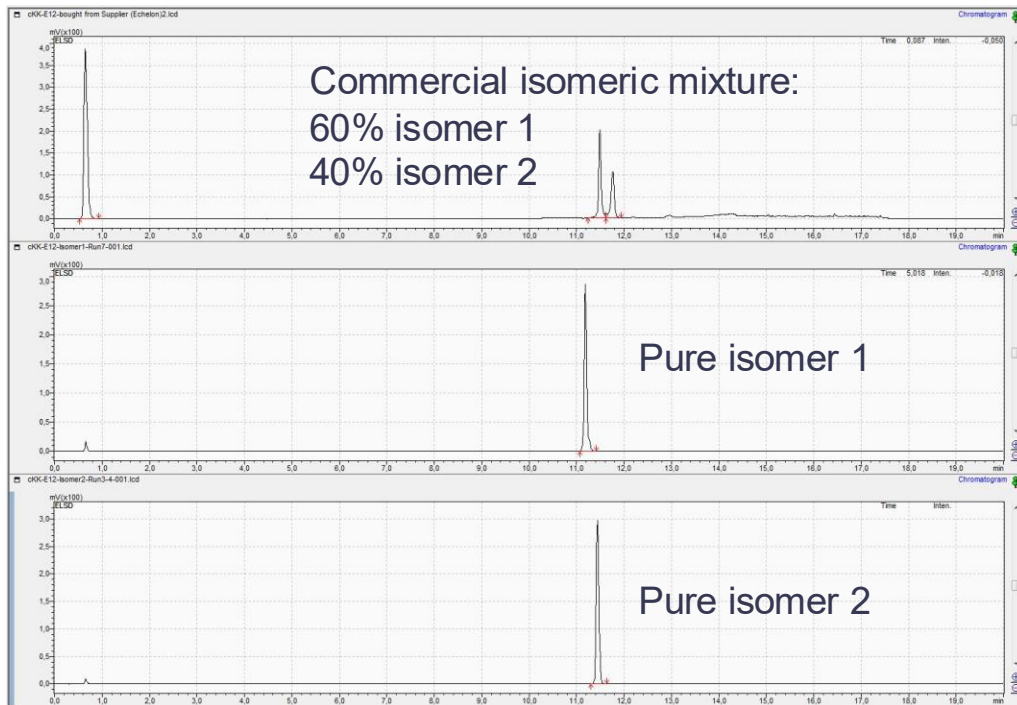
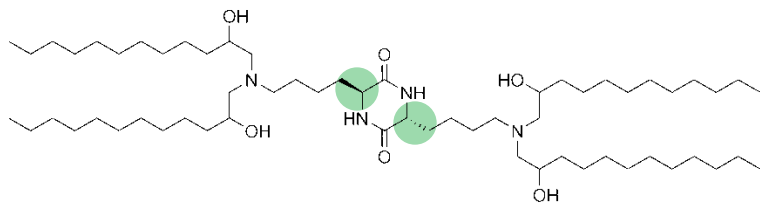


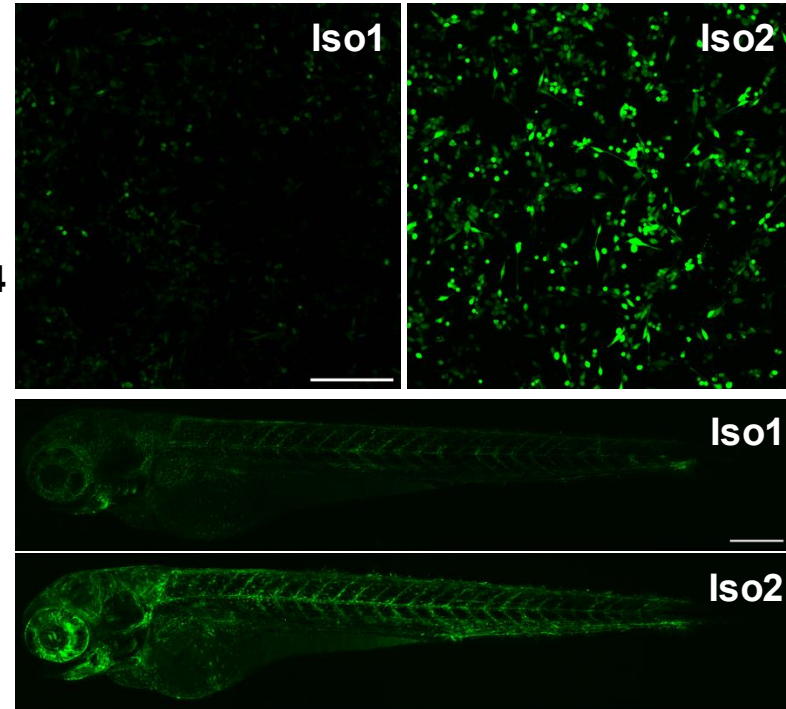
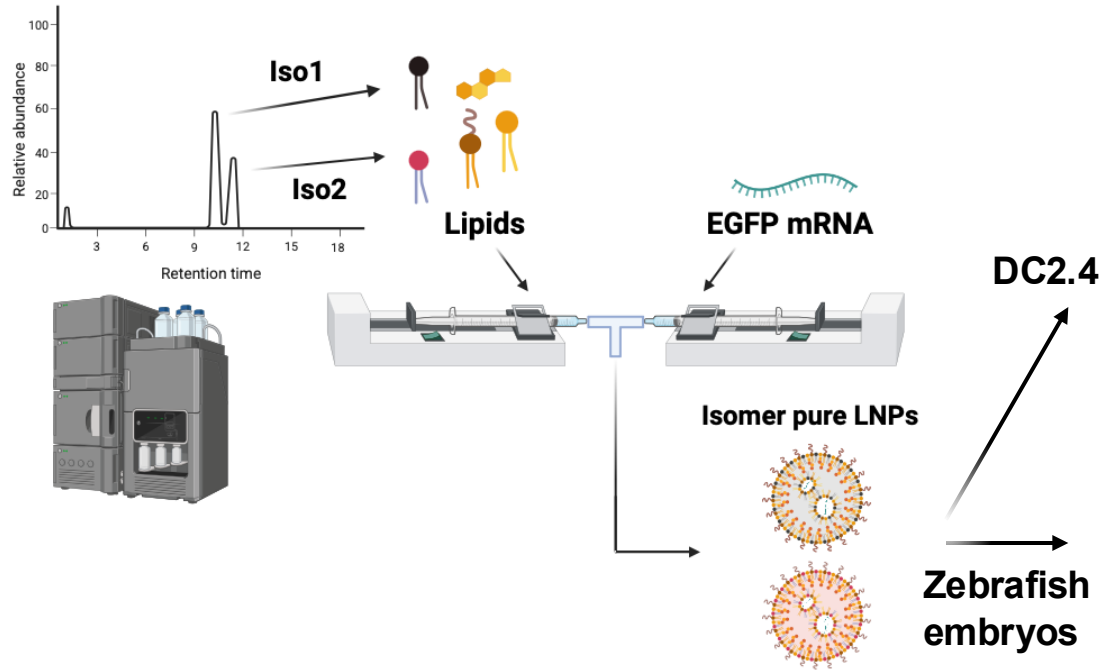
Lipid stereochemistry of lipid nanoparticles significantly influences mRNA expression levels *in vivo*

Renzo Knol
Leiden University
July 16th 2025

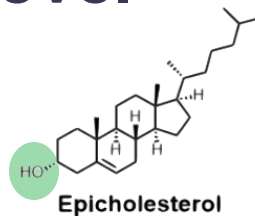
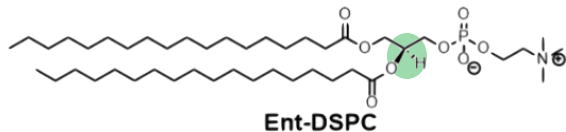
cKK-E12 has two distinct isomer groups



Isomer 2 provides higher mRNA expression



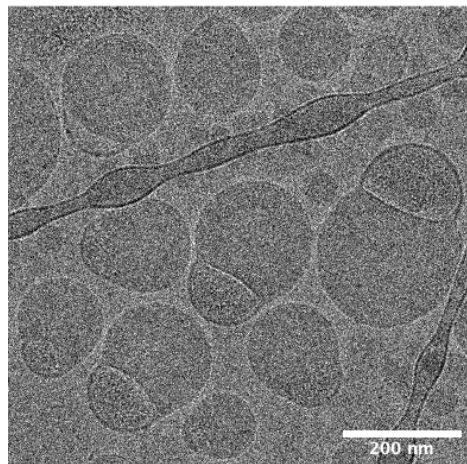
Stereochemistry of helper lipids influences mRNA expression level



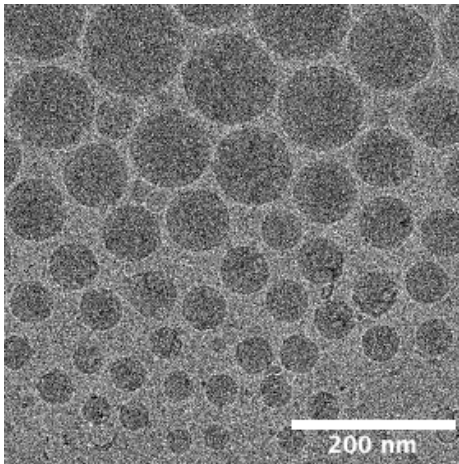
Differences in internal lipid organization determine mRNA expression levels

DSPC

Iso1

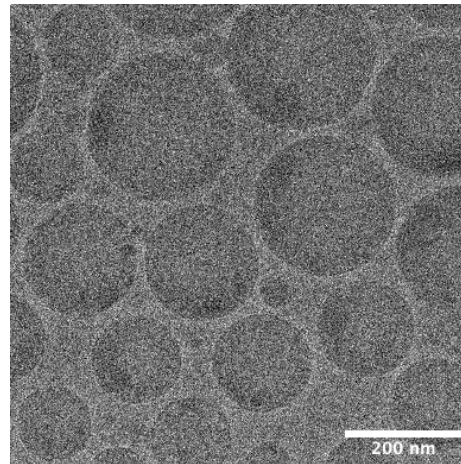


Iso2

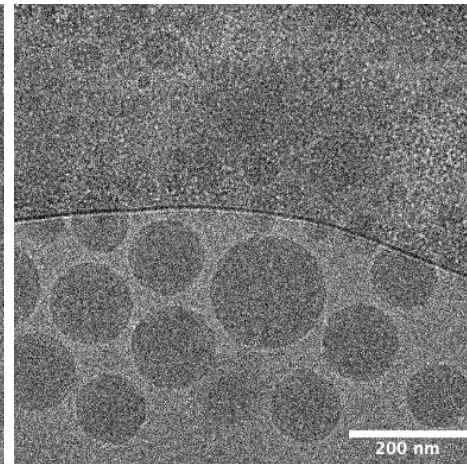


DOPE

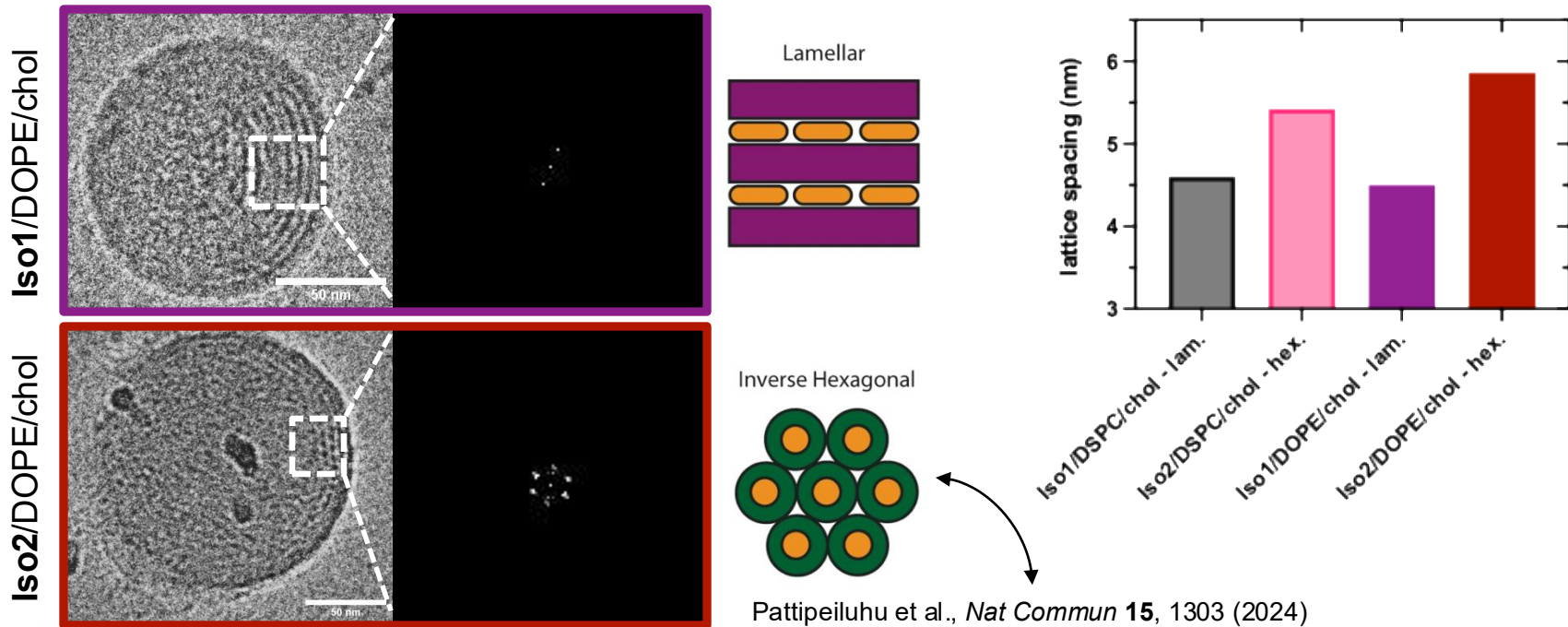
Iso1



Iso2

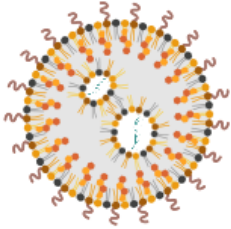


Differences in internal lipid organization determine mRNA expression levels

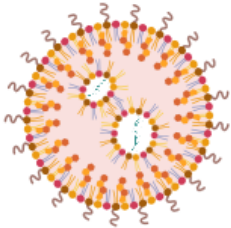


Conclusion

Iso1 LNP



Iso2 LNP





Universiteit
Leiden
The Netherlands

Acknowledgements

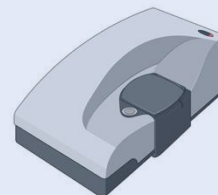
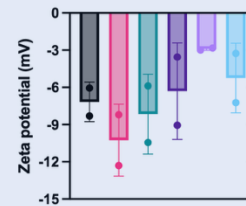
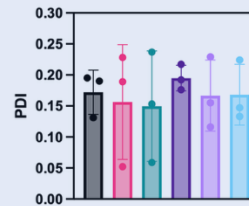
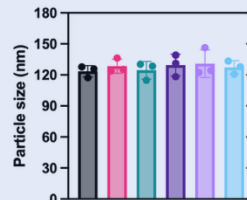
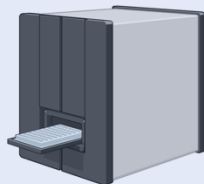
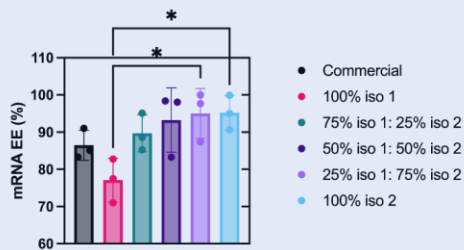
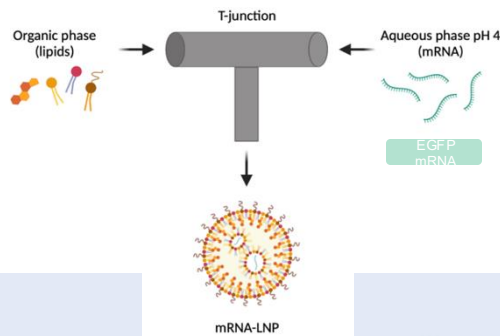
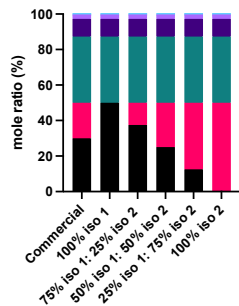
Dennis Aschmann
Inès Pfister
Bram Slütter
Panagiota Papadopoulou
Oscar Escalona Rayo
Prof. Alexander Kros

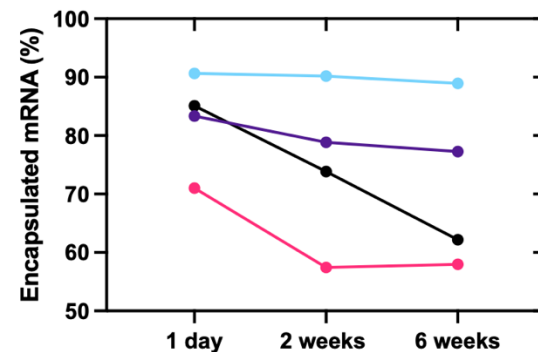
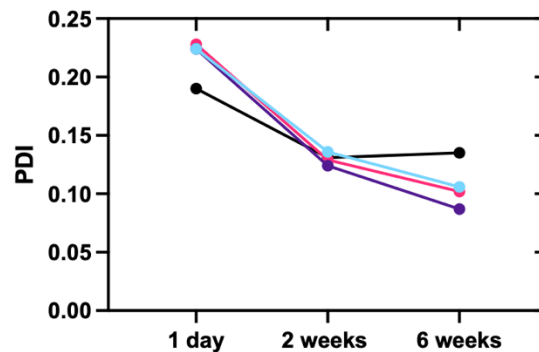
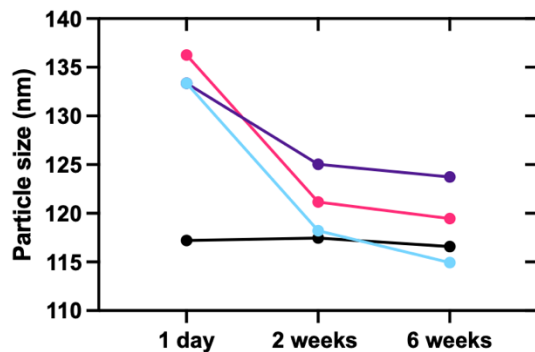
CryoEM:

Karl Bertram (ATEM Bio)

SAXS:

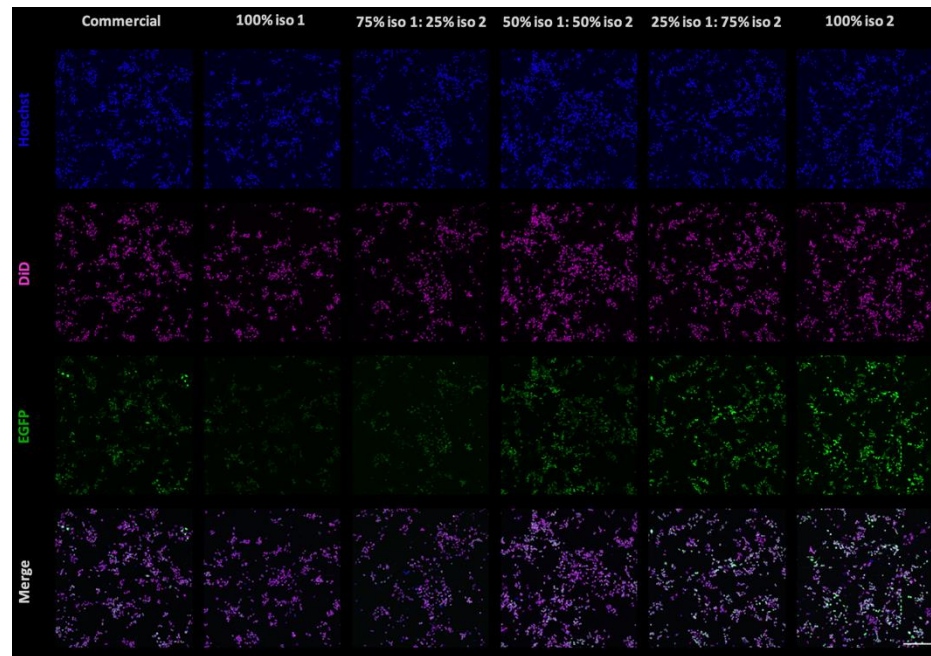
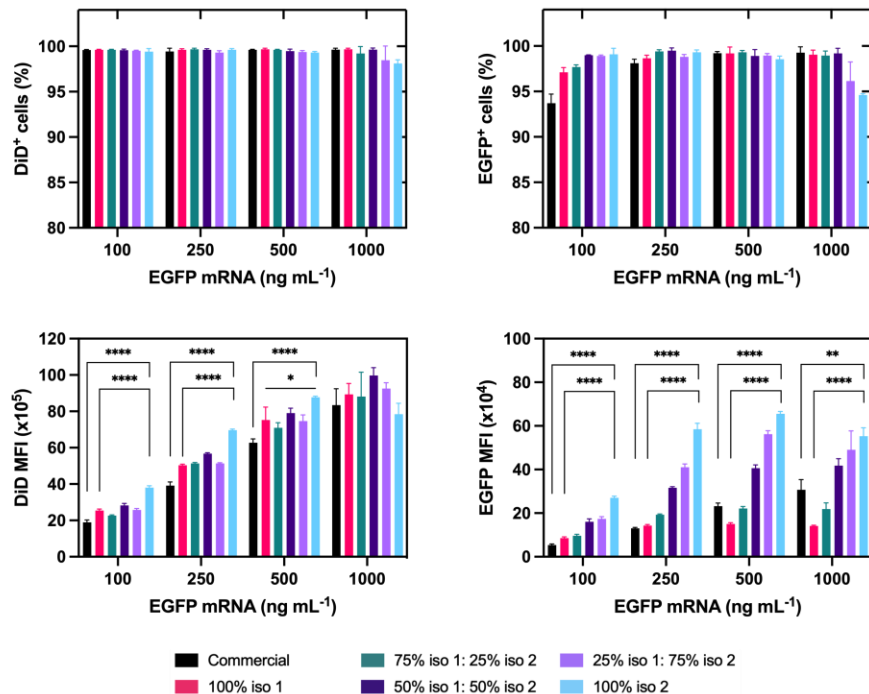
Rafael Vasconcelos de Melo Freire & Prof. Ilja Voets



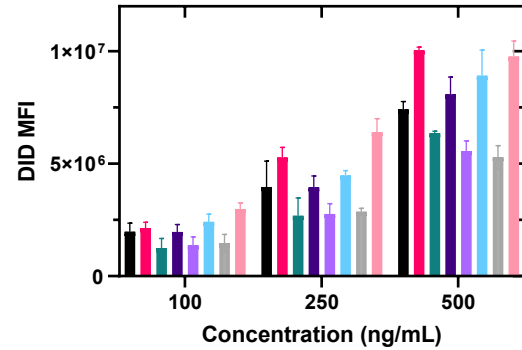


—●— Commercial —●— 100% iso 1 —●— 50% iso 1: 50% iso 2 —●— 100% iso 2

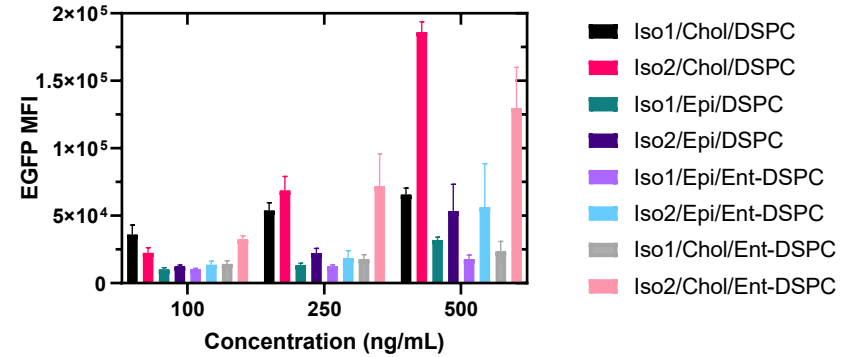
DC2.4 immortalized murine dendritic cell line



DC2.4

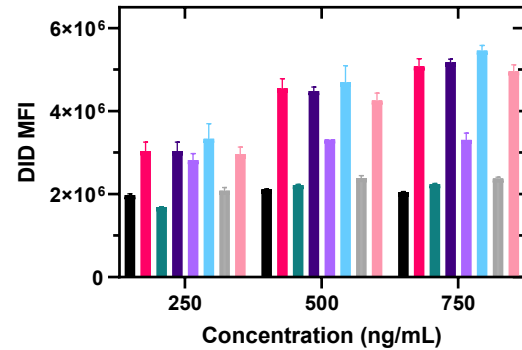


DC2.4

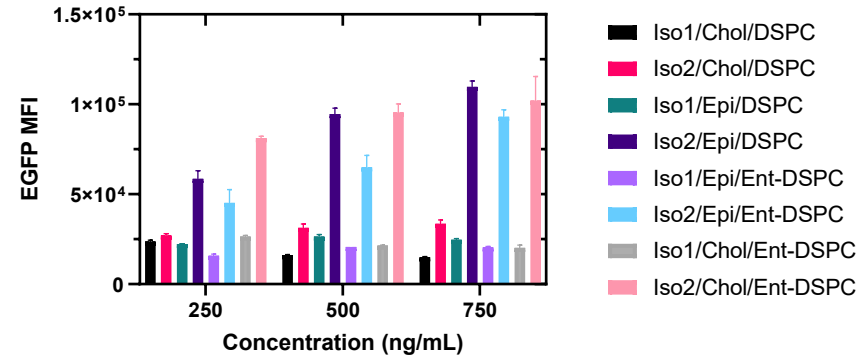


- Iso1/Chol/DSPC
- Iso2/Chol/DSPC
- Iso1/Epi/DSPC
- Iso2/Epi/DSPC
- Iso1/Epi/Ent-DSPC
- Iso2/Epi/Ent-DSPC
- Iso1/Chol/Ent-DSPC
- Iso2/Chol/Ent-DSPC

RAW264.7



RAW264.7

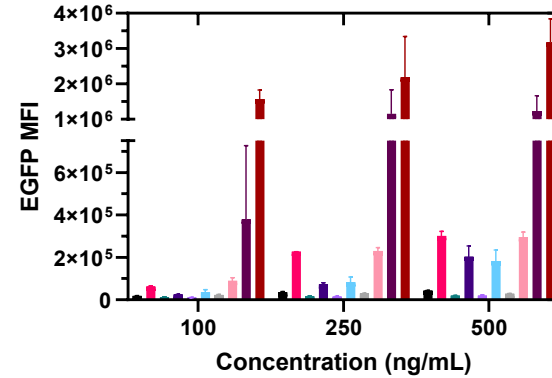
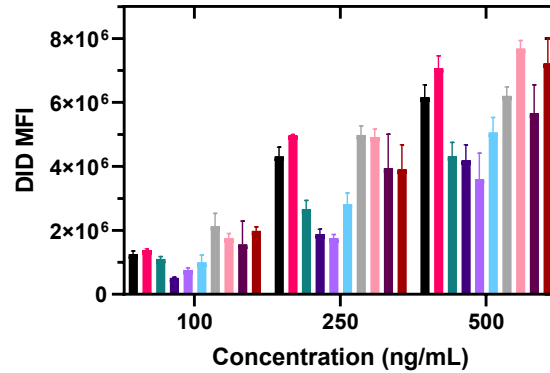


- Iso1/Chol/DSPC
- Iso2/Chol/DSPC
- Iso1/Epi/DSPC
- Iso2/Epi/DSPC
- Iso1/Epi/Ent-DSPC
- Iso2/Epi/Ent-DSPC
- Iso1/Chol/Ent-DSPC
- Iso2/Chol/Ent-DSPC

HUVEC

HUVEC

175-fold
difference in
transfection level



- Iso1/Chol/DSPC
- Iso2/Chol/DSPC
- Iso1/Epi/DSPC
- Iso2/Epi/DSPC
- Iso1/Epi/Ent-DSPC
- Iso2/Epi/Ent-DSPC
- Iso1/Chol/Ent-DSPC
- Iso2/Chol/Ent-DSPC
- Iso1/Chol/DOPE
- Iso2/Chol/DOPE

Jurkat

Jurkat

30-fold
difference in
transfection level

