

# CureVac's tailored LNP platforms to deliver mRNA for prophylactic and therapeutic applications

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## Prophylactic Vaccines





- Strong **humoral responses**, induction of **antibodies**
- High **tolerability**, minimize side effects and reactogenicity
- High **stability** for easy large-scale delivery and **long-term storage**

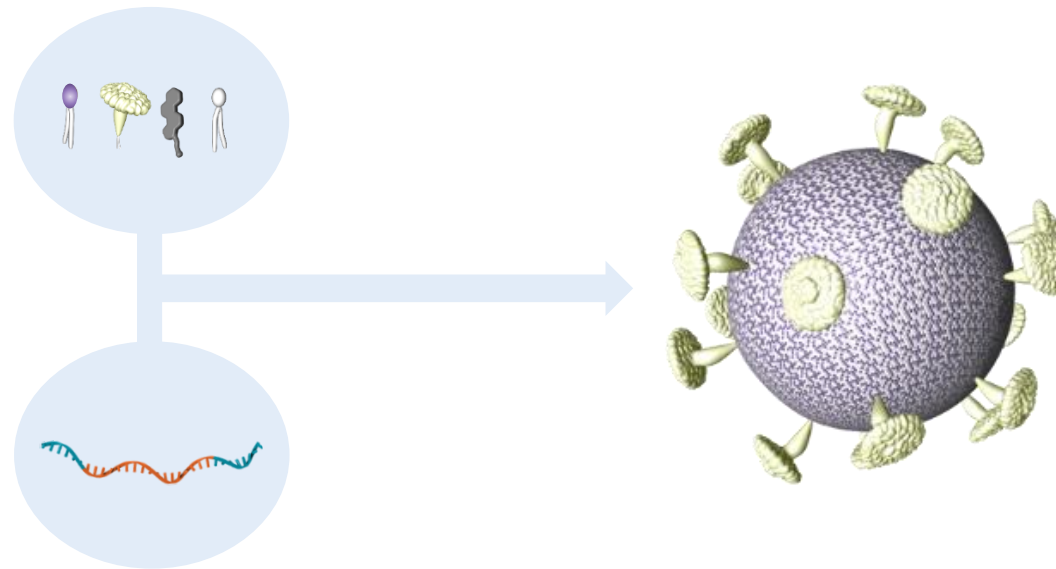
## Cancer Vaccines

- Strong **cellular responses**, induction of **tumor-killing T cells**
- Strong systemic activation of **signaling pathways** to maximize immune response
- Maximized **mRNA uptake** into immune cells for highest **efficacy**

**Aim: Tailor LNP design for improved activity of Prophylactic or Cancer mRNA vaccines.**

# CureVac's proprietary mRNA-LNP delivery platform

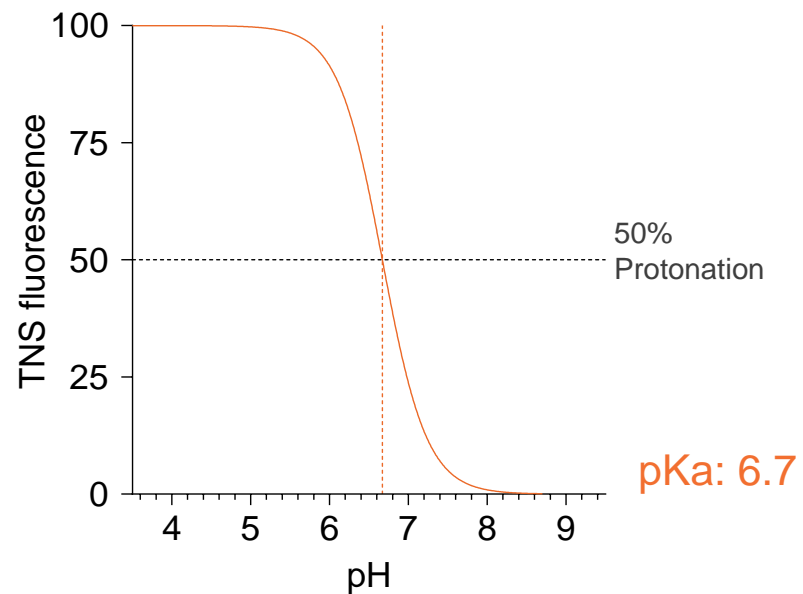
- **Proprietary ionizable lipid** 
- **Novel helper lipids** 
- **Proprietary PEG alternatives** 
- **Cholesterol** 



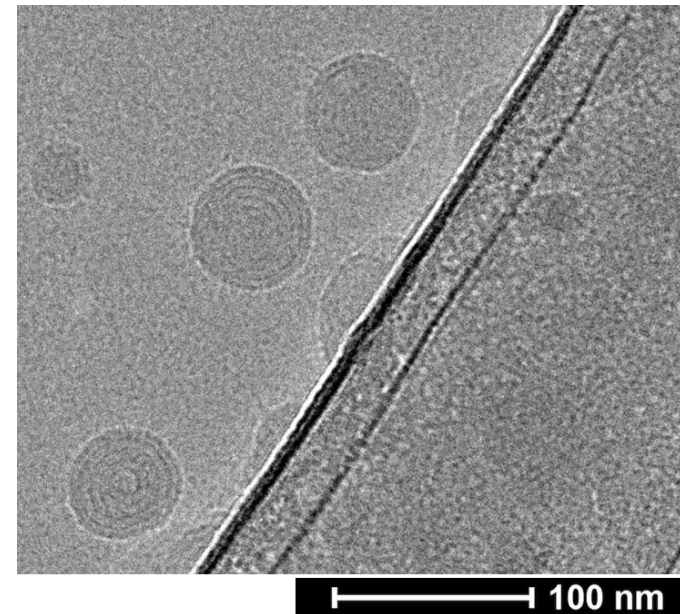
# CV-LNP physico-chemical properties

- Small size **below 80 nm**
- High pKa of  $\sim 6.7$
- Uniform structure without significant bleb formation

### TNS Assay

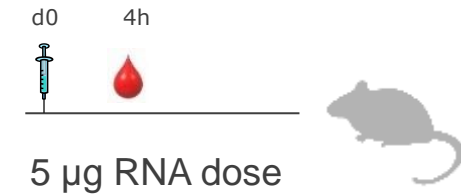
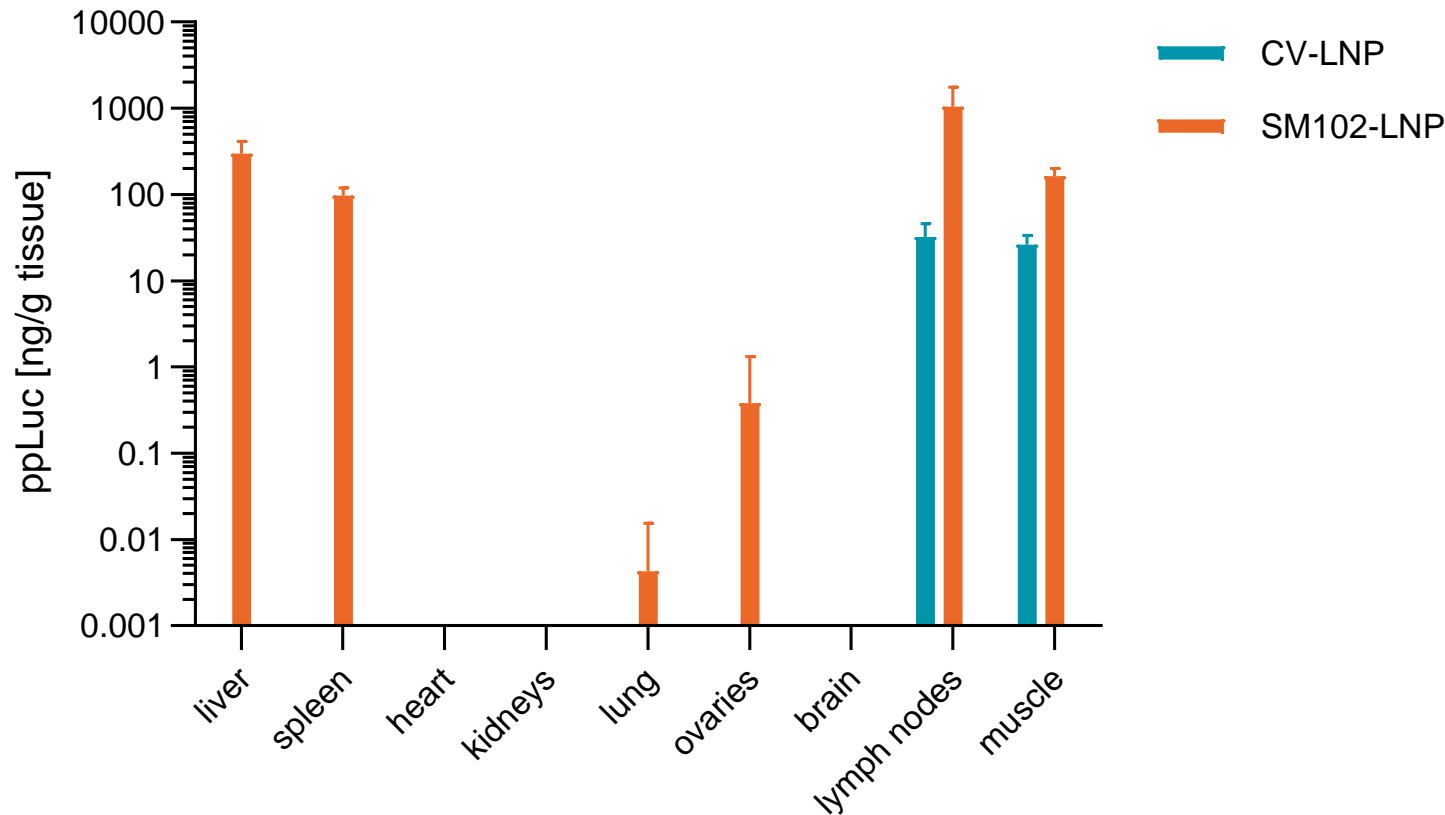


### Cryo-TEM



# CV-LNP is optimized for a local biodistribution through rational design

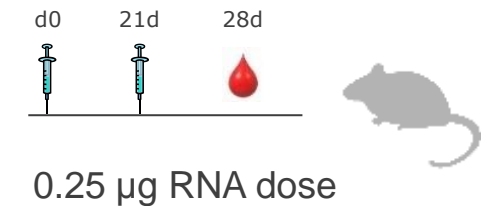
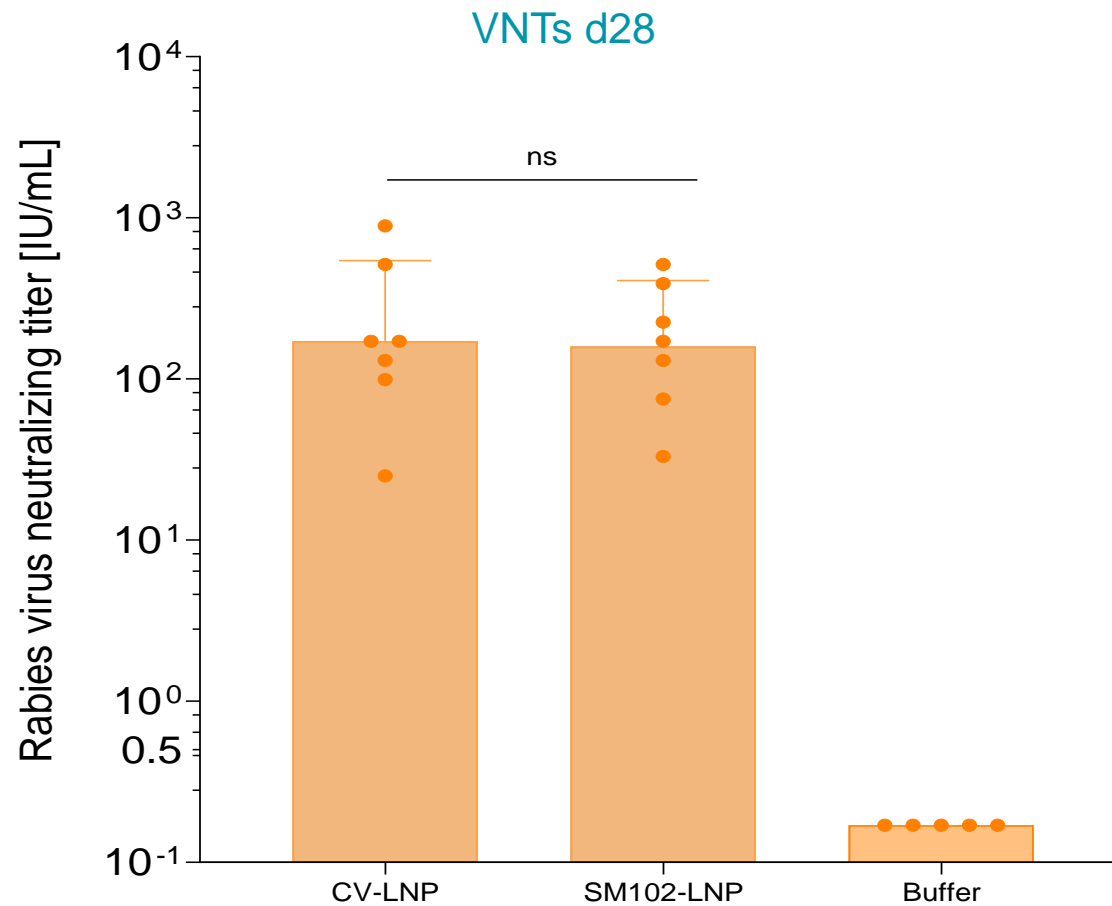
- Biodistribution of CV-LNP encapsulating luciferase RNA upon i.m. injection of 5  $\mu$ g
- CV-LNP delivers RNA exclusively to muscle and lymph nodes while avoiding expression in distal organs such as liver and spleen



Formulation	Muscle/Liver ratio (4h)
CV-LNP	1693
SM102-LNP	0.55

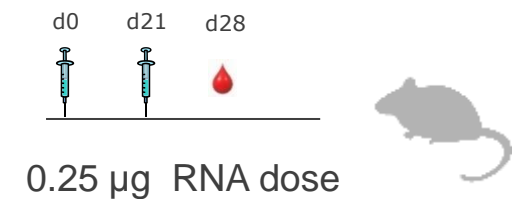
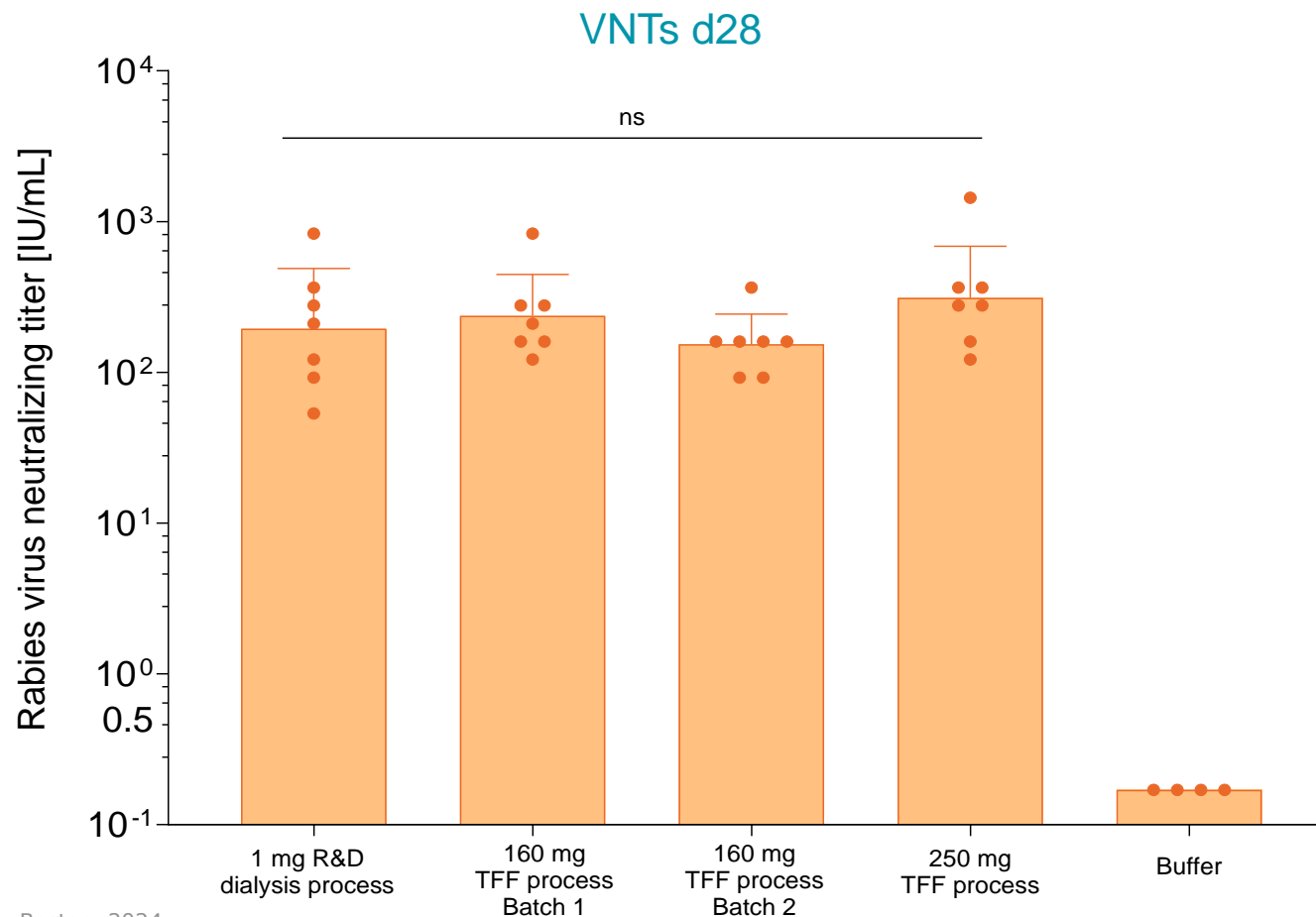
# CV-LNPs enable a potent immune response

- CV-LNP encapsulating modified RAVG-RNA enable significant immune response in Rabies vaccination mouse study
- Rabies virus neutralizing titers were comparable to state-of-the-art SM102-LNP used in Spikevax



# CV-LNPs are seamlessly scalable

- CV-LNPs encapsulating modified RAVG-RNA were upscaled from 1 mg R&D dialysis process to **250 mg batch TFF process**
- *In vivo* potency was retained at different manufacturing scales
- **First successful up-scaling of an LNP using PEG alternatives**





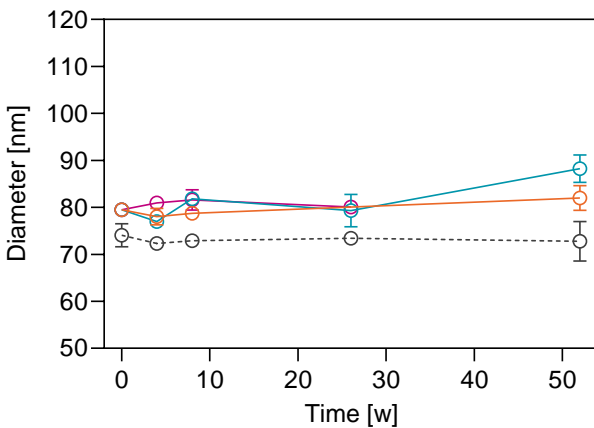
# Lyophilised CV-LNPs stable at room temperature for 1 year

- Slight size increase upon drying and **no change of particle size after 1 year of storage at 2-8 °C and 25 °C.**
- RNA integrity: No change at 2-8°C, modest reduction to 53% within 1 year 25 °C, no effect on EE%.

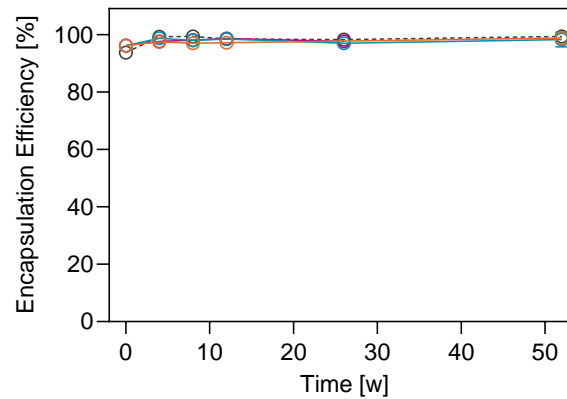


—○— 2-8°C    —○— 25°C    —○— 40°C    -○- Liquid LNP at -80°C

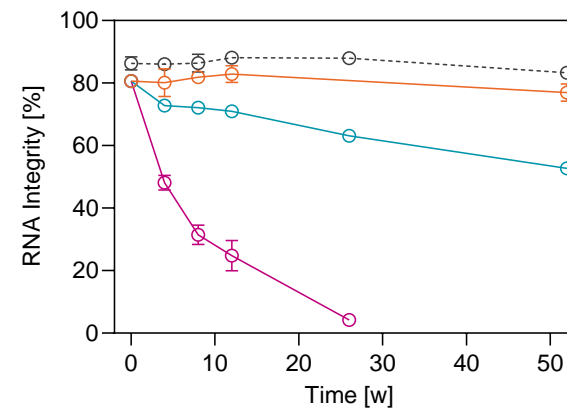
### DLS-Size



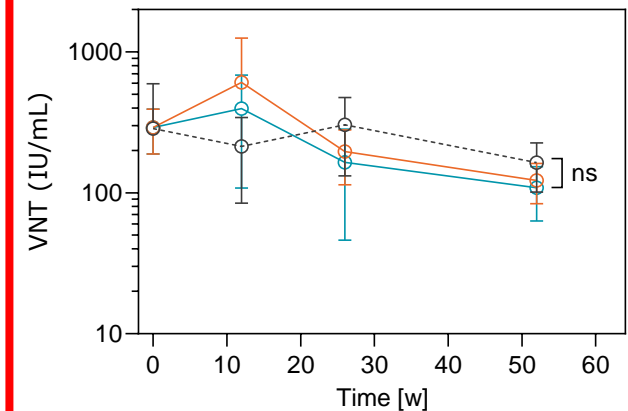
### RiboGreen



### RNA Integrity



### Rabies VNT d28



- **Vaccination efficiency of lyophilized vaccine retained after 1 year storage at 2-8°C and 25°C.**
- Study is currently extended up to 3 years.



## CureVac LNP platform for Oncology

## Prophylactic Vaccines






- Strong **humoral responses**, induction of **antibodies**
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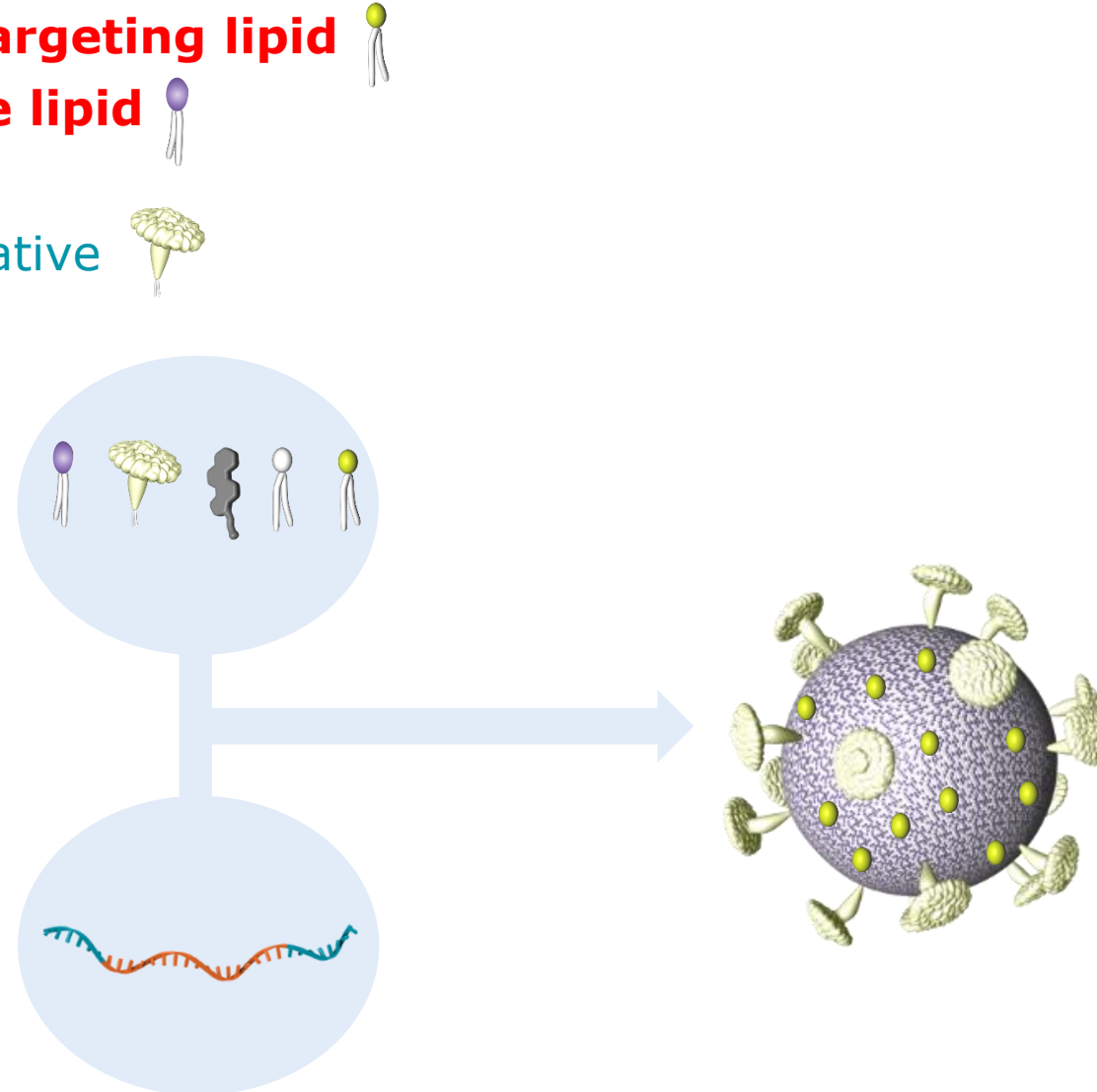
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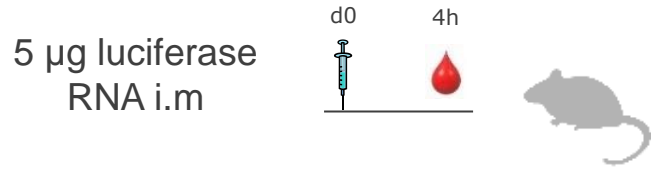
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# CureVac 5-component LNP for therapeutic cancer vaccines

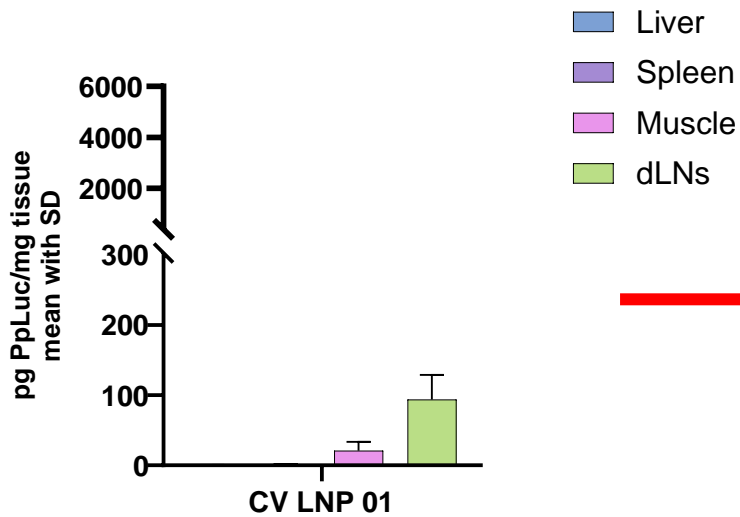
- **Novel immune cell targeting lipid** 
- **Proprietary ionizable lipid** 
- **New helper lipids** 
- **Proprietary PEG alternative** 
- **Cholesterol** 



# Systematic changes in LNP composition increase expression in the immune compartments after IM administration

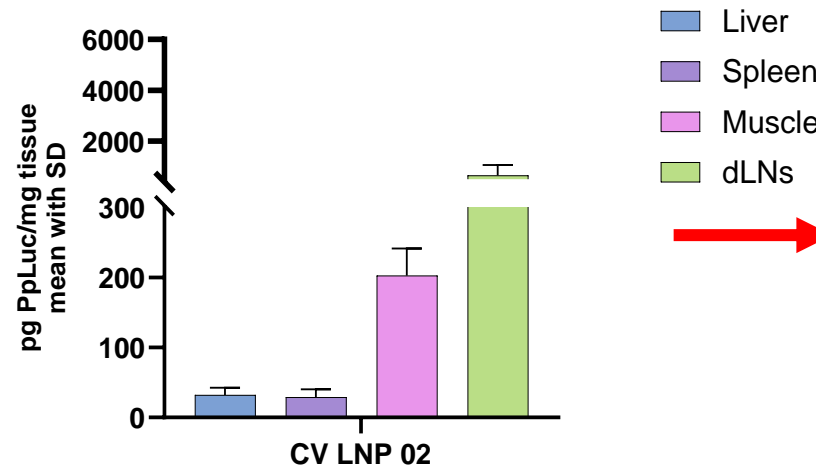


## Unoptimized CV LNP composition



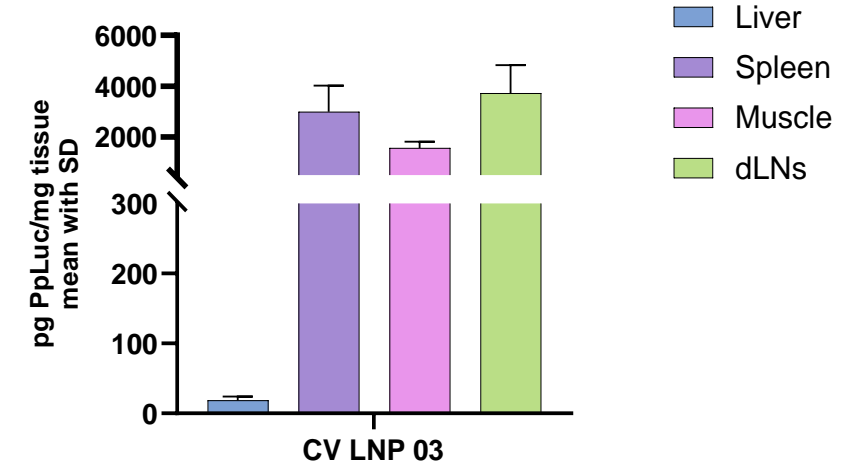
Spleen to liver ratio: 2.1

## New ionizable lipid + helper



Spleen to liver ratio: 1

## Novel immune cell targeting lipid

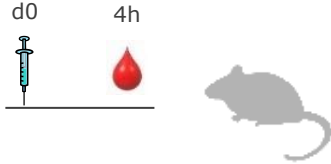


Spleen to liver ratio: 160.6

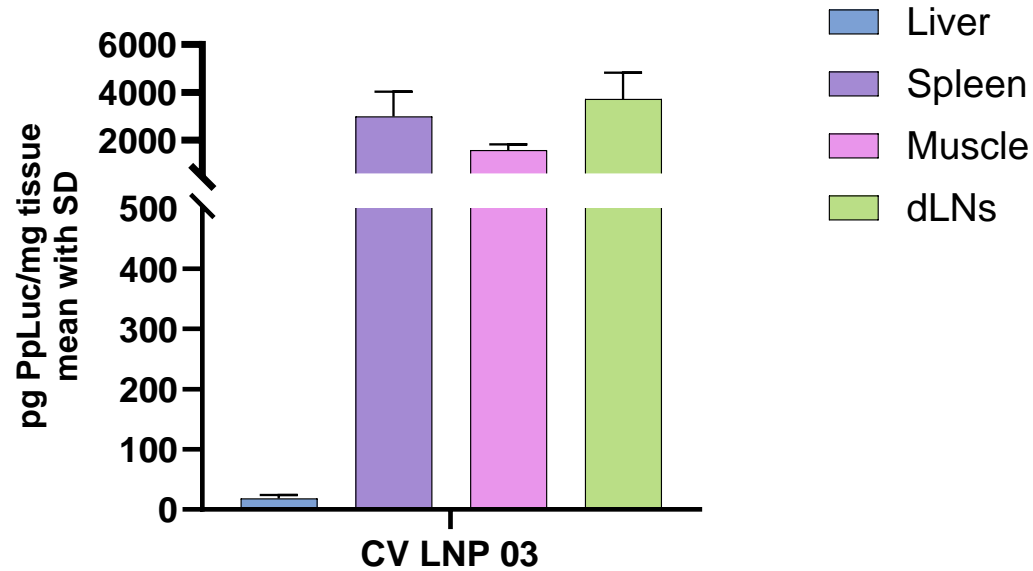
- Most prominent increase in systemic **immune compartments** (spleen and draining lymph nodes)
- Consistently low expression in liver and other distal organs

# Comparison to unoptimized state-of-the-art LNP – importance of tailoring for therapeutic area application

5 µg luciferase RNA i.m.

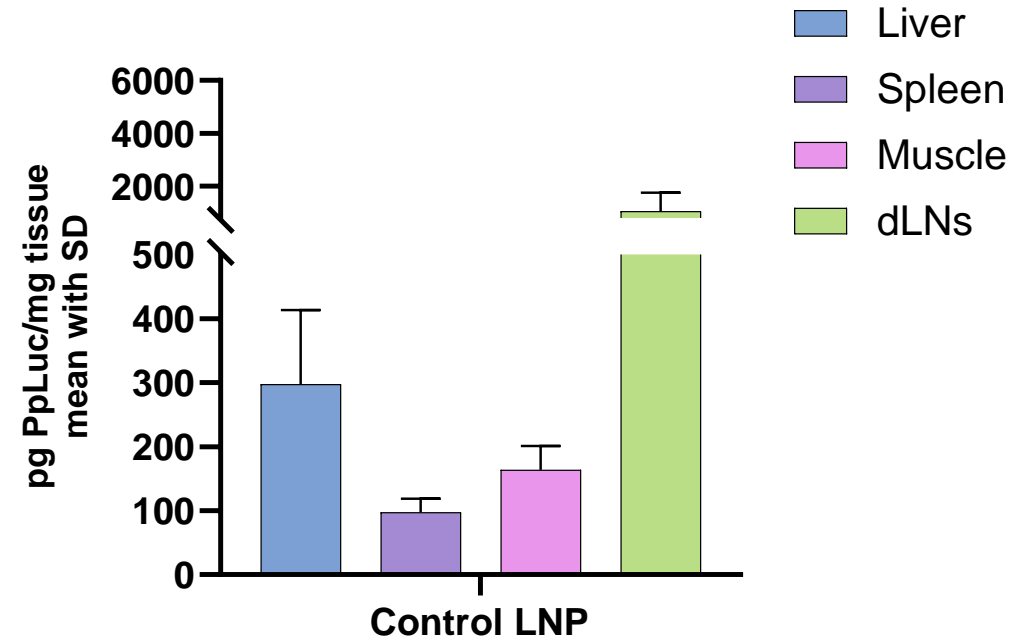


## CureVac LNP for Oncology



**Spleen to liver ratio** **160.6**

## SM102 LNP



**Spleen to liver ratio** **0.3**

# Acknowledgements

Contact: [Paula.Muresan@curevac.com](mailto:Paula.Muresan@curevac.com)

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**Thank you for your  
attention**

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