A Novel RNA **Lipid Nanoparticle** Platform: **Gene-Edited CAR T Cells** for Off-the-Shelf Cancer Therapy

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Director of Product Development

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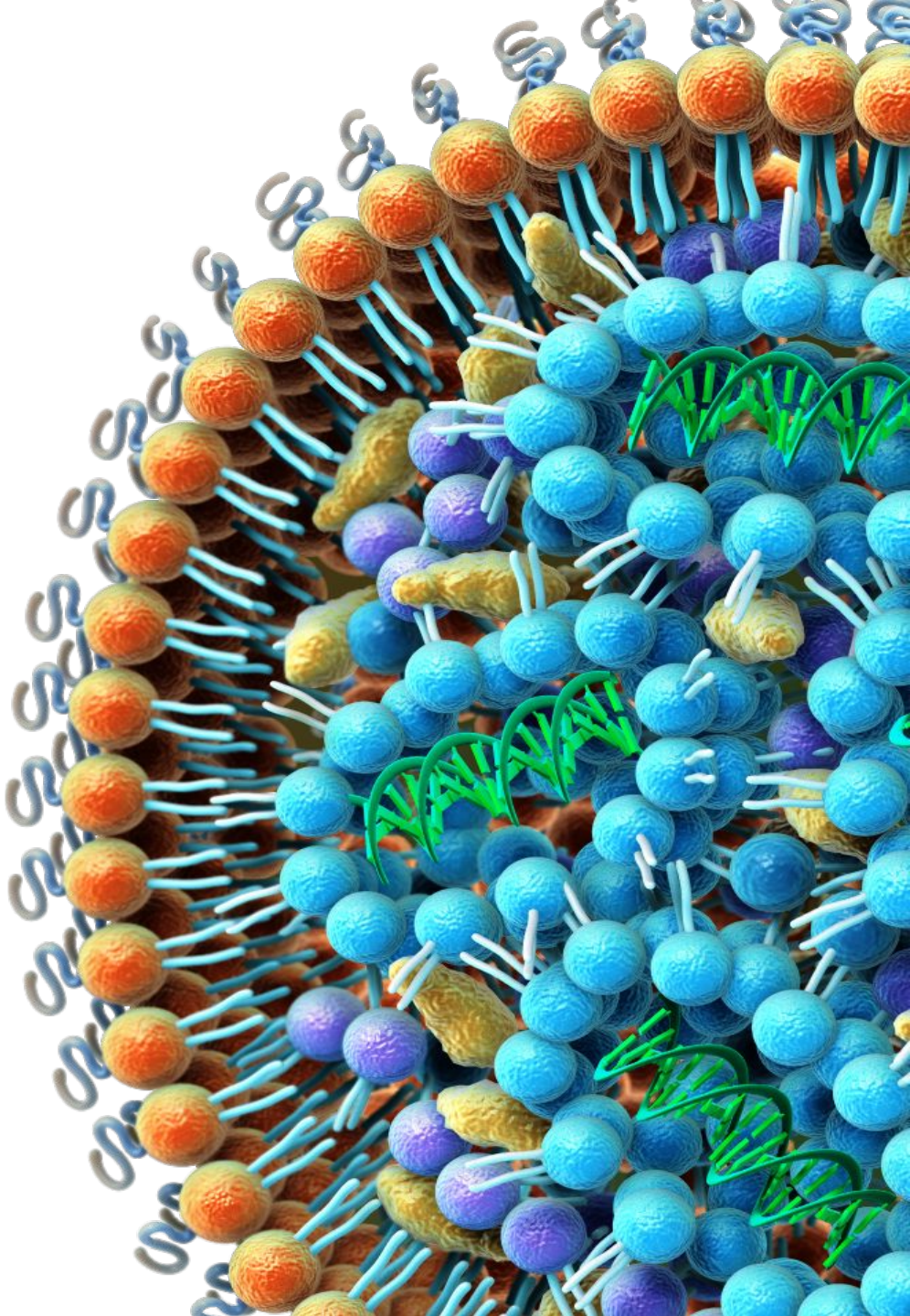

Next Generation Immune Cell Therapies

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Today

- High response in some advanced blood cancers
- Moderate toxicities
- Limited efficacy in solid tumors
- On-demand manufacturing
    - Autologous
    - Viral Vectors

Tomorrow

- Additional cancers and earlier lines of therapy
- Reduced toxicities
- Extension to solid tumors
- Off-the-shelf manufacturing
    - **Allogeneic**
    - **Gene-Edited**
    - **Non-Viral Delivery**

Lipid Nanoparticles for Genetic Engineering of T Cells

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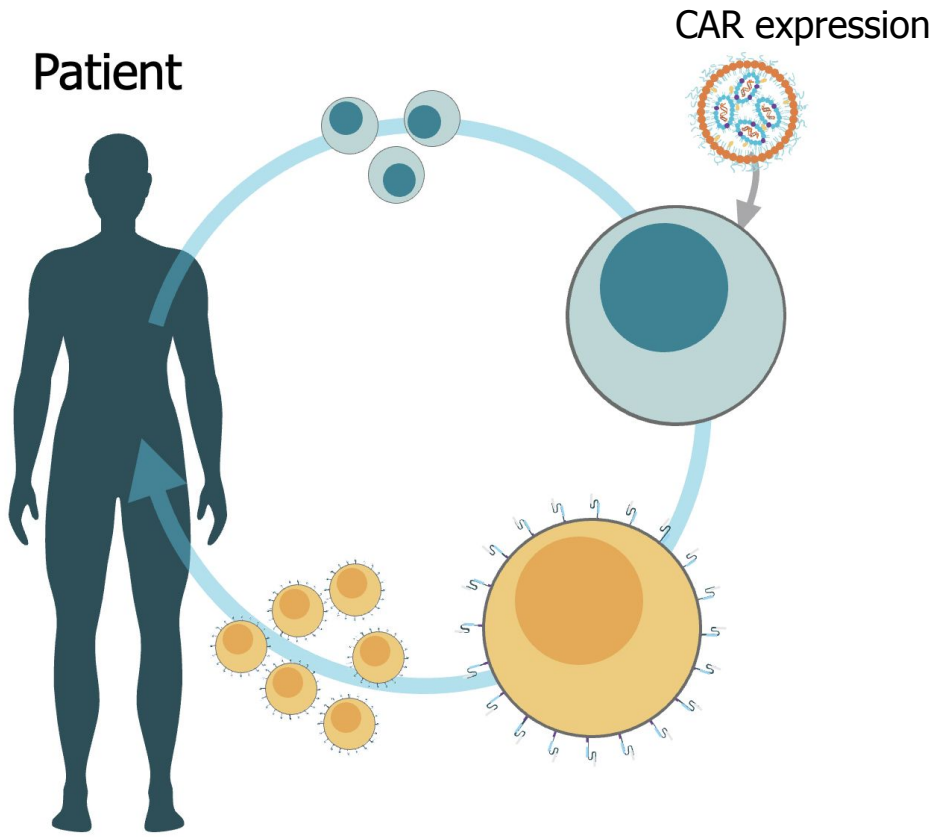
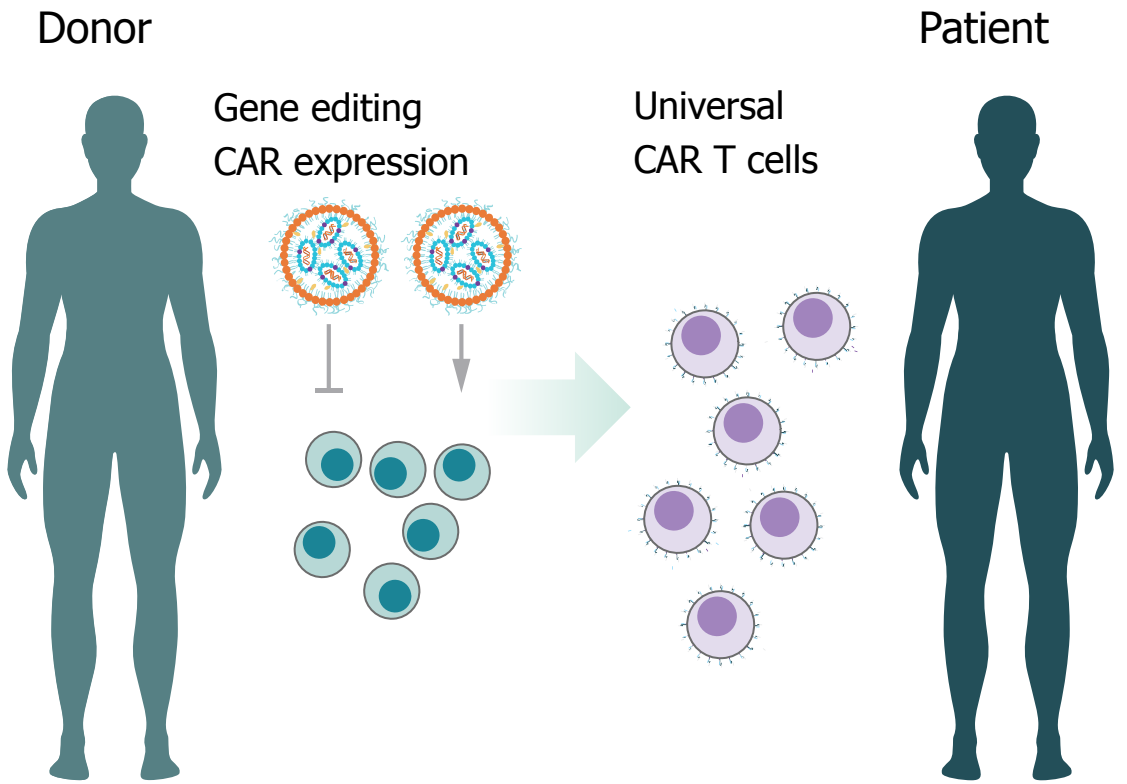
Autologous CAR T therapy



Single LNP Addition

"Off-the-shelf" allogeneic CAR T therapy



Multiple LNP Additions

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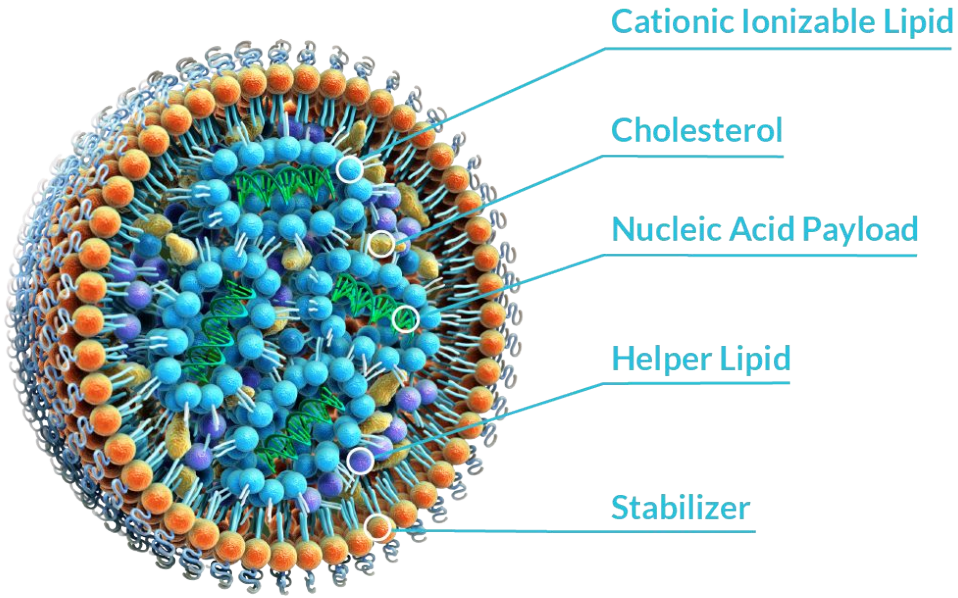
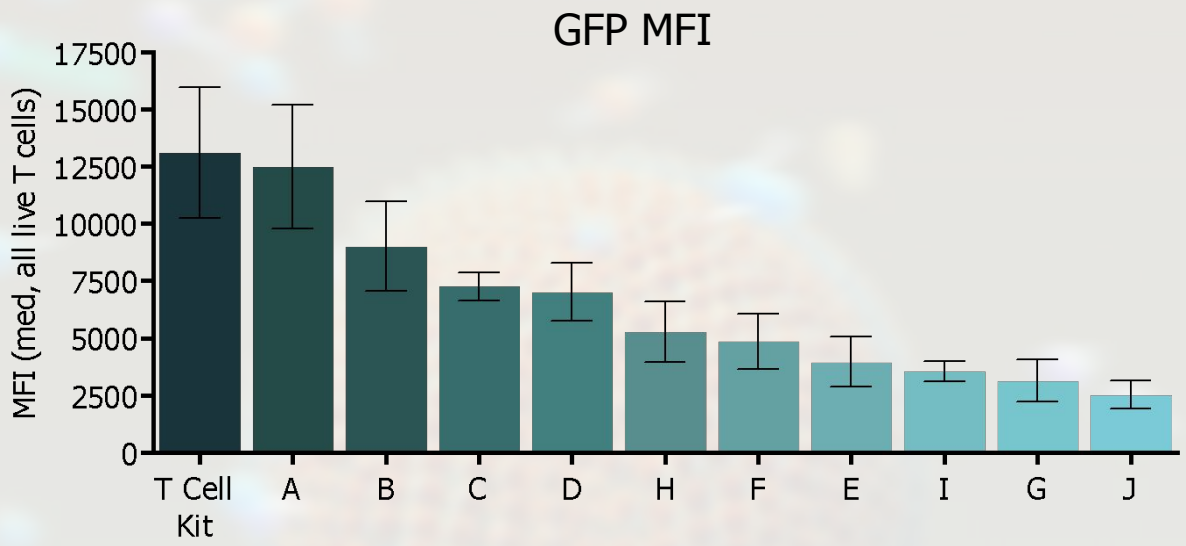
T Cell Kit Composition was Selected for Superior Performance in Primary T Cells



We have a **novel lipid library** comprising ionizable lipids and compositions that are **designed** for applications in **vaccines**, **gene therapy**, and **cell therapy**.



Methods: All component mole ratios maintained with only the ionizable lipid varied. GFP intensity and transfection efficiency was measured via flow cytometry 48 h post treatment. LNP treatment was performed following the T Cell Kit for mRNA on Spark protocol.

Proof-of-Concept Demonstration of *Ex Vivo* T Cell Engineering

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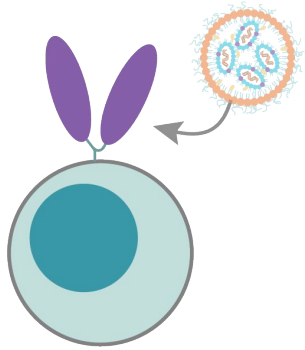
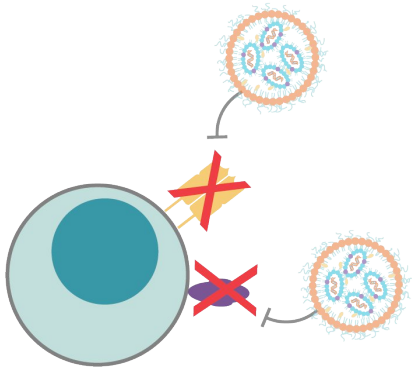
1 Gene Expression



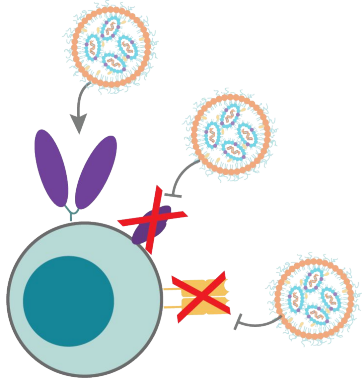
2nd generation CD19 CAR expression

2 Gene Knockout



TCR and/or CD52 double knockout

3 Gene Knockout and Expression



TCR knockout and subsequent CAR expression

1 LNPs Show High Transfection Efficiency and High Cell Viability

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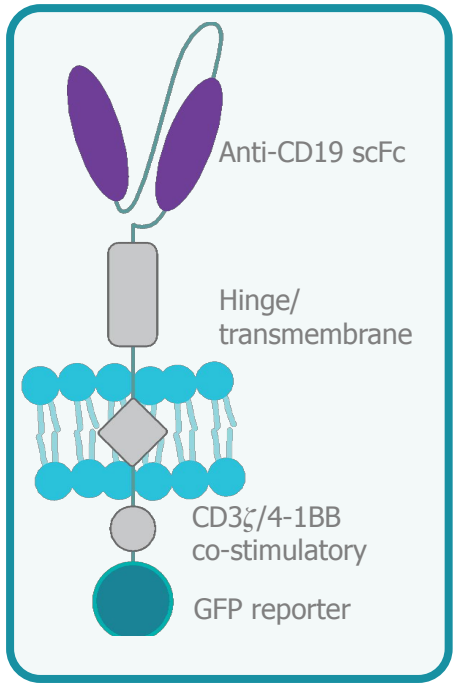
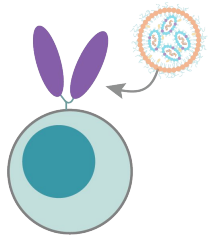
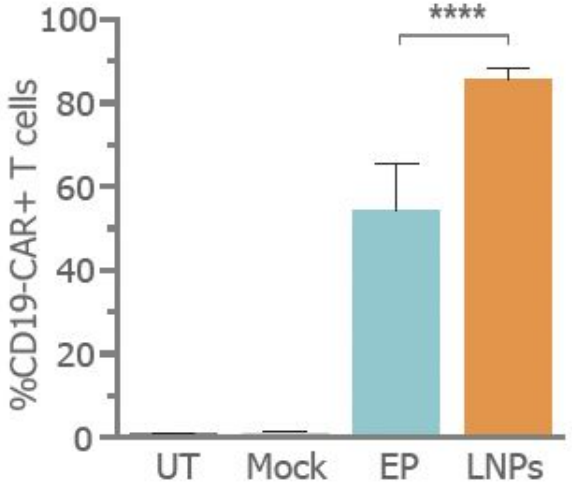




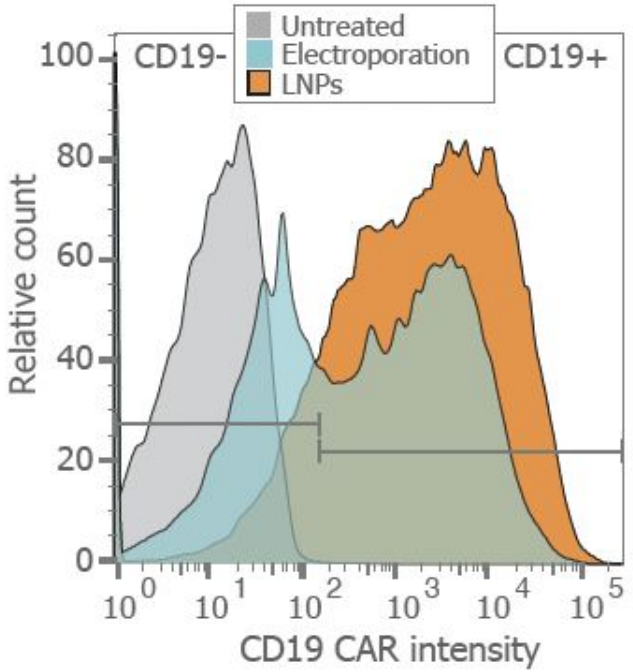
CAR mRNA LNP

Primary T cell

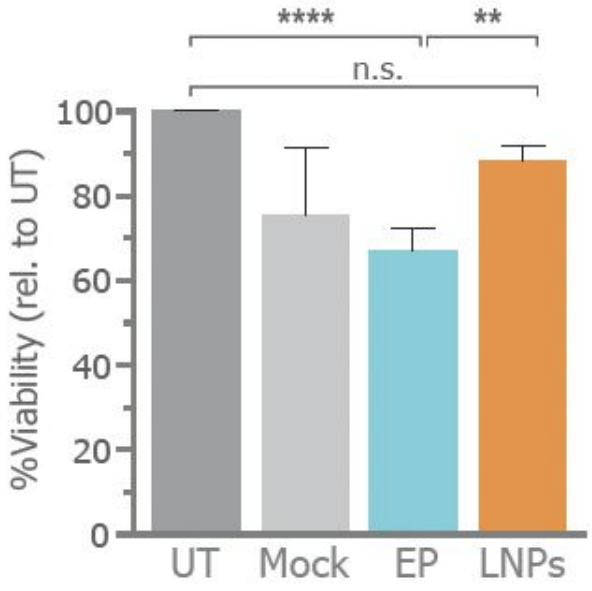
Transfection Efficiency



Protein Expression



Viability



2 Gene Knockout: Dose-dependent Knockout Efficiency with High Cell Viabilities

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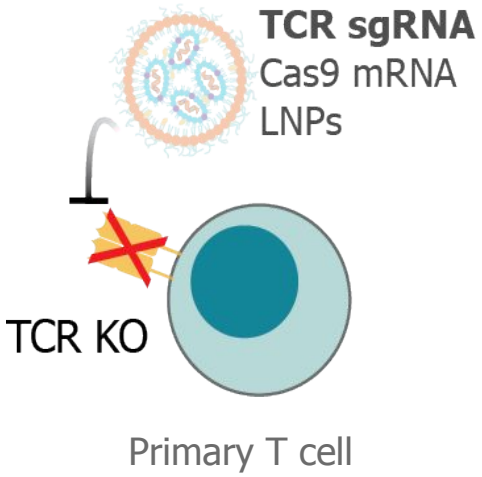
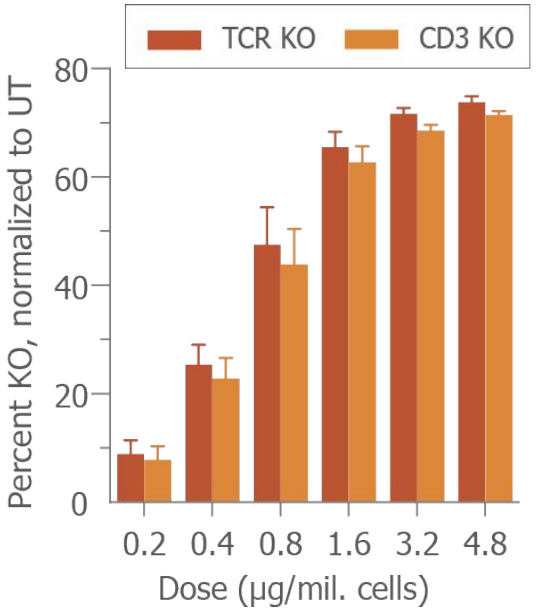
A



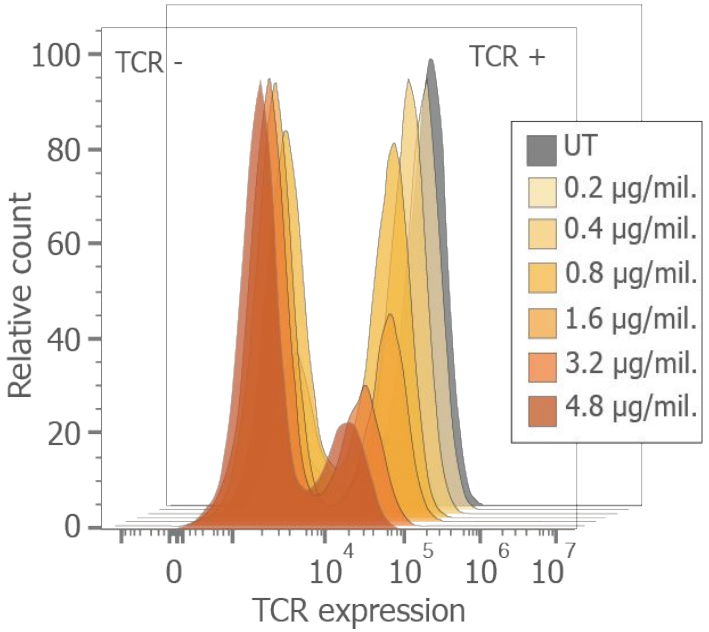
B

Knockout Efficiency



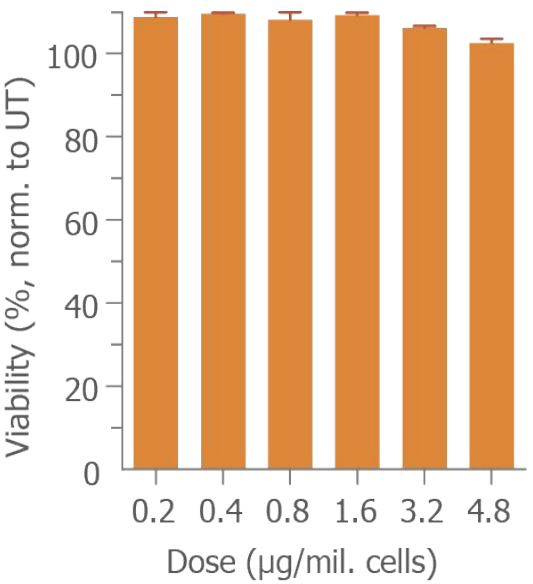
C

Protein Expression



D

Viability



3 Multi-step Engineering using LNPs: Knockout and Expression

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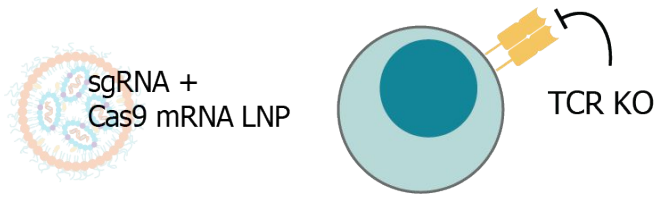
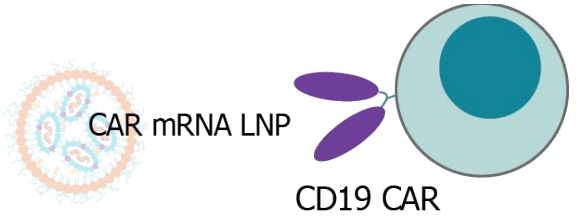
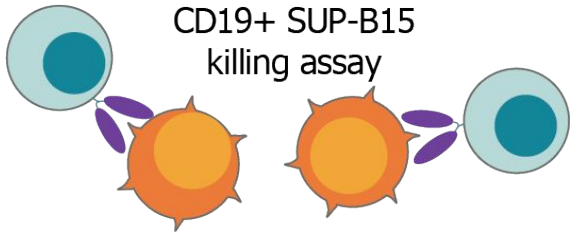
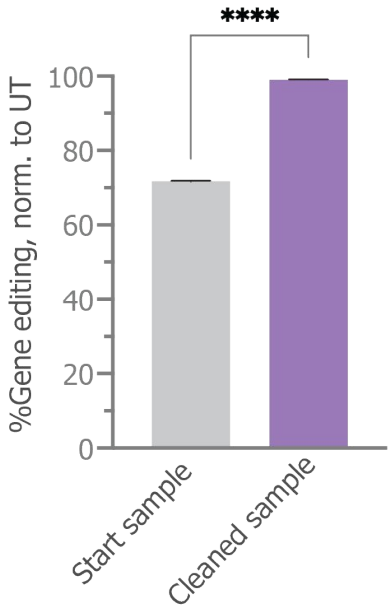
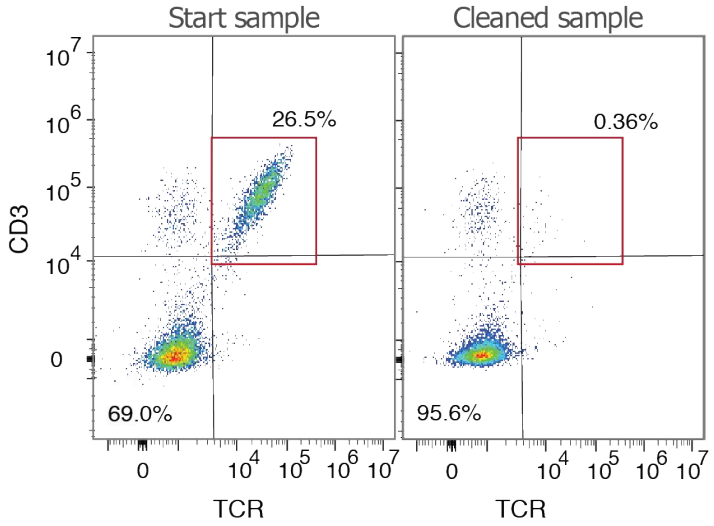
TCR Knock Out → **CAR Expression** → ***In Vitro* Killing Assay**

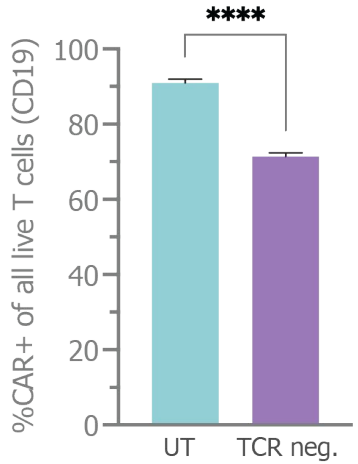


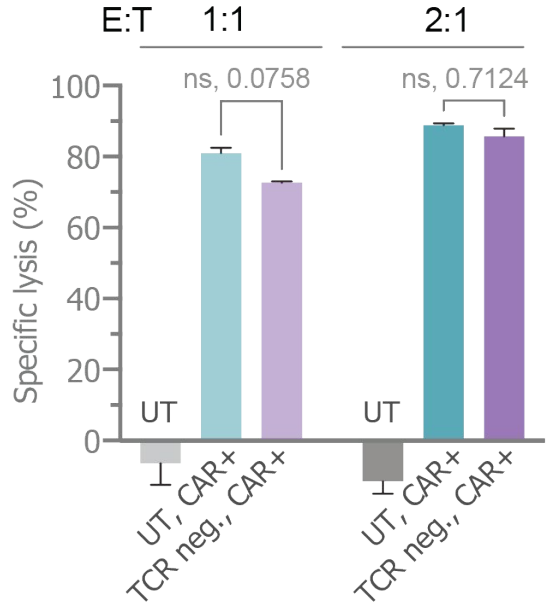












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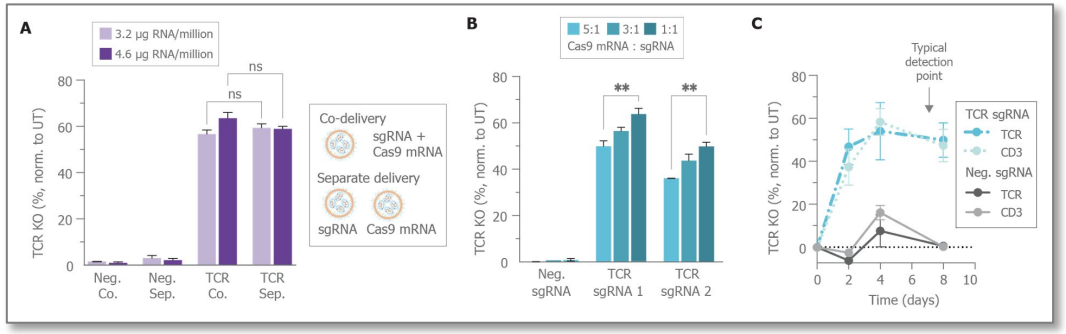

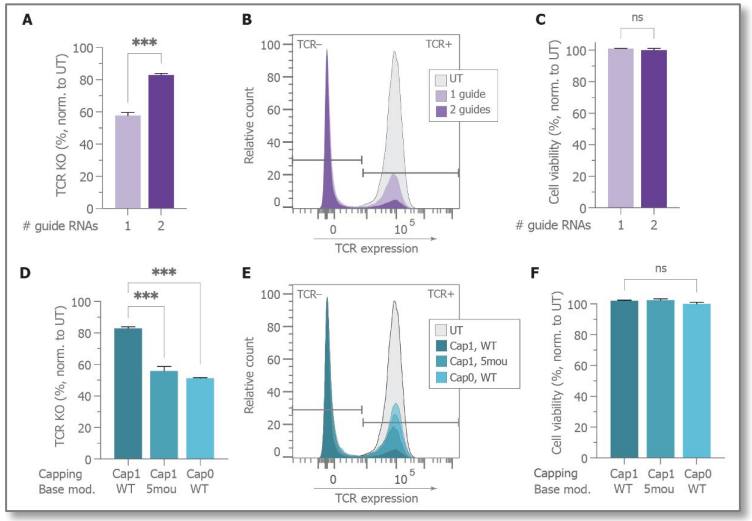

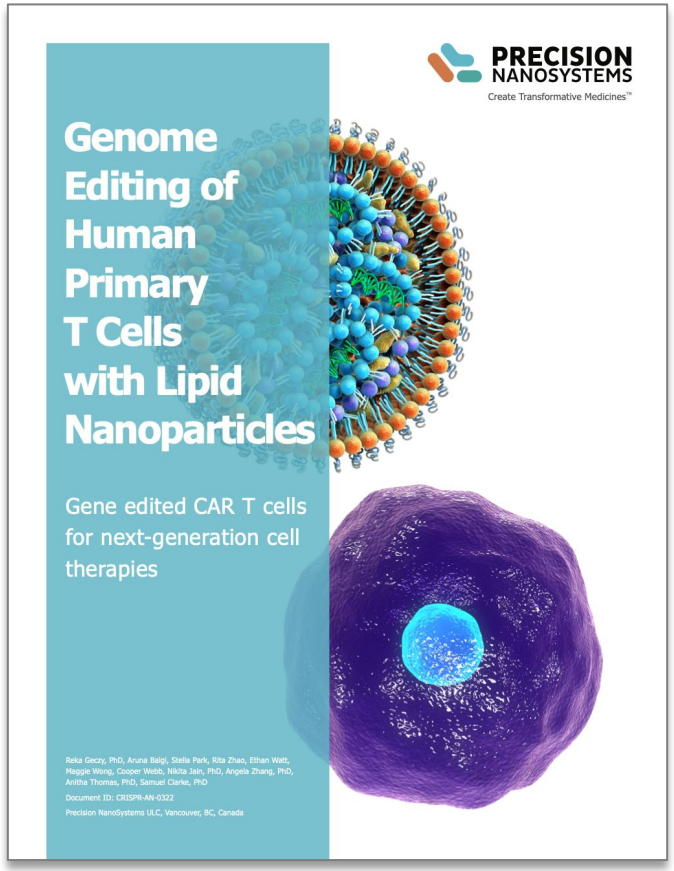

Providing Complete Solutions that Translate through Drug Development

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Discovery | Early Preclinical | Late Preclinical | Clinical | Commercial

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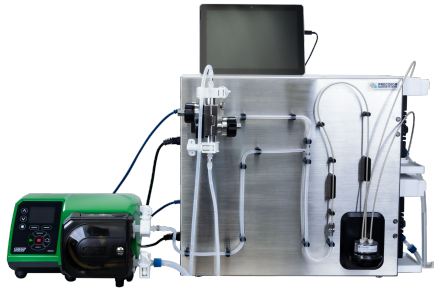

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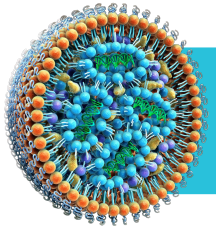

GenVoy® Reagents

Biopharmaceutical Services

- Screening
- Formulation Development
- Process Development
- Scale-up
- Technology Transfer & Manufacturing
- Chemistry, Manufacturing & Controls (CMC) Support

Acknowledgements

PNI Reagents & Delivery Teams

- Reka Geczy
- Aruna Balgi
- Stella Park
- Rita Zhao
- Anitha Thomas
- Nikita Jain
- Angela Zhang

Funding

- Government of Canada IRAP-NRC Program

PNI Departments:

- Clinical Manufacturing
- Research
- Engineering & Operations
- Preclinical
- Process Development
- Product Development
- Analytical Development
- Quality Control
- Quality Assurance
- Project Management
- RNA Development Services
- Sales and Marketing

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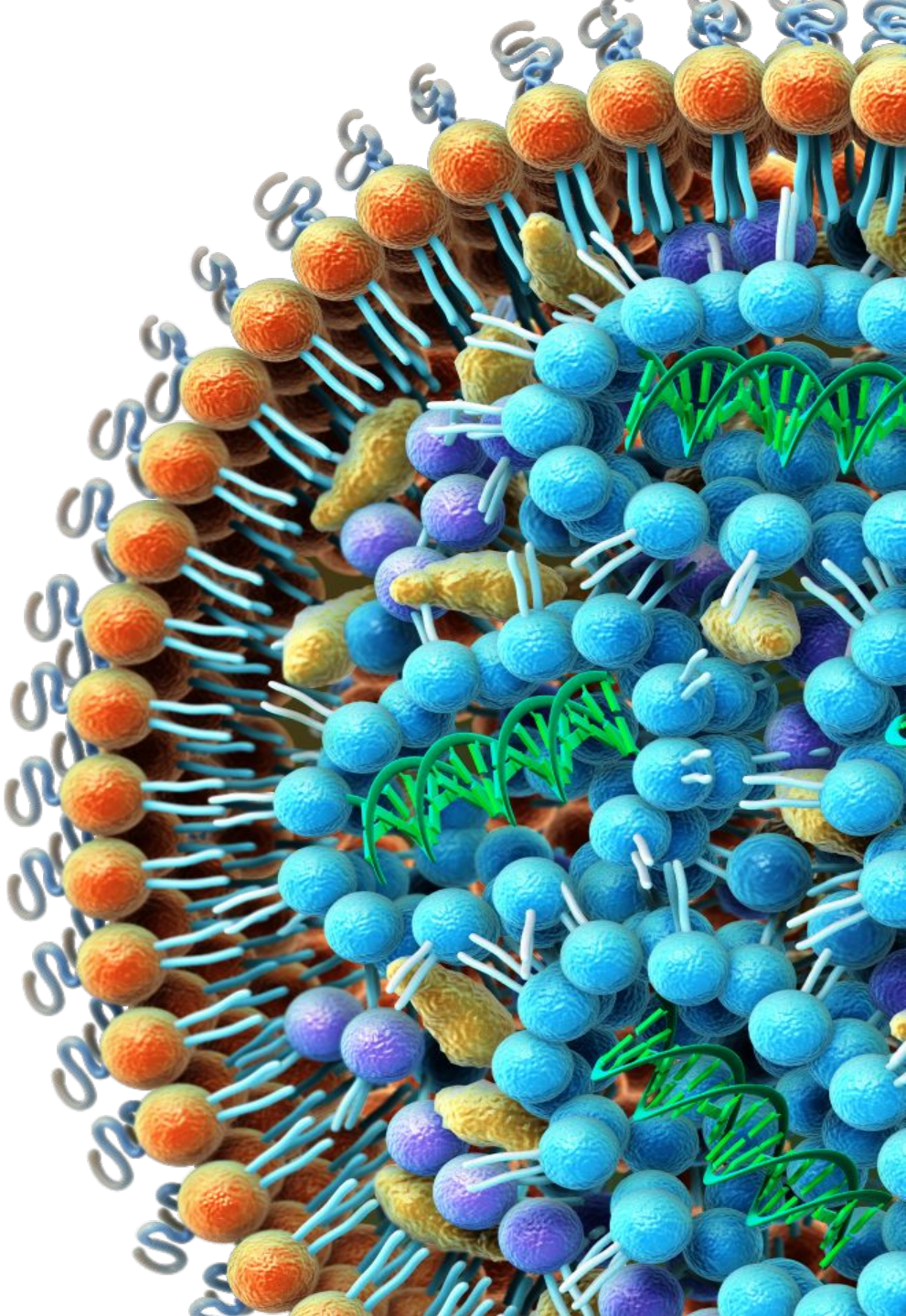
Thank you for listening!

Questions?



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