Peptide Functionalized Enhanced Lipid Nanoparticles Dendritic Cells Inducing Memory T Cell Response

*Peeter Graham-Vilo[a,b], Daniel Fernandez Ruiz[b,c] and Pall Thordarson[*a,b]*

[a]School of Chemistry, The University of New South Wales, Sydney, NNSW 2052, Australia
[b]UNSW RNA Institute, The University of New Sout Wales, NSW 2025, Australiac
[c]School of Biomedical Sciences, The University of New South Wales, NSW 2052, Australia
p.grahamvilo@student.unsw.edu.au; p.thordarson@unsw.edu.au

Dendritic Cells (DCs) are the most effective immune cells in our biological systems, regulating both adaptive and innate immune systems and are considered central components in promoting anti-tumour T-cell response. With their high expression of membrane and cytosolic receptors that identify different types of danger signals, including pathogens and tumour cells.[1] With RNA therapies being worldwide interest with the COVID-19 mRNA vaccine, lipid nanoparticles (LNP) are emerging as an ideal candidate for immunotherapy, with its enhanced pharmacodynamics and pharmacokinetics and lower side effects compared to other cancer therapies. These properties are further enhanced with a peptide functionalized bioconjugates with the well-known click chemistry of thiol-maleimide Michael type addition or the Strain-promoted alkyne-azide cycloaddition reactions.[2] This increases stability, immunogenicity, targeting specificity and intracellular uptake over antibody bioconjugates.

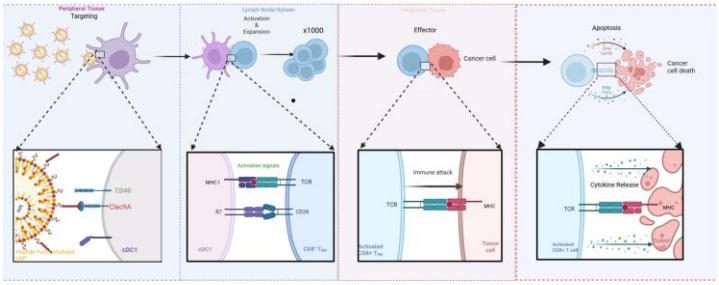

Figure 1 Schematic illustration of conjugation of functionalized peptide to LNP Targeting DC allowing T cell activation and expansion of effector T cells with the ability toward cancer cell apoptosis

This study investigates targeting DC's endosomal receptor types found of DCs; with C-type lectin receptor Clec9a,[3] and tumour necrosis receptor (TNF) CD40[4] with a functionalised peptide that have been reported to exhibit high binding affinity towards there targeted receptor, and bioconjugate to mRNA LNPs for delivery to possibly further promote effector T cells and induce tissue resident memory T cells (T_{RM}). This will be determined via OT1 express cells injeced in mice followed by the injection of CpG ODN with peptide functionalized mRNA LNP. On days 7 and 28 the mice spleen and liver with be analysed for T effector cells and T memory cells respectively.

References:

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(2) Martínez-Jothar, F.;*Journal of Controlled Release* **2018**, *282*, 101-109.
(3) Gou, S.;et al. *Theranostics* **2021**, *11* (15), 7308-7321.
(4) Mamuti, M.; et al. *Adv Mater* **2022**, *34* (24), e2109432.