

Triazine lipids as a platform for subunit vaccine development

Kaysi M. Lee, PhD Candidate
The Venditto Lab
University of Kentucky
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Subunit vaccines are a safe and targeted approach to immunity

Subunit Vaccines: use of *recombinant proteins, peptides, or polysaccharides* to induce immunity

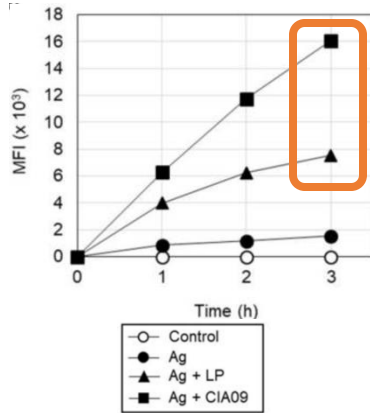
Examples: Novavax (COVID-19), GARDASIL 9 (HPV), and RECOMBIVAX HB (Hepatitis B)

Can require an adjuvant for long-term protection

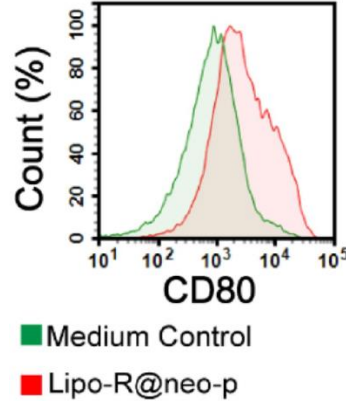
Office of Infectious Disease and HIV/AIDS Policy, 2022 – Package Inserts via FDA, 2024, 2014, 2018 – CDC 2024

Liposomes are a versatile tool for subunit vaccines

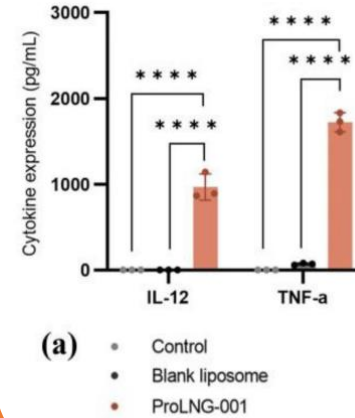
1. Antigen Uptake



2. DC Maturation

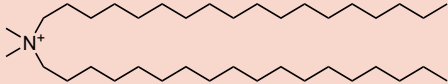
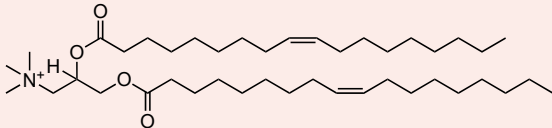
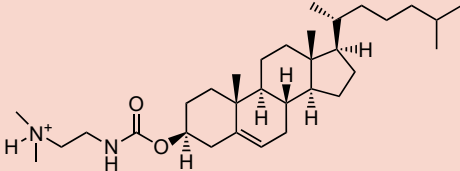


3. Cytokine Production

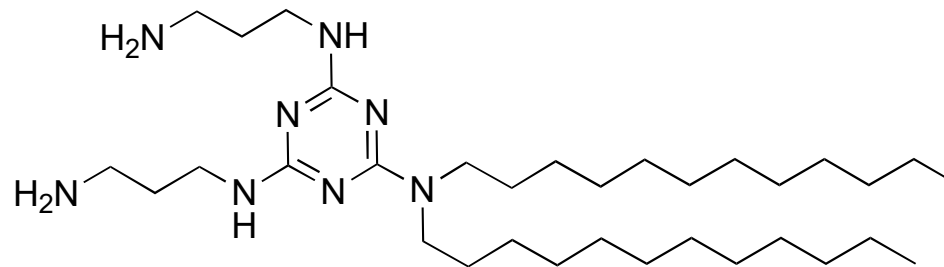


Wui, Seo Ri et al., *Pharmaceutics*, 2021 – Shi, L. and Gu. H, *Nanomedicine: Nanotechnology, Biology, and Medicine*, 2023 – Kim, S. et al. *Vaccines*, 2023

Cationic lipids used in subunit vaccines

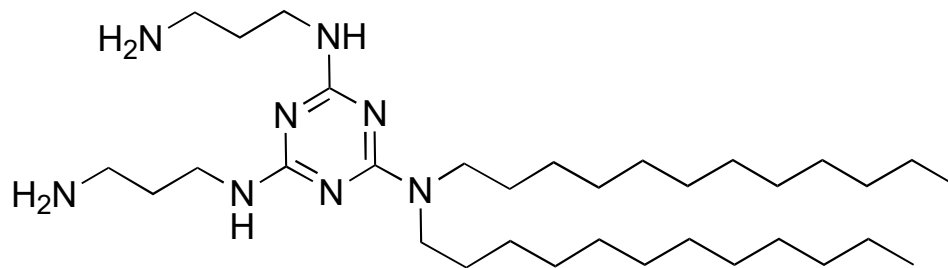
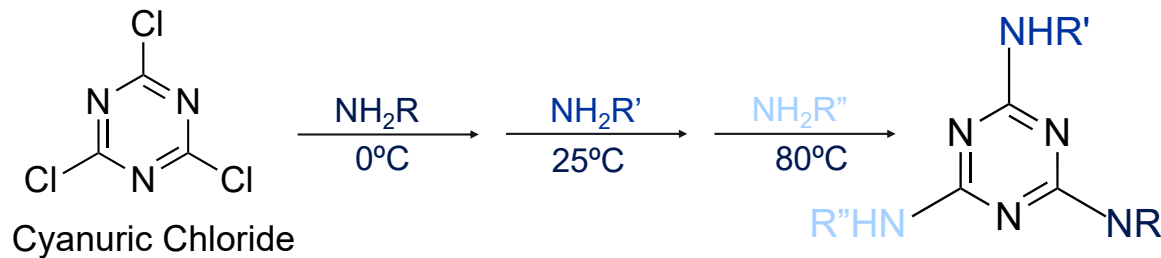
Name	Structure
DDA (Dimethyldioctadecylammonium)	
DOTAP (1,2-dioleoyl-3-trimethylammonium-propane)	
DC-Chol (3β-[N-(N',N'-dimethylaminoethane)-carbamoyl]cholesterol)	
DOTMA (1,2-di-O-octadecenyl-3-trimethylammonium propane)	

Henriksen-Lacey, M. et al, *Molecular Pharmaceutics*, 2010 – Anderluzzi, G. et al *Journal of Control release*, 2021 – Vangasseri, D.P. et al *Molecular Membrane Biology*, 2005



Nardo et al. *RSC Advances*, 2021 – Nardo et al. *Biomaterial Sciences*, 2022

Cyanuric chloride has thermally controlled chemo-selective reactivity



TZ3

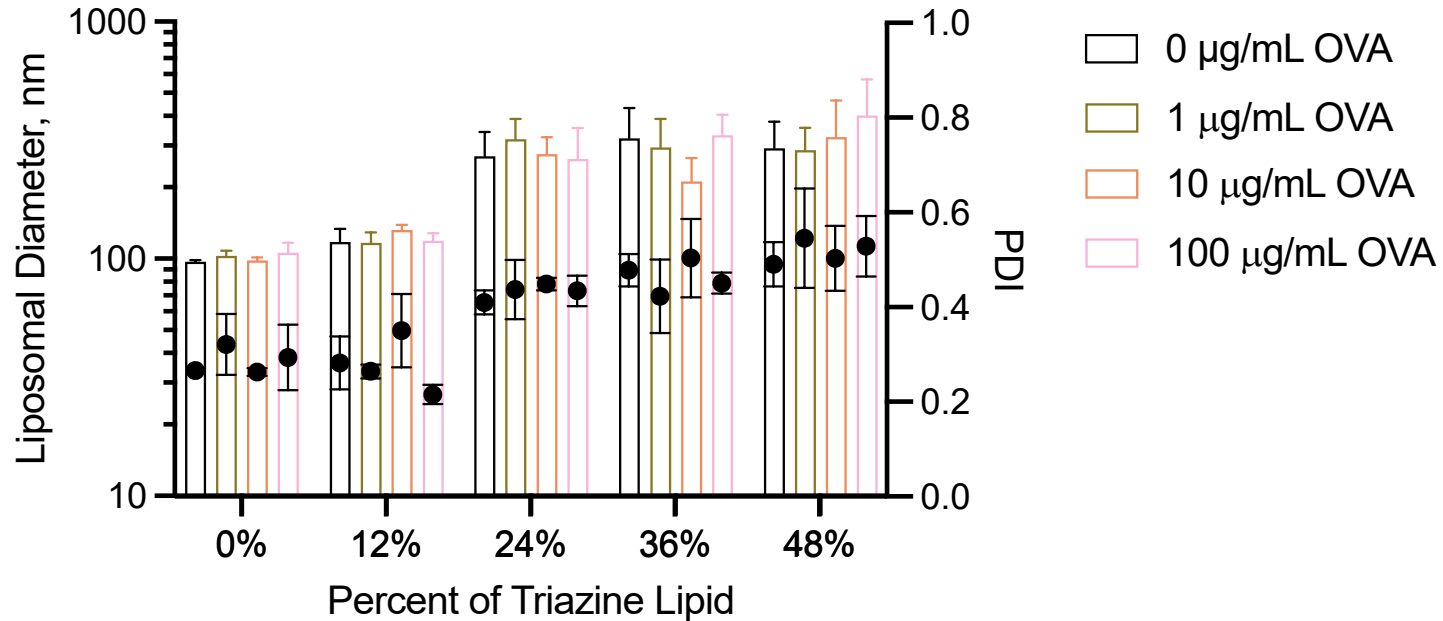
Julian Mory
Poster #131

Nardo et al. *RSC Advances*, 2021 – Nardo et al. *Biomaterial Sciences*, 2022

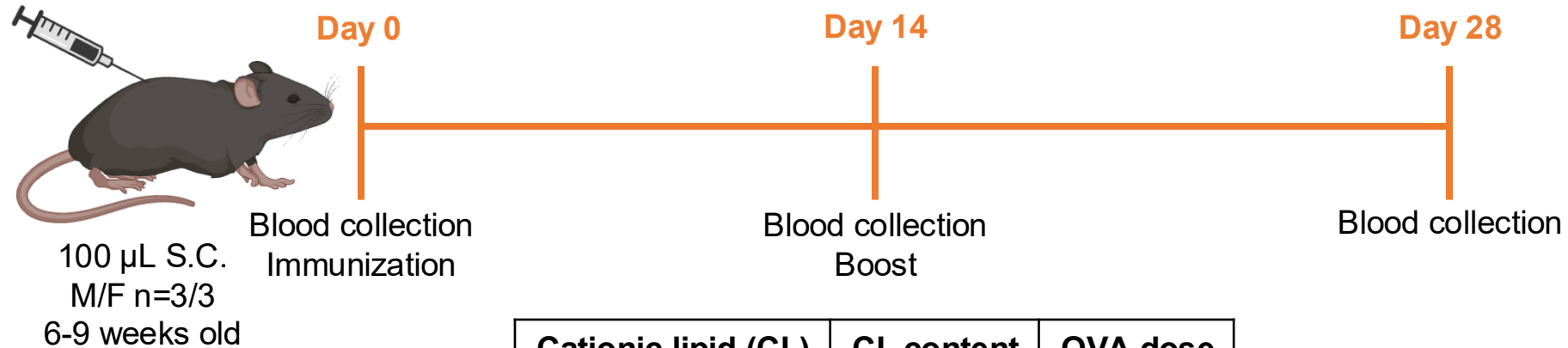
Formulating TZ3 liposomes

	Molar Ratio of Lipids			
Label	TZ3	DOPC	Cholesterol	DSPE-PEG2000
0%	0	60	39	1
12%	12	48	39	1
24%	24	36	39	1
36%	36	24	39	1
48%	48	12	39	1

OVA does not affect the stability of the formulation as an admixture

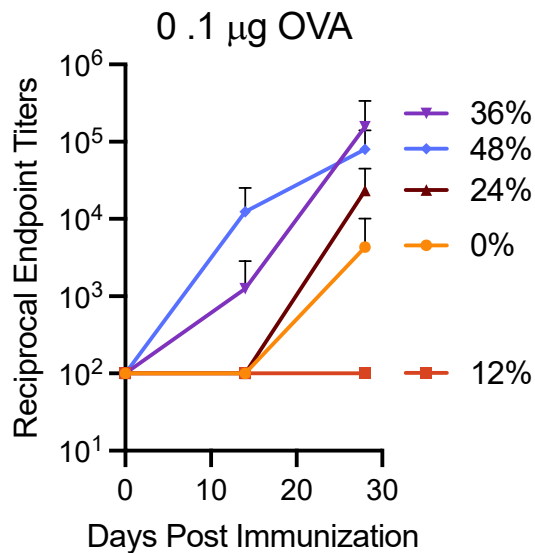


In vivo assessment of formulations

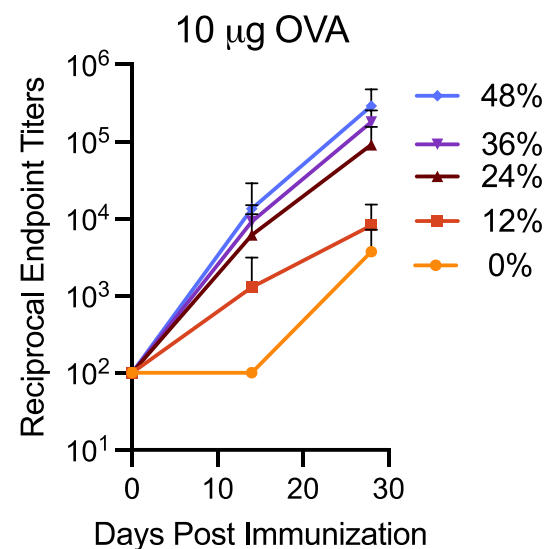
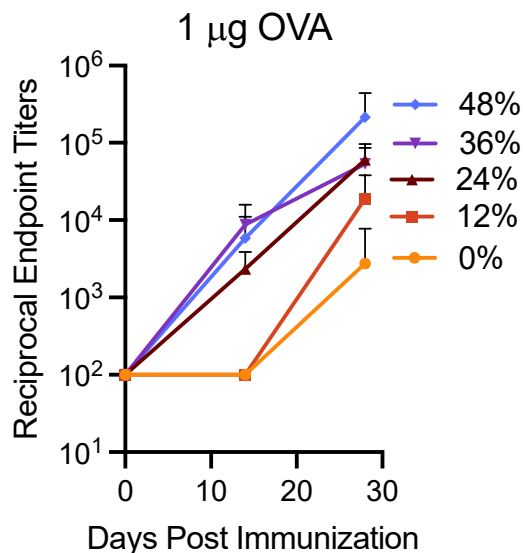
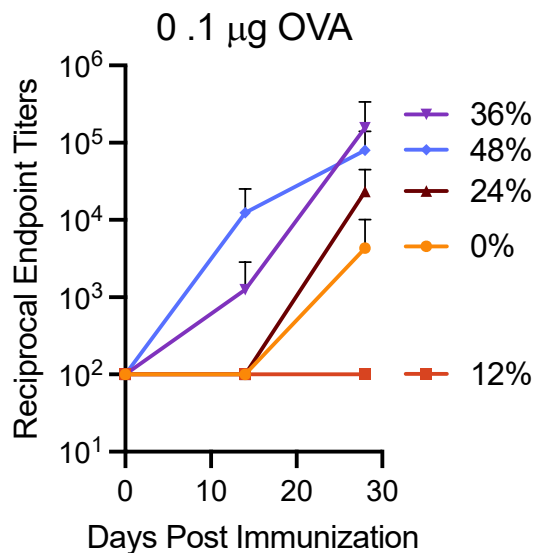


Cationic lipid (CL)	CL content	OVA dose
TZ3	0%	0.1 μ g
	12%	1 μ g
	24%	10 μ g
DOTAP	36%	0.1 μ g
	48%	

TZ3 induces robust OVA-specific IgG titers

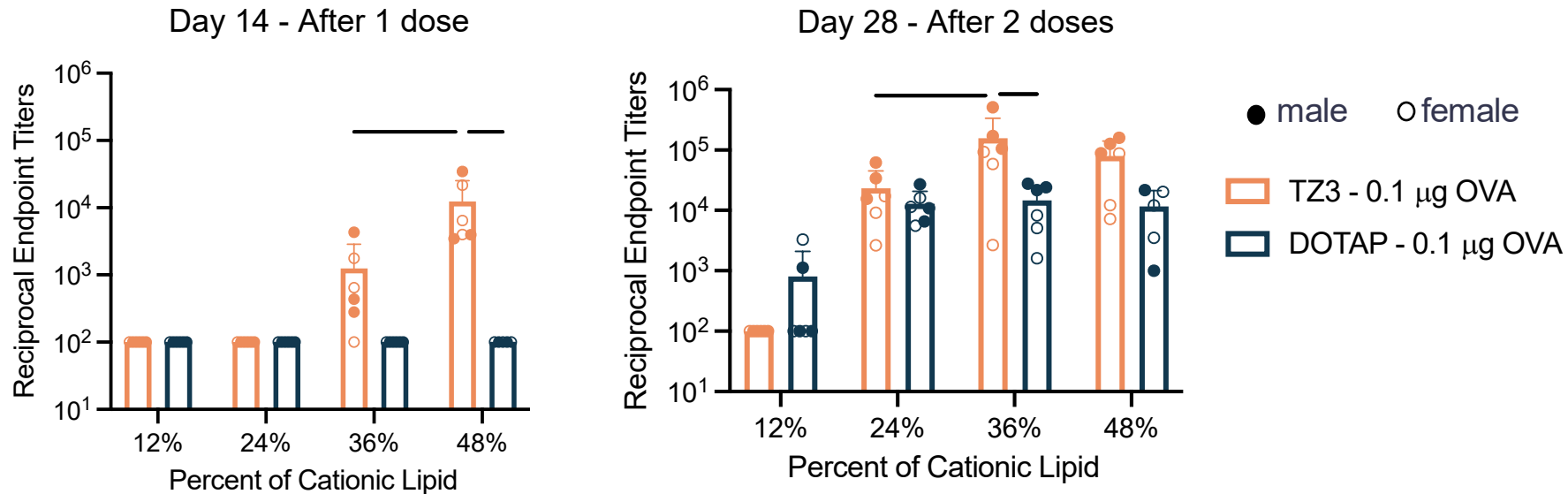


TZ3 induces robust OVA-specific IgG titers



Immune response influenced by TZ3 content and OVA dose

TZ3 exhibits a higher immune response than DOTAP



Two-Way ANOVA with Tukey * $p < 0.05$, ** $p < 0.01$

Triazine lipids offer a versatile platform for subunit vaccine development

TZ3-based formulations are stable with and without antigen
TZ3-based formulations induce a robust immune response in mice

Ongoing and Future Studies

- In vitro cellular uptake and liposomal trafficking of the formulations
- In vivo memory and subclass immunity
- Applications to clinically relevant models

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Kaysi M. Lee

Thank you!



University of Kentucky –
College of Pharmacy



KaysiMLee@uky.edu



www.linkedin.com/in/KaysiMLee