Targeted-LNPs capable of functional DNA delivery to T cells enable *in vivo* CAR-T generation

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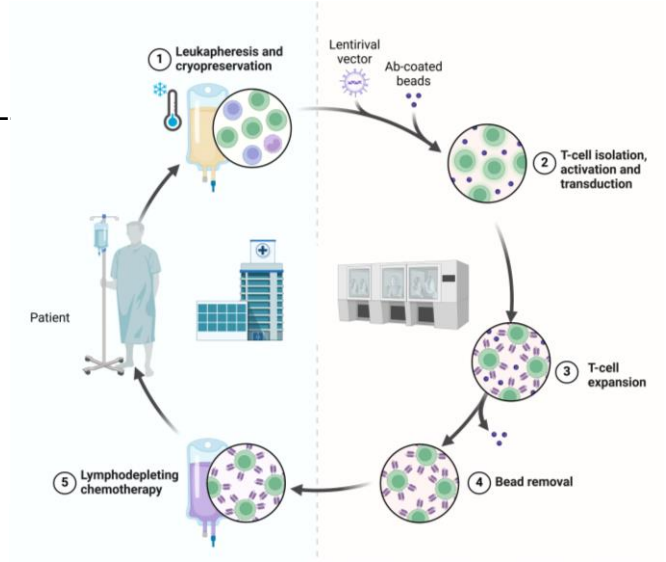
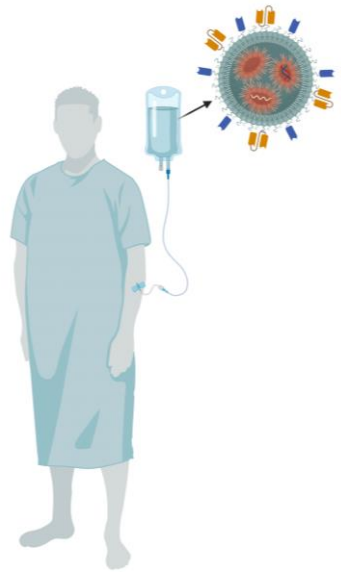
NEXT-GENERATION DELIVERY INNOVATIONS

In vivo CAR-T therapy possesses several advantages over *ex vivo* CAR-T and will improve patient access

Cons of *ex vivo*

- ✗ Prohibitive Cost of Goods
- ✗ Prohibitive Cost of Time
- ✗ Prohibitive operational constraints
- ✗ Requires hospitalization, chemo-conditioning
- ✗ Limited patient access





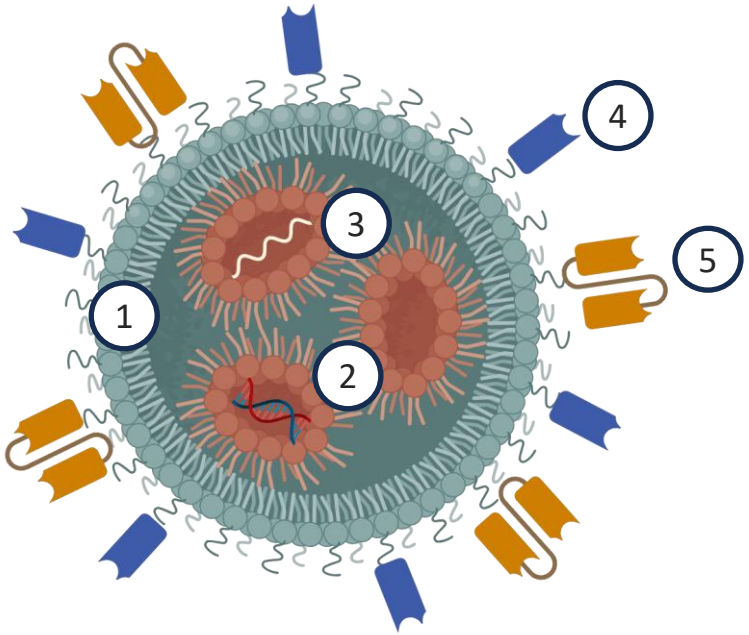
Pros of *in vivo* CAR-T

- ✓ Off the shelf gene therapy; NOT a cellular product
- ✓ Superior safety and efficacy:
  - Slower onset of action = potential for lower CRS and ICANS
  - Potential for more durable clinical efficacy with longer CAR-T persistence
- ✓ Out-patient / community treatment center setting
- ✓ Small fraction of COGS compared to rival technologies

NanoCell's tLNP platform: targeted, non-viral, DNA-based gene delivery

tLNP platform:

Non- viral gene delivery vector



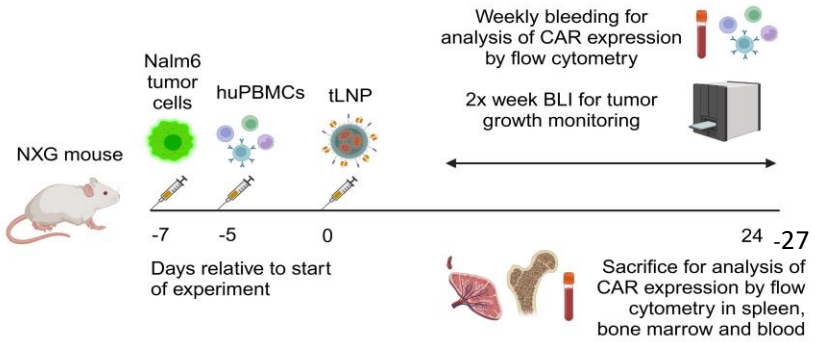
NanoCell targeted LNP (tLNP)

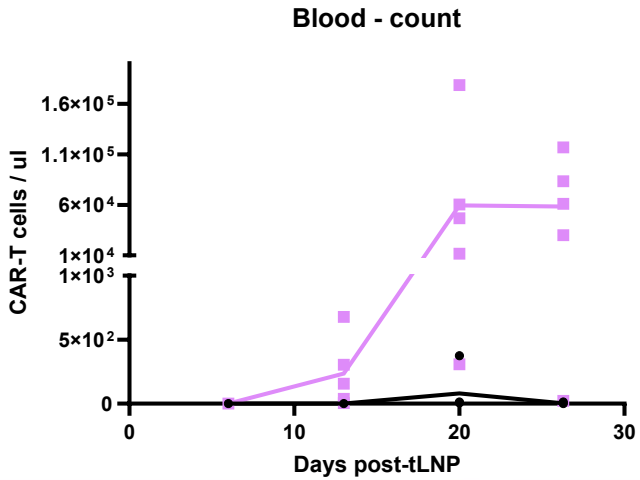
A single product for non-viral delivery of nucleic acids to T cells

1. LNP formulation designed to deliver DNA into the nucleus of the target cell
2. Minicircle DNA (mcDNA) expressing CAR or TCR
3. Transposase in RNA format for stable integration of mcDNA
4. T cell specific binder to target T cells
5. T cell-specific agonist binder to activate T cells

Wide-ranging and growing IP portfolio

NCTX-01 induced robust CAR expression in blood, spleen and bone marrow in a huPBMC model

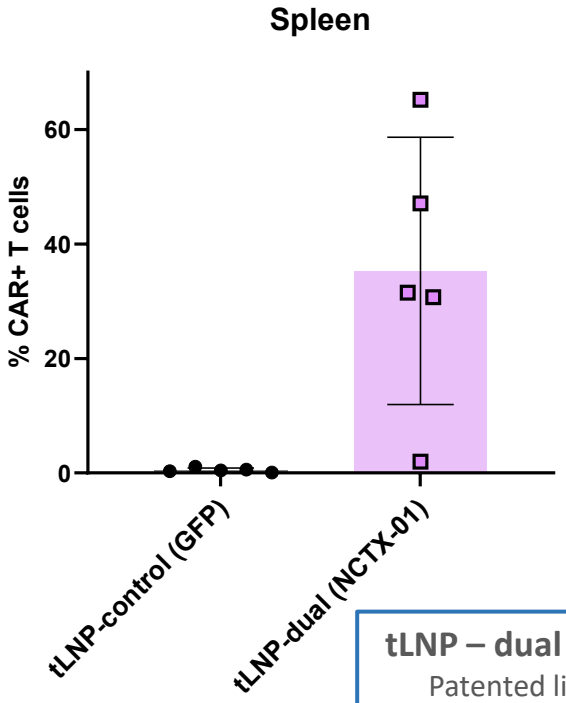


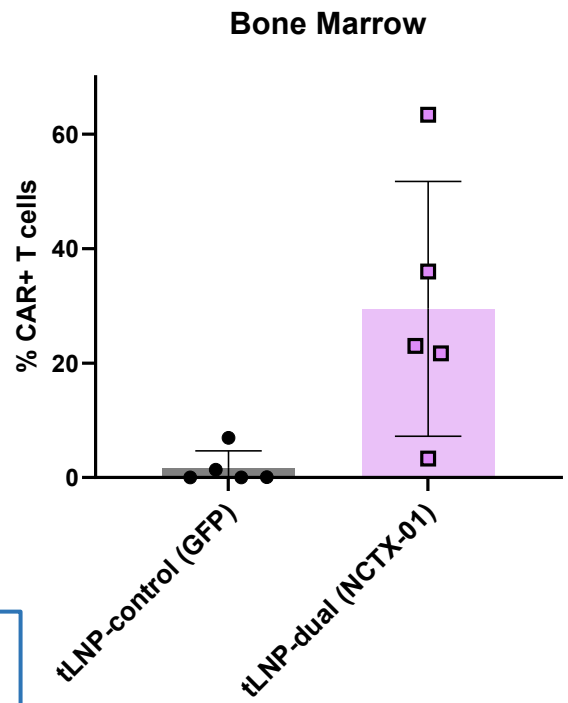


mcGFP control

tLNP-dual (NCTX-01)

Dose = 50µg/kg



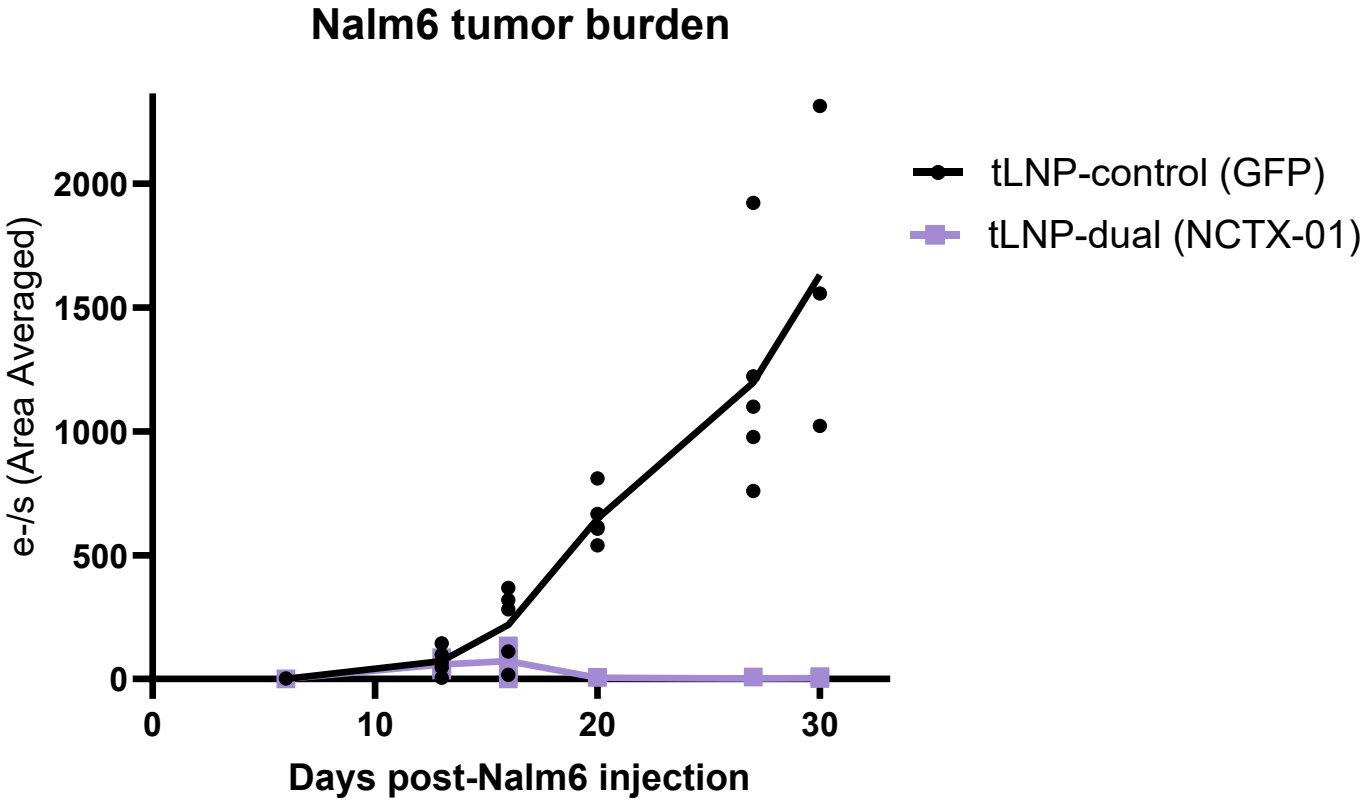


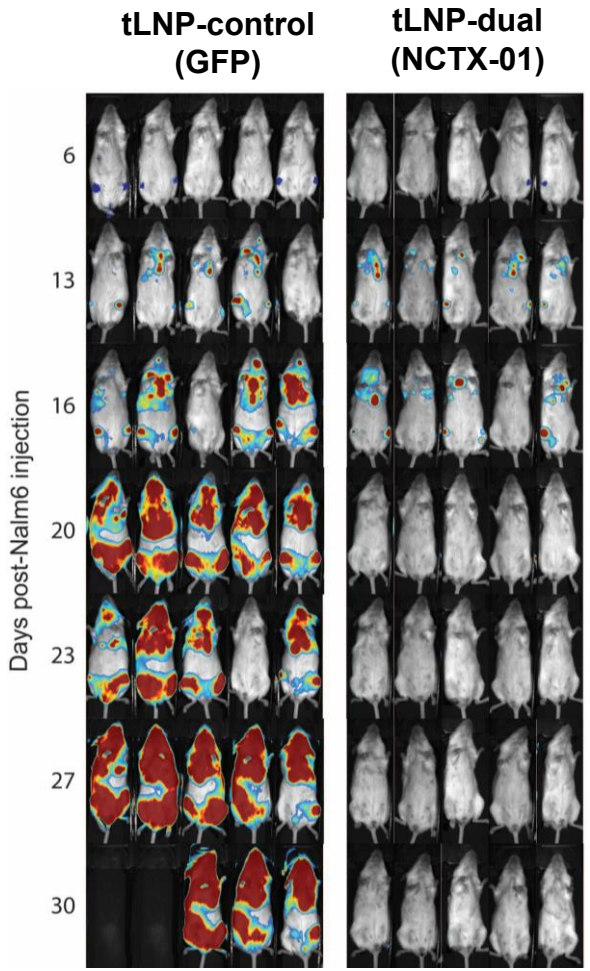
tLNP – dual (NCTX-01) LCC

Patented lipid compositions under license

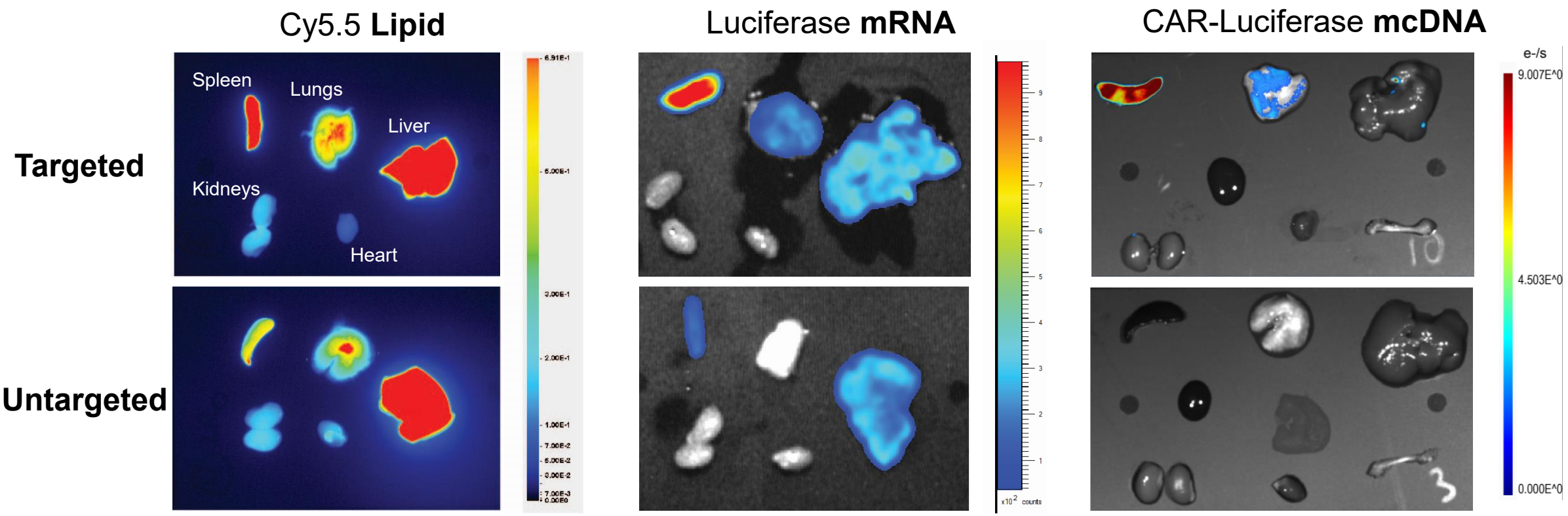
Patented dual CD19/CD22 CAR construct under license -

Complete Nalm6 tumor clearance in NCTX-01-treated mice





Targeting steers particle to T cell rich spleen and is required for mcDNA expression



Conclusions

- NCTX-01 induces efficient stable T cell transfection with CD19-CD22 dual CAR mcDNA *in vivo*
- *In vivo* generated CAR-T cells effectively target tumor cells, inducing complete tumor eradication
- Targeting promotes biodistribution to the spleen
- CAR-Luciferase expression is only detected using BLI when particles are targeted
- Nanocell's non-viral NCTX-01 vector promises to greatly enhance patient access to CAR-T therapy

Thank you for listening!

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NANO-ENGINE

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