Immunodelivery

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CONTROLLED RELEASE SOCIETY
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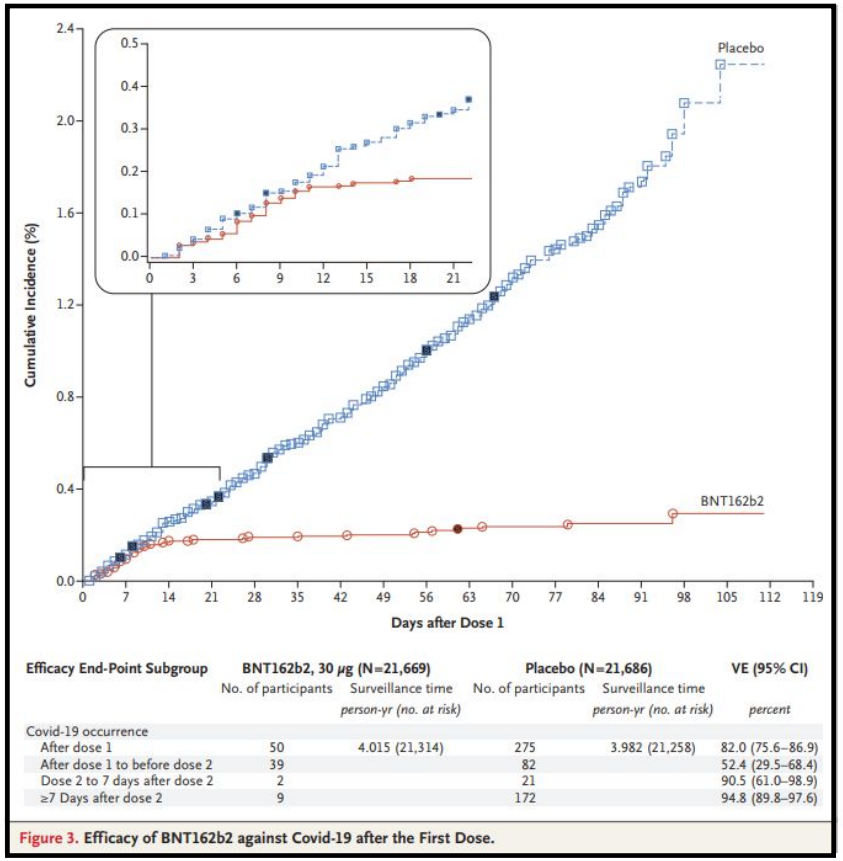
THE FUTURE OF DELIVERY SCIENCE

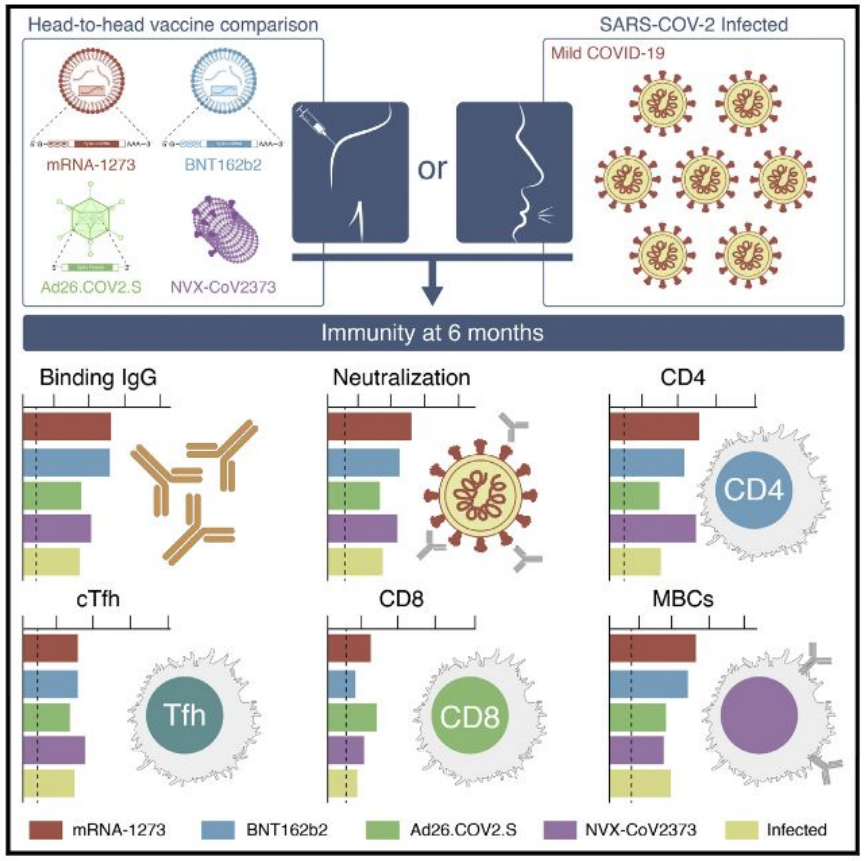
The dawn of mRNA Vaccines



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669) No. of participants	BNT162b2, 30 μg (N=21,669) Surveillance time person-yr (no. at risk)	Placebo (N=21,686) No. of participants	Placebo (N=21,686) Surveillance time person-yr (no. at risk)	VE (95% CI) percent
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

Figure 3. Efficacy of BNT162b2 against Covid-19 after the First Dose.

Polack et al. Lancet 2020 (Dec)



Zhang et al. Cell 2022

Verbeke R. et al. JCR 2021

Galsome approach to strengthen mRNA vaccines

Our path from proof of concept study (in 2019) to mRNA vaccines for clinical use

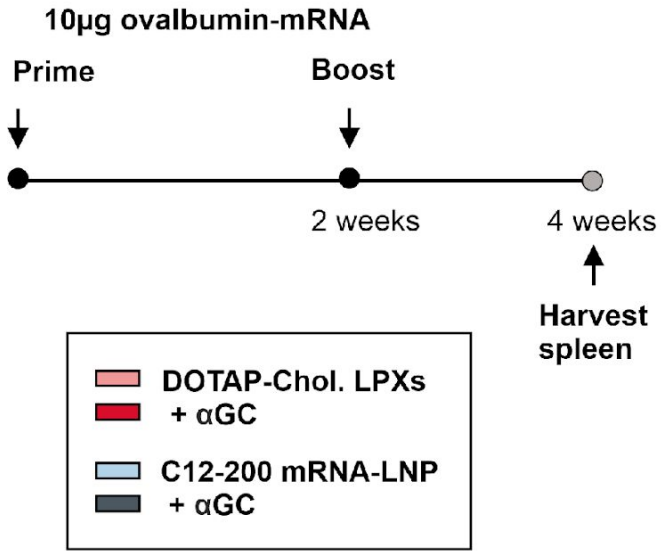
This includes:

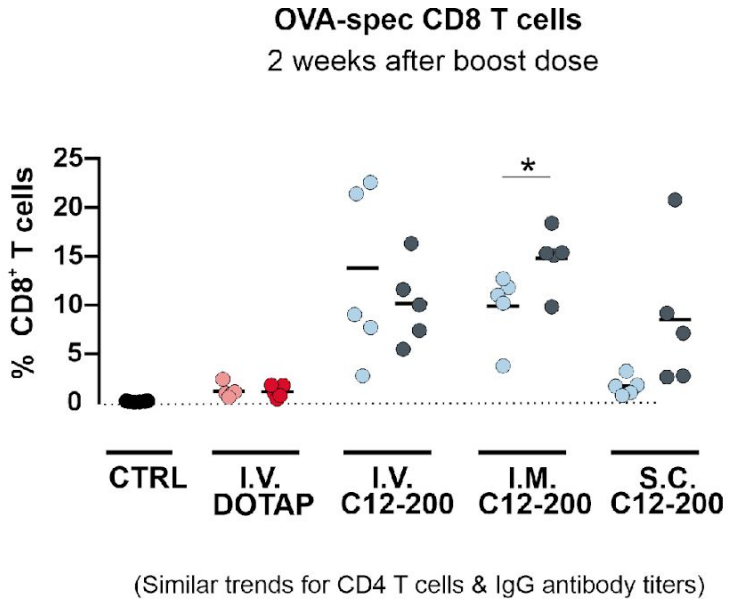
- Switch from cationic lipoplexes to ionizable LNP system
- Role of administration route and dose
- Optimization of LNP production and composition
- Optimization of mRNA sequence
- Type of ionizable lipid

Focused on the induction of robust cytotoxic (CD8) T cell immunity

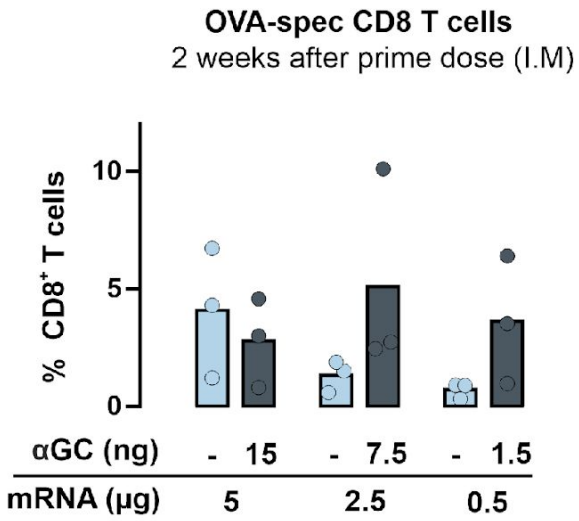
Vaccine applications in cancer – (intracellular) bacterial diseases

Role of lipid carrier & administration route





(Similar trends for CD4 T cells & IgG antibody titers)

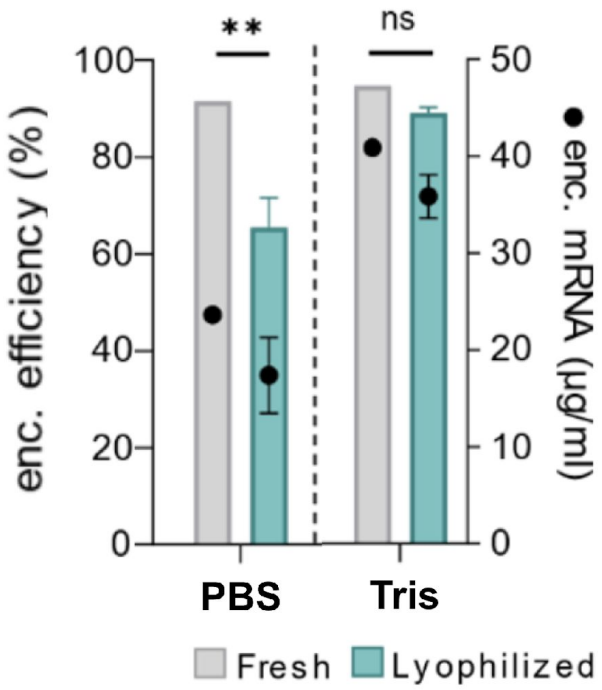


- C12-200 iLNPs outperform DOTAP LPXs
- IM route offered best levels of antibodies & T cells

- αGC empowers T cell responses
- αGC as adjuvant exerts dose-sparing effects

Optimizations along the way…

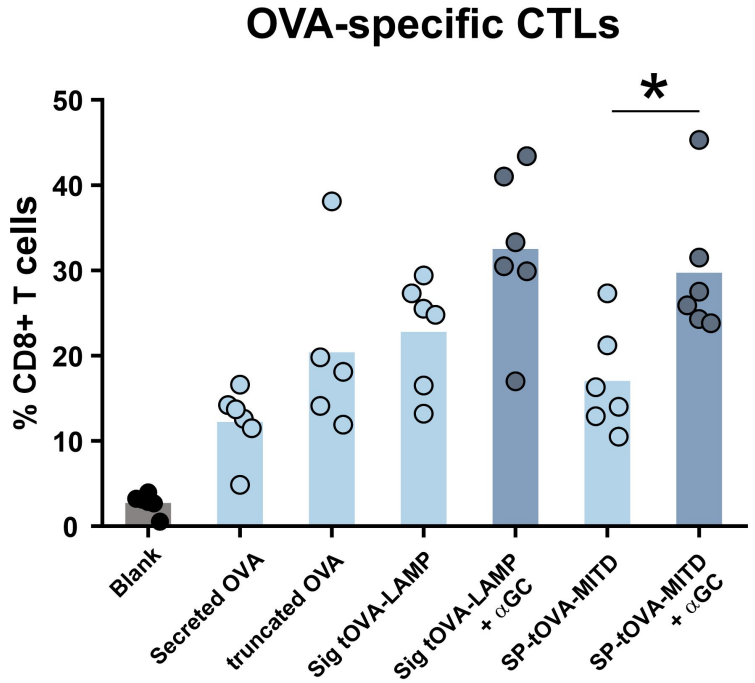
- **Enhancing the stability**



C12-200:mRNA 10 to 20 (~NP=6)
Dialysis buffer from PBS to Tris (+9% Sucrose)

De Meulewaeter, Sofie et al. JCR 2023

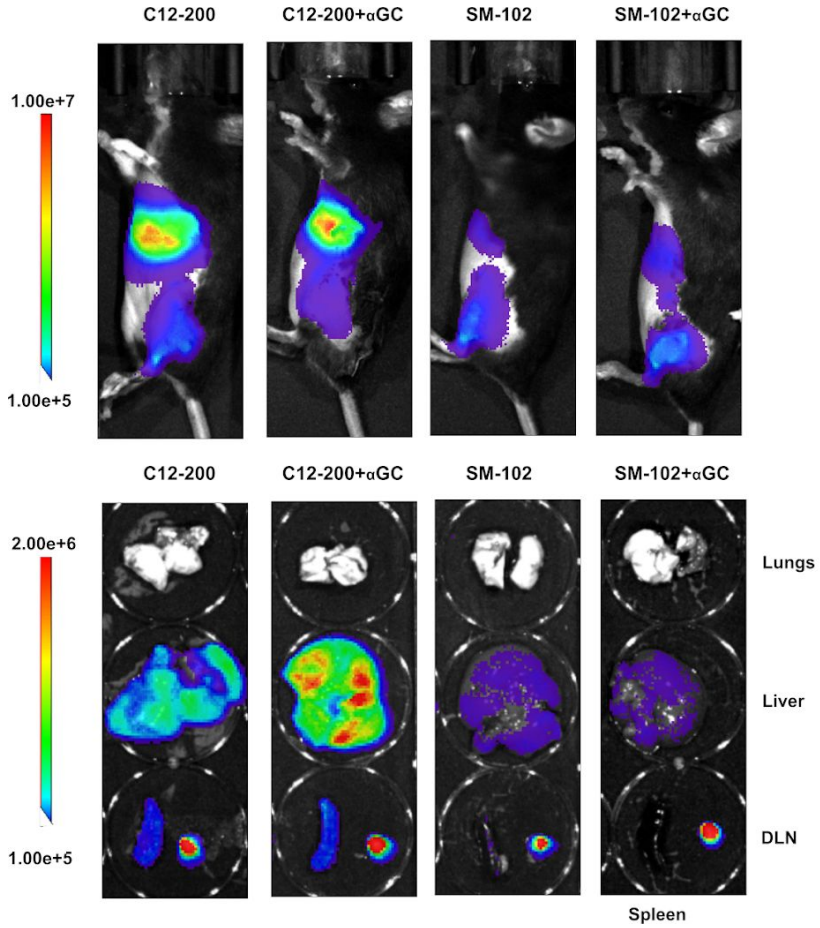
- **Inclusion of trafficking sequences***



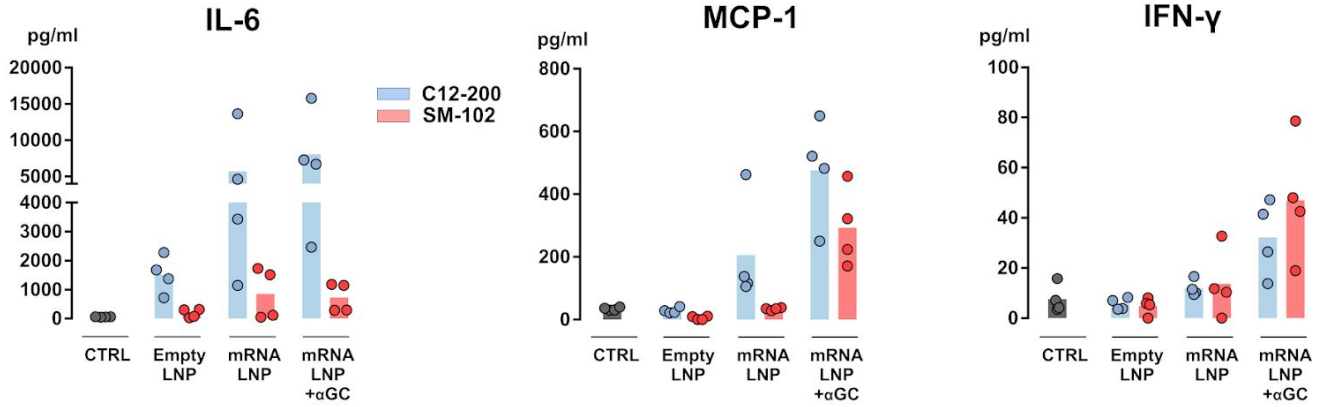
(2 weeks post-boost vaccine – 2µg dose)
Study by Ilke Aernout

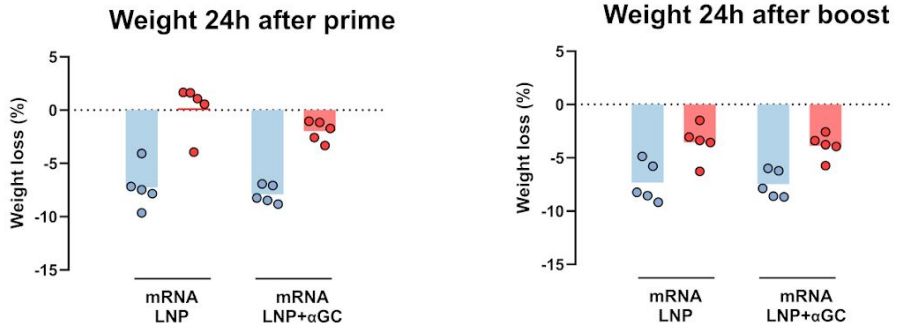
*Kreiter et al. J. Immunol 2008
Bonehill et al. J. Immunol 2004

Role of ionizable lipid as immune-activator



(6h post-injection of 2.5µg luciferase mRNA)

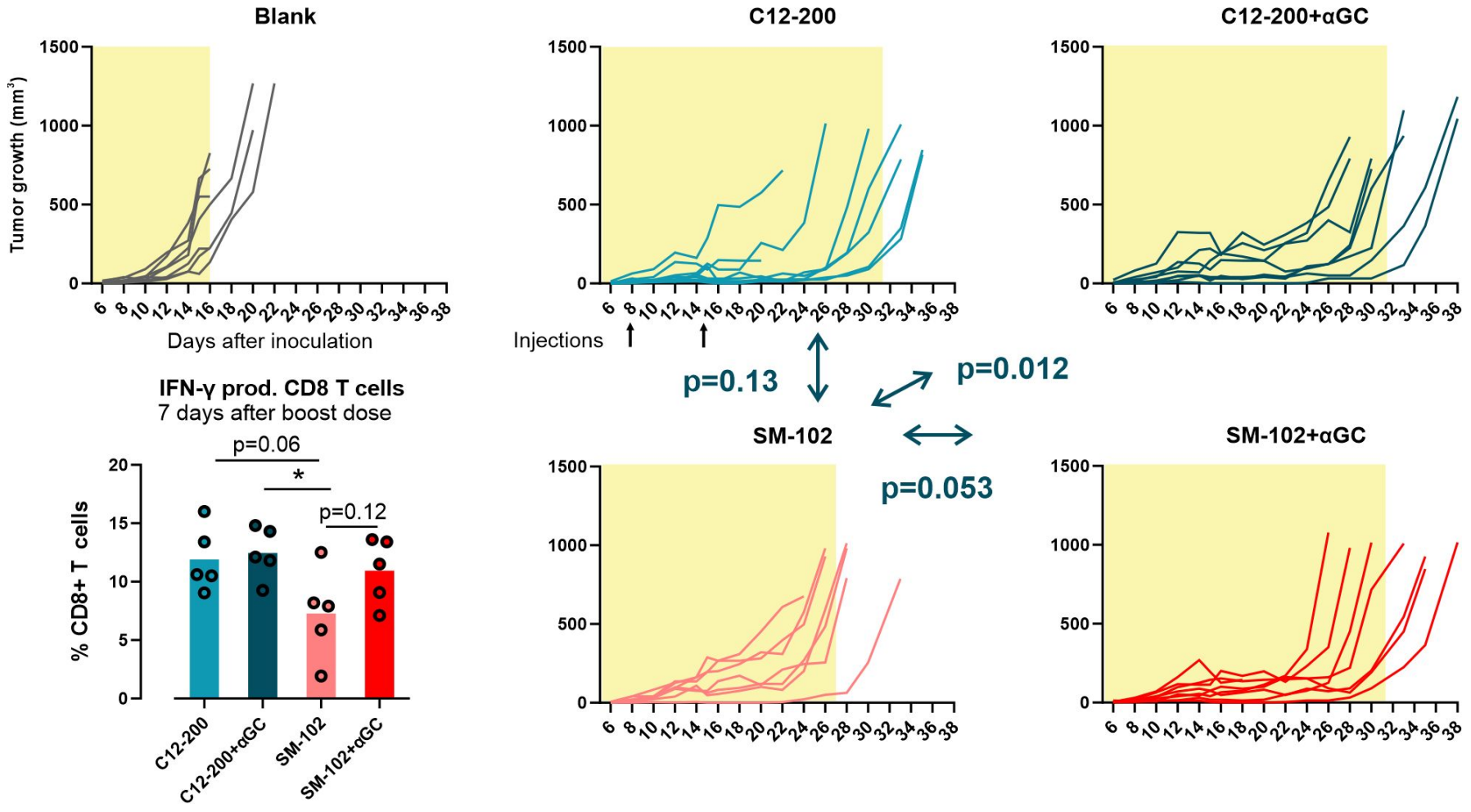




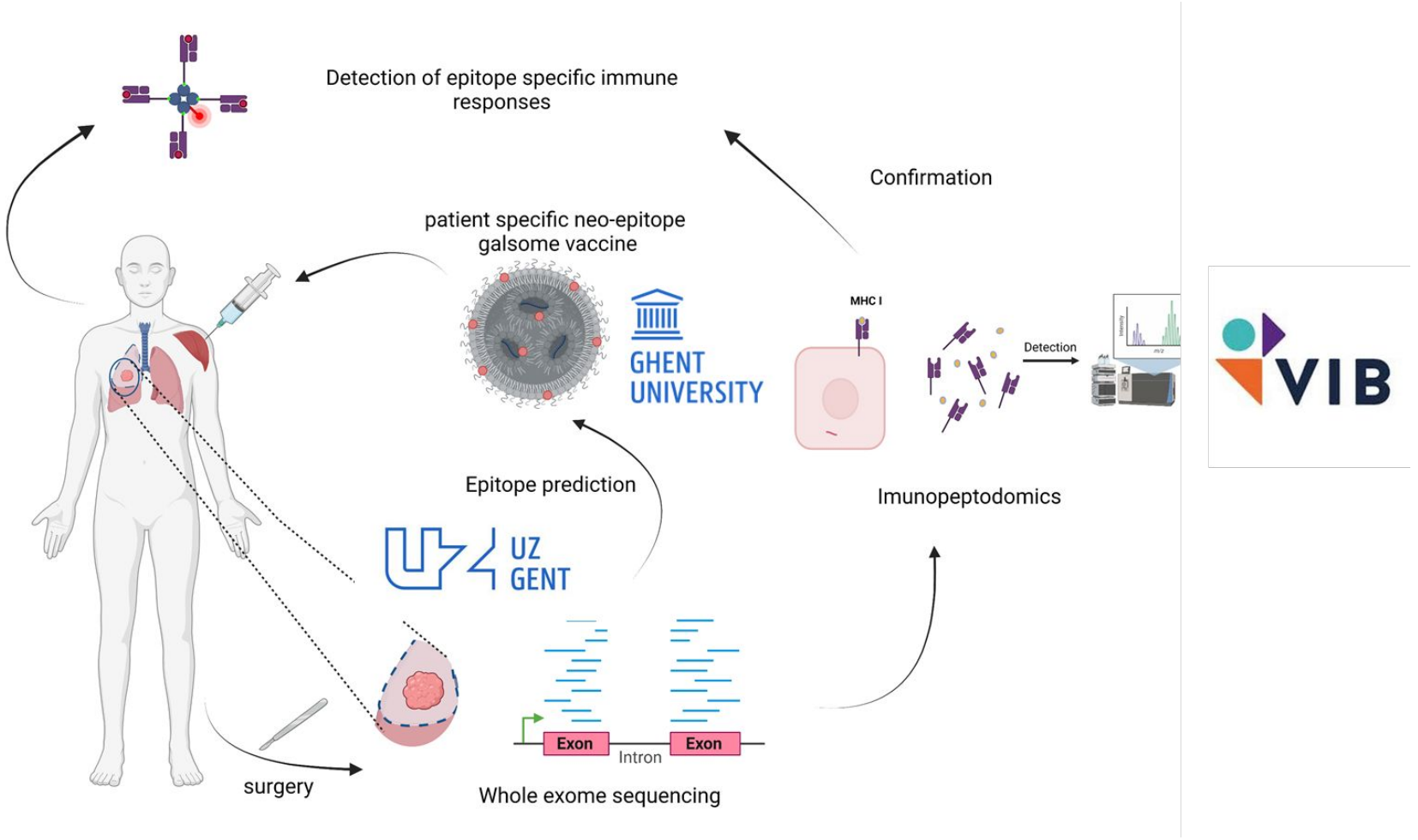
- **C12-200 is more reactogenic than SM-102 (Moderna)**
- **C12-200 is slightly better in transfection than SM-102**

Alameh MG et al. Immunity 2021
Verbeke R. et al. Immunity 2022

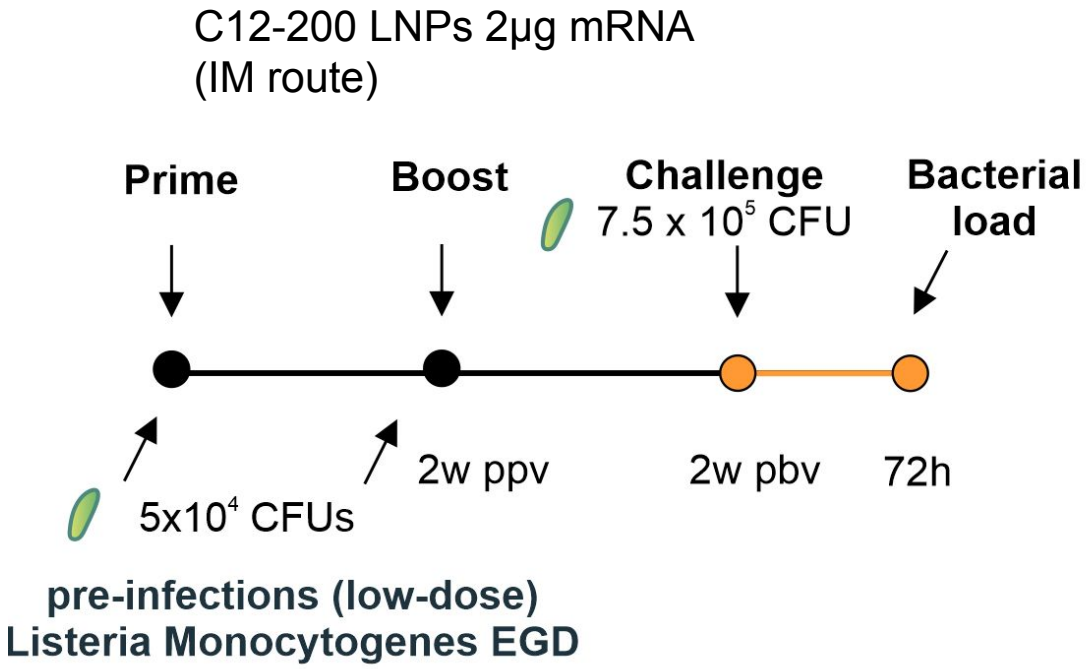
Therapeutic effects in B16 melanoma model

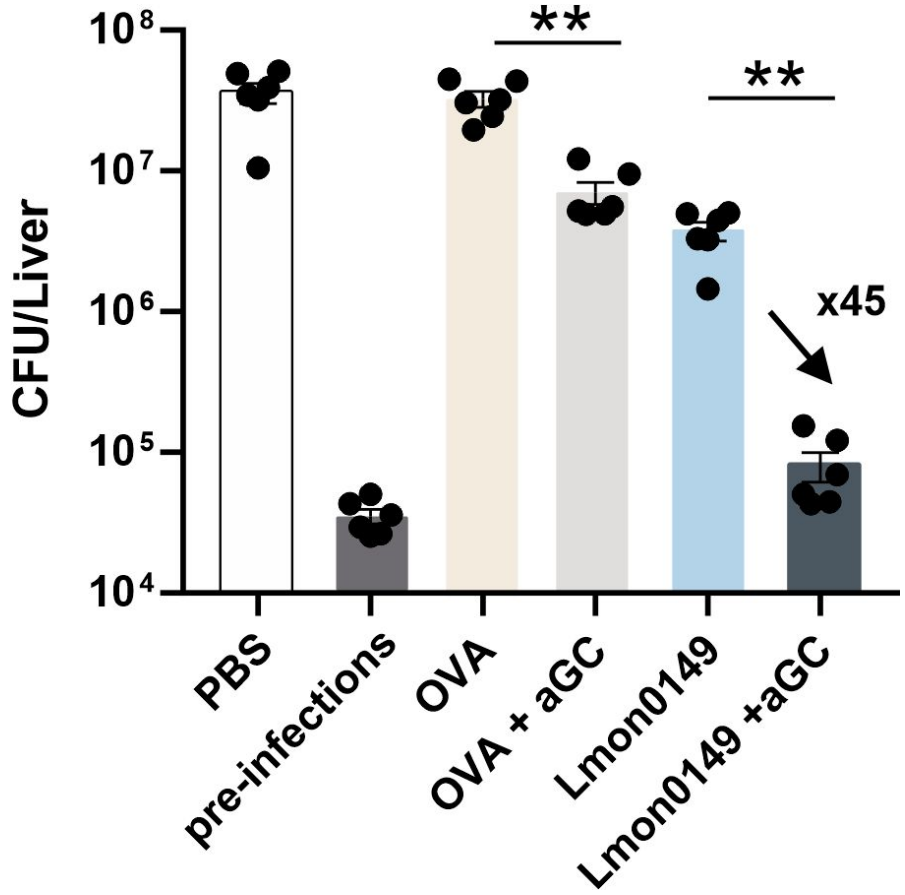


Neo-Galsomes for Non-Small Cell Lung Cancer (Phase 1 2024)



Proof of concept of Galsome potential for intracellular bacteria





- **Synergistic protective effects of αGalCer & mRNA-LNP vaccine**

Mayer R. et al. Nat. Commun. 2022
EP22170792.0

Baxerna project - development of bacterial mRNA vaccines
(EU funded – 9 million)

Institut Pasteur

Demangel
Mycobacteria
Tuberculosis & Buruli Ulcer

Van der Henst & Muraille
Acinetobacter baumannii
AMR

VIB ULB

VIB Impens
MS Proteomics
Immunopeptidomics

VIB Martens
MS Bio-IT
Immunopeptidomics

Antigen discovery

mRNA vaccine development

Breckpot
mRNA design
immunotherapy

De Smedt
mRNA vaccines
adjuvantia

Netea
trained immunity
innate immunity

Loré
vaccine mechanisms
In vivo models

VUB VRIJE UNIVERSITEIT BRUSSEL

GHENT UNIVERSITY

Radboud umc

Karolinska Institutet

Vandekerckhove
GMP mRNA-LNP
production

Vermaelen
Pneumology
Tuberculosis

Leroux-Roels
Center for Vaccinology
Clinical trials

U4 GENT GMP unit Cell Therapy

CEVAC

clinical trial

VFI VACCINE FORMULATION INSTITUTE — Analytical Methods

RheaVita — Vaccine lyophilization & storage

Quantoom Biosciences — Cheaper en local Vaccine production

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