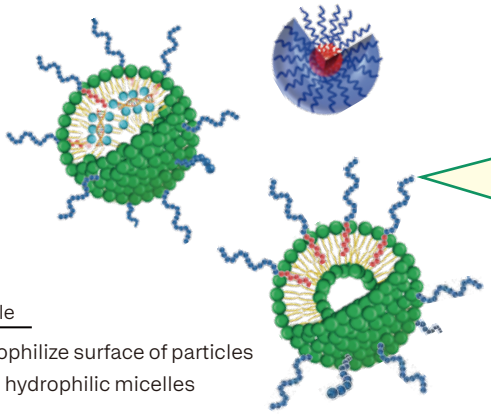
Low Immunogenicity　High gene expression

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.

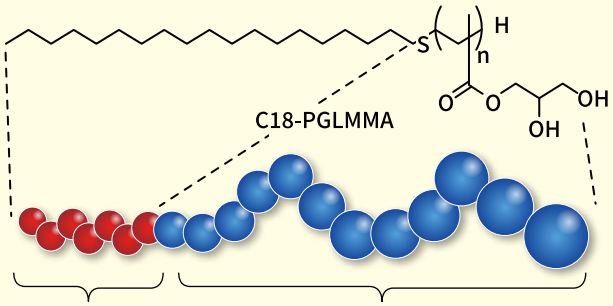


Example

- Hydrophilize surface of particles
- Form hydrophilic micelles

Biocompatible polymer PGLMMA

Average molecular weight (Mw) of about 12,000



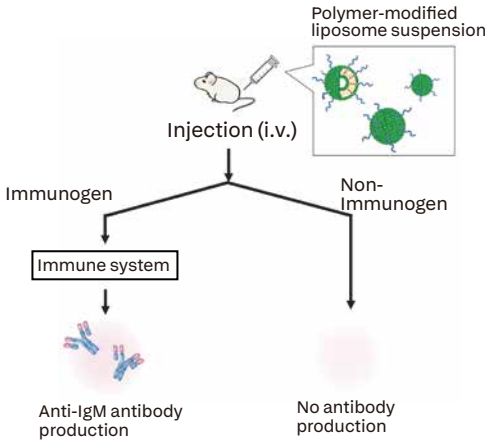
*PGLMMA is an abbreviation for poly (glycerol monomethacrylate).

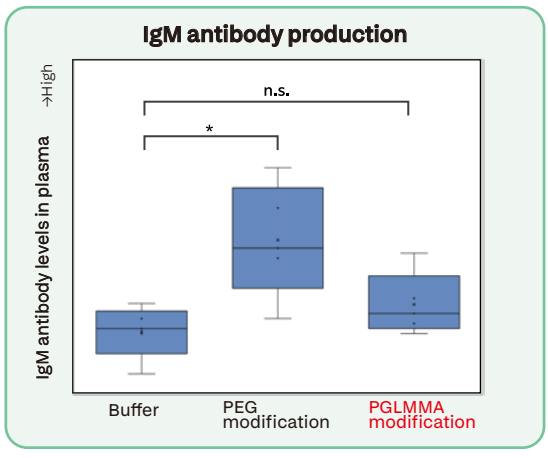
Features

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.*

IgM antibody production

PGLMMA-modified liposomes induce little IgM antibody.





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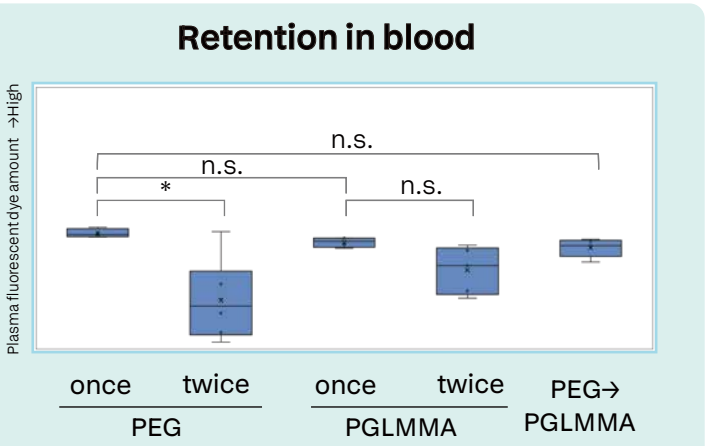
Retention in blood after multiple doses

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, DiI 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

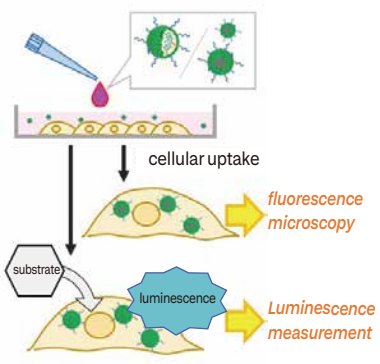
The particle size of polymer-modified liposomes is about 60 nm.

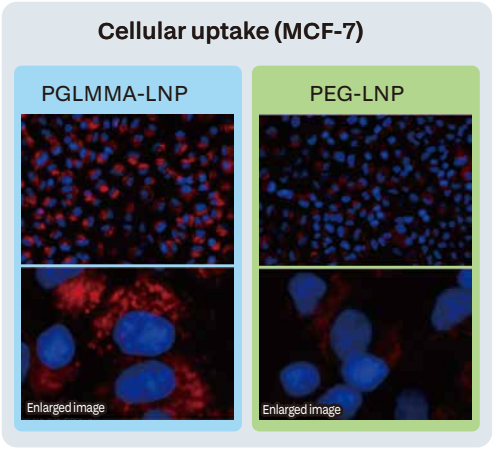


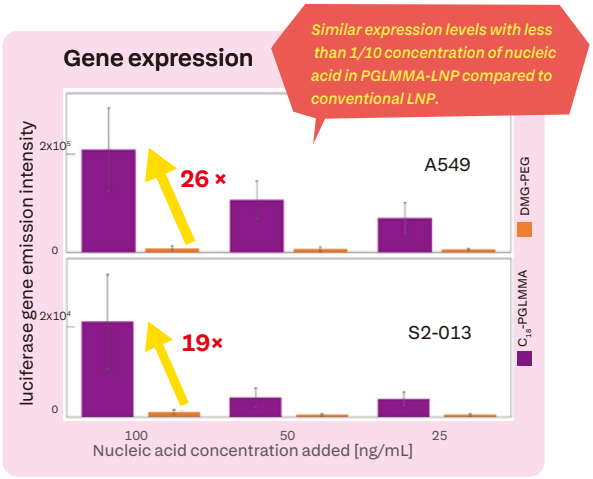
Cellular Uptake and Gene Expression

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*

Safety studies

No toxic findings in acute toxicity and Ames studies.

Items	Study details	Results
Single dose in rats (acute toxicity) study	Study category : Non-GLP study Study group : 3 males and 3 females per group Route of administration : Intravenous administration Dosage : 10 or 100 mg/kg Evaluation items : General symptoms, body weight, necropsy Observation period : 14 days	No findings
Ames tests	Study category : GLP study (Industrial Safety and Health Act, Chemical Substances Control Law, OECD) Guideline : OECD-TG471 Strains : TA98, TA100,TA1535,TA1537, and WP2uvrA	Negative

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