SARTORIUS

Product Datasheet

LipidBrick®

A Library of Innovative Proprietary Cationic Lipids for Lipid Nanoparticle Formulation

Product Information

LipidBrick® is a unique library composed of innovative proprietary imidazolium-based cationic lipids dedicated to the formulation of lipid nanoparticles (LNPs). These active lipids safeguard mRNA molecules and enhance the transfection ability of LNPs. Each LipidBrick® lipid is permanently charged; therefore, unlike ionizable lipids, it confers an overall positive charge to LNPs, which induces extra-hepatic tropism. In addition, delivery efficacy and biodistribution can be fine-tuned by screening the LipidBrick® library to select the most suitable LipidBrick® lipid for each specific application | therapeutic need.

Features and Benefits

- **Efficient:** Modulate LNP properties to adapt biodistribution to therapeutic goals
- **Secure:** Unique structure protected by an independent patent held by Polyplus (now part of Sartorius)
- **Time-Saving:** In vitro and in vivo proof of concept studies have been successfully performed
- **Flexible:** Versatile library for selecting the best LipidBrick® lipid for each application

Introduction

Relevant Applications

- LNP formulation
- mRNA vaccines
- mRNA therapeutics
- Protein replacement therapy
- Gene therapy
- Genome editing
- Ex vivo cell therapy
- Proof of concept studies
- Academic research

Relevant Process Steps

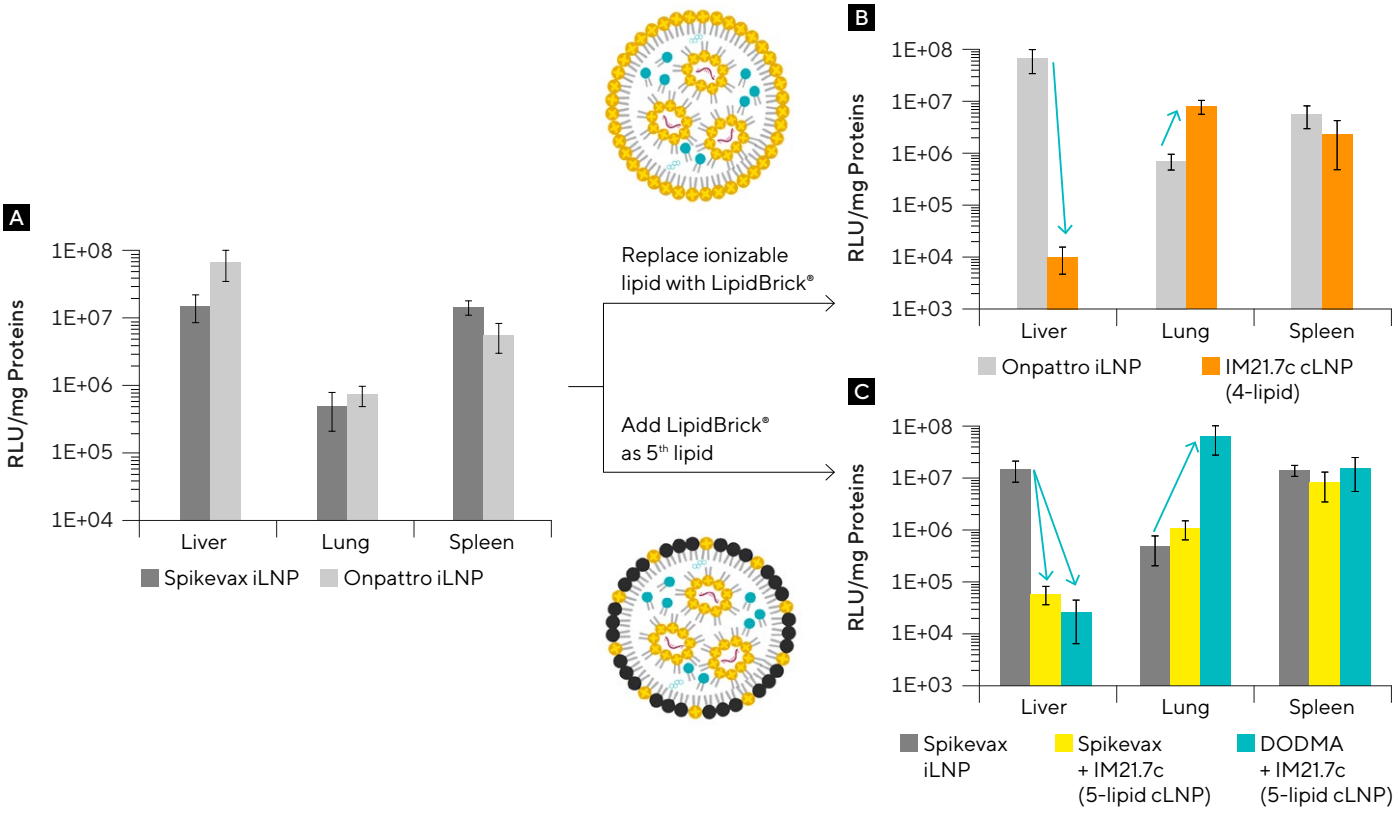
- mRNA-LNP formulation
- Drug product formulation
- Delivery | transfection

Performance

Extra-Hepatic Biodistribution

LipidBrick® lipids are all based on an imidazolium polar head, which gives them a permanent charge and, therefore, differentiates them from ionizable lipids (Figure 1A). LipidBrick® lipids can be used as a complete replacement for the ionizable lipid (Figure 1B) or as a fifth lipid in LNP formulations (Figure 1C). In both cases, their use in the formulation confers an overall positive charge on LNPs, enabling biodistribution beyond the liver.

Figure 1: *Biodistribution Profiles of Different mRNA-LNP Formulations Using Common Ionizable Lipids and | or LipidBrick® IM21.7c*

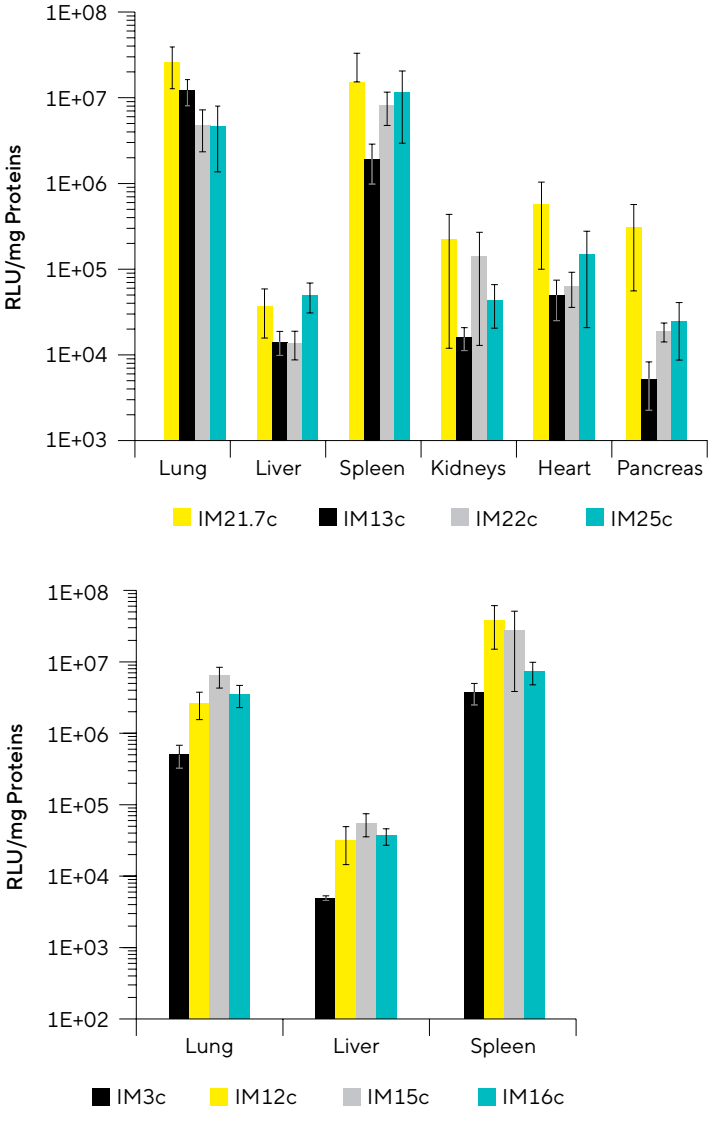


Note. A) Ionizable-based LNPs (iLNP) accumulate in the liver. In contrast, LipidBrick®-based LNPs (cLNP) bypass the liver, whether they (B) replace the ionizable lipid or (C) are added as a fifth lipid. mRNA-LNPs were formulated using common ionizable lipids (SM-102, Dlin-MC3-DMA, DODMA) and | or a cationic lipid (IM21.7c). Luc mRNA (10 µg) was intravenously injected in each mouse and luciferase expression was measured 24 h after injection.

Tunable Delivery Properties

The difference in the chemical structure of each of the LipidBrick® lipids (around their imidazolium-based polar head) can induce differences in affinity with other lipid components, affinity with the payload, encapsulation efficiency, cellular uptake, and affinity with certain tissues or cell types, which leads to different profiles of biodistribution, immunogenicity, stability, etc. Therefore, by working with the LipidBrick® library, it is possible to screen and fine-tune the selection of the most appropriate LipidBrick® depending on the therapeutic applications and target organ or tissue (Figure 2).

Figure 2: *The LipidBrick® Library Makes it Possible to Fine-Tune the Delivery Properties and Tropism of LNPs According to the Therapeutic Objective*

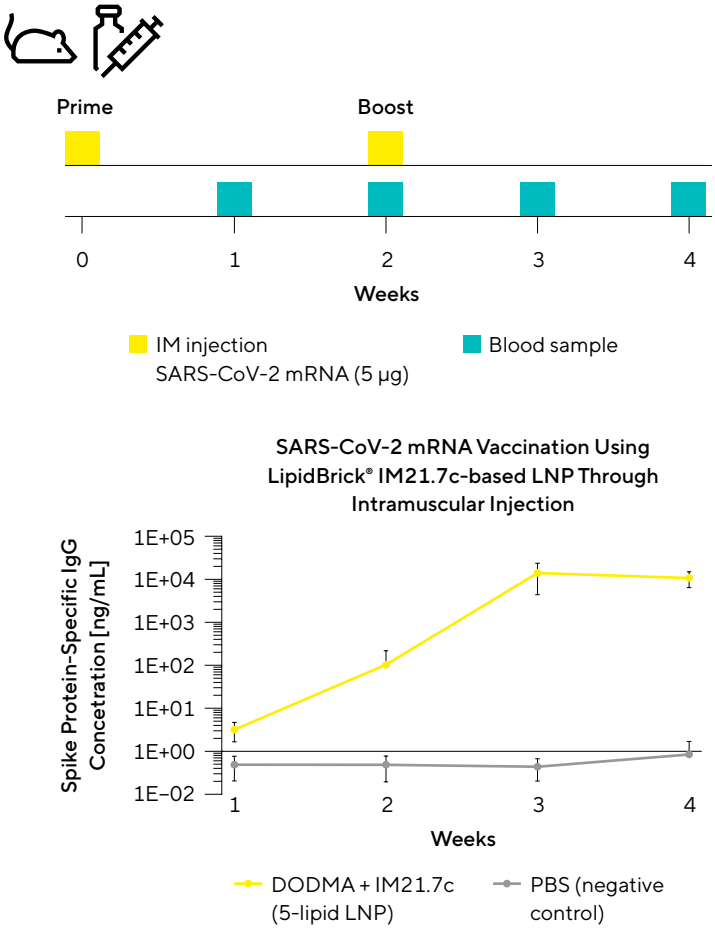


Note. All mRNA-LNPs have the same formulation (DODMA + IMXXc; 5-lipid, cLNP) with the exception of the LipidBrick® lipid used. This single adjustment modulates the tropism of the LNPs, offering additional options for screening.

Vaccination

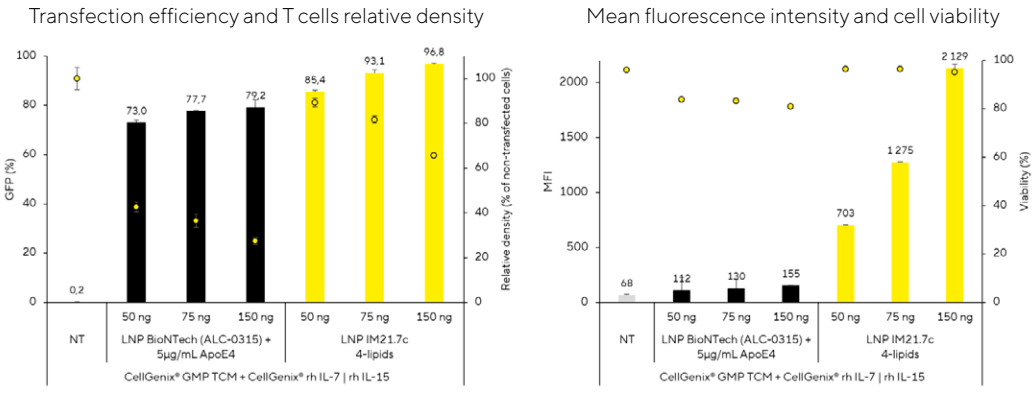
In addition to modulating the biodistribution of LNPs, LipidBrick® has also proved to be a valuable tool for intramuscular vaccinations or immunizations. In addition to its effectiveness and safety, a particularly interesting aspect of LipidBrick® is its secure intellectual property; the unique structure is protected by a patent exclusively owned by Polyplus, now part of Sartorius.

Figure 3: *LipidBrick® IM21.7c-Based LNPs are Efficient for mRNA Vaccination*



Note. mRNA-LNPs (5 µg SARS-CoV-2 mRNA) were injected through intramuscular injection on day 0 and day 14. Blood was collected every seven days for four weeks, and the levels of spike protein-specific IgG were measured by ELISA. PBS was administered as a negative control.

Figure 4: *IM21.7c-LNPs lead to Very High Transfection Efficiency & Cell Viability of Primary Human T Cells Ex Vivo*



Note. mRNA encoding GFP was transfected into primary human T-cells using LipidBrick® IM21.7c-based LNPs and ionizable LNPs (ALC-0315) with 50, 75 or 150 ng mRNA for 187,500 activated primary T-cells in CellGenix® GMP TCM in a 96-well plate. GFP expression, relative cell density, mean fluorescence intensity and viability were assessed 48 hours post-transfection. Activation of T-cells was performed using T-Cell TransAct™ (Miltenyi) and CellGenix® rh IL-7 and rh IL-15.

Technical Specifications

Attribute	LipidBrick® IM21.7c 50 mg	LipidBrick® IM21.7c 250 mg	LipidBrick® IM21.7c 1 g	LipidBrick® Library Kit (8 × 50 mg)
Quality grade	Research grade	Research grade	Research grade	Research grade
Type	Cationic lipid (powder)	Cationic lipid (powder)	Cationic lipid (powder)	Cationic lipids (powder and oil)
Amount	50 mg	250 mg	1 g	8 × 50 mg (50 mg of each of the 8 different LipidBrick® lipids)
Container	Borosilicate glass vial	Borosilicate glass vial	Borosilicate glass vial	Borosilicate glass vials
Storage	–20 ± 5 °C	–20 ± 5 °C	–20 ± 5°C	–20 ± 5°C
Expiry date	Indicated in the certificate of analysis and on the product	Indicated in the certificate of analysis and on the product	Indicated in the certificate of analysis and on the product	Indicated in the certificate of analysis

Ordering Information

Item	Description	Quantity	Order Number
LipidBrick® IM21.7c 50 mg	50 mg of LipidBrick® IM21.7c for LNP formulation	50 mg	101000232
LipidBrick® IM21.7c 250 mg	250 mg of LipidBrick® IM21.7c for LNP formulation	250 mg	101000172
LipidBrick® IM21.7c 1 g	1 g of LipidBrick® IM21.7c for LNP formulation	1 g	101000173
LipidBrick® Library kit (8 × 50 mg)	50 mg of each of the 8 different LipidBrick® lipids	8 × 50 mg	101000241

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