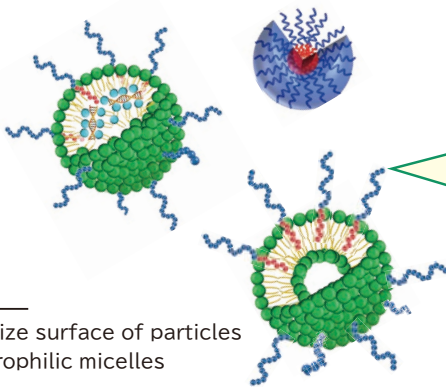


Polymer for Drug Delivery Systems (DDS) (PGLMMA)

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

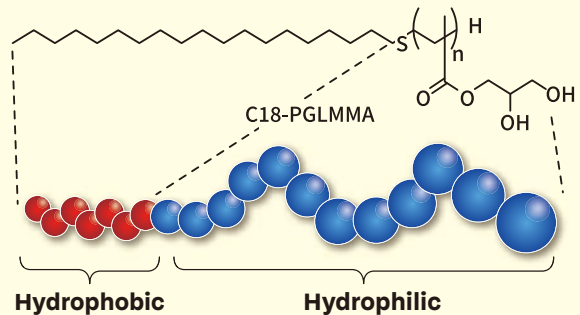


Example

- Hydrophilize surface of particles
- Form hydrophilic micelles

A novel Drug Delivery System (DDS) polymer, **PGLMMA**

Average molecular weight (Mw) of about 12,000



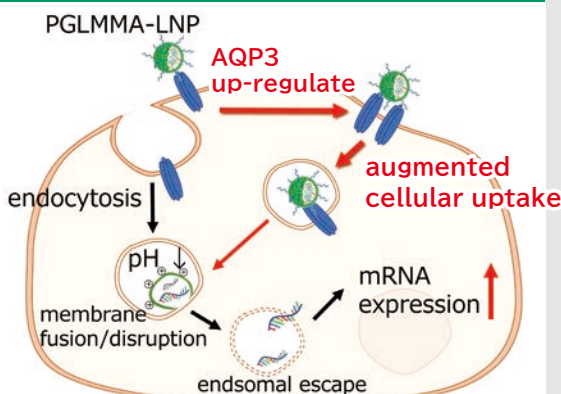
*PGLMMA is an abbreviation for poly (glycerol monomethacrylate).

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.

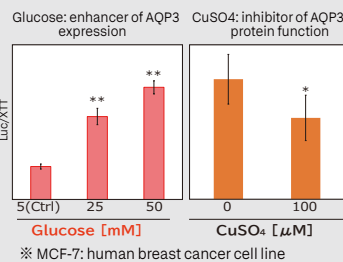
Mechanisms : augmentation of cellular uptake

AQP3 mediates cellular uptake of PGLMMA



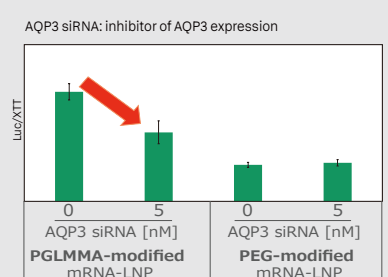
Correlation of mRNA expression with the amount of AQP3 protein

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



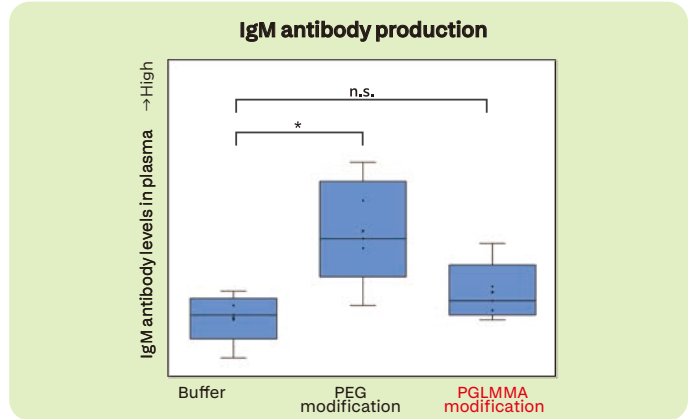
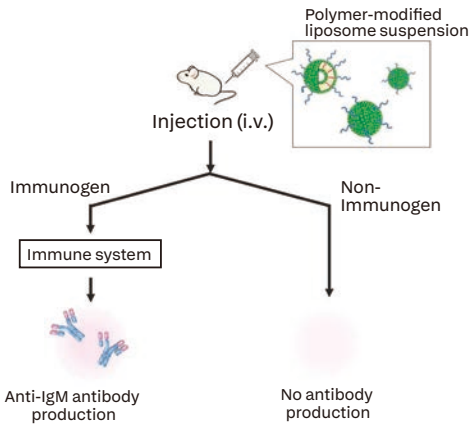
Recognition of PGLMMA by AQP3 promotes the uptake of PGLMMA-LNP

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



1. IgM antibody production

➔ PGLMMA-modified liposomes induce little IgM antibody.



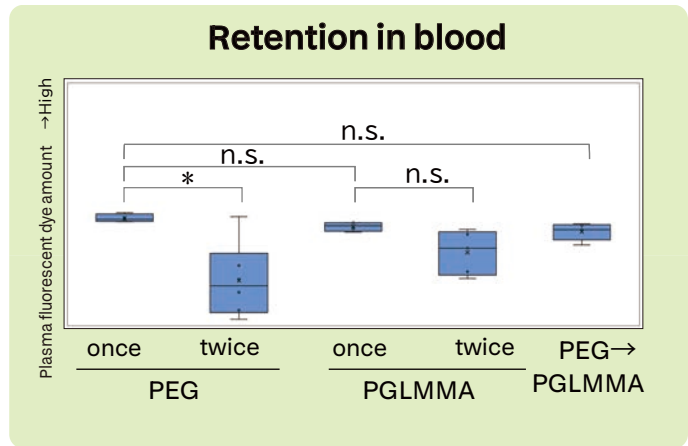
2. Retention in blood after multiple doses

➔ 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

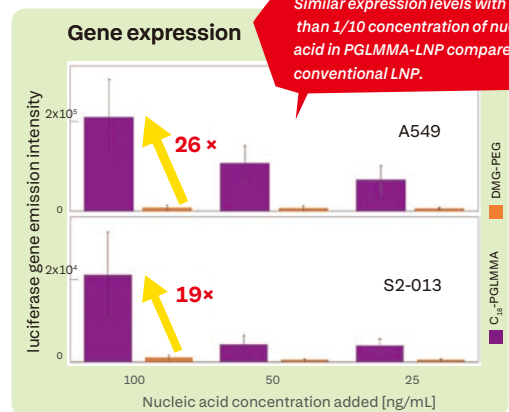
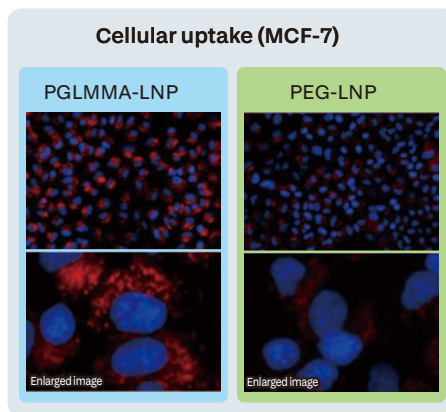
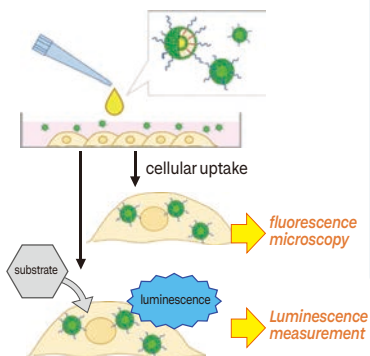
The particle size of polymer-modified liposomes is about 60 nm.



3. 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



Similar expression levels with less than 1/10 concentration of nucleic acid in PGLMMA-LNP compared to conventional LNP.

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