Therapeutic Cell Engineering Using Surface-Conjugated Synthetic Nanoparticles

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High loading efficiency of a wide range of therapeutic agents (recombinant proteins, small molecule drugs, siRNA, magnetic imaging agents)

Protect cargo from premature degradation or premature interaction with the biological environment

Tailored drug release kinetics
Can we device a facile bioengineering tool to enhance the therapeutic potential of cytoreagents?

☐ No cell pre-conditioning (Immediately before infusion of cell product into the patient)

☐ 100% efficiency

☐ Quick, easy scale up

☐ Wide range of therapeutic agents
The chemical surface conjugation of adjuvant drug-loaded NPs prior to adoptive transfer permits continuous pseudo autocrine stimulation and can endow their carrier cells with substantially superior proliferative and reconstitutive capabilities than achieved with systemic drug adjuvant injection.
a Liposomes

“stapled” lipid vesicles

Lipid-coated PLGA nanoparticles
Average 91 (+/- 28, n=30) liposomes / T cell
Average 102 (± 21, n=30) Multilamellar lipid NPs/T cell
PLGA NPs on T cells
Does nanoparticle attachment interfere with key cellular functions? (no therapeutic cargo in NPs)
PLGA NPs on T cells
Does nanoparticle attachment interfere with key cellular functions? (no therapeutic cargo in NPs)
T cells without nanoparticles

MFI (CFSE) = 360

T cells with 100 nanoparticles

MFI (CFSE) = 339

MFI (DiD) =
Day 0 T cell imaging

Untreated

Pmel-1

Pmel-1 + syst. IL15Sa/21

IL15Sa/21 NP conj. Pmel-1
Summary

This strategy does not require cell preconditioning and complements traditional genetic engineering approaches to augment or reprogram cell function.

We have devised a facile and generalizable strategy to robustly augment the therapeutic potential of cytoreagents.

Adjuvant agent-releasing NPs can be retained on the cell surface, follow the characteristic in vivo migration pattern of their cellular vehicle, and endow them with substantially enhanced effector functions using low doses that have no effect when given systemically.
Thanks to:
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