte [2], Rima Budvytyte [1]

[1] Vilnius University, Institute of Biochemistry, Vilnius, Lithuania

[2] Vilnius University, LSC-EMBL Partnership Institute for Genome Editing Technologies, Vilnius, Lithuania

Aceruloplasminemia is a rare genetic disorder caused by ceruloplasmin deficiency, leading to iron accumulation and neurodegeneration. Lipid nanoparticles (LNPs) are a promising, non-viral platform for delivering gene-editing tools to correct genetic defects. Despite significant progress in LNP-based delivery systems, challenges remain in optimizing their composition to enhance specificity and therapeutic efficacy. This study investigates the optimization of LNP formulations to achieve an optimal balance between loading efficiency, stability, and targeted delivery. LNPs were characterized for particle size and size changes over time using dynamic light scattering, while nanoparticle stability was assessed via calcein leakage assays. Fluorescence-labeled cargo allowed for the quantification of loading efficiencies and real-time tracking of cellular uptake and release. Results indicate that while established lipid compositions exhibited comparable or slightly higher loading efficiencies, they were less effective for targeted delivery due to insufficient specificity. Furthermore, the incorporation of various sterols led to a reduction in loading efficiency, yet these formulations demonstrated similar targeted release rates to the original LNP composition. These findings help guide LNP design improvements for gene editing, advancing potential aceruloplasminemia therapies.