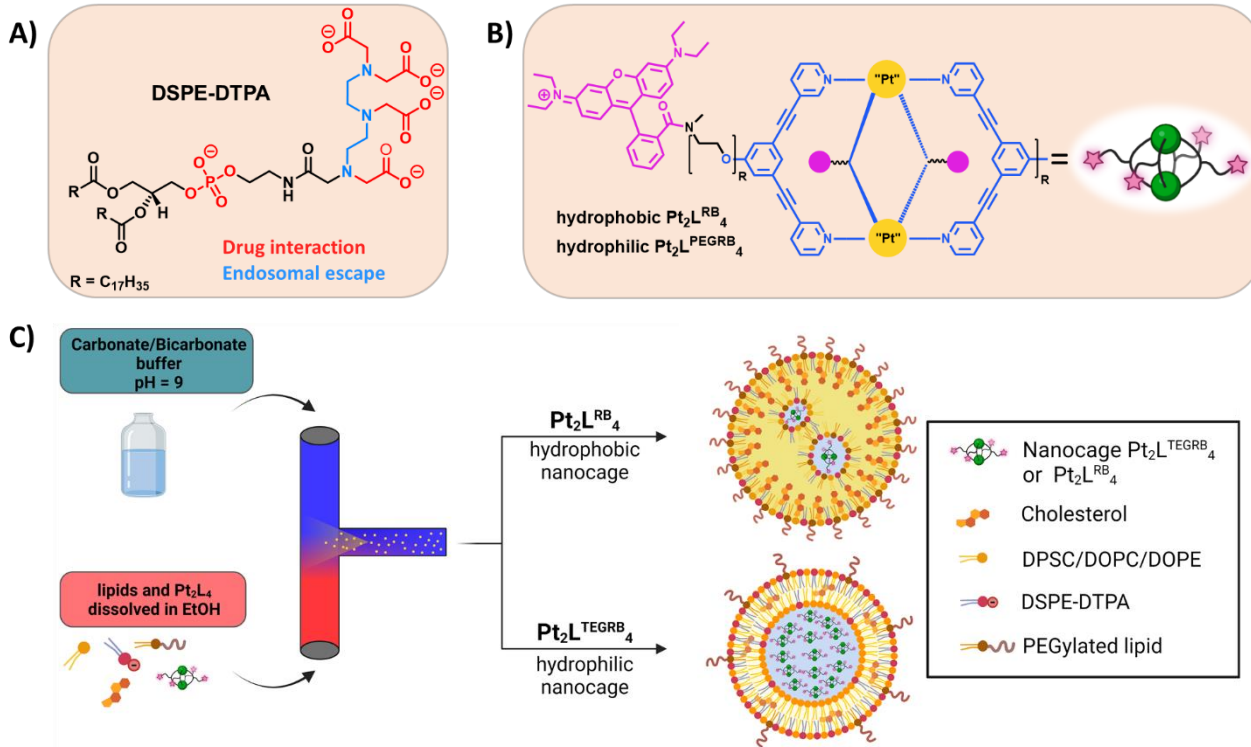


Charge-Reversed Lipid Nanoparticles Containing Metal-Organic Cages for *In Vivo* Anti-Cancer Treatment

Dr. Dennis Aschmann

revLNPs are used for cationic drugs



classic LNPs vs. revLNPs

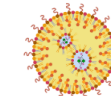
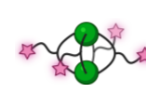
classic LNPs

- Using cationic ionizable lipids (cILs) like MC3, SM-102 or ALC-0315
- Encapsulation of anionic payloads like RNA



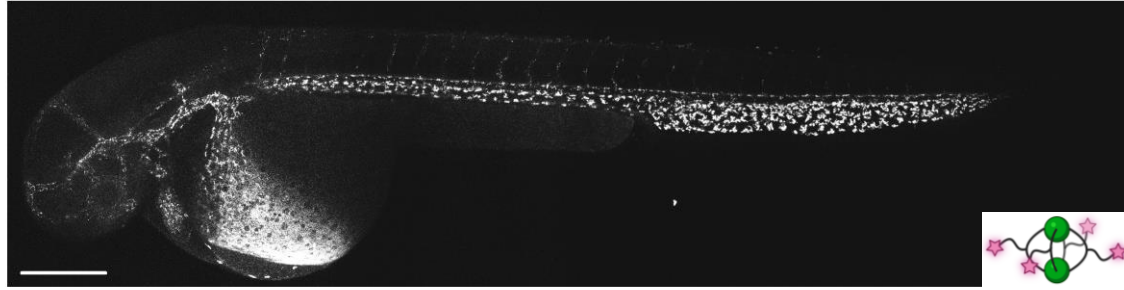
revLNPs

- Using anionic ionizable lipids (aILs) like PE-DTPA
- For the encapsulation of cationic payloads like Nanocage or cationic drugs



revLNPs improve the circulation of nanocages

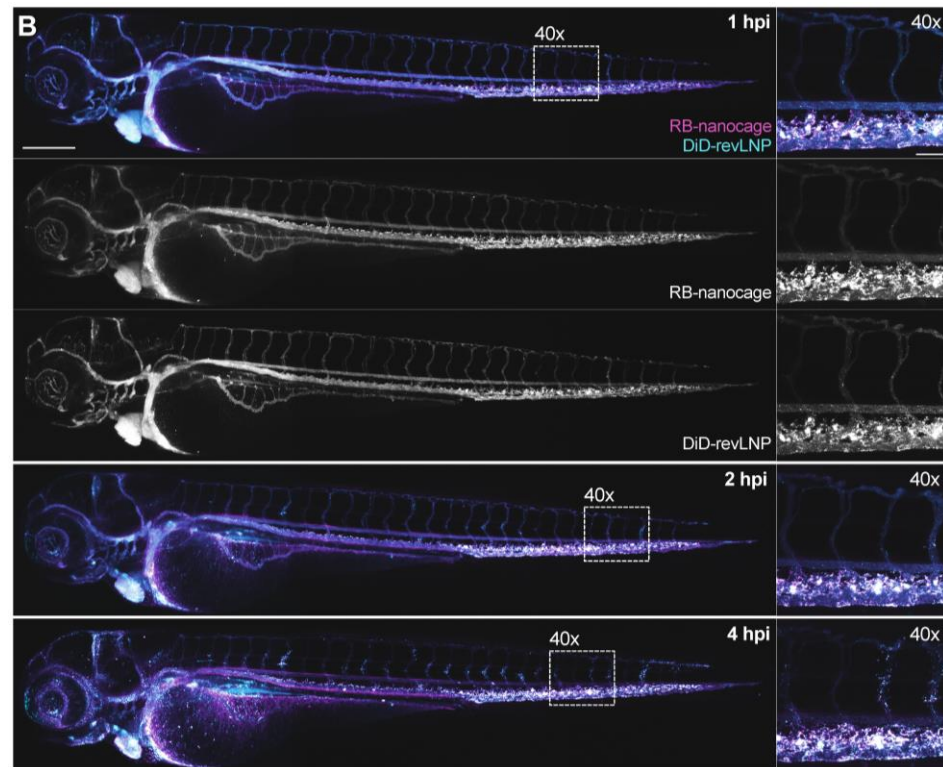
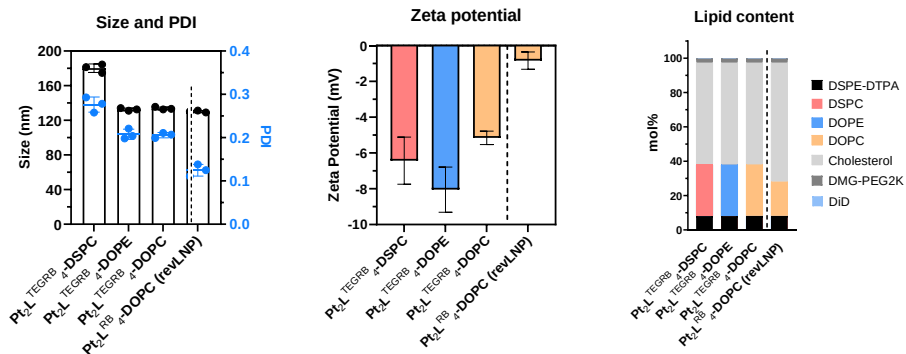
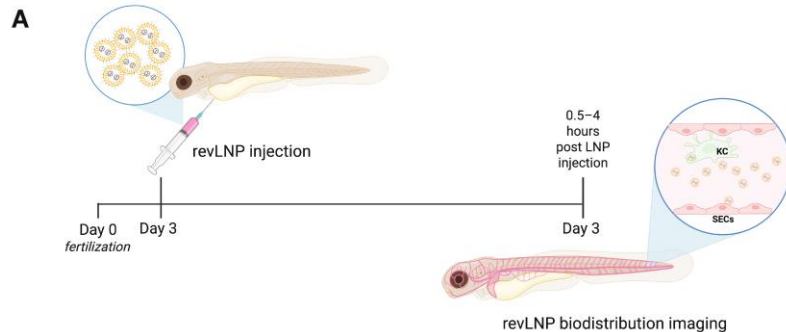
Free cage



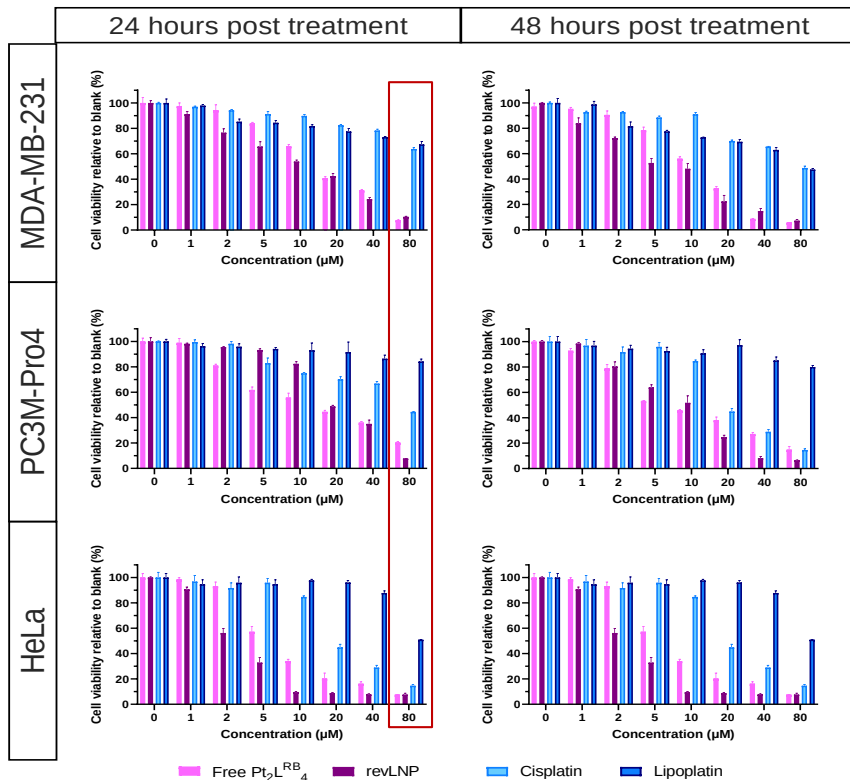
- Free nanocages show fast internalization!



revLNPs exhibit uniform and stable particles still circulating after 4 h



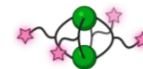
Nanocages are more potent than cisplatin



LNPs vs. revLNPs

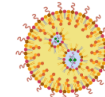
Nanocage ($Pt_2L_4^{RB_4}$)

- ~10 times more toxic in prostate and breast cancer compared to cisplatin

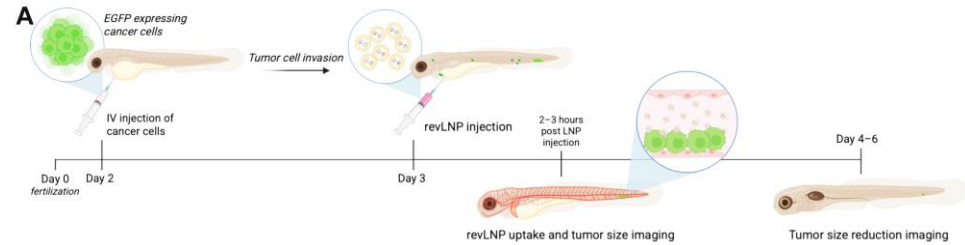
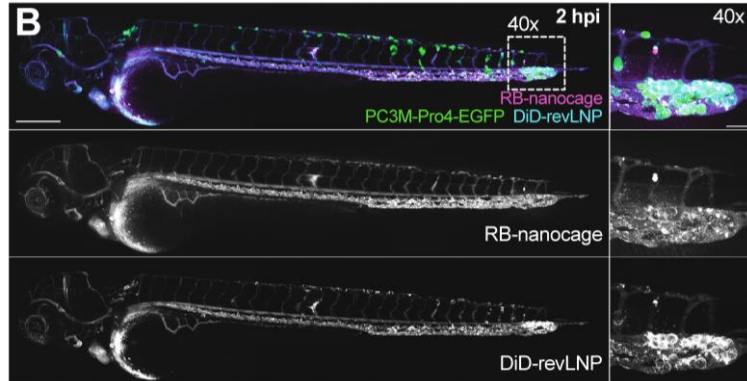


revLNPs

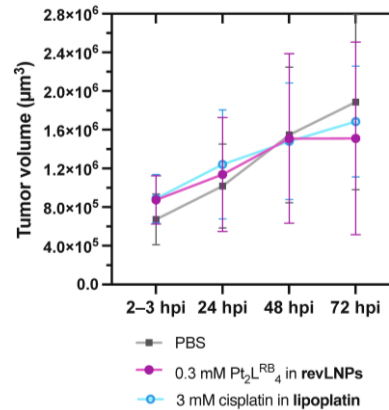
- MDA – IC_{50} : 7.5 μM
- PC3 – IC_{50} : 9.1 μM
- HeLa – IC_{50} : 2.5 μM
- Similar toxicity compared to the free nanocage



revLNPs adsorb on prostate cancer cells



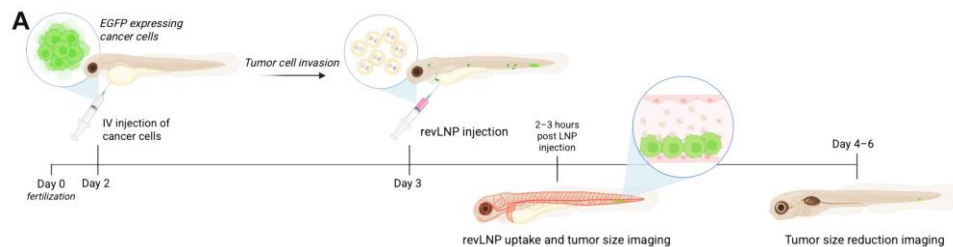
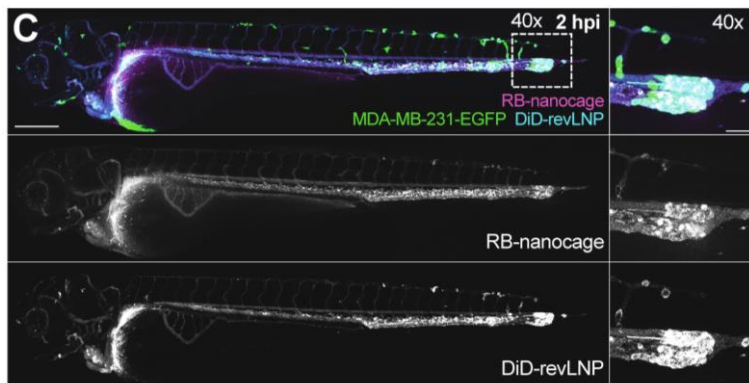
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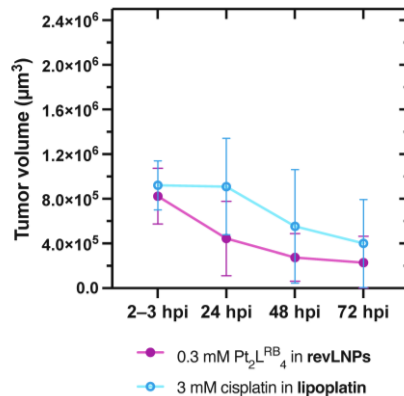
Prostate cancer response

- Progression in cancer growth
- Slightly reduced cancer volume after 3 days compared to control group and lipoplantin

revLNPs kill breast cancer efficiently



E



Breast cancer response

- Most of the individual in the PBS control died
- Reduced tumor volume over 3 days for lipoplatin and revLNPs
- revLNPs caused a **tumor volume reduction of 89%**
- revLNPs contain a **10-fold lower drug dose**



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Universiteit
Leiden



Cat4CanCenter

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Amsterdam University

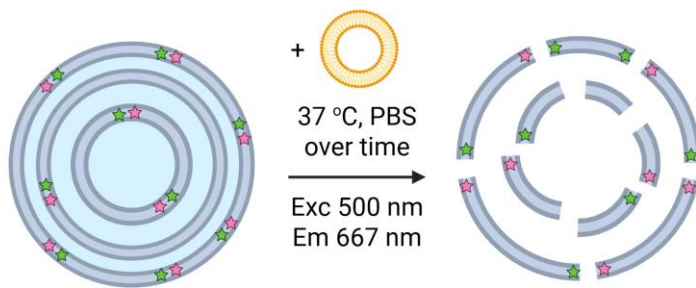
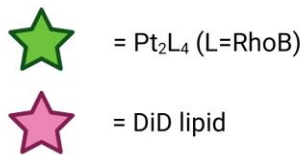
- Eduard Bobylev
- Pieter Laan
- Prof. Joost Reek



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revLNPs show endosomal escape which is improved at pH 5.5



Dissociation Efficiency (%) =

$$\frac{F_{\text{Endosome}} - F_{\text{Intact LNP}}}{F_{\text{Triton-X}} - F_{\text{Intact LNP}}} \times 100\%$$

