Cationic lipids offer new possibilities in liposome and LNP engineering for RNA therapeutics

Malik Hellal, PhD – Director Chemistry R&D

Claire Guéguen, PhD – R&D Life Science Manager

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Polyplus

This is Polyplus

- Headcount: 270
- Global Headquarter located in Strasbourg, France
  - Building size: 3.634 sqm
  - Offices: ~2,000 sqm and Lab space: ~ 1.600 sqm
- Facilities in Europe
  - R&D Nucleic delivery
  - R&D of Plasmid engineering
  - Molecular biology services (Plasmid, NGS, etc...)
  - Plasmid and protein manufacturing
  - GMP Fill & Finish
- End-to-end capabilities
  - Product & Service development
  - Process Development
  - Manufacturing
  - Quality
  - Regulatory & Scientific Support

Strasbourg France

Nucleic acid delivery

Lille France

Plasmid Engineering

Liège Belgium

Plasmid & Prot. CDMO

Lyon France

GMP Fill/Finish & CT

Our vision and mission

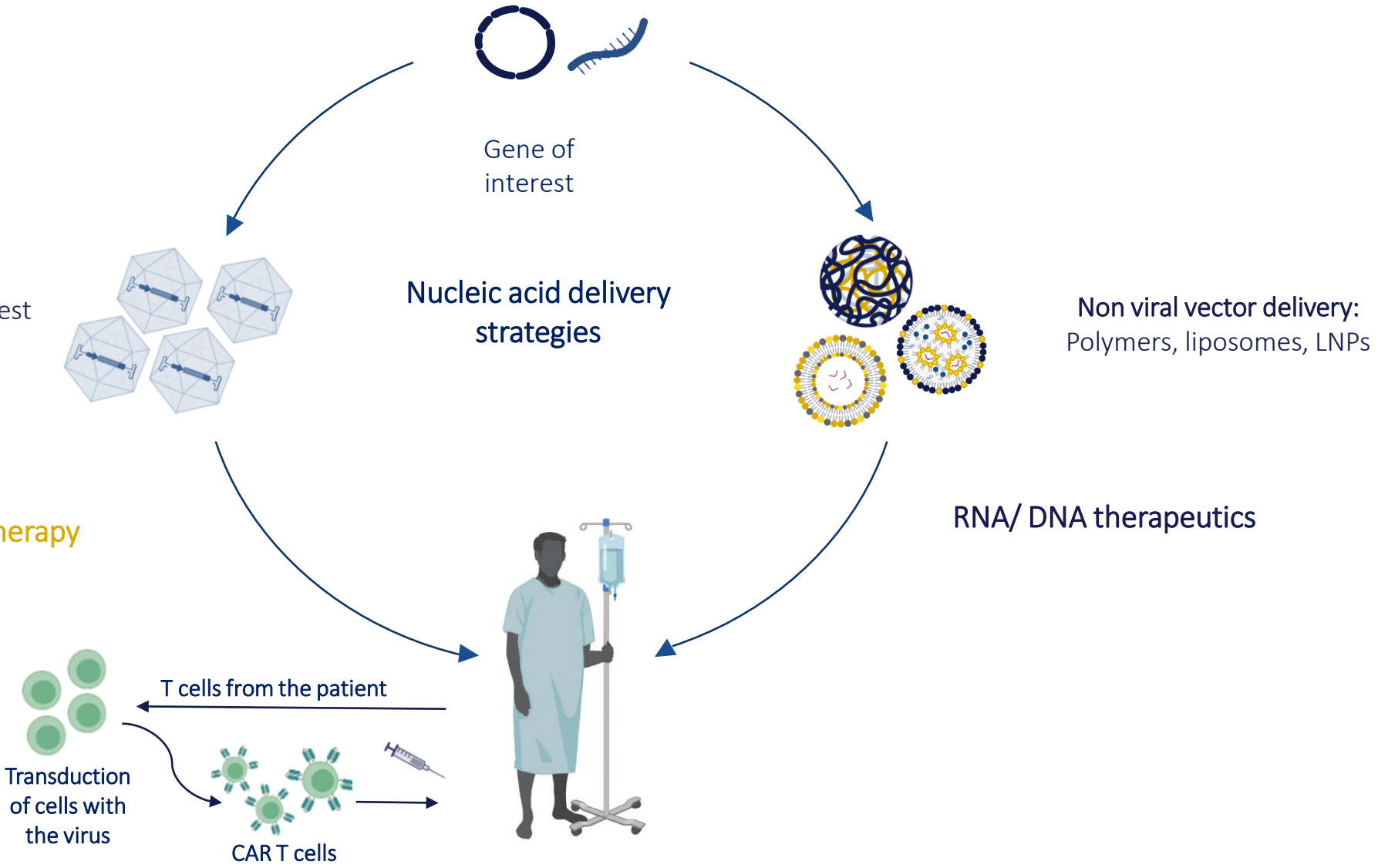
Vision

Our vision is to help drug developers and manufacturers innovate with greater confidence and quality while reducing cost and time to market for cell and gene therapies and RNA & DNA therapeutics

Our mission is to develop cutting-edge genetic engineering and delivery technologies that enable scientists to develop breakthrough nucleic acid-based therapies that improve human health

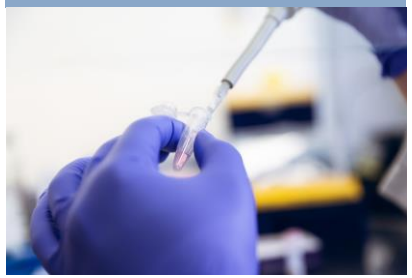
Mission

Powering delivery of nucleic acid therapies



Our pillars to revolutionize delivery of nucleic acid therapies

Polyplus

Unique Synthesis And Formulation Know-how	Deep Understanding of Molecular & Cell Biology and Applications	Extensive advanced biologics process expertise (CGT, RNA therapeutics)	Vertically Integrated Manufacturing and Supply Chain (R&D/GMP)	End-to-end customer support Scientific & Regulatory Support
				

Unique, integrated and highly scalable platform supported by +20-year experience & industry-leading science

+20 years of Innovation, Expertise and Quality

2001 — *in vivo*-jetPEI®

2002 — ISO 9001

2007 — *in vivo*-jetPEI® GMP

2012 — PEIpro®

2018 — PEIpro®-GMP

2020 — FectoVIR®-AAV

2021 — FectoVIR®-AAV GMP

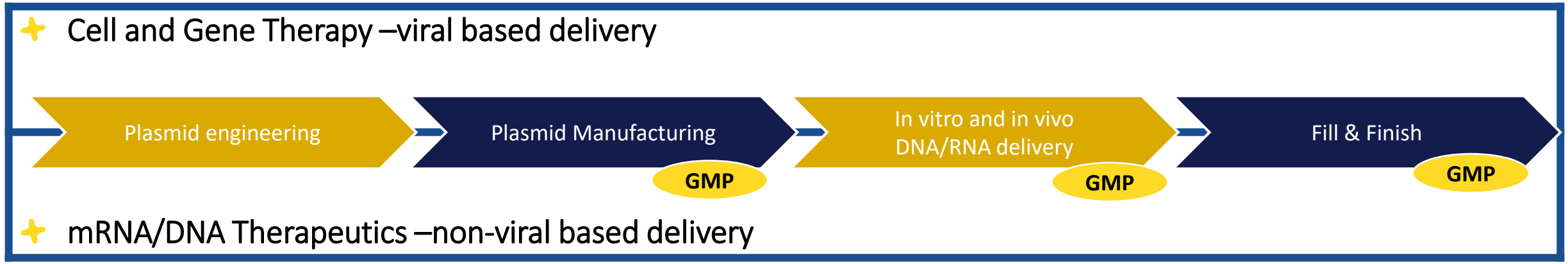
2022 — pDNA Engineering & Manufacturing

2023 — FectoVIR®-LV

2023 — LipidBrick® for LNP

Polyplus' solution for delivery and manufacturing of nucleic acid therapies

- Complete Product & service portfolio for Gene-therapy viral vector & DNA/RNA therapeutics manufacturing
- Extensive **scientific and regulatory support** to support projects from discovery to commercial through clinical phases



mRNA Therapeutics main challenges

Biodistribution

- Current ionizable lipids are mainly accumulating in the liver → Possible toxicity
- Need for innovative technology to widen therapeutic applications

Safety

- Better mRNA-LNP stability
- GMP raw material and processes

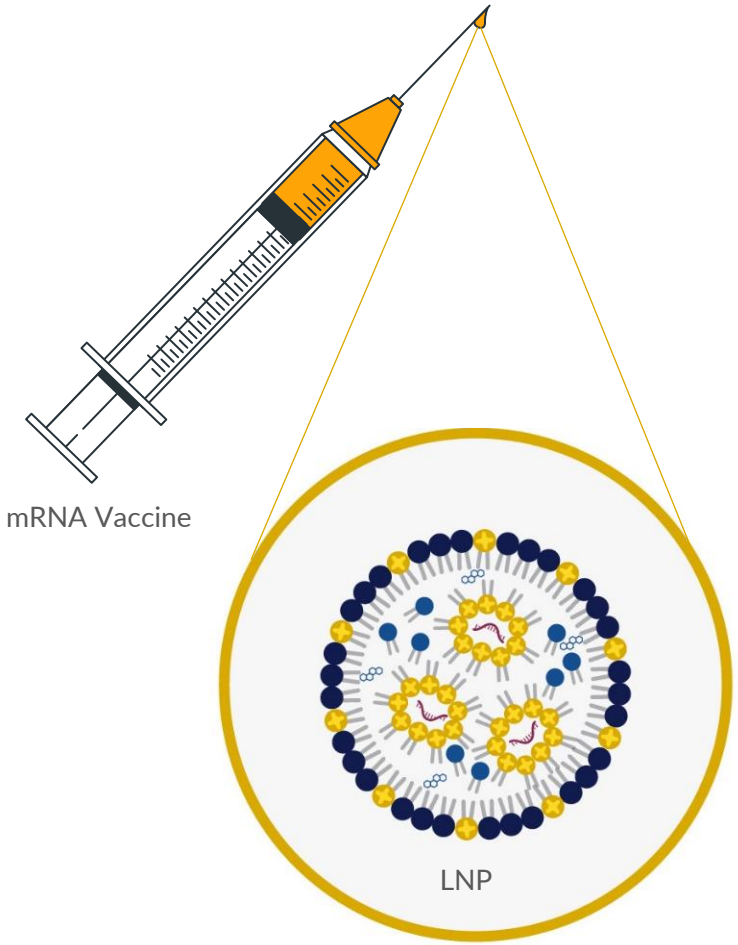
Supply

- Optimal storage conditions
- Sufficient quantities for large scale manufacturing → kg scale needed for prophylactic vaccine

IP

- Possibility to use innovative technology to broaden therapeutic areas
- Clearer IP landscape regarding LNP components

Typical mRNA vaccine composition



Active substance = Nucleic acids

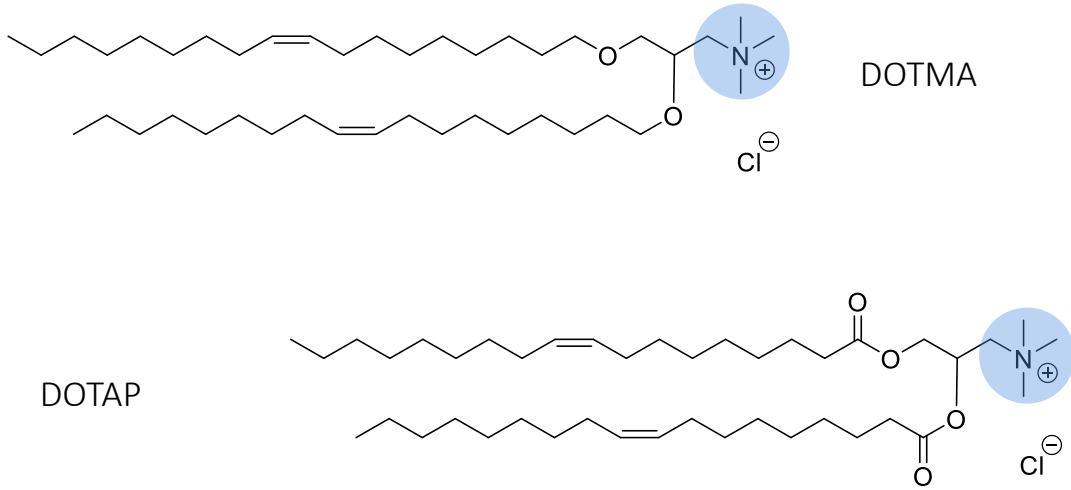
- mRNA
  - **mRNA**: carry the genetic information to be translated, *in fine*, into a protein of interest

Excipient/Carrier = LNP (lipid nanoparticles) composed of a lipid mix

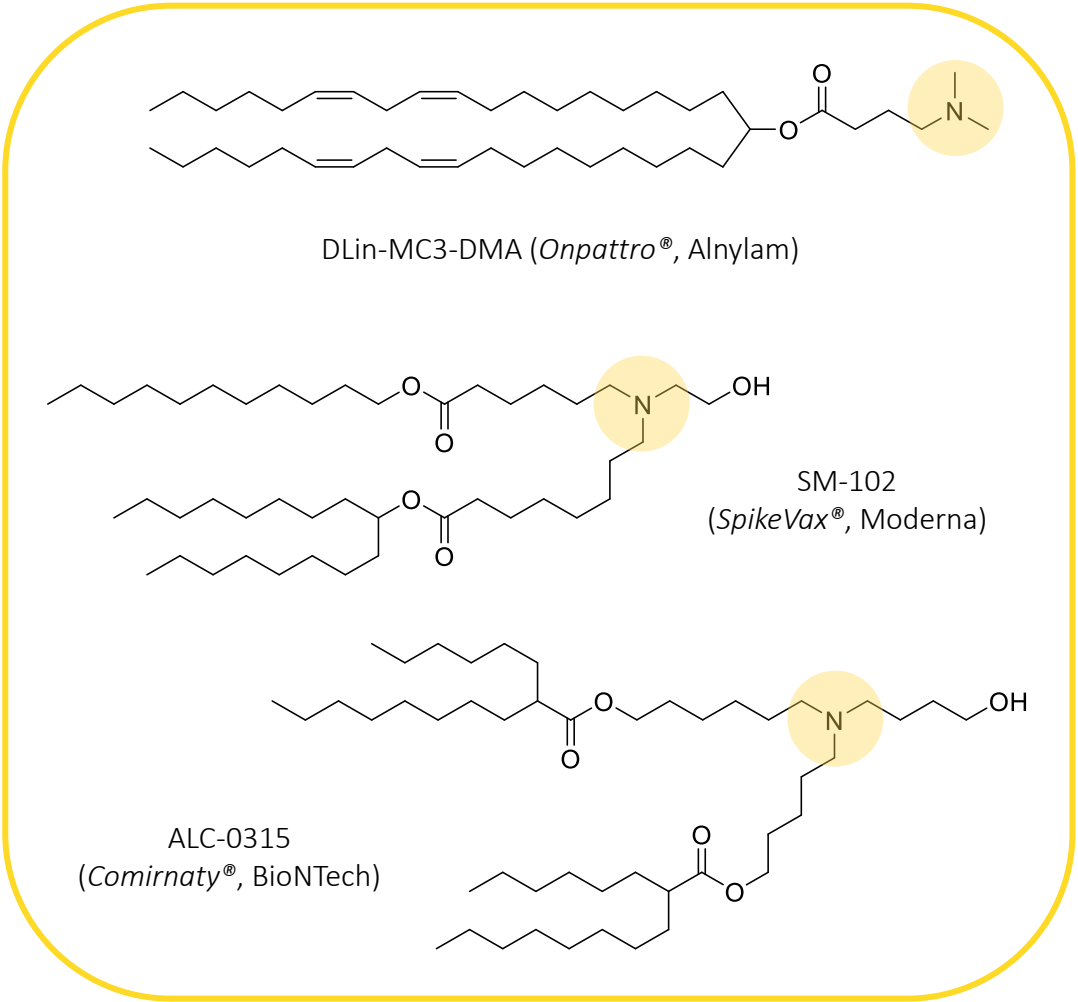
- Cationic / ionizable lipids
  - **Active lipids** (cationic and/or ionizable lipids): positively charged lipids will interact with negatively charged nucleic acids and cell membrane (improve cell uptake)
- Helper lipid
  - **Structural/Helper lipids** (phospholipids): Provide LNP rigidity and stability
- PEGylated lipid
- Cholesterol
  - **Modulators**:
    - PEG-lipids: Provide steric stabilization and prolong blood circulation
    - Cholesterol: Increase membrane fluidity and stability, promote membrane fusion

Cationic and Ionizable Lipids

Cationic lipids = Permanent charge



Ionizable lipids = Charge depends on pH



- Both Lipids share the ability to interact with Nucleic Acids
- Ionizable lipids are generally considered less toxic than fixed cationic lipids → True for Lipids based on quarternary ammonium group such as DOTMA and DOTAP, but…

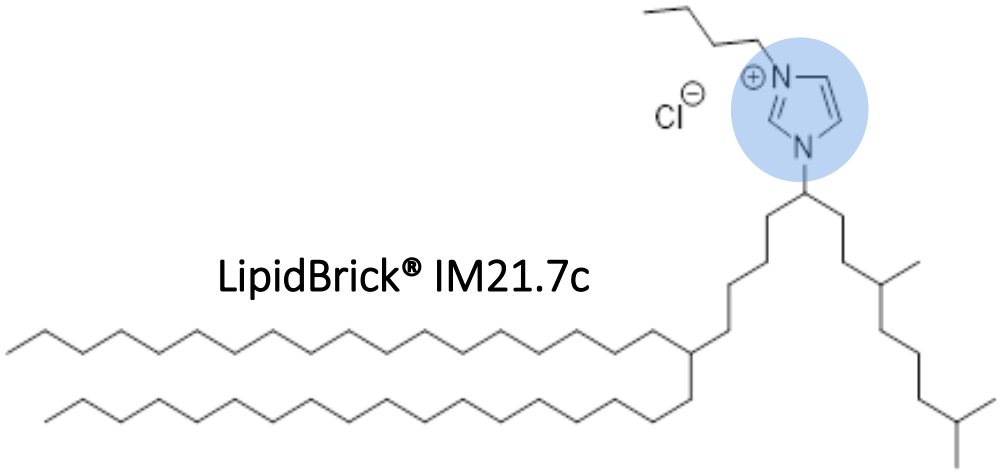
LipidBrick® IM21.7c

Innovating cationic lipids for LNP formulation

LipidBrick® IM21.7c = Breakthrough technology

- Polyplus® new generation of cationic lipids

  - Based on **IM**idazolium **polar head** (heterocycle = less toxic)
  - Proof of concept using IM21.7c in LNP formulation has been performed *in vivo* with no toxicity nor inflammatory response
  - Same IM21.7c already used in Liposomal Formulations jetMESSENGER® and *in vivo*-jetRNA®+ proving to be really efficient and safe
  - Sole Proprietary Technology of Polyplus®
    - Patent n° EP18306417 (Granted in EU – US under examination)
    - Patent n° EP22306027.8 (submitted but not published yet)

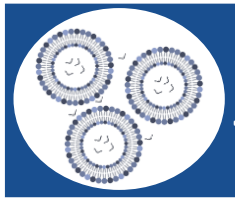
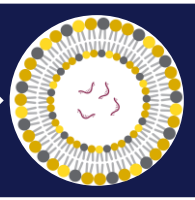
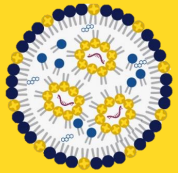


LipidBrick® IM21.7c

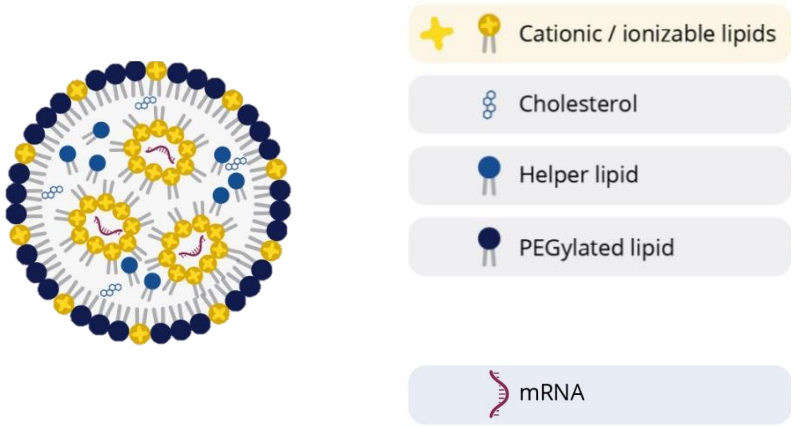
Cationic lipid
= Fixed positive charge

Polyplus' aim is to provide pathway from Research to Clinic trials

- Exact same cationic lipid shared by commercial products from Polyplus®

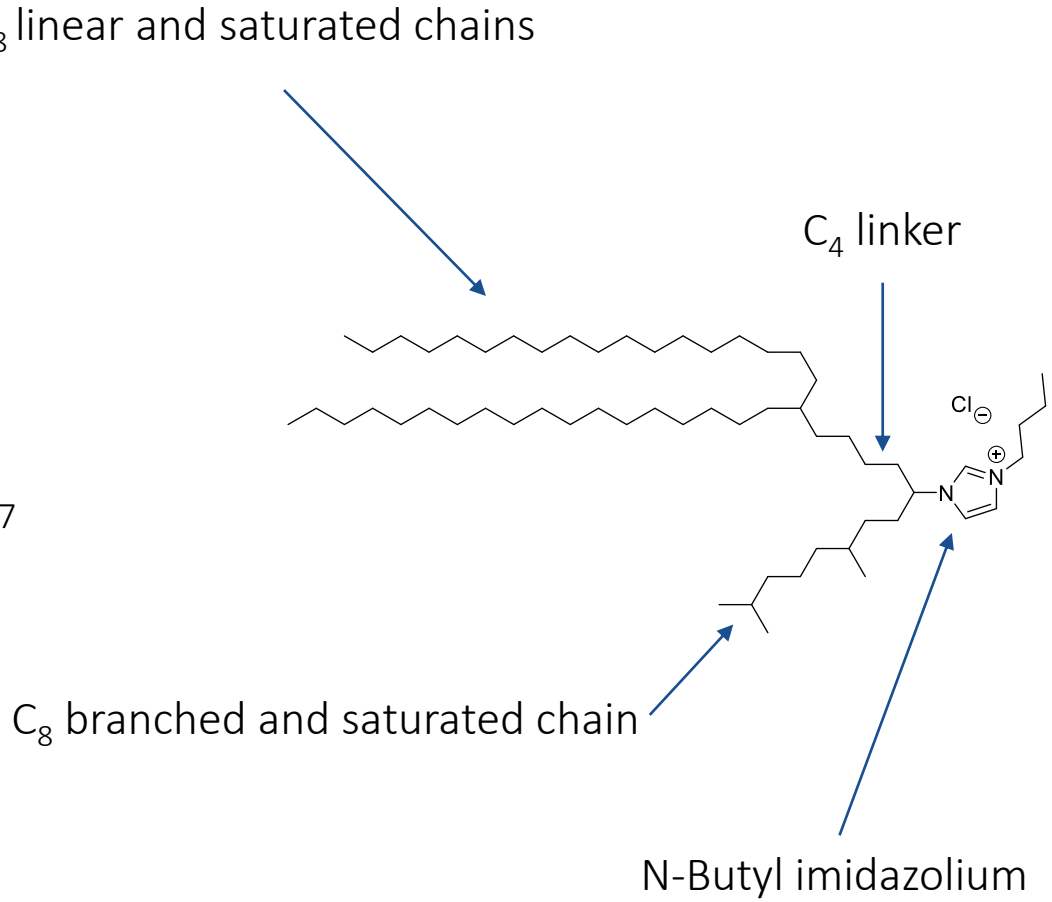
	In vitro POC	*In vivo* POC & preclinical study	Clinical trials & commercialization
Ready-to-use solution	 jetMESSENGER®	 *in vivo*-jetRNA®+	*in vivo*-jetRNA®+ GMP [Development upon request]
Lipid Nanoparticle formulation	 LipidBrick® IM21.7c (RUO)		LipidBrick® IM21.7c GMP [Under development]

Optimization of LNP formulation

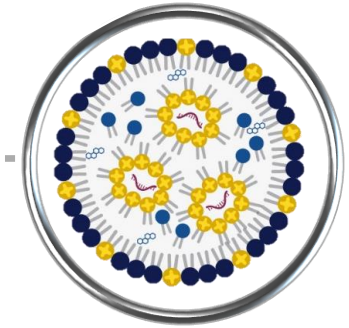


IM21.7c

CAS n°: 2416939-42-7

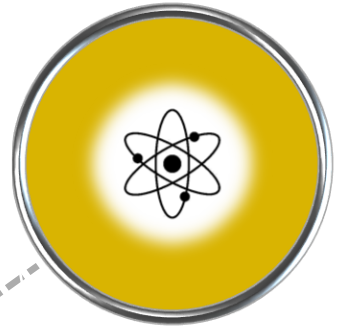


Discovery process – evaluation of proprietary library

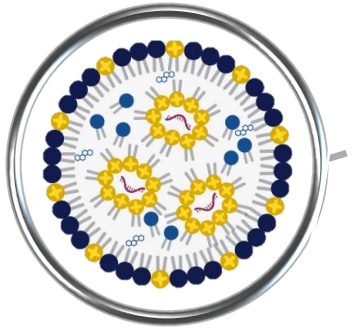


Self-assembly
- screening
- methods
- buffer

Physical properties
- Size
- Zeta potential



Synthesis
- Scalability
- Identity
- Purity



Encapsulation efficiency

Transfection efficiency
- In vitro & in vivo
- Toxicity

LipidBrick® IM21.7c advantages

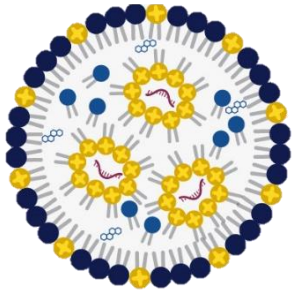
Efficient: Modulate LNP properties to adapt the biodistribution depending on the therapeutic purpose
→ IM21.7c shows a great potential by enlarging the biodistribution

Accelerate your project: *in vitro* and *in vivo* proof of concept have been successfully performed
→ LNP characterization, stability study, biodistribution and immune response have been studied

Secure: Use a unique lipid structure protected by an independent patent owned by Polyplus®
→ Independent IP covering the use of LipidBrick® with nucleic acid in LNP formulation

LipidBrick® IM21.7c is efficient

Our optimized LNP formulation



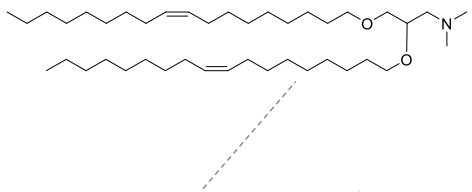
Cationic / ionizable lipids — **LipidBrick® IM21.7c** + DODMA

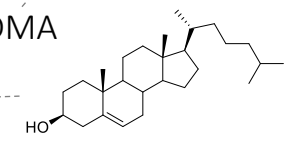
Cholesterol — Cholesterol

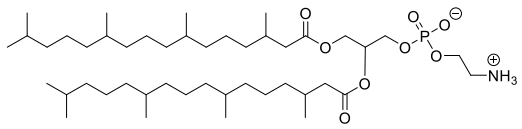
Helper lipid — DPyPE

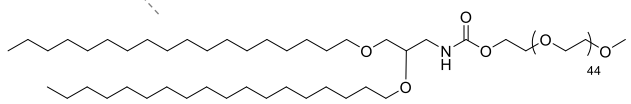
PEGylated lipid — DSG-PEG$_{2k}$

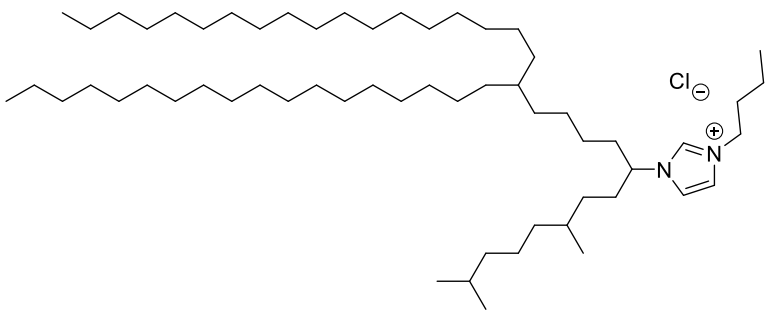
mRNA — **CleanCap® Fluc mRNA**







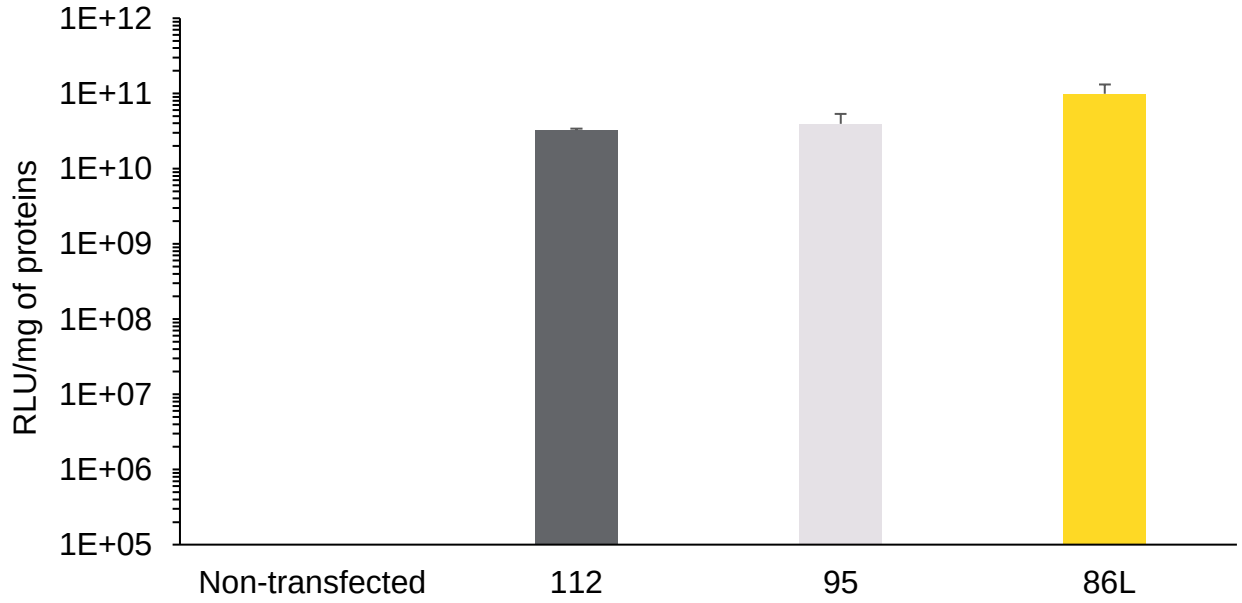




Determination of the number of lipids

Name	Cationic lipid (mM)		Ionizable lipid (mM)		HelperLipid (mM)		Cholesterol (mM)	DSG-PEG$_{2k}$ (mM)	Size	PDI	Zeta	EE%
112	IM21.7c	4	DODMA	0	DPyPE	1	1.85	0.15	71±3	0.152	+17	98%
95			DLin-MC3-DMA	3					80±3	0.077	+12	100%
86L			DODMA	3					64±2	0.068	+12	98%

Caco-2 cells – Luciferase expression (500 ng)



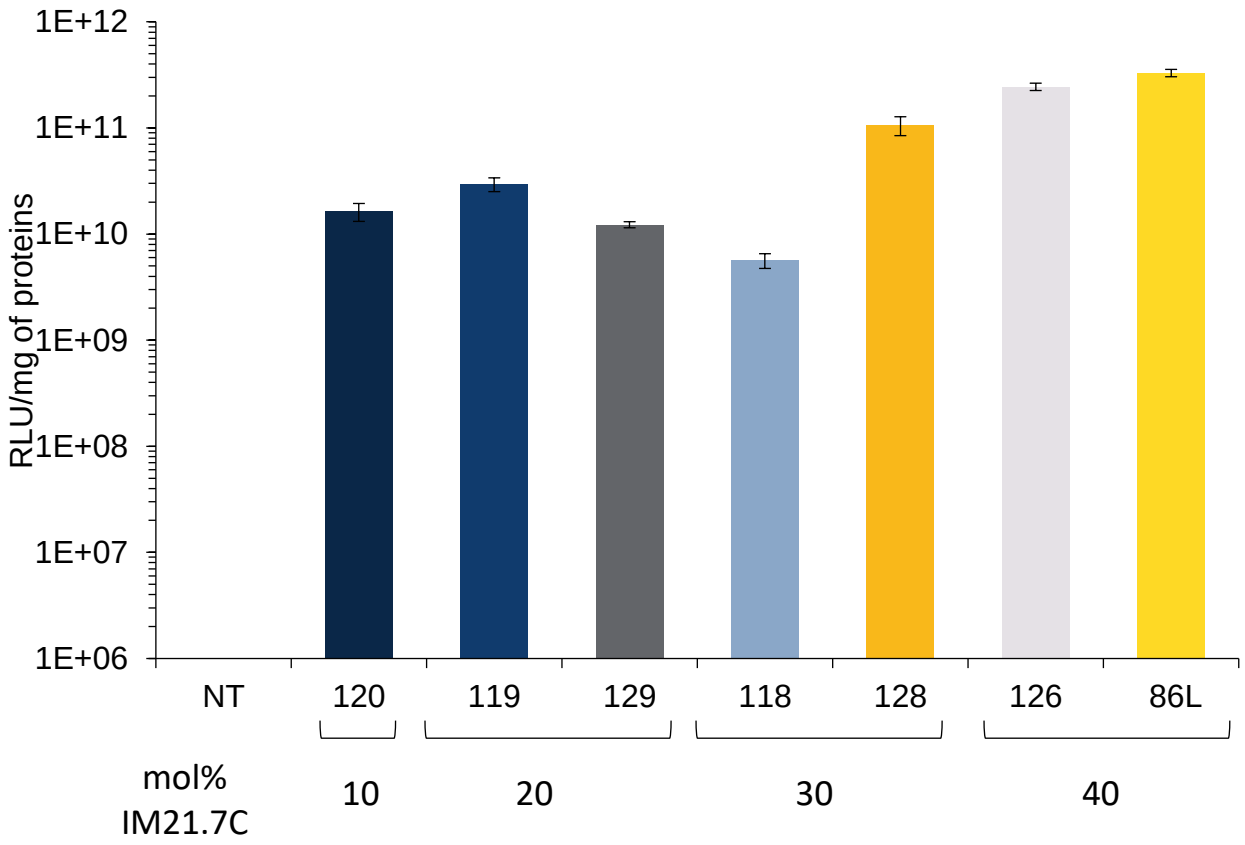
- 5 lipids were used for optimisation of LNP formulation with IM21.7c

Impact of the amount of IM21.7c on delivery efficiency

N°	IM21.7c (mM)	DODMA (mM)	DPyPE (mM)	Cholesterol (mM)	DSG-PEG_{2k} (mM)	Size	PDI	Zeta	EE%
120	1	3	1	2.85	0.15	26±1	0.144	+9	98%
119	2	3	1	2.85	0.15	72±3	0.042	+12	97%
129	2	5	1	1.85	0.15	51±1	0.131	+11	99%
118	3	3	1	2.85	0.15	43±1	0.085	+9	98%
128	3	4	1	1.85	0.15	59±4	0.107	+11	98%
126	4	2	1	1.85	0.15	61±3	0.11	+12	97%
86L	4	3	1	1.85	0.15	64±2	0.068	+12	98%

- Zeta potential not correlated to amount of **IM21.7c**
- Size range: 30-70 nM
- PDI < 0.2

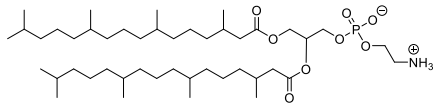
Caco-2 cells – Luciferase expression (500 ng)



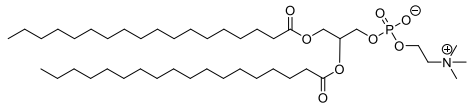
Influence of phospholipid

N°	IM21.7c (mM)	DODMA (mM)	Helper Lipid (mM)		Cholesterol (mM)	DSG-PEG$_{2k}$ (mM)	Size	PDI	Zeta	EE%
86AC	IM21.7c 4	DODMA 3	DPyPE	1	1.85	0.15	54±1	0.085	+16	100
237			PLPE	1			52±9	0.197	+14	100
239			DOPE	1			60±5	0.155	+13	100
238			DOPC	1			50±10	0.163	+17	100
240			DPPC	1			59±8	0.134	+17	100
241			DSPC	1			43±3	0.162	+15	100

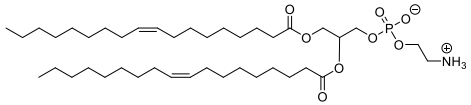
DPyPE



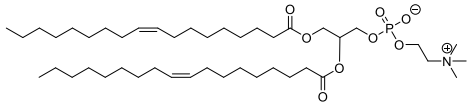
DSPC



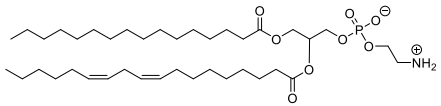
DOPE



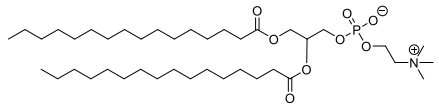
DOPC



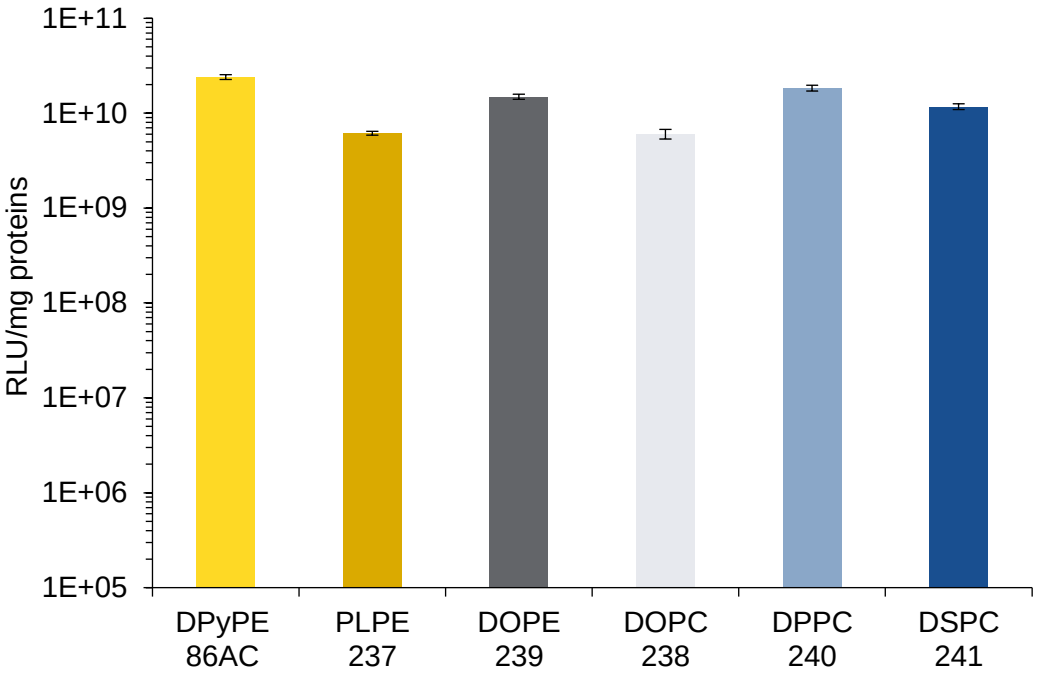
PLPE



DPPC



Caco-2 cells – Luciferase expression (500 ng)

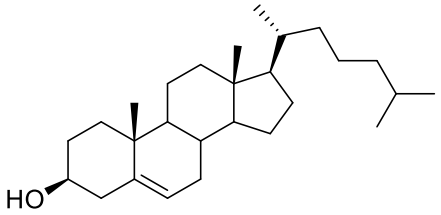


- A large variety of phospholipids are compatible with the use of IM21.7c

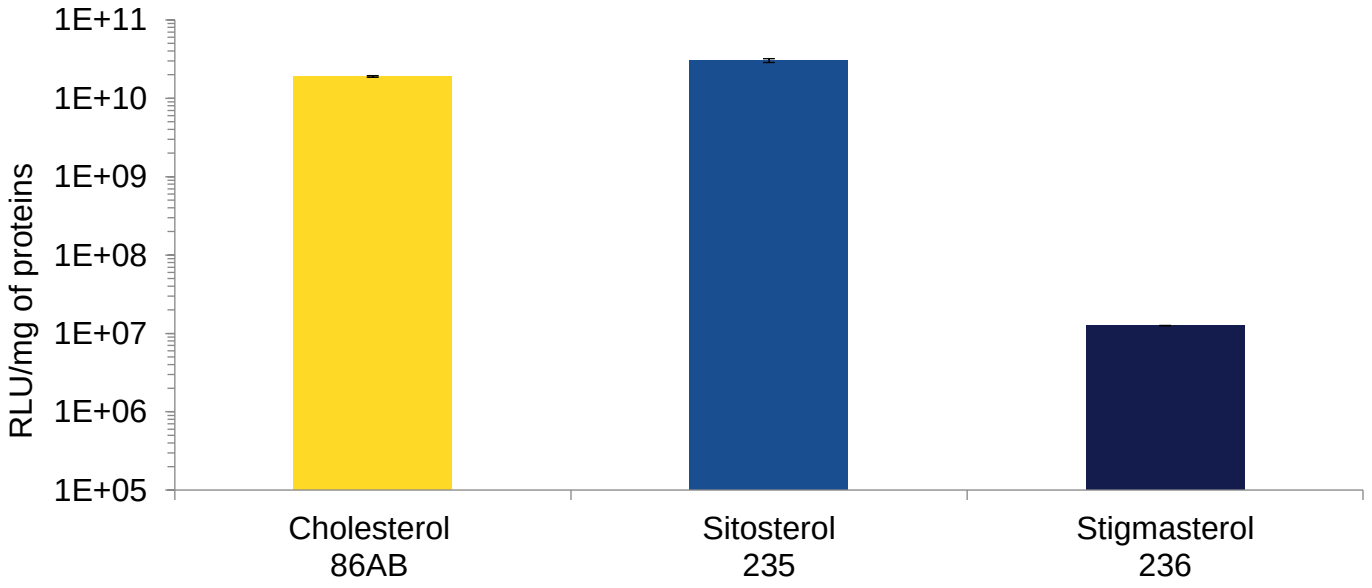
Influence of sterol

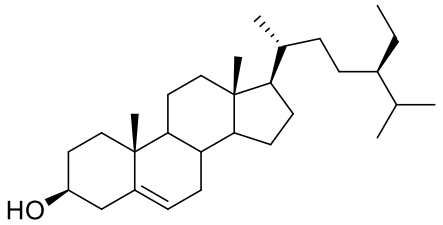
N°	Cationic lipid (mM)	Ionizable lipid (mM)	Helper Lipid (mM)	Sterol (mM)		DSG-PEG$_{2k}$ (mM)	Size	PDI	Zeta	EE%
86AB	IM21.7c	DODMA	DPyPE	Cholesterol	1.85	0.15	55±3	0.152	+14	100
235	4	3	1	β-sitosterol	1.85		77±9	0.163	+14	100
236				Stigmasterol	1.85		127±11	0.177	+7	100

Caco-2 cells – Luciferase expression (500 ng)

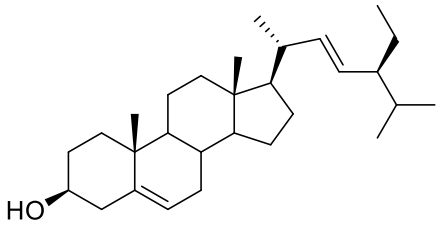


Cholesterol





β-sitosterol



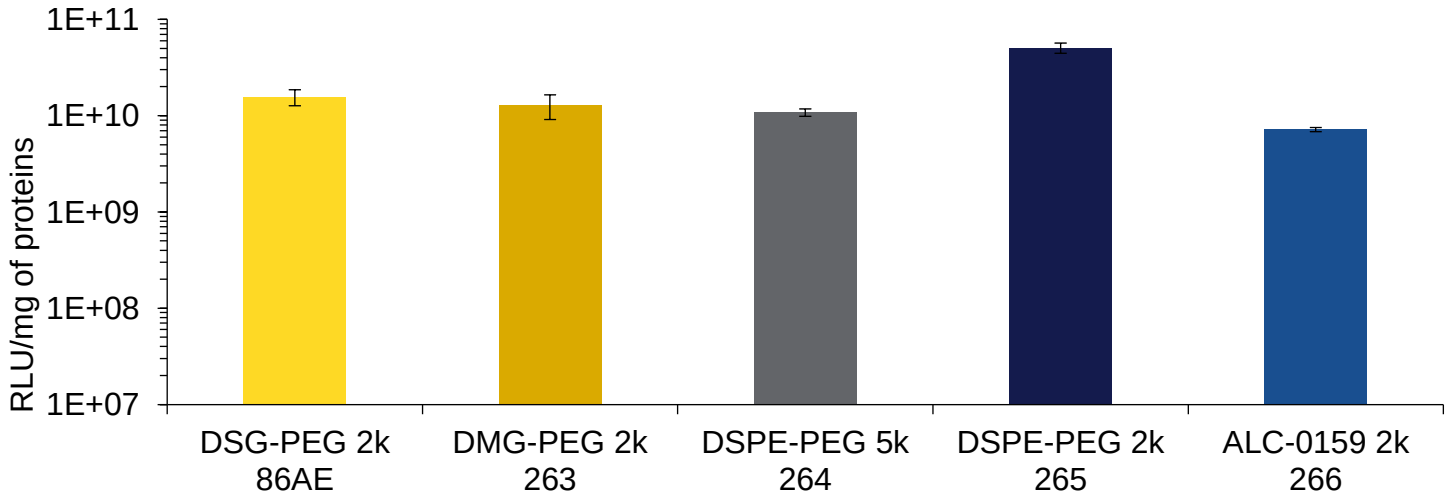
Stigmasterol

- Cholesterol and sitosterol are recommended with IM21.7c

Influence of PEG-lipid

N°	Cationic lipid (mM)	Ionizable lipid (mM)	Helper Lipid (mM)	Cholesterol (mM)	PEG-lipid (mM)		Size	PDI	Zeta	EE%
86AE	IM21.7c 4	DODMA 3	DPyPE 1	1.85	$DSG\text{-}PEG_{2k}$	0.15	75±5	0.050	+11	100
263					$DMG\text{-}PEG_{2k}$	0.15	40±3	0.198	+18	100
264					$DSPE\text{-}PEG_{5k}$	0.15	61±4	0.082	+2	100
265					$DSPE\text{-}PEG_{2k}$	0.15	85±3	0.056	+24	100
266					ALC-0159	0.15	36±6	0.216	+18	100

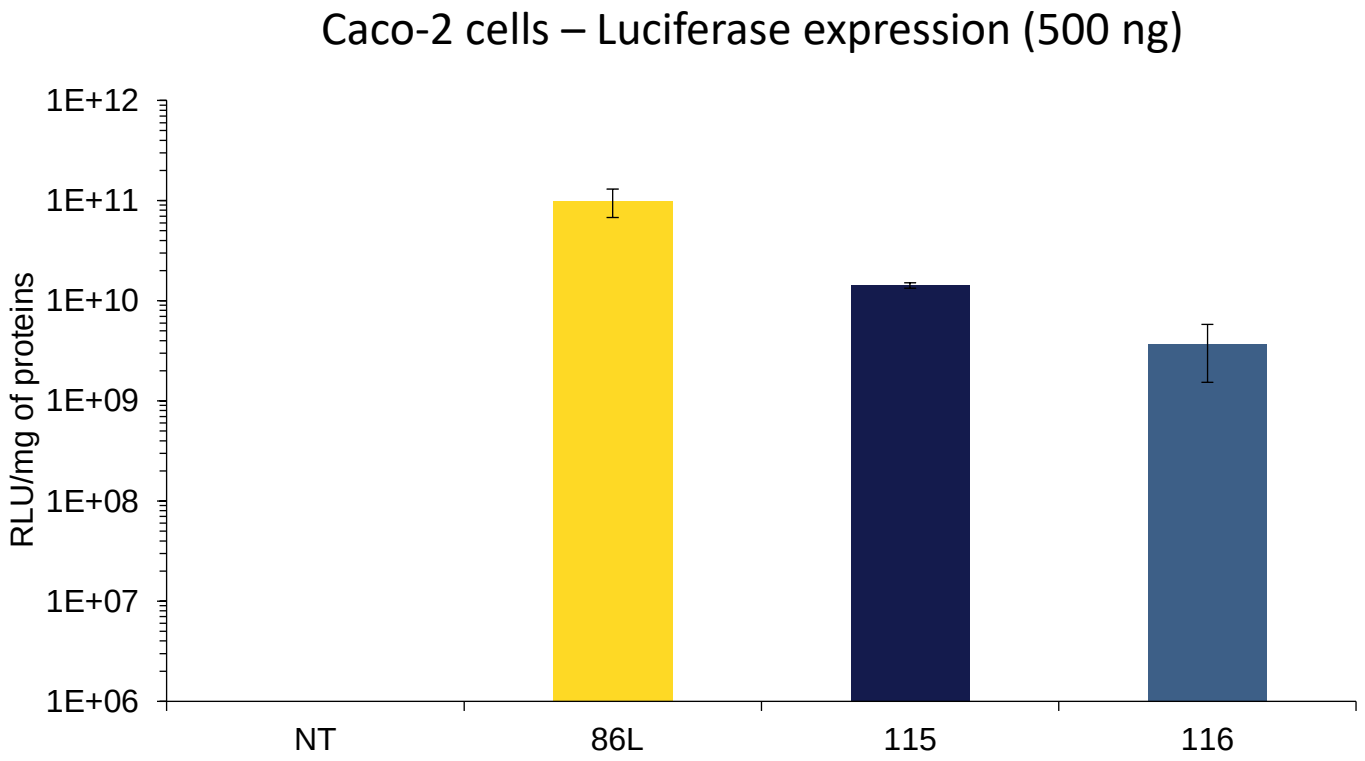
Caco-2 cells – Luciferase expression (500 ng)



- DSG, DMG, DSPE-PEG and ALC-0159 are recommended with IM21.7c

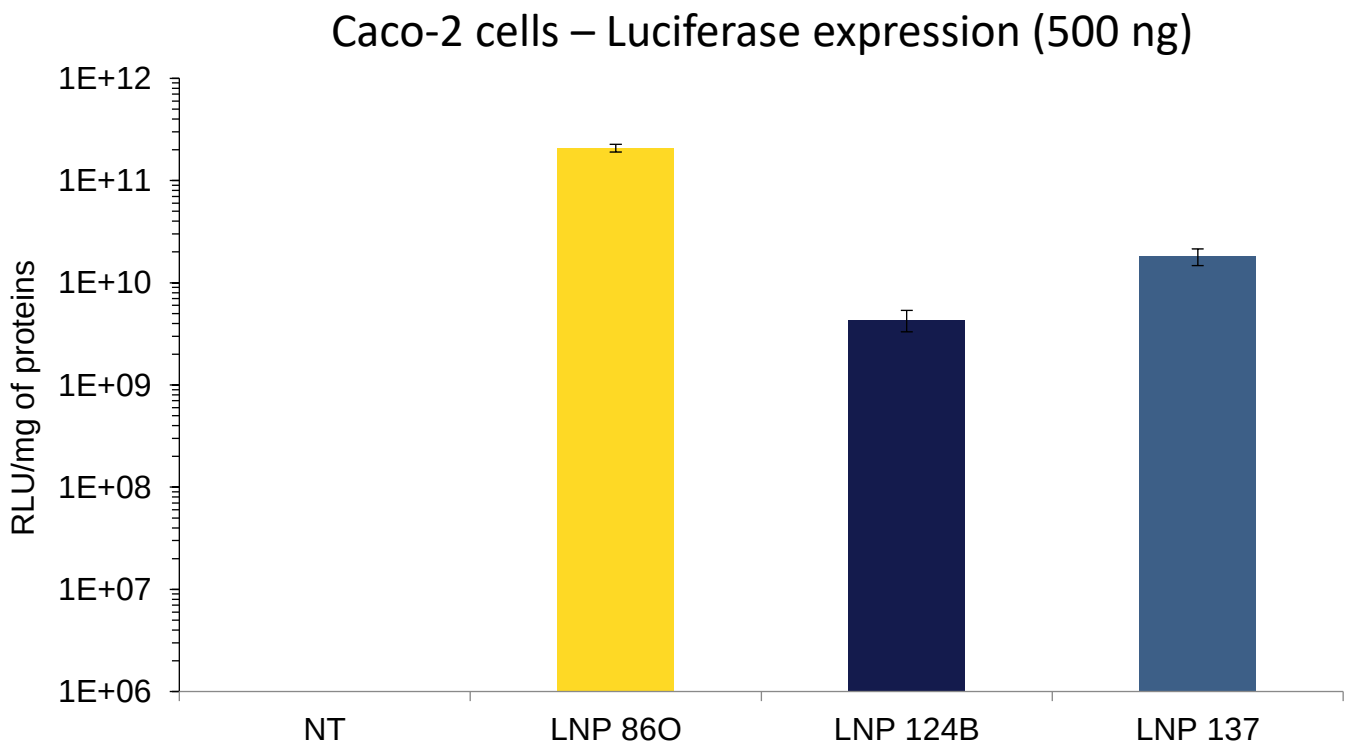
Influence of the amount of PEG-lipid

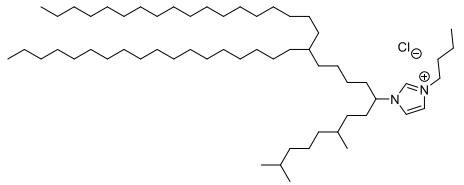
N°	Cationic lipid (mM)	Ionizable lipid (mM)	Helper Lipid (mM)	Cholesterol (mM)	DSG-PEG$_{2k}$ (mM)	Size	PDI	Zeta	EE%
86L	IM21.7c 4	DODMA 3	DPyPE 1	1.85	0.15	64±2	0.068	+12	98%
115				1.70	0.3	32±1	0.221	+17	99%
116				1.50	0.5	22±2	0.292	+12	98%

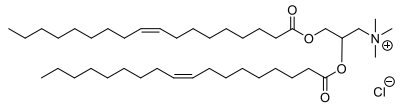


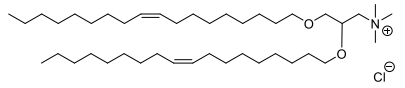
Comparison with DOTAP or DOTMA

N°	Cationic lipid (mM)		Ionizable lipid (mM)	Helper Lipid (mM)	Cholesterol (mM)	DSG-PEG$_{2k}$ (mM)	Size	PDI	Zeta	EE%
86O	IM21.7c	4	DODMA 3	DPyPE 1	1.85	0.15	64±2	0.068	+12	98%
124B	DOTAP	4					40±1	0.018	+12	86%
137	DOTMA	4					35±2	0.1788	+12	95%





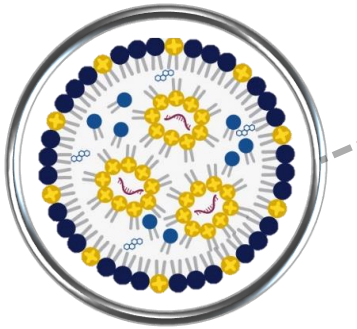




Evaluation of LNP formulation with LipidBrick® IM21.7c

Physical properties

- Size
- Zeta potential



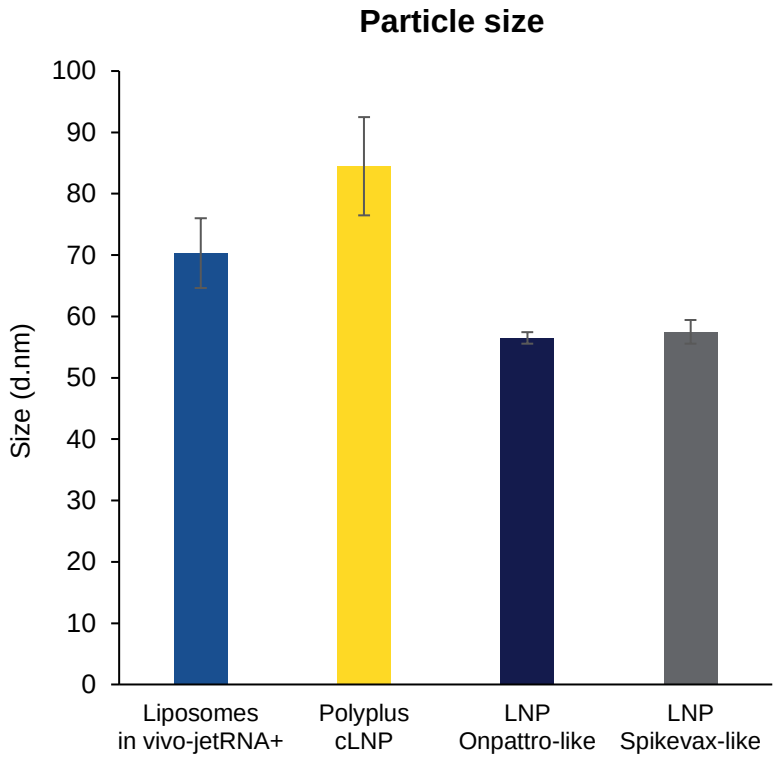
Encapsulation efficiency

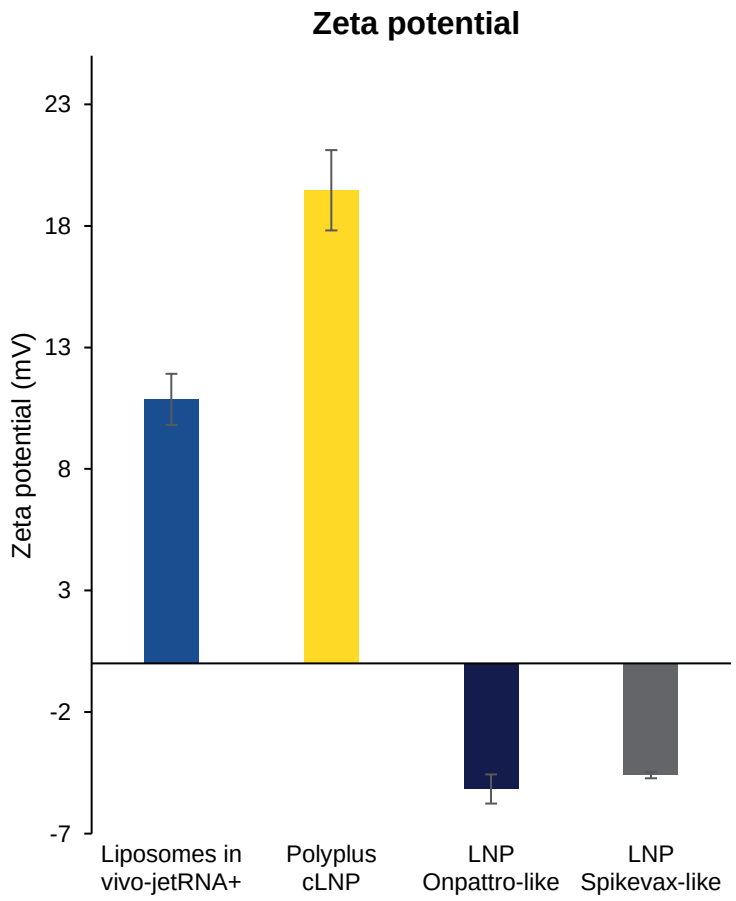
Name	Cationic / Ionizable lipid (mM)		Helper Lipid (mM)		Cholesterol (mM)	PEG (mM)	
Polyplus cLNP	IM21.7c/DODMA	4/3	DPyPE	1	1.85	$DSG\text{-}PEG_{2k}$	0.15
LNP Onpattro-like	DLin-MC3-DMA	2.75	DSPC	0.55	2.118	$DMG\text{-}PEG_{2k}$	0.086
LNP Spikevax-like	SM-102	5	DSPC	1	3.85	$DMG\text{-}PEG_{2k}$	0.15

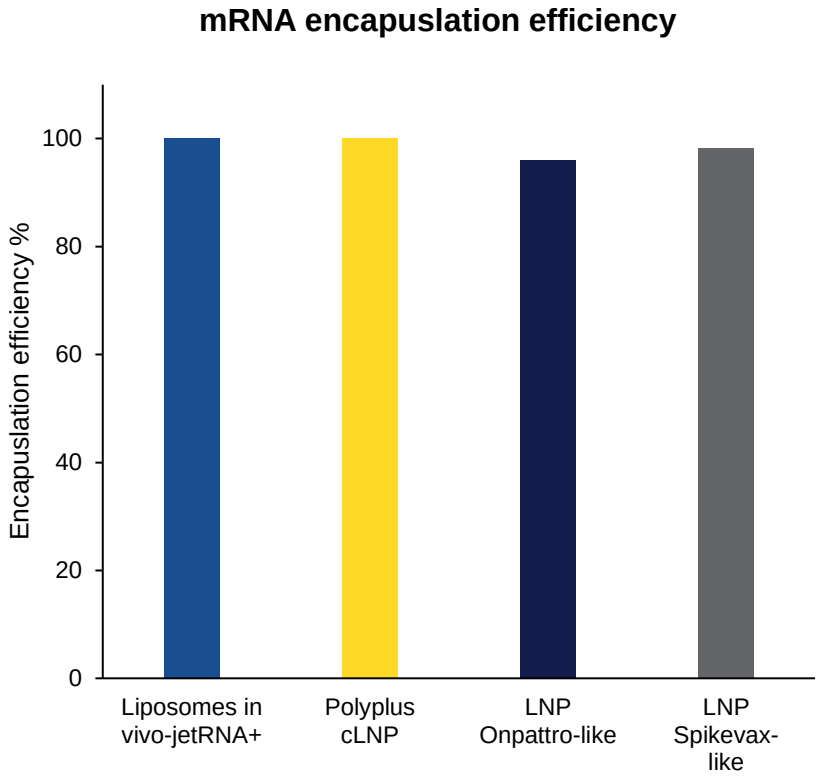
Transfection efficiency

- *In vitro*
- *In vivo*
- Toxicity

Polyplus cLNP using LipidBrick® IM21.7c allows to modify LNP properties



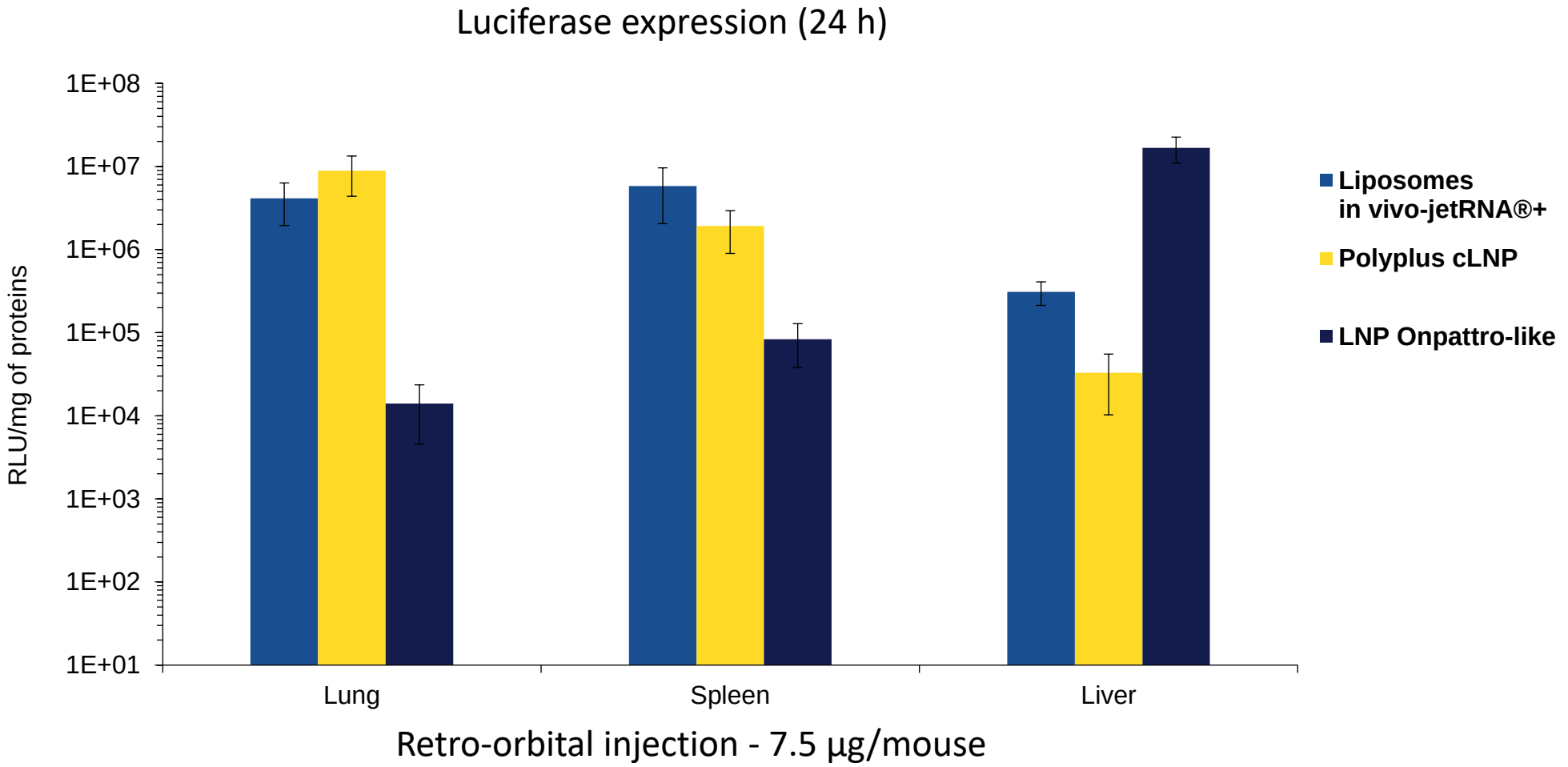




Liposomes with *in vivo*-jetRNA®+ at 50ng/µl after 1h of complexation & LNPs at 250 or 200ng/µl

Polyplus cLNP leads to a different biodistribution than LNP with ionizable lipids

- After IV injection, less accumulation in the liver but global repartition compared to LNP with ionizable lipids



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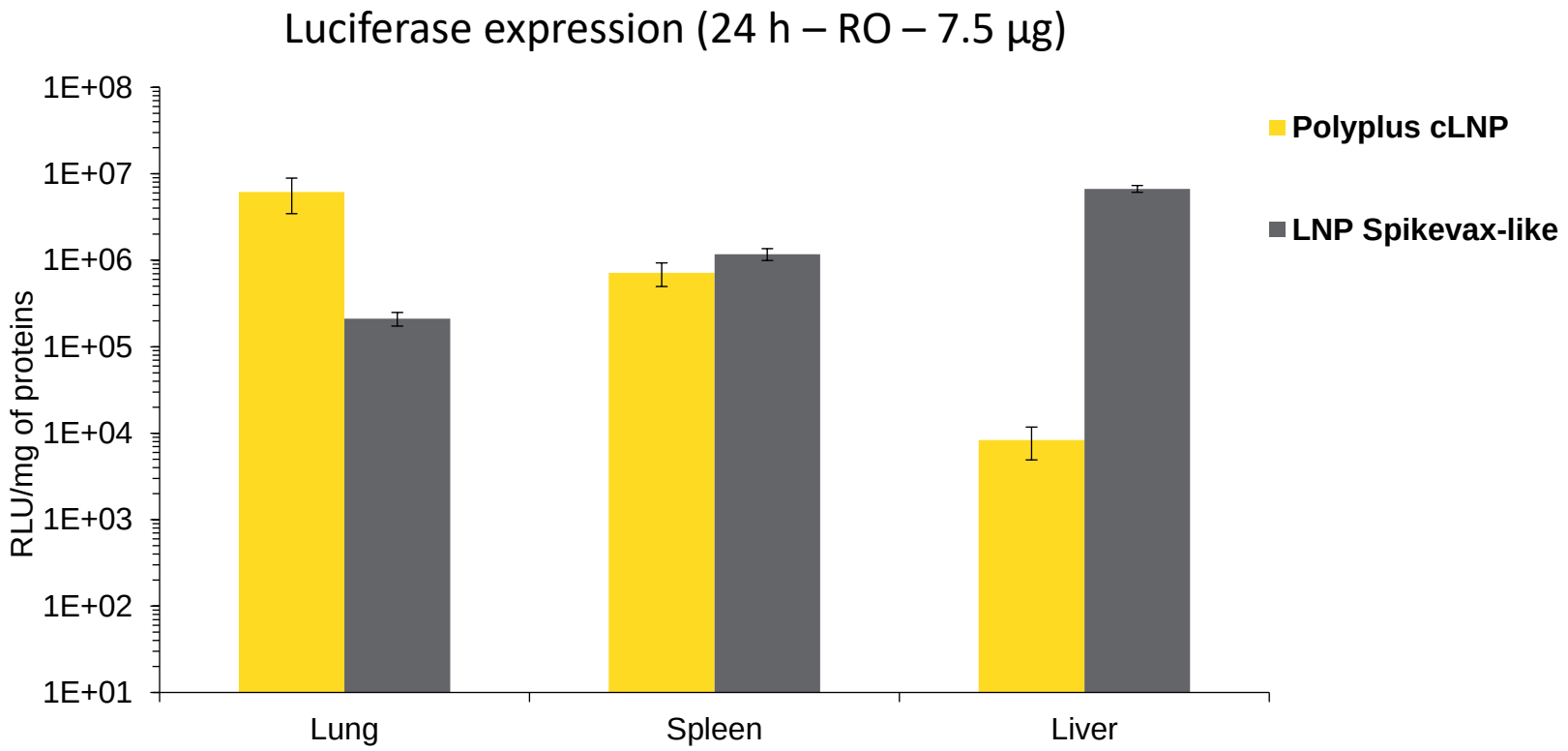
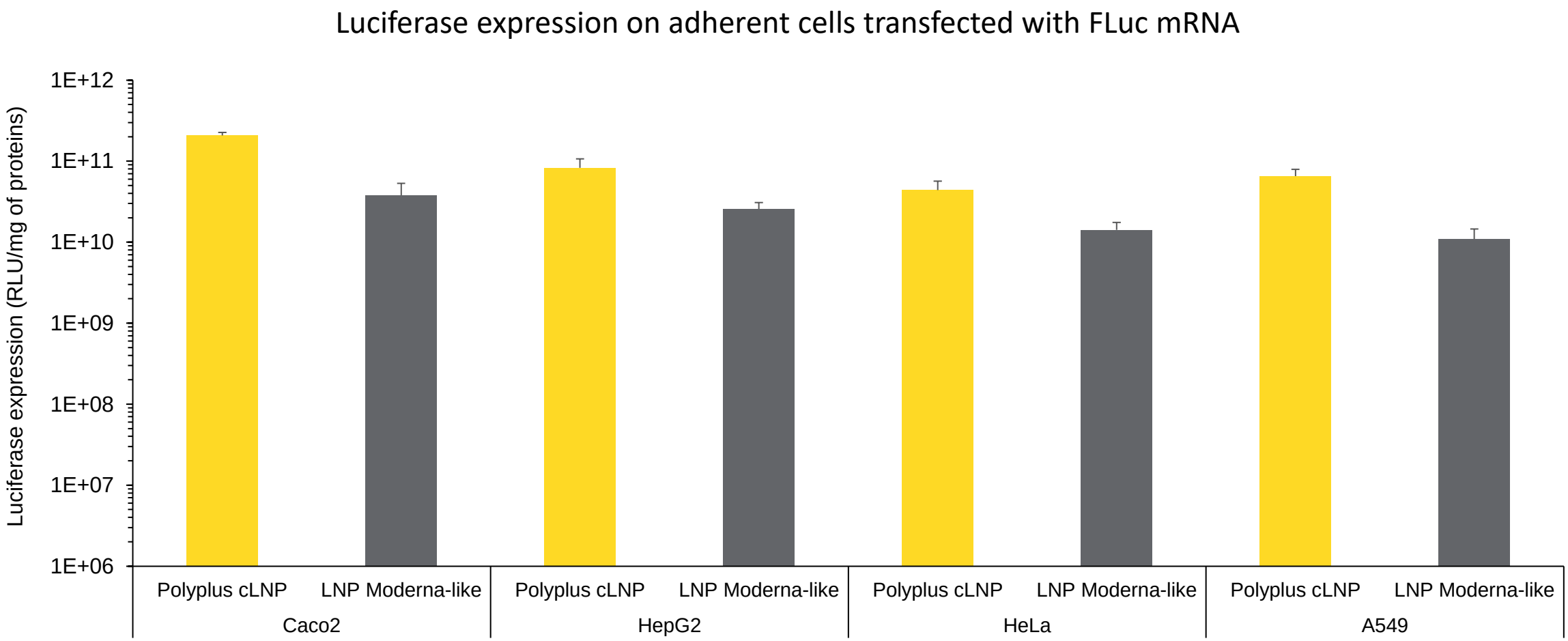


- LipidBrick® IM21.7c is efficient → Modulates LNP properties to adapt the biodistribution depending on the therapeutic purpose

LipidBrick® IM21.7c accelerates your project

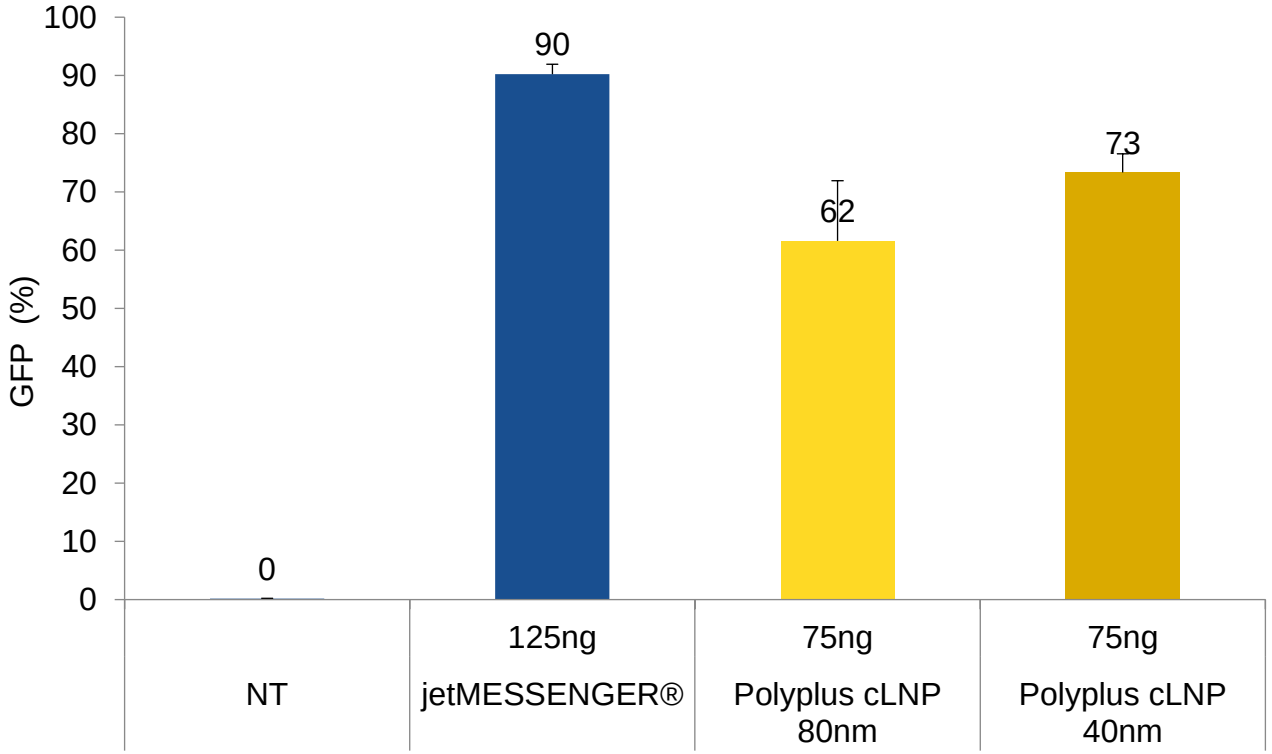
Efficient transfection on adherent cell lines with Polyplus cLNP



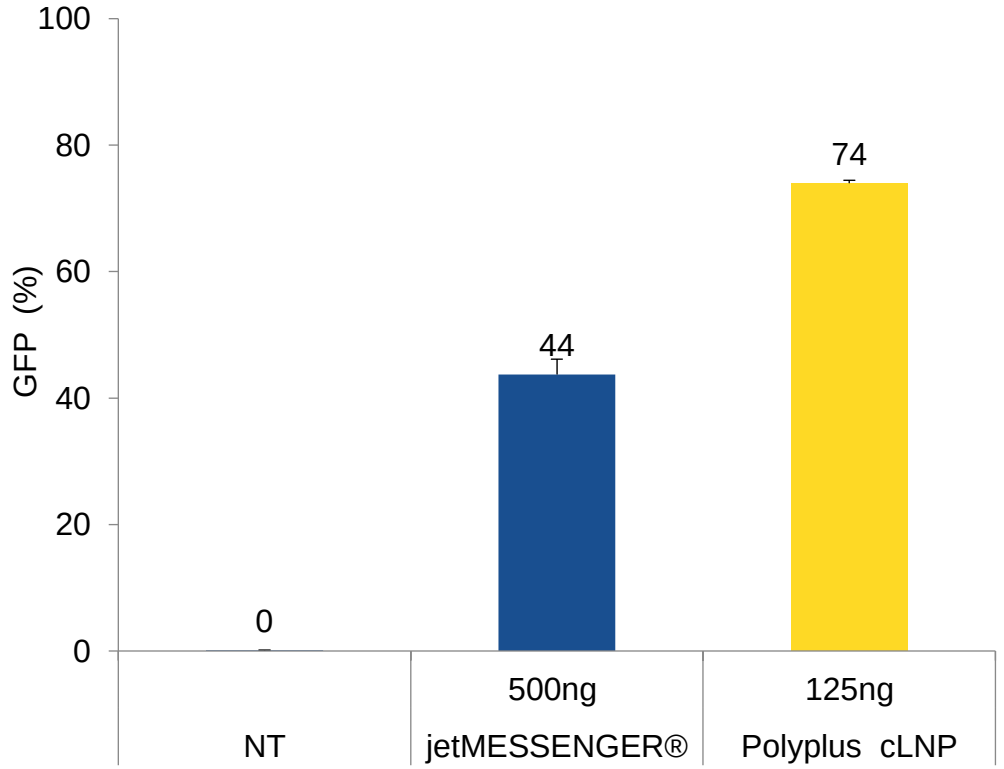
Efficient transfection of human T cells and CD34+ HSC with Polyplus cLNP

- Efficient transfection of immune cells: T cells and CD34+ HSC

Primary Human T cells from peripheral blood



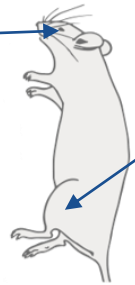
Primary Human CD34+ HSC from placental blood



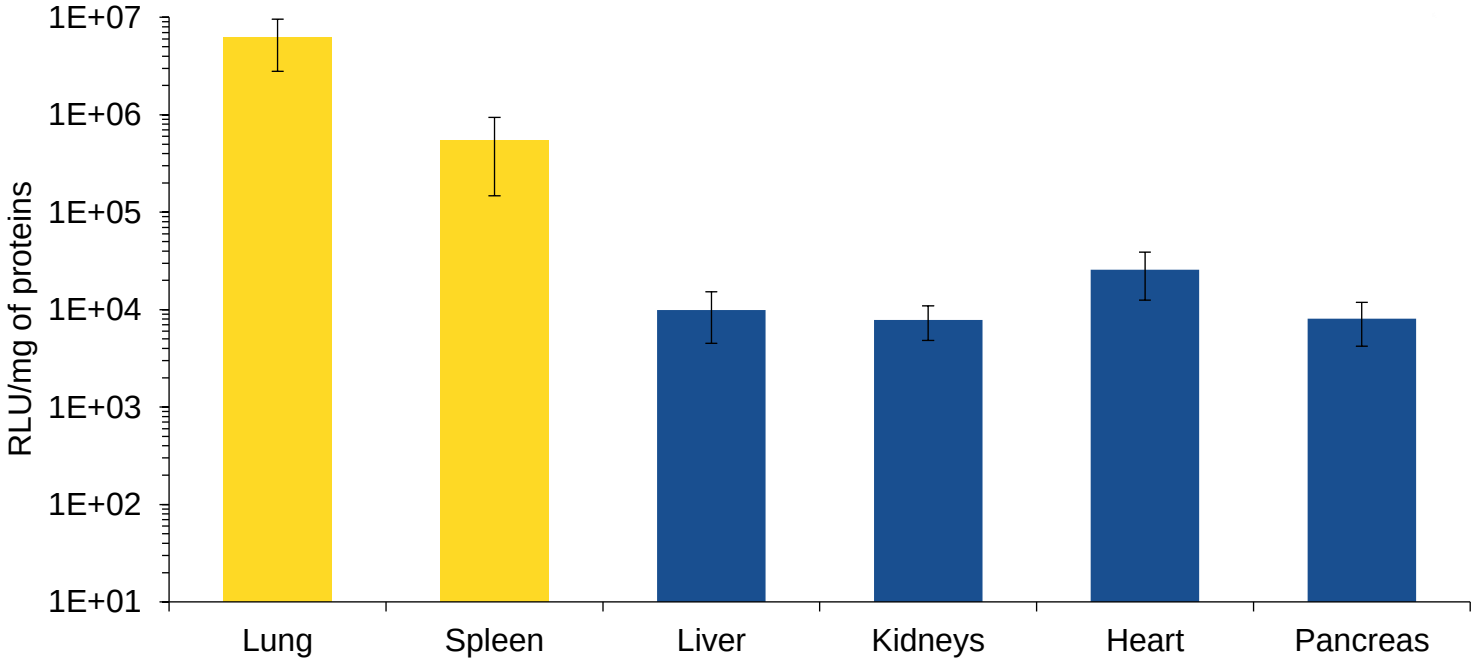
Efficient mRNA delivery with Polyplus cLNP via different routes of administration (1/2)

Retro-orbital injection

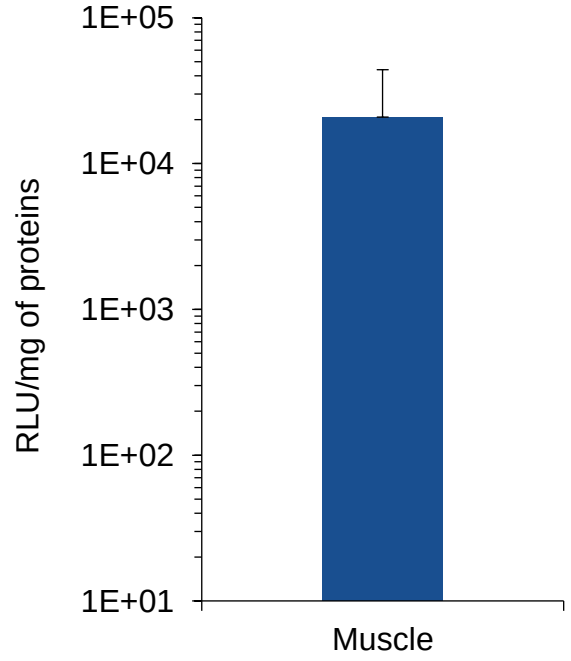
Intramuscular injection



Luciferase expression (24 h – 10 µg/mouse)

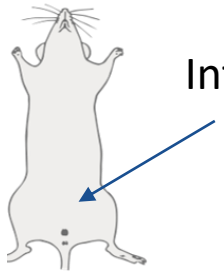


Luciferase expression (24 h – 5 µg/mouse)



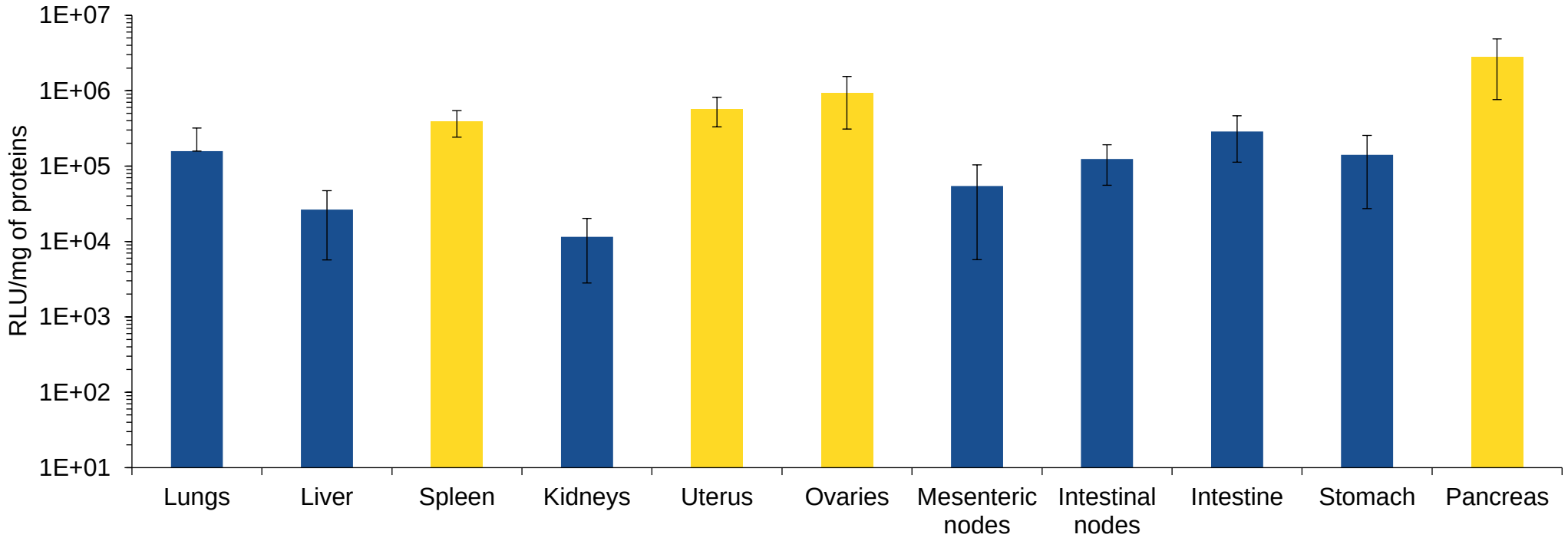
- Successful expression after IV (RO) and IM injection routes

Efficient mRNA delivery with Polyplus cLNP via different routes of administration (2/2)



Intraperitoneal injection

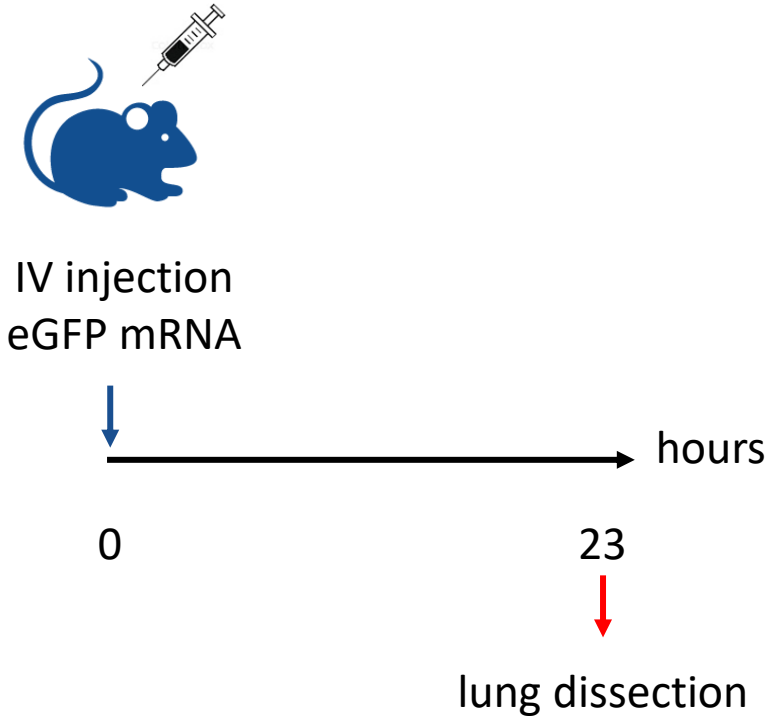
Luciferase expression (24 h– 20 µg/mouse)

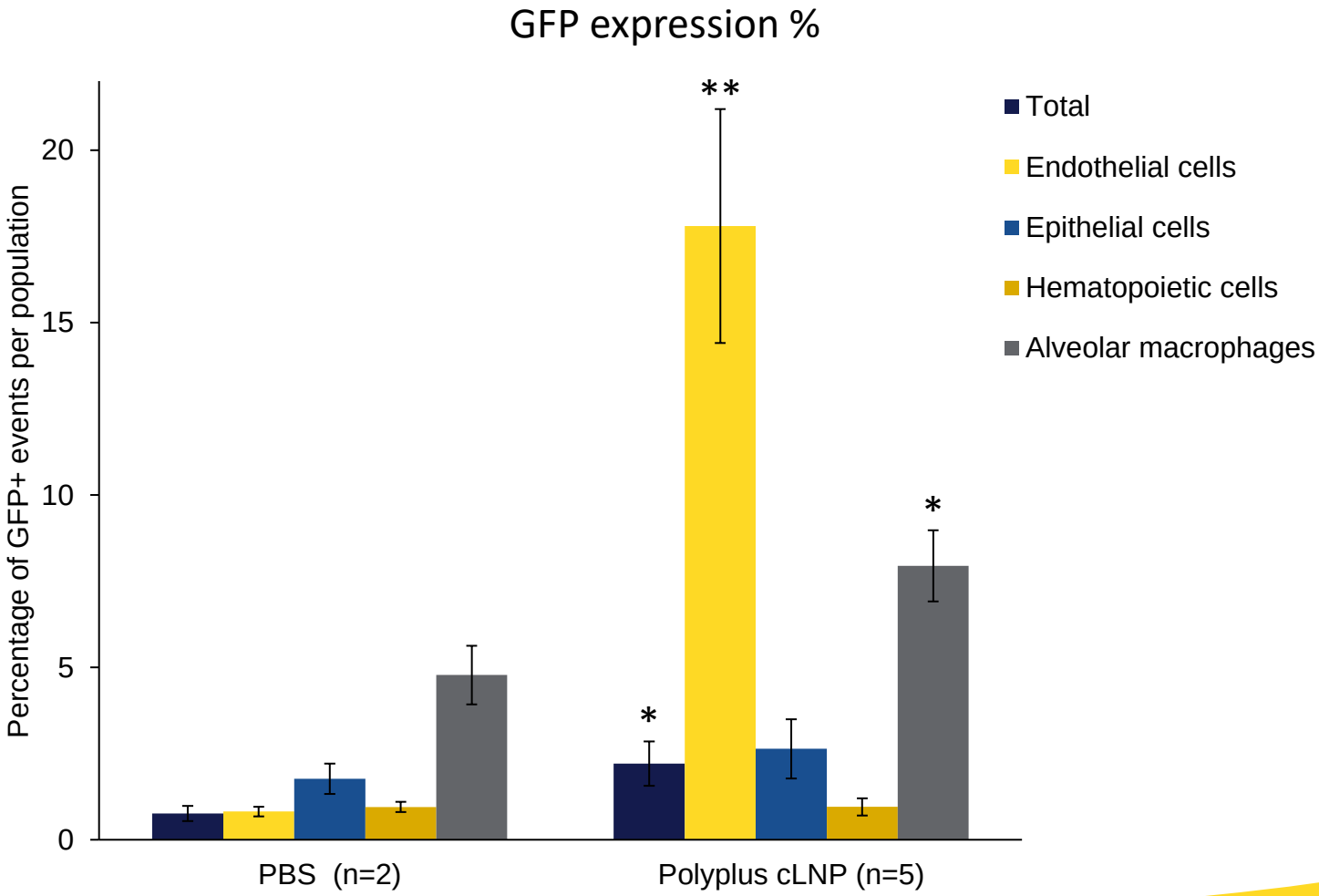


- Successful expression after IP injection routes

Polyplus cLNP mainly targets endothelial cells and alveolar macrophages

- In the lung, Polyplus cLNP using LipidBrick® IM21.7c mainly target endothelial cells (CD45- CD31+ EpCAM-) and alveolar macrophages (CD45+ CD11b+ F4/80+)



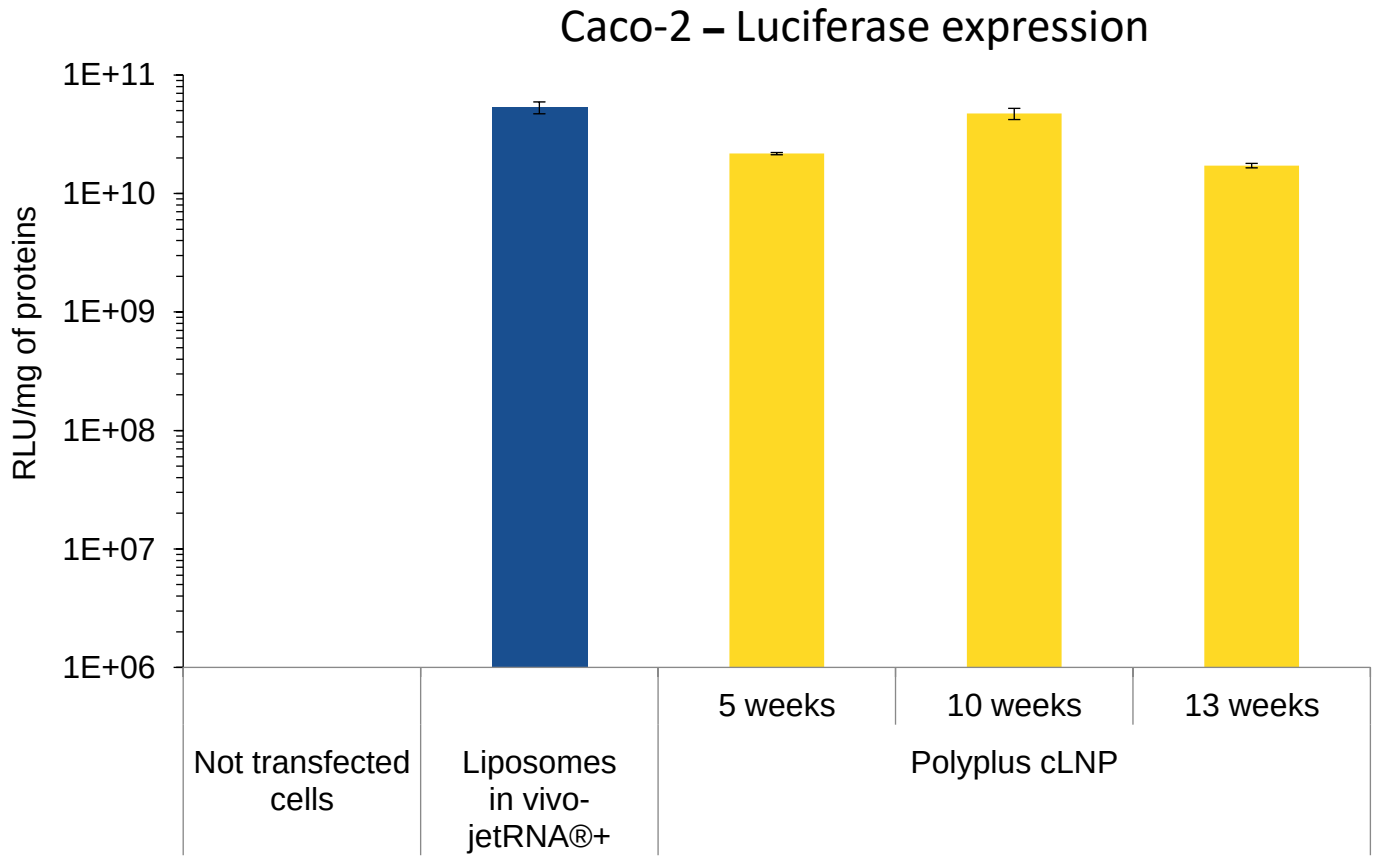


t-test *p<0.05 and **p<0.01

Polyplus cLNP using LipidBrick® IM21.7c is very stable over the time

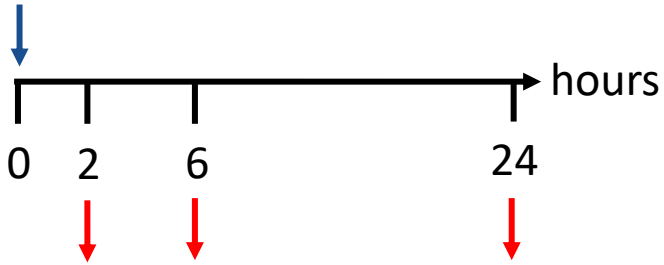
- Polyplus cLNP are stable up to 13 weeks at 4°C

Time at 4°C	Size (d.nm)	Pdi	Zeta potential (mV)
Fresh	67	0.092	+12
10 months	77	0.099	+17



Polyplus cLNP triggers the same cytokine profile as LNP with ionizable lipids

IV injection
CleanCap® Fluc mRNA (5moU)

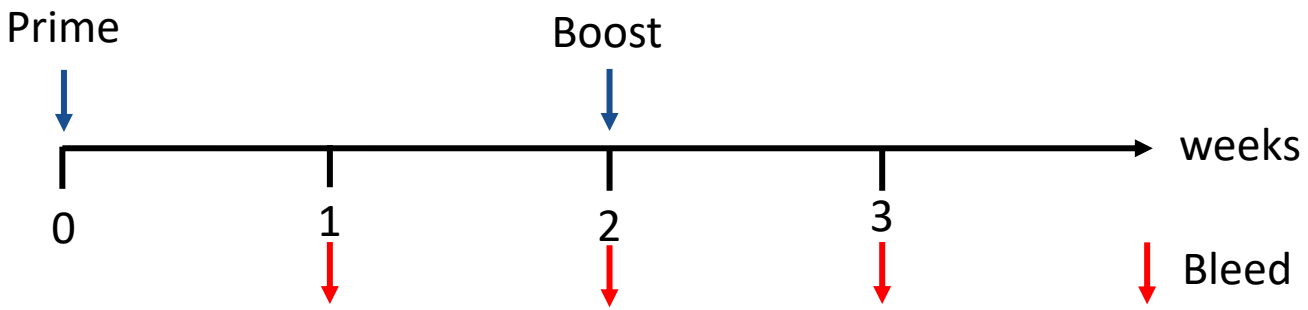


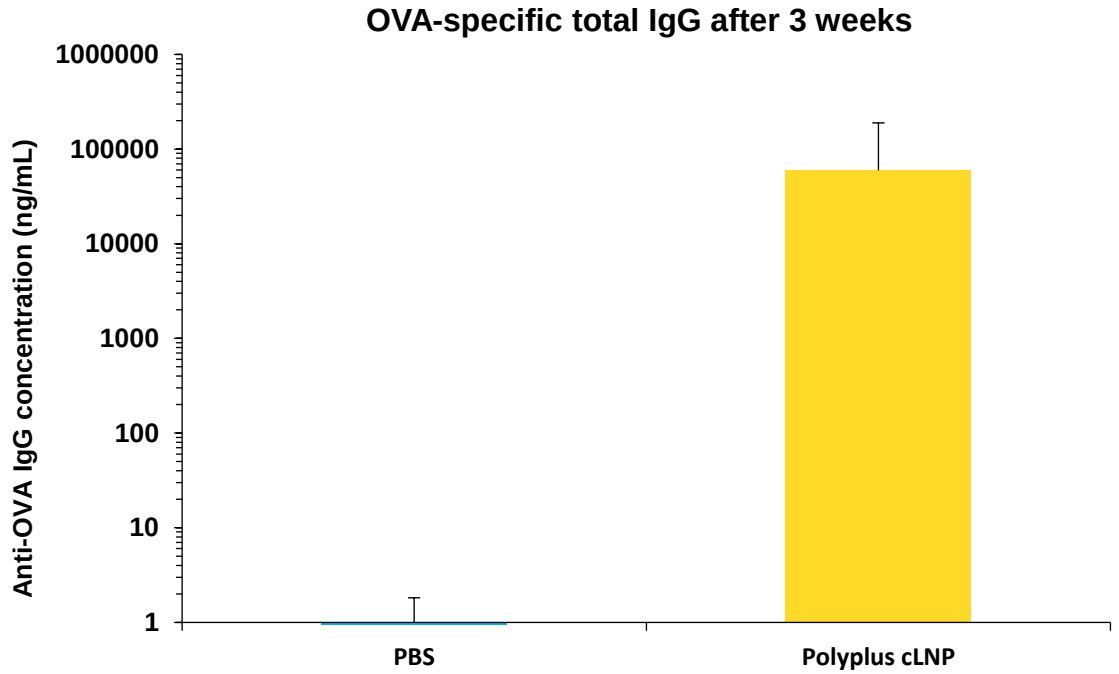
Average (N=6 mice)	PBS			LPS			LNP Onpattro-like			Polyplus cLNP with LipidBrick® IM21.7c		
Cytokine	2 h	6 h	24 h	2 h	6 h	24 h	2 h	6 h	24 h	2 h	6 h	24 h
IFN-γ												
TNF-α												
GM-CSF												
IL-1α												
IL-1β												
IL-2												
IL-4												
IL-5												
IL-6												
IL-10												
IL-12												
IL-17A												
IL-23												

Legend in pg/mL
> 10^4
10^3 - 10^4
101-1000
21-100
0-20

Polyplus cLNP gives strong humoral immune response against OVA

IM injection
OVA mRNA

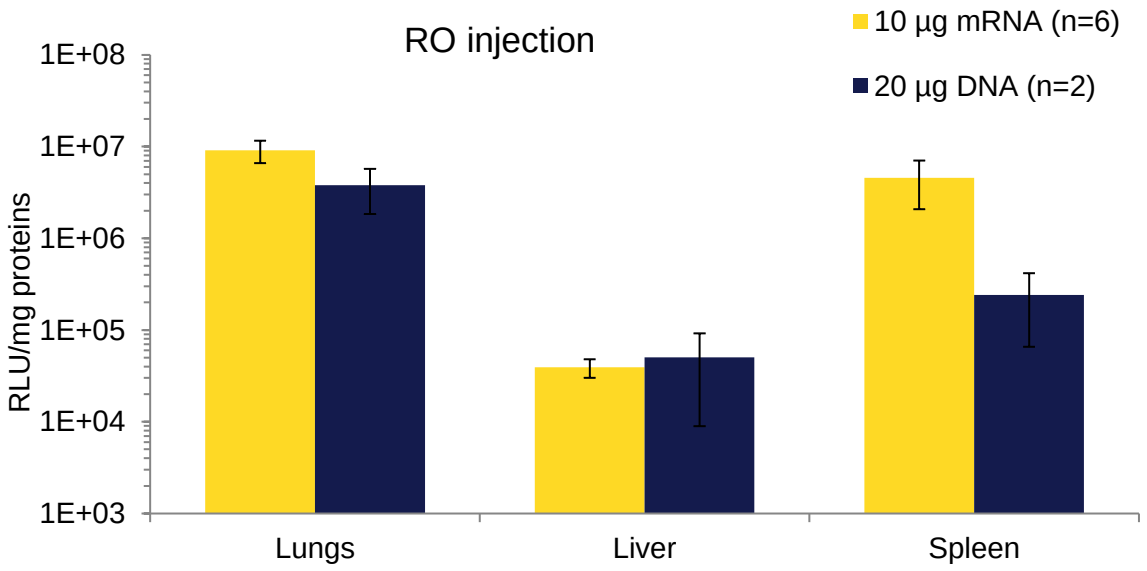




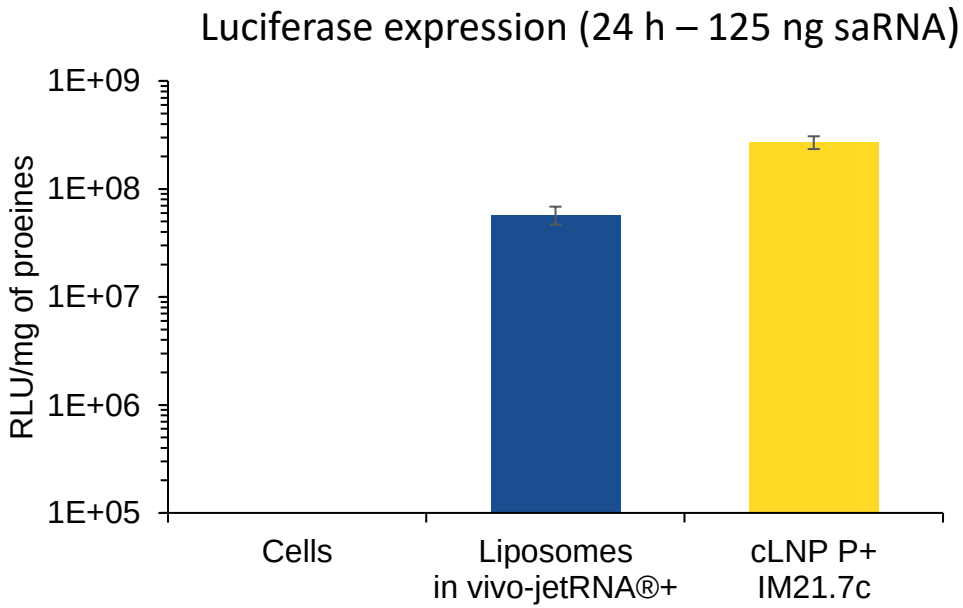
LipidBrick® IM21.7c can be used with other nucleic acids

Nucleic acid	Size	Lipids (mM)	Size	PDI	Zeta	EE%
mRNA FLuc	**2 kb**	IM21.7c / DODMA / DPyPE / Cholesterol / DSG-PEG$_{2k}$ 4 / 3 / 1 / 1.85 / 0.15	44±2	0.156	+12	100
DNA pCMV_FLuc			55±3	0.107	+12	100
saRNA nLuc	**8.4 kb**		87±2	0.097	+12	91

- DNA: *in vivo*



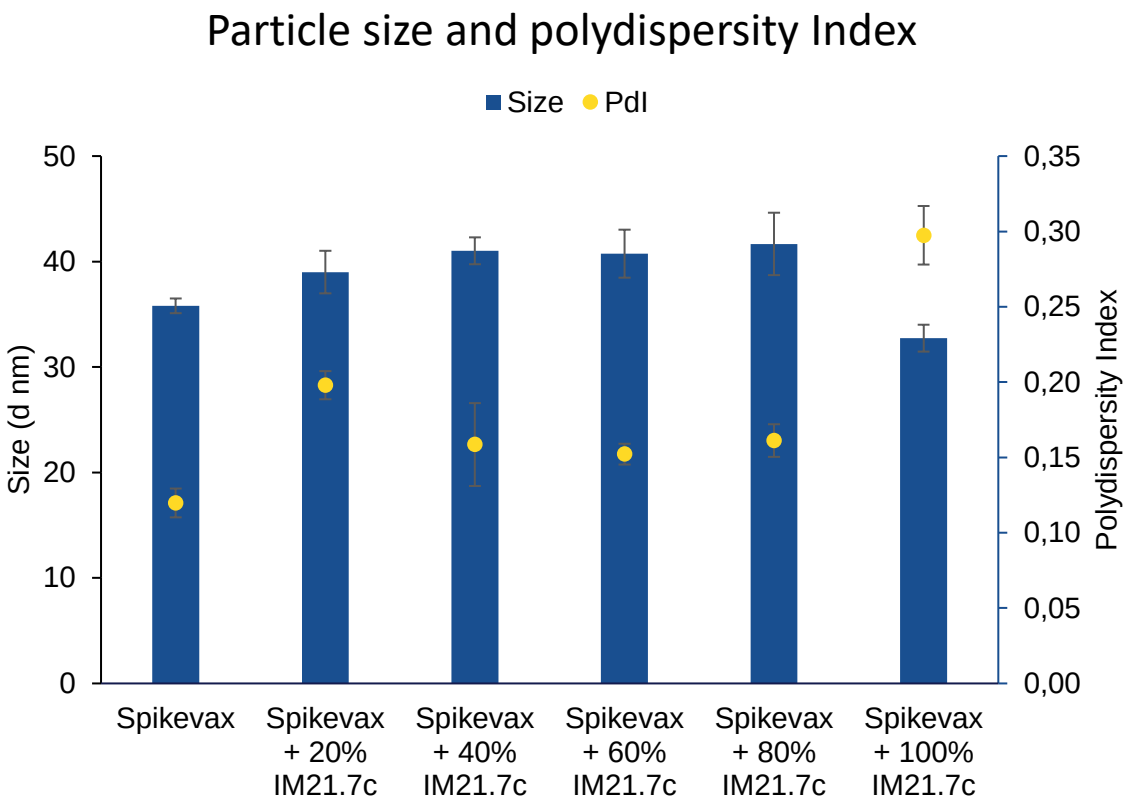
- saRNA: *in vitro* – HEK-293T(a)

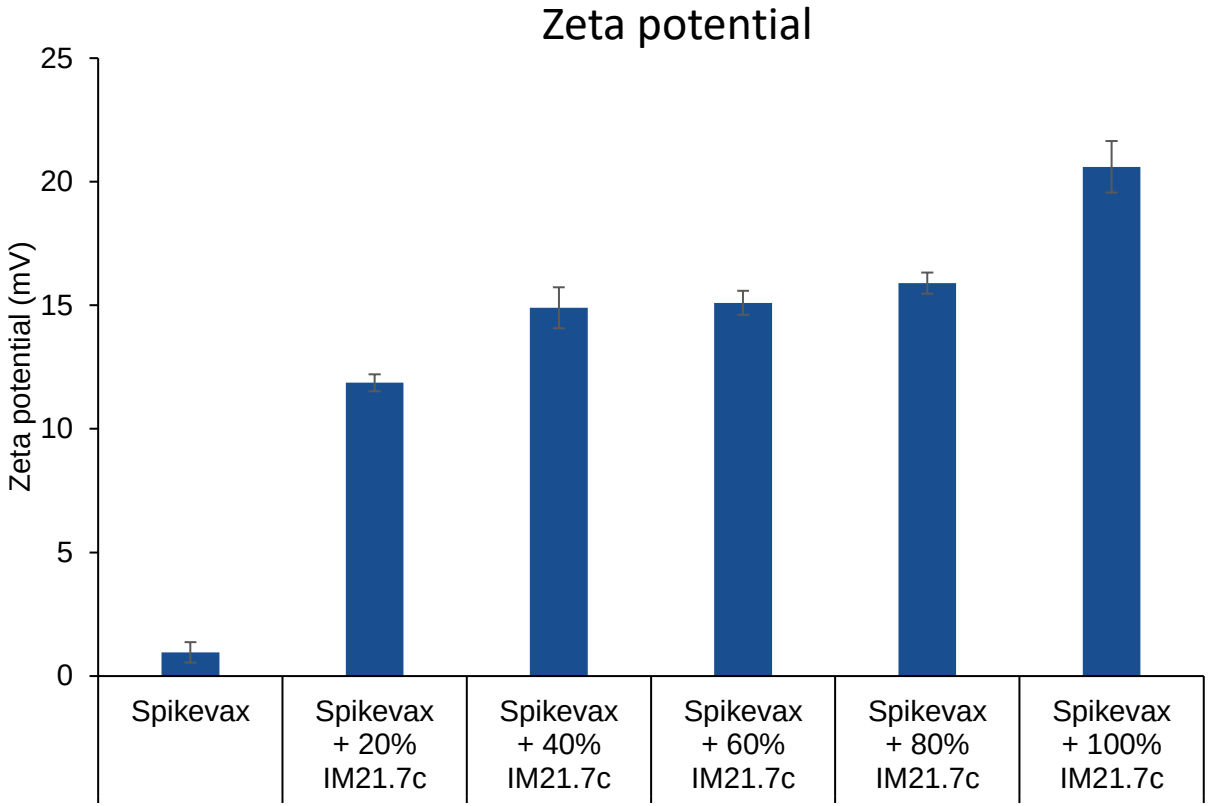


- LipidBrick® IM21.7c accelerates your project: *in vitro* and *in vivo* proof of concept have been successfully performed

Plug&Play formulation with LipidBrick® IM21.7c

Addition of IM21.7c in Spikevax's formulation increases zeta potential

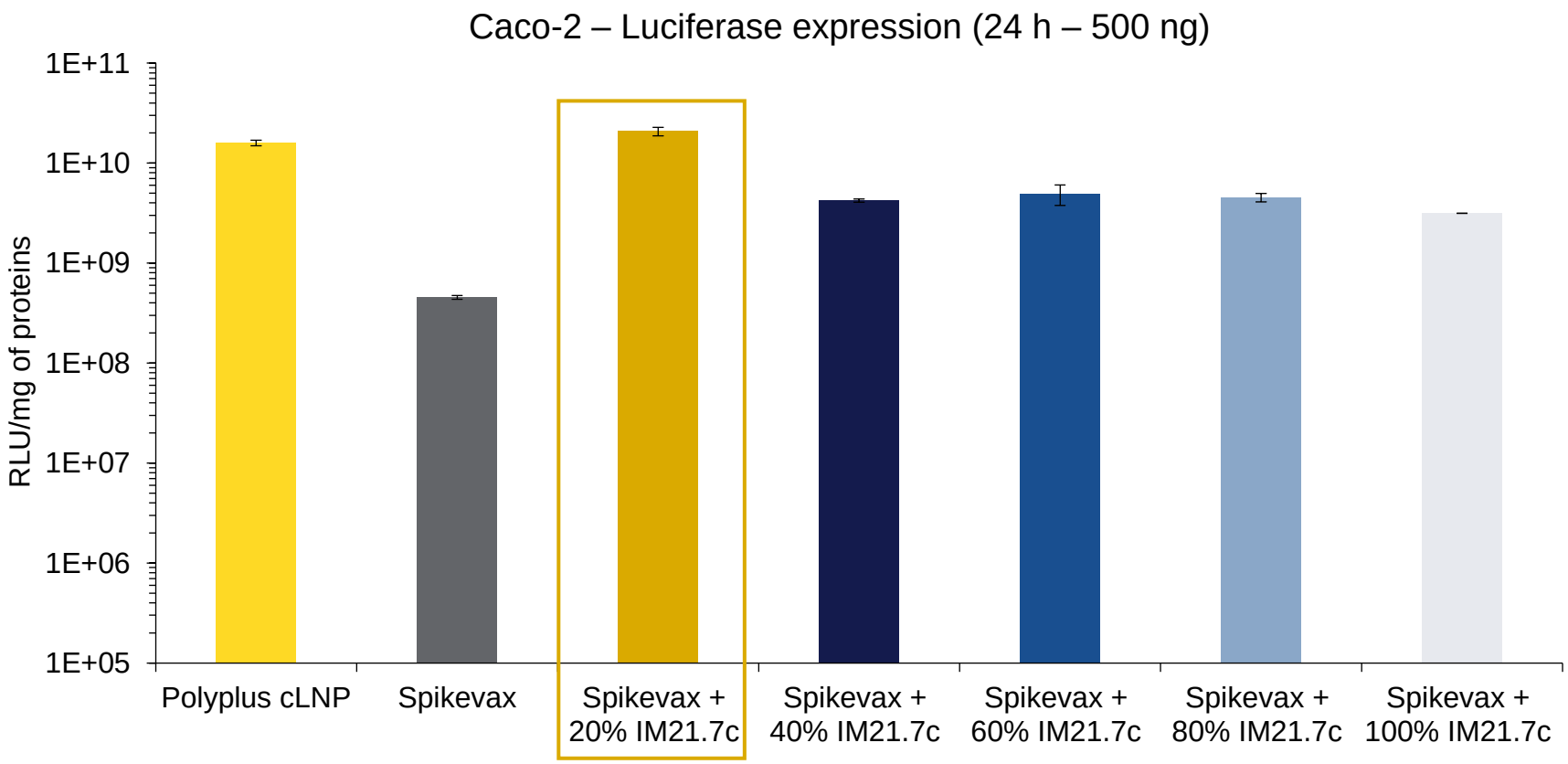




- Addition of 20% of IM21.7c in Comirnaty and Onpattro's formulations also increases LNP zeta potential

Addition of IM21.7c in Spikevax's formulation increases transfection efficiency *in vitro*

Lipid composition	Size	Zeta
Polyplus cLNP	63±2	+12
Spikevax	36±1	+1
+ 20% IM21.7c	39±2	+12
+ 40% IM21.7c	41±1	+15
+ 60% IM21.7c	41±2	+15
+ 80% IM21.7c	42±3	+16
+ 100% IM21.7c	33±1	+21

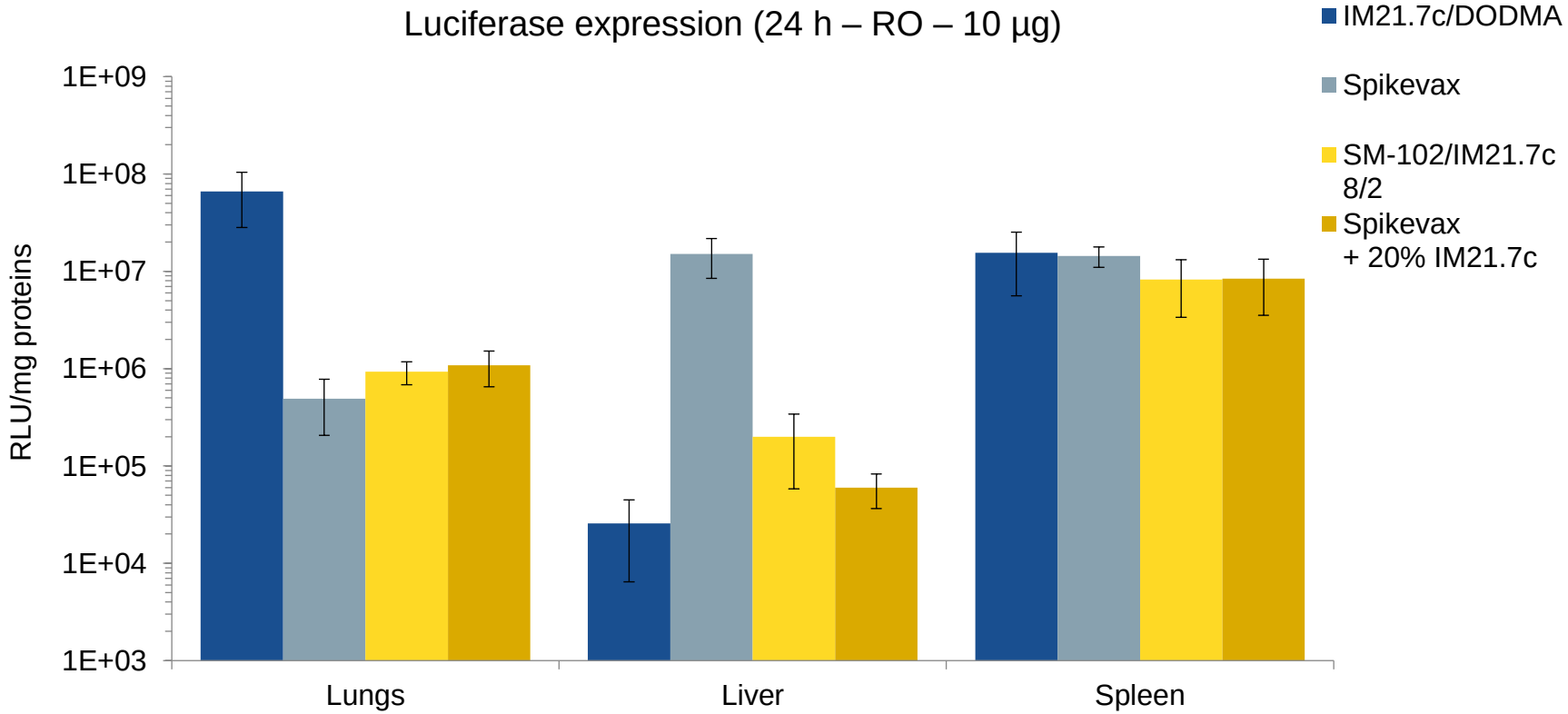


- Same increased transfection efficiency *in vitro* on HEK cells with addition of 20% of IM21.7c in Spikevax, Comirnaty and Onpattro's formulations

Less accumulation in the liver with 20% of IM21.7c in Spikevax's formulation

- Addition of 20 % of IM21.7c in Spikevax's formulation gives same expression in the spleen but less accumulation in the liver following IV injection

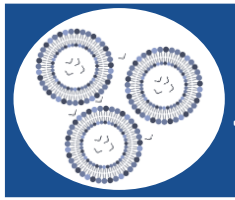
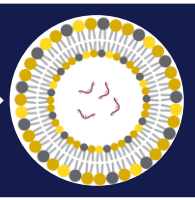
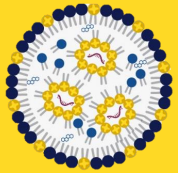
Cationic/ionizable lipid	Size (nm)	Zeta (mV)
IM21.7c/DODMA	57±4	+13
Spikevax	39±2	+1
SM-102/IM21.7c 8/2 in Spikevax	37±3	+11
Spikevax + 20% IM21.7c	37±1	+11



- LipidBrick® IM21.7c is efficient → Modulates LNP properties to adapt the biodistribution depending on the therapeutic purpose

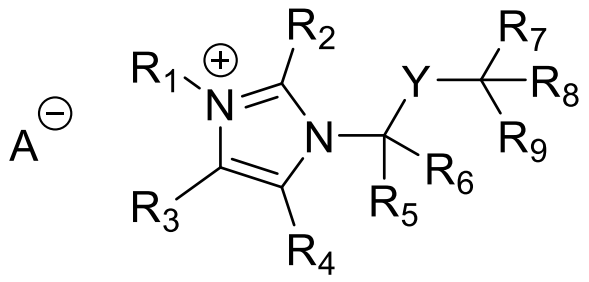
Polyplus' aim is to provide pathway from Research to Clinic trials

- Exact same cationic lipid shared by commercial products from Polyplus®

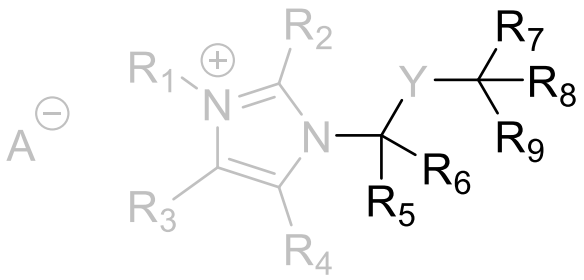
	In vitro POC	*In vivo* POC & preclinical study	Clinical trials & commercialization
Ready-to-use solution	 jetMESSENGER®	 *in vivo*-jetRNA®+	*in vivo*-jetRNA®+ GMP [Development upon request]
Lipid Nanoparticle formulation	 LipidBrick® IM21.7c (RUO)		LipidBrick® IM21.7c GMP [Under development]

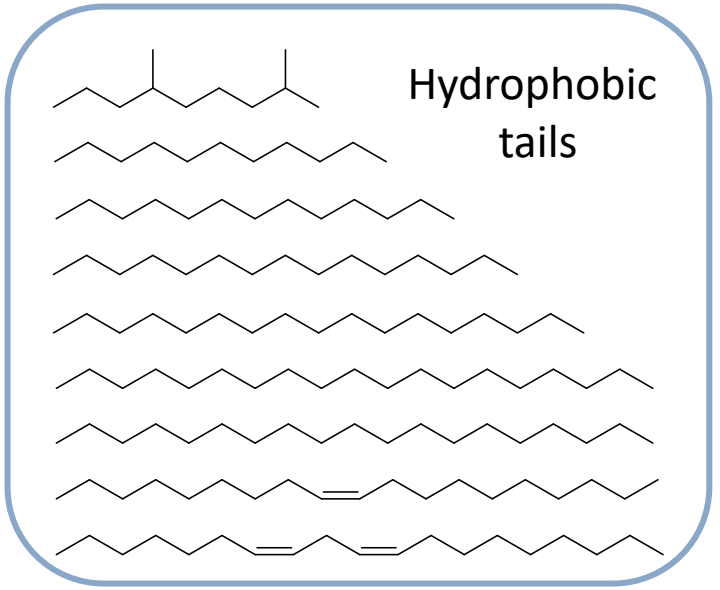
LipidBrick®: New Library

Design a library of innovative cationic lipids

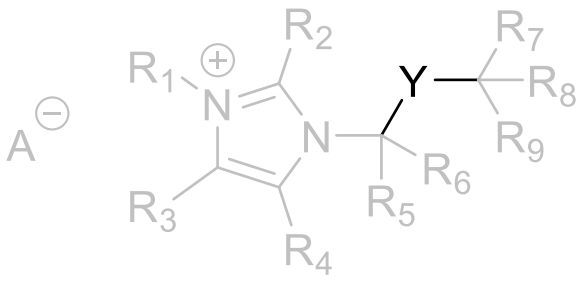


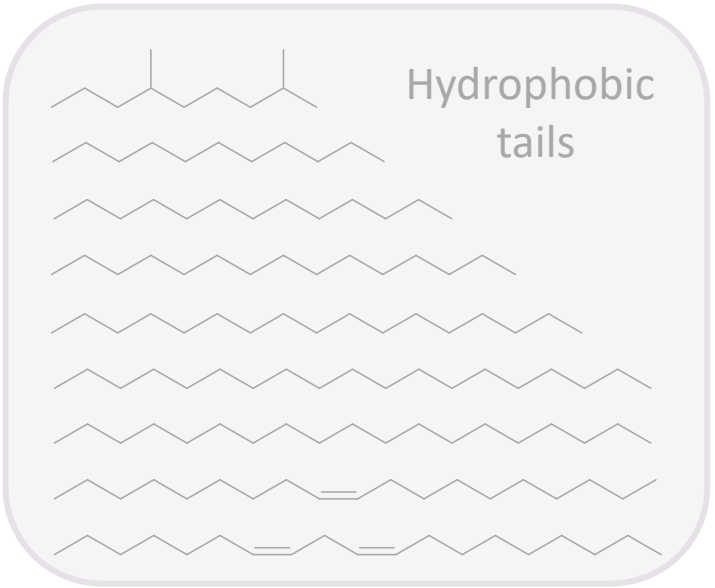
Design a library of innovative cationic lipids





Design a library of innovative cationic lipids





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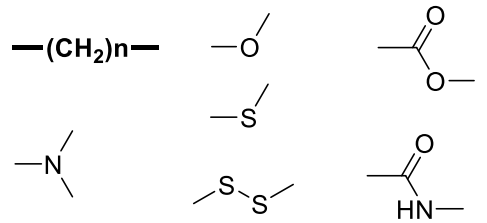
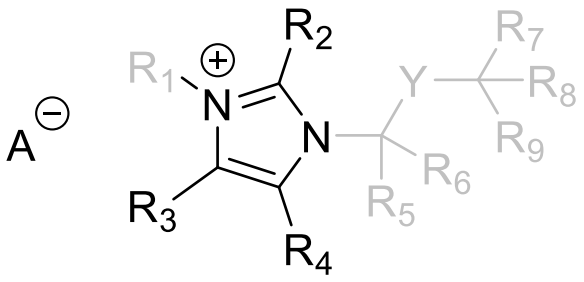
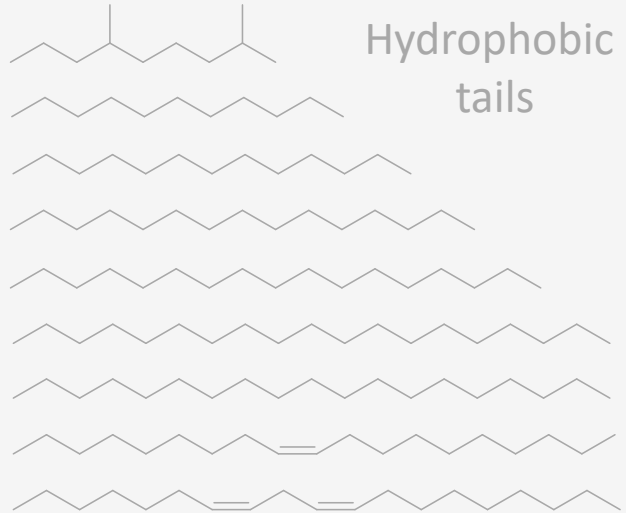


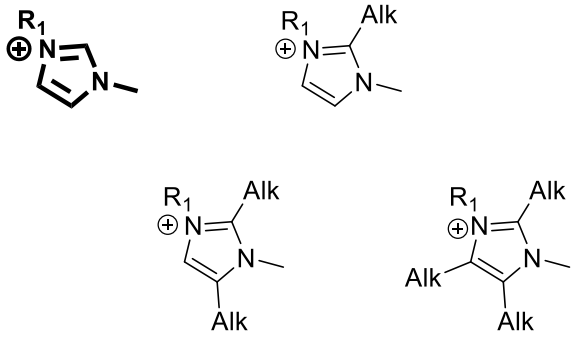
Design a library of innovative cationic lipids



Hydrophobic tails



Polar head



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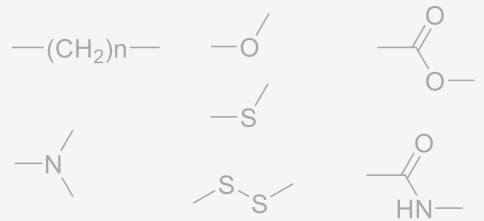
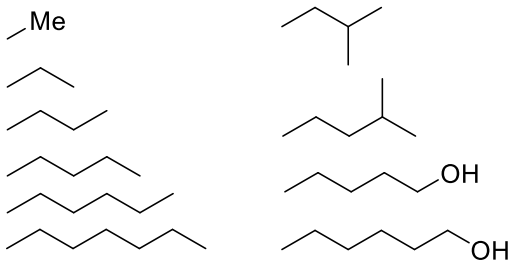
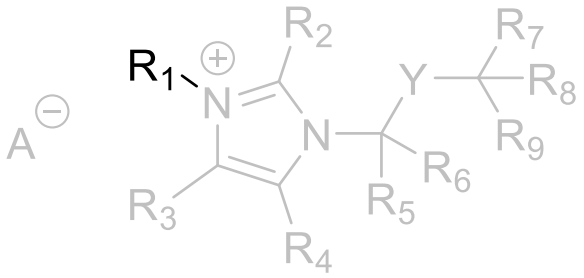


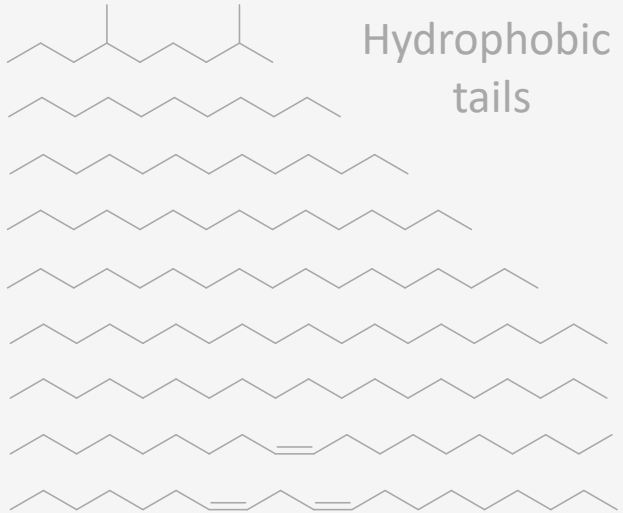
Design a library of innovative cationic lipids

Functional group

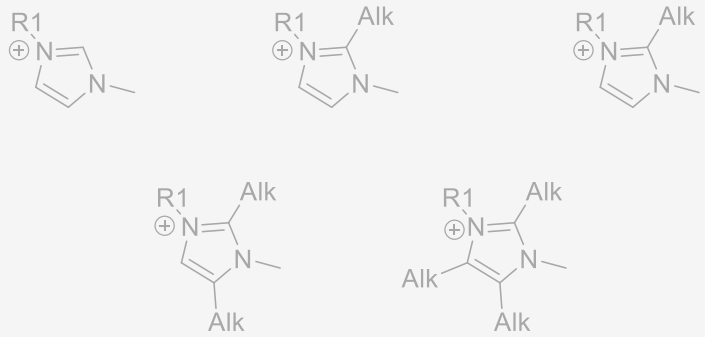




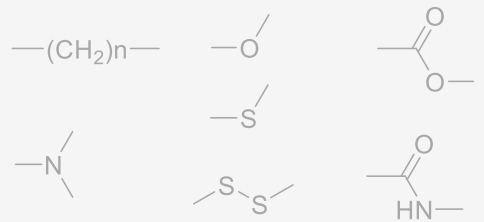
Hydrophobic tails



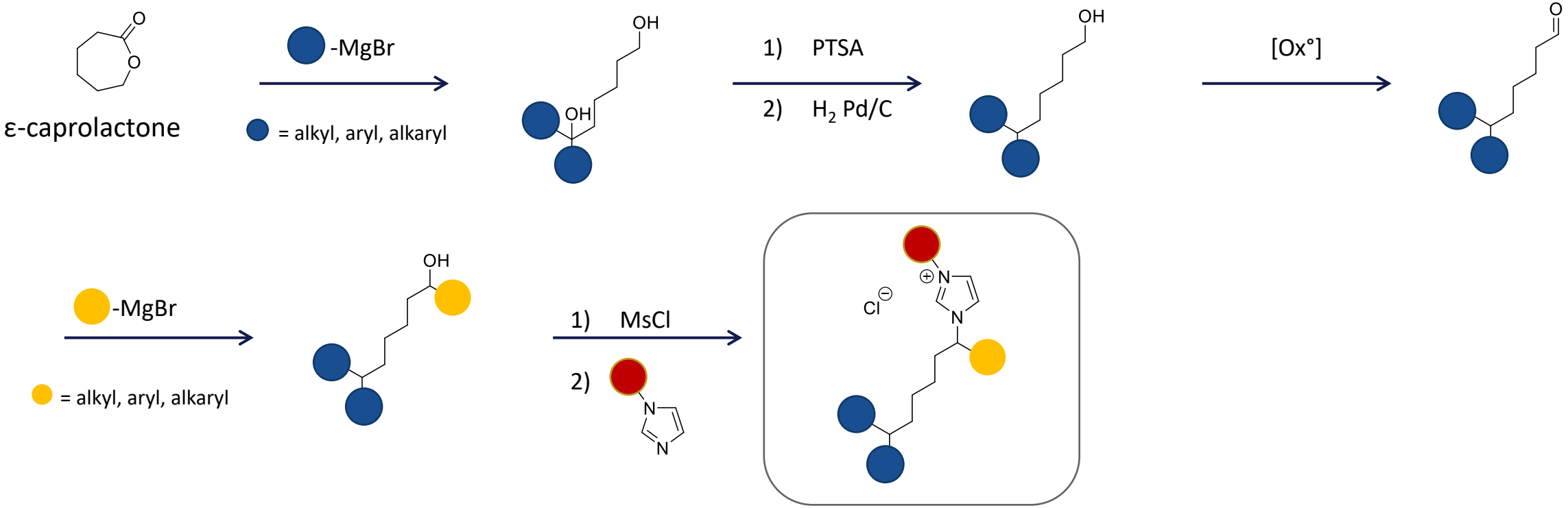
Polar head



Linker

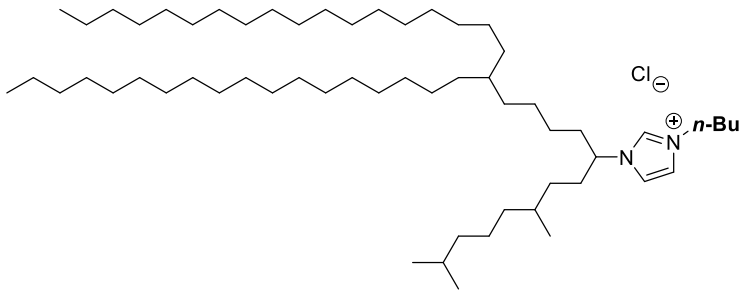


LipidBrick® library – Development of a synthetic platform



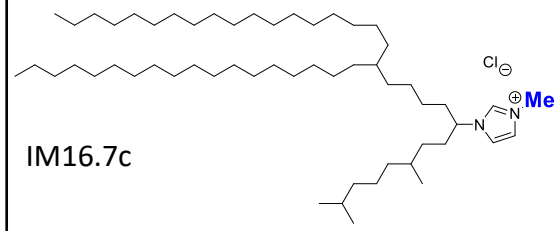
- 7-steps synthesis
- Scalable, tunable and GMPable

LipidBrick® library - Structures

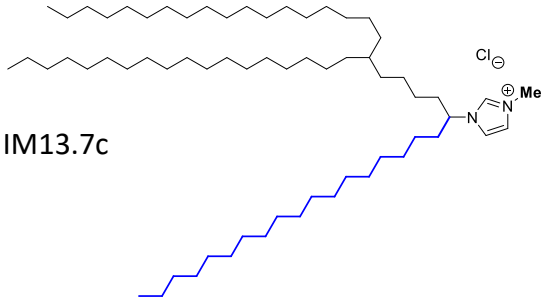


IM21.7c

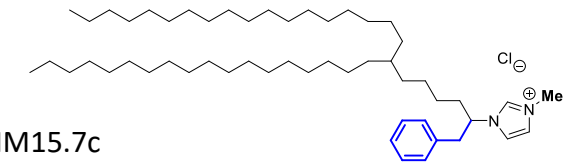
CAS n°: 2416939-42-7



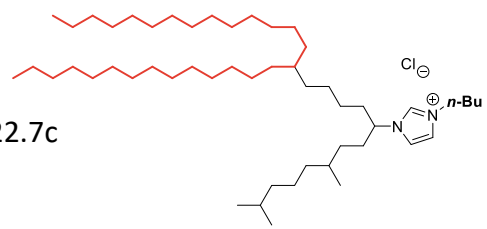
IM16.7c



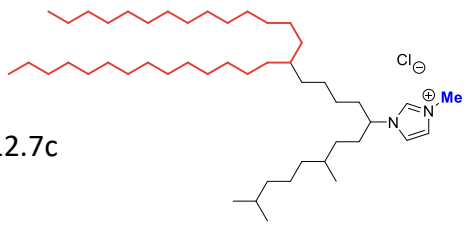
IM13.7c



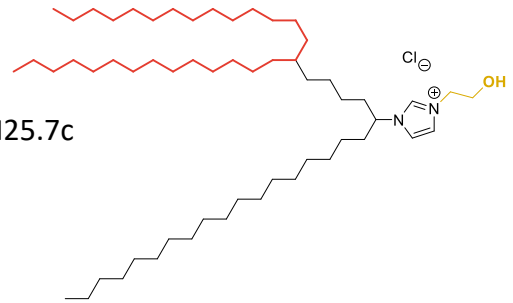
IM15.7c



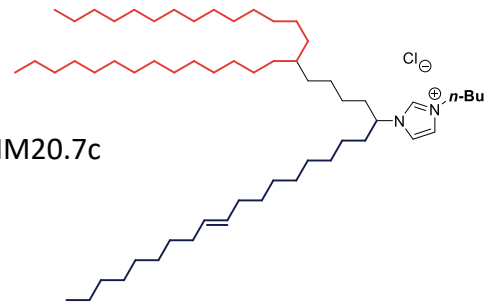
IM22.7c



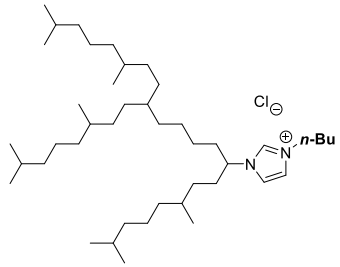
IM12.7c



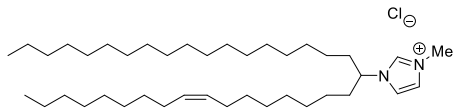
IM25.7c



IM20.7c



IM23.7c

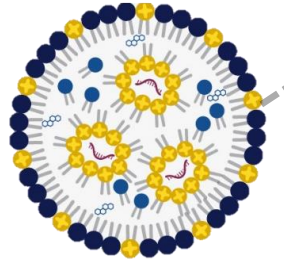


IM3.5c

LipidBrick® library – cLNP characterization

Cationic / Ionizable lipid (mM)		Helper Lipid (mM)		Cholesterol (mM)	DSG-PEG (mM)
IMXX.Xc/DODMA	4/3	DPyPE	1	1.85	0.15

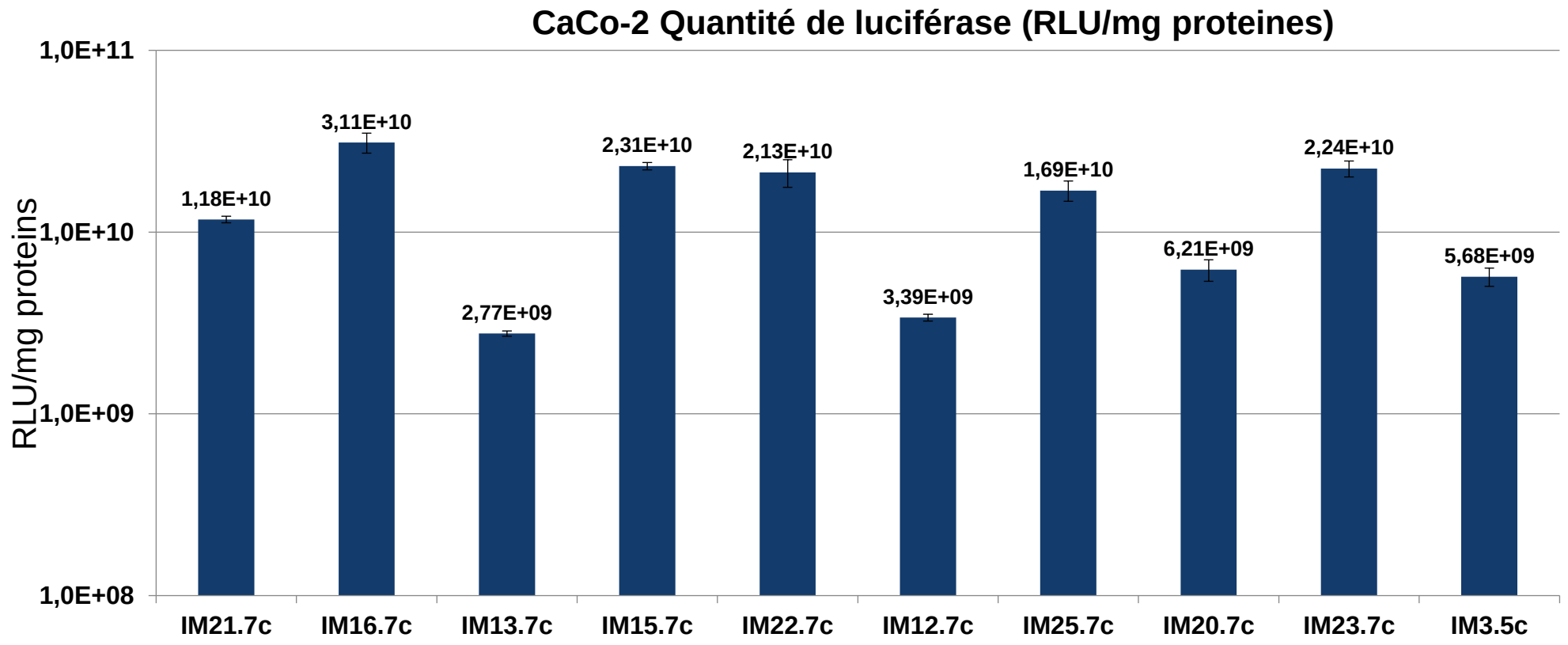
- Physical properties
  - Size
  - Zeta potential
  - PDI



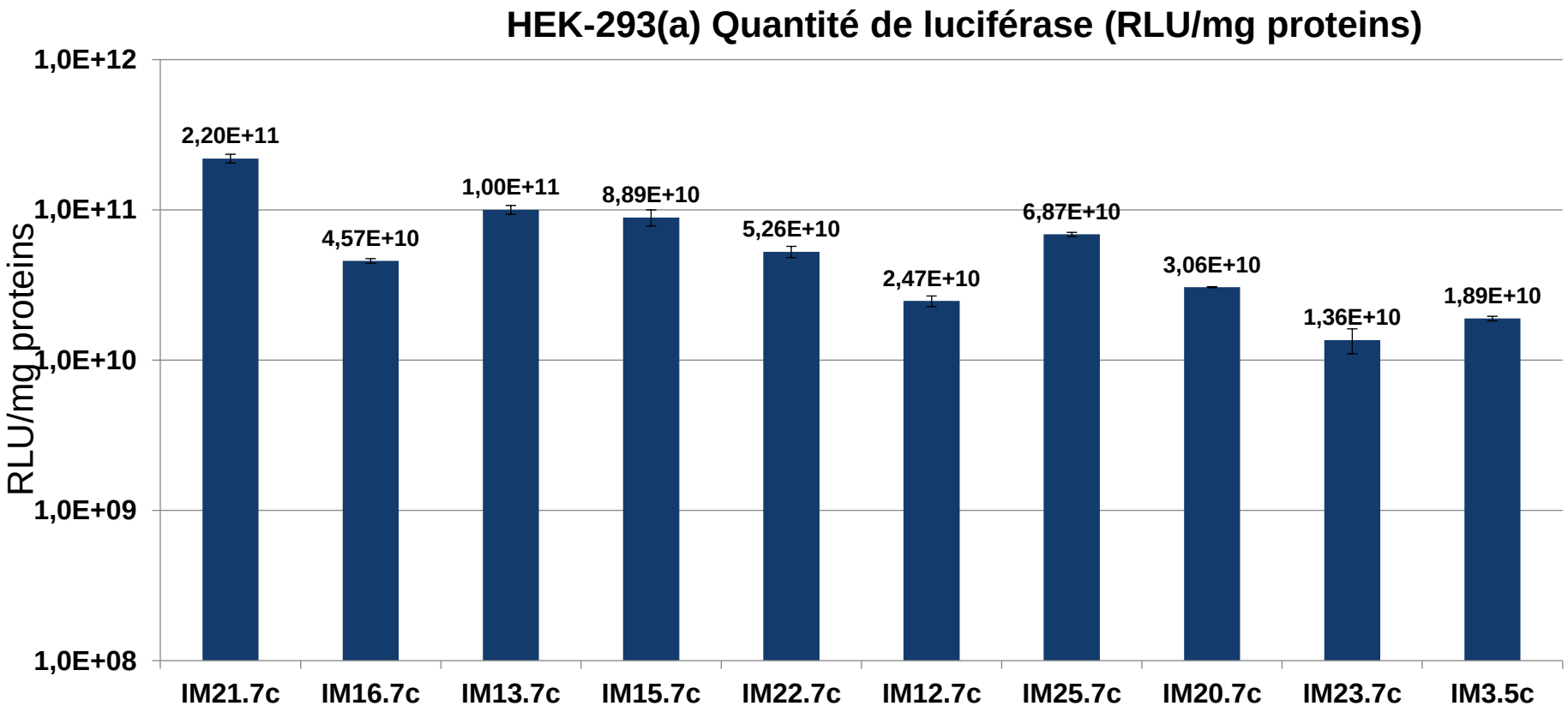
- Encapsulation efficiency

	IM21.7c	IM16.7c	IM13.7c	IM15.7c	IM22.7c	IM12.7c	IM25.7c	IM20.7c	IM23.7c	IM3.5c
Size (nm)	45±2	56±3	74±4	66±6	40±2	29±1	86±2	46±2	58±1	41±2
Zeta (mV)	+10	+13	+11	+9	+14	+12	+10	+12	+15	+16
PDI	0.158	0.132	0.090	0.113	0.140	0.120	0.053	0.130	0.066	0.104
EE (%)	99	99	99	99	99	99	99	99	99	99

LipidBrick® library - transfection efficiency on CaCo-2 cells



LipidBrick® library - transfection efficiency on HEK-293 cells



Conclusion

LipidBrick® IM21.7c advantages

Efficient: Modulate LNP properties to adapt the biodistribution depending on the therapeutic purpose
→ IM21.7c shows a great potential by enlarging the biodistribution

Accelerate your project: *in vitro* and *in vivo* proof of concept have been successfully performed
→ LNP characterization, stability study, Biodistribution and immune response have been studied

Secure: Use a unique lipid structure protected by an independent patent owned by Polyplus®
→ Independent IP covering the use of LipidBrick® with nucleic acid in LNP formulation

LipidBrick® IM21.7c – Commercially Available

- 2 pack sizes:

Part number	Designation
101000172	LipidBrick® IM21.7c 250 mg
101000173	LipidBrick® IM21.7c 1 g

Custom pack size possible if request >10 g

- State: Powder
- Storage temperature: -20°C
- Documentation: CoA and MSDS available

- **Direct orders** (via our local BM or at order@polyplus-transfection.com)
- **Distribution network**

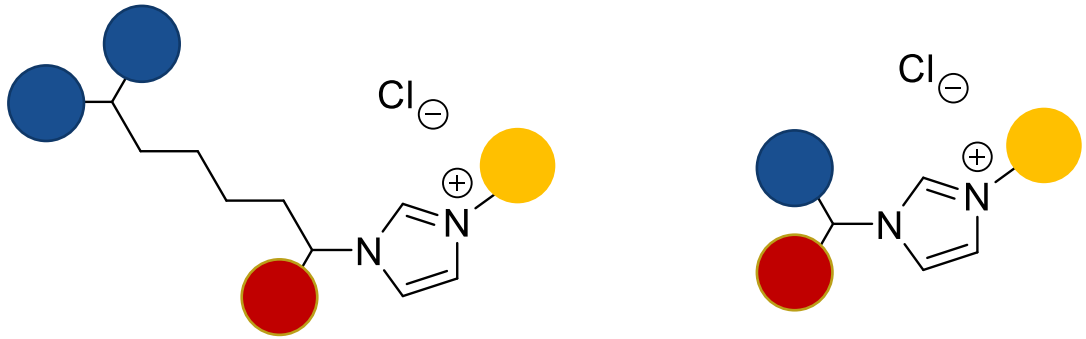
LipidBrick® library – Early Access

- 1 pack size composed of 10 proprietary lipids:

Part number	Designation
Coming soon	LipidBrick® range 10 x 100 mg

IM21.7c	IM16.7c	IM13.7c	IM15.7c	IM23.7c
IM22.7c	IM12.7c	IM20.7c	IM25.7c	IM3.5c

Custom pack size possible if request >10 g



- State: Powder or oil
- Storage temperature: -20°C

- Early access (at booth #211 or at support@polyplus-transfection.com)

LipidBrick® = Polyplus®' Proprietary Lipids

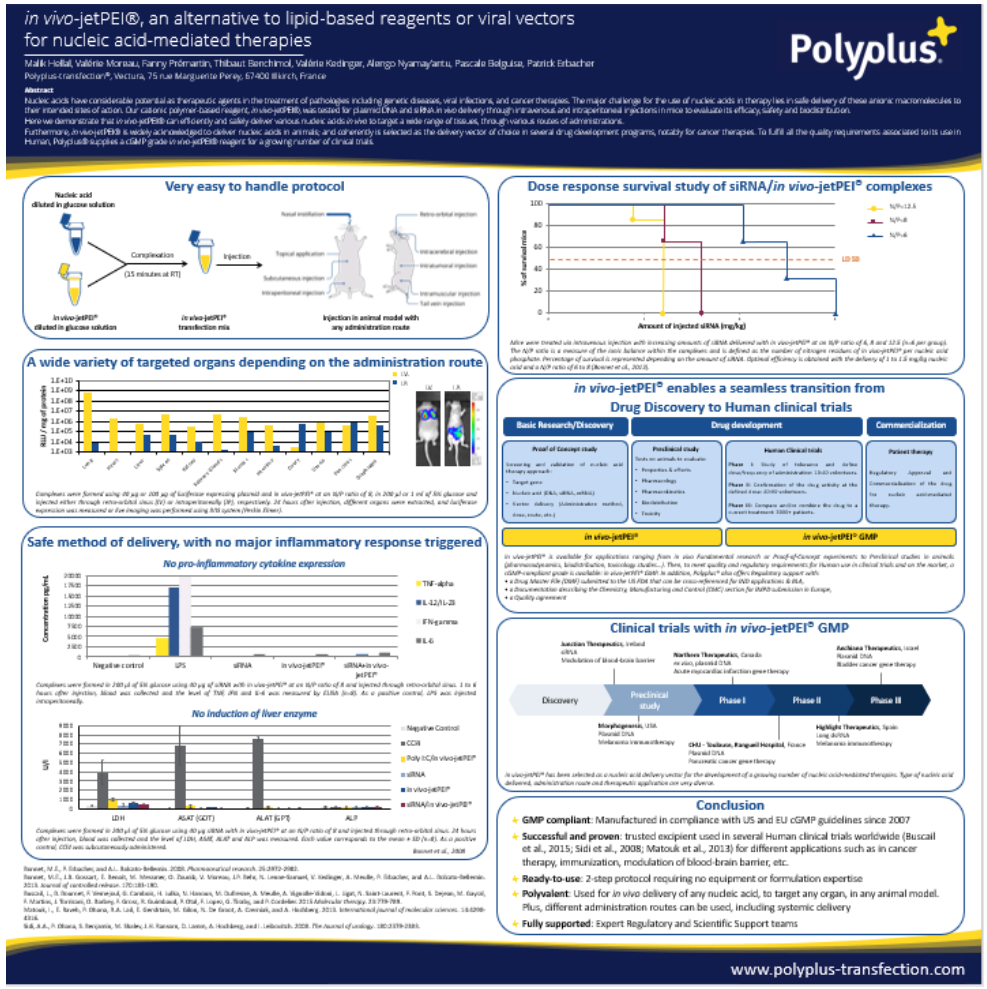
- Use a **unique lipid structure** protected by an **independent patent owned by Polyplus®**
  - Patent n° EP18306417 (Granted in EU – under examination in US & other countries)
  - Patent n° EP22306027.8 (Applied in July 2022)

- A Freedom To Operate (FTO) analysis has been performed by a qualified IP attorney
  - Based on US and EU patents, **LipidBrick® can be used as a component of LNP without infringing the intellectual property rights** of any other party

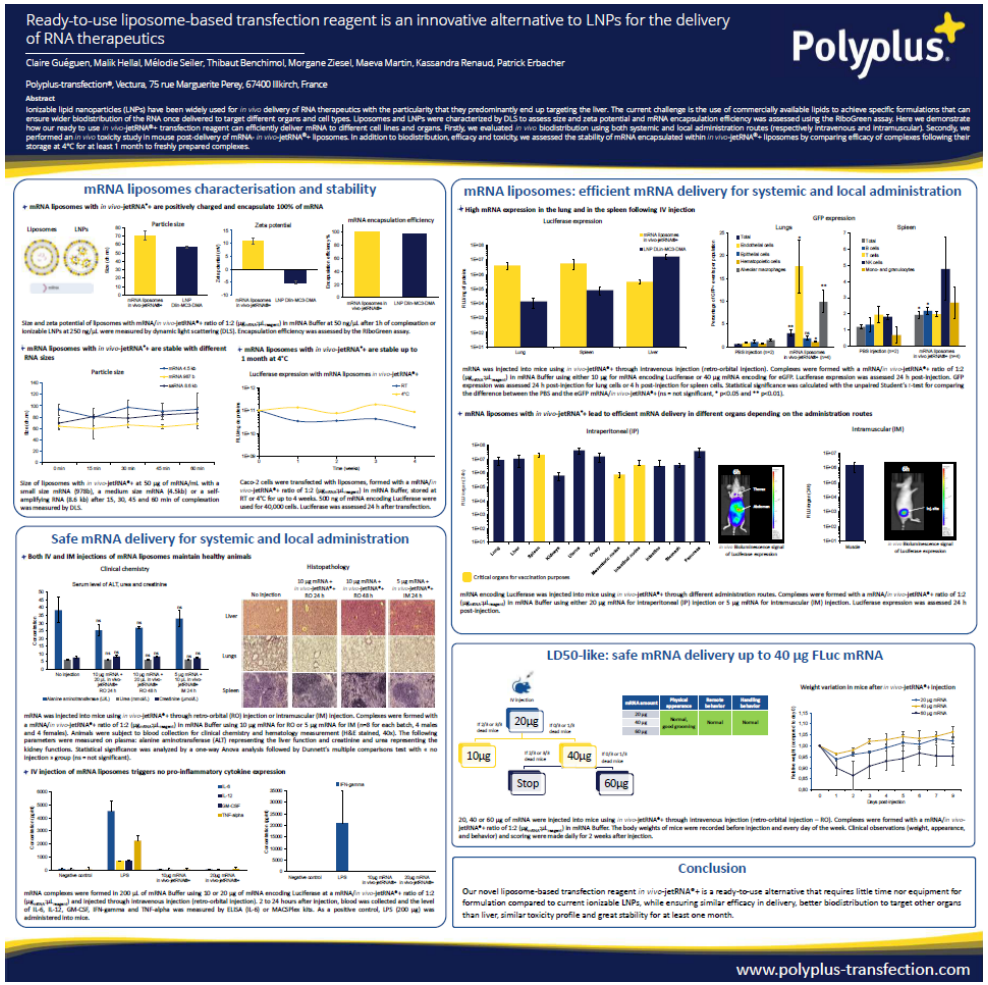
- Polyplus® offers a range of proprietary cationic lipids : **LipidBrick®**

Poster session dedicated to our off-the-shelf non-viral delivery solutions

- Poster #820 *in vivo*-jetPEI®



- Poster #821 *in vivo*-jetRNA®+



Polyplus®

Thank you!