Ocular delivery

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Absolute quantitation of barcoded liposomes in ocular tissues

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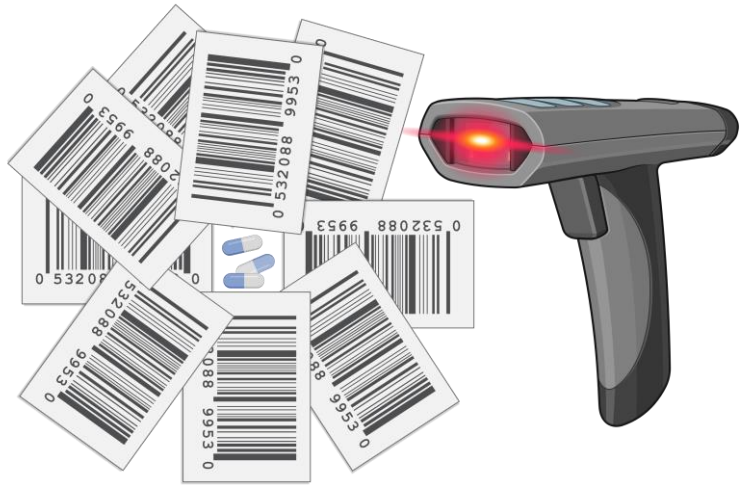

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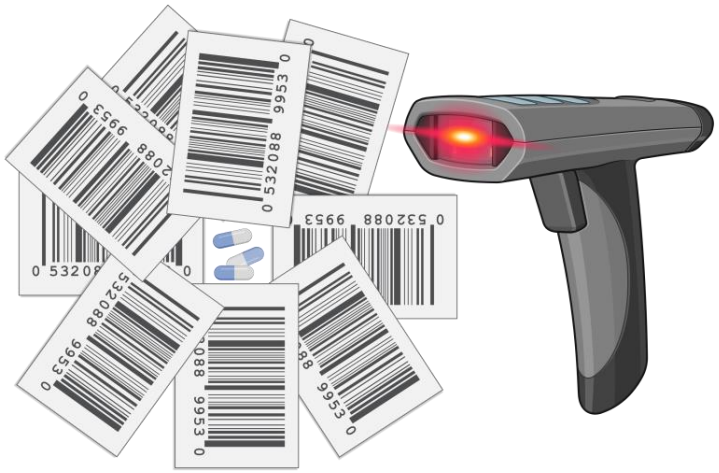
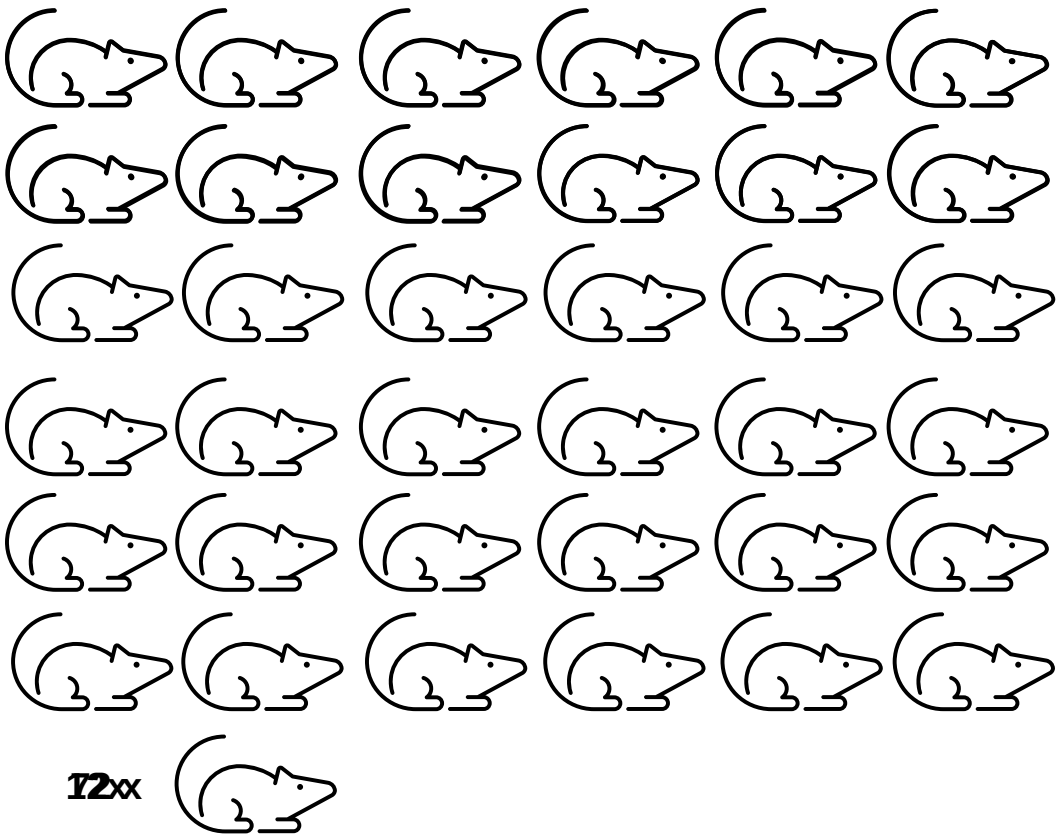
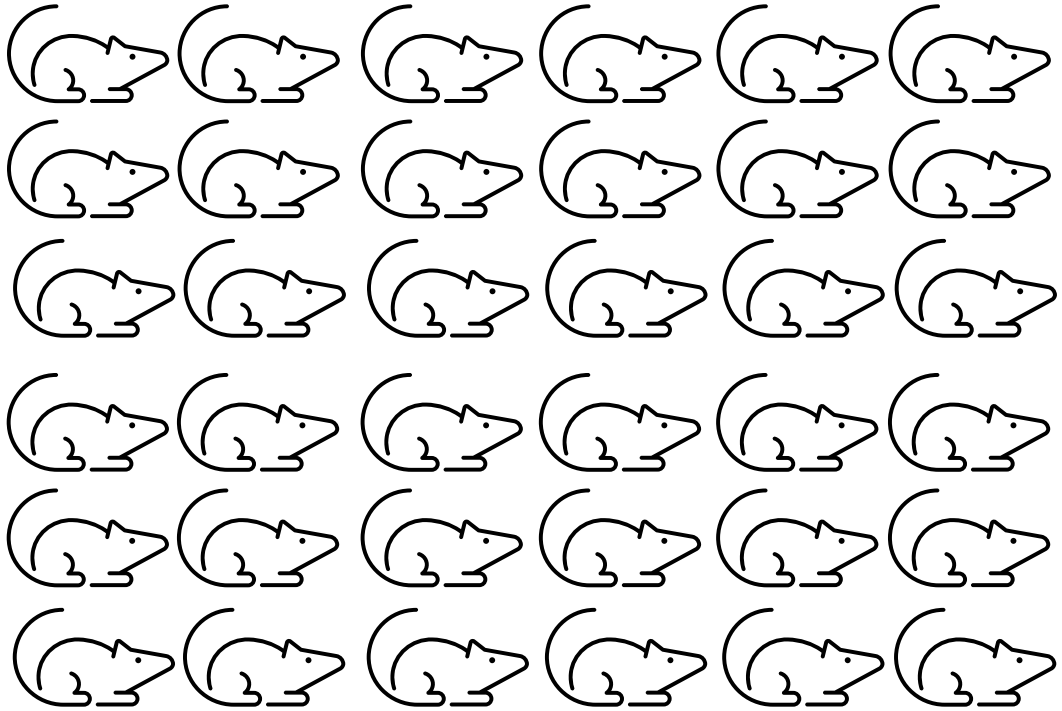
Barcoded drug delivery systems?

- Drug delivery systems (DDS) labeled with different tags that do not alter their properties
- Barcoding enables screening of multiple DDS within the same subject
- Rule of 3R's!
- Reducing the number of animals required
- Refinining the results



Why we need barcoding?





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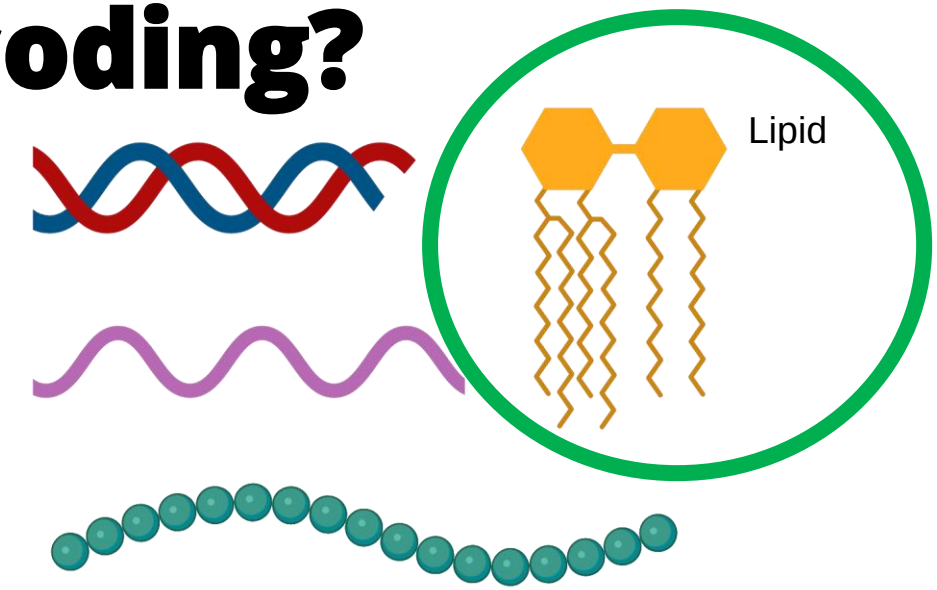
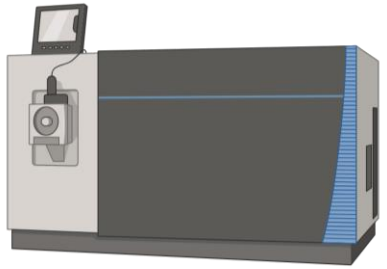
How can we do barcoding?

1. Barcode

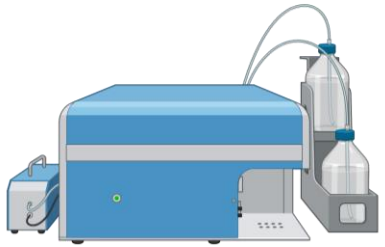


2. Reader



LC-MS

PCR



Flow cytometry

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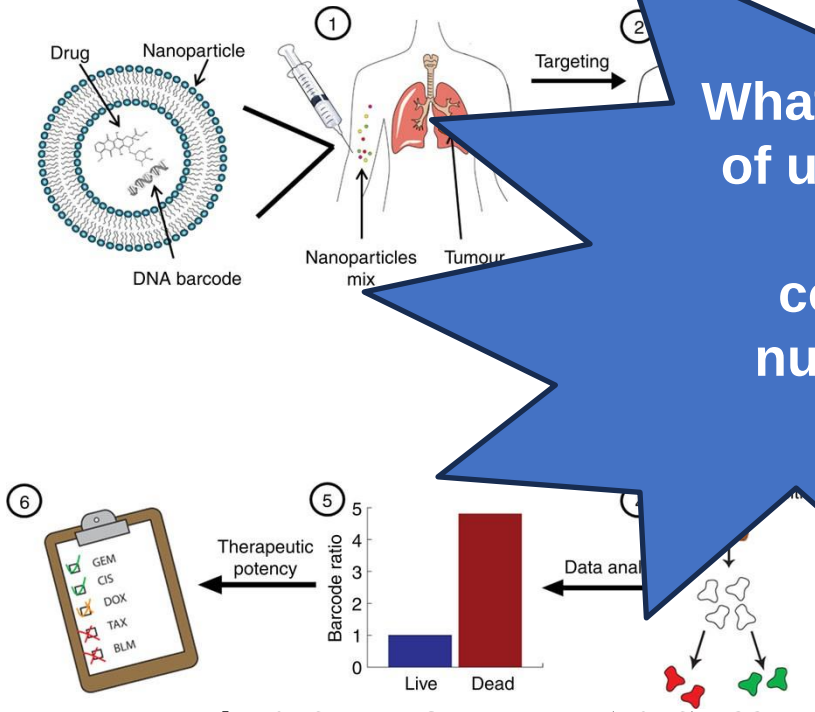
Barcoding of liposomes

- DNA barcodes for a theranostic application: PCR analysis of DNA combined with live-dead cell imaging to study drug efficacy
- DNA/mRNA barcodes for LNP screening: Studying the efficacy of mRNA delivery & protein production

What is the benefit of using lipids as barcodes compared to nucleic acids?



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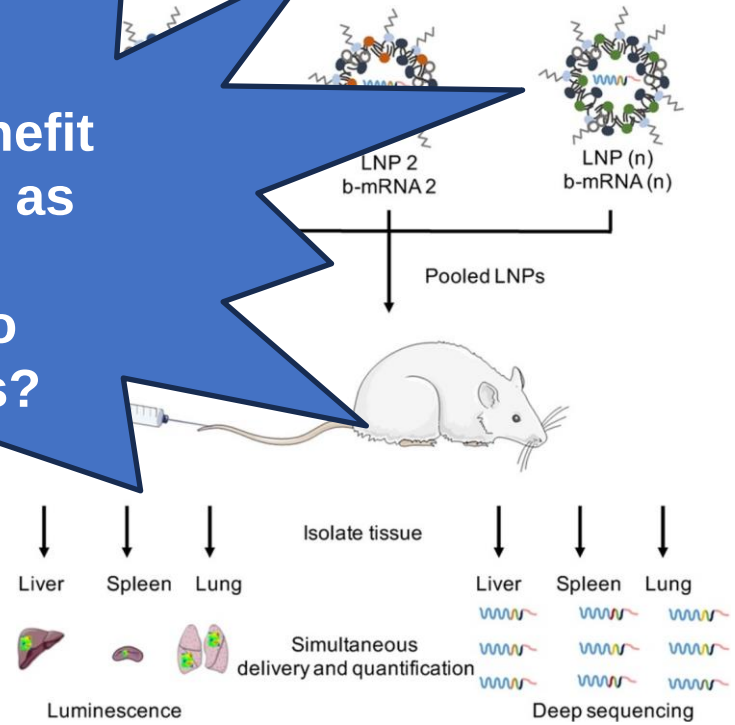

P.P.G. Guimaraes, et al. (2019) J. Control. Release. 316 (2019) 404–417.

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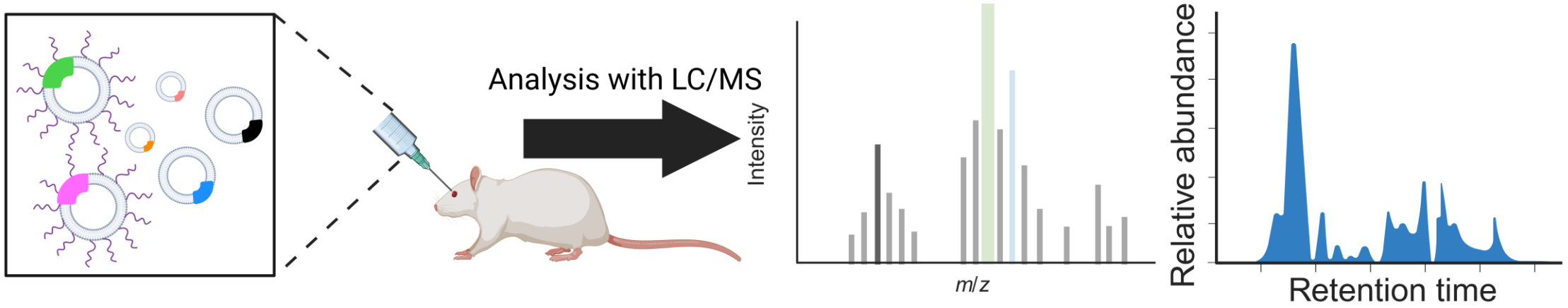
Absolute quantitation of barcoded liposomes in ocular tissues

AIM To develop a quantification method that allows studying of multiple liposome formulations within the same animal.

HYPOTHESIS Ocular pharmacokinetics of various liposome formulations can be studied within the same animal when the liposomes are labeled with barcode lipids.



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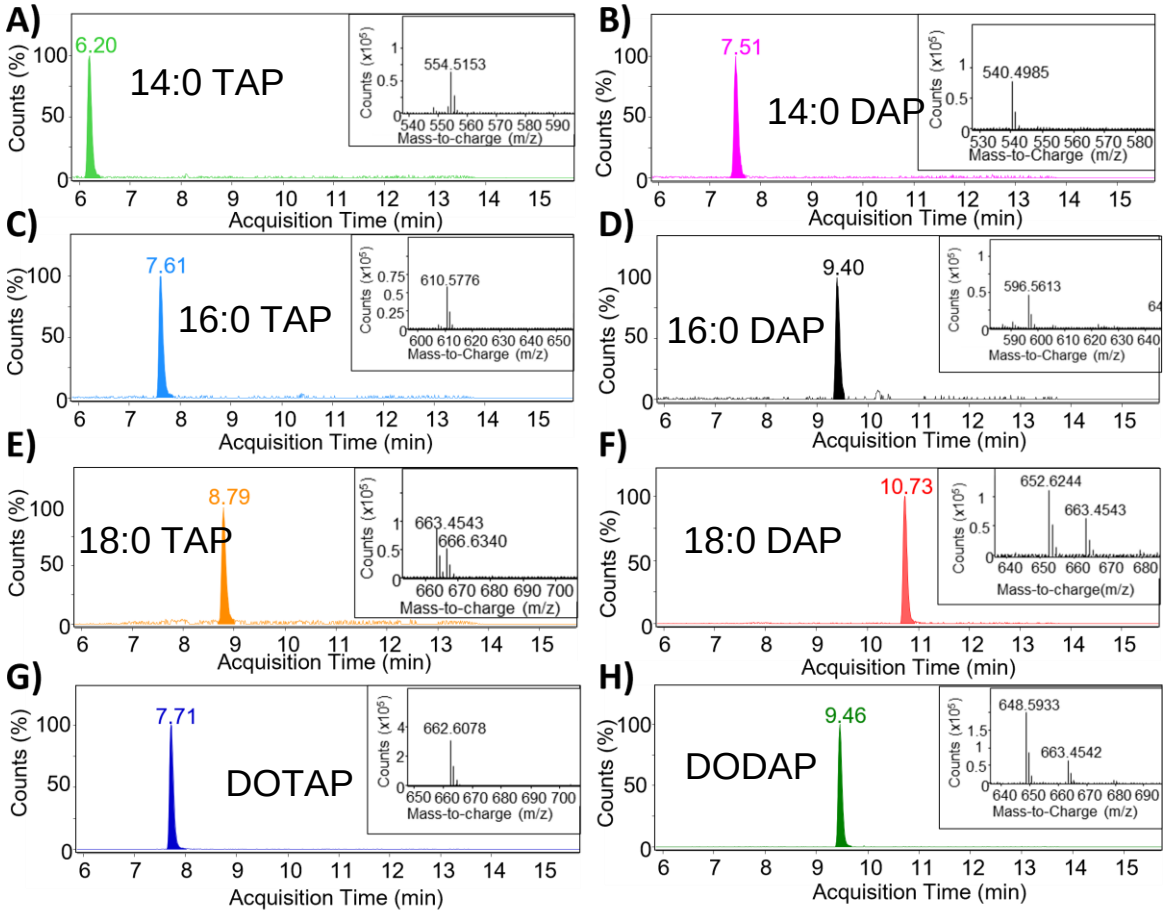
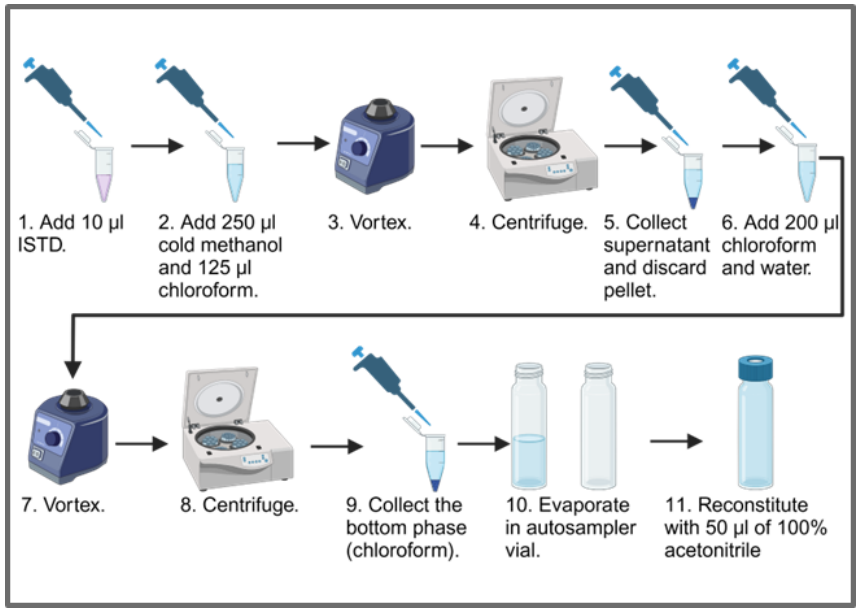
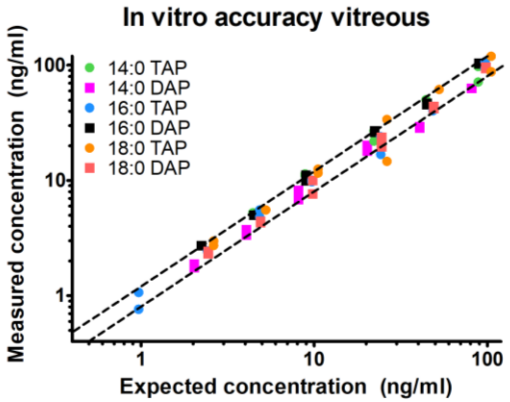
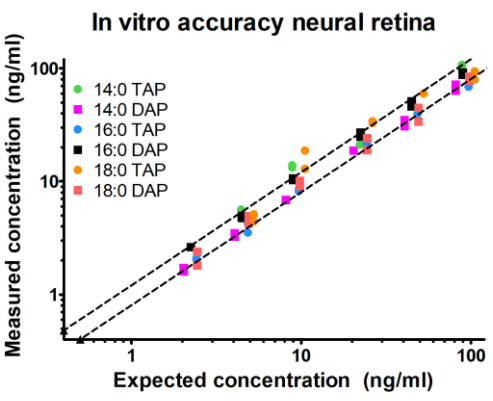
Sample preparation and method validation





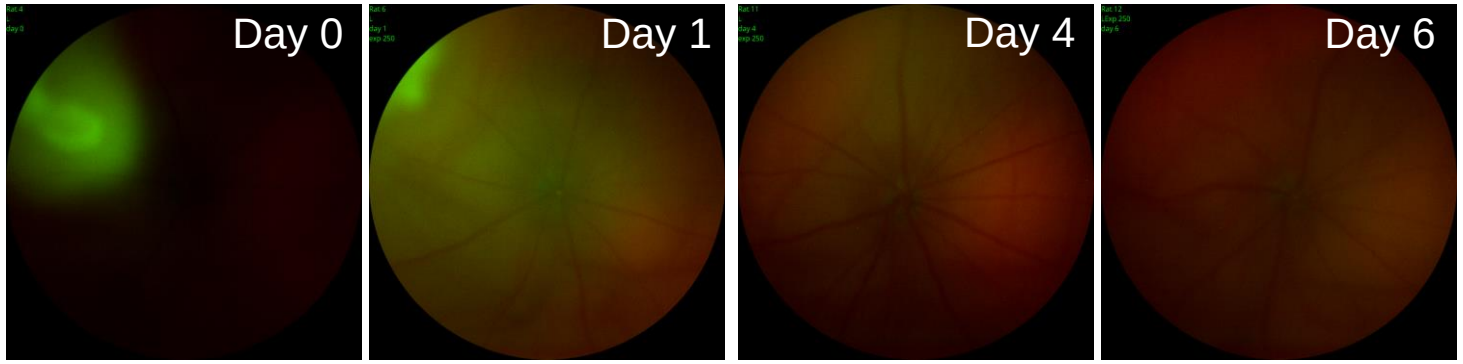


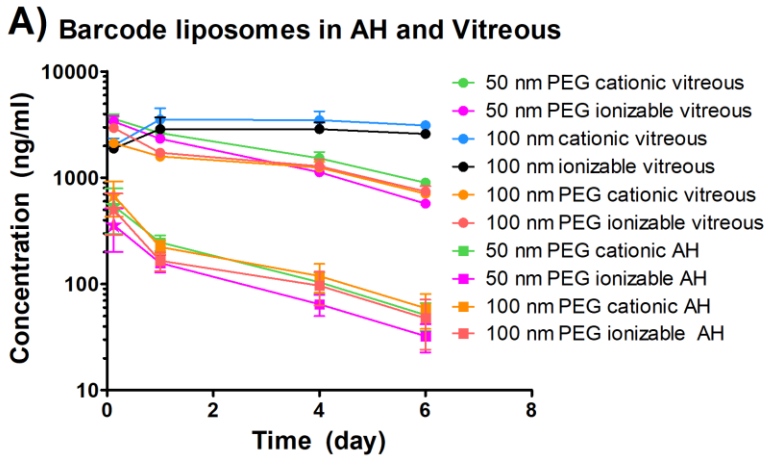


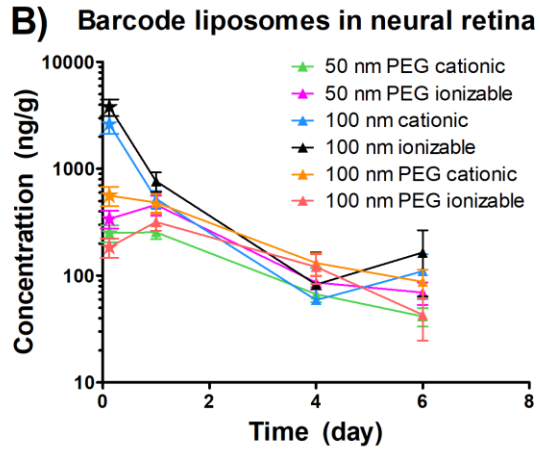
Merivaara, Arto, et al. *Journal of Controlled Release* 370 (2024): 1-13.

Concentration of barcode liposomes in ocular tissues

- Rats: intravitreal injections, injection volume 3 µl
- 6 barcode liposome formulations in one injection
- Fluorescent label to confirm succesful injection and to compare with barcode results
- Injection on day 0, tissues collected on day 0, day 1, day 4, and day 6.







Dose normalized concentrations

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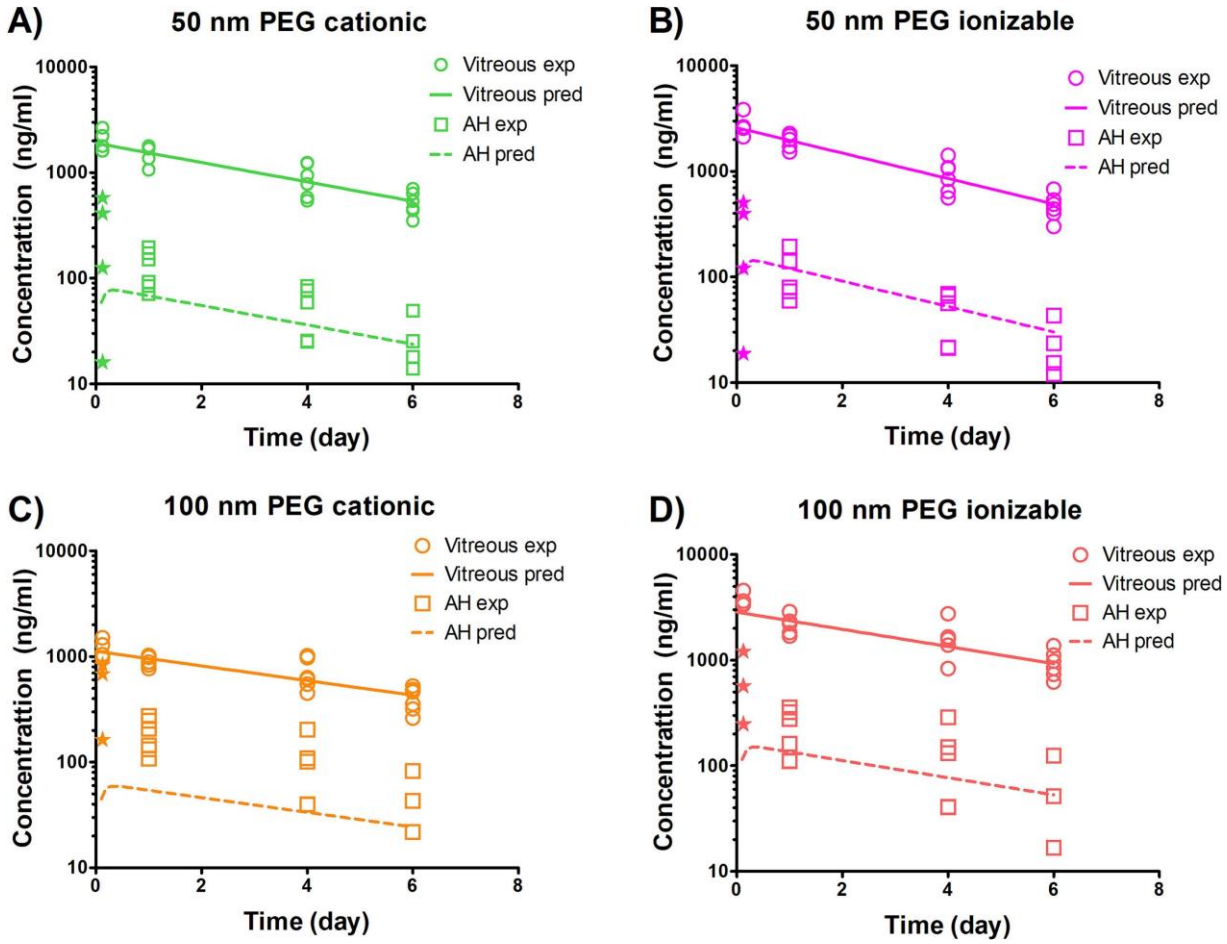
Evaluation of pharmacokinetics



Vitreous	50 nm PEG pos	50 nm PEG ionizable	100 nm PEG pos	100 nm PEG ionizable
Dose (ng)	74	106	74	162
C0 (ng/ml)	1888	2571	1115	2822
Ke (day-1)	0.211	0.277	0.160	0.187
T½ (day)	3.3	2.5	4.3	3.7
Vd (ml)	39	41	66	57
AUC(0-inf)	8959	9274	6982	15051
Aqueous humor	**50 nm PEG pos**	**50 nm PEG ionizable**	**100 nm PEG pos**	**100 nm PEG ionizable**
Ke (day-1)	0.305	0.311	0.249	0.229
T½ (day)	2.3	2.2	2.8	3.0

Merivaara, Arto, et al. *Journal of Controlled Release* 370 (2024): 1-13.

Conclusions and take home message

- Barcode lipids offer an accurate, precise, and reliable method to study the in vivo intraocular pharmacokinetics of liposomes even in rats.
- The number of animals decreased from 72 to 12 by using the barcoded liposomes. This is important from an ethical point of view as well as from an economic point of view.
- The approach can be transferred to other tissues such as plasma and liver, to study the drug delivery with liposomes.

Acknowledgements

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