

Nanoparticules biomimétiques

Session Stratégies innovantes en transfusion plaquettaire :
des plaquettes de culture aux nanoparticules biomimétiques

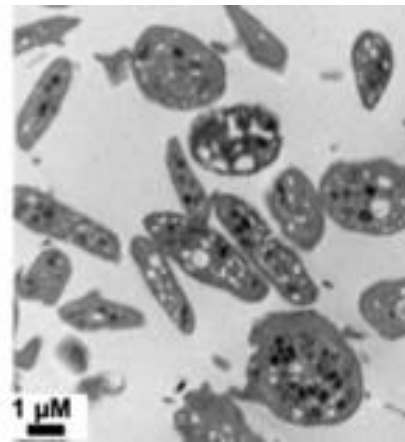
Dr Stéphanie Roulet



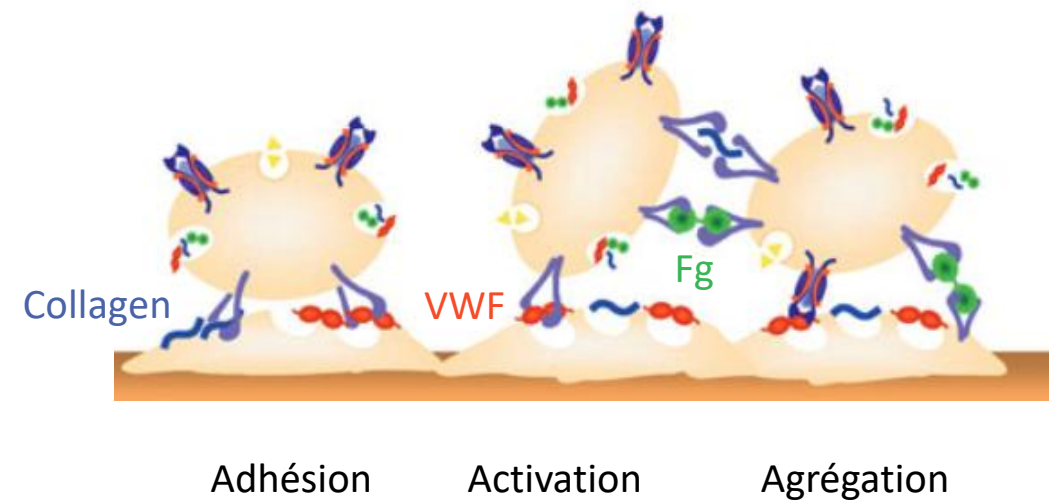
Liens d'intérêt

- CSL Behring
- LEO Pharma
- LFB
- Sanofi
- Stago BioCare

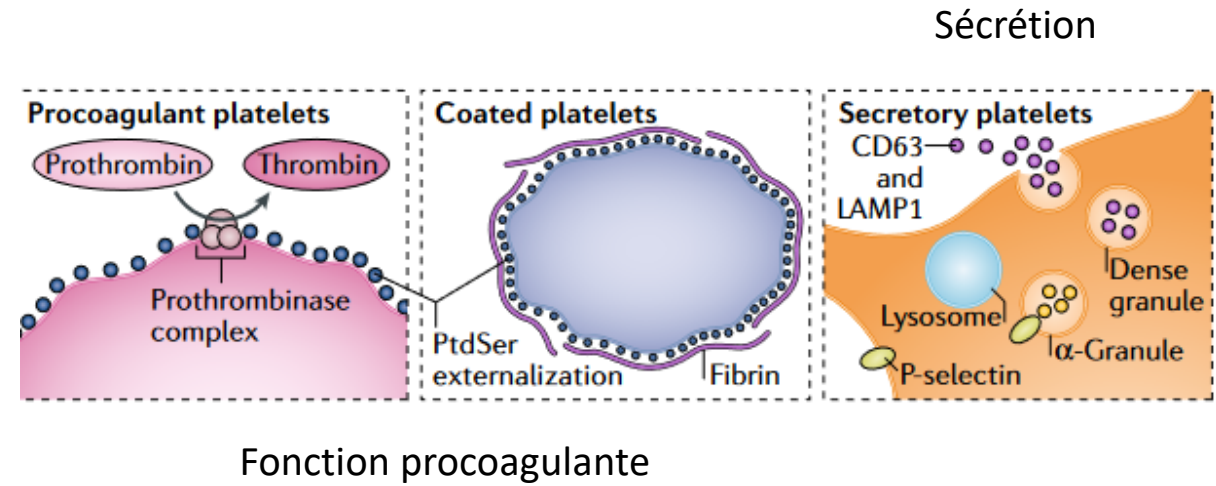
Les plaquettes



Rauch et al. *Circ Res* 2023



Wei et al. *Br J Haematol* 2009



van der Meijden & Heemskerk. *Nat Rev Cardiol* 2019

Indications de la transfusion plaquettaire



Chirurgie hémorragique

Thrombopénie

Thrombopathie

Greffe de cellules souches

Syndromes myélodysplasiques



Réversion des AAP

Insuffisance médullaire chronique

Anémie aplasique

Polytraumatisme



Les écueils de la transfusion plaquettaire



Manque de donneurs

Courte durée de vie (7-10 j)



Courte durée de conservation (3-5 j)



Contamination
bactérienne ou virale



Coût



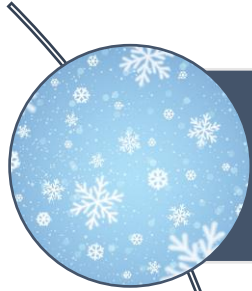
Pas de disponibilité
préhospitalière



Réaction immunologique
(TRALI)

HLA

Quelles alternatives à la transfusion de plaquettes ?



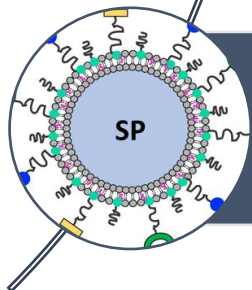
Augmenter la durée de conservation des plaquettes



Production à partir de mégacaryocytes en culture

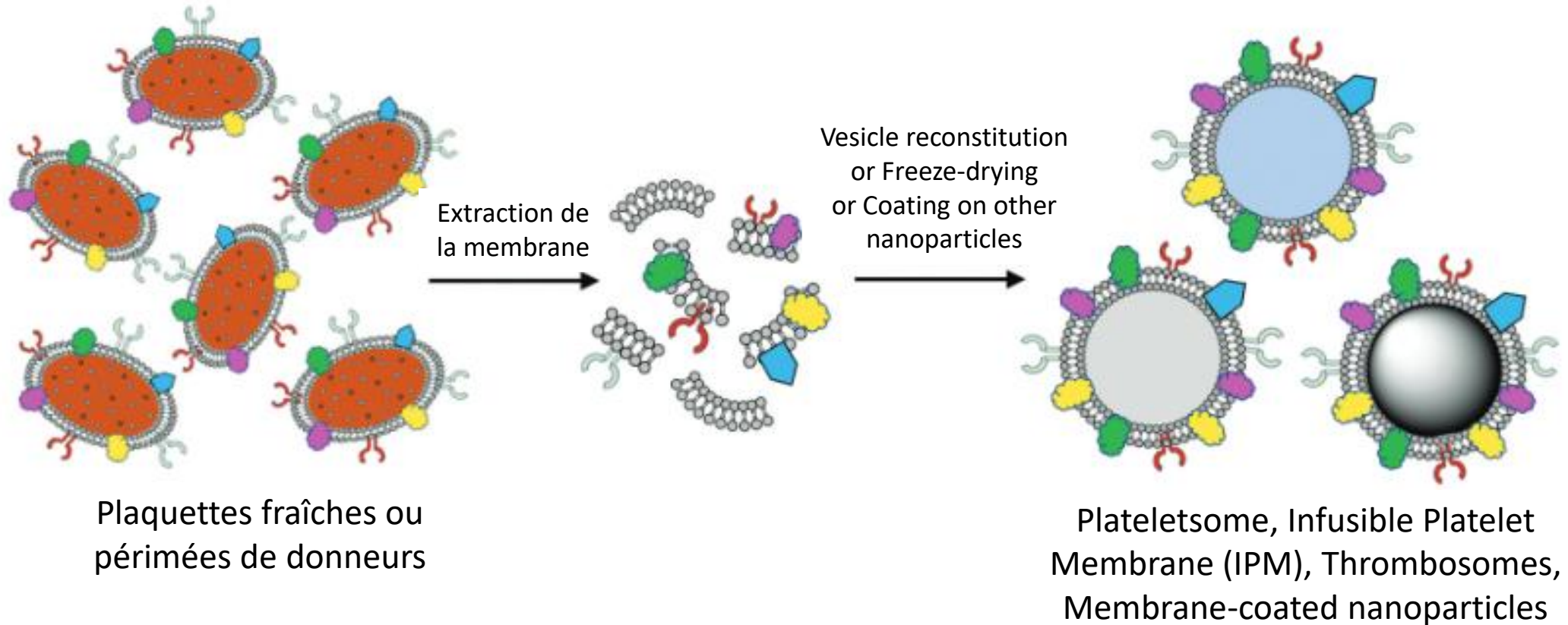


Plaquettes artificielles à base de membrane plaquettaire



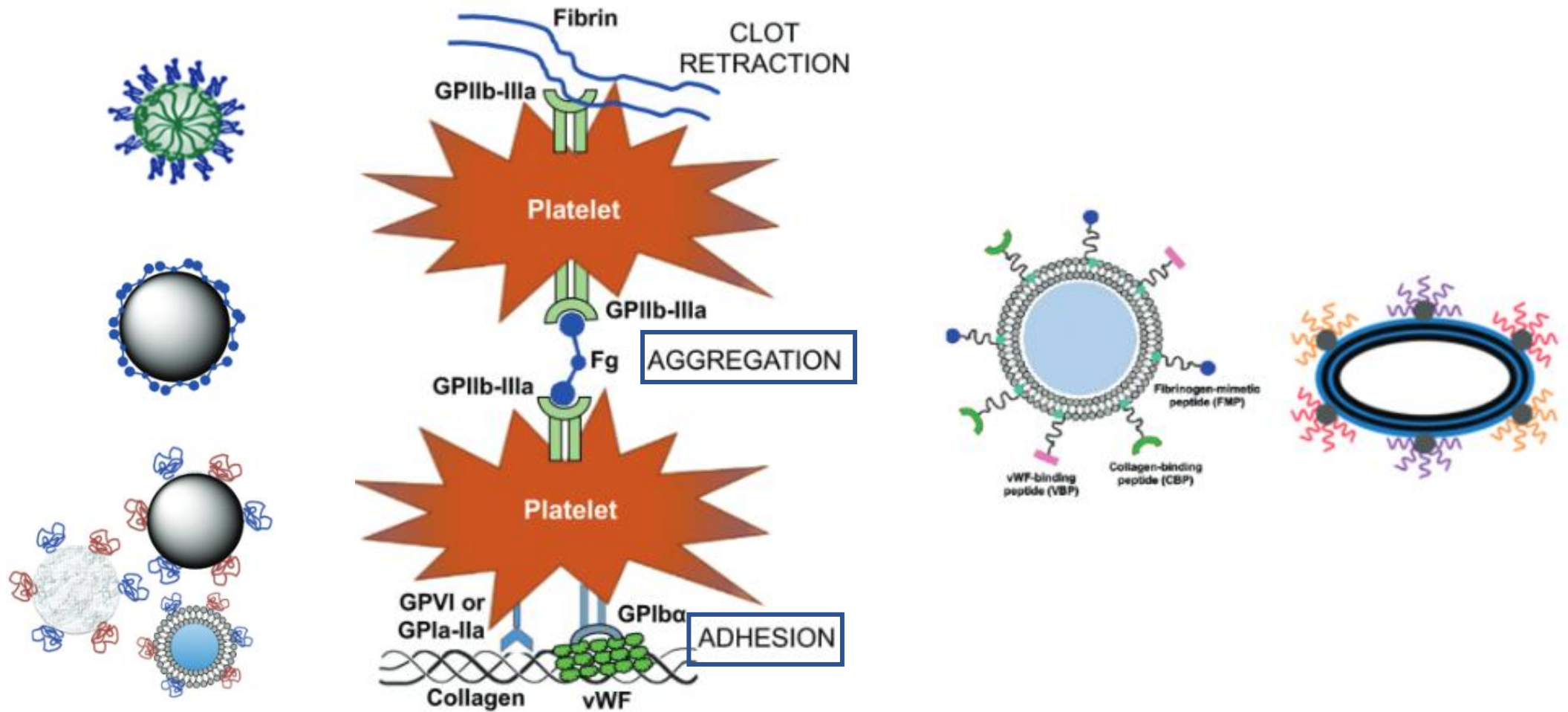
Nanoparticules inspirées des plaquettes

Plaquettes « artificielles » à base de membrane plaquettaire



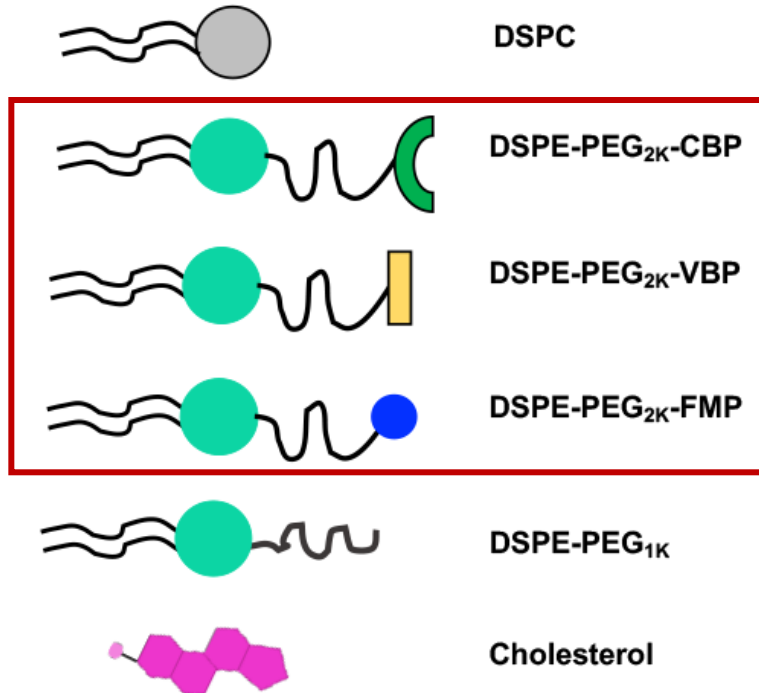
Luc et al. *Platelets* 2022

« Plaquettes artificielles biomimétiques »



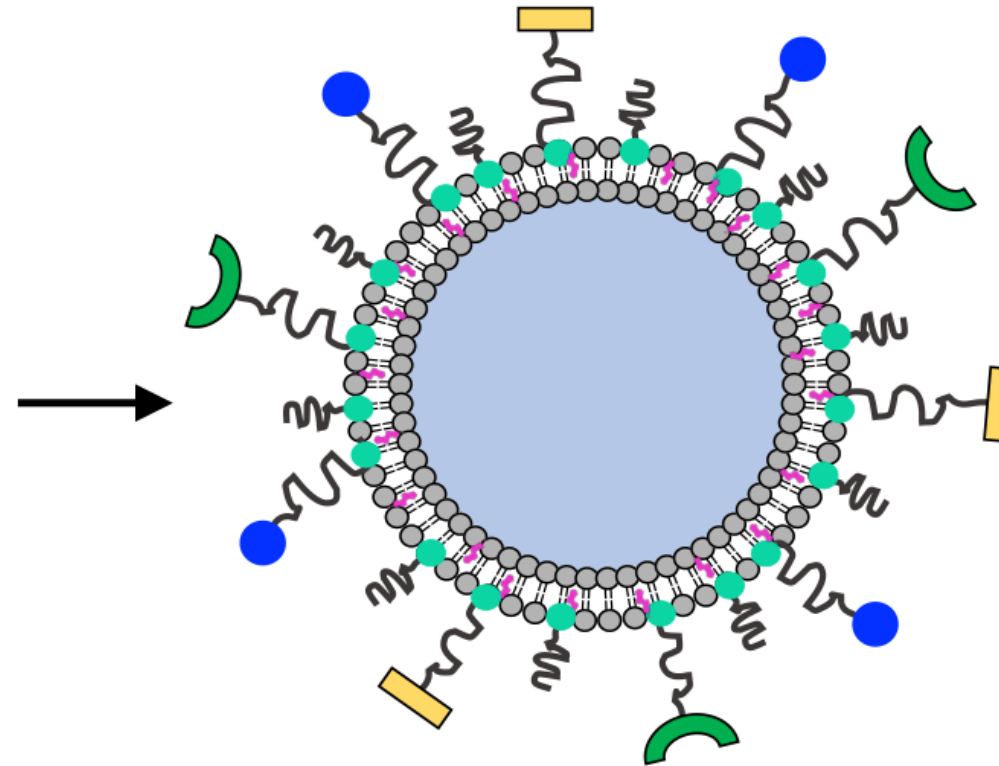


SynthoPlate Components

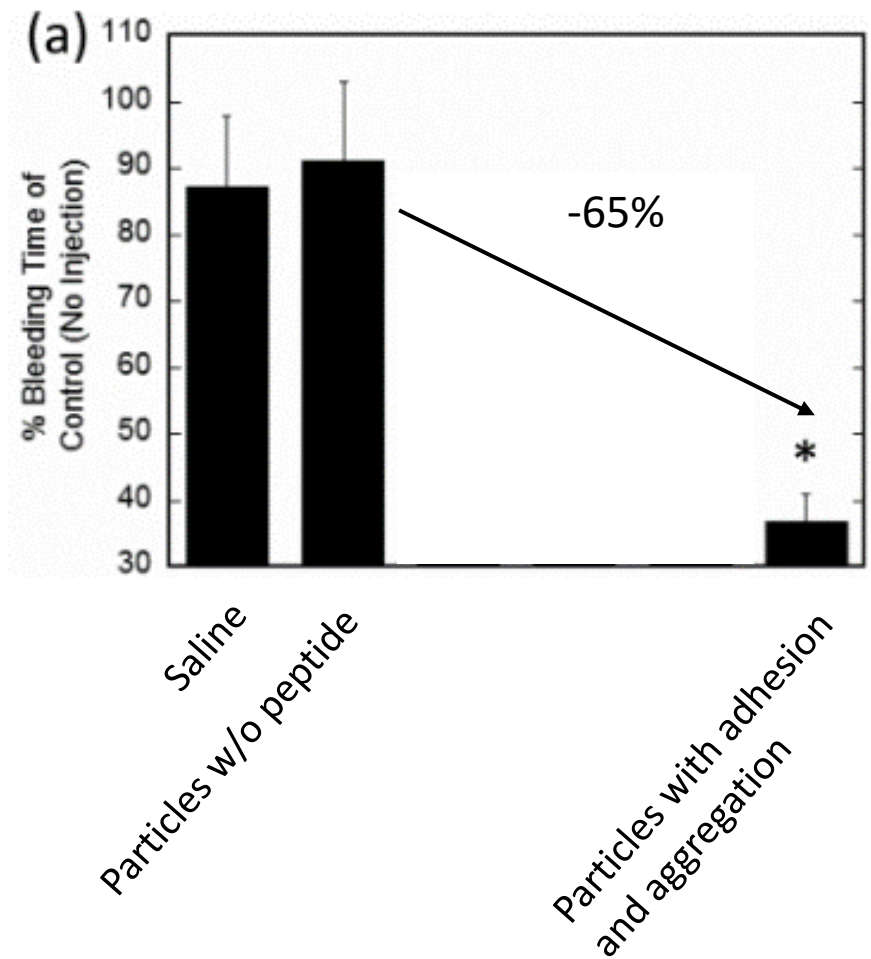
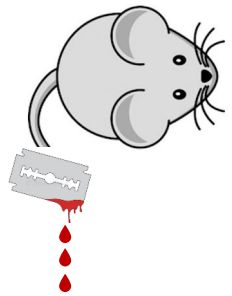
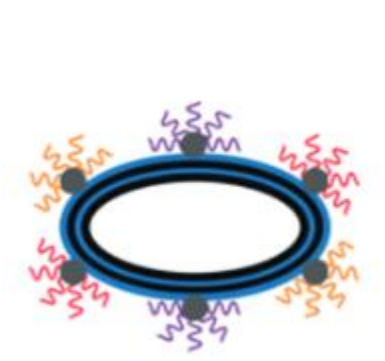
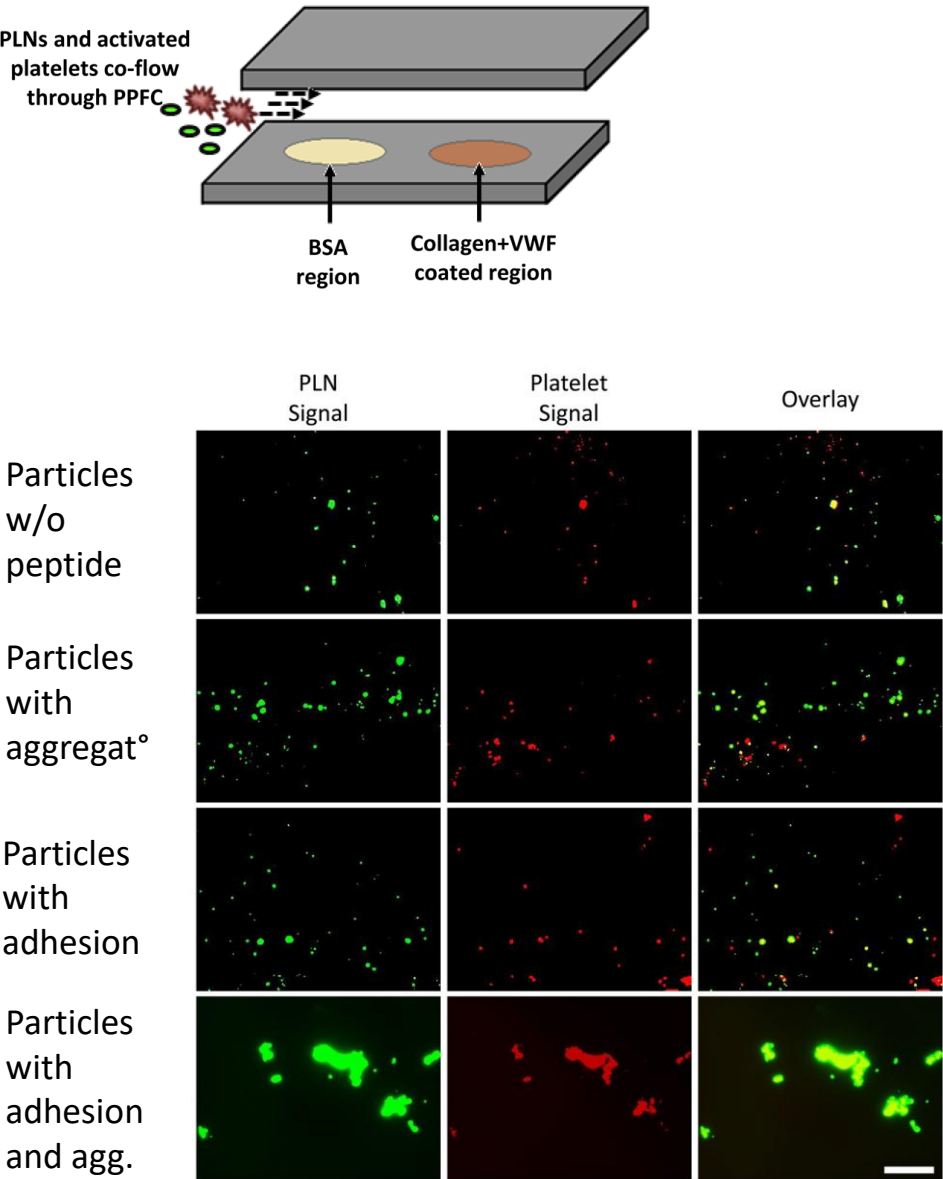


CBP: collagen binding peptide
VBP: VWF binding peptide
FMP: fibrinogen mimetic peptide

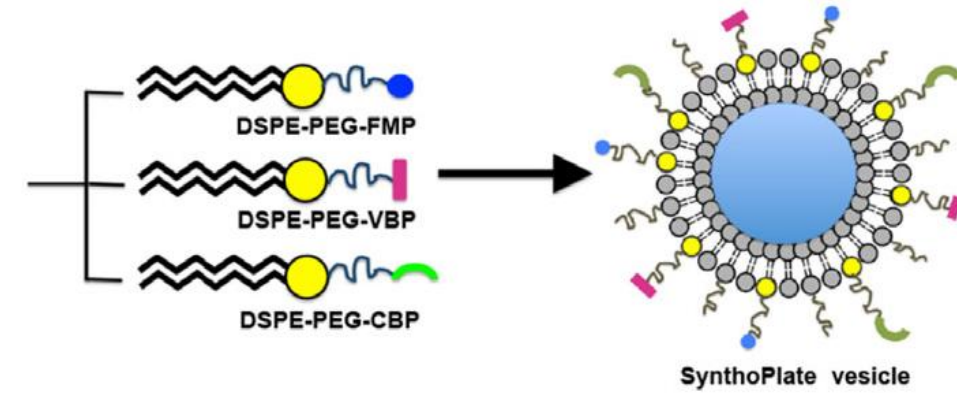
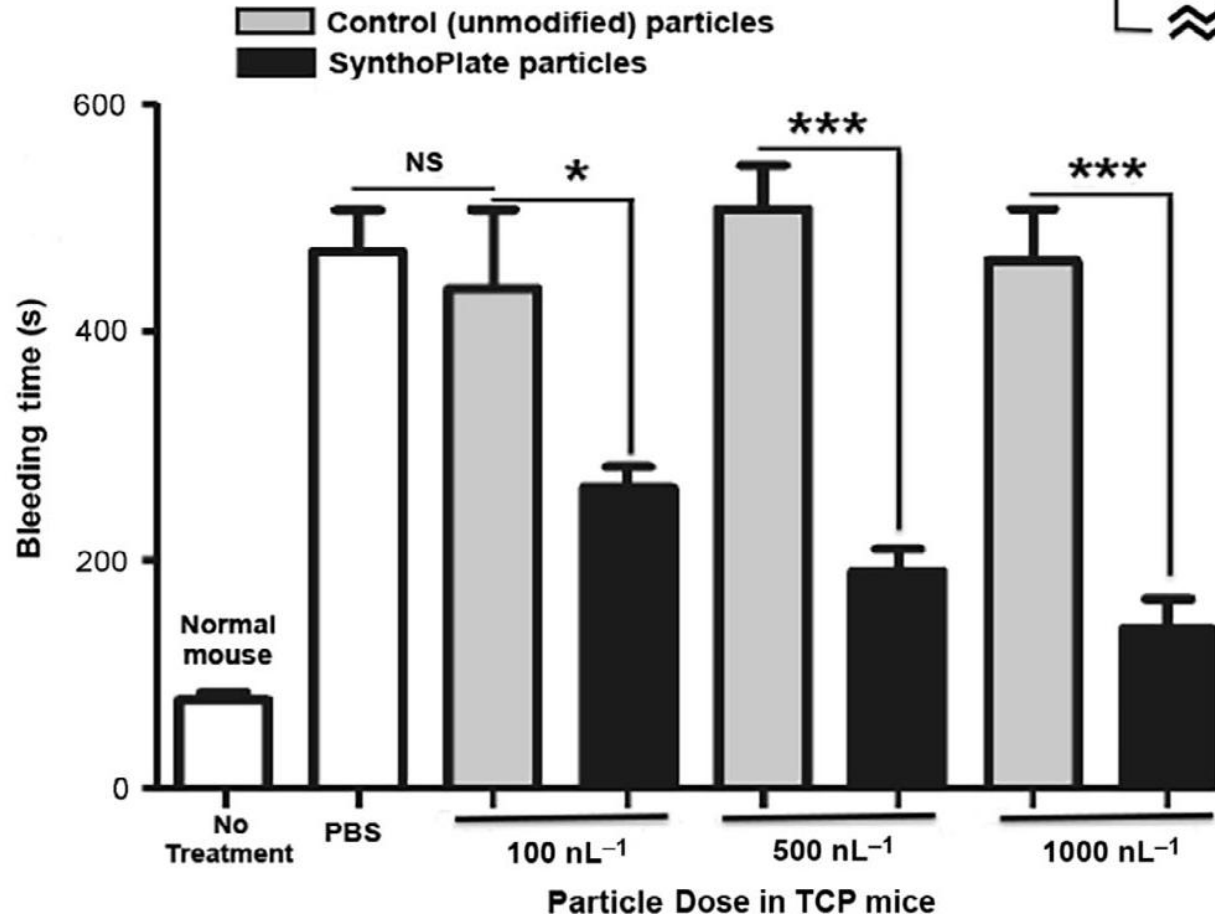
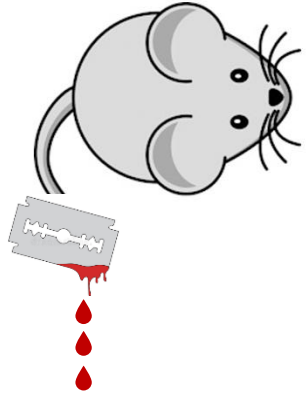
SynthoPlate



Les « PLN » diminuent le temps de saignement chez la souris

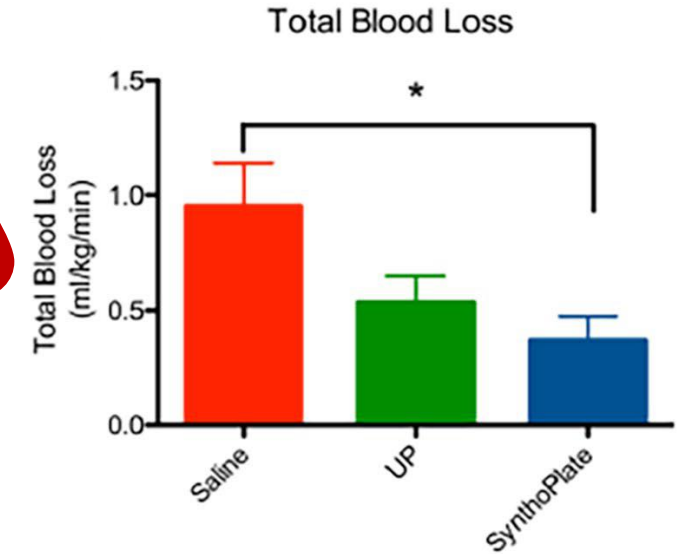
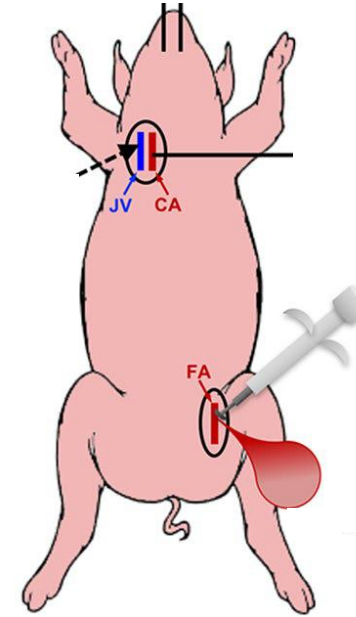
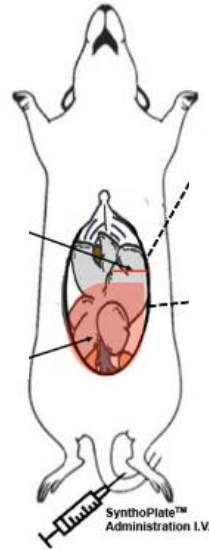
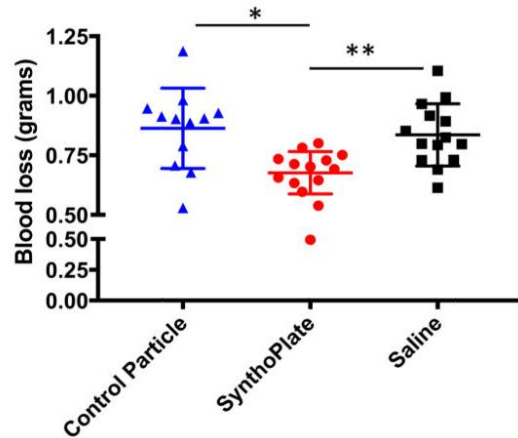


Les « PLN » réduisent le temps de saignement des souris thrombopéniques

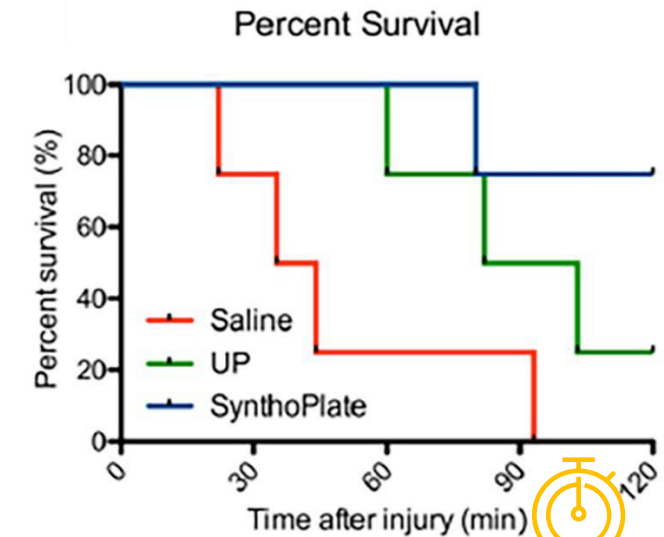
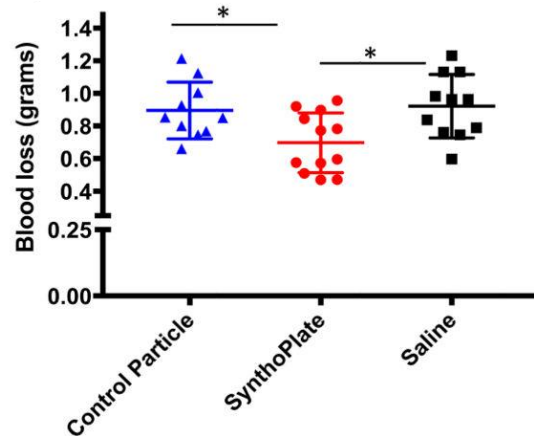


Les SynthoPlate™ améliorent l'hémostase dans des modèles de trauma

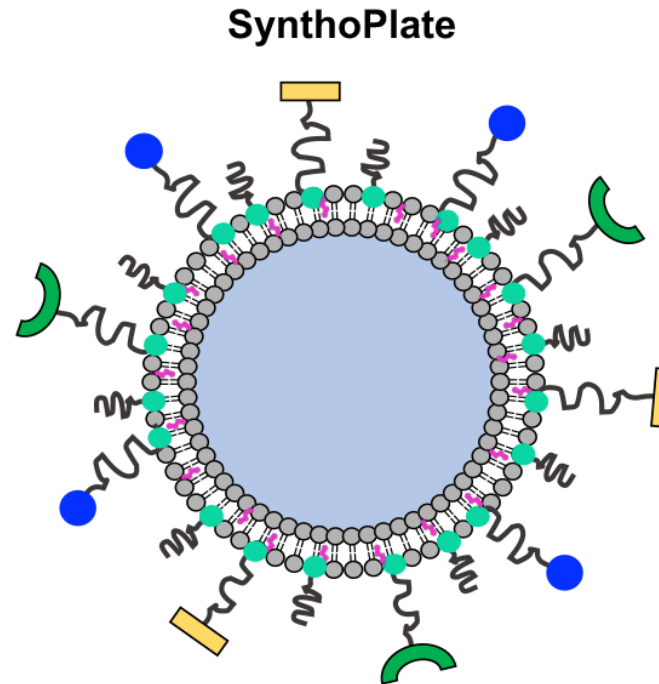
Pre-treatment protocol



Rescue protocol



Les nanoparticules inspirées des plaquettes



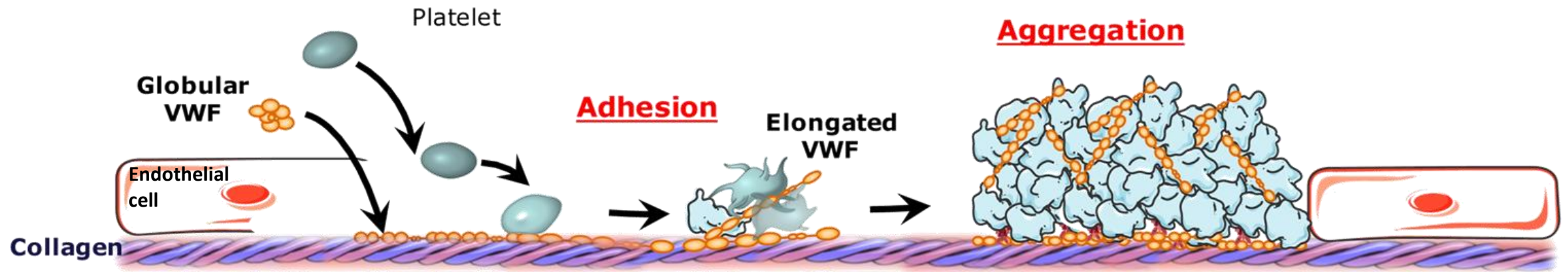
Dysfonction plaquettaire



Hémophilie

Maladie(s) de Willebrand

Rôle du facteur Willebrand dans l'hémostase primaire



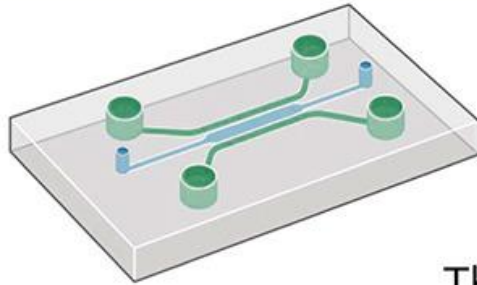
Le VWF plasmatique globulaire se lie et se déplie sur la surface de collagène sous-endothélial

Les plaquettes adhèrent à ce VWF déplié

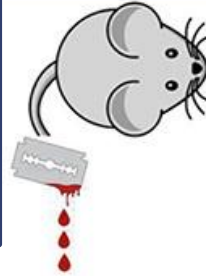
Le VWF participe à la croissance du thrombus

Synthetic platelets improve platelet adhesion and thrombus formation on collagen using blood from VWD murine models

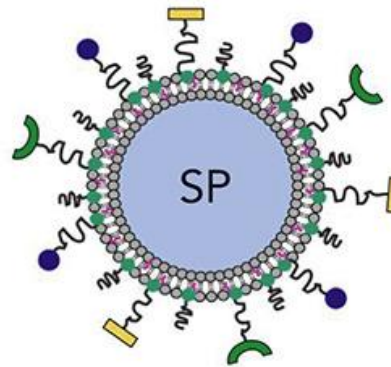
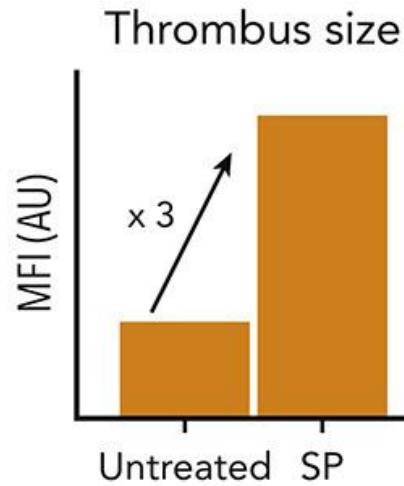
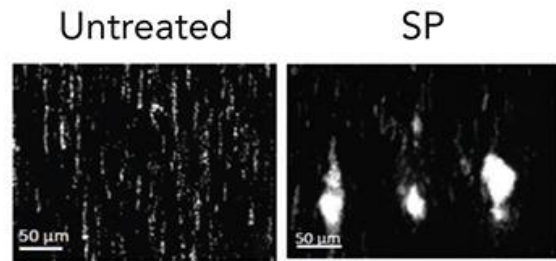
Synthetic platelet treatment reduces blood loss in murine models of VWD



Roullet et al. *Blood* 2023



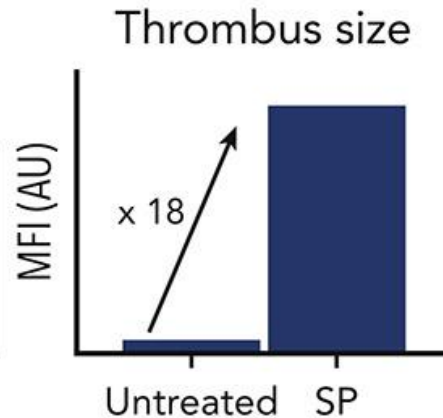
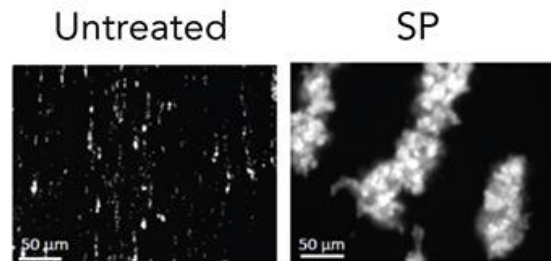
VWD 2B



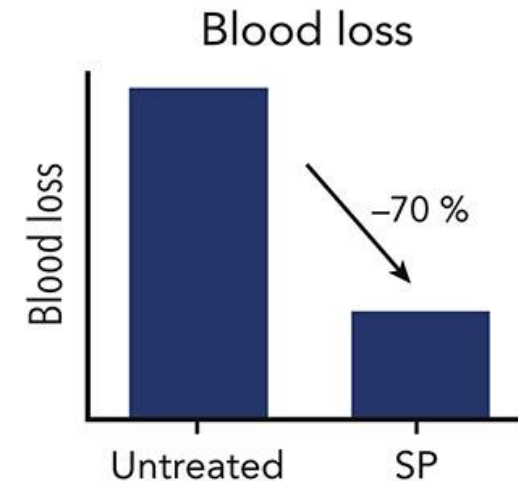
VWD 2B



VWF KO

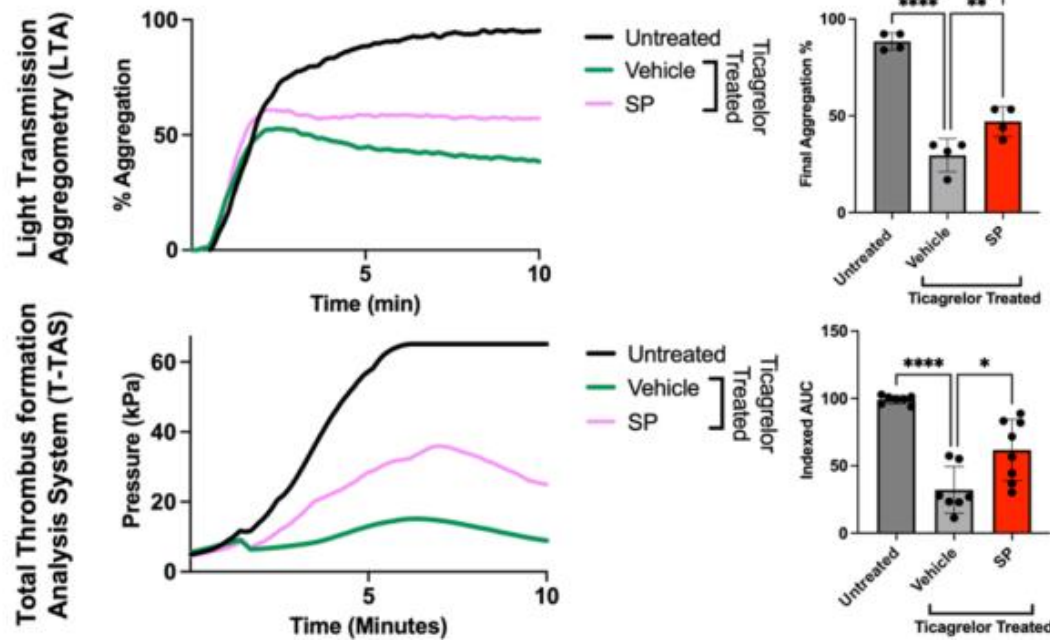


VWF KO



Oral Communication Presenter: **Ujja Didar Singh Sekhon**, PhD Oral Communication Co-Author: Emily Gahagan
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Communication Co-Author: Rebecca Ahn Oral Communication Co-Author: Anirban Sen Gupta, PhD Oral
Communication Co-Author: Macky Neal Oral Communication Co-Author: Christa Pawlowski Oral
Communication Co-Author: Michael Bruckman

Image 1 :



Ticagrelor

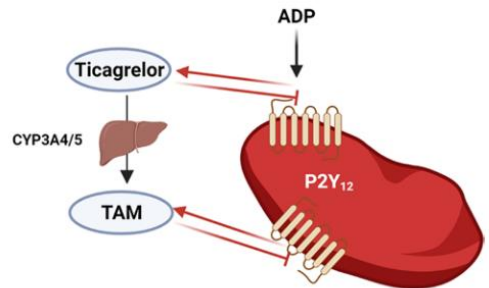
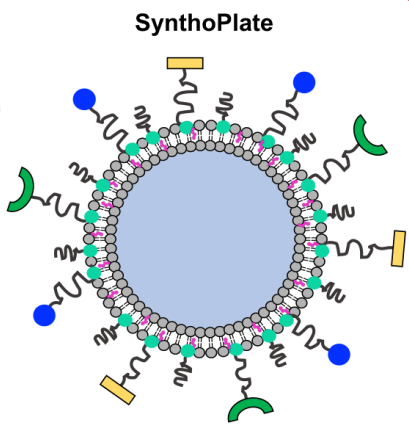
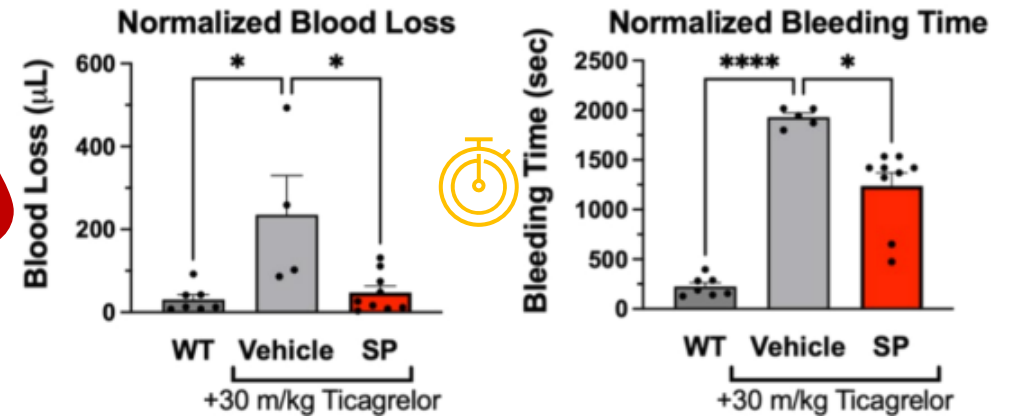
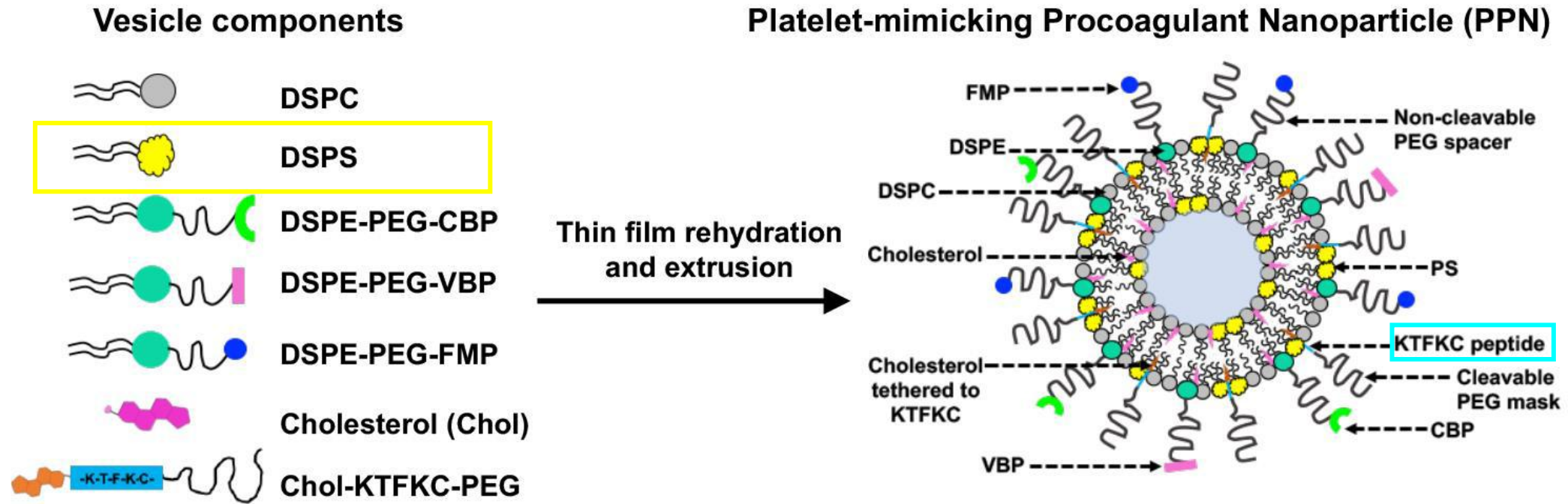


Image 2 :



Les particules procoagulantes mimant les plaquettes



DSPC: distearoylphosphatidylcholine

DSPS: distearoylphosphatidylserine

DSPE: distearoylphosphatidylethanolamine

PEG: polyethylene glycol

Chol-PEG: hides PS in bloodstream

KTFKC: plasmin-cleavable peptide sequence

Fluorescence by rhodamine if needed

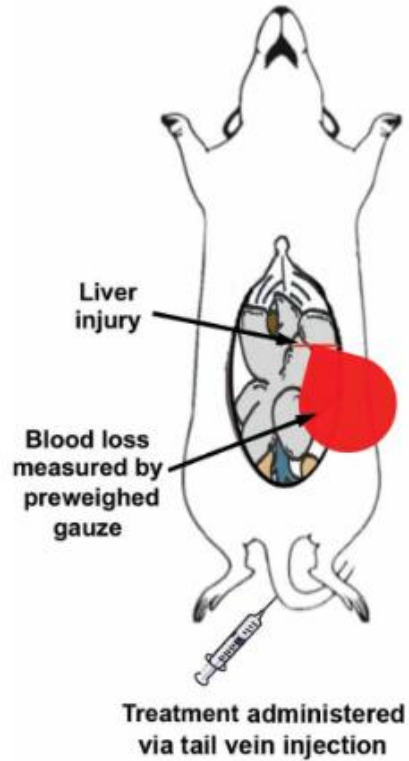
CBP: collagen binding peptide

VBP: Von Willebrand binding peptide, derived from FVIII C2 domain, and interacts with VWF D'D3 domains

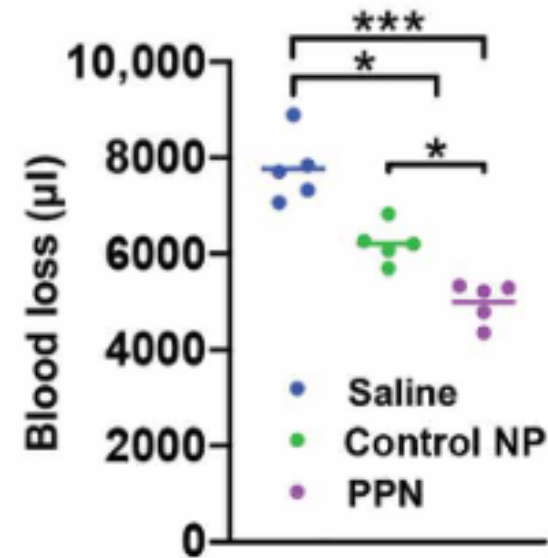
FMP: fibrinogen mimetic peptide

Les particules procoagulantes améliorent l'hémostase et la survie

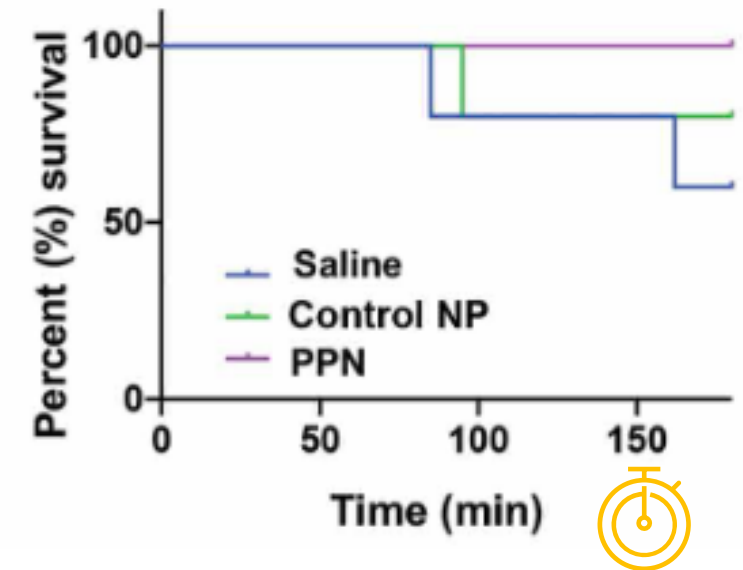
A Rat model of traumatic liver injury



B Blood loss at 1 hour

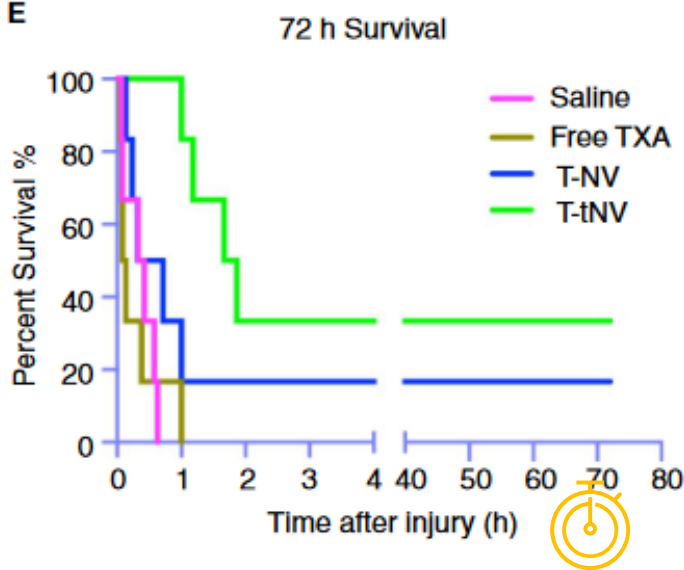
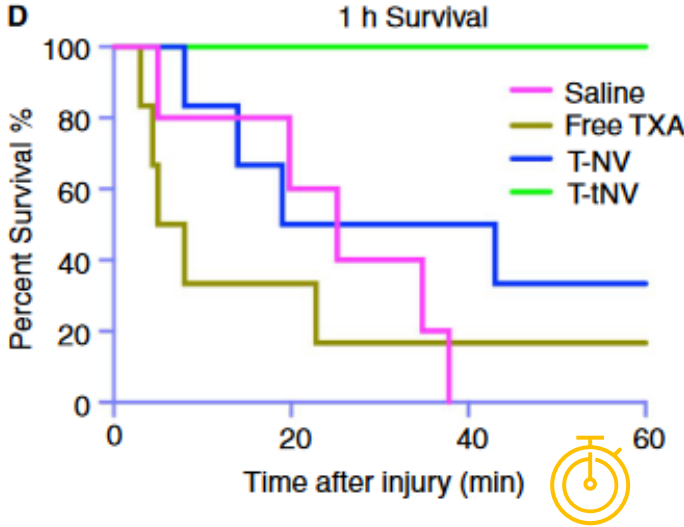
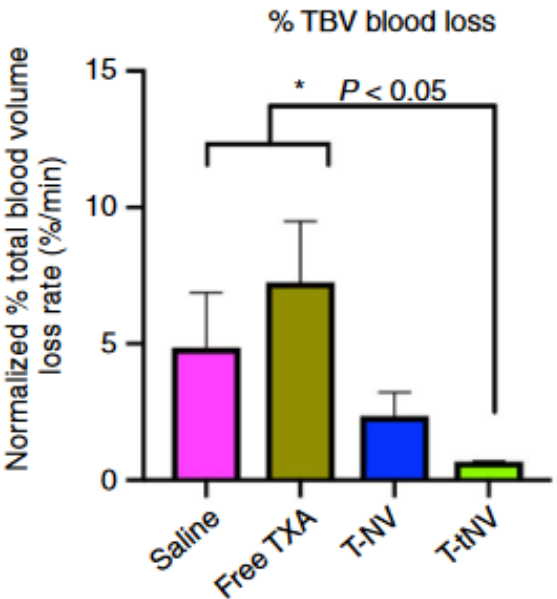
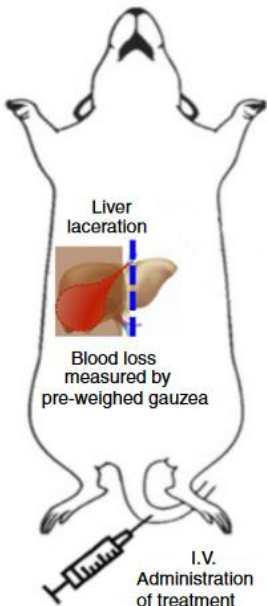
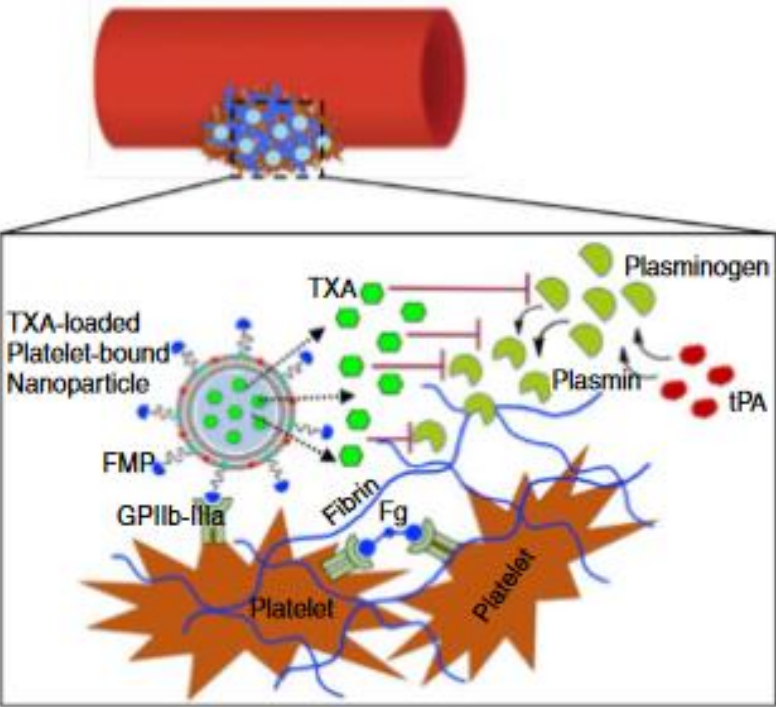


C Survival at 3 hours

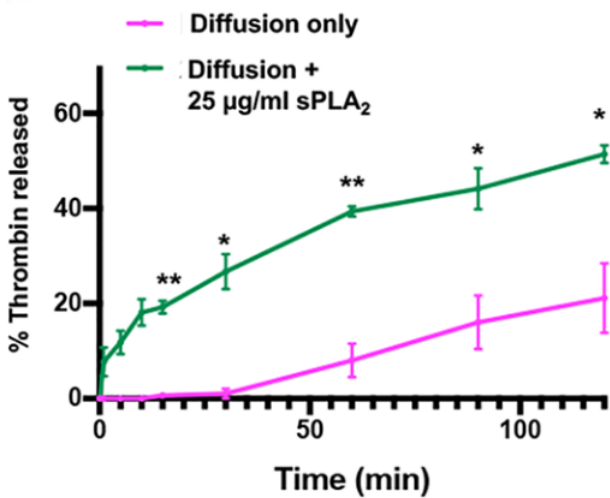
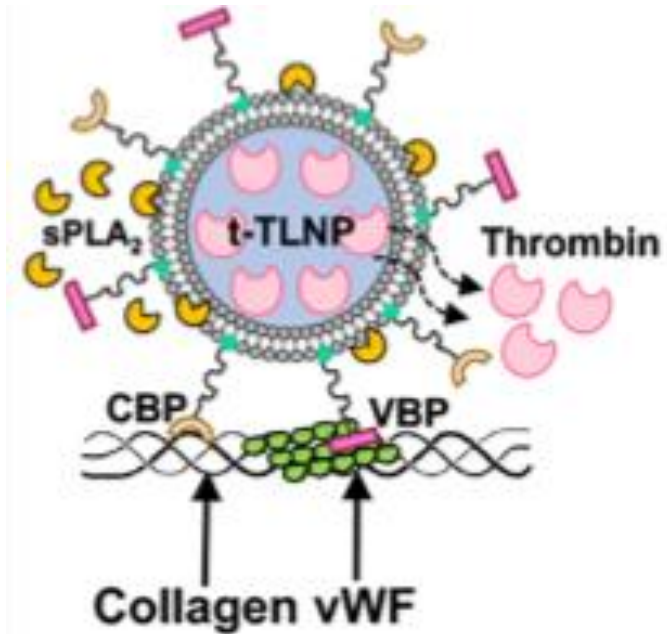


Sekhon et al. *Science Transl Med* 2022

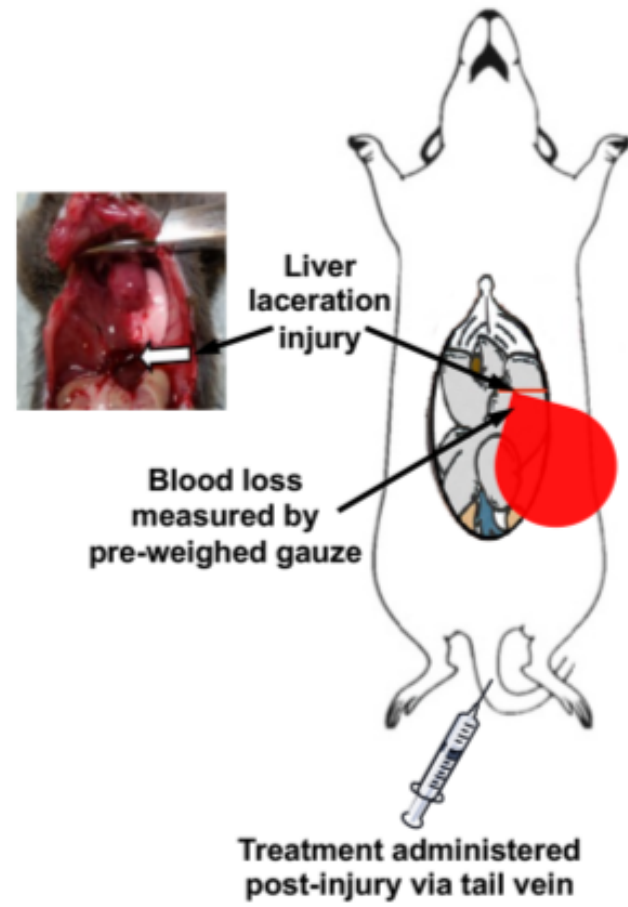
Administration d'acide tranexamique ciblée sur le traumatisme



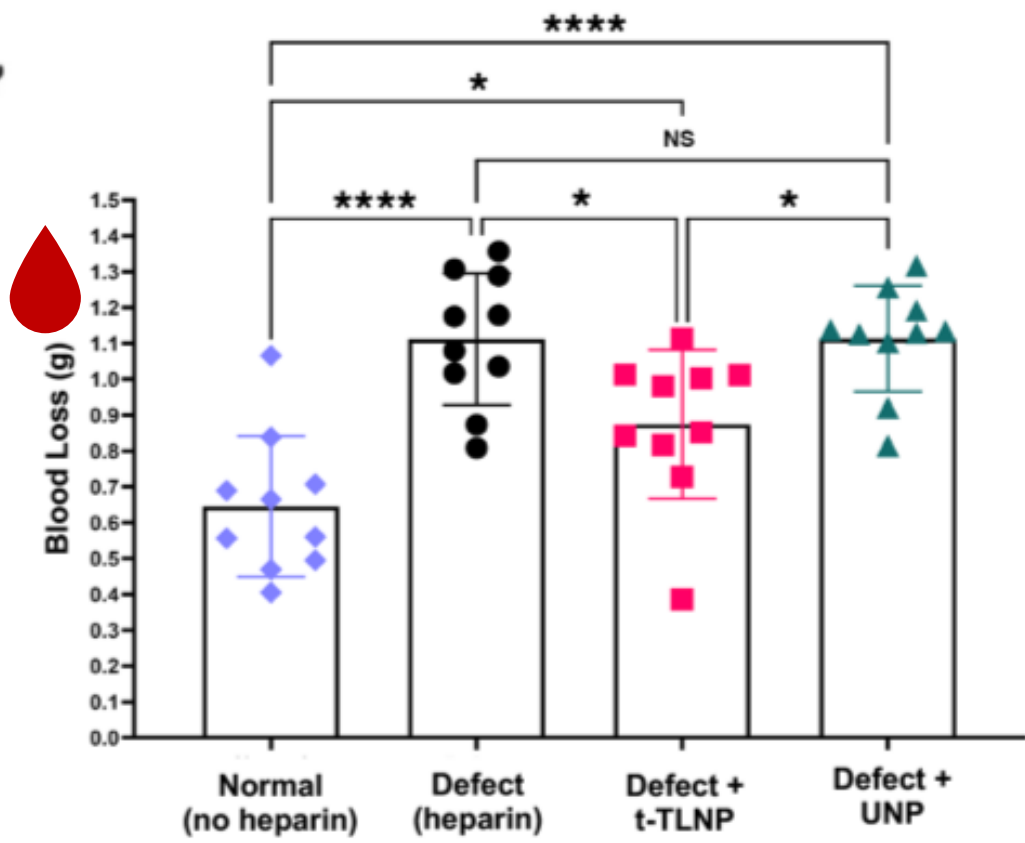
Administration de thrombine ciblée sur le traumatisme



A. Mouse liver laceration model



B. Blood loss analysis



Synthèse sur les nanoparticules inspirées des plaquettes

