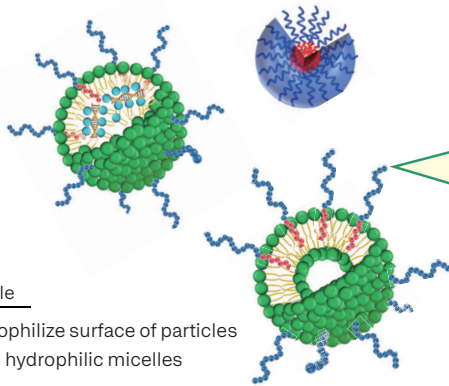


Low Immunogenicity

High gene expression

New Biocompatible Polymer (for DDS)

A novel biocompatible polymer "PGLMMA" offers numerous advantages, such as being less likely to induce IgM antibody production and maintaining blood retention even after multiple doses.

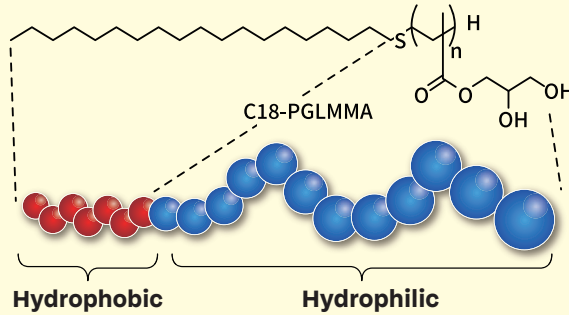


Example

- Hydrophilize surface of particles
- Form hydrophilic micelles

Biocompatible polymer **PGLMMA**

Average molecular weight (Mw) of about 12,000



Hydrophobic

Hydrophilic

*PGLMMA is an abbreviation for poly (glycerol monomethacrylate).

Features

1

IgM antibody production is low.

2

Retention in blood is maintained even after multiple doses.

3

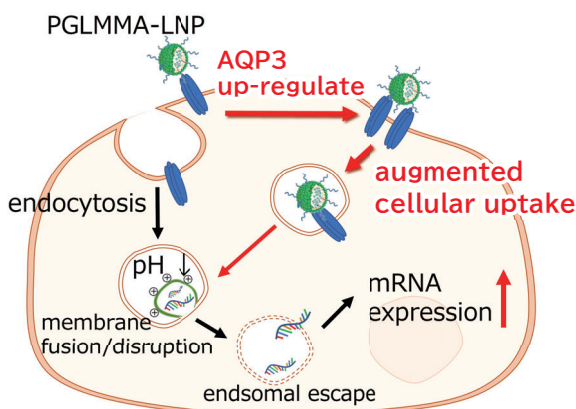
Even if the surface is hydrophilic, it is easily taken up by cancer cells.

4

Safety concerns such as acute toxicity are low.

Mechanisms : augmentation of cellular uptake

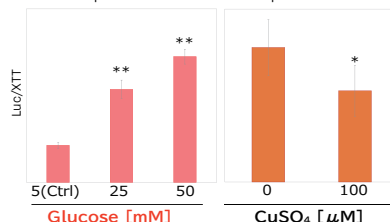
AQP3 mediates cellular uptake of PGLMMA



Correlation of mRNA expression with the amount of AQP3 protein

→ AQP3 upregulation leads high mRNA-LNP uptake. Functional inhibition of AQP3 protein cause reduction of the uptake.

Glucose: enhancer of AQP3 expression CuSO₄: inhibitor of AQP3 protein function

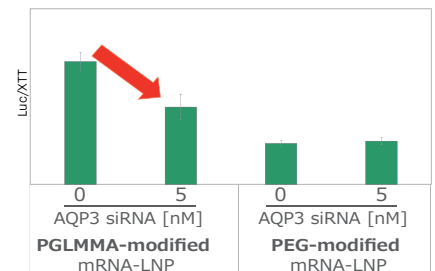


※ MCF-7: human breast cancer cell line

Recognition of PGLMMA by AQP3 promotes the uptake of PGLMMA-LNP

→ Organs or cells with high AQP3 expression are expected to show efficient uptake of LNP.

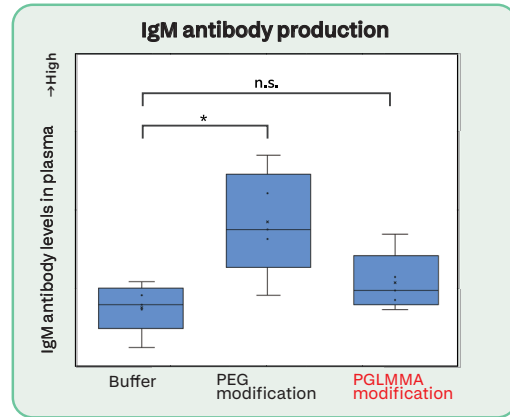
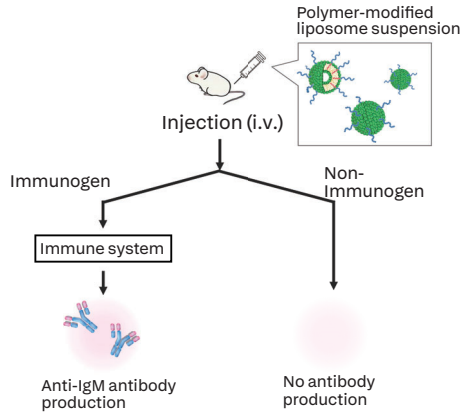
AQP3 siRNA: inhibitor of AQP3 expression



1

IgM antibody production

➔ PGLMMA-modified liposomes induce little IgM antibody.



2

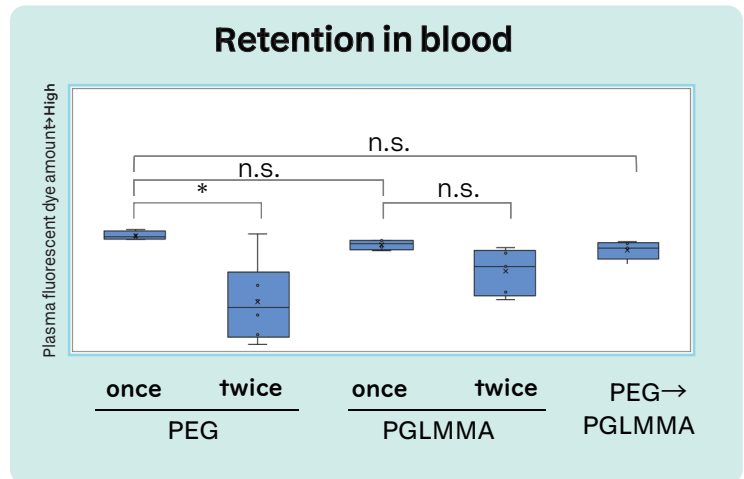
Retention in blood after multiple doses

➔ PGLMMA-modified liposomes showed no decrease in blood retention after the second dose.

Animal species : BALB/cCrSlc mice
 Administration method : Tail vein injection , 2 doses
 Drug : Polymer-modified liposomes(About 60 nm, in PBS, Dil staining)
 Dose : First 0.1 μmol/kg
 Second 5 μmol/kg
 Dosing interval : 7 days

Study group	Modification of the drugs	
	1st	2nd
PEG once	PBS	PEG
PEG twice	PEG	PEG
PGLMMA once	PBS	PGLMMA
PGLMMA twice	PGLMMA	PGLMMA
PEG → PGLMMA	PEG	PGLMMA

The particle size of polymer-modified liposomes is about 60 nm.

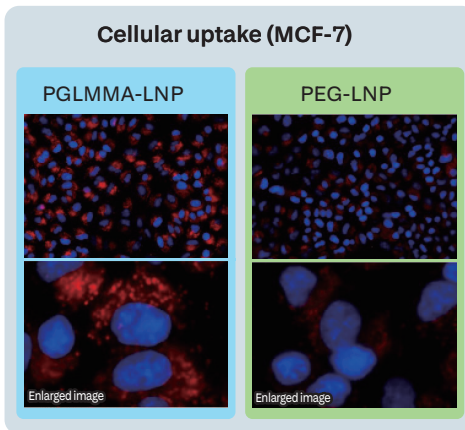
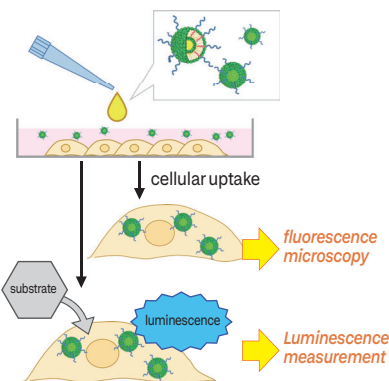


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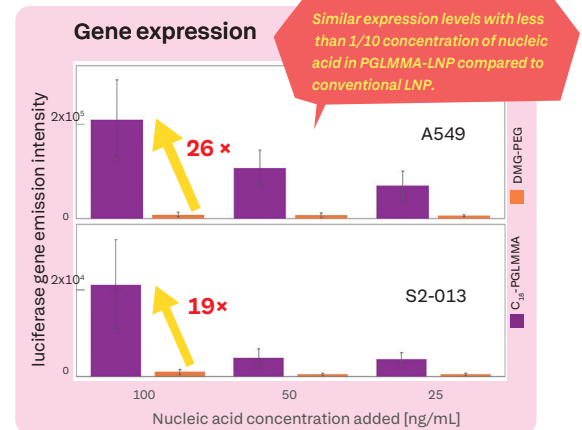
Cellular Uptake and Gene Expression

➔ PGLMMA-modified particles are easily taken up by cancer cells.

Polymer-modified lipid nanoparticles (LNP) encapsulating fluorescent dye and Luc mRNA



※MCF-7 : human breast cancer cell A549 : human lung cancer cell S2-013 : human pancreatic cancer cell



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