ACID DEGRADABLE SOLID LIPID NANOPARTICLES

Tech ID: 32514 / UC Case 2022-022-0

PATENT STATUS

Patent Pending

BRIEF DESCRIPTION

The inventors demonstrate that polyethylene glycol (PEG) conjugated to cholesterol via an acid degradable linkage composed of an azide-benzaldehyde acetal has the potential to allow solid lipid nanoparticles (SLNs) to be PEGylated with mole ratios up to 50%.

The azide-benzaldehyde acetal, has its azide in the para position, and generates stable acetals with a t ½ of > 1000 minutes at pH 7.4. These PEG-acetals can be formulated into SLNs, and stored, and then reduced prior to biological use, to generate an amino acetal that has t ½ < 60 minutes at pH 7.4 and several minutes at pH 5.0. The ultra-PEGylated lipids were efficient at transfecting a variety of organs, including the muscle, the lung, spleen and liver and were also able to transfect the blood.

Acid degradable PEG-lipids have great potential for overcoming the PEG dilemma, but have previously been challenging to develop due to the synthetic challenges associated with working with acetals and their instability at pH 7.4. (SLNs contain a PEGylated lipid, generally in the 1-5% range, which is needed to maintain SLN stability, size, and tissue diffusion, and lower toxicity. However, excessive PEGylation also results in lower cell uptake and endosomal disruption — a paradox referred to as the PEG dilemma.)
The inventors anticipate numerous applications of the azide-benzaldehyde acetal linker, given its unique ability to be stable prior to reductive activation.

SUGGESTED USES

This technology can be used for delivering mRNA to a variety of organs such as the heart, liver, lungs, spleen, or brain, for vaccine development, gene editing and numerous other medical applications.

ADVANTAGES

This technology overcomes the PEG dilemma, which has limited the efficacy of solid lipid nanoparticles (SLNs), despite their tremendous potential for delivering mRNA to treat a wide variety of diseases.

RELATED MATERIALS

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Small Molecule Endosomal Disruptor for Biotherapeutic Delivery
- Quaternized-Zwitterionic Ionizable Lipids
- Compositions and Methods for Identifying Functional Nucleic Acid Delivery Vehicles
- New Acid Degradable Lipids Based On Self Assembling Peptides

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OTHER INFORMATION

KEYWORDS

nanoparticle, mRNA, PEGylation, macrogol, PEG dilemma

CATEGORIZED AS

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» Gene Therapy
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