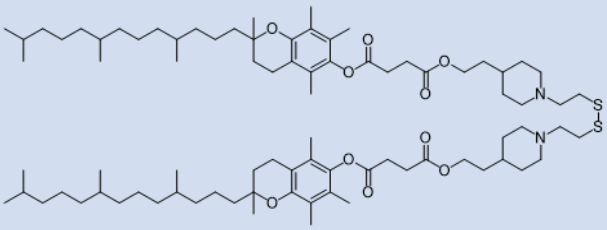
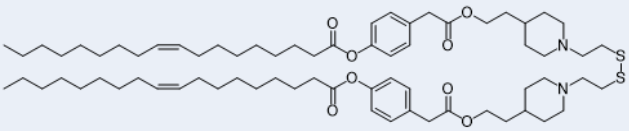
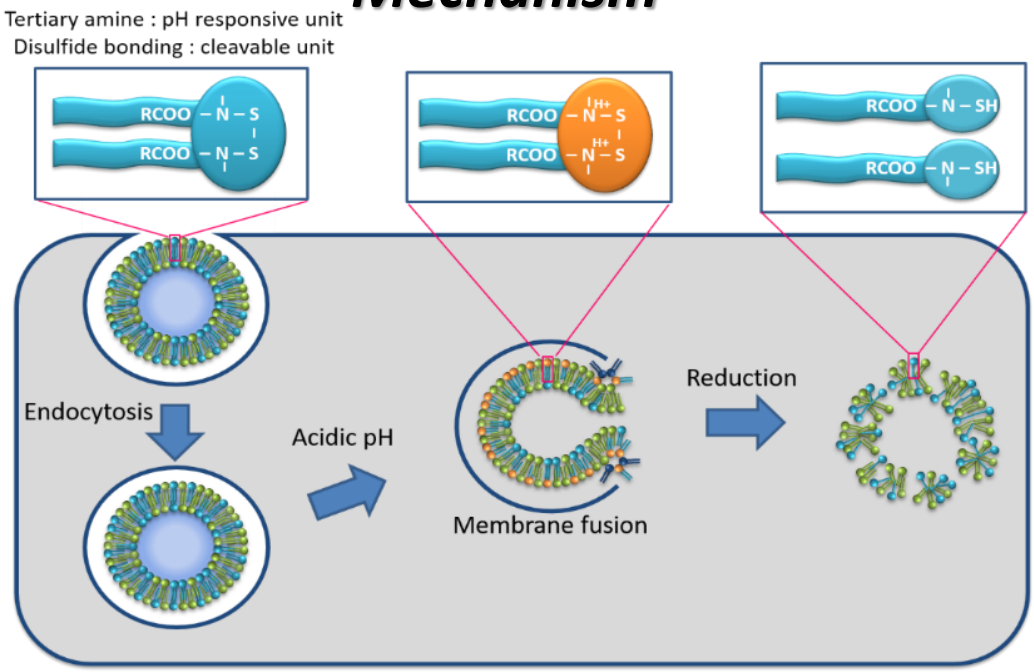
COATSOME® SS-series

Novel Lipid Nanoparticle Platform for Nucleic Acid Therapeutics

Product name	Structure	MW
COATSOME® SS-EC (ssPalm E-P4C2)		1402.2
COATSOME® SS-OP (ssPalm O-Phe)		1173.8

Mechanism



SS lipid applications

Application	Nucleic acid
In vitro transfection	mRNA, pDNA
Liver targeting (I.V.)	siRNA
	mRNA, pDNA
Spleen targeting (I.V.)	mRNA, pDNA
Cancer vaccine (I.M., S.C.)	mRNA, pDNA
Infectious disease vaccine (I.M., S.C.)	mRNA, pDNA
Topical administration	mRNA, pDNA

*Please inquire for detail information on formulation.

Features

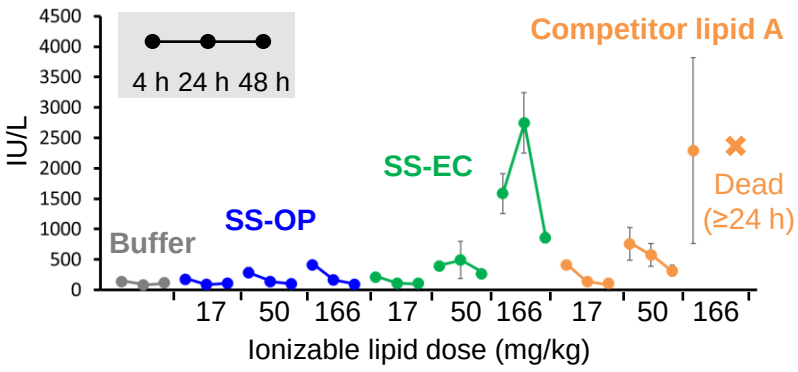
- ✓ Encapsulation: siRNA, mRNA, pDNA
- ✓ Efficient drug delivery and low toxicity
- ✓ Controlled targeting of organs: liver, spleen, or lymph nodes
- ✓ Long-term storage of lyophilized / freeze-thaw LNP
- ✓ Applicable for cancer / infectious disease vaccine
- ✓ Applicable for active targeting

Hepatic delivery

Hepatotoxicity

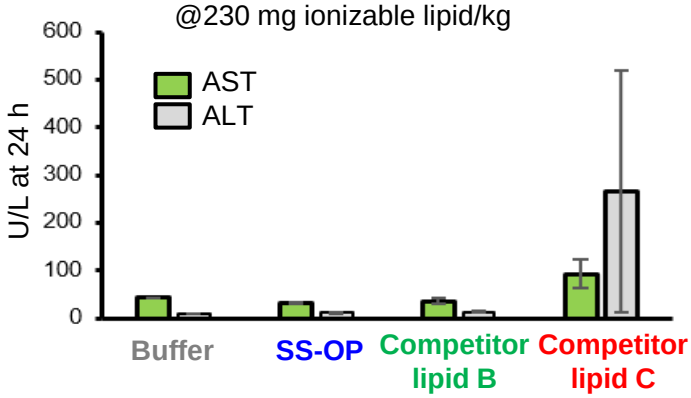
Serum AST level (4, 24, 48 h)

BALB/c mouse, 6w, female (I.V.)



Serum AST/ALT level

BALB/c mouse, 6w, female (I.V.)
@230 mg ionizable lipid/kg

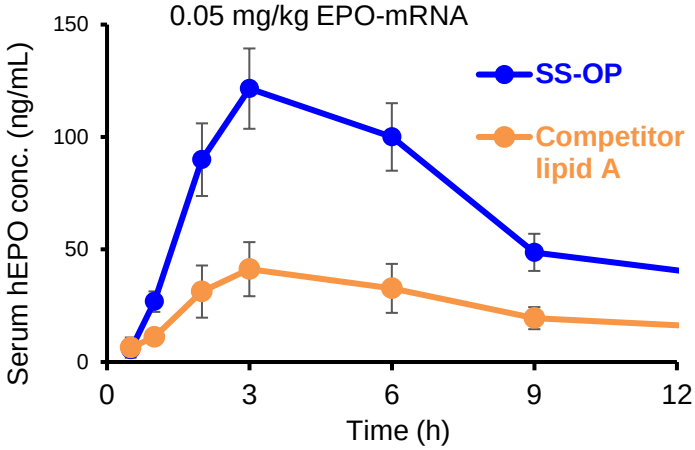


LNP-mediated hepatotoxicity was remarkably suppressed with our SS series.

Gene expression

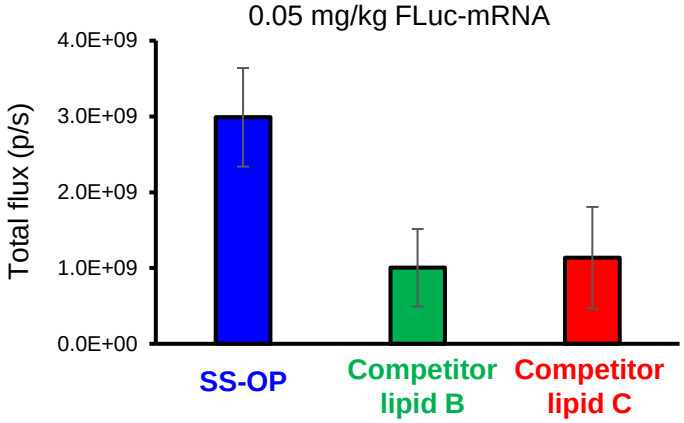
Human erythropoietin (hEPO)

BALB/c mouse, 6w, female (I.V.)
0.05 mg/kg EPO-mRNA



Firefly luciferase (FLuc)

BALB/c mouse, 6w, female (I.V.)
0.05 mg/kg FLuc-mRNA

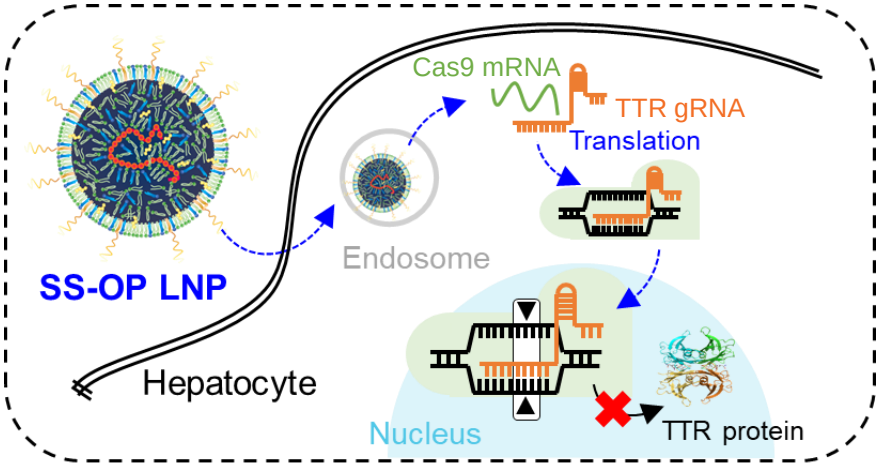


Higher hepatic gene expression than three competitor lipids used in marketed drugs.

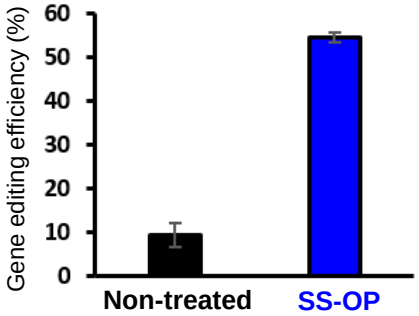
Gene Editing (CRISPR/Cas9)

C57BL/6J mouse, 6w, male (I.V., week 0, 1)

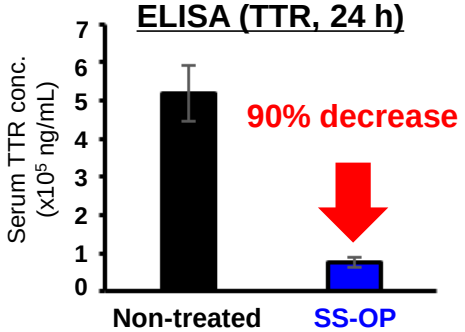
0.375 mg/kg Cas9 mRNA
0.375 mg/kg TTR gRNA
} Co-encapsulation



Gene editing efficiency



ELISA (TTR, 24 h)

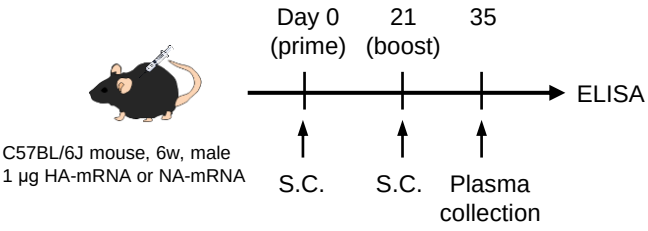


55% of TTR-encoding genome are edited and serum TTR levels are reduced by ~90%.

mRNA vaccine

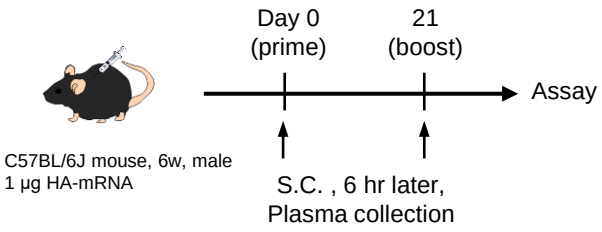
For infectious disease vaccine

Antibody response of the influenza virus

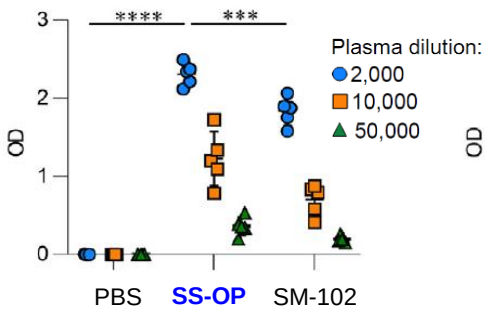


HA: Hemagglutinin, NA: Neuraminidase

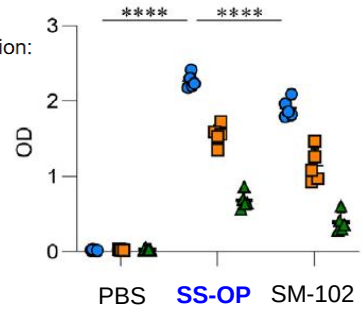
Inflammatory cytokine production



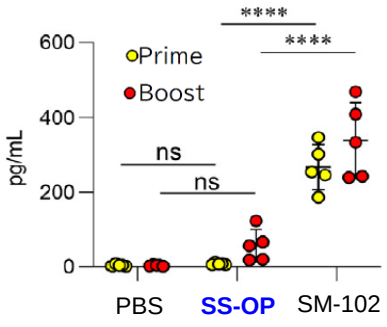
HA-specific IgG1 (boost)



NA-specific IgG1 (boost)



IL-6



Other cytokines (IFN-α, IFN-β, IFN-γ, CCL2, CXCL10) were also suppressed in SS-OP LNP.

SS-OP LNP had comparable IgG production and low inflammatory in comparison with SM-102.

"SS-OP" and "SM-102" notations in the figures on this page are modified from "LNP ssPalmO" and "LNP SM-102" in the reference; Kawai et al., Low-inflammatory lipid nanoparticle-based mRNA vaccine elicits protective immunity against H5N1 influenza virus with reduced adverse reactions, Molecular Therapy (2024), https://doi.org/10.1016/j.ymthe.2024.12.032).
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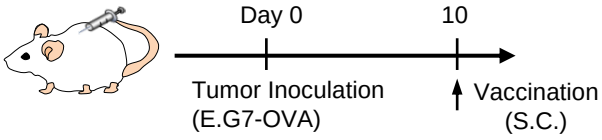
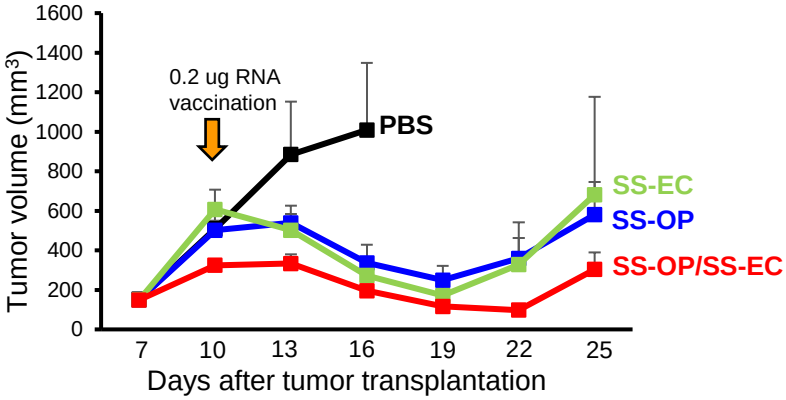
For cancer vaccine

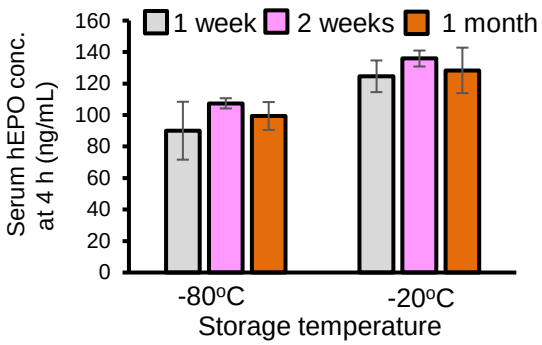


SS-OP/SS-EC LNP$_{OVA\text{-}mRNA}$ shows a remarkably high antitumor effect.



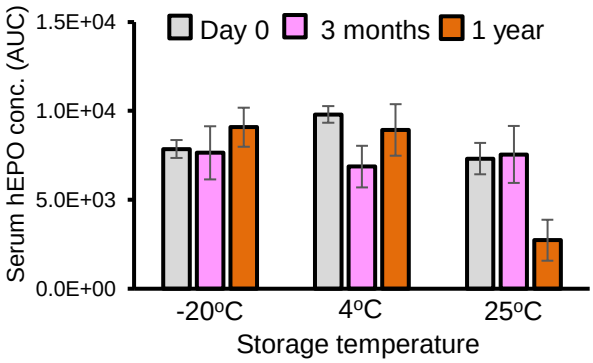
Stability of mRNA-LNP

Freeze-thaw LNP



Further stability tests are ongoing.

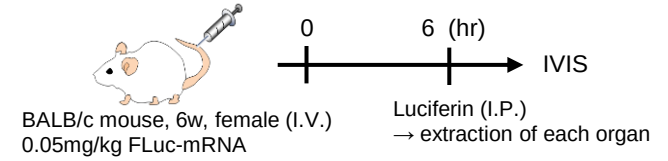
Lyophilized LNP

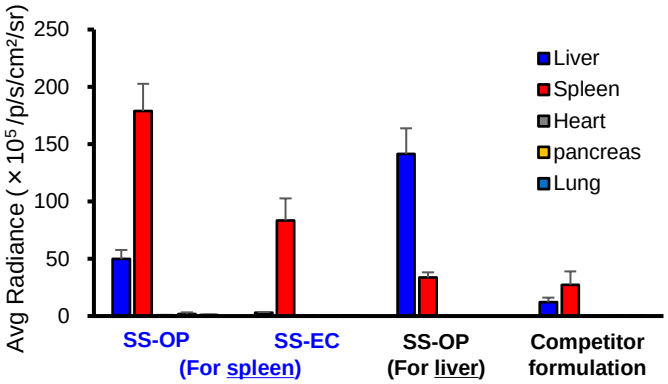


Freeze-thaw LNP is stable at least 1 month, and Lyophilized LNP is stable at least 3 months.

Extrahepatic delivery

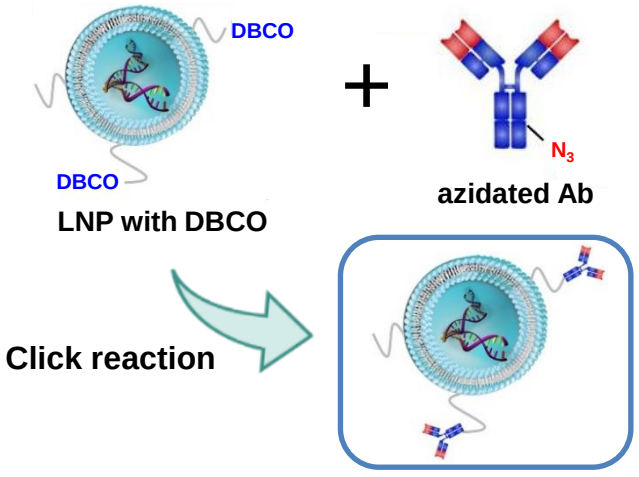
Splenic delivery





Successful mRNA delivery to spleen

Active targeting (e.g. Antibody conjugation)



Applicable for ligand modified LNP

Articles and Patents

- **Liver targeting**

(1) Hepatic pDNA delivery :
M. Ukawa et al., Adv. Healthc. Mater., 3, 1222-1229 (2014)
(2) Hepatic siRNA delivery :
H. Akita et al., ACS Biomater. Sci. Eng., 1, 834–844 (2015)
(3) Hepatic mRNA delivery by SS-OP LNP :
H. Tanaka et al., Adv. Funct. Mater., 1910575 (2020)
(4) Hepatic oligonucleotide delivery :
H. Tanaka et al., Pharmaceutics, 13, 544-561 (2021)

- **Spleen targeting**

(5) Splenic mRNA delivery by PS loaded LNPs :
Y. Sakurai et al., Adv. Healthc. Mater., Dec 19, e2202528 (2022)
(6) Self-Antigen mRNA delivery for treatment of EAE model :
M. Gomi et al., Pharmaceuticals, 16, 1270 (2023)

- **Vaccine (cancer and infection)**

(7) DNA vaccine for cancer immunotherapy (S.C.) :
H. Akita et al., Nanomedicine, 14, 2587-2597 (2018)
(8) DNA vaccine for cancer and Protozoan infection :
M. Maeta et al., Mol. Pharm., 17, 1237-1247 (2020)
(9) mRNA vaccine for infectious disease :
A. Kawai et al., Mol. Ther., 2024 Dec 17:S1525-0016(24)00831-1

- **Active targeting (ligand modified LNP)**

(10) Lung delivery by peptide ligand LNP (I.V.) :
S. Santiwarangkool et al., J. Pharm. Sci., 106, 2420-2427 (2017)
(11) Targeted delivery of LNP to lymphatic endothelial cells :
Y. Sakurai et al., J. Control. Release, 349, 379-387 (2022)

- **Lymphatic endothelial cell targeting**

(12) siRNA delivery to lymphatic endothelial cells :
Y. Sakurai et al., J. Control. Release, 353, 125-133 (2022)

- **Brain targeting**

(13) pDNA delivery to brain (I.C.V.) :
H. Akita et al., Int. J. Pharm., 490, 142-145 (2015)
(14) mRNA delivery to brain (I.C.V.) :
H. Akita et al., Mol. Pharm., 15, 2060−2067 (2018)
(15) Efficient mRNA transfection in brain capillary endothelial cells :
Y. Sakurai et al., Pharmaceutics, 14, 1560-1571 (2022)

- **Tumor targeting**

(16) Tumor pDNA delivery :
H. Akita et al., J. Control. Release, 200, 97–105 (2015)

- ***In vitro* transfection**

(17) *In vitro* pDNA delivery :
H. Akita et al., Adv. Healthc. Mater., 2, 1120-1125 (2013)
(18) Efficient mRNA transfection in T cell line :
H. Tanaka et al., Pharmaceutics, 13, 2097-2112 (2021)

- **Other articles**

(19) Small molecule drug encapsulated particle :
H. Tanaka et al., Colloids Surf. B, 151, 95-101 (2017)
(20) Inflammatory site small molecule delivery (I.V.) :
A. Watanabe et al., Int. J. Pharm., 509, 118–122 (2016)
(21) Lyophilized LNP encapsulating siRNA :
D. Shirane et al., Biol. Pharm. Bull., 41, 1291-1294 (2018)
(22) Improvement of gene expression activity by anti-inflammatory drug delivery (I.V.) :
T. Ohto et al., Biol. Pharm. Bull., 42, 299-302 (2019)

- **Patents**

(1) Cationic lipid having improved intracellular kinetics
Patent number: US9708628, EP2781507, JP6093710, CN201280056417.9
(2) Cationic lipid
Patent number: US10385030, EP3252043, JP6640750, CN107406396
(3) Novel cationic lipid exhibiting improved intracellular dynamics
Application number: WO2019188867A1

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