

SITUATIONS HÉMOLYTIQUES & LEURS CONSÉQUENCES

Pr Pablo BARTOLUCCI

Univ Paris Est Créteil, Hôpitaux Universitaires Henri Mondor, APHP Coordinating Referral Center for Sickle Cell Disease and Red Blood Cell Disorders – UMGGR, Créteil, France

IMRB INSERM EFS, Team Pirenne, Créteil, France

Member of the ERN Eurobloodnet

Clinical Investigation Center 1430

Réseau Erythrocyte Drépanocytose RED

CONFLITS D'INTÉRÊT

- Consultant for THERAVIA, ROCHE, PFIZER, NOVONORDISK
- Lecture fees for THERAVIA, AGIOS, VERTEX, ROCHE
- Steering committee for ROCHE, THERAVIA, PFIZER
- Research support from THERAVIA, EMMAUS
- Cofounder of INNOVHEM

ANÉMIE

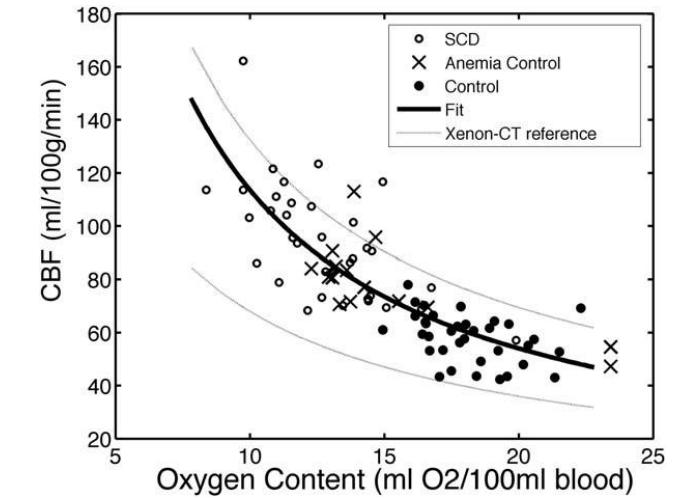
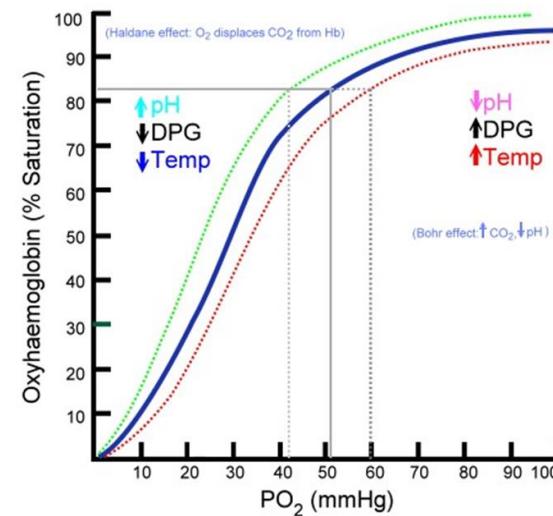


↓ Apport d'oxygène

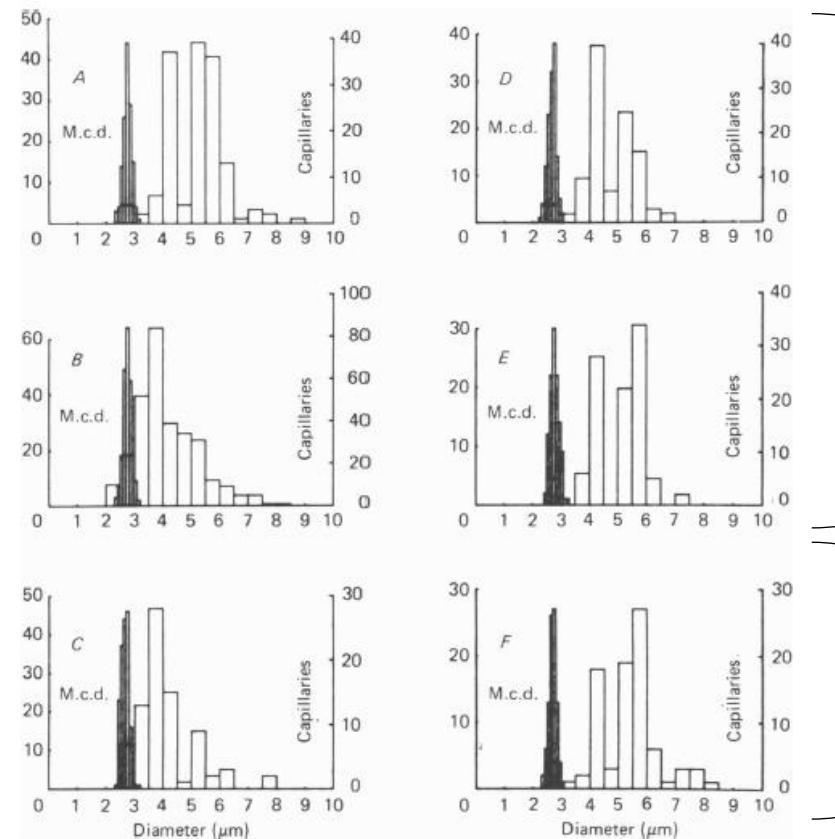
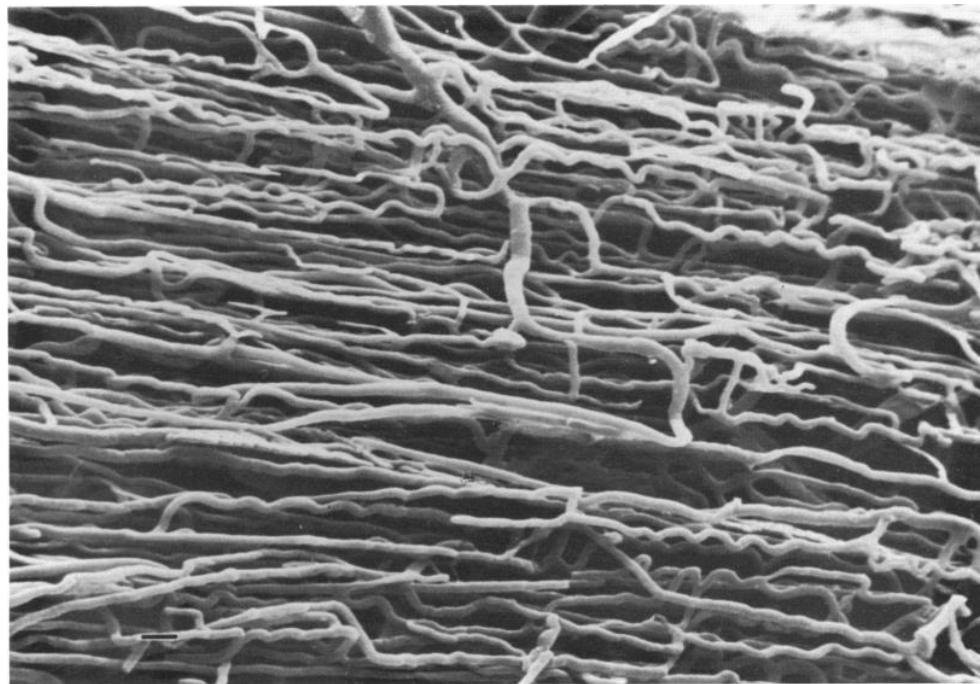
Maintien des apports en oxygène



↑ Débits
↑ 2-3 DPG



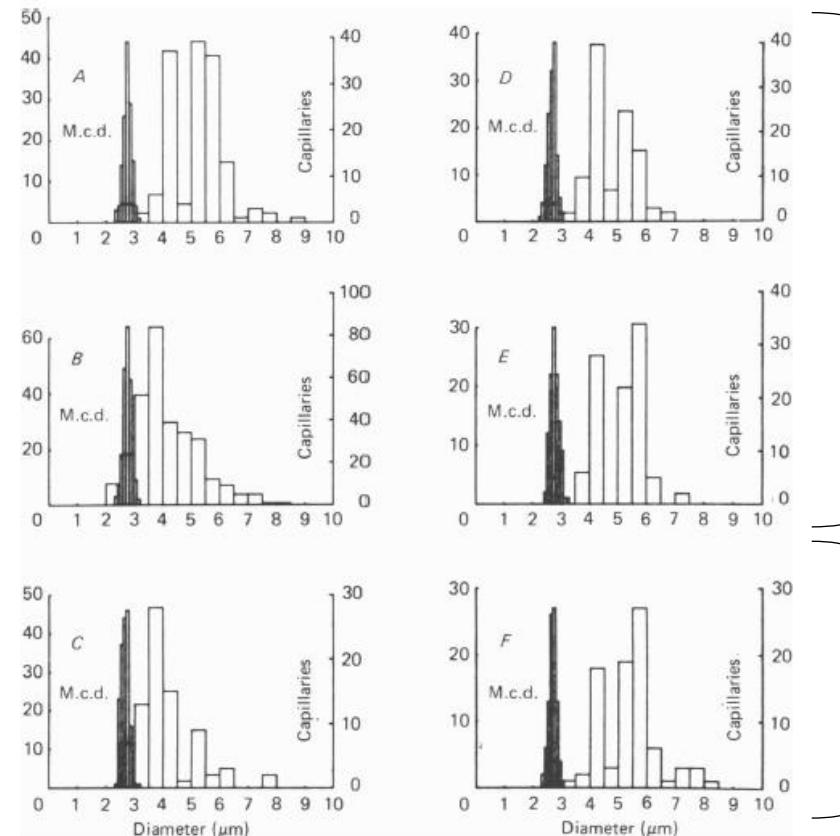
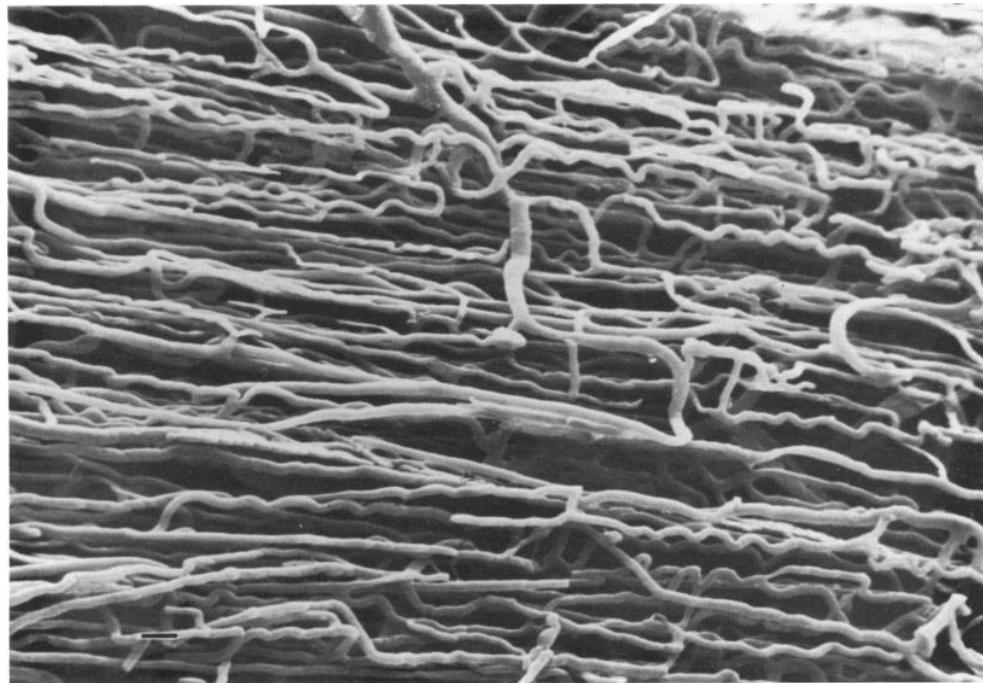
LES ÉCHANGES GAZEUX AU NIVEAU VASCULAIRE



Capillaires myocardiques

Capillaires musculaires

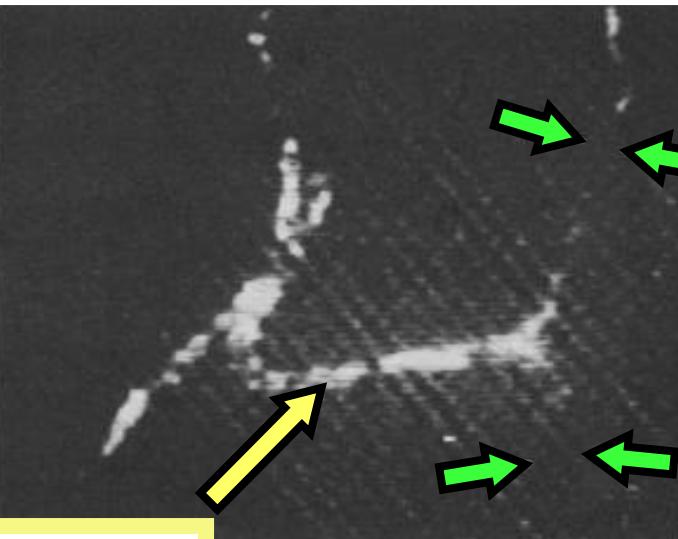
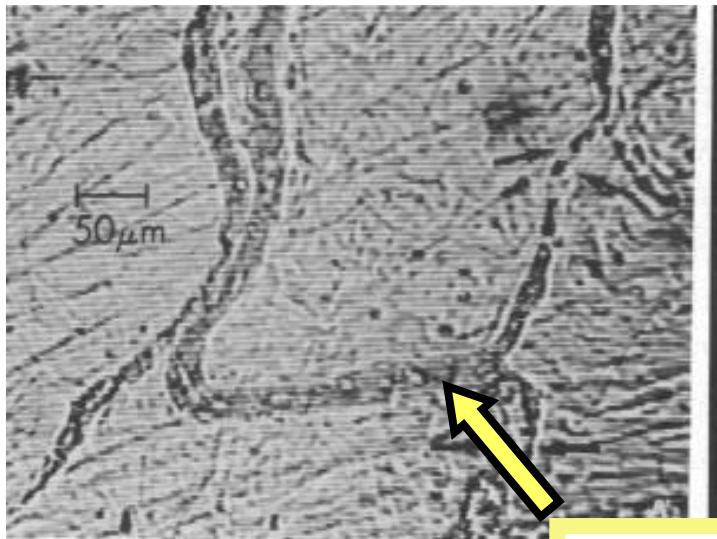
LES ÉCHANGES GAZEUX AU NIVEAU VASCULAIRE



Capillaires myocardiques

Capillaires musculaires

LA VASO-OCLUSION UN PROCESSUS COMPLEXE EST-CE EXCLUSIF DE LA DRÉPANOCYTOSE ?

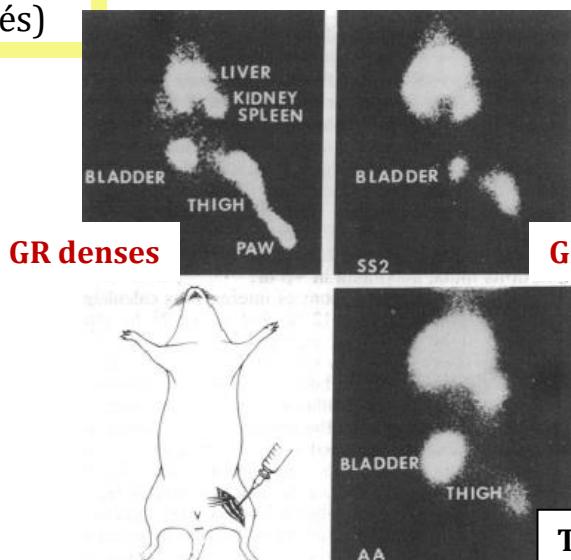
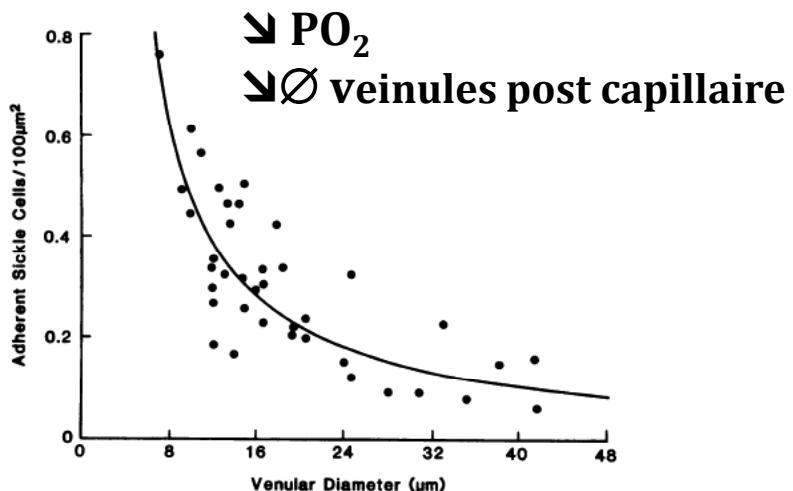


GR denses (FITC)
(GR falciformés)

Kaul et al 1989

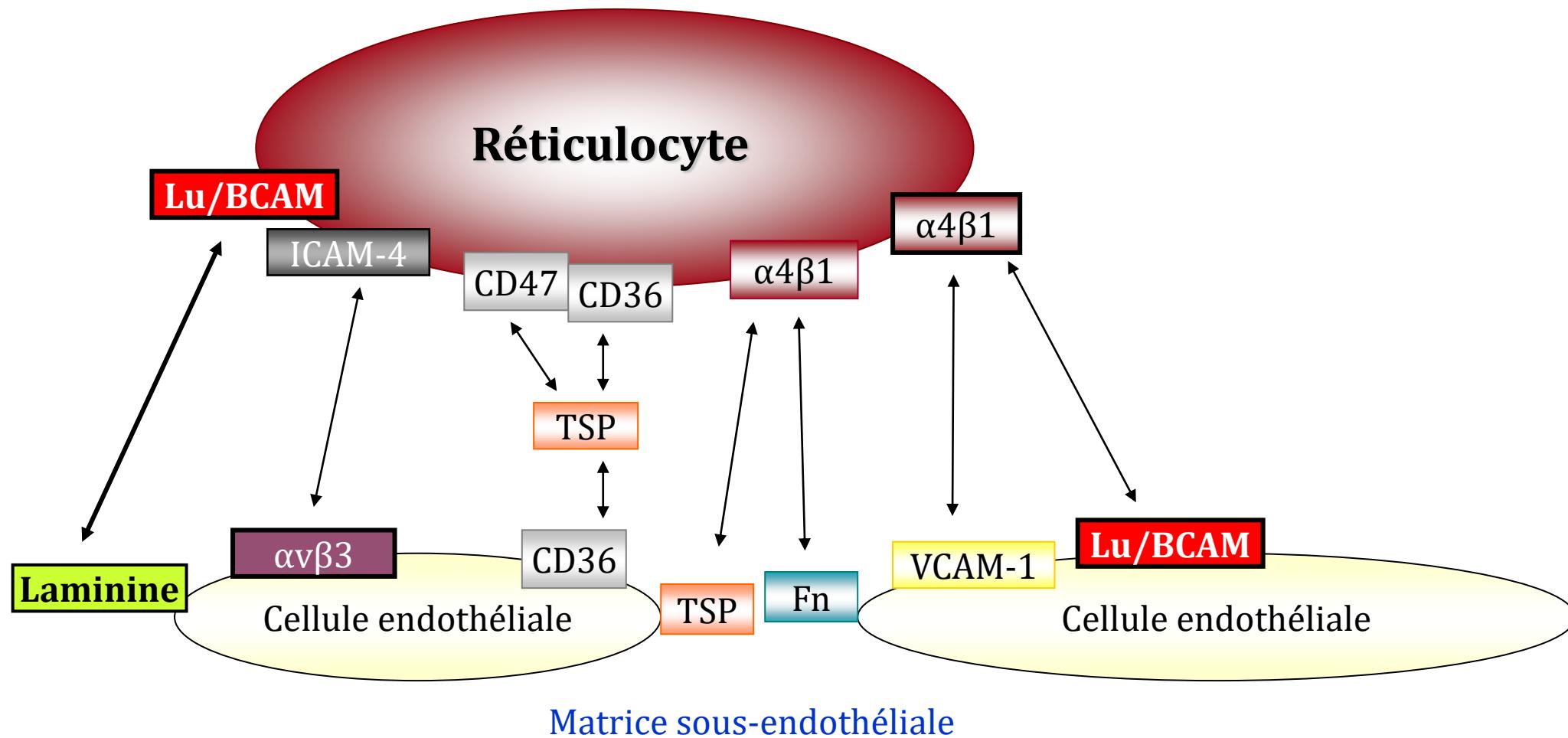
GR non falciformés
(non marqués FITC)

Phénomènes
d'adhérence
non spécifiques
à la drépanocytose

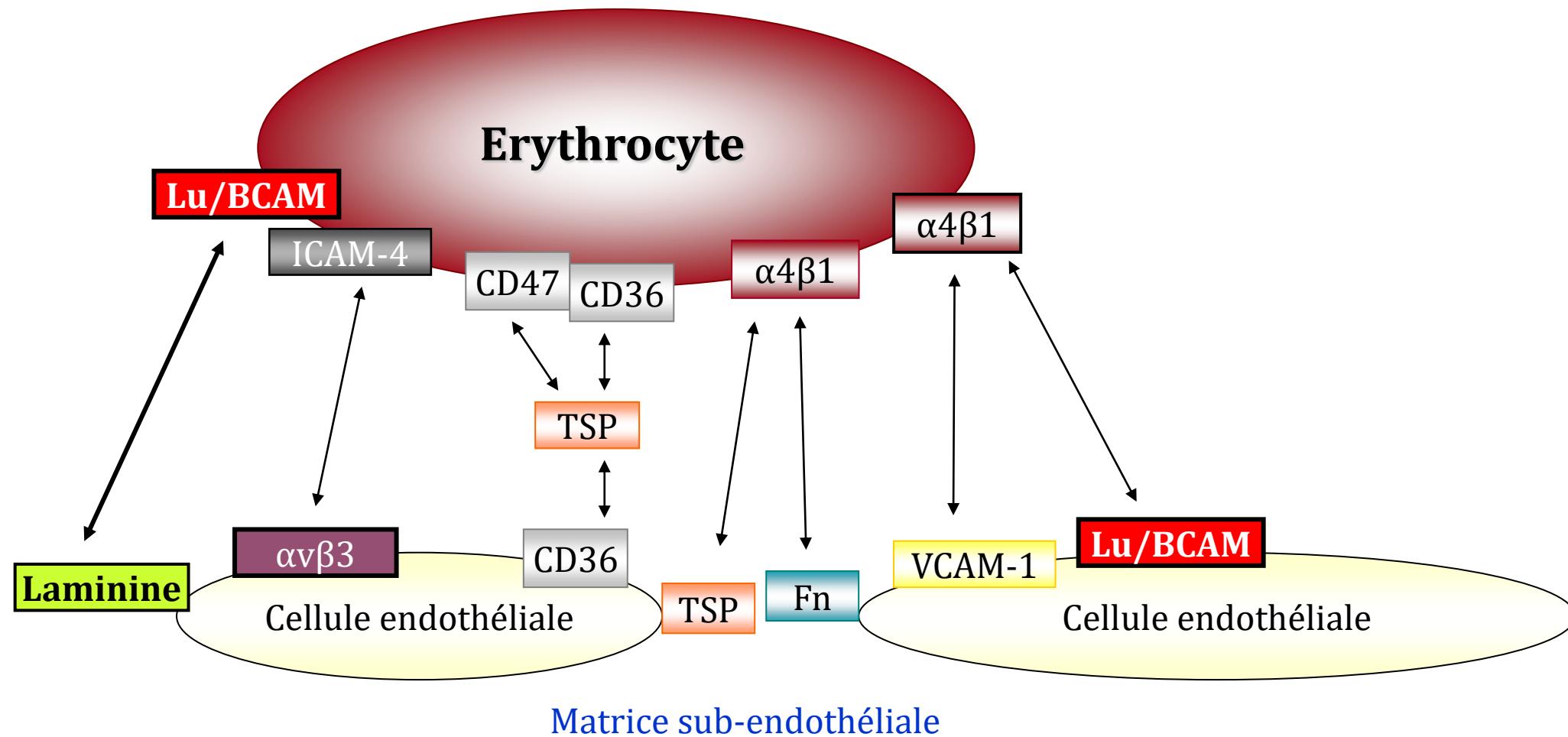


Fabry et al 1989

INTERACTIONS GR – ENDOTHÉLIUM PAROI VASCULAIRE



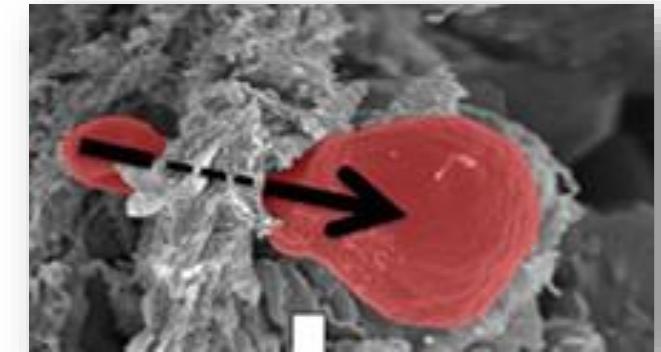
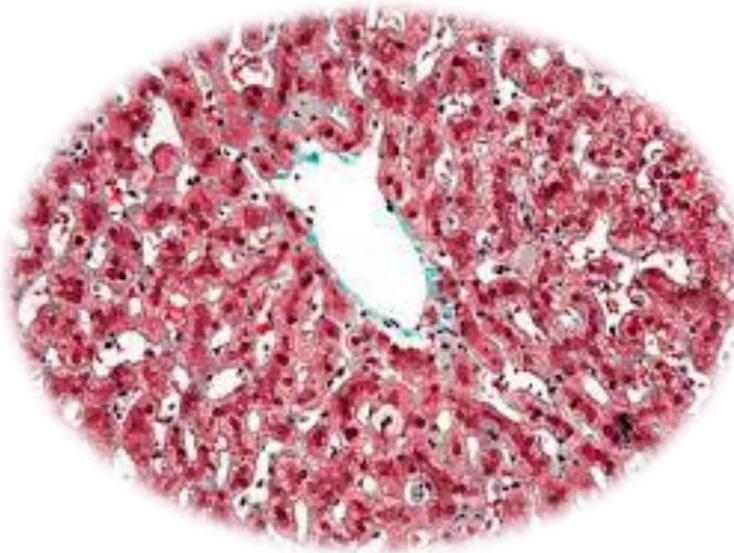
INTERACTIONS GR – ENDOTHÉLIUM PAROI VASCULAIRE



Hémolyse extra vasculaire



Séquestration
Activation macrophagique



Buffet, données personnelles

Zafrani, données personnelles

Drépanocytose

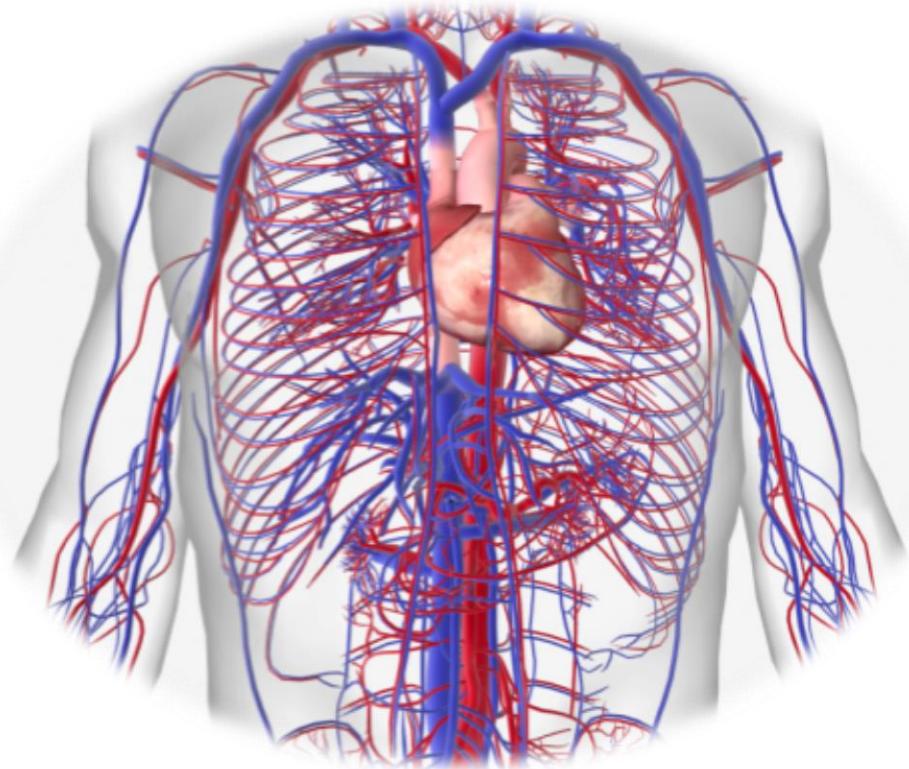
Occlusion de la veine centrale de la rétine

↑ adhérence
GR

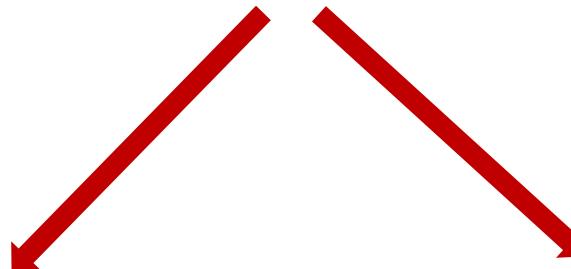
Sphérocytose

Maladie de Gaucher

Paludisme



Hémolyse intra vasculaire



**Vasculopathie
aigüe**

**Vasculopathie
chronique**

Hémoglobinurie paroxystique nocturne

Drépanocytose

b thalassémie

AHAI

Hémoglobinose H

Hémolyse intra vasculaire

DHTR

Stomatocytose splénectomisé
Pyropoikilocytose

Déficit G6PD

ECMO

Déficit PK

Hémoglobinurie paroxystique nocturne

Drépanocytose

b thalassémie

AHAI

Hémoglobinose H

DHTR

**Hémolyse intra vasculaire
avec discordance
Hème - Hémoglobine plasmatique
(Hème médullaire ou cinétique ?)**

Stomatocytose splénectomisé
Pyropoikilocytose

Déficit G6PD

ECMO

Déficit PK

Hémoglobinurie paroxystique nocturne

Drépanocytose

b thalassémie

AHAI

Hémoglobinose H

**Hémolyse intra vasculaire
avec activation du complément**

Stomatocytose splénectomisé
Pyropoikilocytose

DHTR

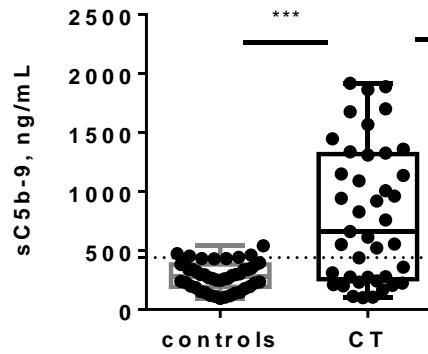
ECMO

Déficit G6PD

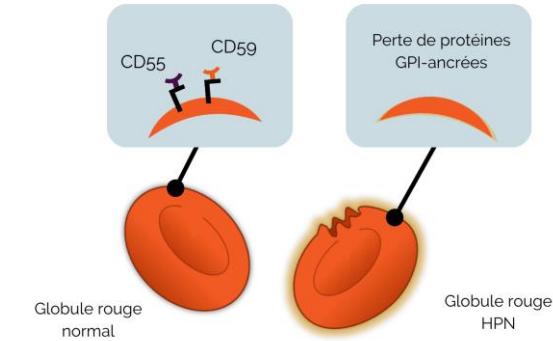
Déficit PK

Hémoglobinurie paroxystique nocturne

Drépanocytose

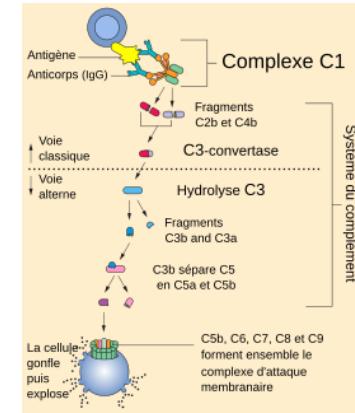


Hémolyse intra vasculaire avec activation du complément

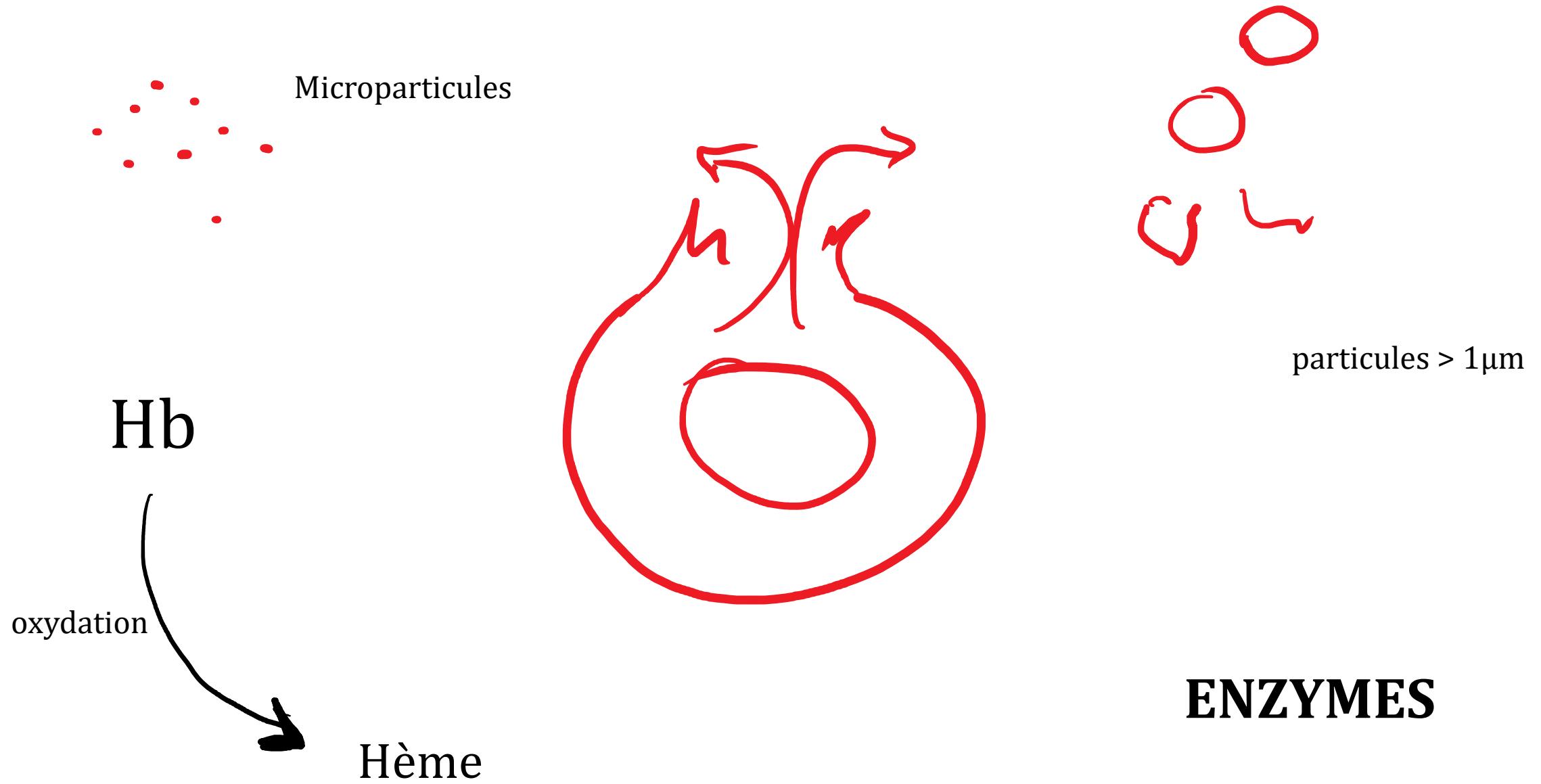


DHTR

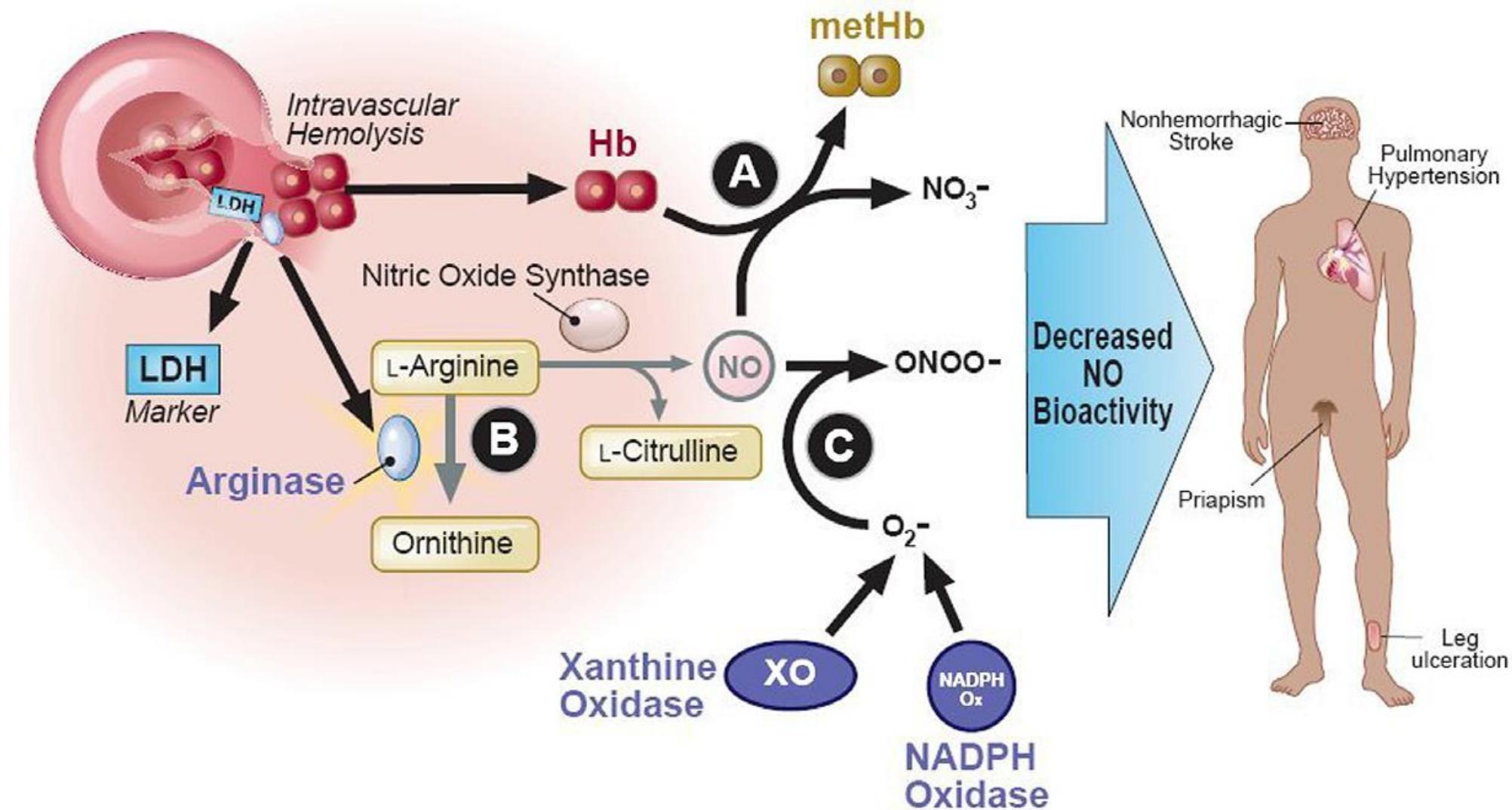
	Day*	C3 level (mg/L)	C4 level (mg/L)	sC5b9 level (mg/L)
Patient 1				
Before eculizumab infusion	0	1080	266	856
First follow-up assessment	2	1030	283	1223
Second follow-up assessment	14	1050	248	1406
Patient 2				
Before eculizumab infusion	0	—	—	—
First follow-up assessment	7	1270	257	1797
Patient 3				
Before eculizumab infusion	0	1070	220	1527
First follow-up assessment	4	313	104	296
Second follow-up assessment	6	359	129	224
Third follow-up assessment	9	928	526	355
Fourth follow-up assessment	13	1210	290	509



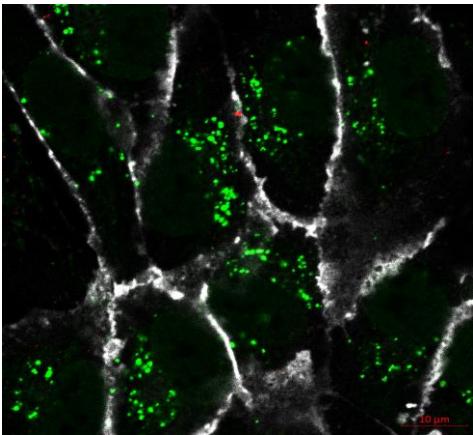
Données IRMB non publiées



HÉMOGLOBINE

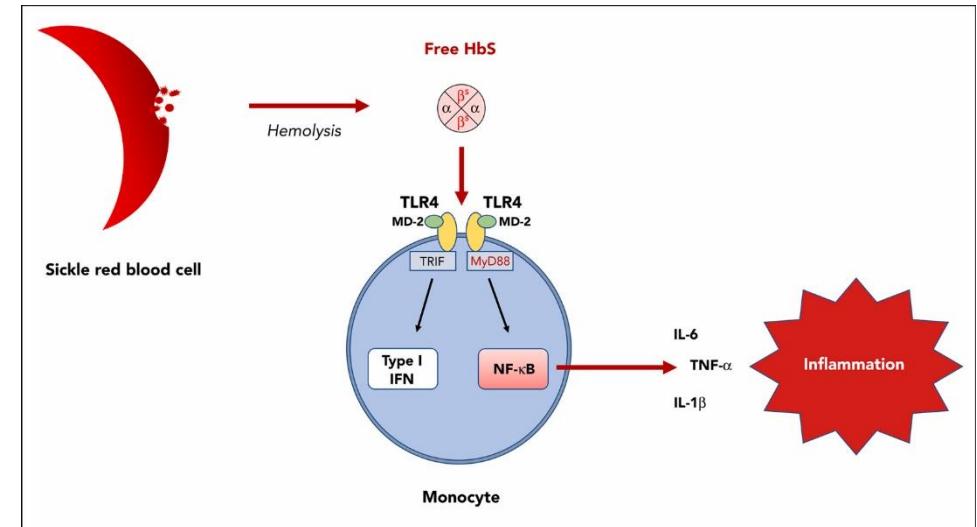


HÉMOGLOBINE



Hb plasma

Pratiquement aucun effet
sur les cellules endothéliales



Allali Blood 2022

HbS → Activation monocyte

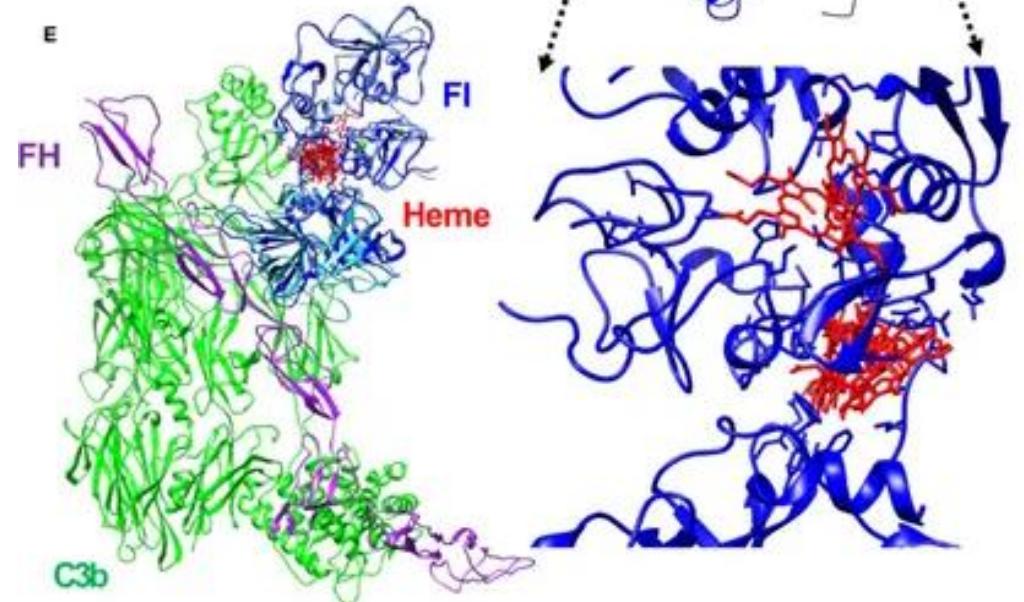
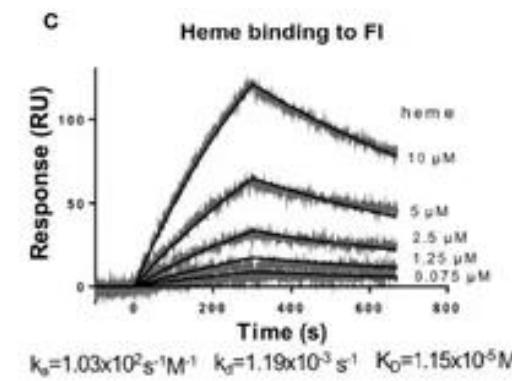
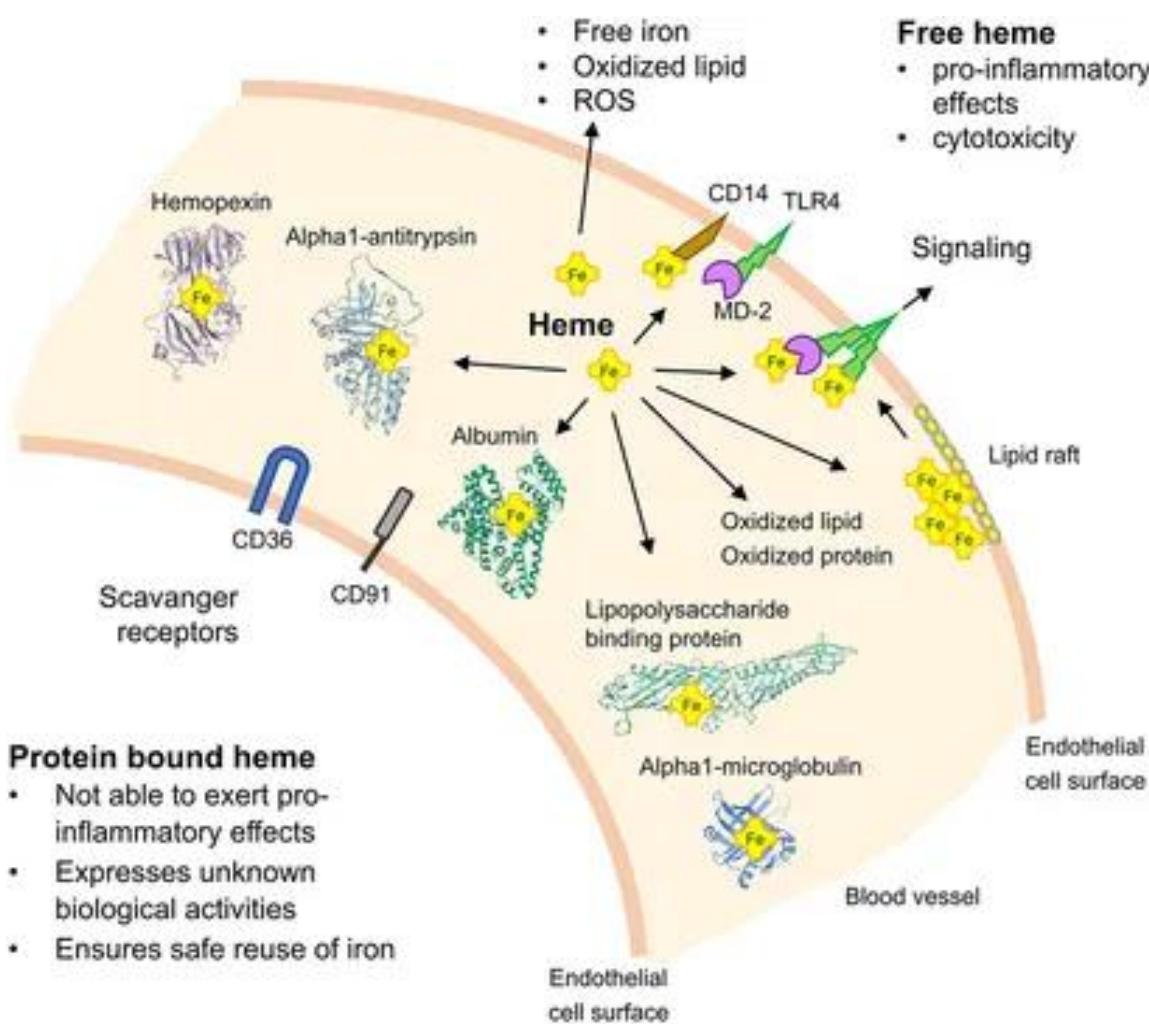
Toxicité tubulaire

Libération Hème
Stress oxydatif

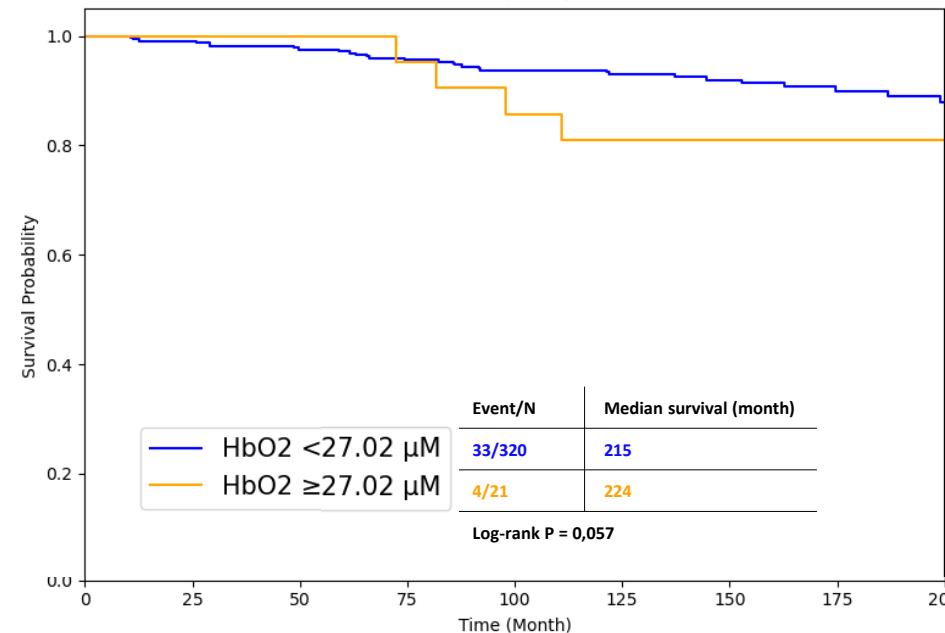
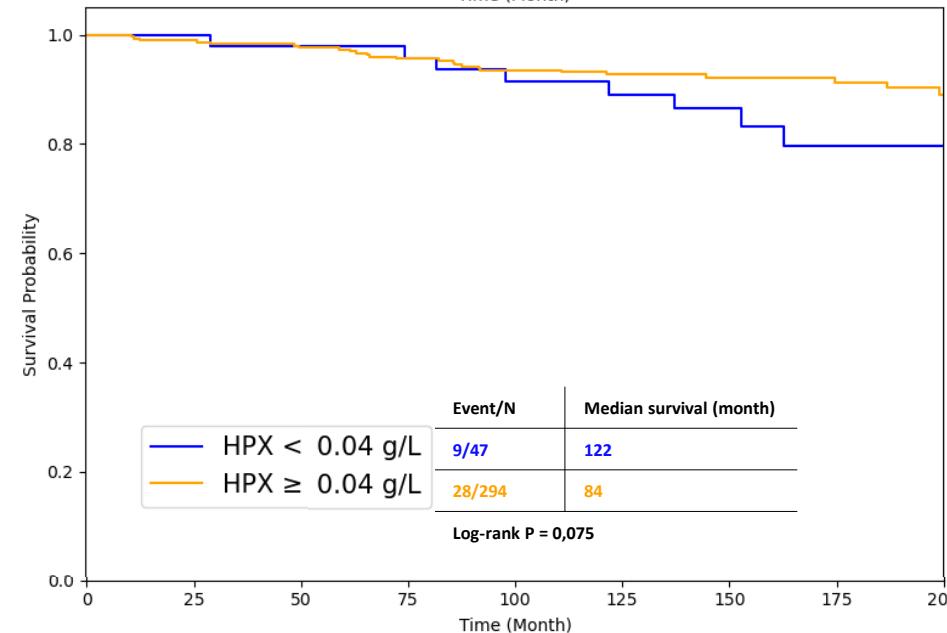
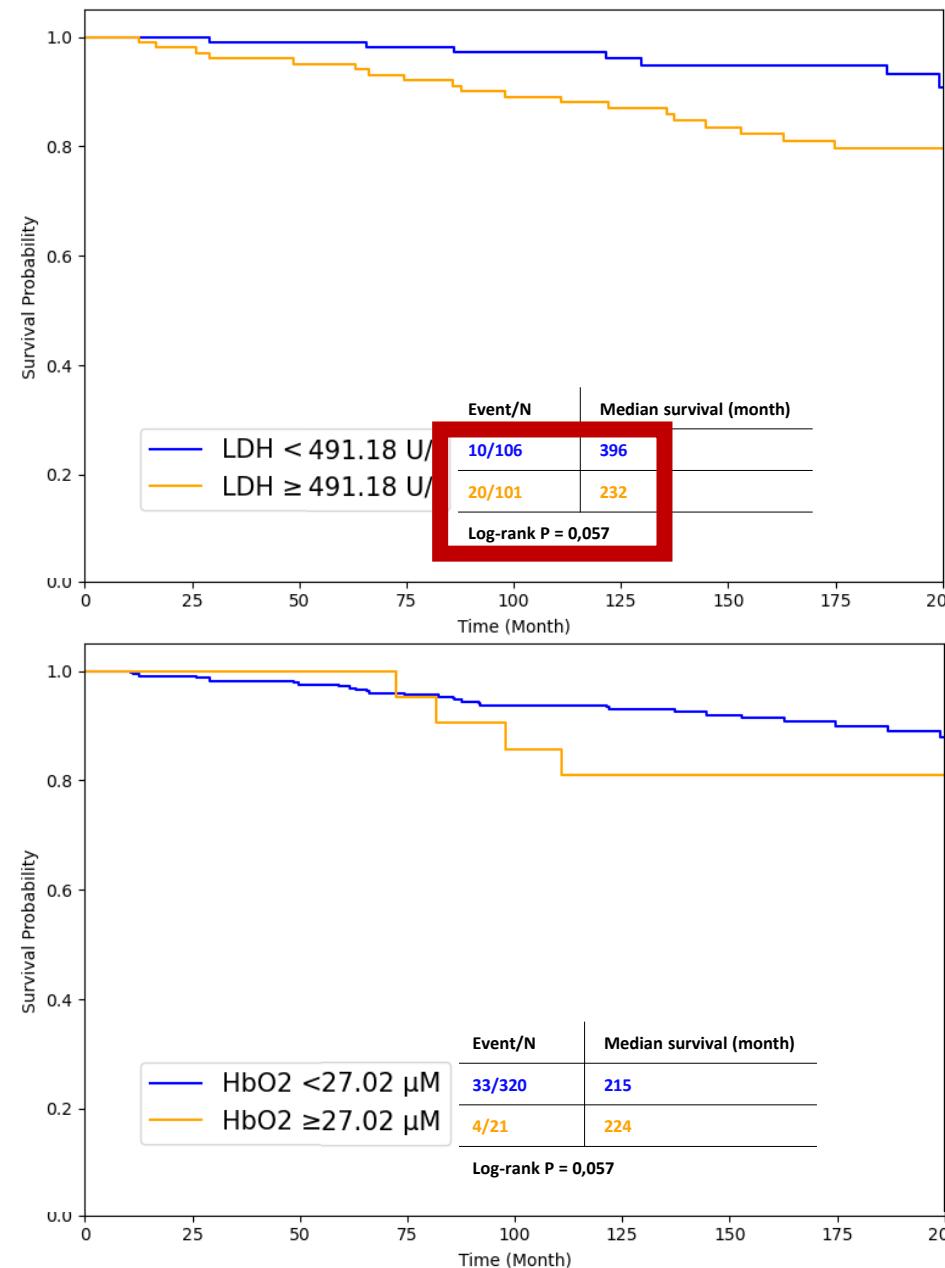
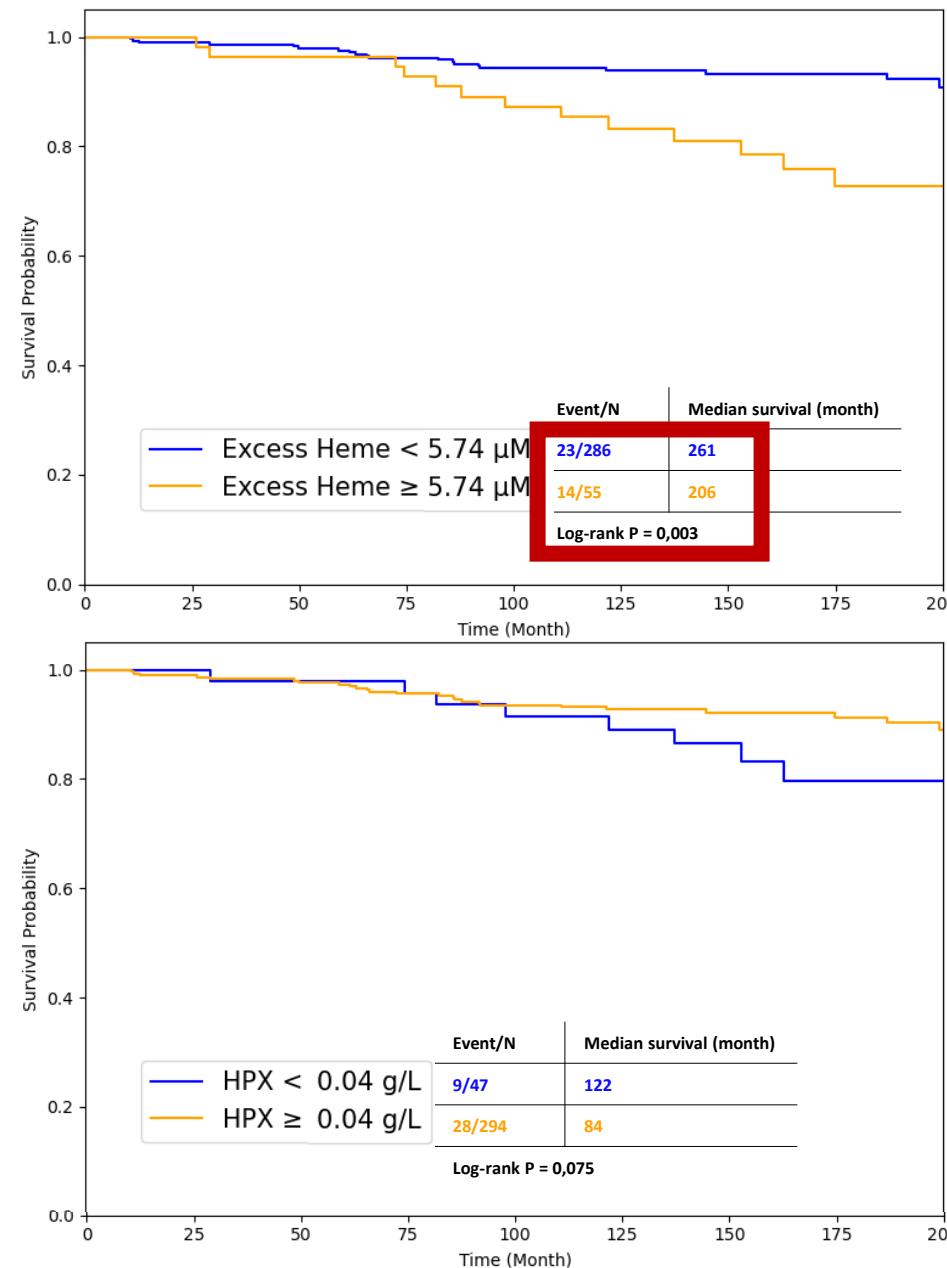
Précipitation
tubulaire

Compétition pour megalin/cubulin
↓ Réabsorption proximale

HÈME

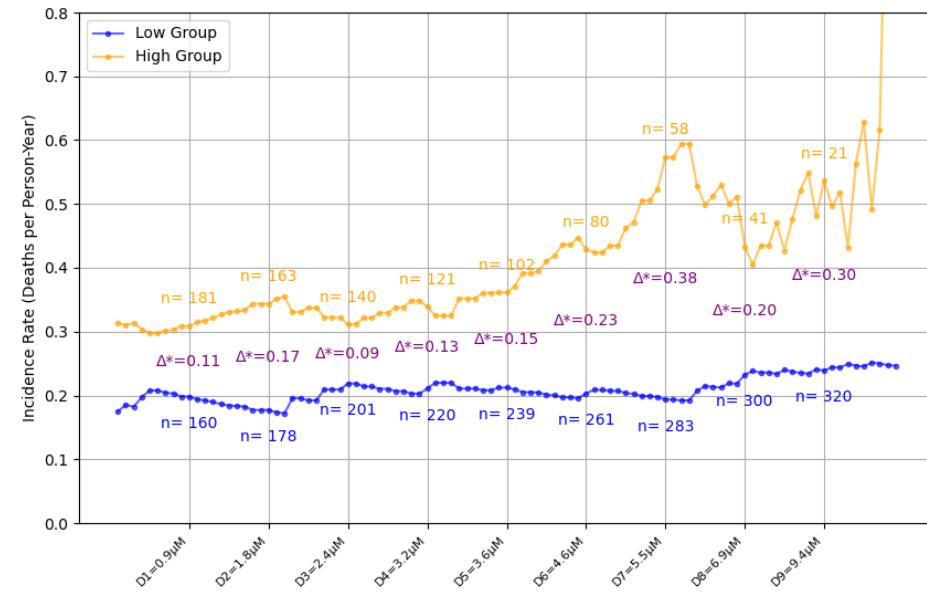


SURVIE À 15 ANS D'UNE COHORTE DE 341 PATIENTS DRÉPANOCYTAIRES (DONNÉES PRÉLIMINAIRES)

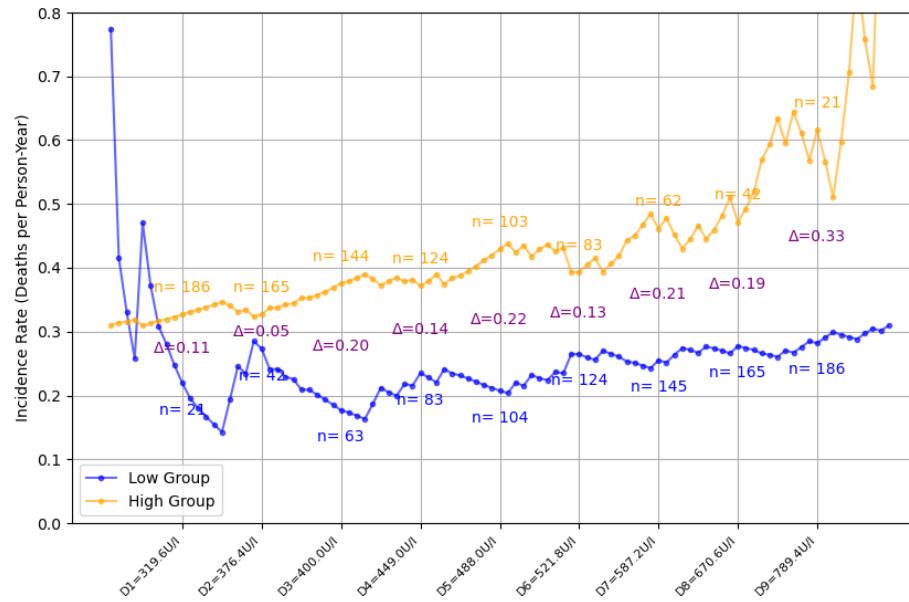


Données personnelles

SURVIE À 15 ANS D'UNE COHORTE DE 341 PATIENTS DRÉPANOCYTAIRES (DONNÉES PRÉLIMINAIRES)



HEME



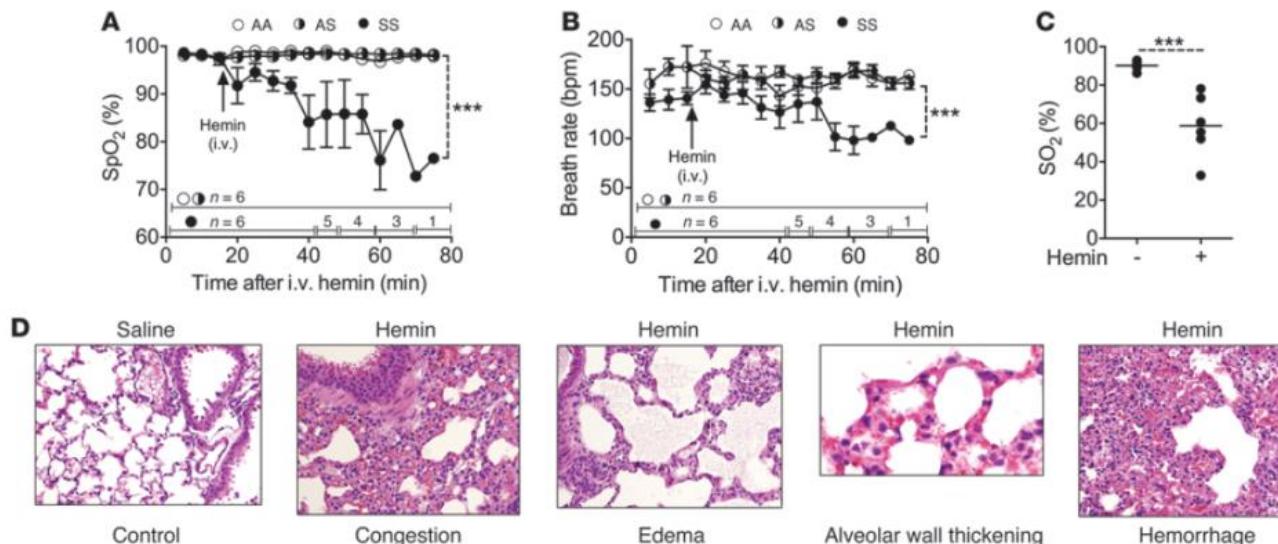
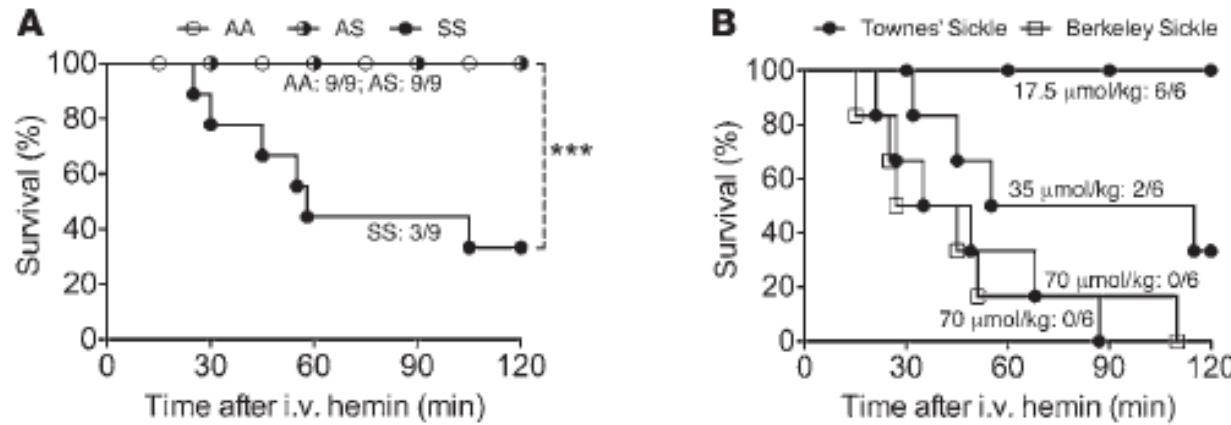
LDH

Cumulative incidence rate trends and differences with statistical significance stratified by hemolytic factor thresholds in sickle cell patients.

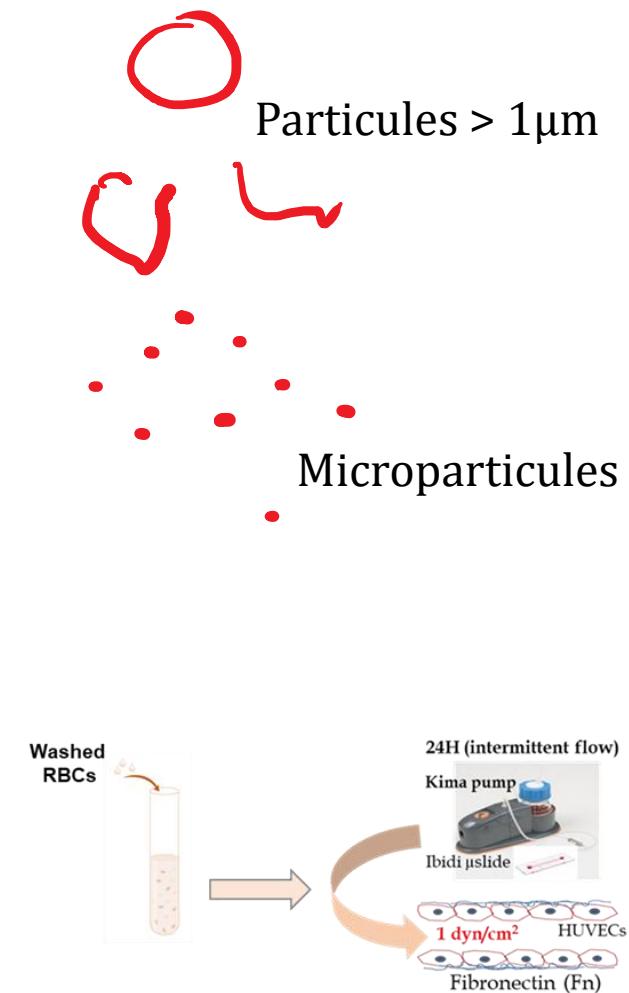
Données personnelles

L'HÈME PROVOQUE UNE VASO-OCCCLUSION SÉVÈRE

MODÈLE MURIN DRÉPANOCYTAIRE



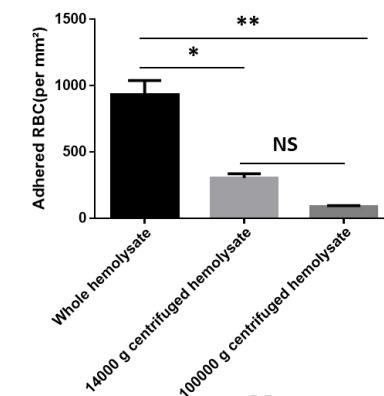
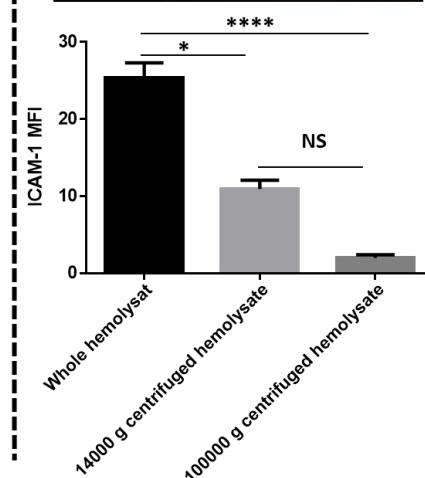
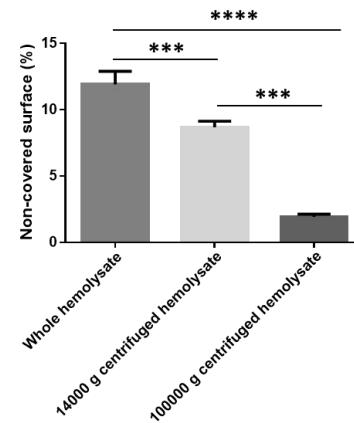
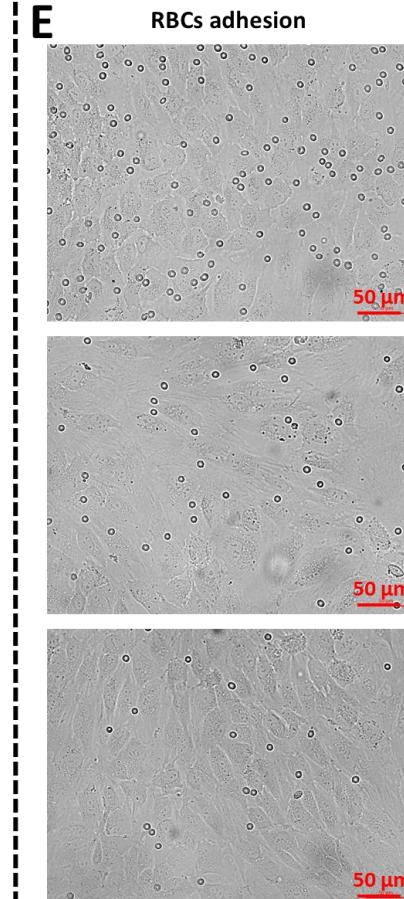
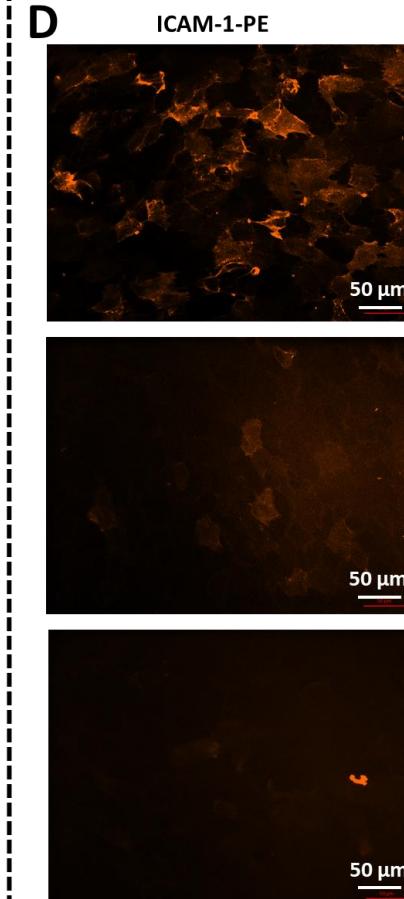
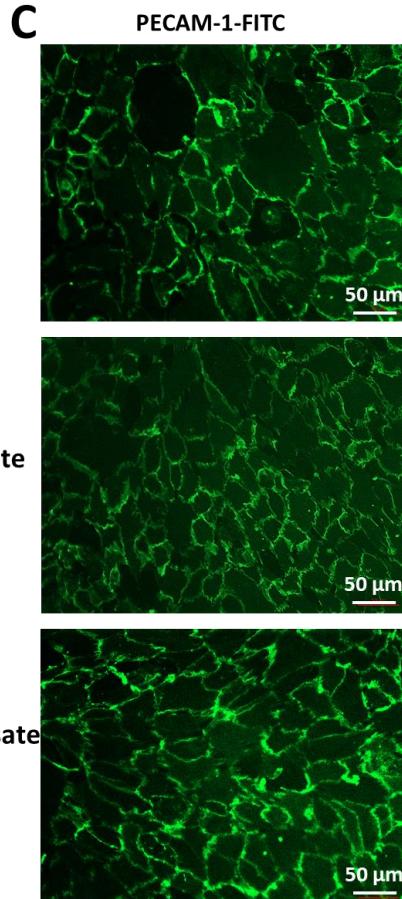
PARTICULES ÉRYTHROCYTAIRES INFLAMMATION



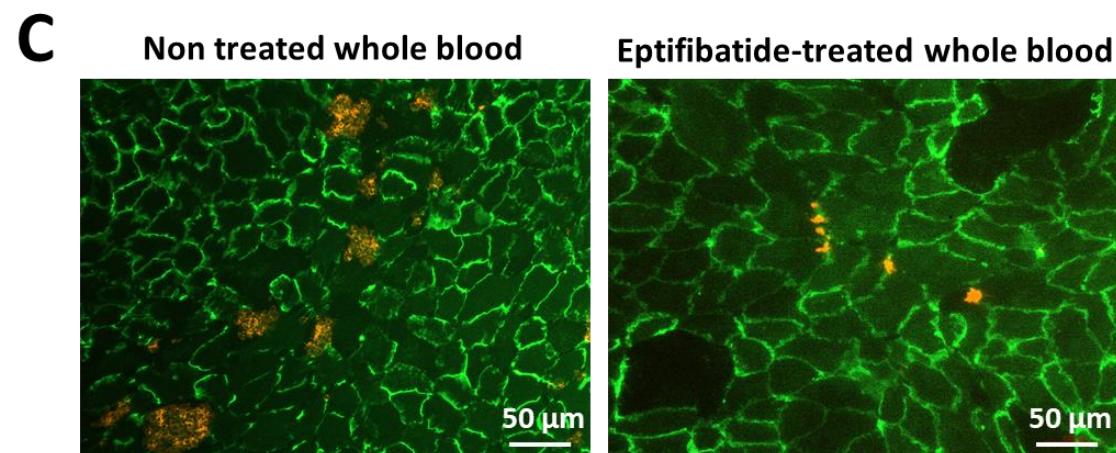
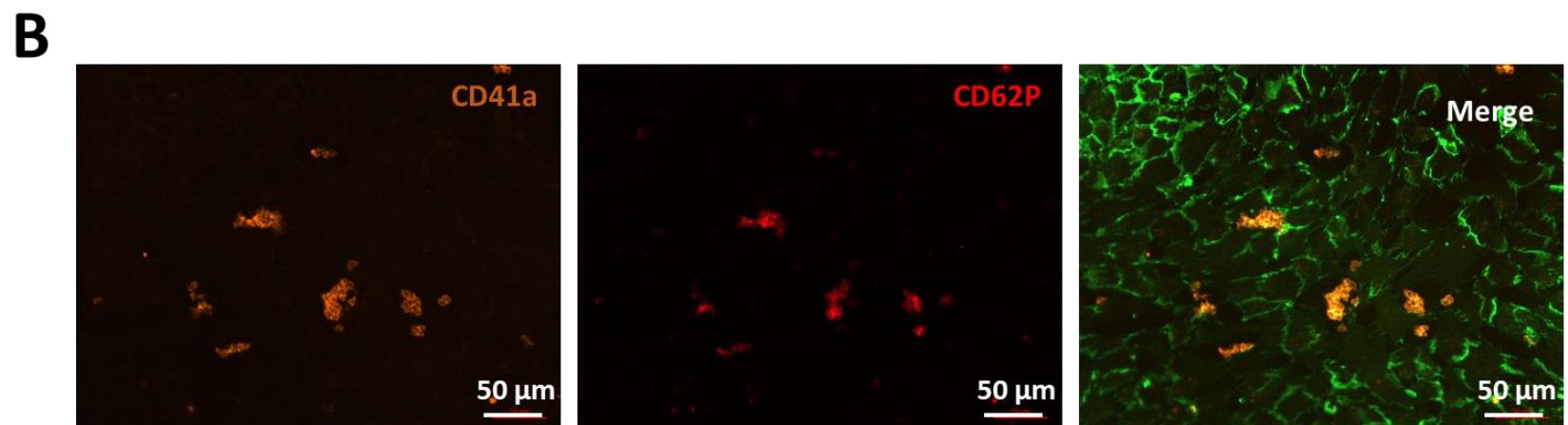
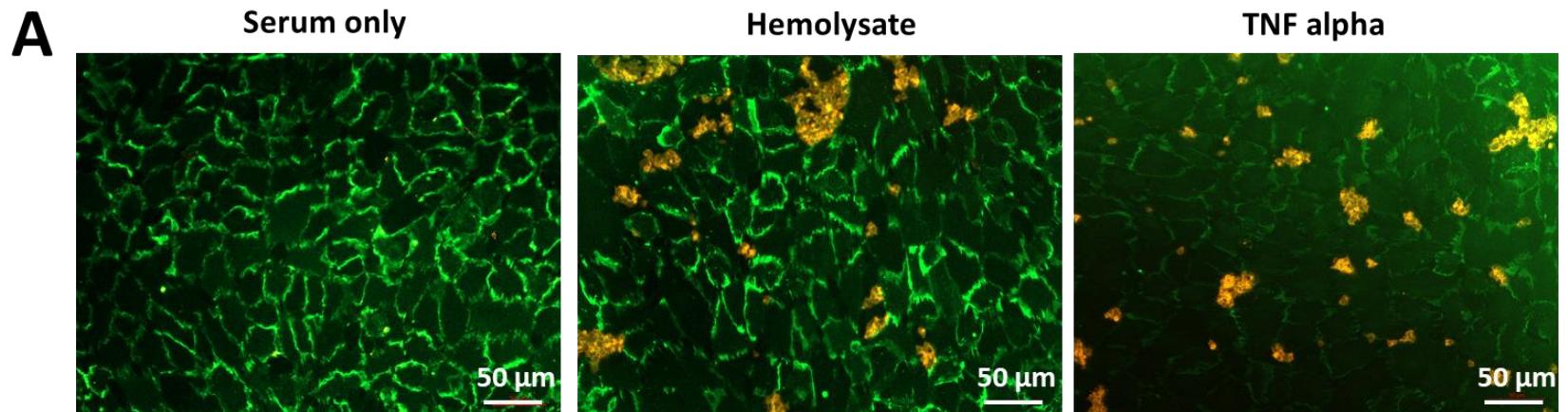
Whole hemolysate

14000 g centrifuged hemolysate

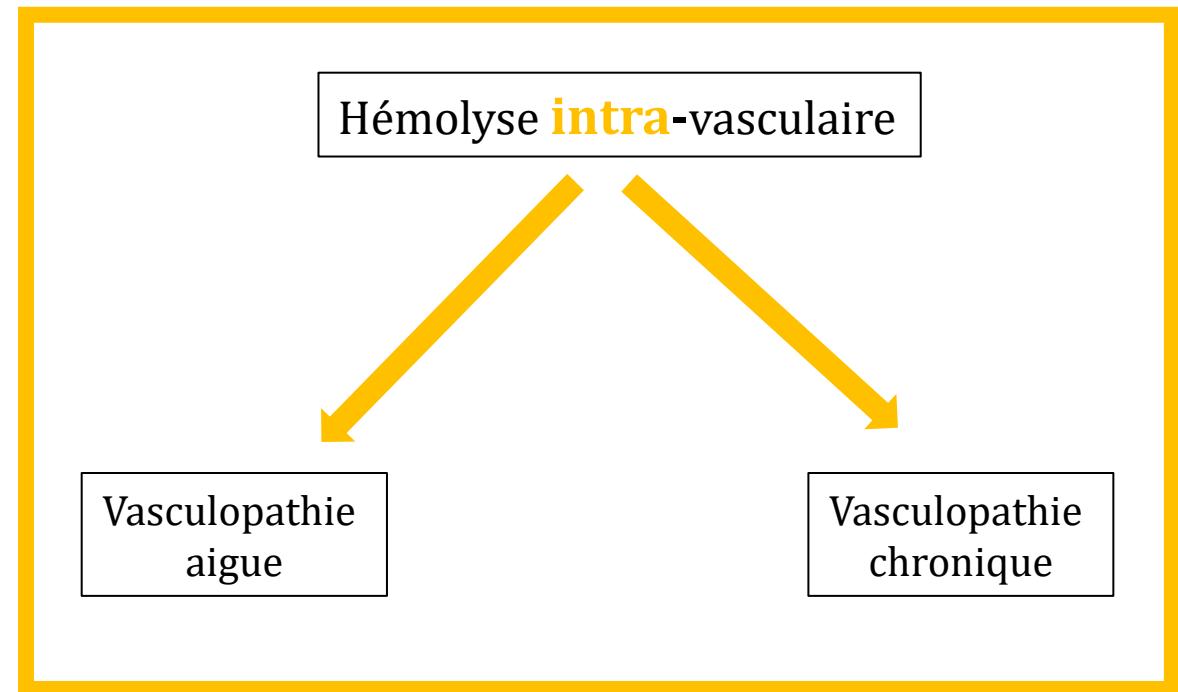
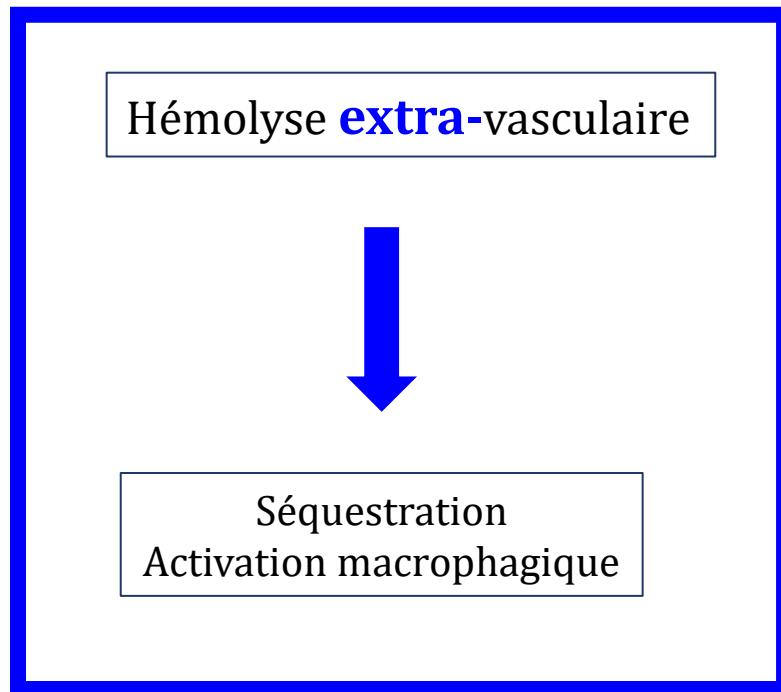
100000 g centrifuged hemolysate



PARTICULES ÉRYTHROCYTAIRES COAGULATION



ASPECTS THÉRAPEUTIQUES GÉNÉRAUX



Traitement de la cause
Splénectomie ?
Traitement visant la ↓ activation macrophagique

Traitement de la cause ++
Inhibiteurs du complément

Hémopexine
Echange plasmatique
avec plasma

Nouvelles approches
plus ciblées sur les voies
effectrices

CONCLUSION

- Les hémolyses recoupent des processus très différents et complexes
- Nécessité de déterminer :
 - La cause de l'hémolyse
 - Le caractère extra ou intra vasculaire
- Besoin d'outils biologiques
- Meilleure compréhension des hémolyses pour adapter les traitements

