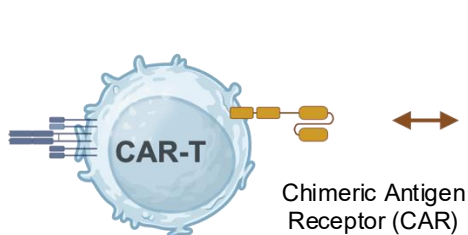


Advancing T cell therapy: mRNA nanocarriers optimization for ex vivo and *in vivo* T cell engineering

Elisa Battistini, Alberto Jiménez, Naiara Doldán, Philipp Lapuhs, Mariona Baliu-Piqué, Lucía Sanjurjo, María José Alonso

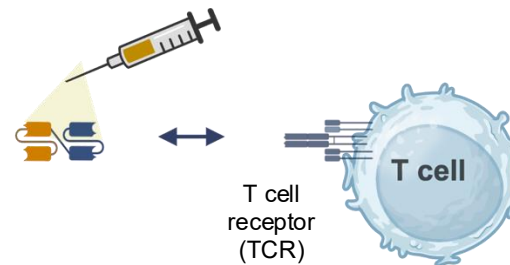
T cell redirecting therapies

CAR engineered T cell



Tumor cell

Bispecific antibody (bsAb)

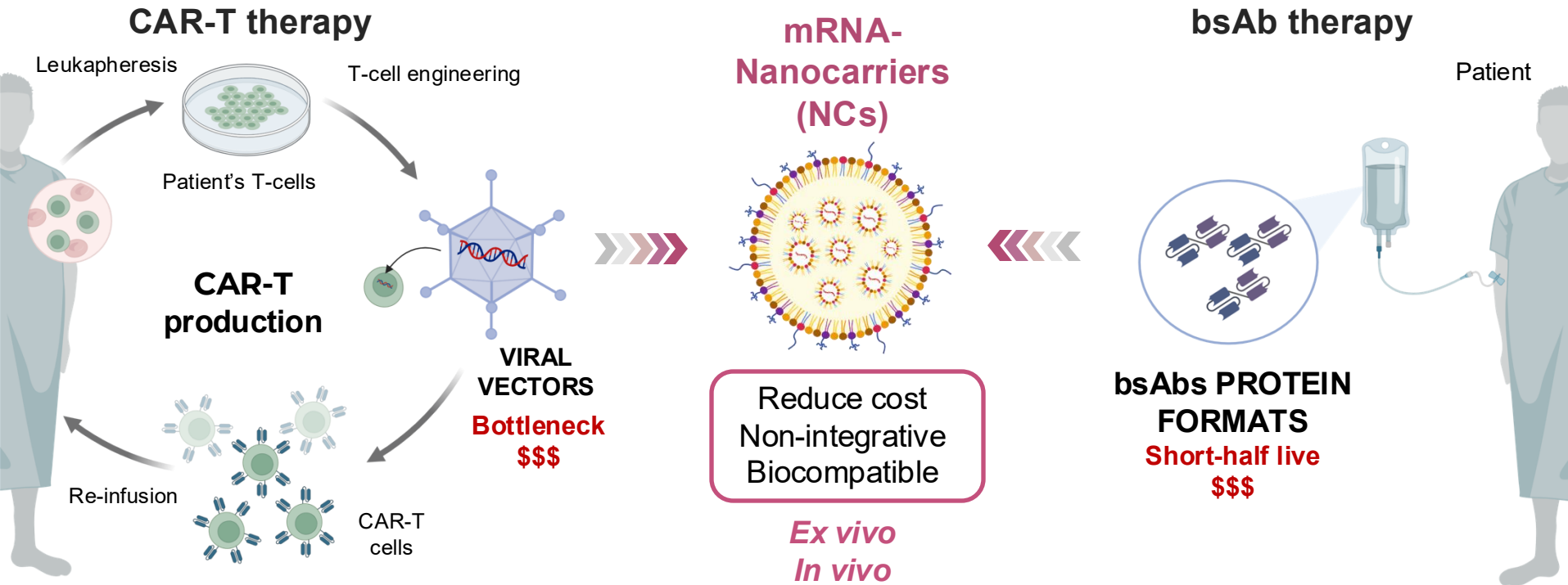


Hematological malignancies (CD19, CD20, BCMA)

Solid tumors (EGFR, Claudin, HER2...)

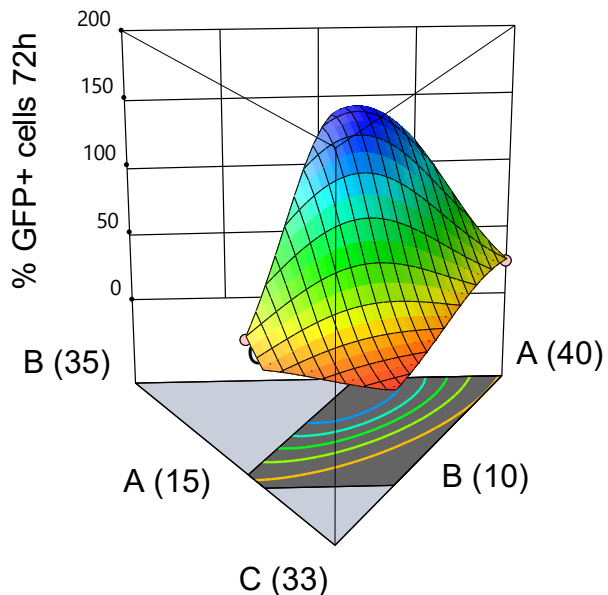
Autoimmune diseases (CD19)

Nanotechnology to advance T cell therapies



mRNA-NCs screening

Design of Experiments (DOE)



Acqueous phase



mRNA



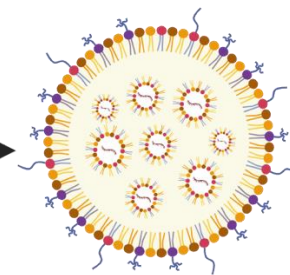
Citrate buffer

Organic phase



Lipid
components

25 NC prototypes:
model mRNA GFP



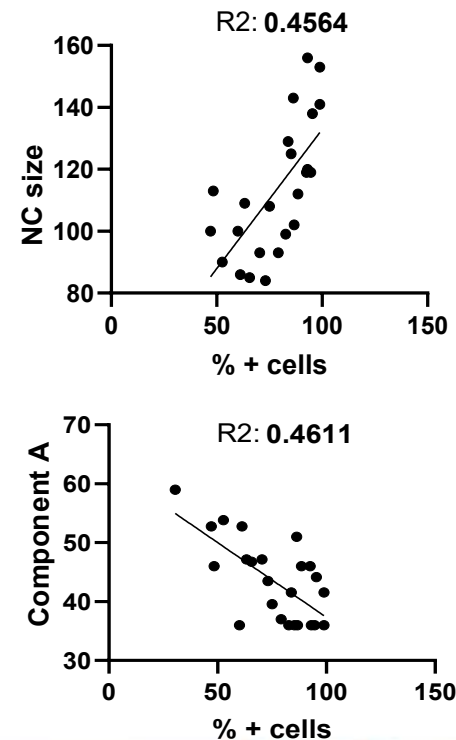
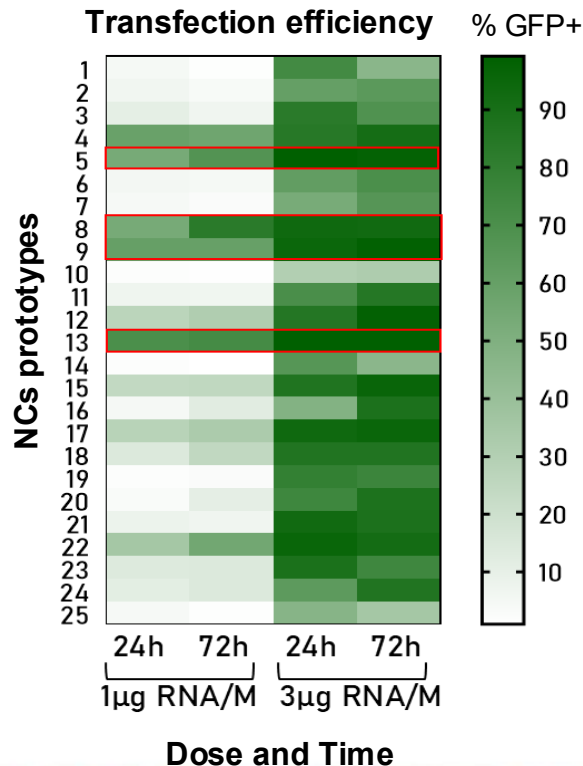
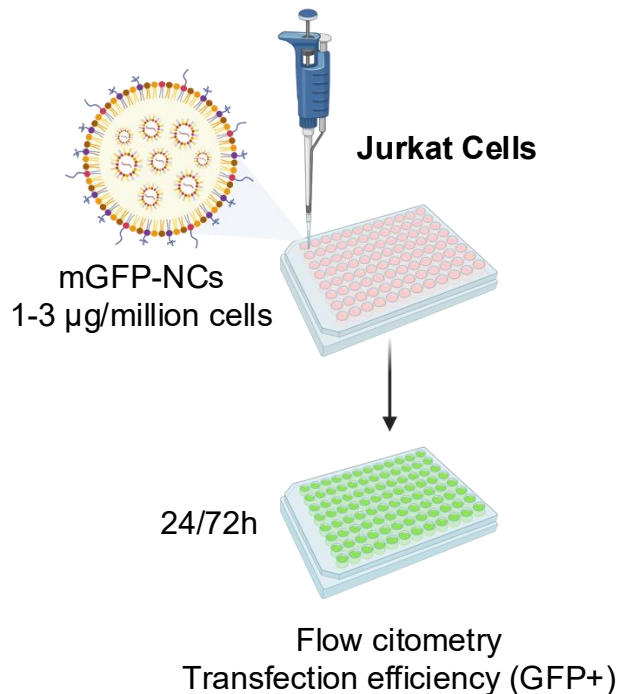
Size: **50-95 nm**

Charge: **neutral**

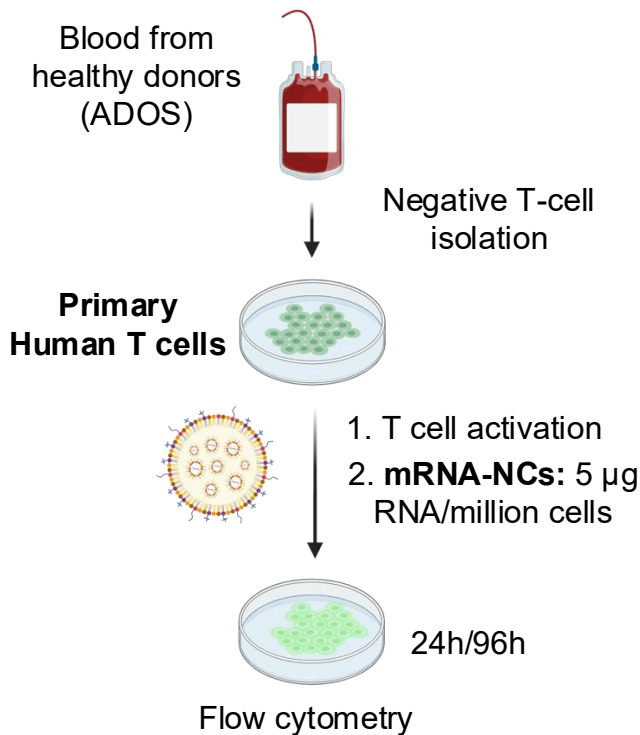
PDI < **0.2**

RNA association: **+85%**
Stable in culture medium

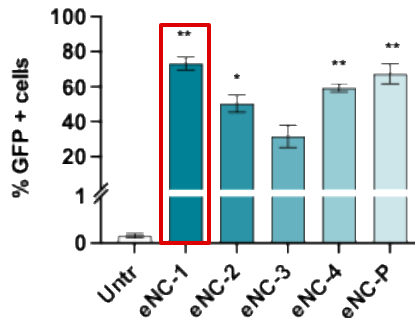
mRNA-NCs screening



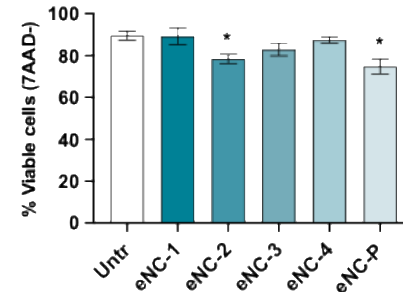
mRNA-NCs efficiency in T cells



Transfection efficiency

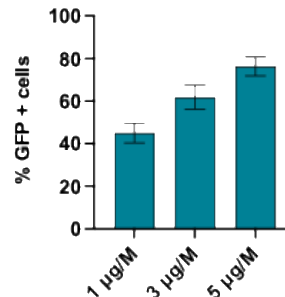


Cell viability

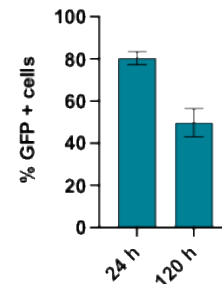


n:3 blood donors; RM one-way ANOVA, *p<0.05, **p<0.01

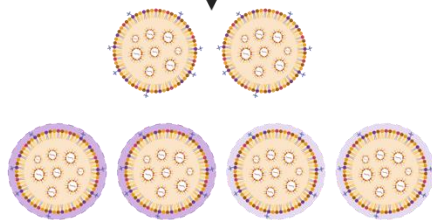
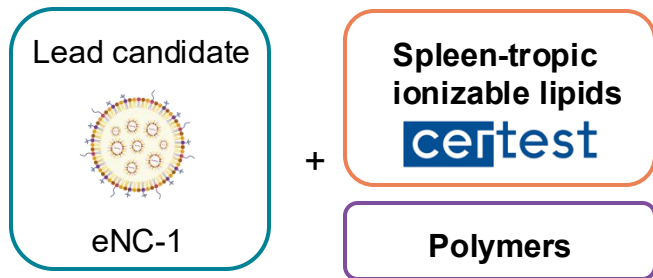
Dose response



Persistence



mRNA-NCs optimization in T cells



Size: **70 – 155 nm**

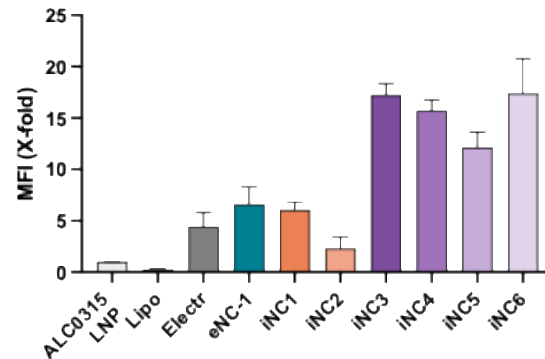
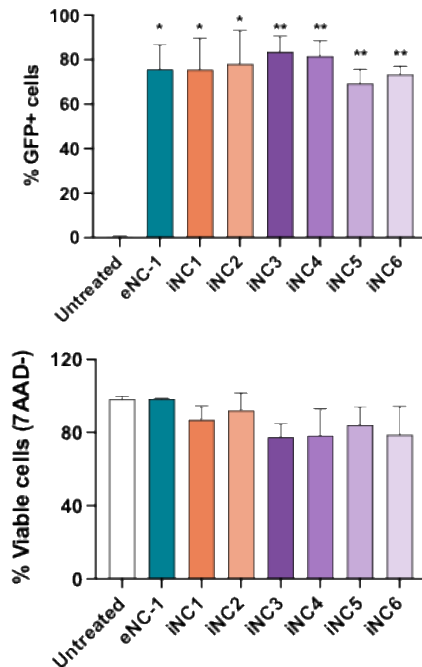
Charge: **neutral**

PDI < **0.2**

RNA association: **+85%**

Stable in culture medium

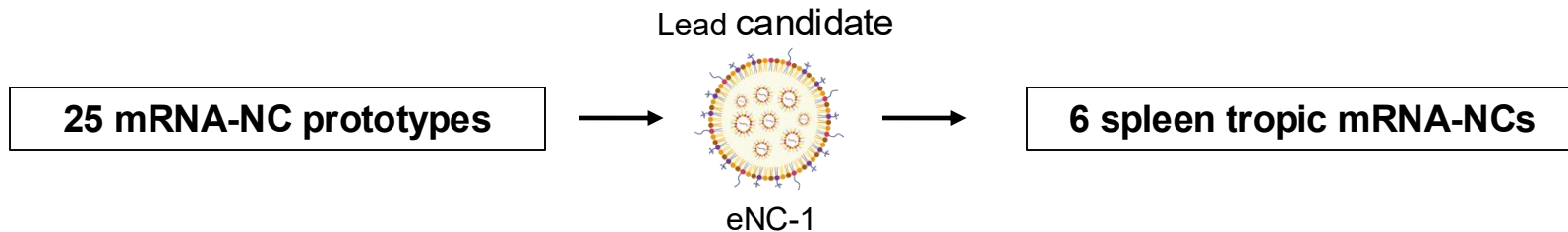
Transfection efficiency and viability, human T cells



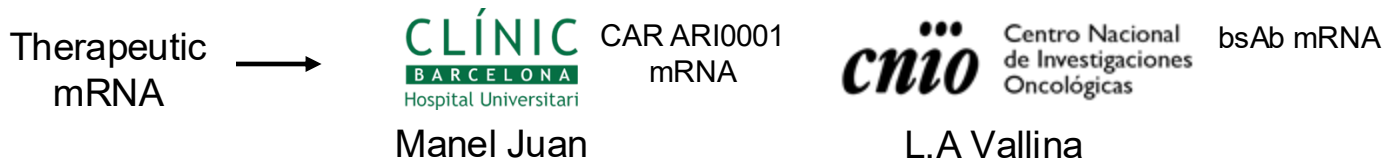
n:3 blood donors; RM one-way ANOVA, *p<0.05, **p<0.01

Summary and conclusions

- Screening → NCs for T cell transfection



- **High T cell transfection efficiency and low toxicity.** Better performance than LNPs (Pfizer), lipofectamine and electroporation.
- **Therapeutic potential and biodistribution studies** are undergoing.



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(IDIBAPS)**

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contra el cáncer

MJ ALONSO'S LAB



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