

# Nanomedicine and Nanoscale Delivery

Professor Khuloud Al-Jamal

**CRS 2022 Annual Meeting & Expo**

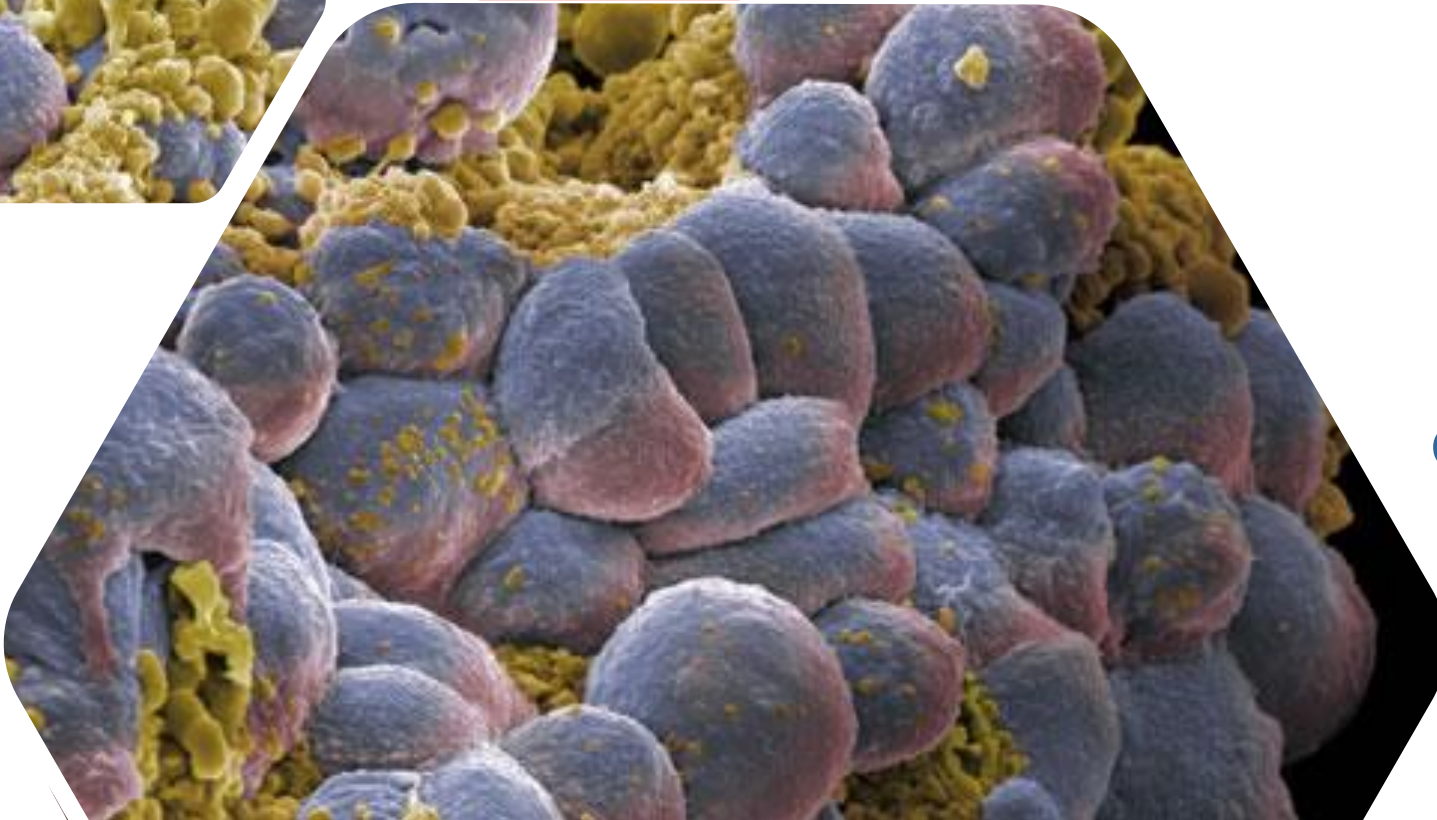
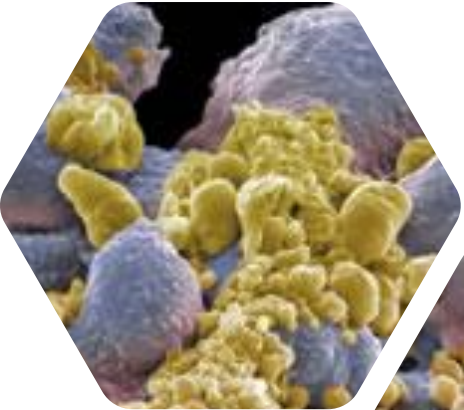
July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

***Advanced Delivery Science***





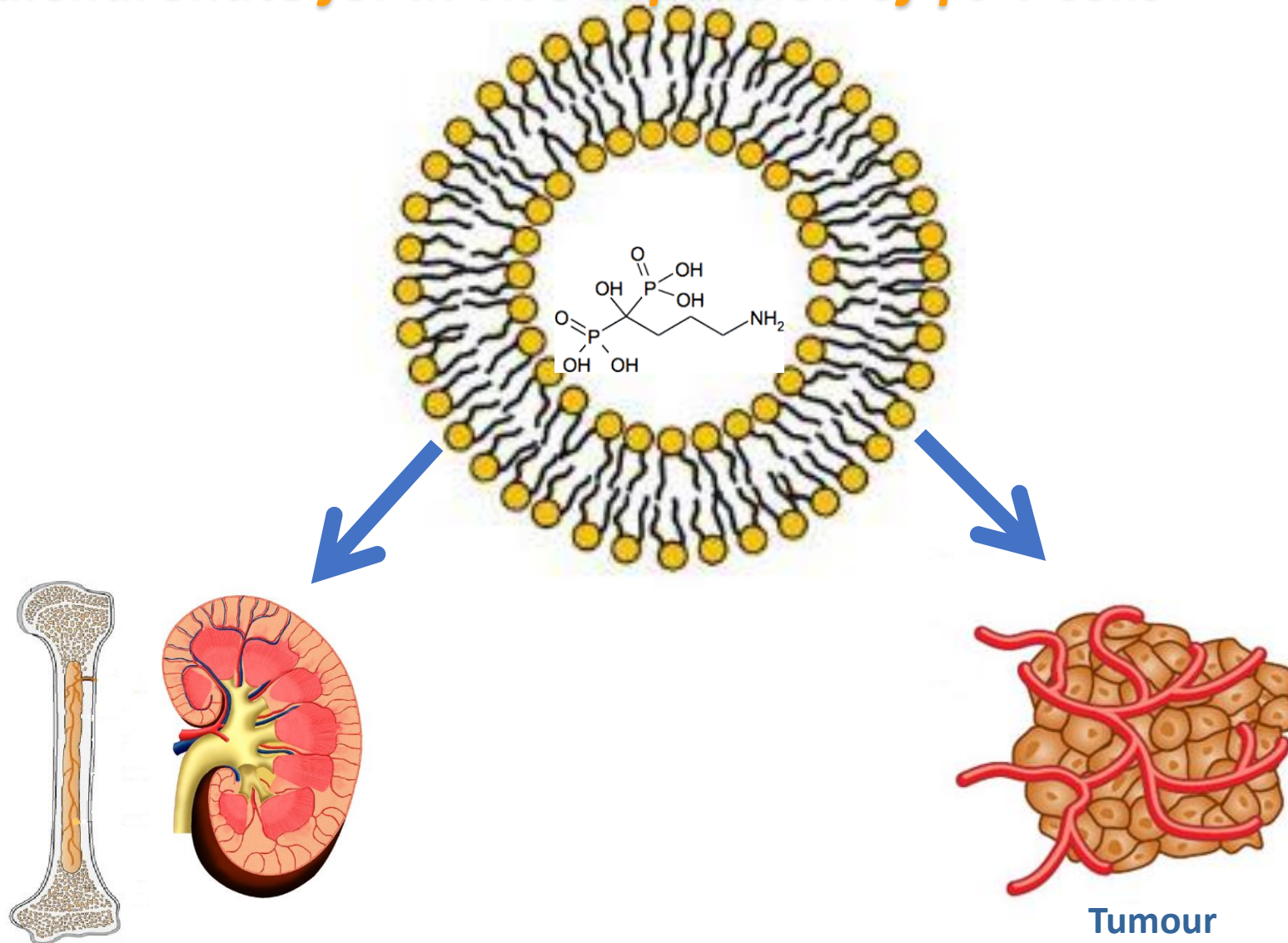
# *Nanoparticle Mediated in Situ Molecular Reprogramming of Immune Checkpoint Interactions for Cancer Immunotherapy*



Khuloud Al-Jamal FRSC,  
BSc, PhD, PGCAP, MRPharmS  
Chair in Drug Delivery & Nanomedicine  
Head of Medicines Development  
Cancer Theme Lead  
Institute of Pharmaceutical Science  
King's College London

# Chemo-immunotherapy

## *Liposomal alendronate for in vivo expansion of $\gamma\delta$ T cells*



2012

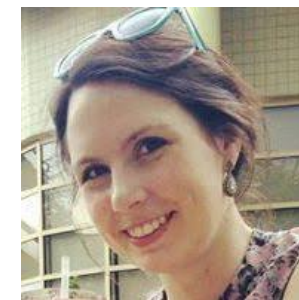


# 2016

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

## Journal of Controlled Release

journal homepage: [www.elsevier.com/locate/jconrel](http://www.elsevier.com/locate/jconrel)



### *In vitro* potency, *in vitro* and *in vivo* efficacy of liposomal alendronate in combination with $\gamma\delta$ T cell immunotherapy in mice

Naomi O. Hodgins<sup>a</sup>, Wafa' T. Al-Jamal<sup>b</sup>, Julie T-W. Wang<sup>a</sup>, Ana C. Parente-Pereira<sup>c</sup>, Mao Liu<sup>a</sup>, John Maher<sup>c,\*</sup>, Khuloud T. Al-Jamal<sup>a,\*</sup>

# 2020

## Nanotheranostics

2020; 4(2): 71-82. doi: 10.7150/ntno.32876

Research Paper

### Organ Biodistribution of Radiolabelled $\gamma\delta$ T Cells Following Liposomal Alendronate Administration in Different Mouse Tumour Models

Julie T-W. Wang<sup>1,\*</sup>, Naomi O. Hodgins<sup>1\*</sup>, Wafa' T. Al-Jamal<sup>2</sup>, John Maher<sup>1</sup>, Jane K. Sosabowski<sup>3</sup> and Khuloud T. Al-Jamal<sup>1</sup>



# 2017

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

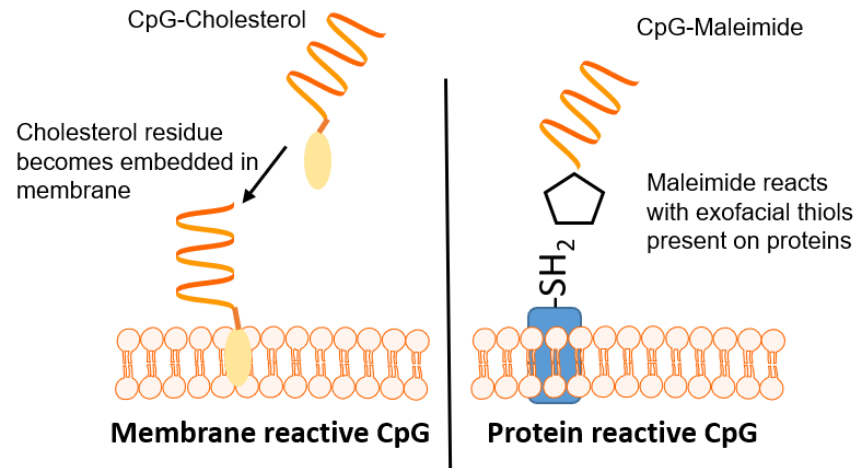
## Journal of Controlled Release

journal homepage: [www.elsevier.com/locate/jconrel](http://www.elsevier.com/locate/jconrel)

### Investigating *in vitro* and *in vivo* $\alpha\beta6$ integrin receptor-targeting liposomal alendronate for combinatory $\gamma\delta$ T cell immunotherapy

Naomi O. Hodgins<sup>a</sup>, Wafa' T. Al-Jamal<sup>b</sup>, Julie T.-W. Wang<sup>a</sup>, Rebecca Klippstein<sup>a</sup>, Pedro M. Costa<sup>a</sup>, Jane K. Sosabowski<sup>c</sup>, John F. Marshall<sup>d</sup>, John Maher<sup>e</sup>, Khuloud T. Al-Jamal<sup>a,\*</sup>

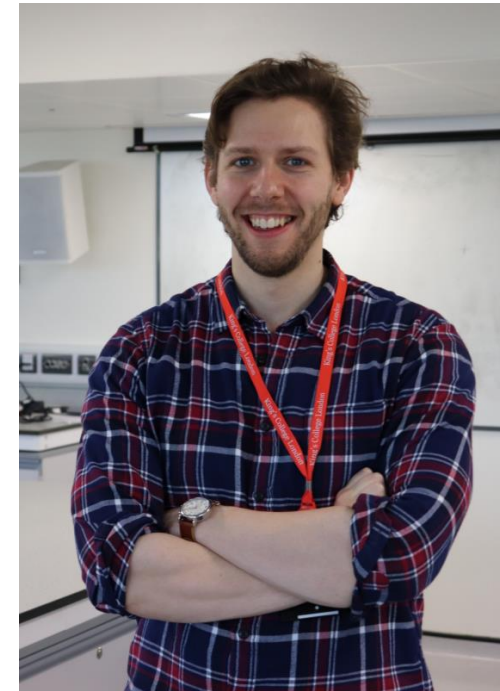
## Immune adjuvants/ICD drugs combinatory therapy



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

**Journal of Controlled Release**

journal homepage: [www.elsevier.com/locate/jconrel](http://www.elsevier.com/locate/jconrel)

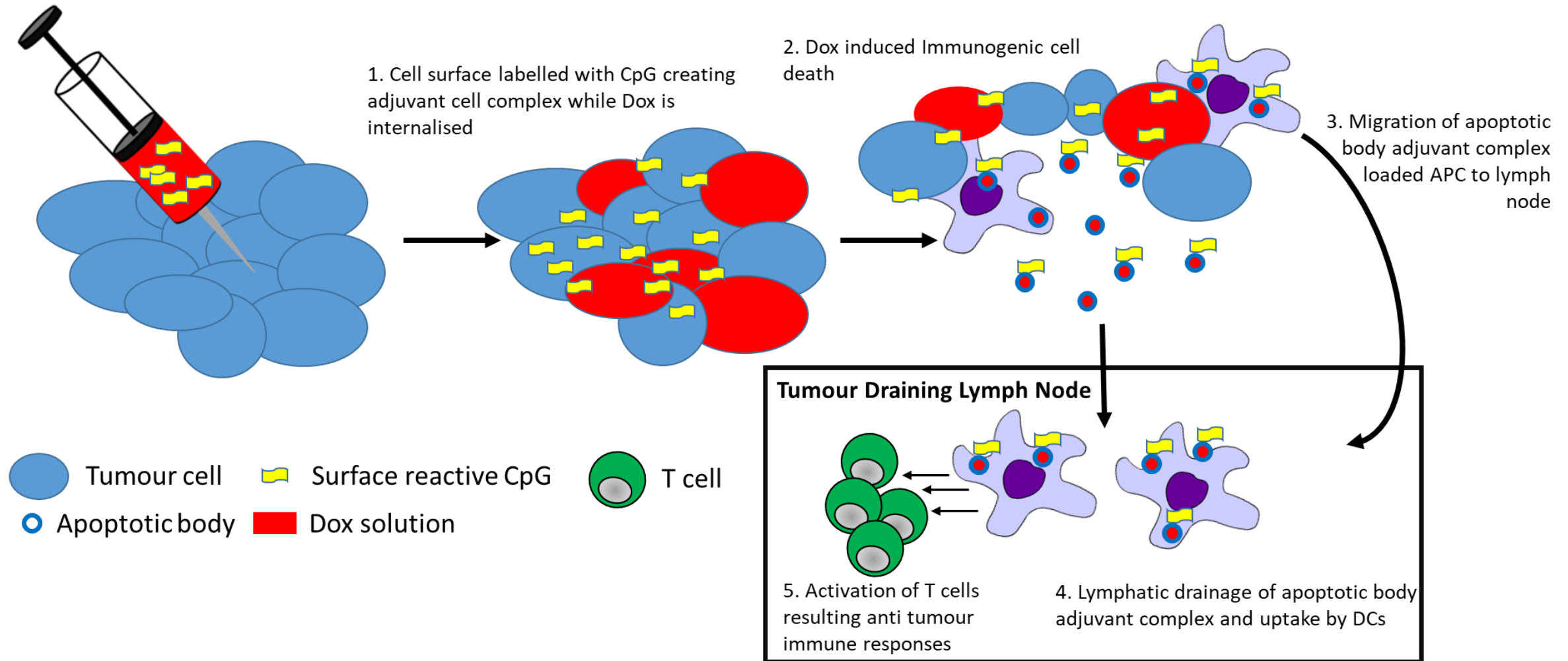


Evaluation of cell surface reactive immuno-adjuvant in combination with immunogenic cell death inducing drug for in situ chemo-immunotherapy

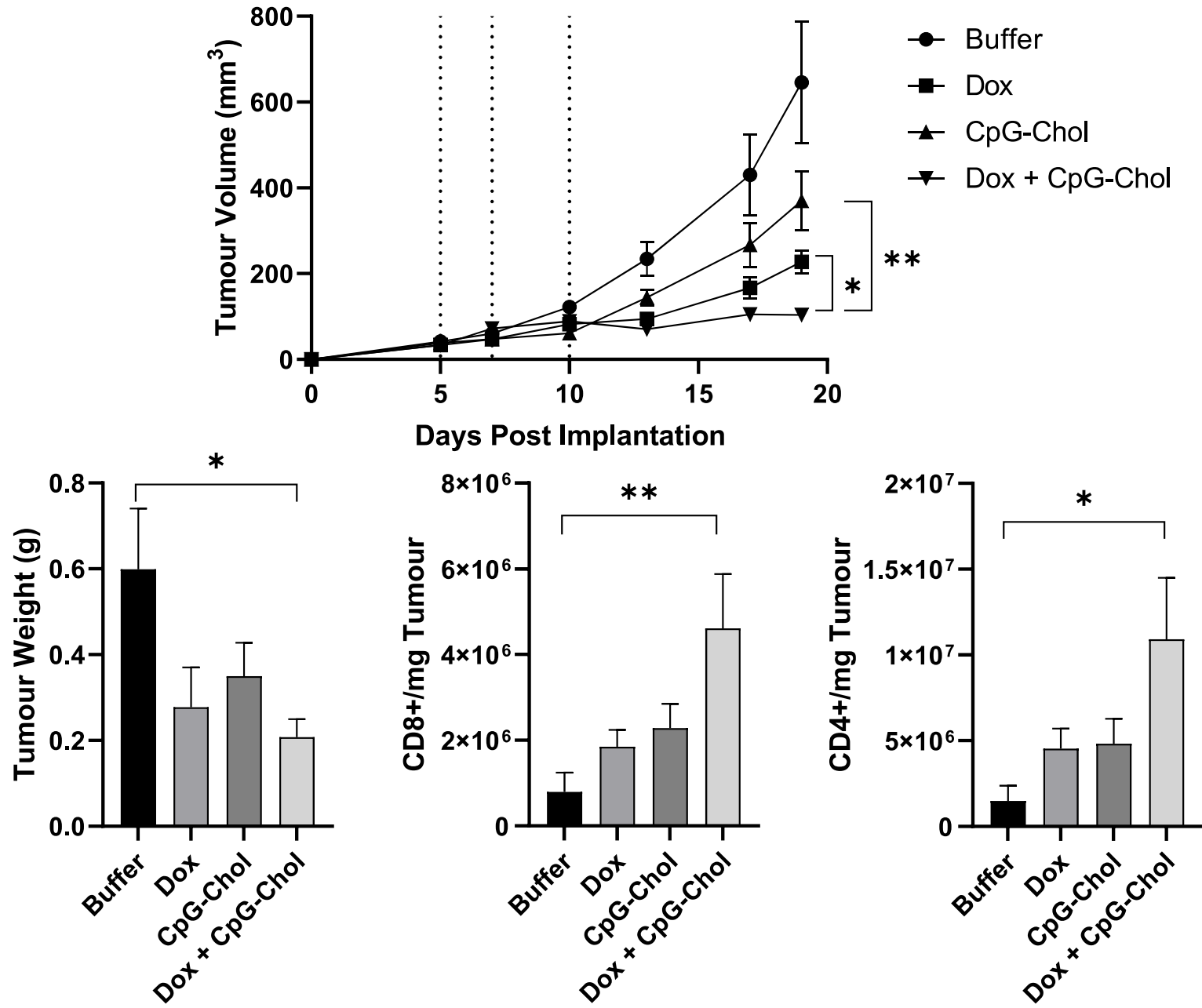
Adam A. Walters\*, Julie Tzu-Wen Wang, Khuloud T. Al-Jamal\*



# Chemo-immunotherapy



# Results: *In vivo* therapy in CT26 mouse model

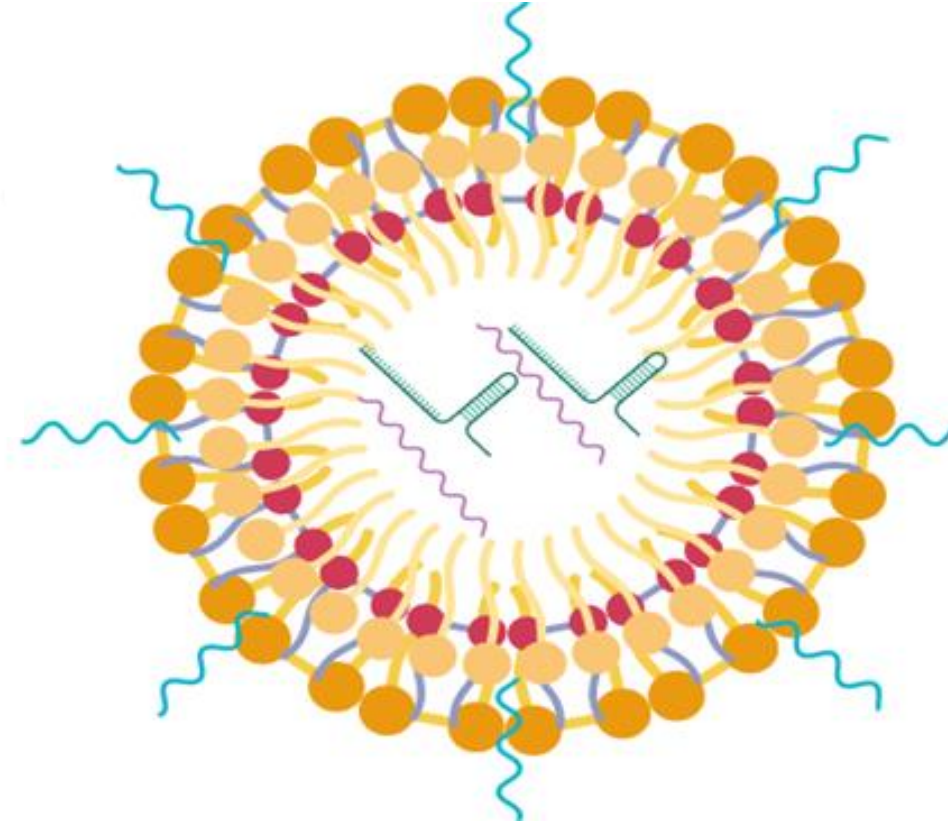


# Stable Nucleic Acid Lipid Nanoparticles (SNALPs)

FDA NEWS RELEASE

## FDA approves first-of-its kind targeted RNA-based therapy to treat a rare disease

For Immediate Release: August 10, 2018



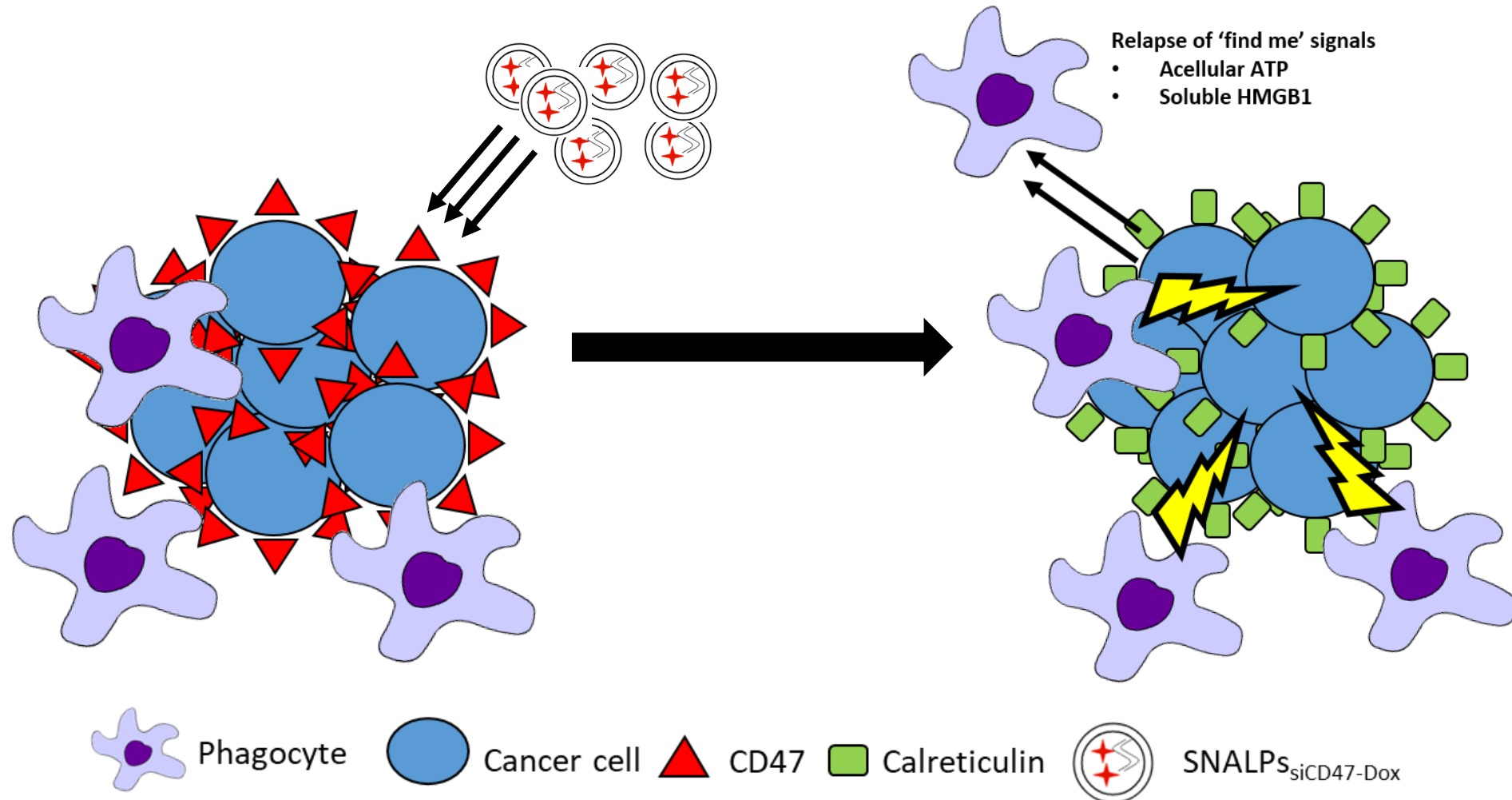
The BioNTech, Fosun Pharma, Pfizer vaccine is a vaccine that aims to protect against COVID-19 was approved for emergency use in UK in Dec 2020.



## An “eat me” combinatory nano-formulation for systemic immunotherapy of solid tumors

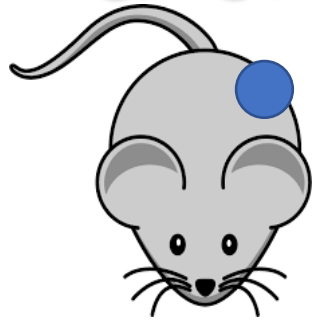
Hend Mohamed Abdel-Bar<sup>1,2#</sup>, Adam A Walters<sup>1#</sup>, Yau Lim<sup>1</sup>, Nadia Rouatbi<sup>1</sup>, Yue Qin<sup>1</sup>, Fatemeh Gheidari<sup>1</sup>, Shunping Han<sup>1</sup>, Rihab Osman<sup>3</sup>, Julie Tzu-Wen Wang<sup>1</sup>, Khuloud T. Al-Jamal<sup>1</sup>✉

# Hypothesis and aims



# Results: In vivo therapy

IV, Dox 5mg/Kg , siRNA 100µg/Kg, 2 injections

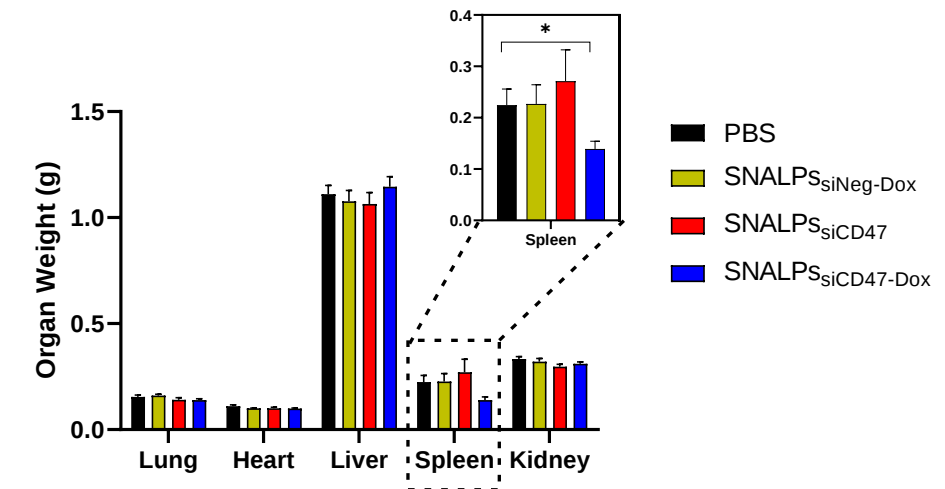
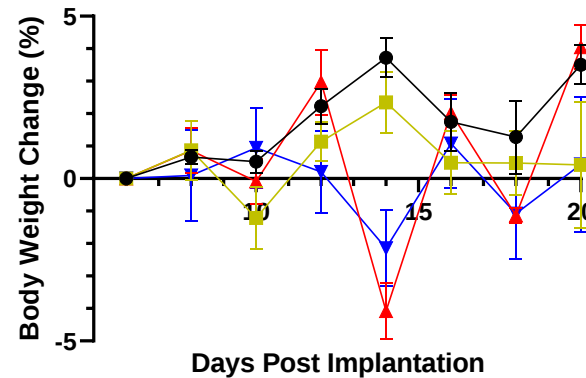
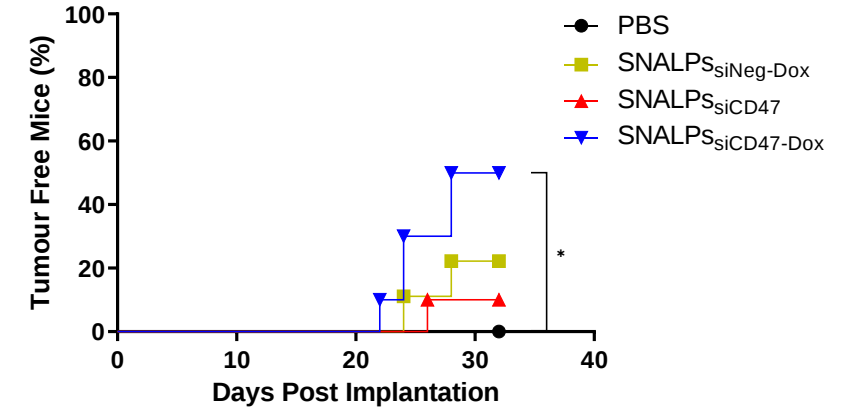
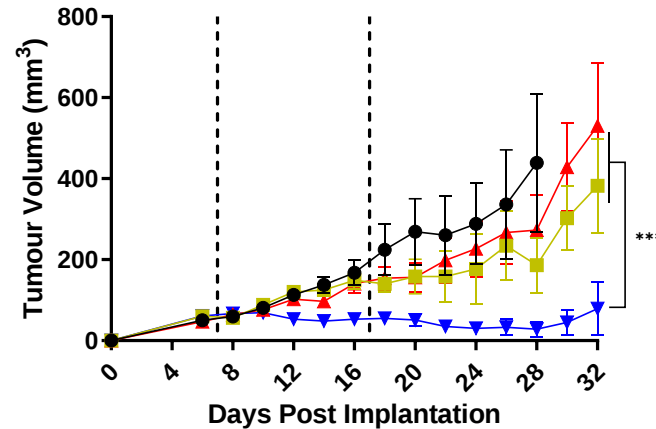


Days 7, 17 (i.v. Injection)

1. PBS
2. SNALPs Negative siRNA+DOX (SNALPs<sub>siNEG-Dox</sub>)
3. SNALPs siCD47 (SNALPs<sub>siCD47</sub>)
4. SNALPs siCD47+DOX (SNALPs<sub>siCD47+DOX</sub>)

Day 32 (or 15 mm diameter)

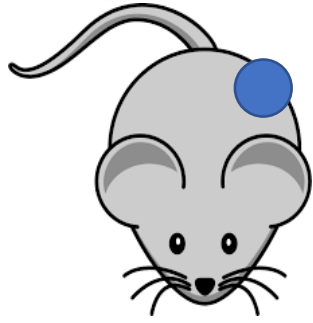
- Tumour volume
- Tumour-free mice number
- Weight changes
- Organ index
- CD47 expression



➤ siCD47-DOX SNALPs significantly reduce tumour growth and leads to remission in 50% mice

# Results: *In vivo* immunogenicity

## Localised/systemic immune response



Days 7, 17 (i.v. Injection)

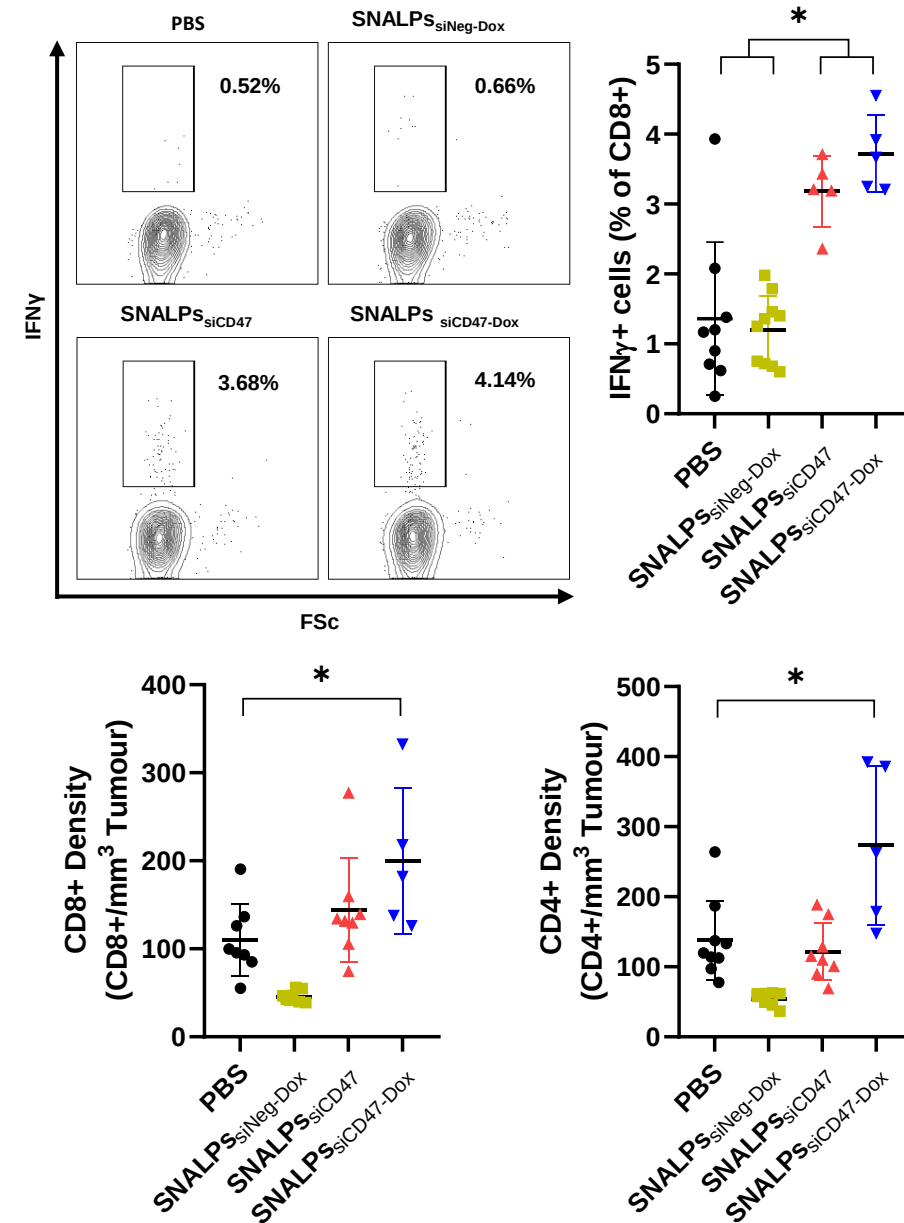


1. PBS
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3. SNALPs siCD47 (SNALPs<sub>siCD47</sub>)
4. SNALPs siCD47+DOX (SNALPs<sub>siCD47+DOX</sub>)

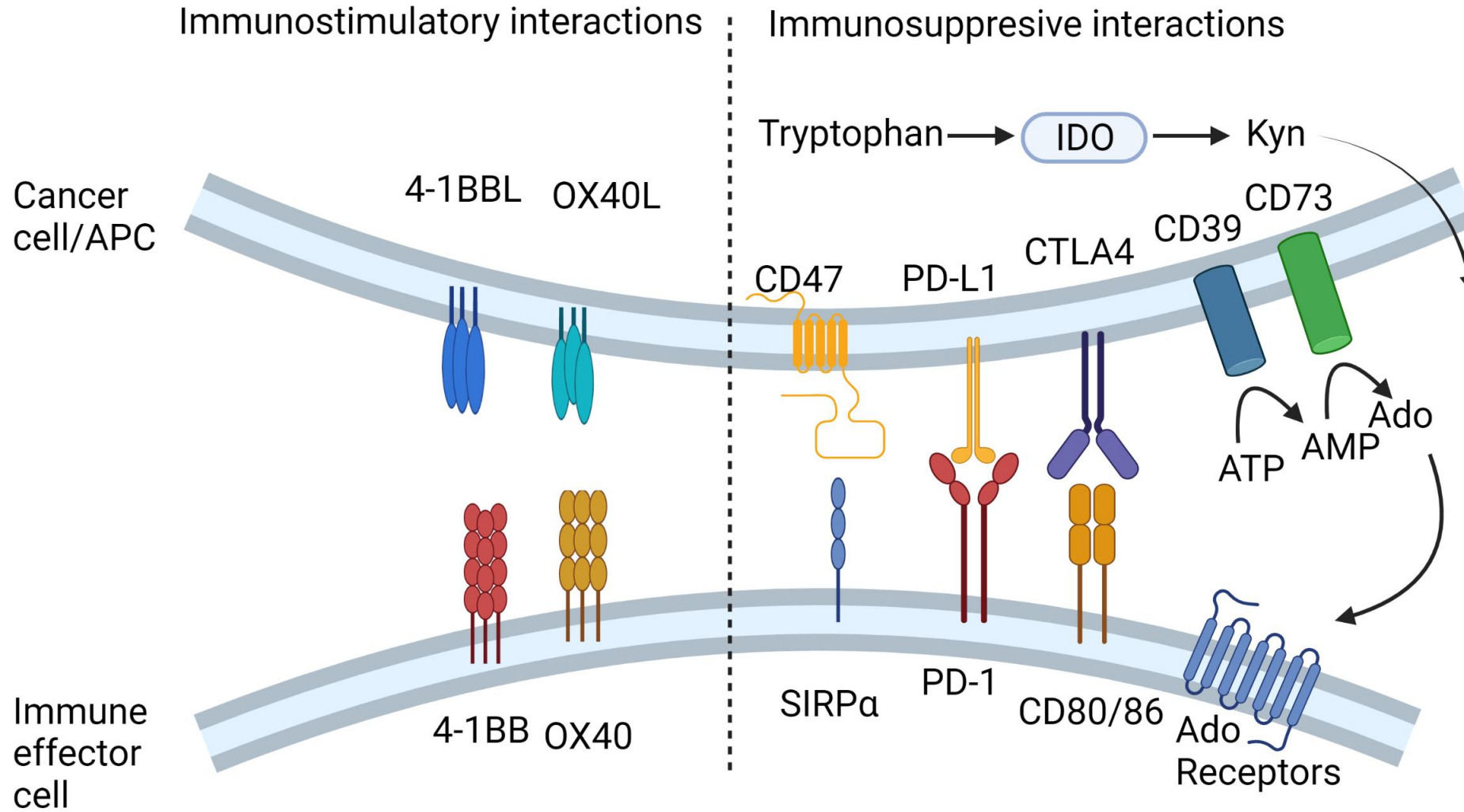
Day 20 (or 15 mm diameter)



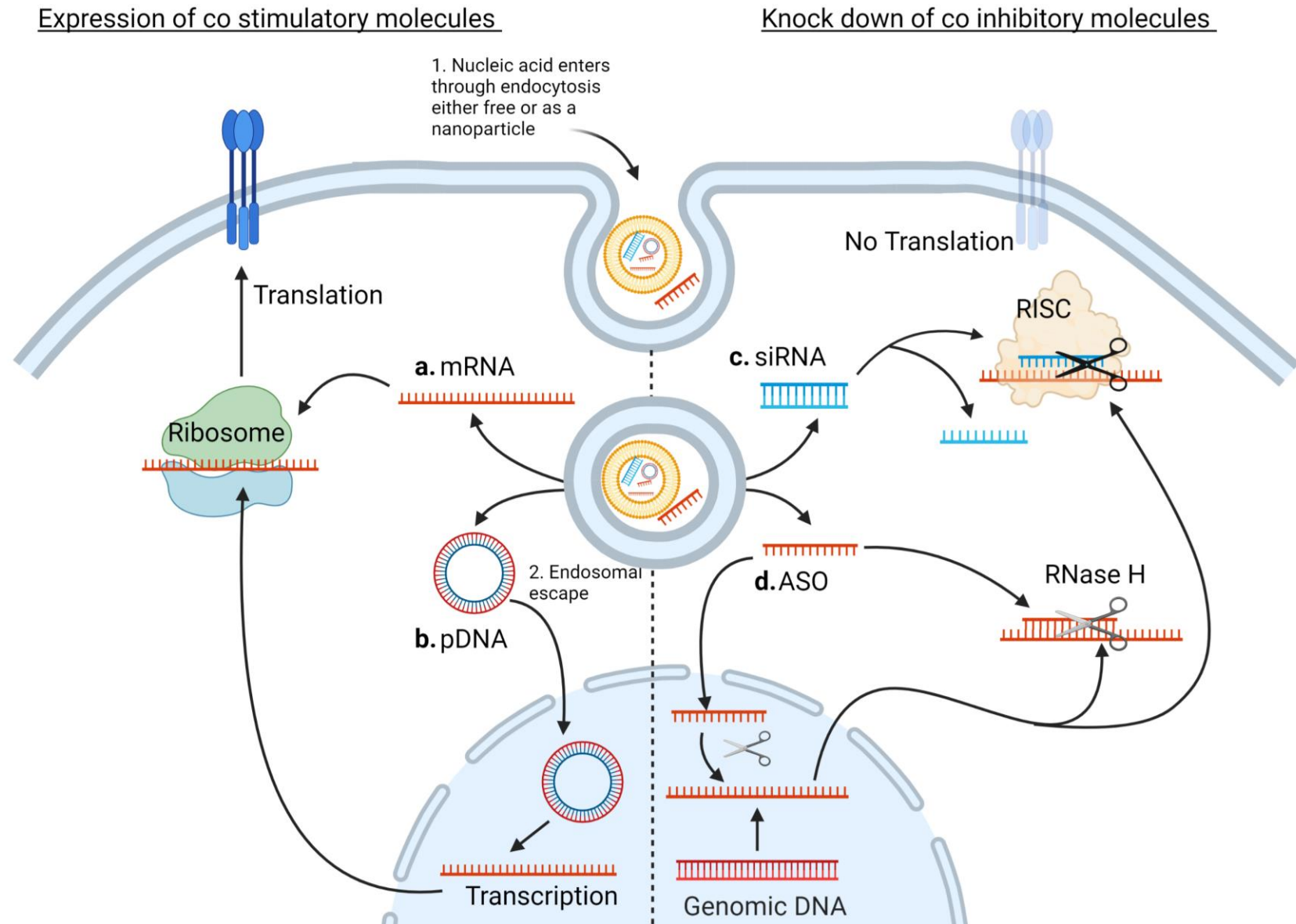
- IFN $\gamma$ + CD8+ cells in spleen (systemic immune response)
- CD4+/CD8+ in tumour microenvironment (localised immune response)



# Inhibitory and stimulatory immune 'checkpoints'



# Nanoparticulate-assisted nucleic acid delivery





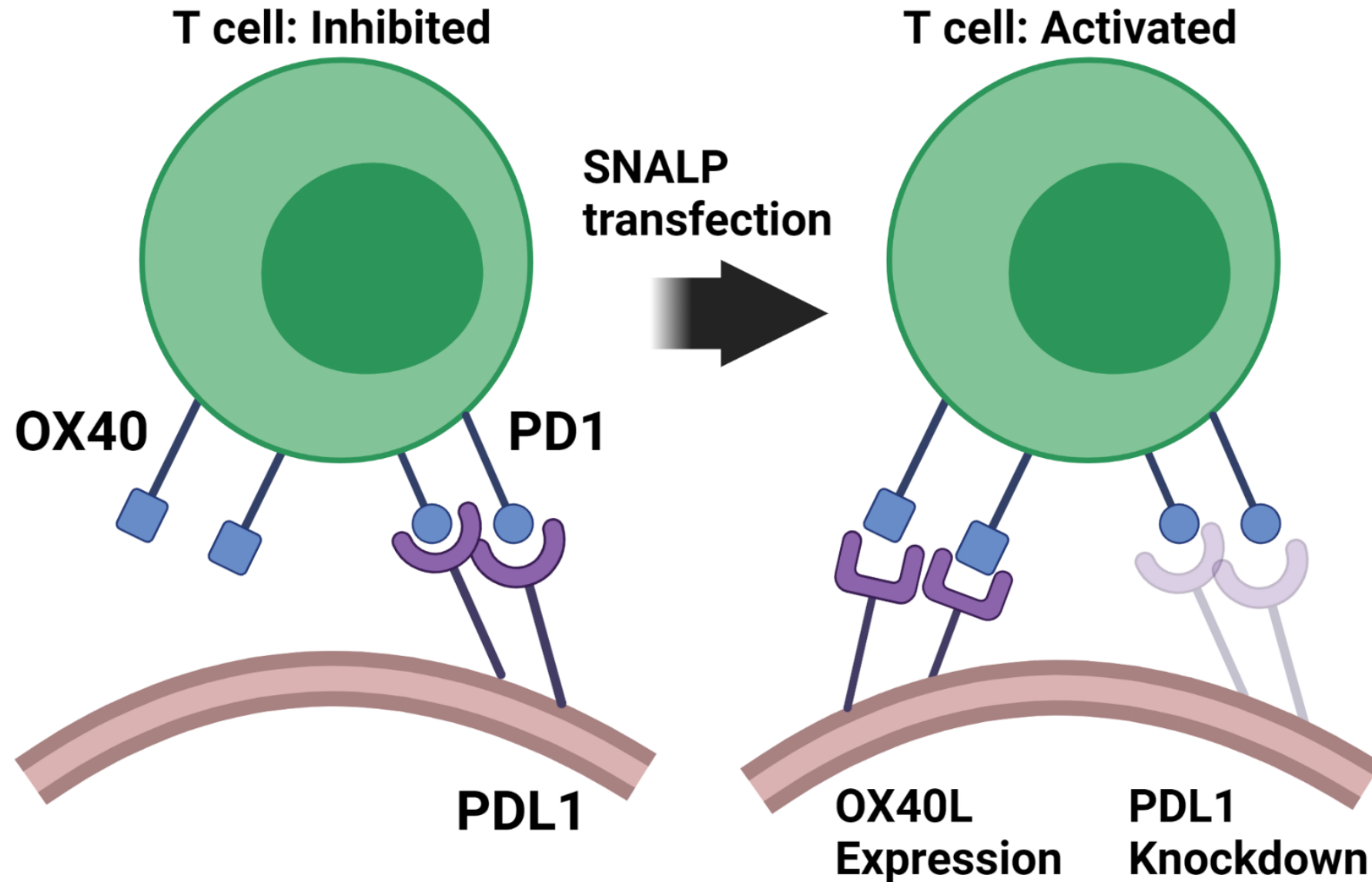
[www.acsnano.org](http://www.acsnano.org)

# Nanoparticle-Mediated *In Situ* Molecular Reprogramming of Immune Checkpoint Interactions for Cancer Immunotherapy

Adam A. Walters,\* Gemma Santacana-Font, Jin Li, Nadia Routabi, Yue Qin, Nathalie Claes, Sara Bals, Julie Tzu-Wen Wang, and Khuloud T. Al-Jamal\*

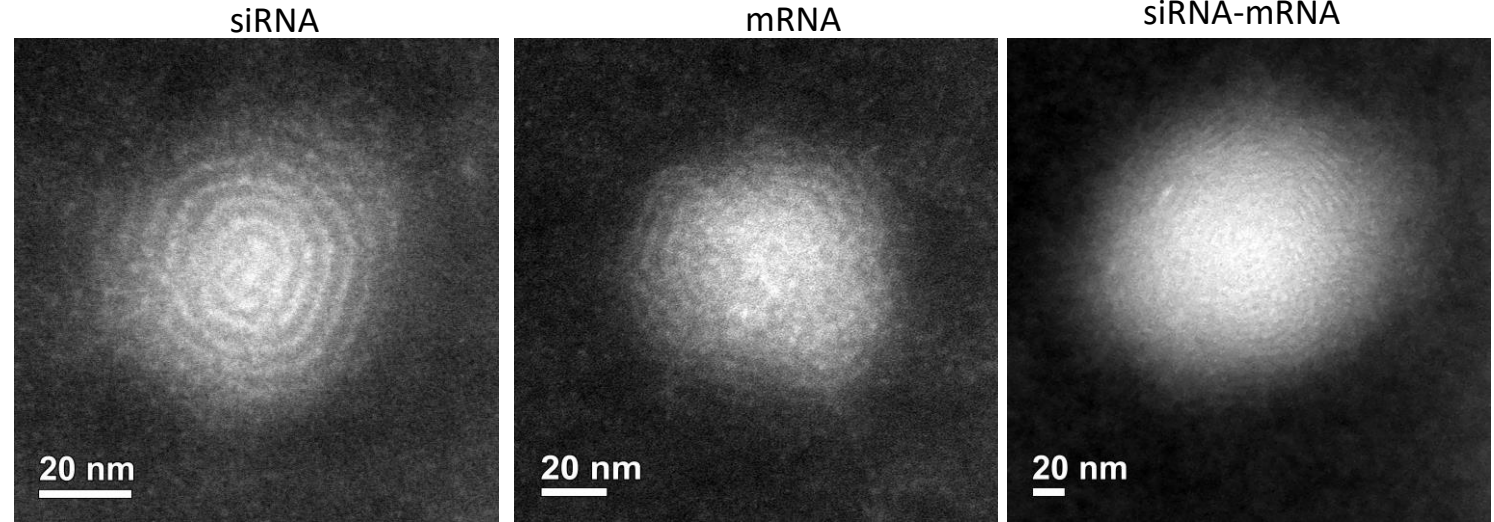
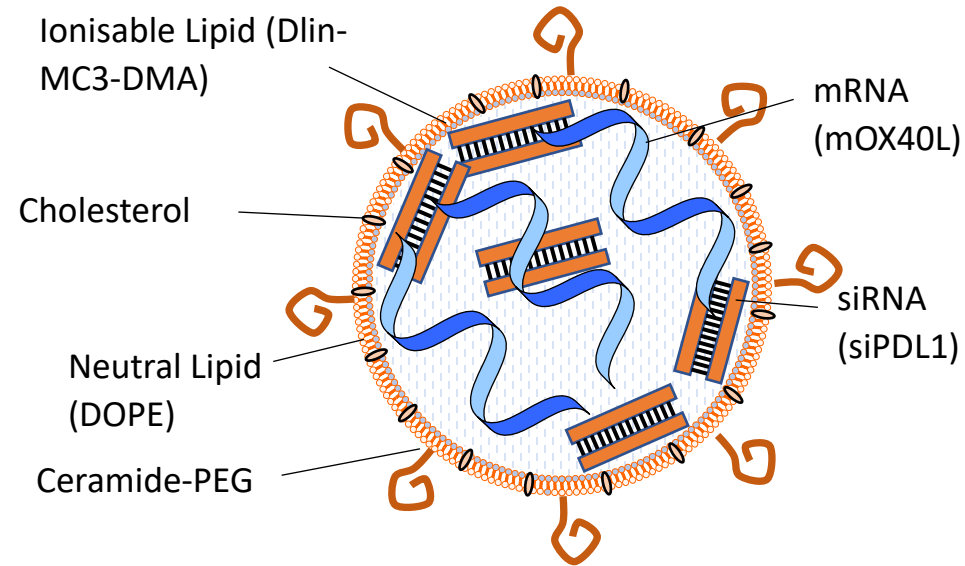


# Hypothesis and aims



# Results: SNALP characterisation

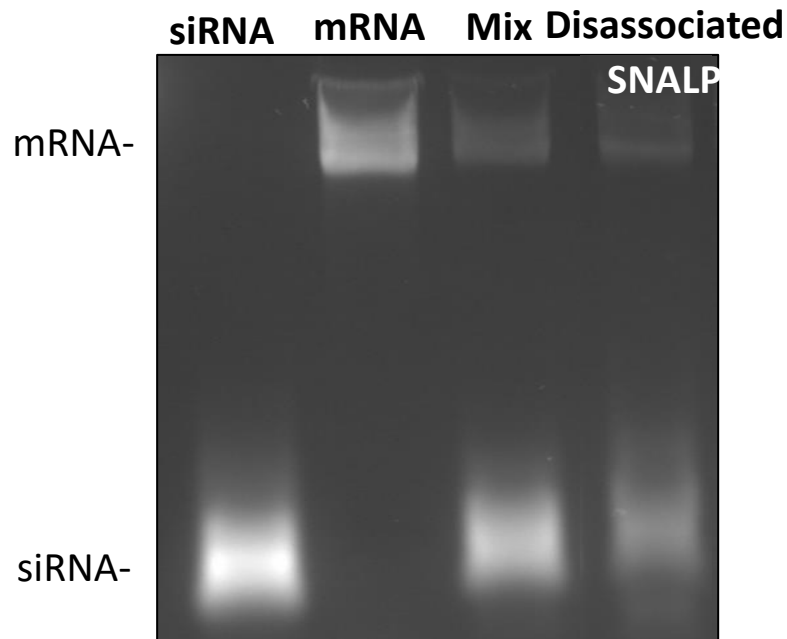
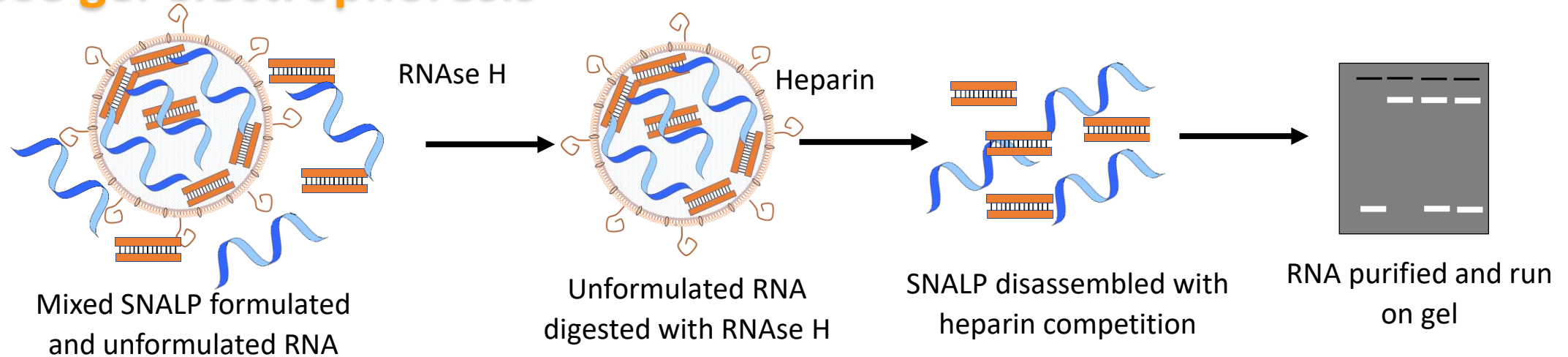
## DLS, TEM, Ribogreen assay



| Type of RNA | Size (d.nm) <sup>a</sup> | PDI <sup>a</sup> | Charge at pH7.4 (mV) <sup>a,b</sup> | Charge at pH4 (mV) <sup>a,c</sup> | EE Loading efficiency (%) <sup>d</sup> |
|-------------|--------------------------|------------------|-------------------------------------|-----------------------------------|----------------------------------------|
| siRNA       | 143.85 ± 2.39            | 0.22 ± 0.02      | +2.39 ± 0.12                        | +16.02 ± 2.31                     | 81.81 ± 5.57                           |
| mRNA        | 144.54 ± 4.22            | 0.19 ± 0.02      | +0.4 ± 3.09                         | +16.58 ± 3.08                     | 87.05 ± 9.37                           |
| mRNA-siRNA  | 149.16 ± 3.06            | 0.22 ± 0.02      | -0.45±0.14                          | +16.53 ± 2.20                     | 93.66 ± 0.59                           |

# Results: SNALP characterisation

## Agarose gel electrophoresis



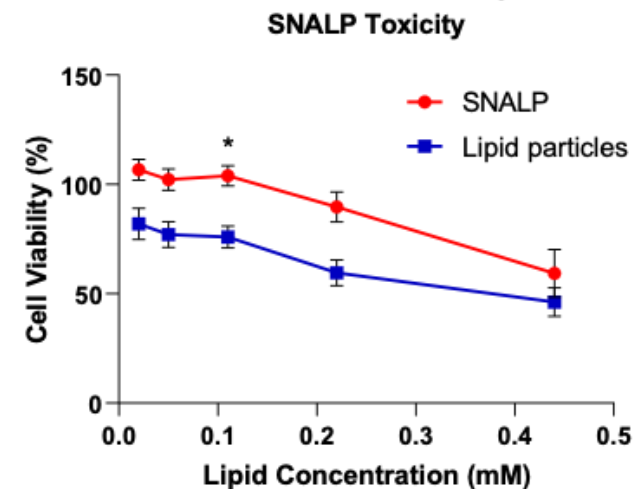
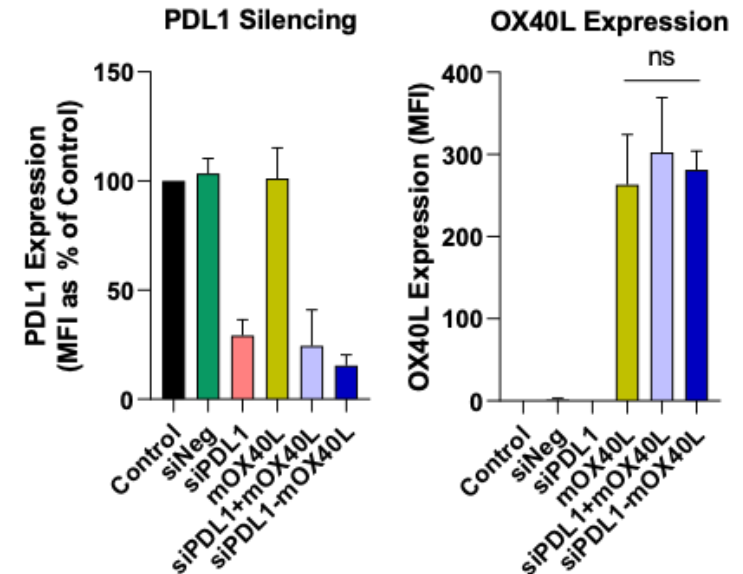
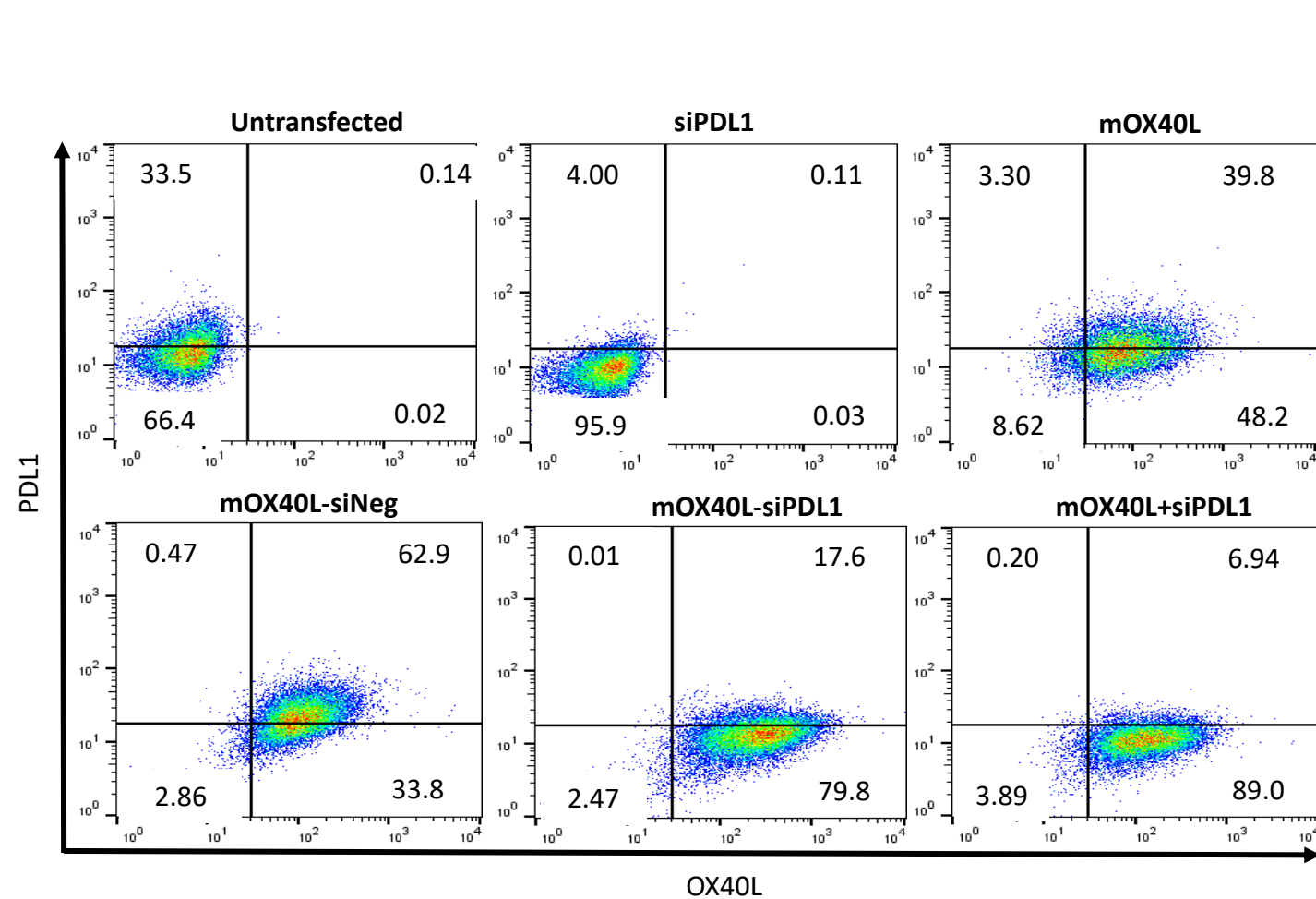
|                              | Mix   | Dissociated SNALP |
|------------------------------|-------|-------------------|
| mRNA Intensity <sup>a</sup>  | 77.9  | 70.9              |
| siRNA Intensity <sup>a</sup> | 154.3 | 115.2             |
| Intensity Ratio <sup>b</sup> | 1.98  | 1.62              |

a: Relative units based on Image J ROI selection

b: siRNA intensity to mRNA intensity

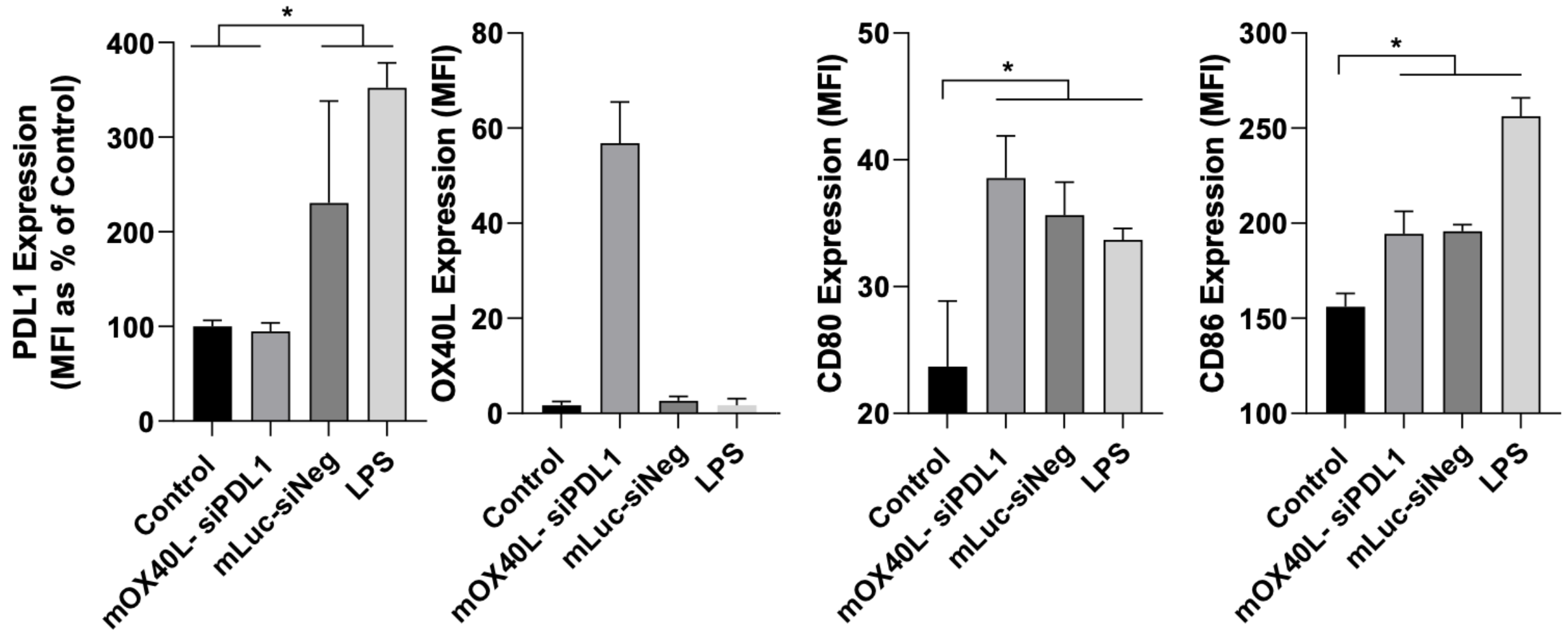
# Results: *In vitro* studies in B16F10 cells

## Gene transfer/flow cytometry



# Results: *In vitro* studies in J774 macrophages

## Gene transfer/immune activation

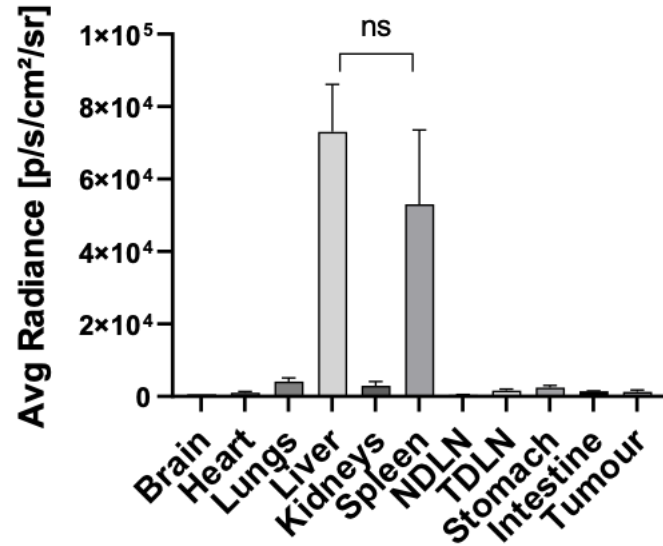




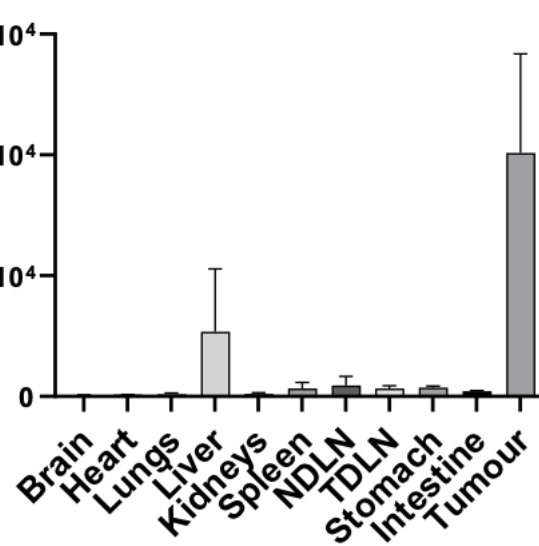
# Results: In vivo tracking & gene transfer

## Optical/BLI imaging & Flow cytometry

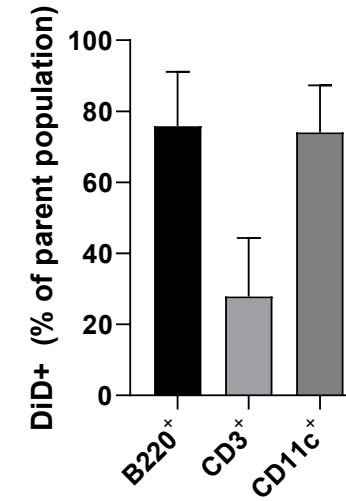
Luc i.v.



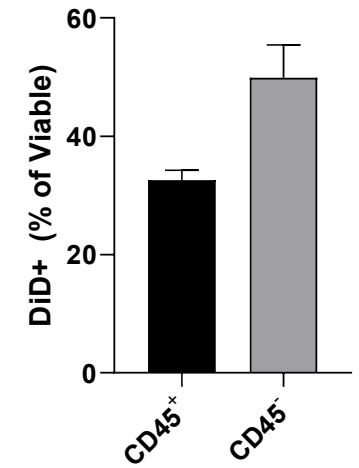
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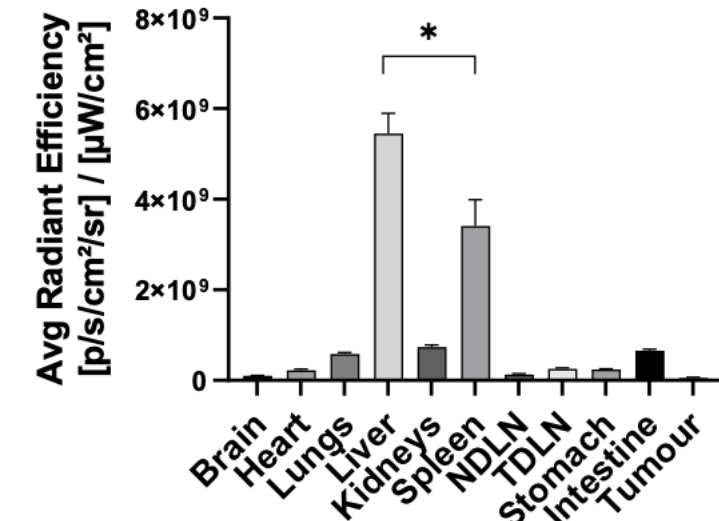
TDLN



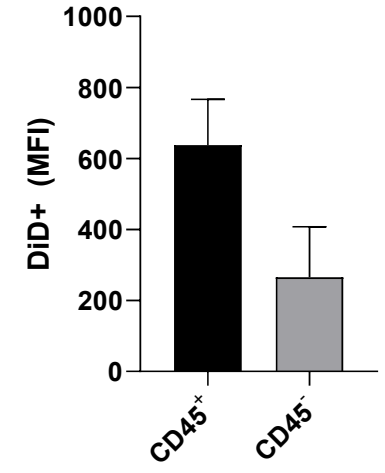
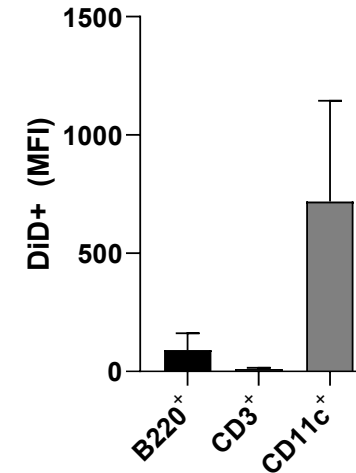
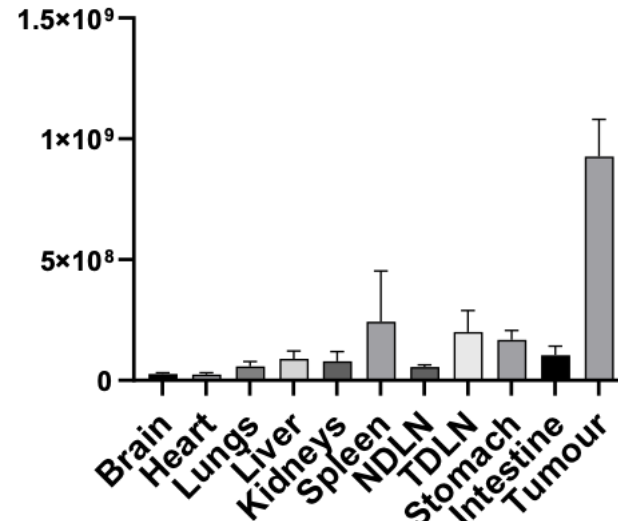
Tumour



DiR i.v.

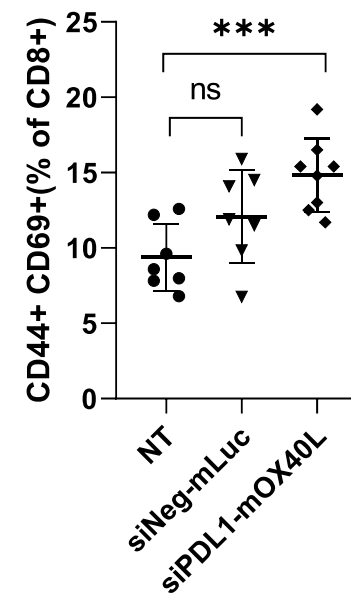
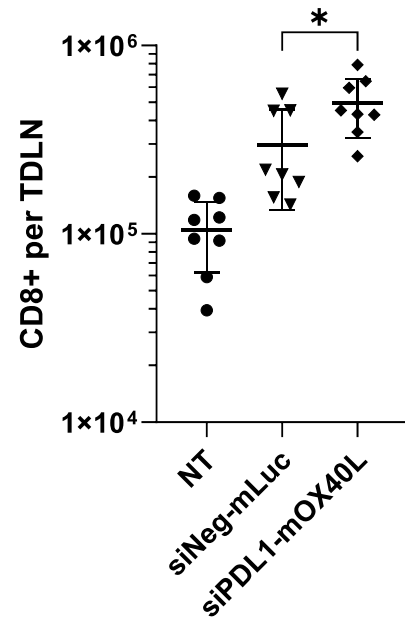
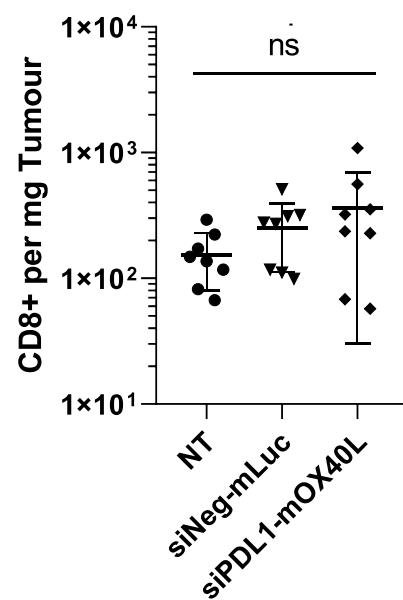
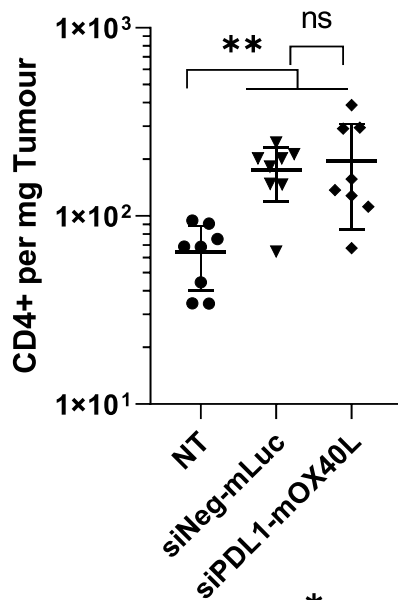
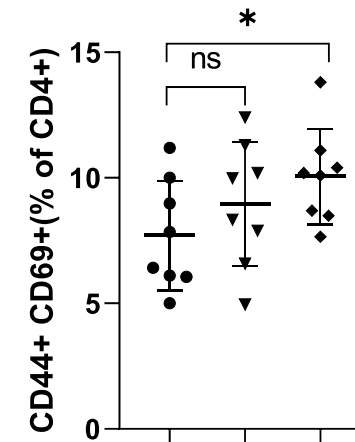
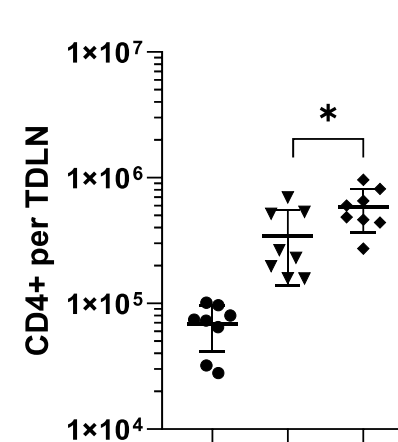
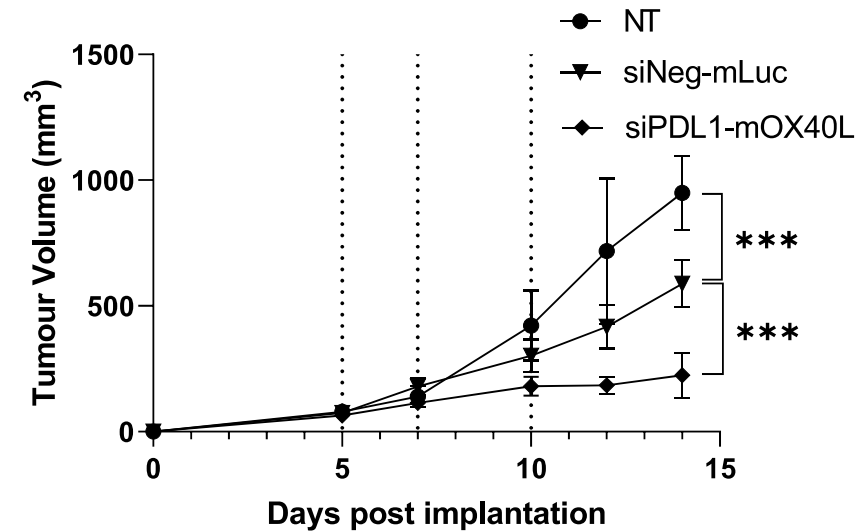


DiR i.t.



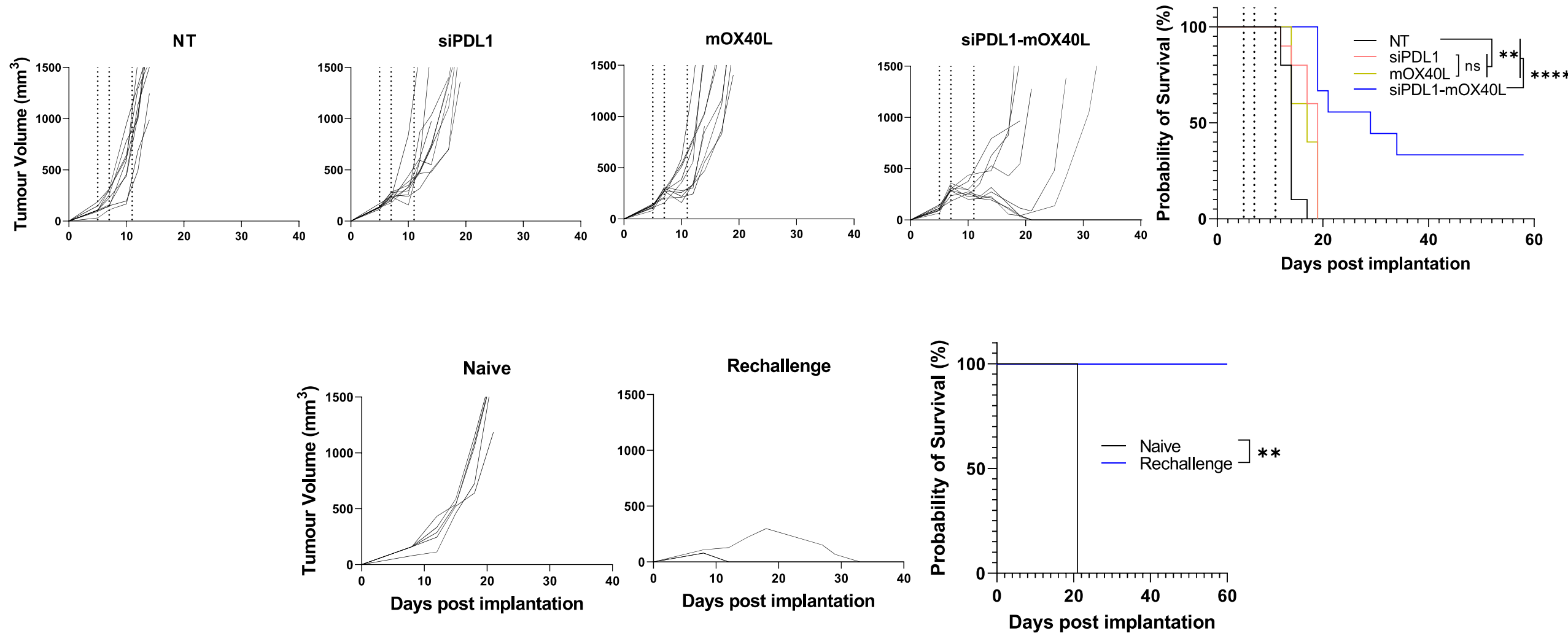
# Results: *In vivo* studies

## Tumour growth delay and immunogenicity

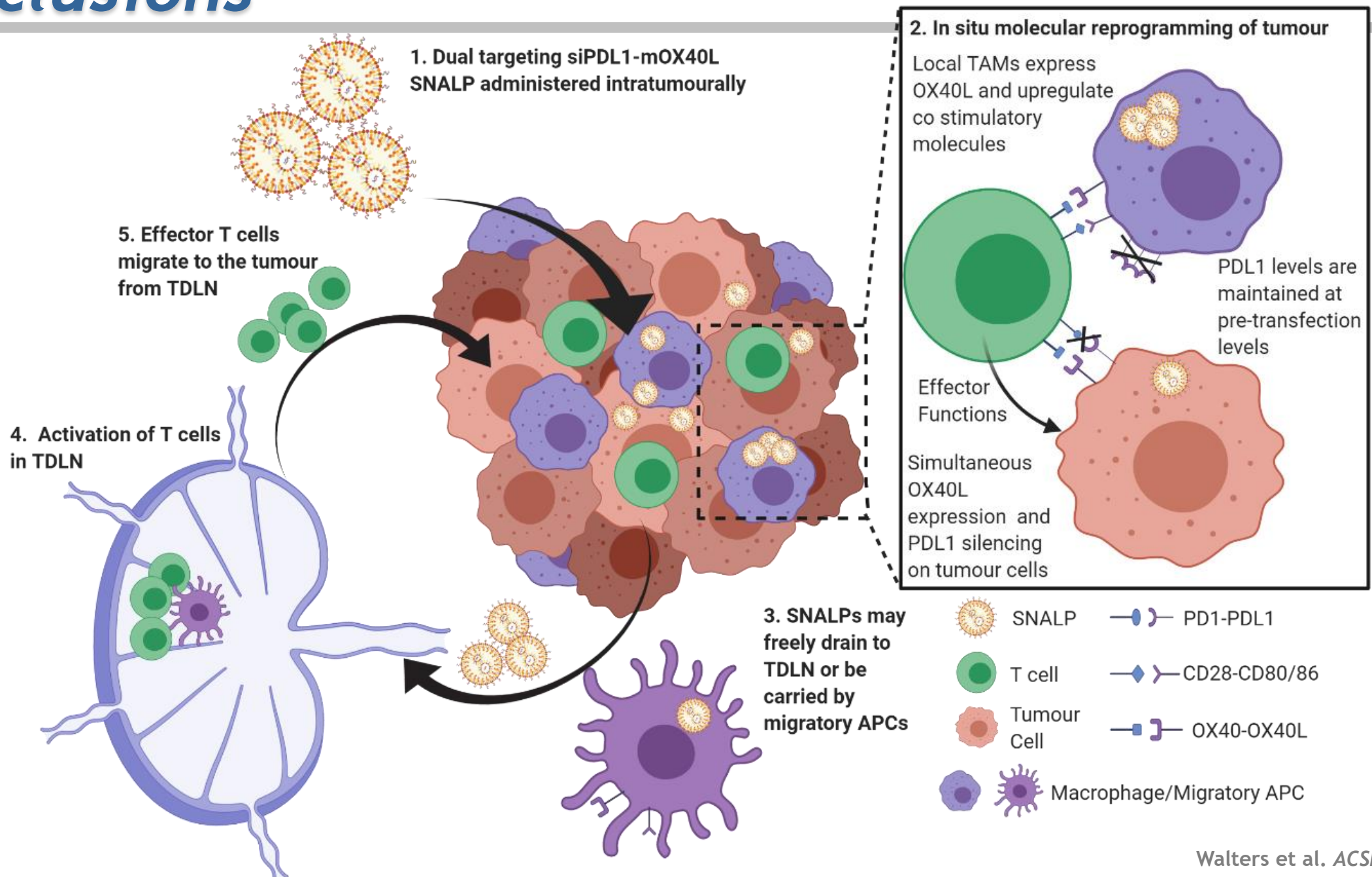


# Results: *In vivo* studies

## Survival and tumour re-challenge



# Conclusions



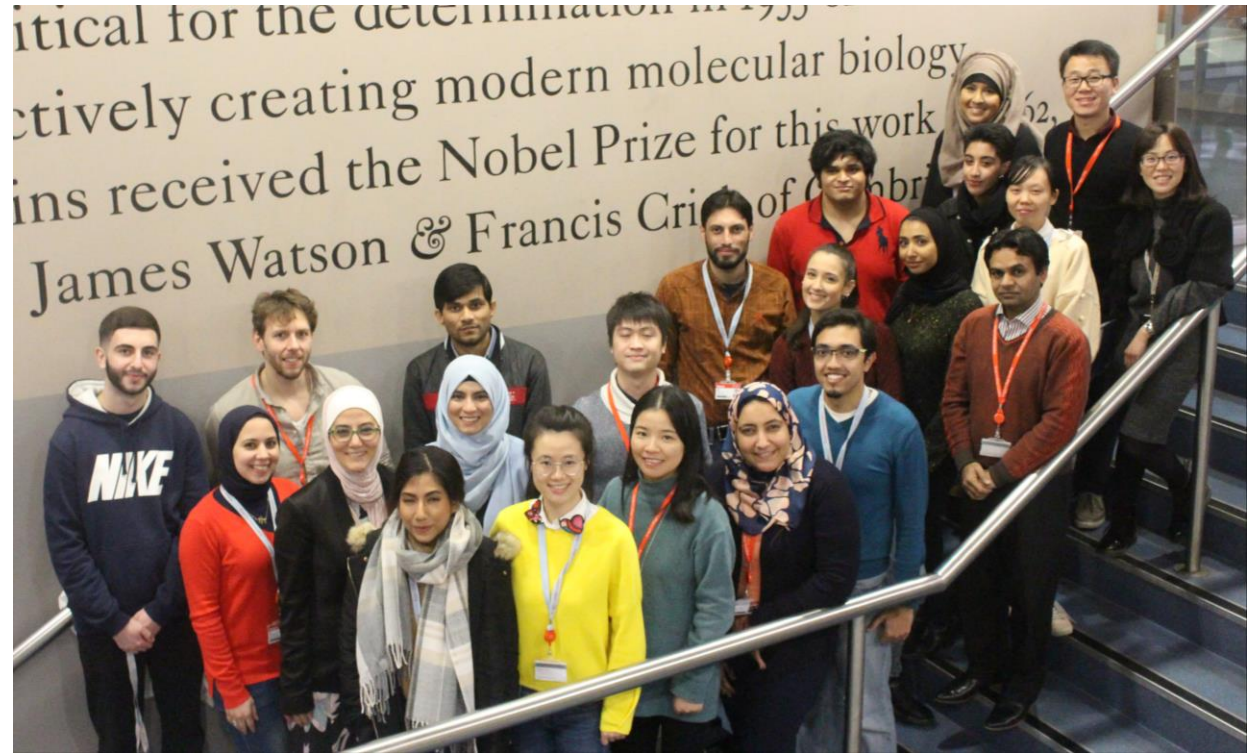
# Acknowledgments

## King's College London

Dr Adam Walters  
Dr Hend Abdelbar  
Dr Fatemeh Gheidari  
Dr Julie Wang  
Dr Naomi Hodgins  
Dr John Maher  
Dr Anna Parente Pereira

## QMUL, UK

Dr Jane Sosabowski  
Prof John Marshall



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