Complement cascade and the biological fate of liposomes in rodents

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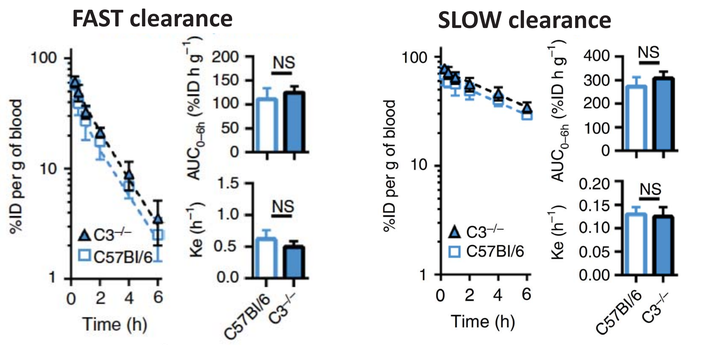
Introduction

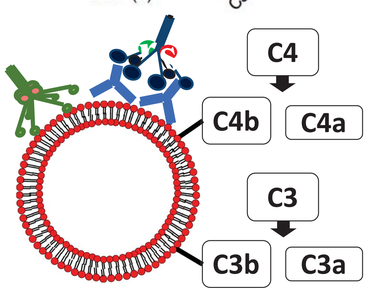
Liposomes

- Vastly used as drug delivery system.
- Large list of approved medicines.
- It has been shown to induce hypersensitivity reactions.

Complement cascade x Pharmacokinetics of nanoparticles

Bertrand et al, Nature Communication 8, 777, 2017





Complement cascade x liposomes

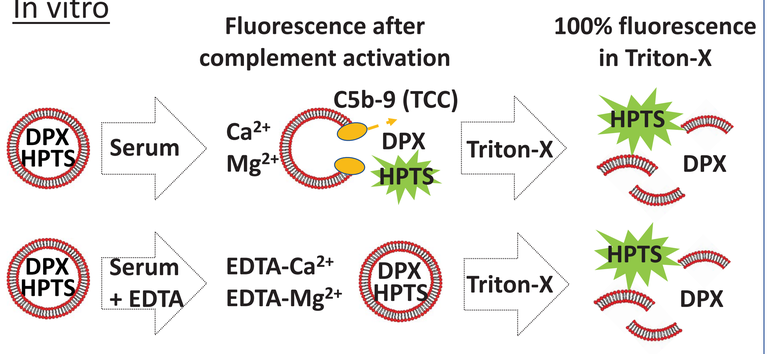
Release of drugs?
Pharmacokinetics?
Biodistribution?

Objectives

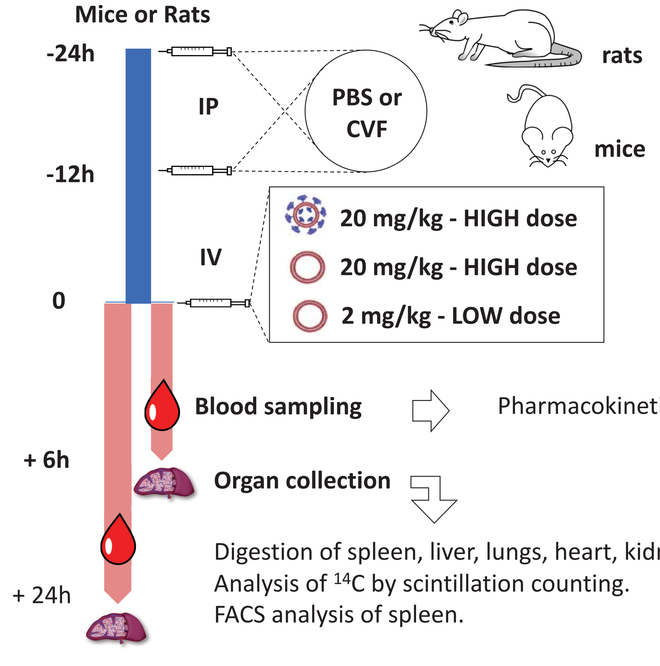
To evaluate the role of complement in the fate of liposomes in mice and rats.

Methods

In vitro



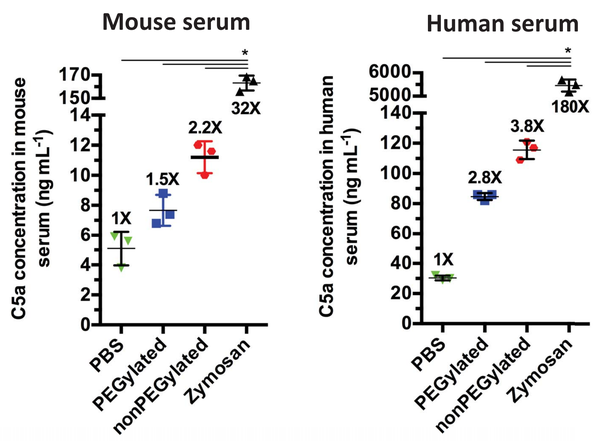
In vivo



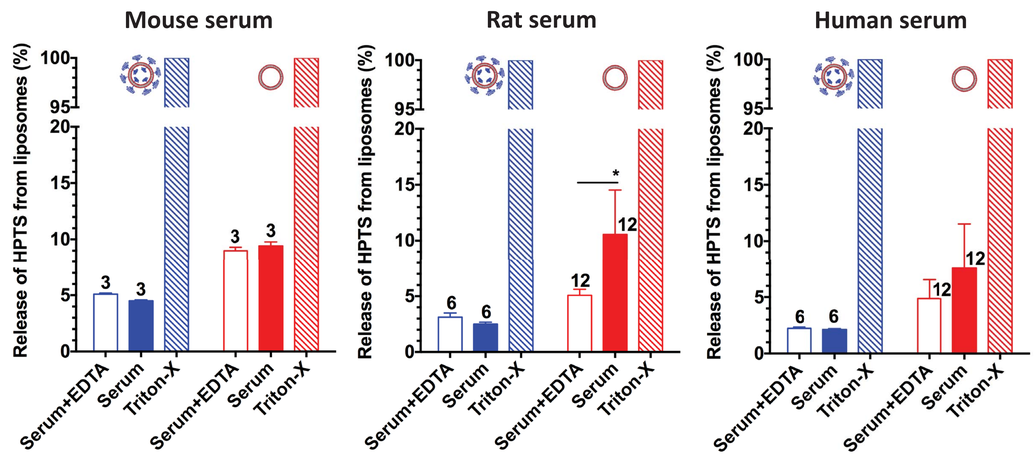
Digestion of spleen, liver, lungs, heart, kidneys.
Analysis of ^{14}C by scintillation counting.
FACS analysis of spleen.

Results

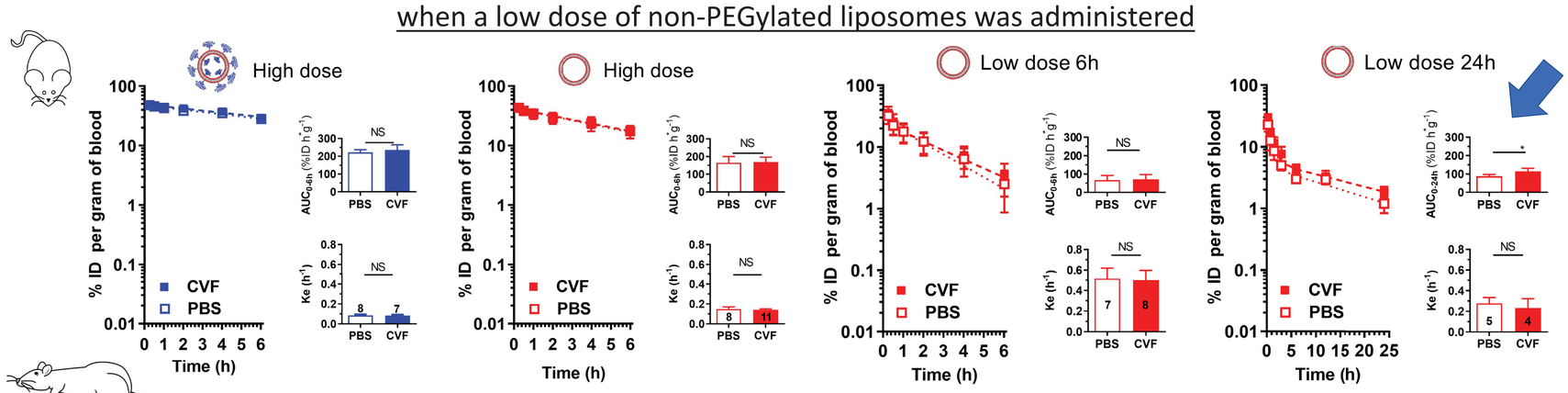
Liposomes are weak activators of the complement cascade

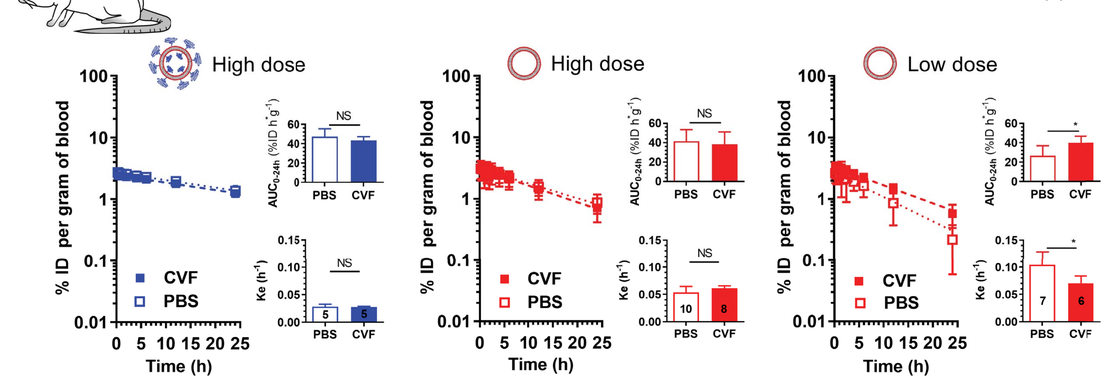


Liposomes are stable in human and rodent sera

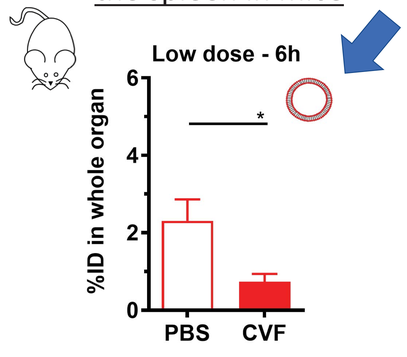


In mice and rats, the only perceivable effect of complement cascade on pharmacokinetics was at later phase of distribution when a low dose of non-PEGylated liposomes was administered

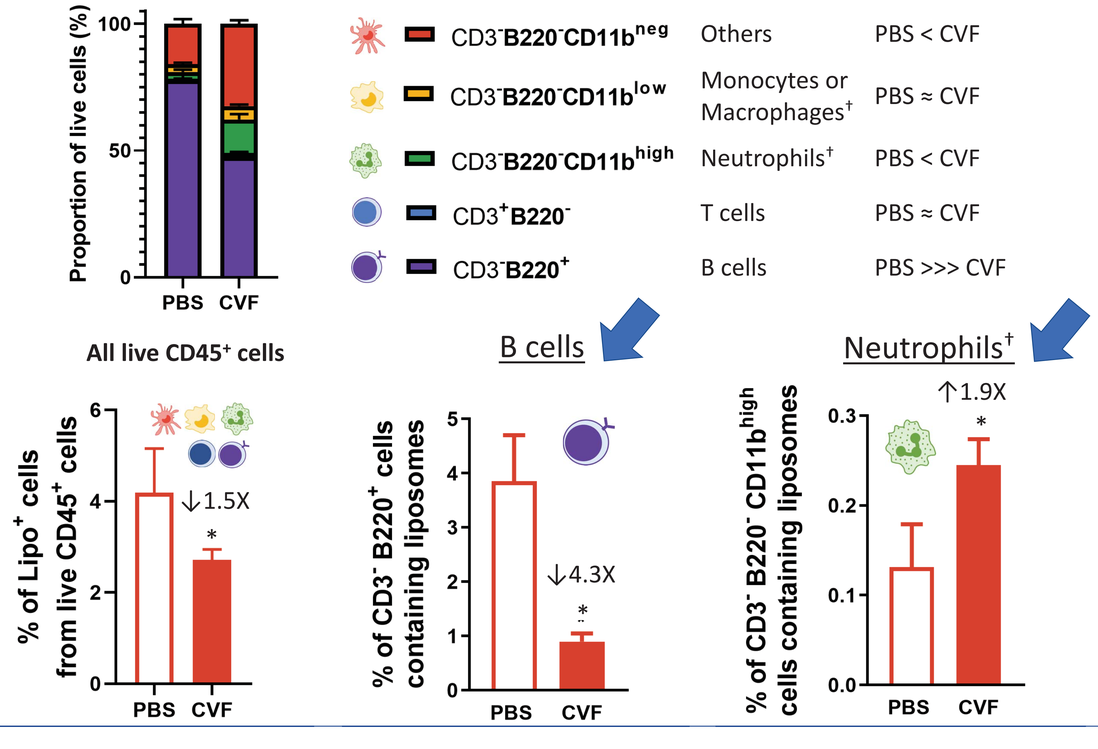




Distribution of liposomes to the spleen in mice



Complement proteins impact the distribution of liposomes to immune cells in mice spleen



Conclusions

- Complement cascade is insufficient to explain the fate of liposomes in rodents.
- Complement proteins seem to trigger the elimination of liposomes through B cells in the spleen of mice.

Further reading - Viana et al, Nanoscale, 2020!
https://tinyurl.com/y6eppjz5

Acknowledgements

CAPES
CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico
CRSNG NSERC
FUNAPE Fundação de Apoio à Pesquisa - UFG
FINEP
Fondation CHU de Québec