66

Exploring the Potential of a Personalized Corona in Lipid Nanoparticles for siRNA delivery

Francia V[1,2], Schiffelers RM[2], Cullis PR[1], Witzigmann D[1]

[1]Department of Biochemistry & Molecular Biology, UBC, Vancouver, BC V6T 1Z3, Canada

[2]Department of Clinical Chemistry and Haematology, UMC Utrecht, 3584 CX, Netherlands

CONTACT:
v.francia@umcutrecht.nl

VANCOUVER NANOMEDICINE DAY

AIM

Develop precise and personalized nucleic acid therapeutics by investigating the biological interactions of clinically relevant lipid nanoparticles

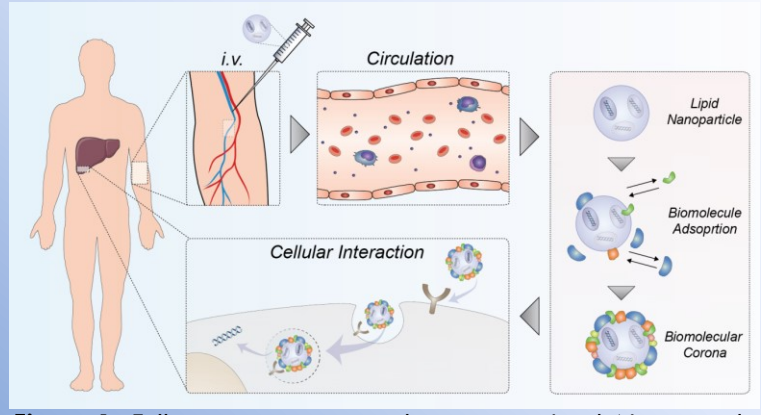


Figure 1: Following intravenous administration, Lipid Nanoparticles (LNPs) adsorb blood biomolecules on their surface forming a "**corona**". Corona proteins (e.g. ApoE) are recognized by cell receptors (e.g on hepatocytes), leading to nucleic acid cytoplasmatic release.

REFERENCES

Akinc, et al. **The Onpattro story and the clinical translation of nanomedicines containing nucleic acid-based drugs.** Nat. Nanotechnol. 14, 1084–1087 (2019).

Francia,V et al. **The Biomolecular Corona of Lipid Nanoparticles for Gene Therapy.** Bioconjugate Chemistry Article ASAP

ACKNOWLEDGEMENTS

Financial support from the University Medical Center Utrecht (Netherlands) and the European Union's Horizon 2020 research and innovation programme "EXPERT" (#825828)

UMC Utrecht · THE UNIVERSITY OF BRITISH COLUMBIA · EXPERT

METHODS

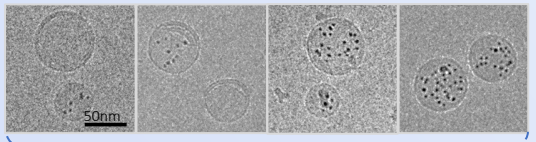
Formulation of magnetic LNPs

Composition	mol %
DLin-MC3-DMA	50.0
DSPC	10.0
Cholesterol	38.5
PEG-DMG	1.5

Figure 2: Magnetic LNPs (IONP-LNP) containing 5nm Iron Oxide NP (IONP) were prepared by rapid mixing through a T-junction mixer. 4 different IONP were used. Only in 4 all LNPs are loaded with IONP.

Sample Name	A	B	C	D
IONP/µmol lipid	$1.1x10^{13}$	$2.2x10^{13}$	$4.4x10^{13}$	$8.8x10^{13}$
LNP Ø (nm)	41.8 ± 8.2	51.4 ± 11.7	49.5 ± 14.2	47.5 ± 12.5
IONP/LNP	2.3 ± 4.6	6.4 ± 6.7	9.7 ± 8.7	12.7 ± 11.9

Miltenyi Biotec



Magnetic Separation

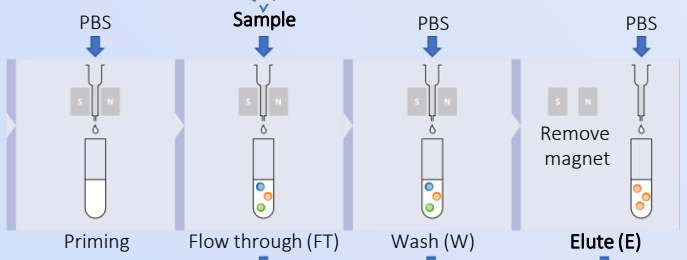
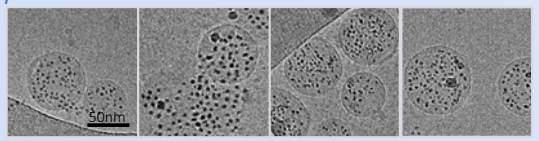
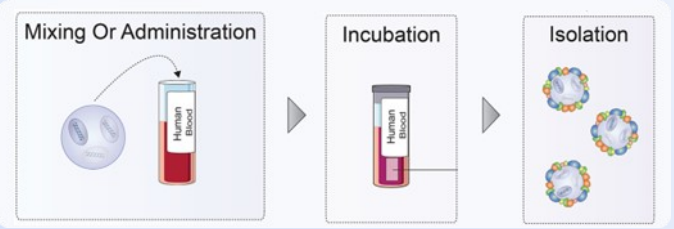


Figure 3: Magnetic LNPs (IONP-LNP) are ritained in the magnetic column. Free IONP and emply LNPs are washed away. Once the magnet is removed, IONP-LNP are eluted.



RESULTS



a) The corona of LNPs in different media

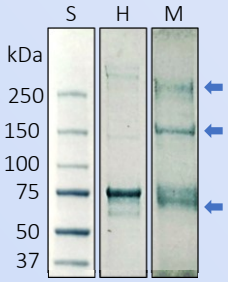


Figure 4: IONP-LNP were incubated in human (H) or mouse serum and the corona-IONP-LNP separated as described in methods. Complexes were run on a polyacrylamide gel and stained with Comassie blue. The 2 samples have different proteins in their corona (blue arrows). S = standard

b) Uptake of corona-LNP complexes

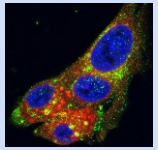


Figure 5: Corona-IONP-LNP complexes were incubated on HEPG2 cells (hepatocytes). Cells were fixed and stained and imaged via confocal.
Blue: nuclei; Red: lysosomes; Green: LNP

CONCLUSIONS

- ❑ **Magnetic IONP-LNPs can be effectively formulated and separated from free IONP and emply LNPs**
- ❑ **Corona of IONP-LNPs formed in different media has a different protein content**