13th International mRNA Health Conference @Berlin

Novel Ionizable Lipids

for in vivo liver, ex vivo CAR knock-in and in vivo liver-detargeting

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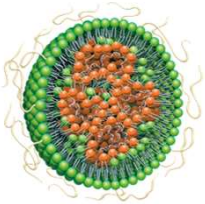
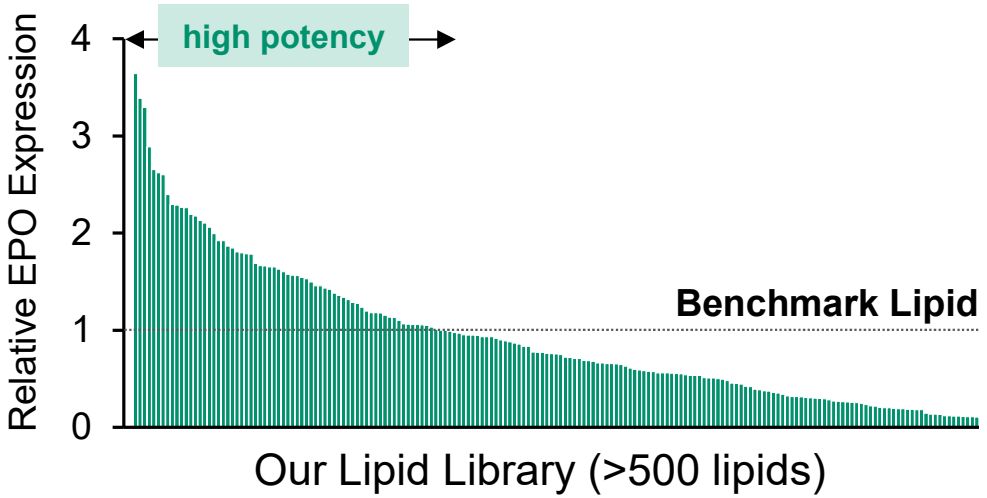
FUJIFILM Ionizable Lipids | Design concept and list



In vivo screening

mouse, 0.1 mg/kg, EPO-mRNA i.v. injection



In vivo mRNA-LNP therapy

i.m.(vaccine)	i.v. liver	extra-hepatic
FL-0445	FL-1245T	FL-1779T
GMP	New	New

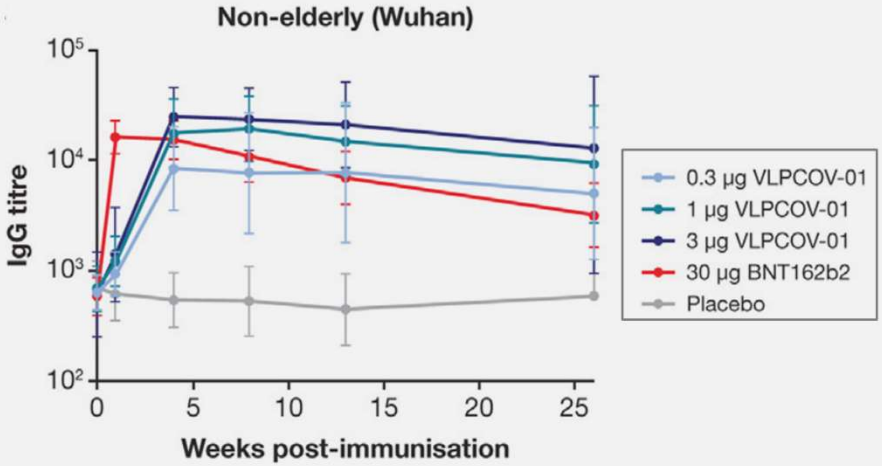
Ex vivo T cell CAR knock-in

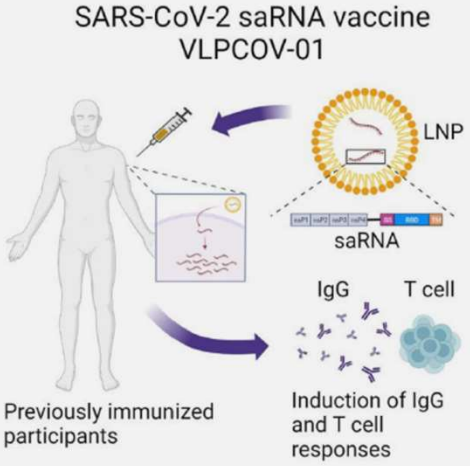
RNA delivery	DNA delivery
FL-1625T	FL-1779T
	New

FL-0445 | GMP-grade, tested in clinical trials

i.m. Vaccine | i.v. Liver | i.v. Liver-detarget. | Ex Vivo CAR-T

Efficient IgG induction with saRNA in clinical trial (Ph 3 ongoing)



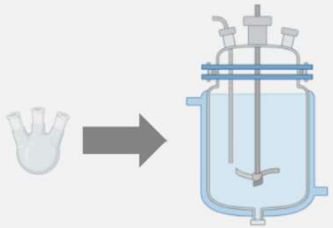


VLP Therapeutics

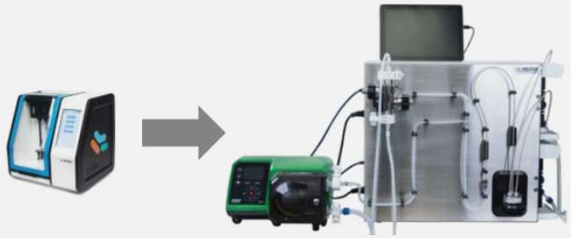
Cell Reports Medicine **2023**, *4*, 101134.

We completed process development and GMP Mfg. in both FL-0445 and its LNP

Ionizable lipid synthesis



LNP production



FL-1245T | Tolerability test in rats

i.m. Vaccine | **i.v. Liver** | i.v. Liver-detarget. | Ex Vivo CAR-T

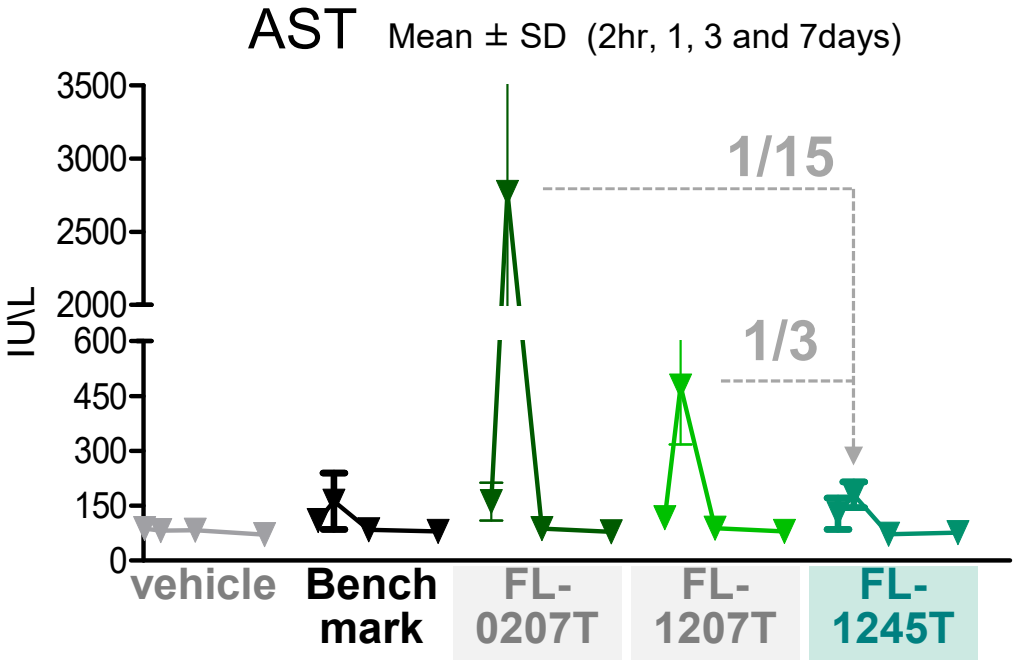
Poster 33

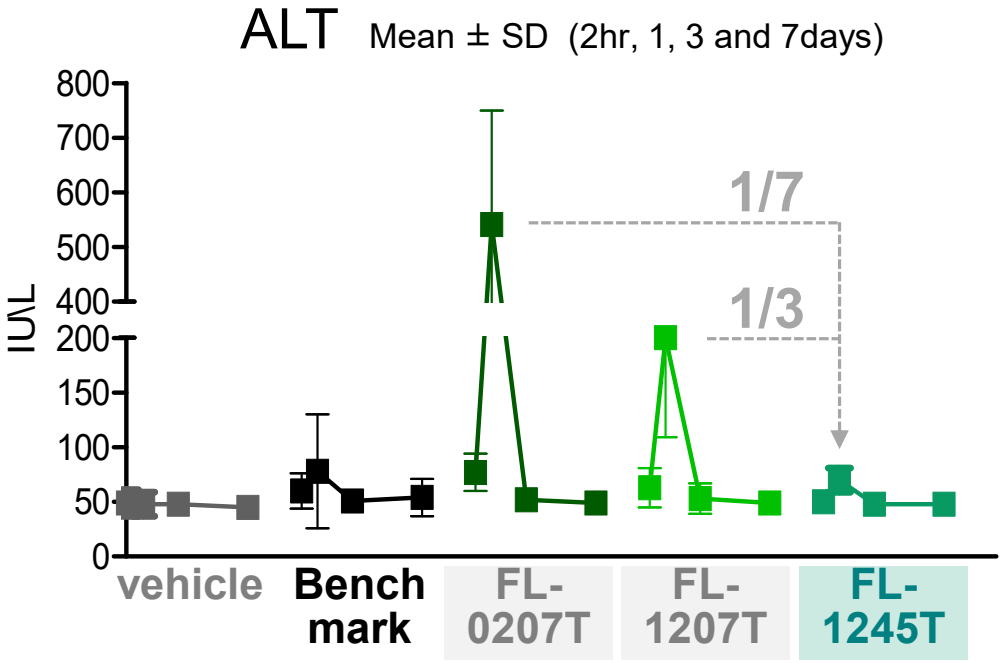
2023 FL-0207T | 2024 FL-1207T | 2025 FL-1245T

hEPO-mRNA

Rat (Sprague-Dawley, male, 7w, N=3)

3 mg/kg (mRNA), i.v. single dose





➢ **Our newest lipid FL-1245T demonstrated high tolerability**

FL-1245T | Tolerability test in rats

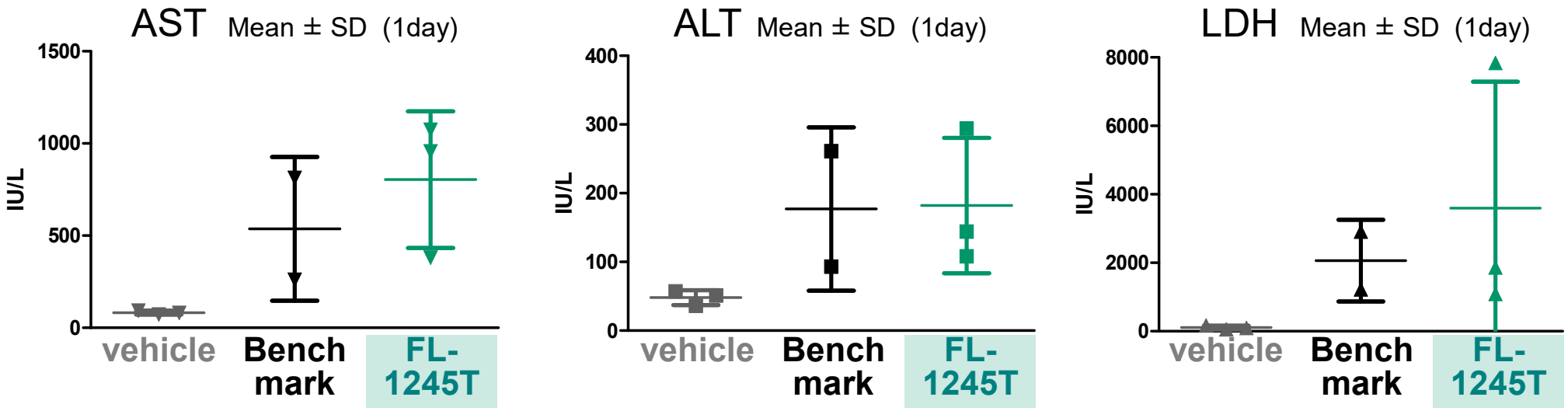
Poster 33

hEPO-mRNA

Rat (Sprague-Dawley, male, 7w, N=3)

6 mg/kg (mRNA), i.v. single dose

Benchmark: 1/3 of the rats died within 1 day, **FL-1245T**: 1/3 of the rats died the next day.



➢ **FL-1245T showed comparable tolerability to the benchmark lipid.**

FL-1245T | Protein expression in NHP

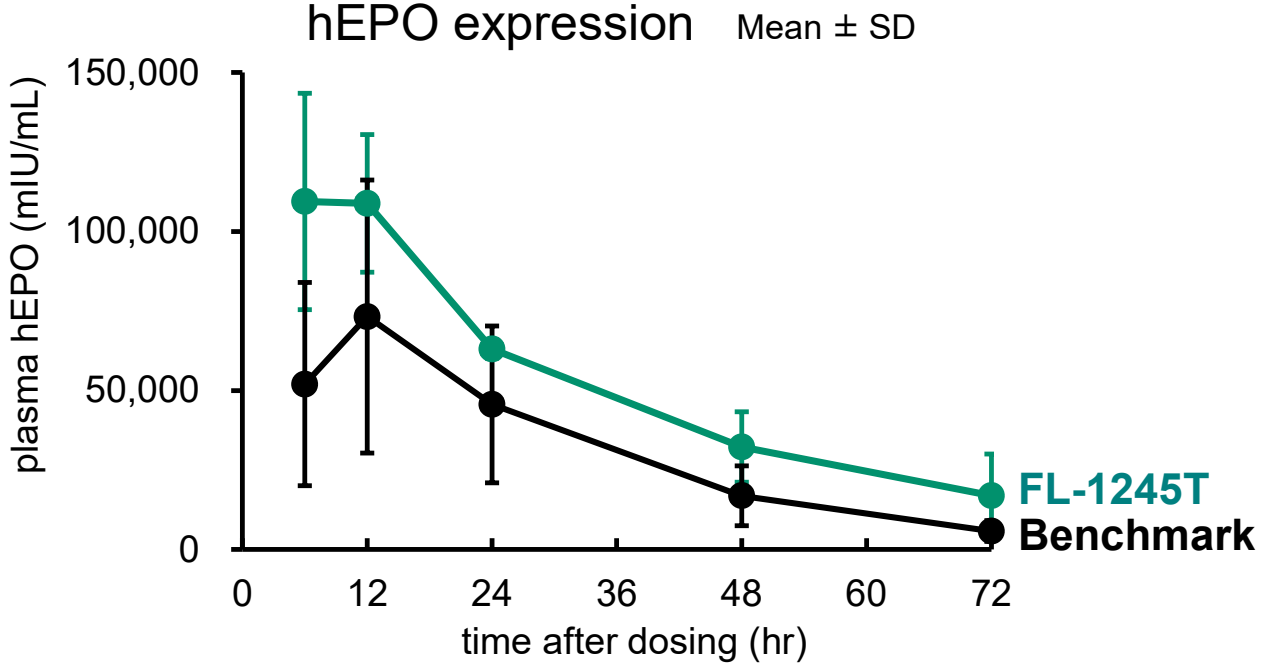
i.m. Vaccine | **i.v. Liver** | i.v. Liver-detarget. | Ex Vivo CAR-T

Poster 33

hEPO-mRNA

Cynomolgus monkey (male, 3y, N=3)

0.05 mg/kg (mRNA), 1hr infusion, i.v.

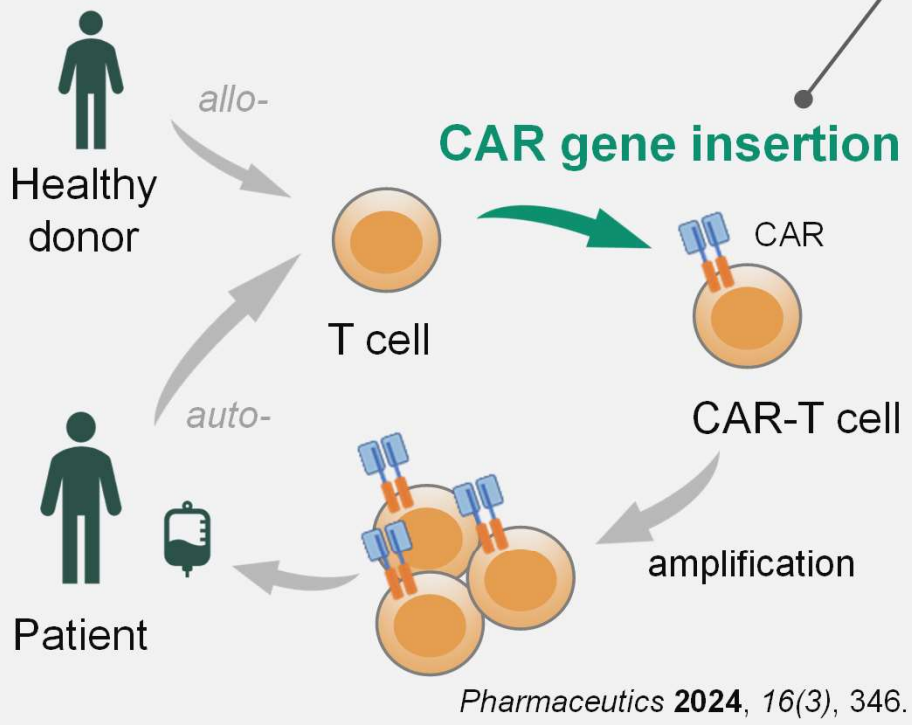


➢ **FL-1245T showed higher protein expression than benchmark lipid.**

We are planning higher dose studies

LNP potential in CAR-T cell manufacturing

i.m. Vaccine	i.v. Liver	i.v. Liver-detarget.	**Ex Vivo CAR-T**



Issues with current methods

- Viral production/QC high costs
- Safety concerns
- Cell damage by electroporation
- Low cell proliferation, low cell yield

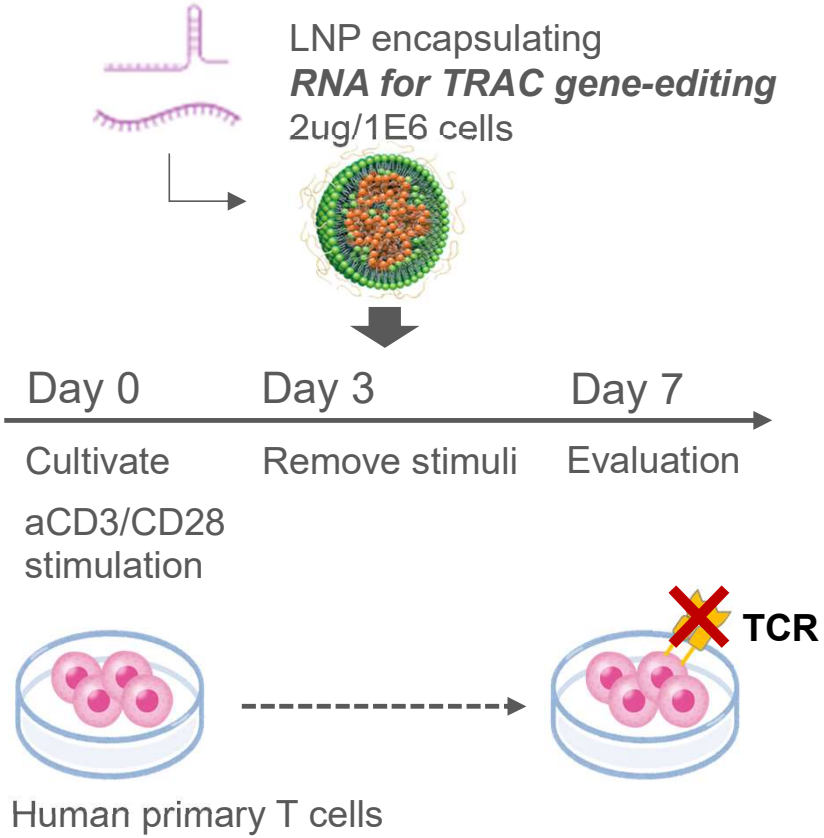
Expectations for LNP methods

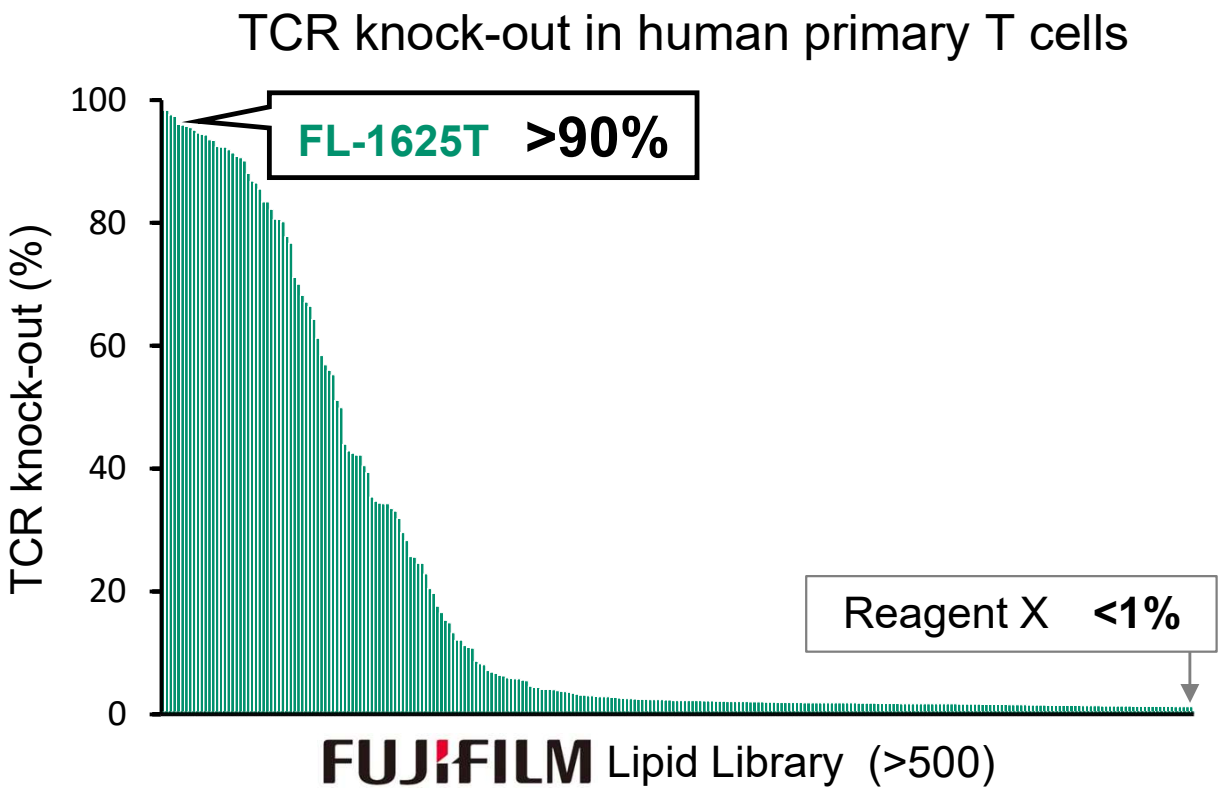
- No use of biological materials
- Reduce cytotoxicity, high yield

➢ **CAR gene insertion with LNP would overcome the current issues**

FL-1625T | T cell RNA delivery, knock-out

i.m. Vaccine | i.v. Liver | i.v. Liver-detarget. | **Ex Vivo CAR-T**

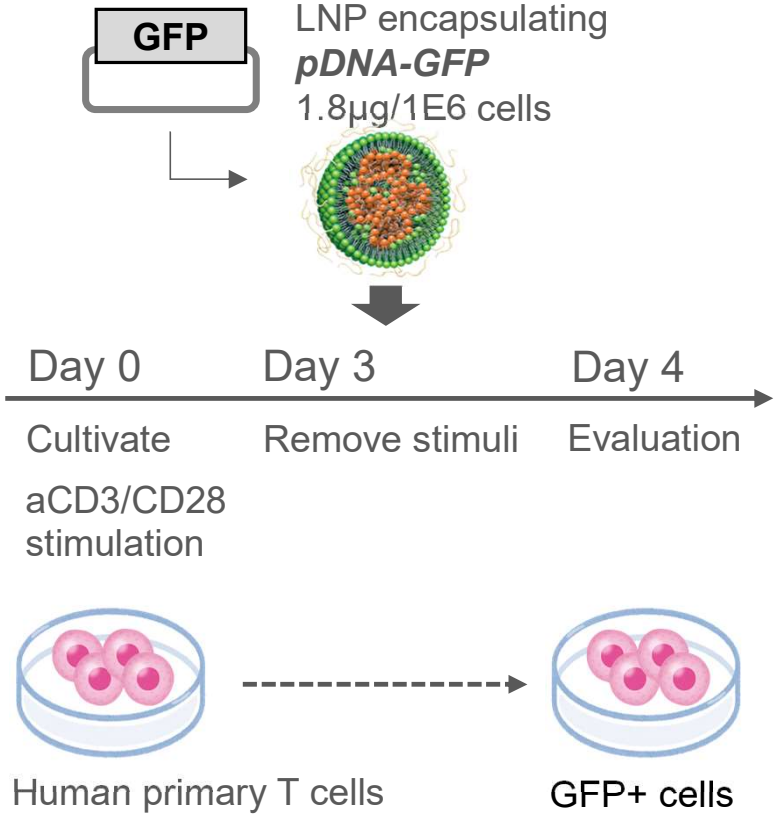


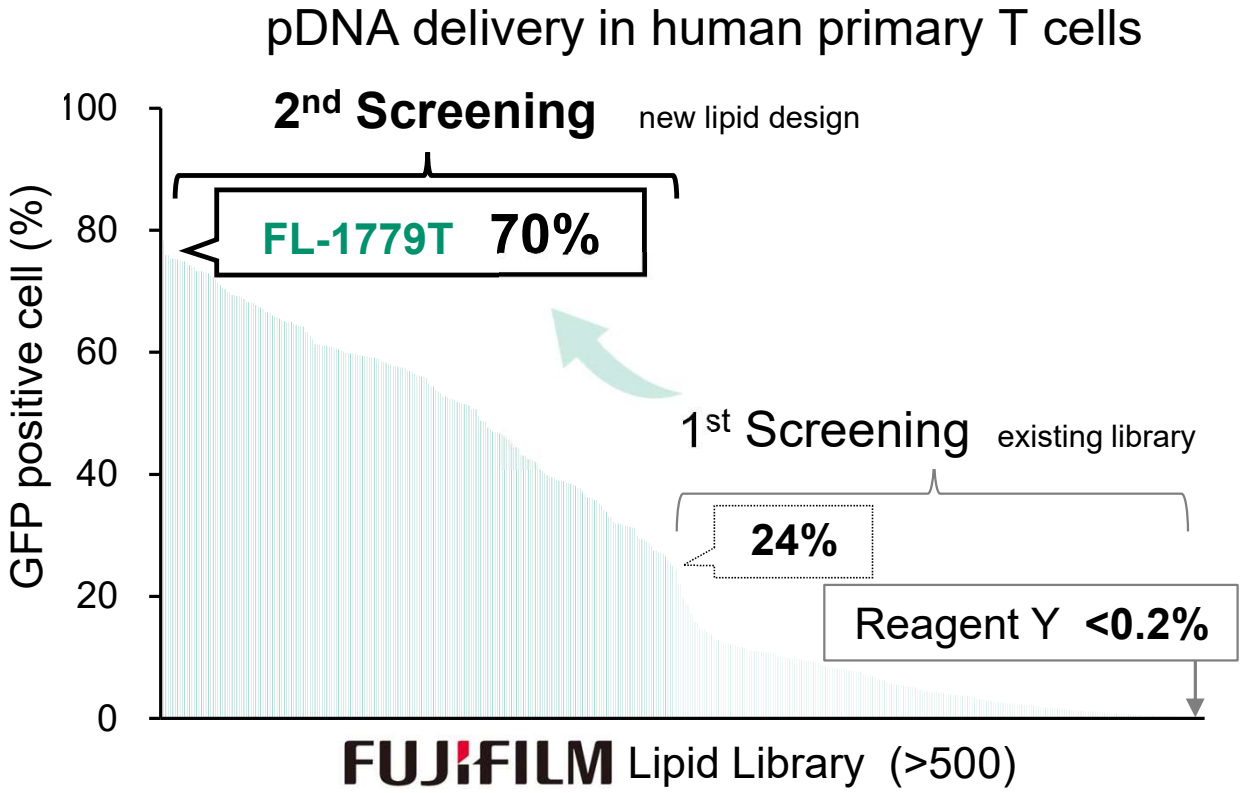


➢ **FL-1625T demonstrated high RNA delivery and >90% TCR knock-out.**

FL-1779T | T cell DNA delivery

i.m. Vaccine | i.v. Liver | i.v. Liver-detarget. | **Ex Vivo CAR-T**

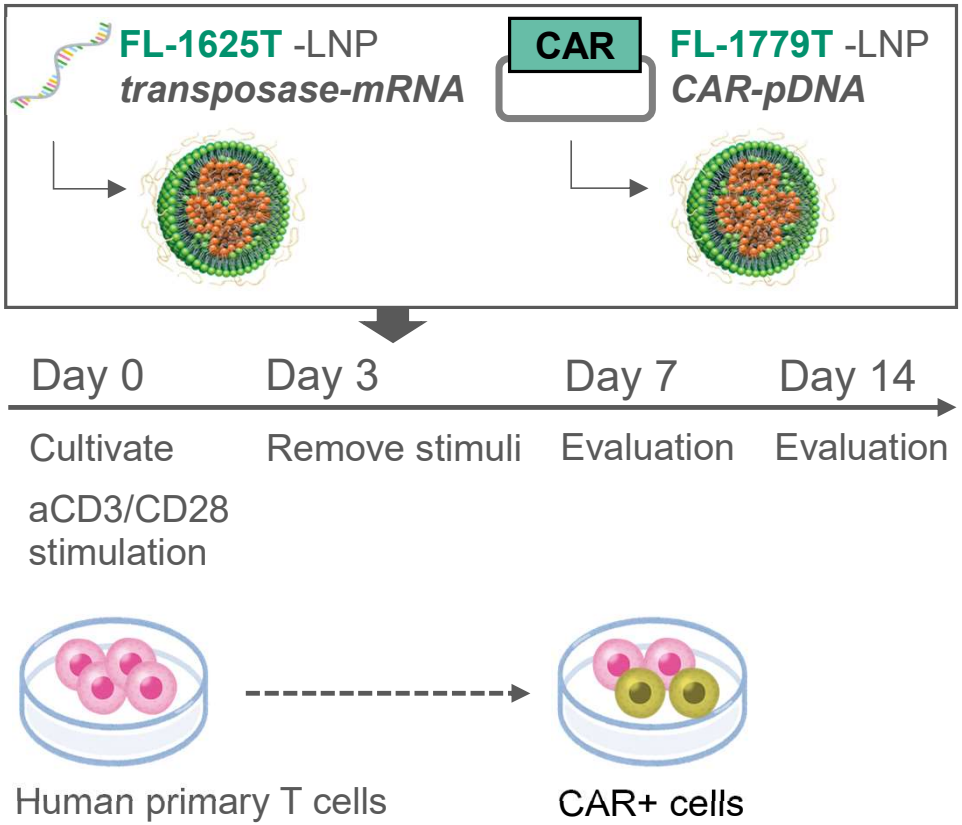


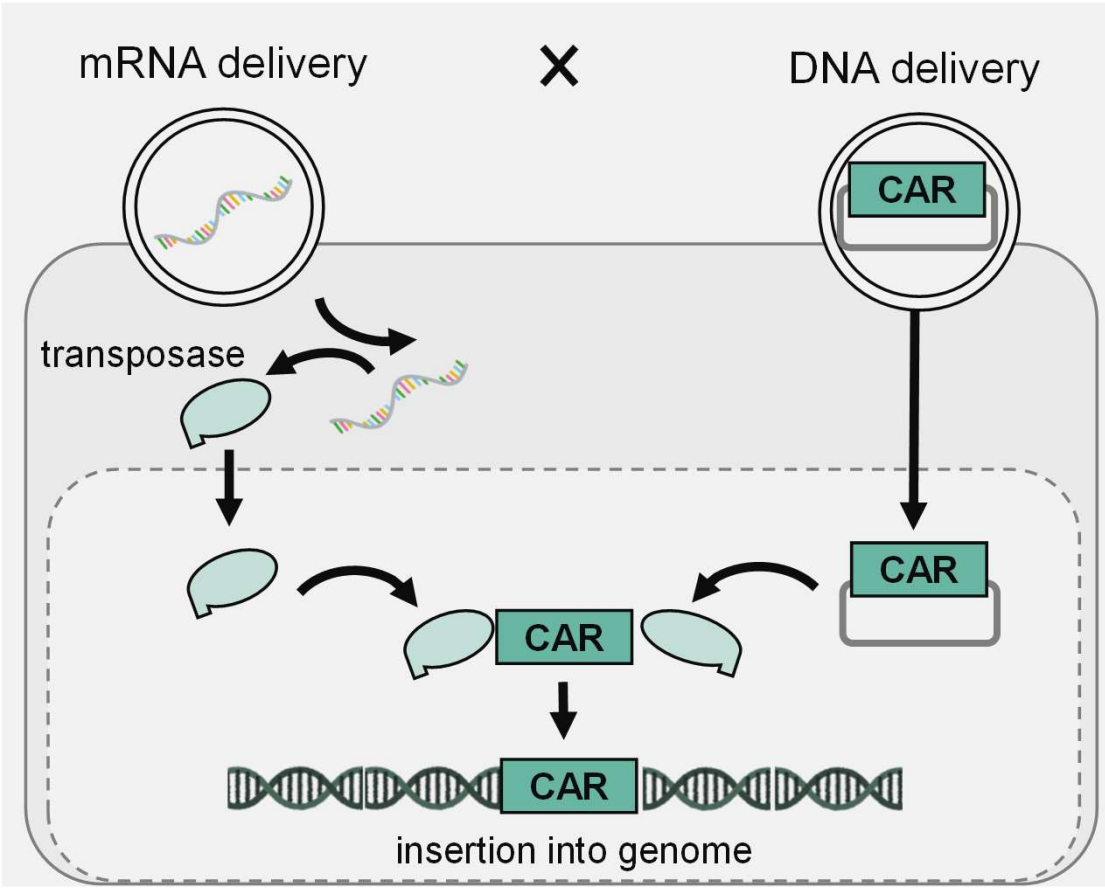


➢ **We designed new lipid FL-1779T, which showed 70% pDNA delivery**

FL-1625T×FL-1779T | T cell CAR knock-In

i.m. Vaccine | i.v. Liver | i.v. Liver-detarget. | **Ex Vivo CAR-T**

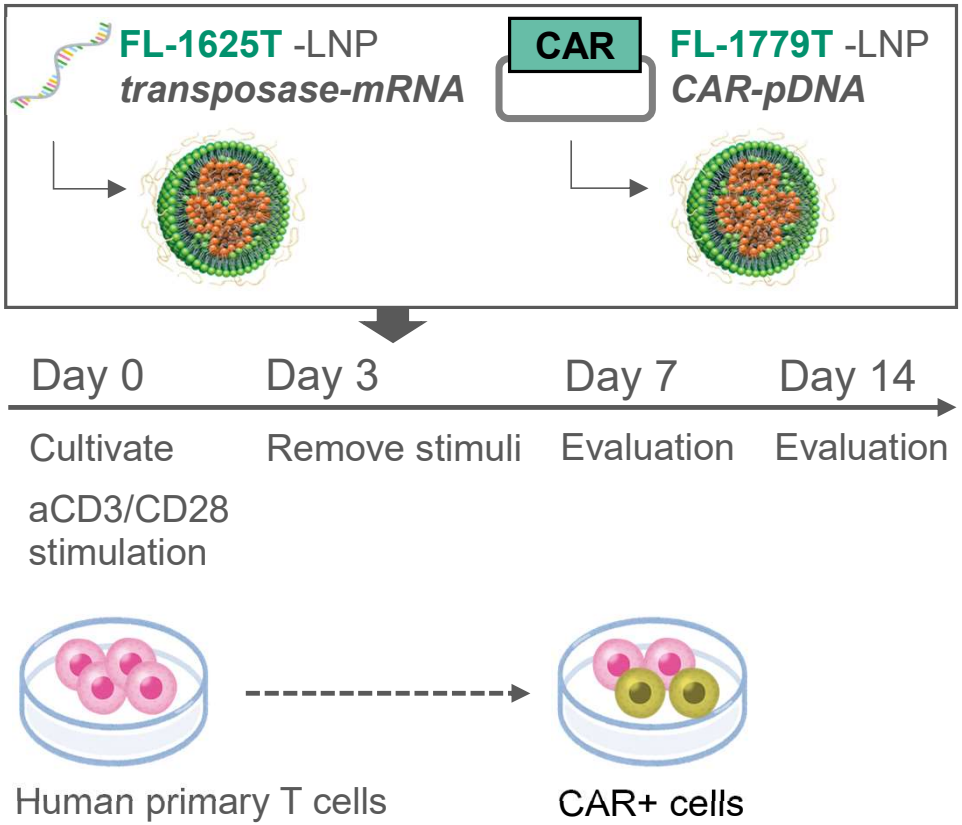




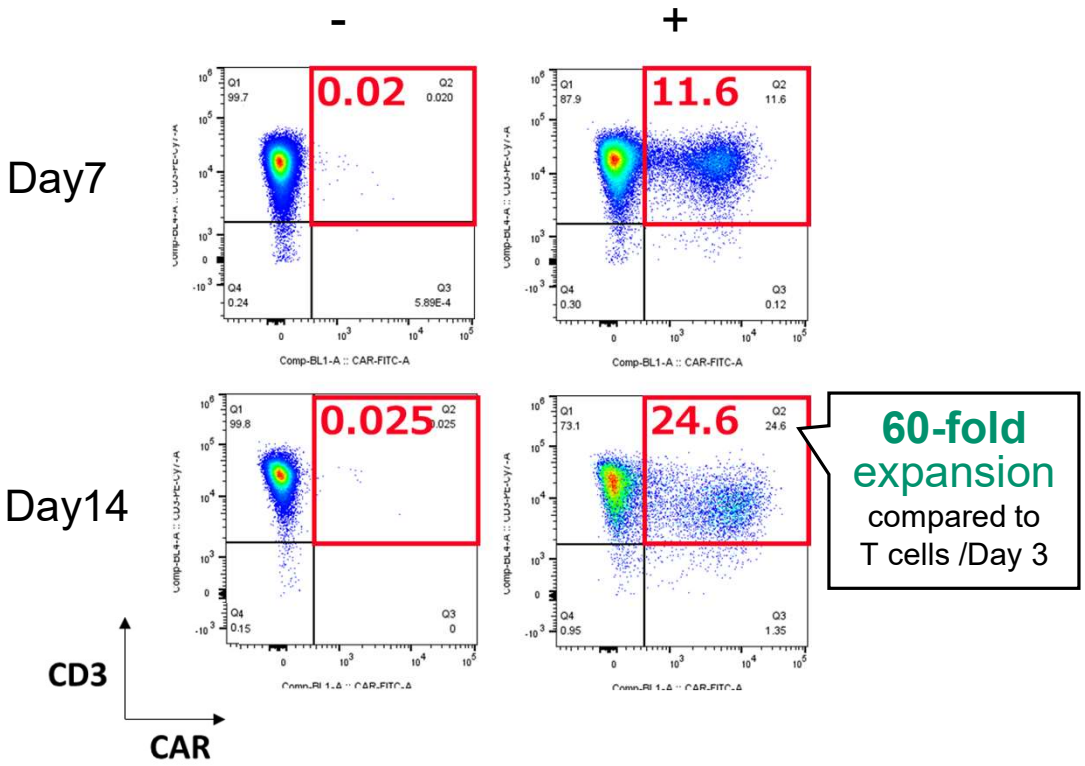
➢ **By using two types of lipids, we tried CAR knock-in application.**

FL-1625T×FL-1779T | T cell CAR knock-In

i.m. Vaccine | i.v. Liver | i.v. Liver-detarget. | **Ex Vivo CAR-T**



CAR-pDNA LNP/ *transposase-mRNA* LNP



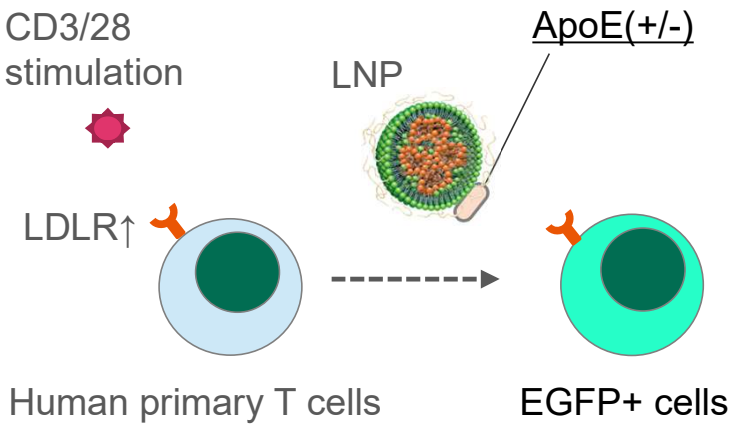
➢ **CAR knock-in was achieved by using FL-1625T and FL-1779T.**

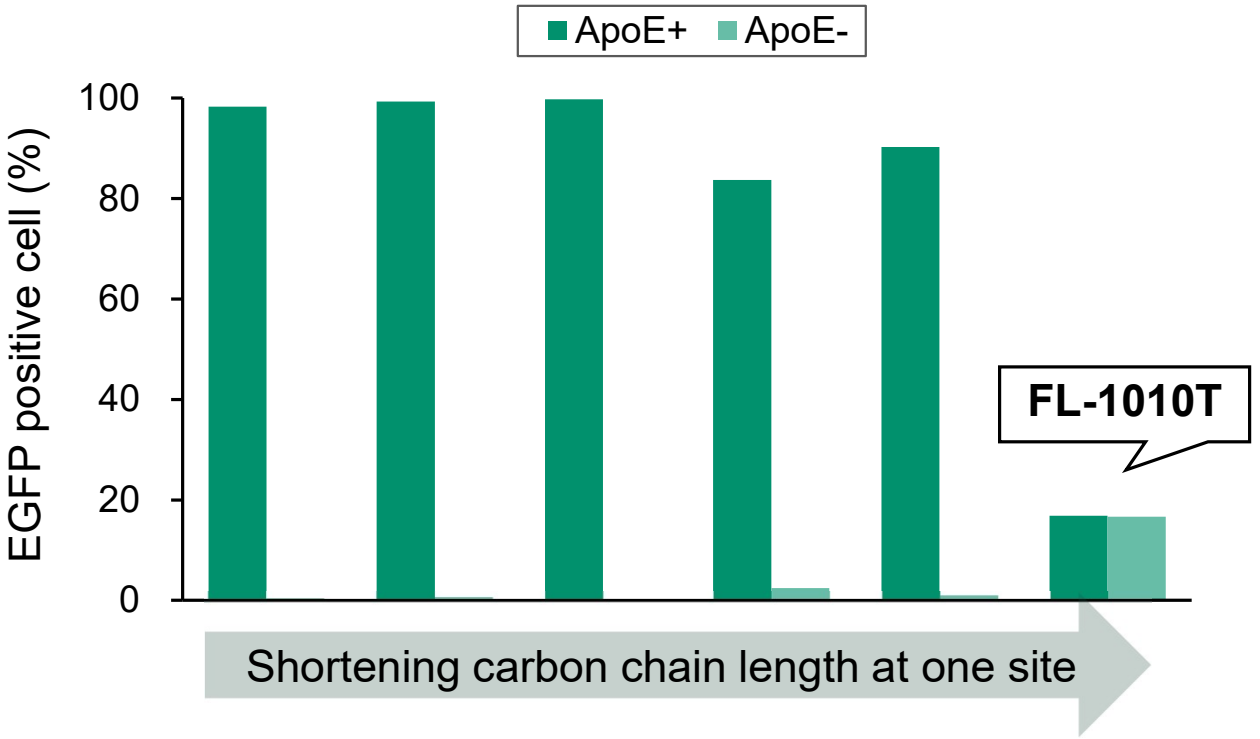
FL-1010T | ApoE-independent uptake

EGFP-mRNA

Ex vivo Activated T cell transfection

1.0μg/ 1E6 cells、ApoE (+/-)





➢ **FL-1010T demonstrated ApoE independent uptake in ex vivo T cell study.**

Then, we conducted in vivo imaging experiments.

FL-1010T | In vivo expression distribution

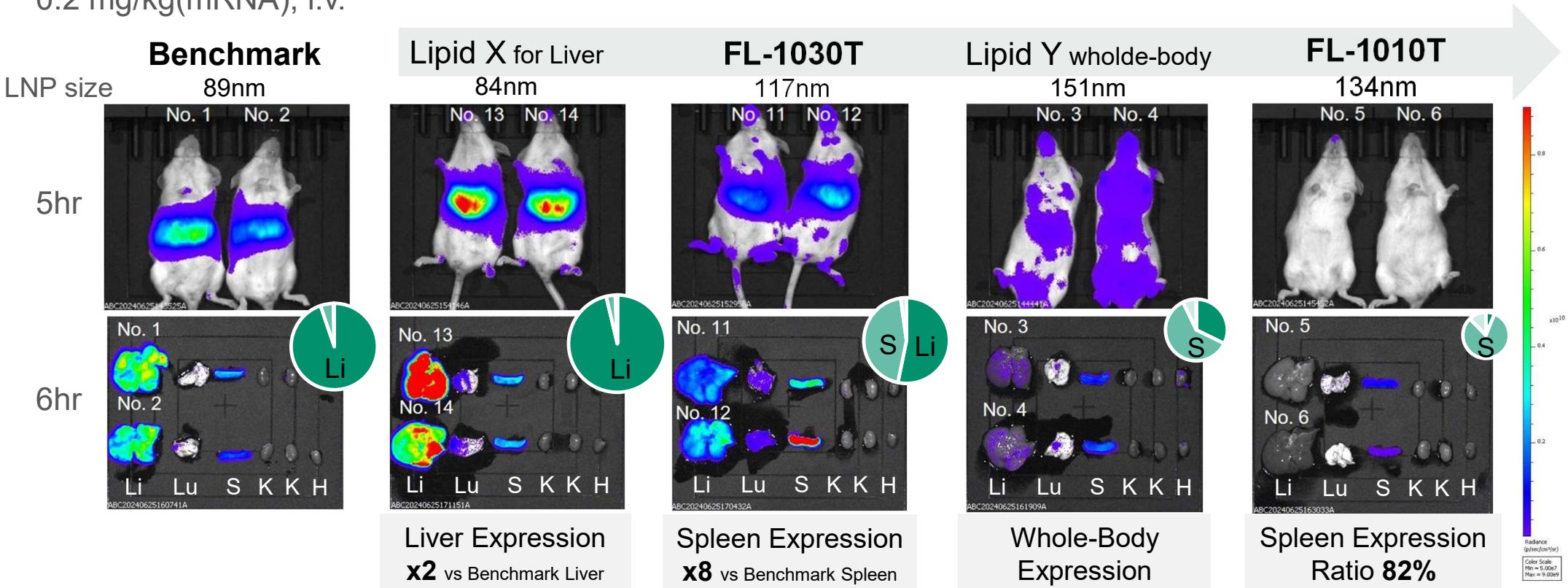
i.m. Vaccine	i.v. Liver	**i.v. Liver-detarget.**	Ex Vivo CAR-T

FLuc-mRNA

Mouse (ICR, female, 5wk, N=2)

0.2 mg/kg(mRNA), i.v.

Li: liver, Lu: lung, S: spleen K: kidney, H: heart
Circle Size indicates the approximate level of expression.
Expression Ratio: Based on Total Flux [p/s]



➢ **Liver-detargeting was accomplished, but LNP size control was a bit delicate.**

FL-1779T | ApoE-independent uptake

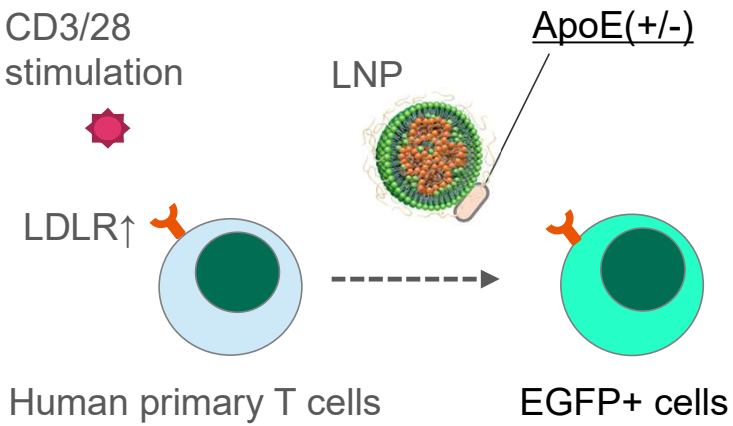
i.m. Vaccine | i.v. Liver | **i.v. Liver-detarget.** | Ex Vivo CAR-T

Poster 35

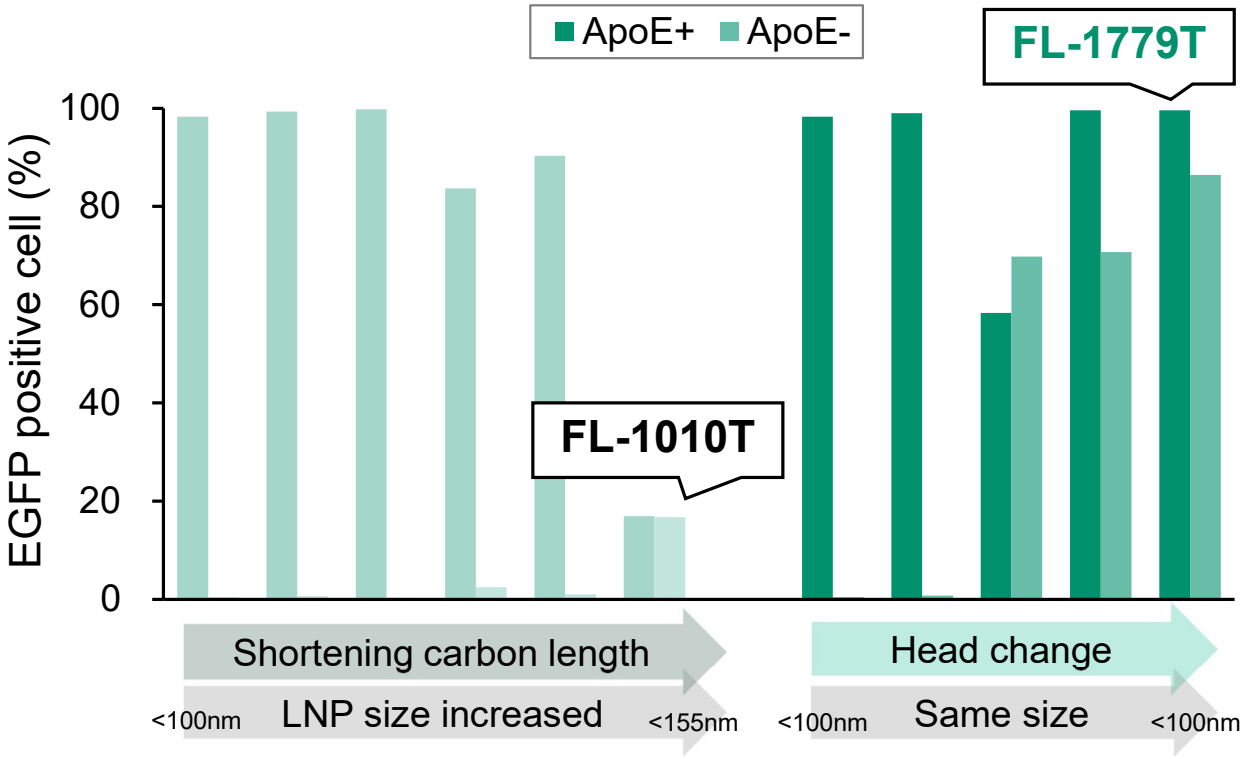
EGFP-mRNA

Ex vivo Activated T cell transfection

1.0μg/ 1E6 cells、ApoE (+/-)



EGFP⁺ cell% in human primary T cells (1day)



➢ **FL-1779T showed higher ApoE independent uptake and easier LNP size control.**

FL-1779T | Potential for extra-hepatic in vivo

i.m. Vaccine | i.v. Liver | **i.v. Liver-detarget.** | Ex Vivo CAR-T

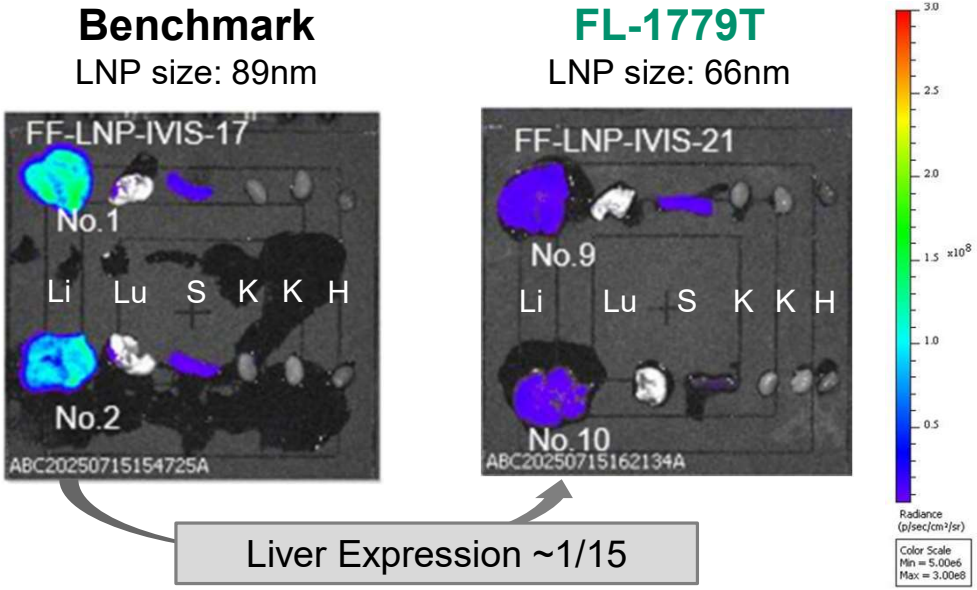
FLuc-mRNA

Mouse (ICR, female, 5wk, N=2)

0.2 mg/kg(mRNA), i.v. 6hr

Benchmark
LNP size: 89nm

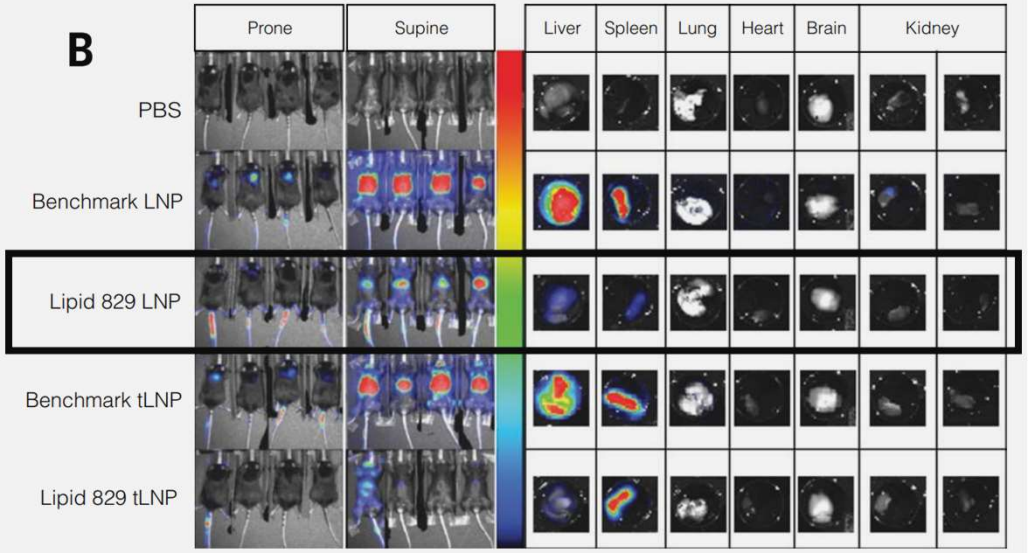
FL-1779T
LNP size: 66nm



Liver Expression ~1/15

Poster 35

Li: liver, Lu: lung, S: spleen K: kidney, H: heart



Science **2025**, *19*, 1311.

Expression pattern was similar to that described in Capstan's paper (LNP without antibody modification)

➢ **FL-1779T showed low expression in liver and spleen.**

Considering ex vivo data together, it may be suitable for in vivo T cell transfection (on-going)

FL-1779T×targeting-LNP | Ex vivo PBMC

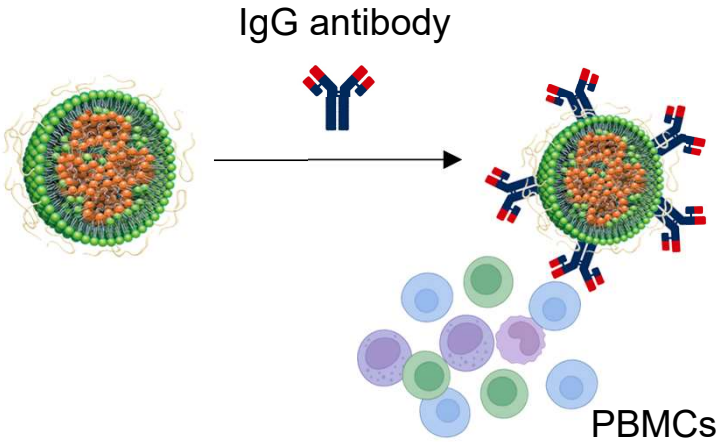
Poster 35

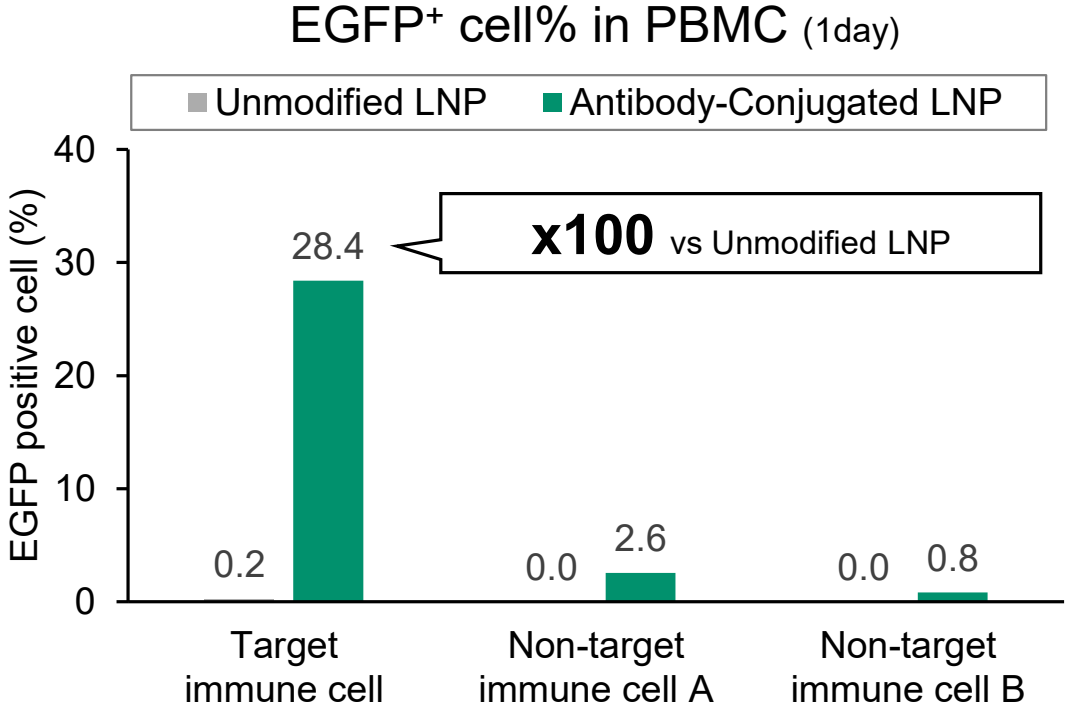
EGFP-mRNA

Specific IgG antibody-conjugated LNP

Ex vivo PBMCs transfection

ApoE (+)





➢ **FL-1779T-LNP conjugated with antibody showed immune cell selective expression.**

FUJIFILM lipids and CDMO services

Booth No. 8

Lipid Licensing

	Lipid	GMP Mfg.	IP	Remarks
i.m. vaccine	**FL-0445**	Established	Issued	Clinical trial (Ph 3)
	FL-2266	Established	Issued	GMP available
i.v. mRNA therapy	**FL-1245T** Poster 33		Pending	Liver mRNA delivery, high dose
	FL-1779T Poster 35		Pending	Liver de-targeting
	FL-1030T		Pending	Spleen mRNA delivery, high expression
Cell Therapy Gene Editing	**FL-1625T**		Pending	T cell RNA delivery (Empty LNP available)
	FL-1779T		Pending	T cell DNA delivery (Empty LNP available)

mRNA-LNP CDMO *@Toyama/ Japan*

Research	mRNA design and synthesis Poster 117 ～ mRNA-LNP formulation optimization
Development	process and analytical methods development
Manufacturing	mRNA-LNP manufacture in GMP

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- Kazuki Himi
- Asuka Ejiri

and many colleagues


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Giving our world more smiles
We bring diverse ideas, unique capabilities,
and extraordinary people together to change the world.
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