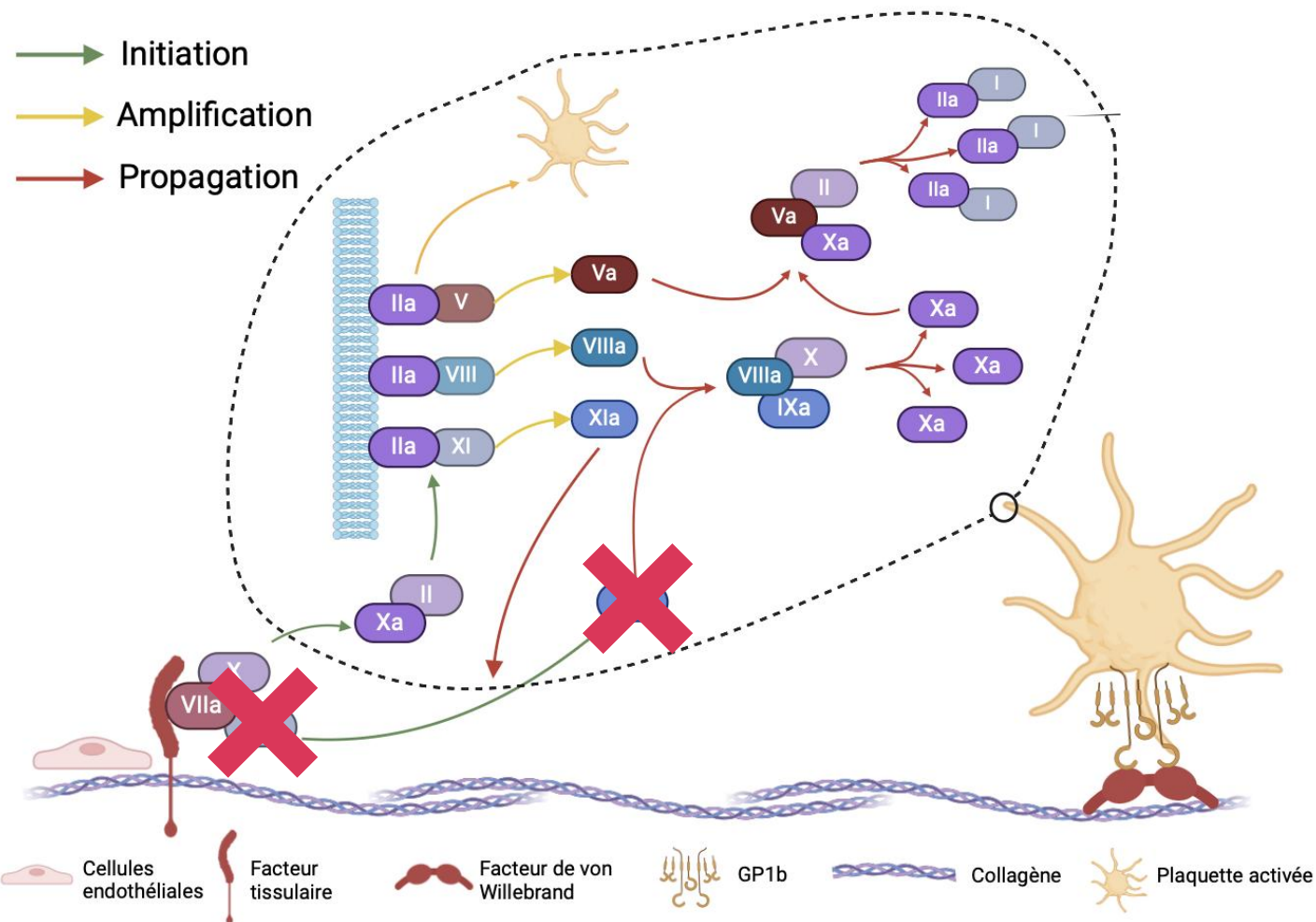


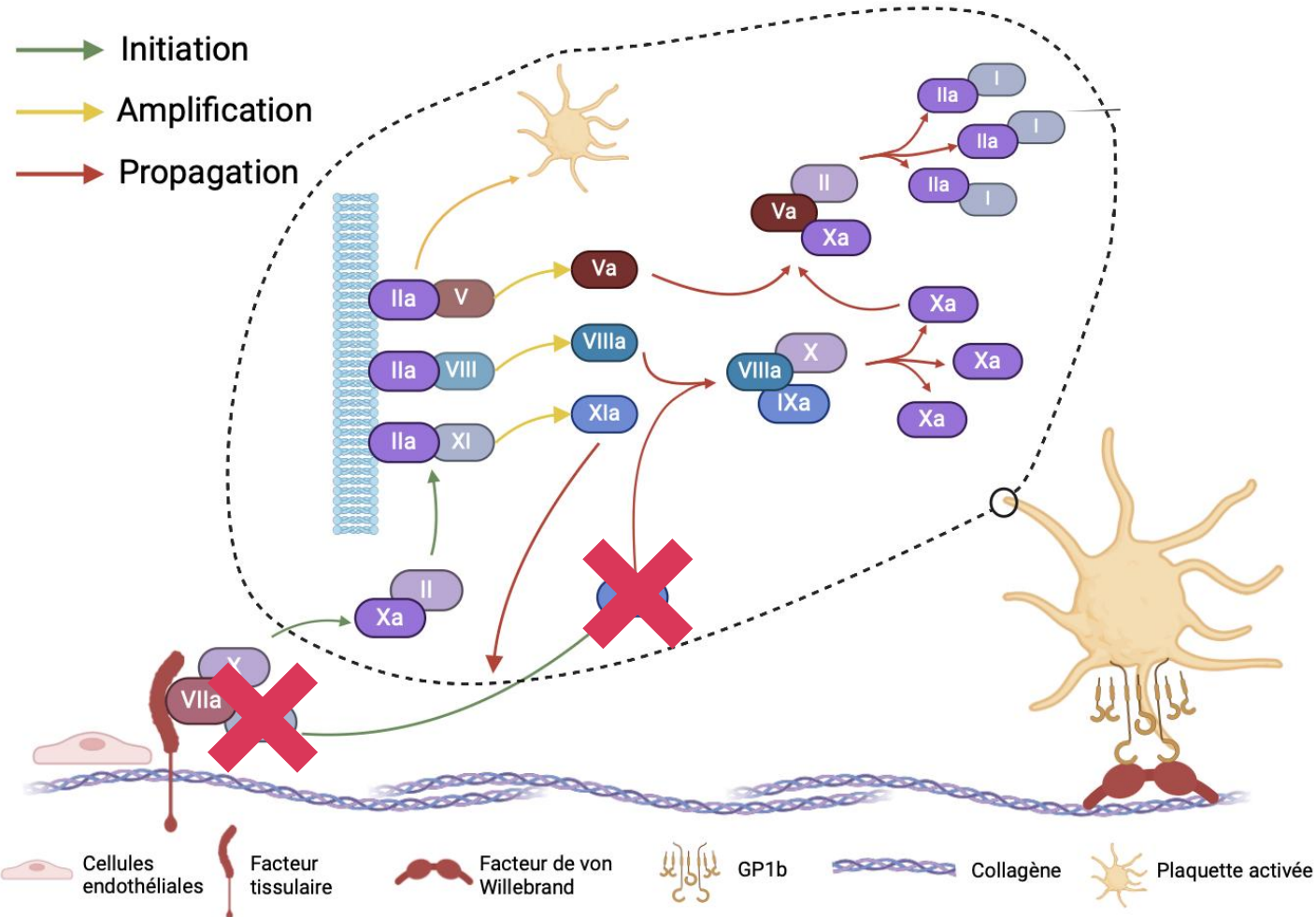
Le réservoir extraplasmatique de Facteur IX

UR-4609 | Hém^ostase & Throm^ob^ose

A. Leuci¹, M. Marano¹, C. Martin¹, Y. Dargaud¹

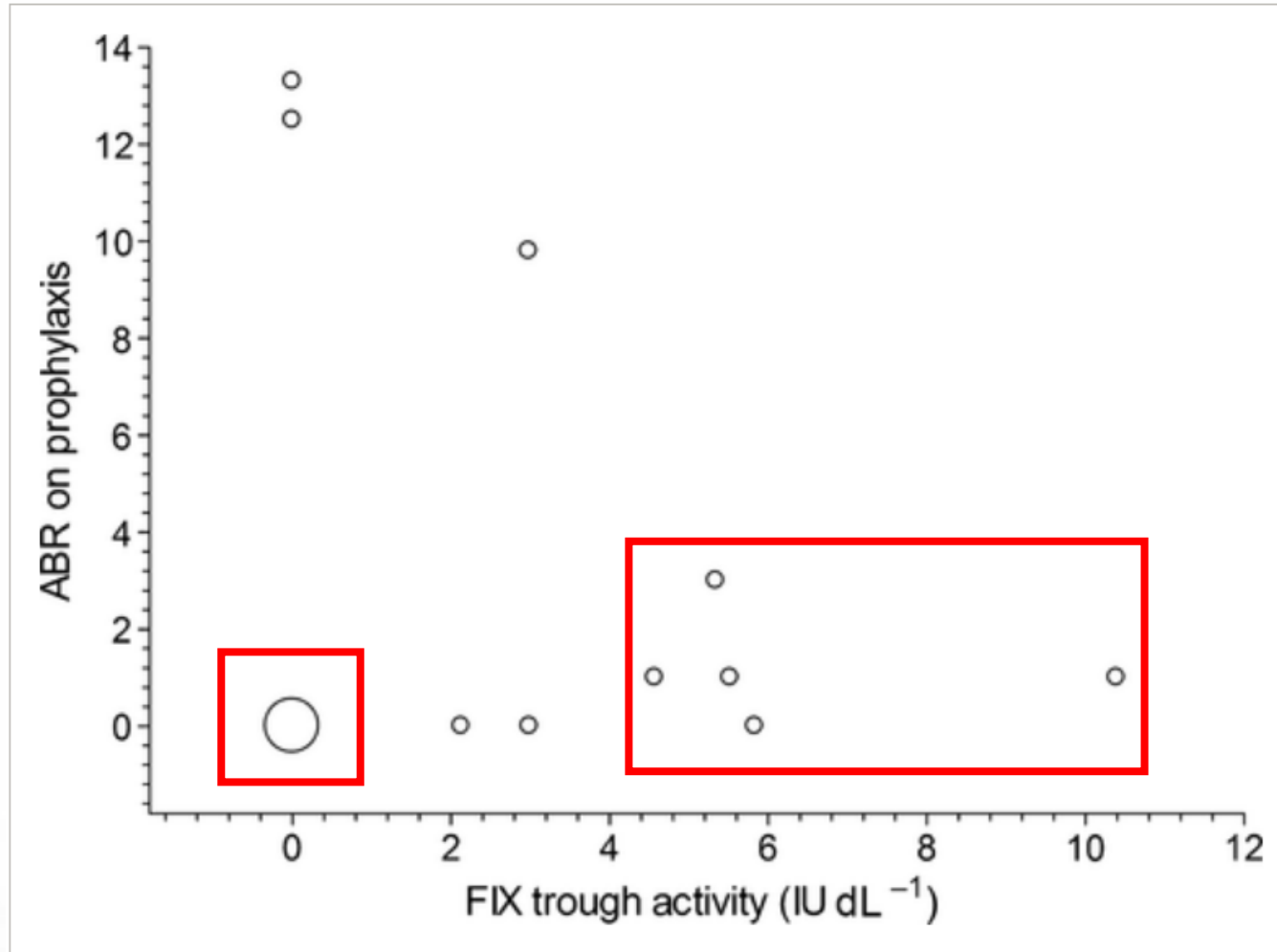
¹Ur4609 Univ Lyon 1 - Lyon (France)

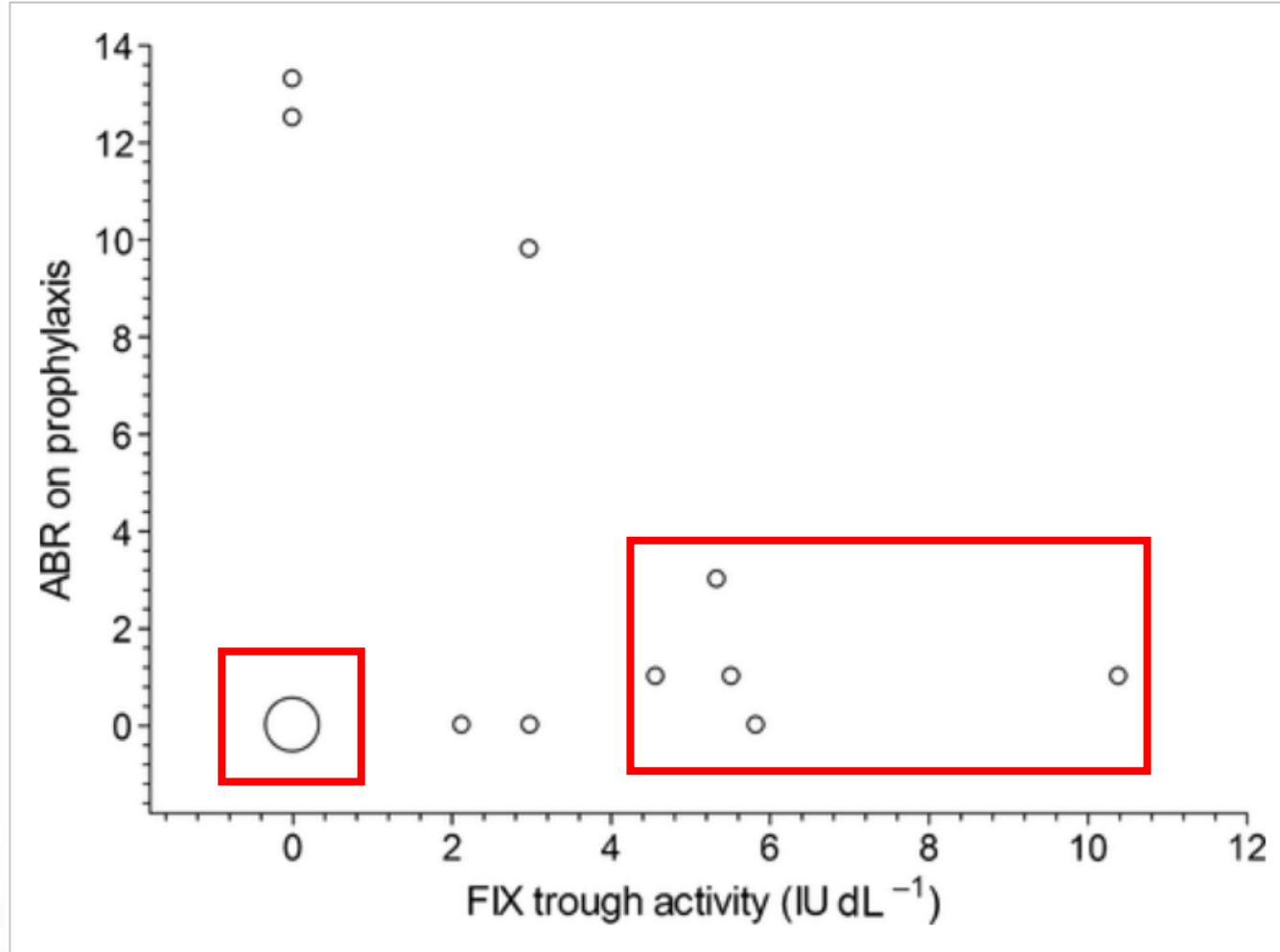




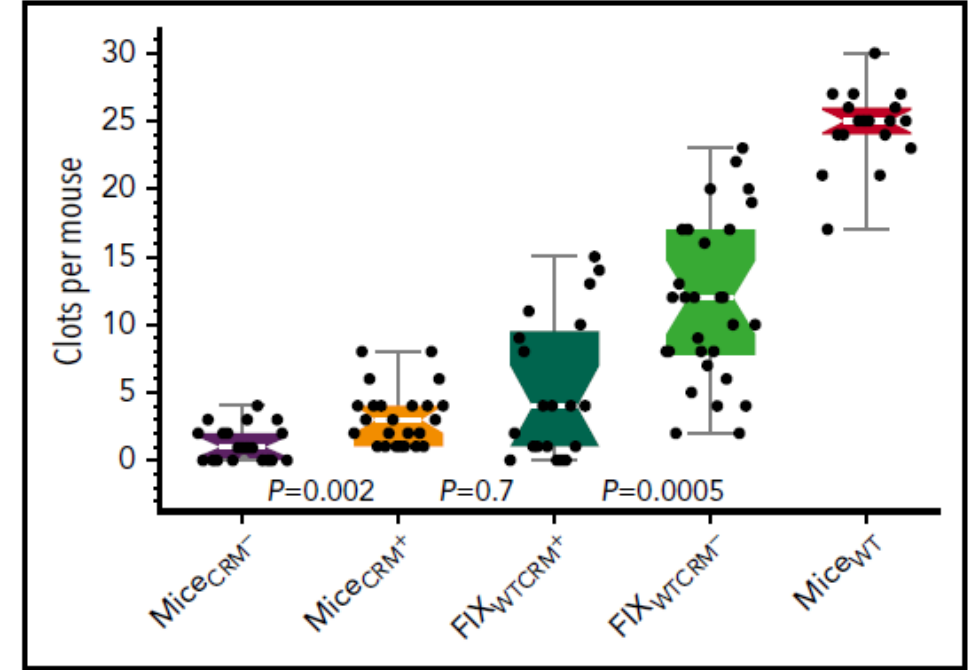
Synovite
 ↓
 Hyperplasie synoviale
 ↓
 Dégradation du cartilage puis de l'os







Kavakli et al. *Haemophilia*. 2016;22(3):381-388.



Cooley et al. *Blood*. 2019;133(22):2445-2451

OC 24.1

Effect of the Type of F9 Mutation on the Pharmacokinetic Profile of Patients with Hemophilia B Treated with Extended Half-Life FIX Concentrates

Matino D et al. ISTH 2023

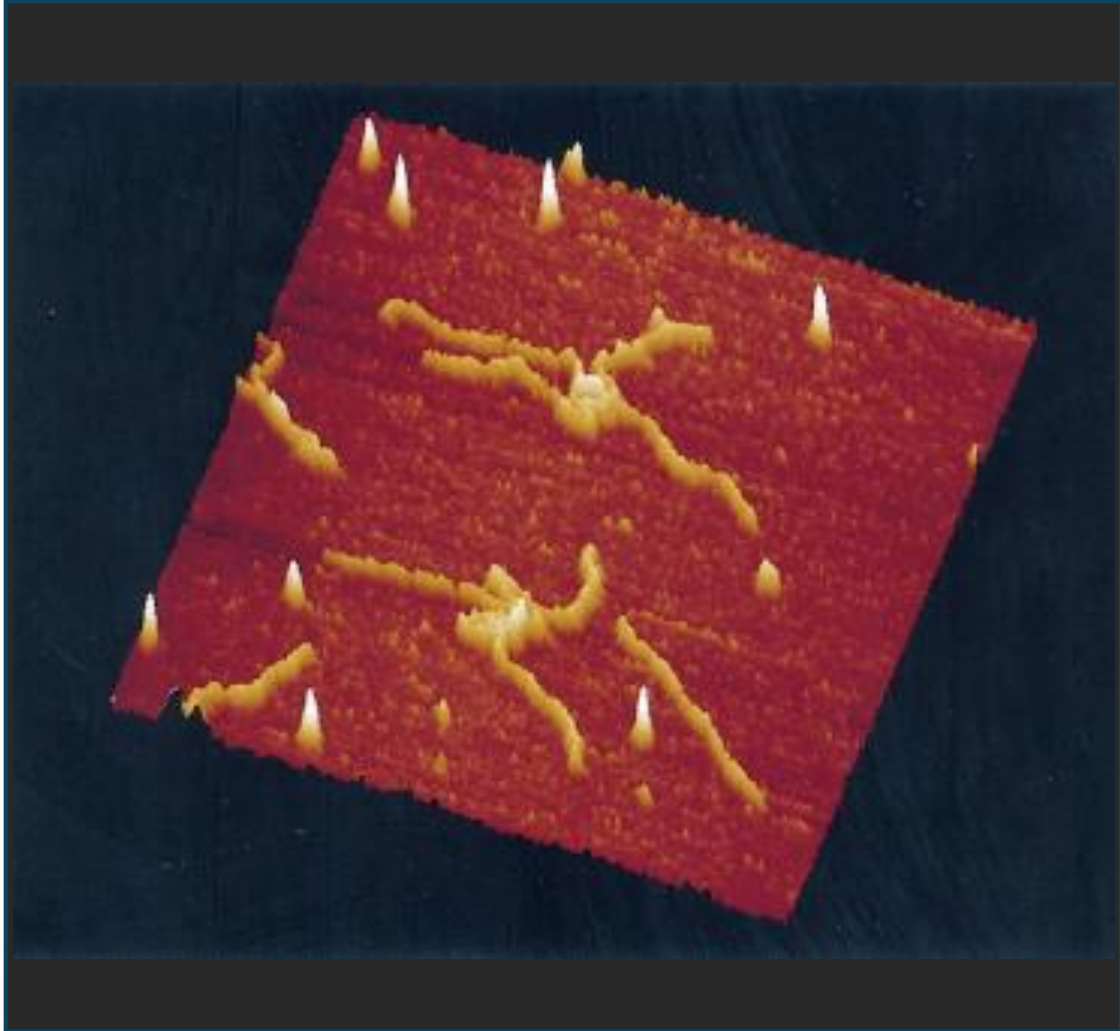
Kleiboer et al. *Haemophilia* 2020; 26:e23-e25



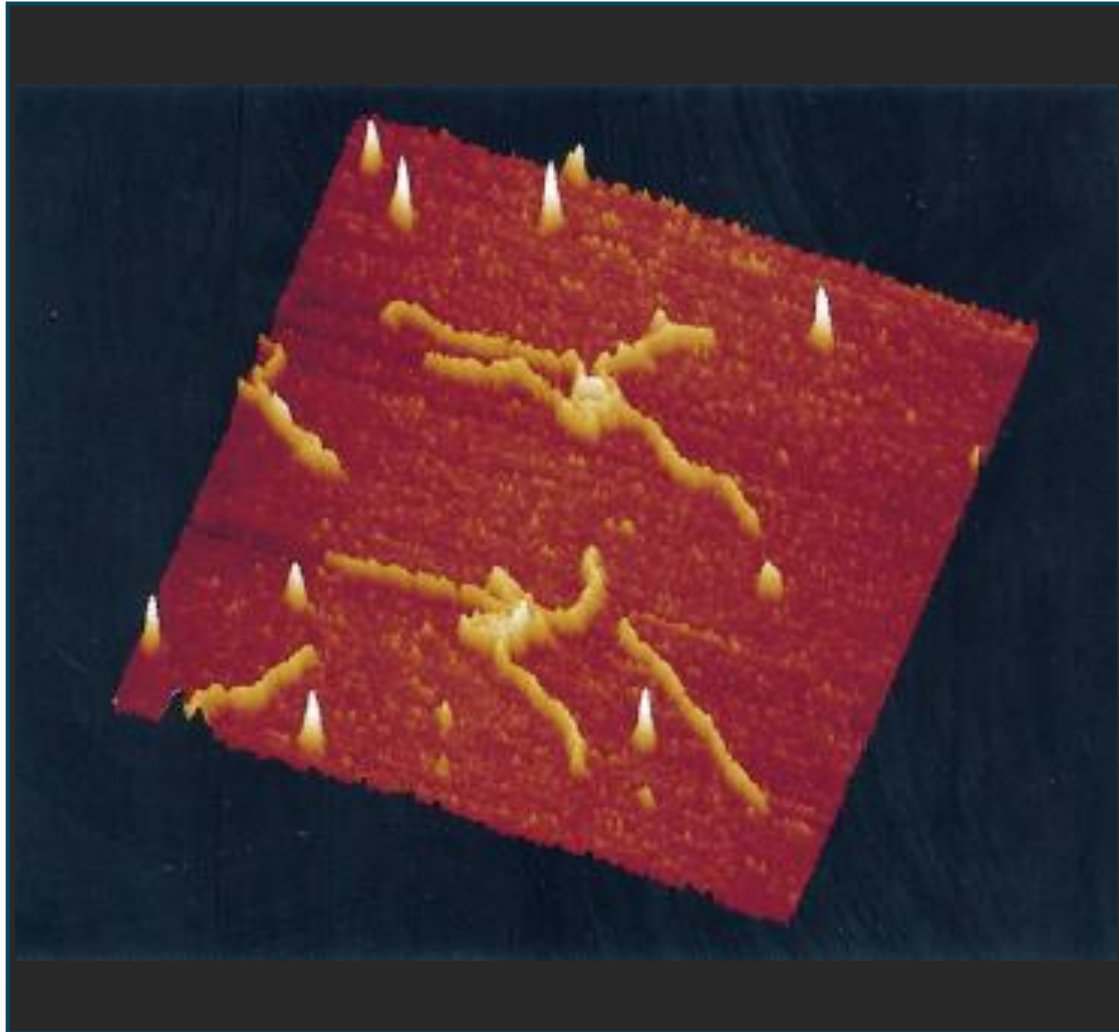
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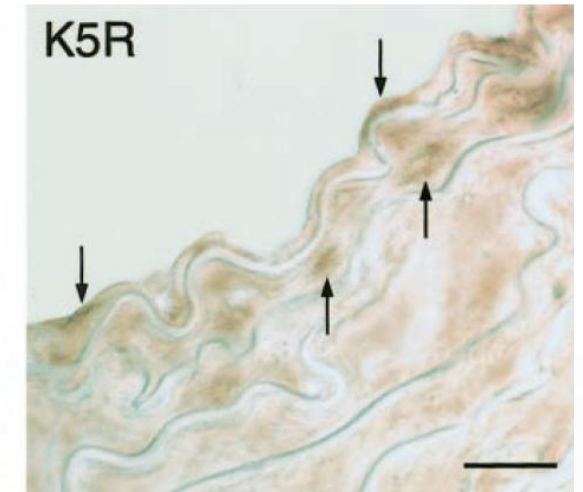
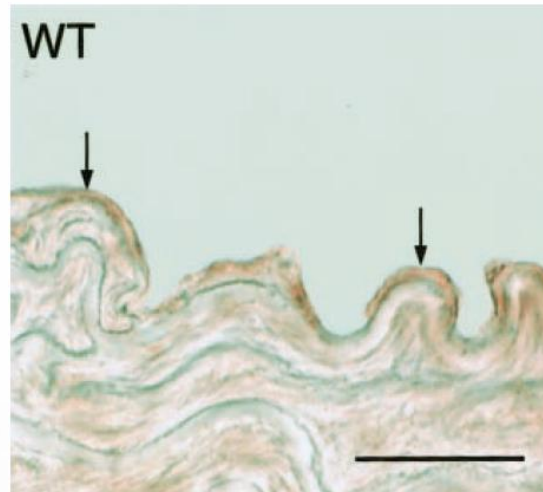
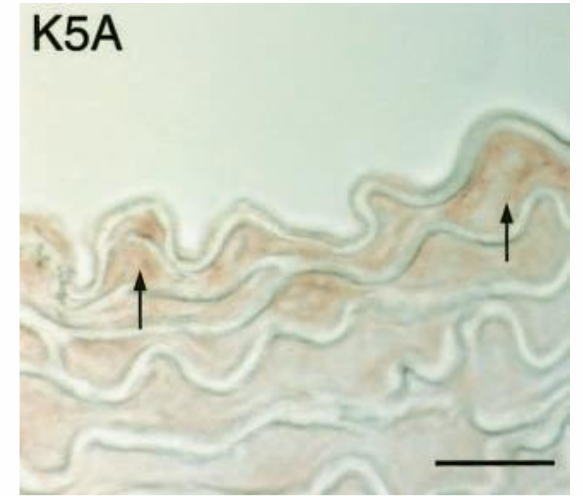
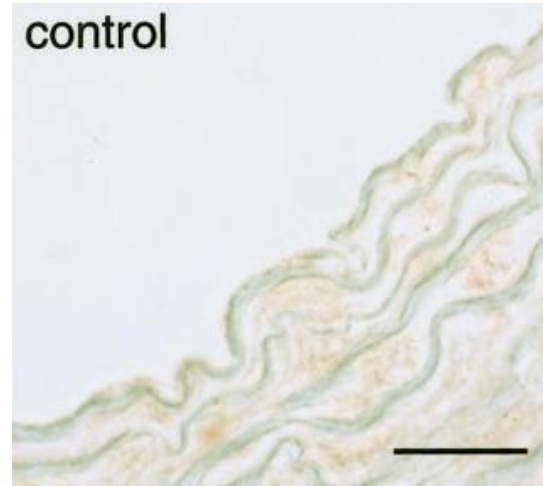
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Wolberg et al. J Clin Biol 1997;272: 16717-20



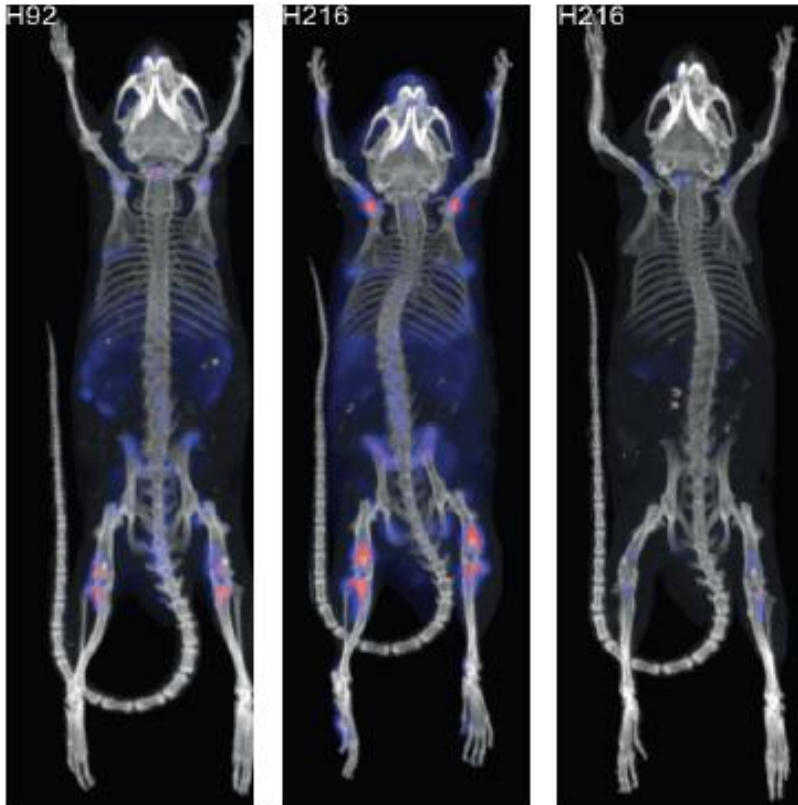
Wolberg et al. J Clin Biol 1997;272: 16717-20



Feng et al. Journal of Thrombosis and Haemostasis, 11: 2176-2196

FIX: 200 UI/kg

5 x half-life

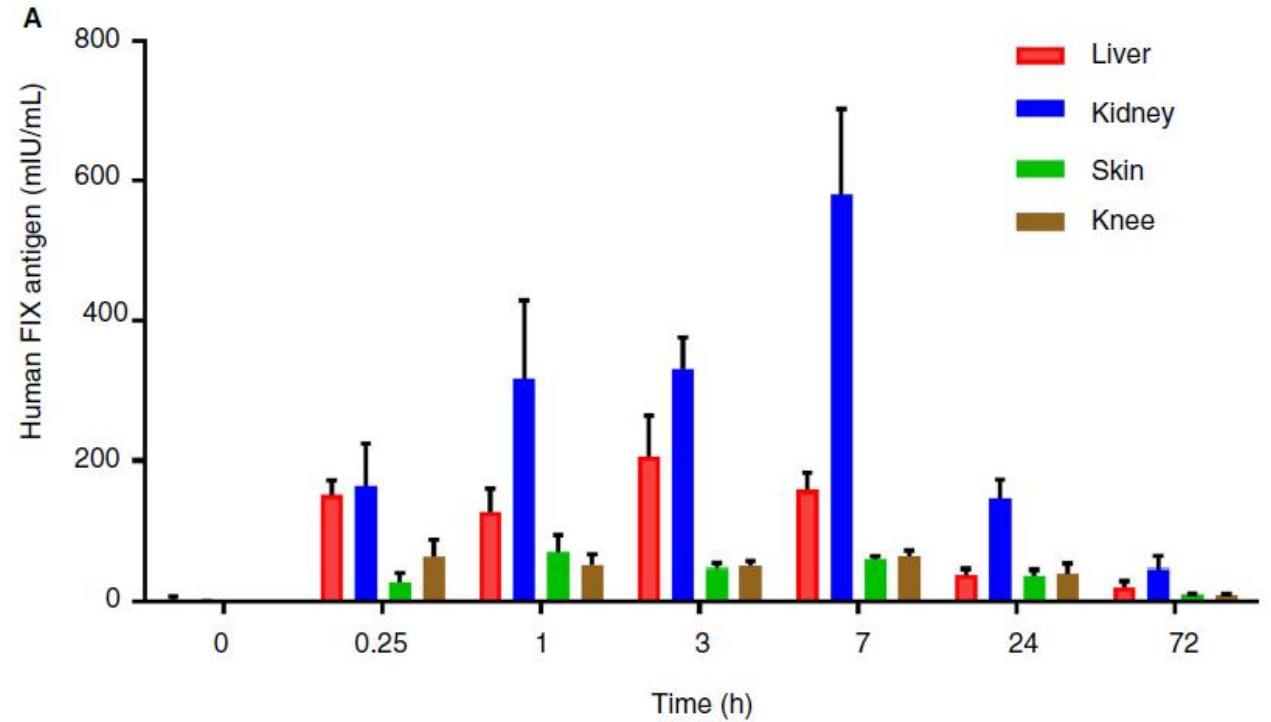


rFIX

rFIXFc

rFIX-GP

FIX-FP: 2000 UI/kg

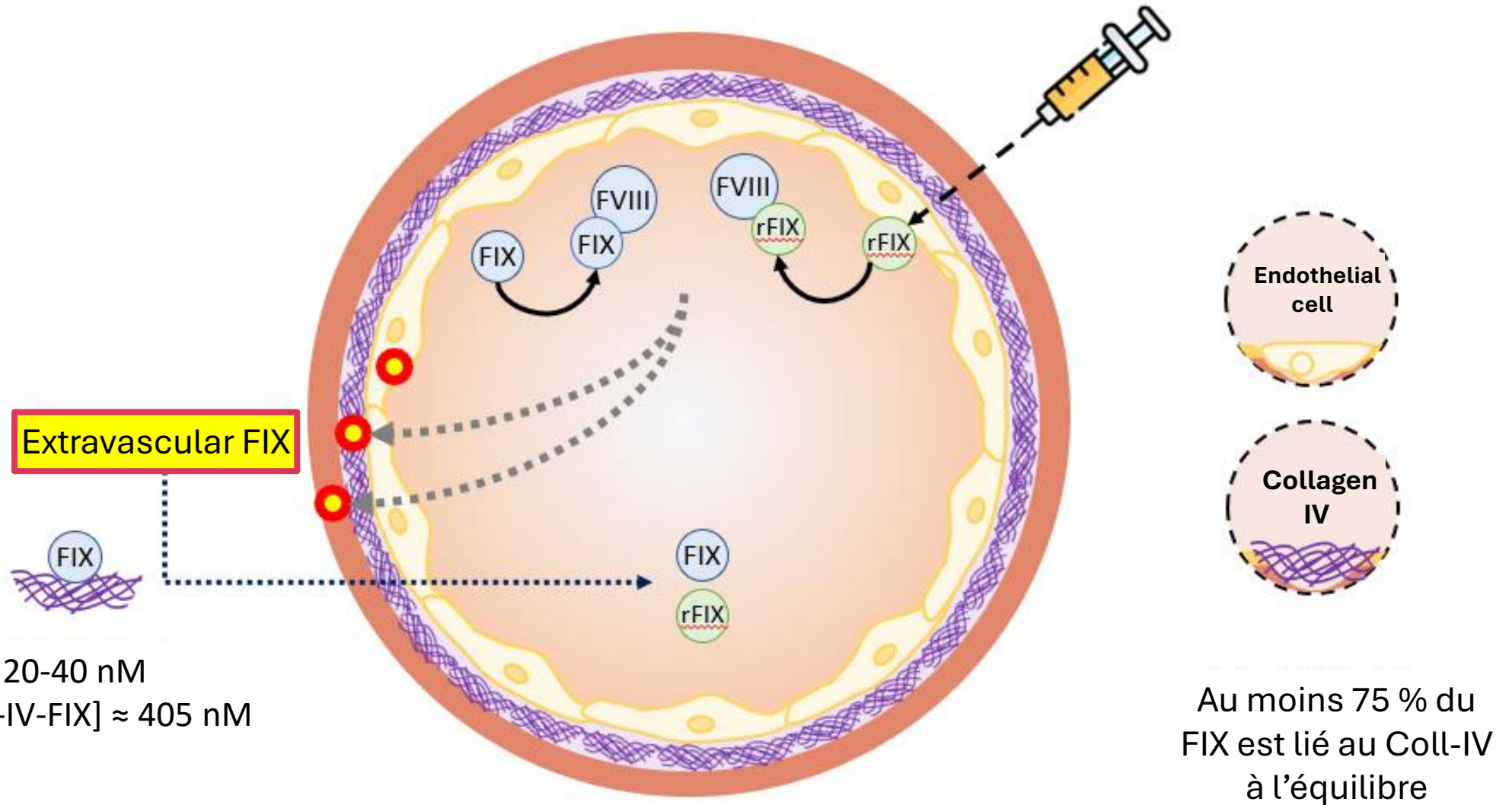




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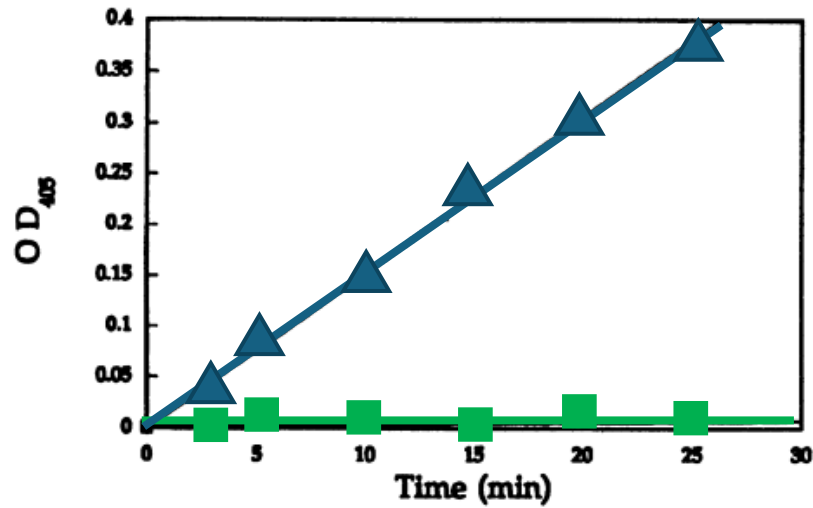


Le FIX lié au Coll-IV est-il actif ?

Le FIX extravasculaire permet-il de protéger contre des saignements ?

Est-ce que le FIX extravasculaire est le seul réservoir de FIX ?





Tenase activity of 0,5n M FIX bound to

▲ endothelial cells

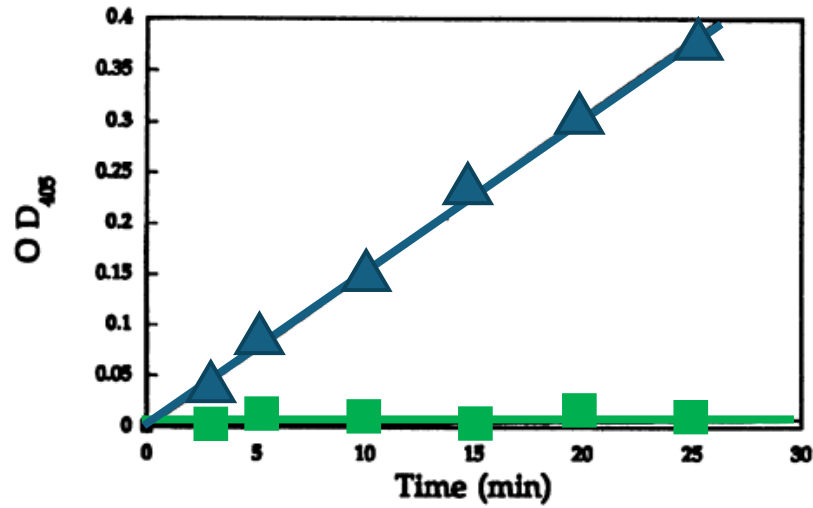
■ ECM protein



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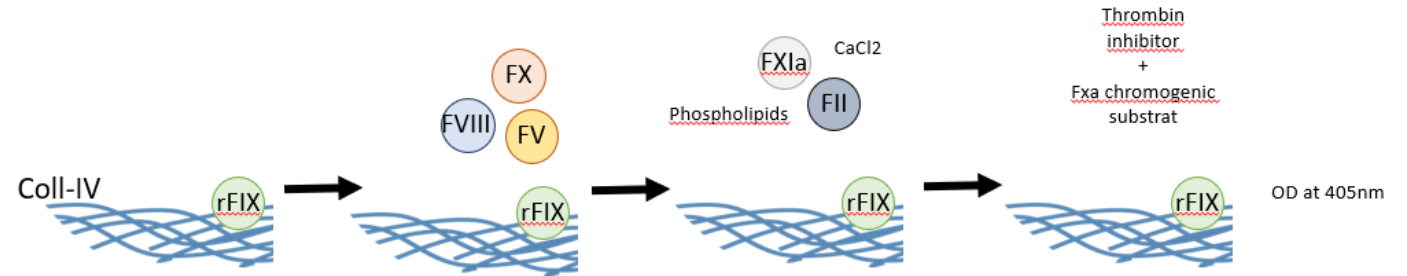
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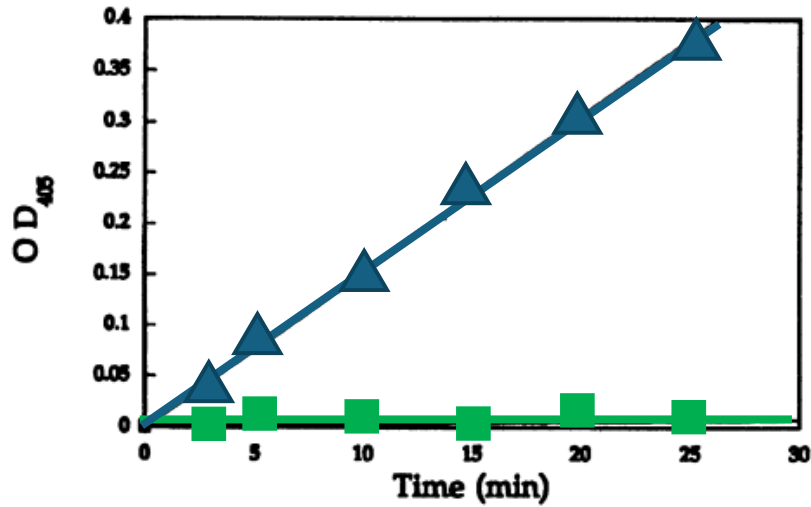


Tenase activity of 0,5n M FIX bound to

▲ endothelial cells

■ ECM protein





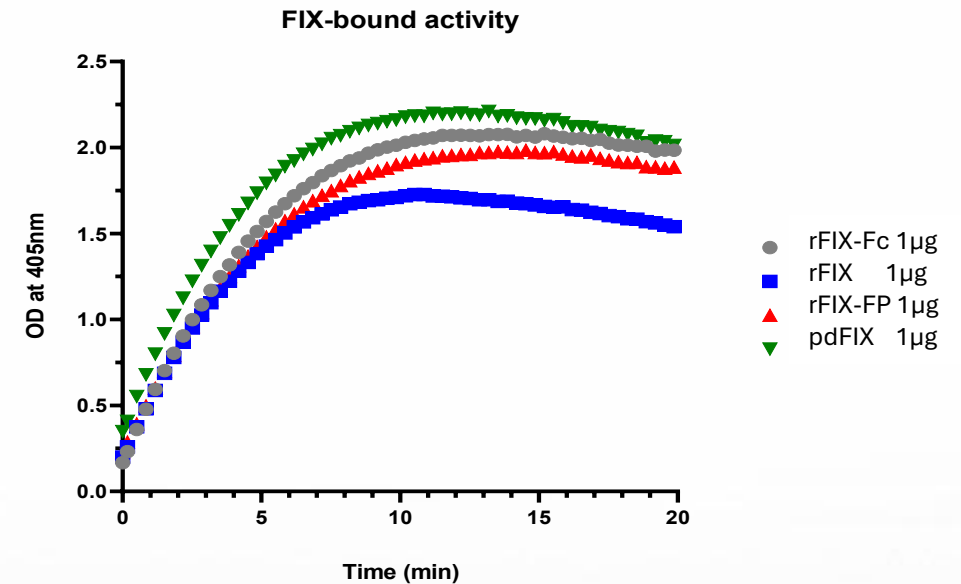
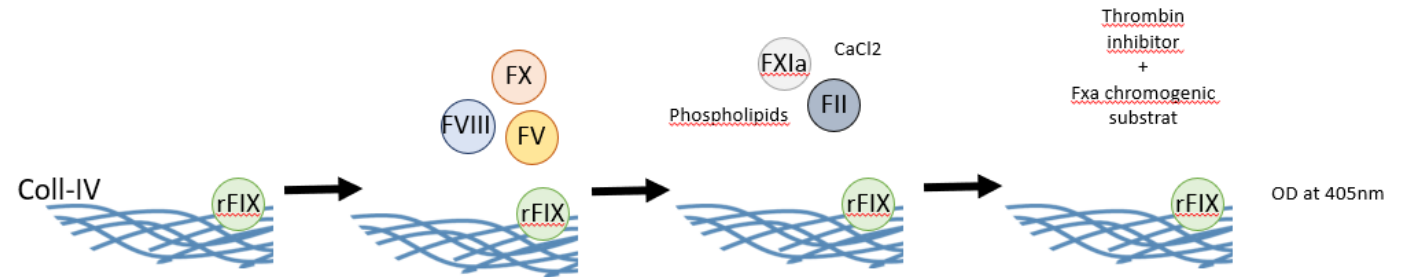
Tenase activity of 0,5n M FIX bound to

▲ endothelial cells

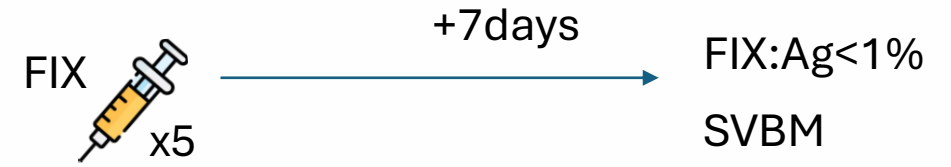
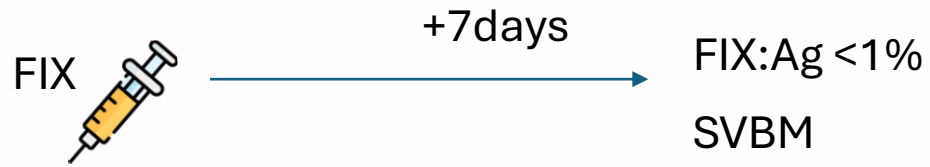
■ ECM protein

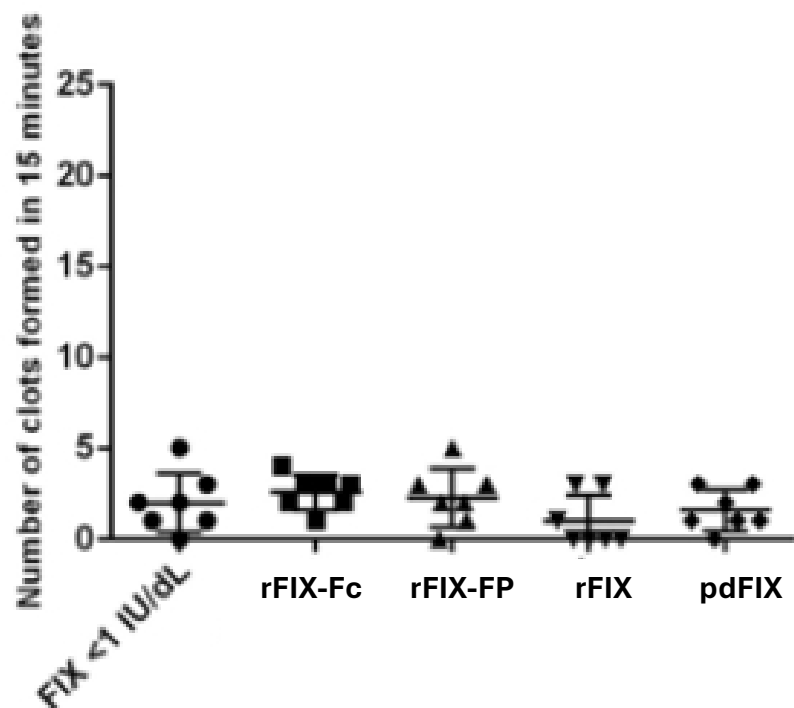
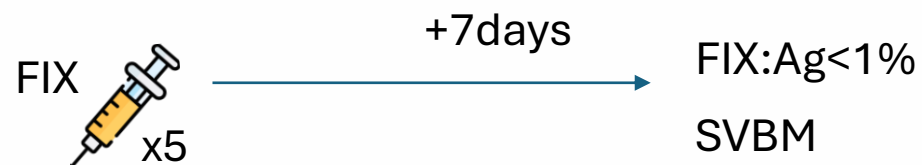
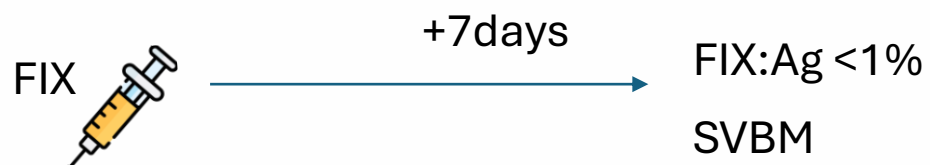
Le FIX lié au Coll-IV est actif
Suffisant pour assurer l'hémostase ?

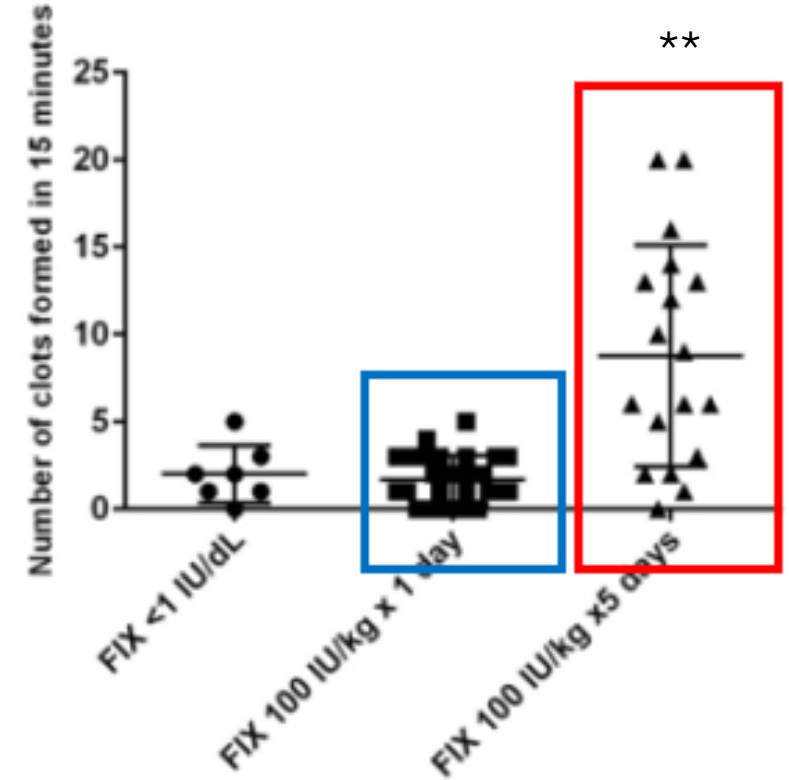
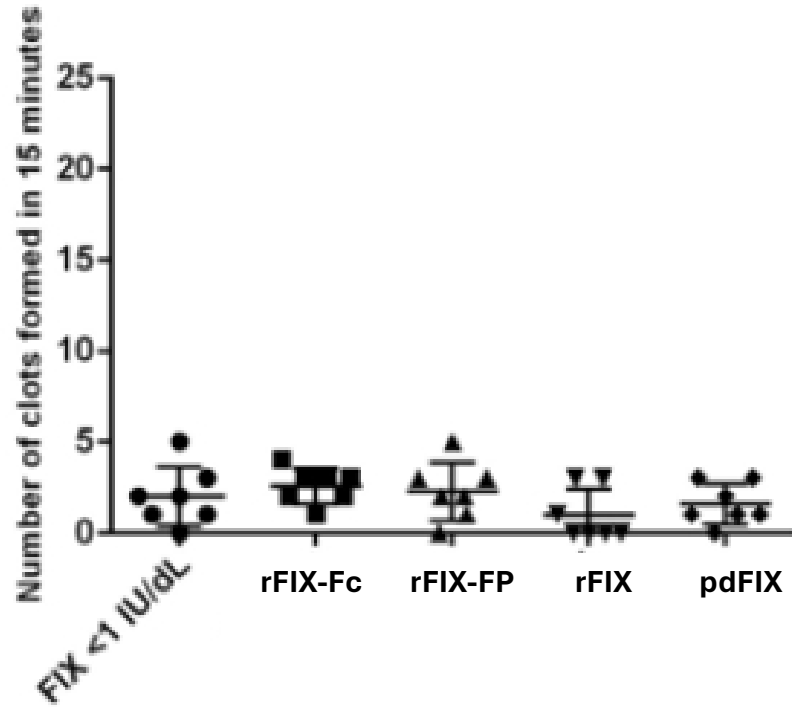
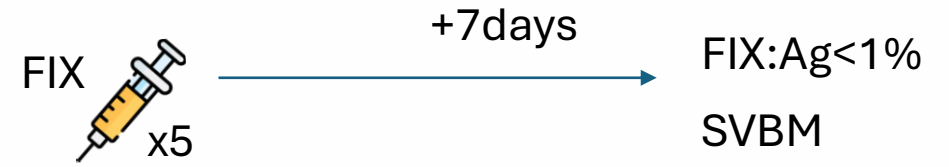
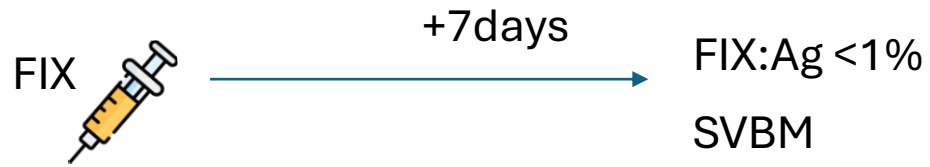
Cheung et al 1996

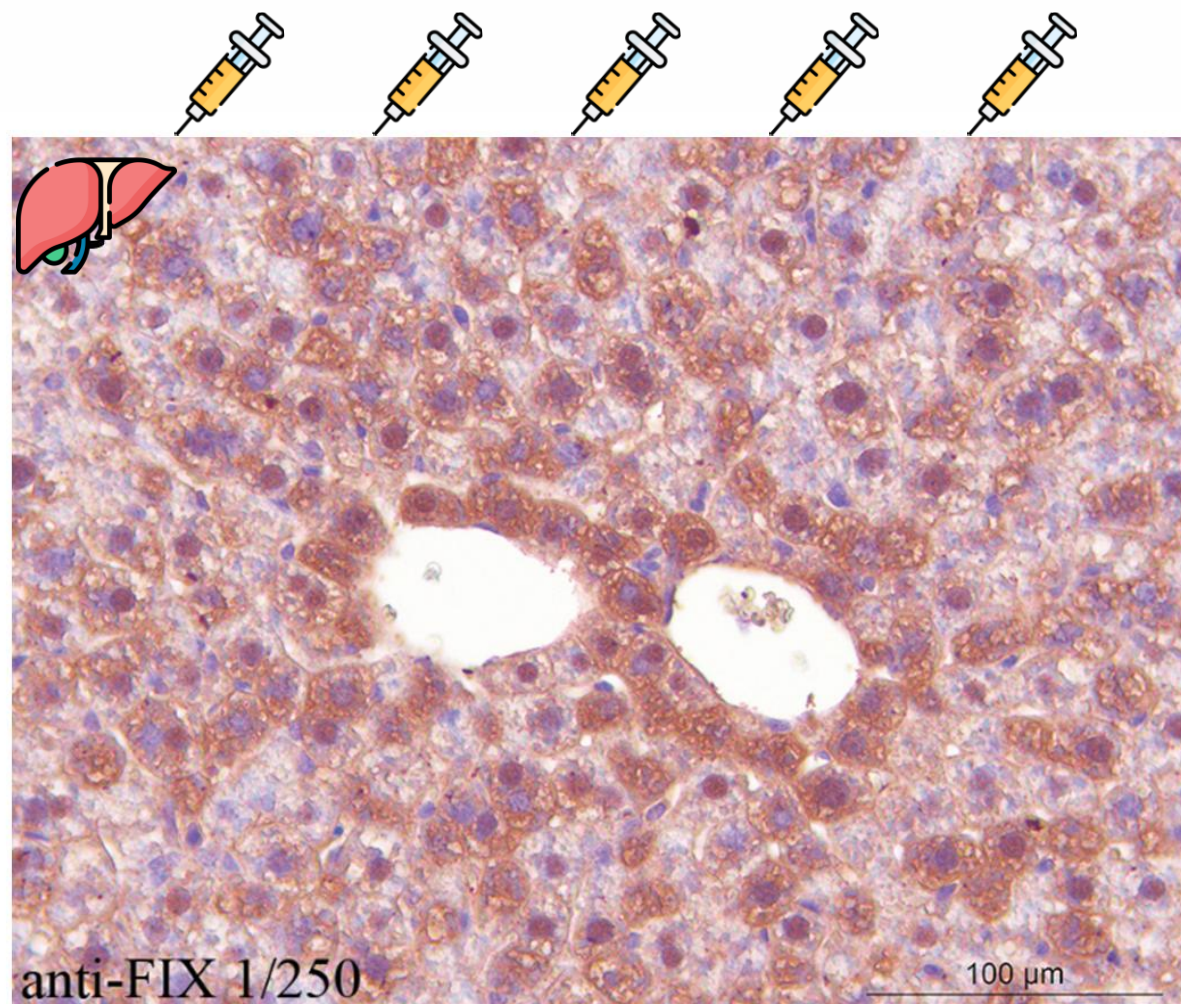
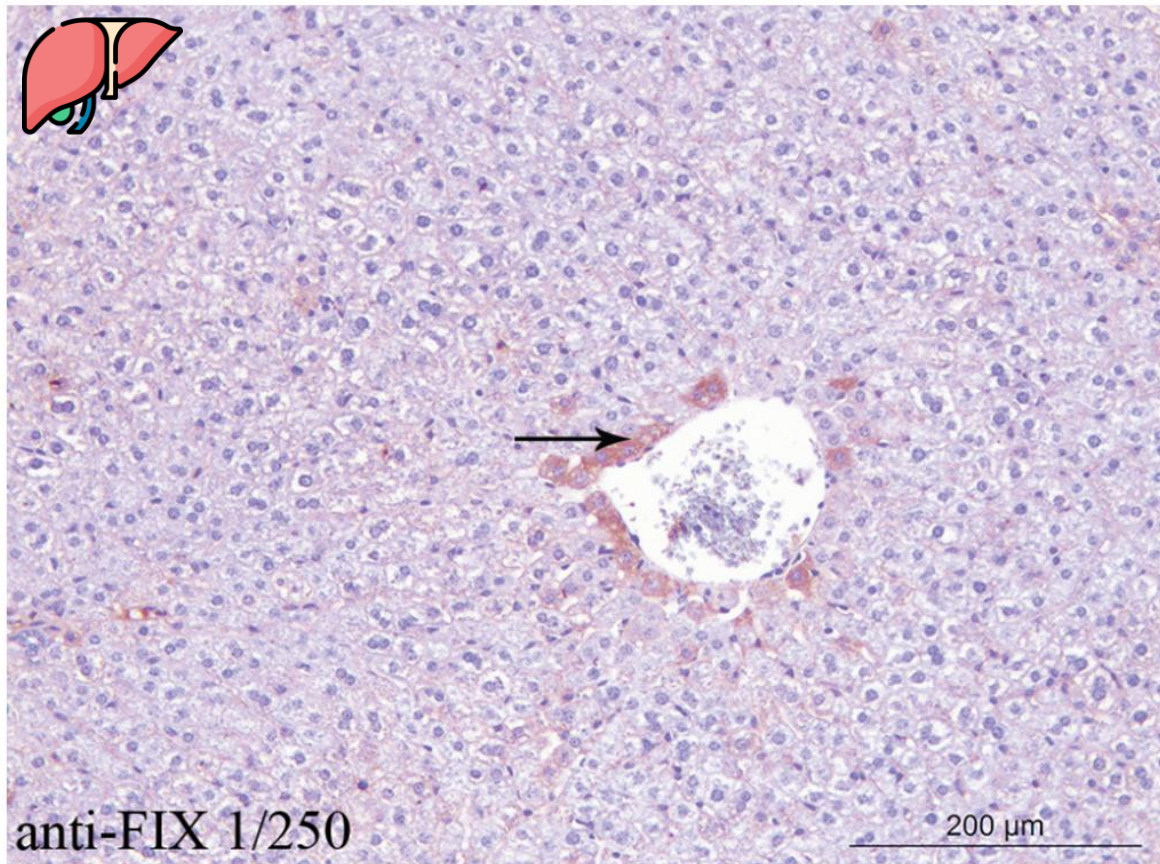


Données personnelles non publiées







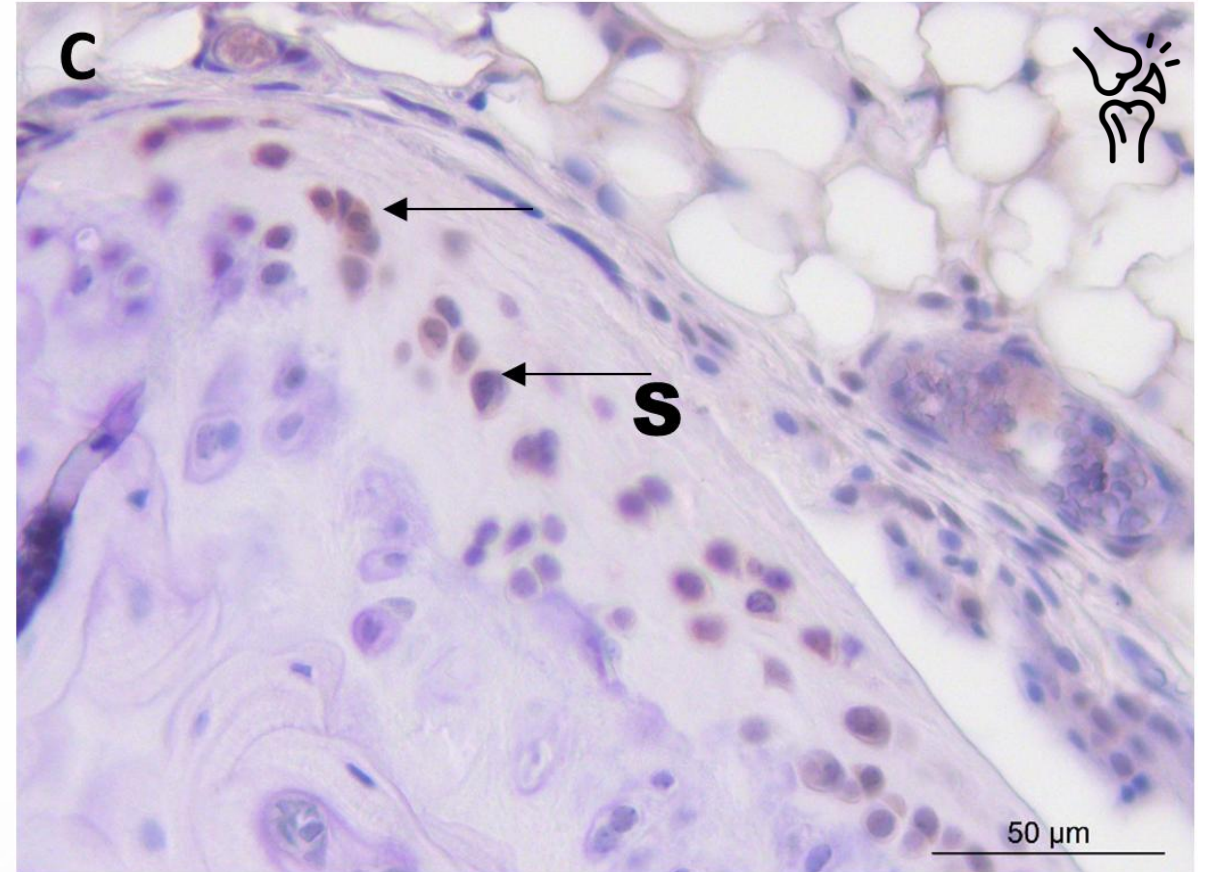
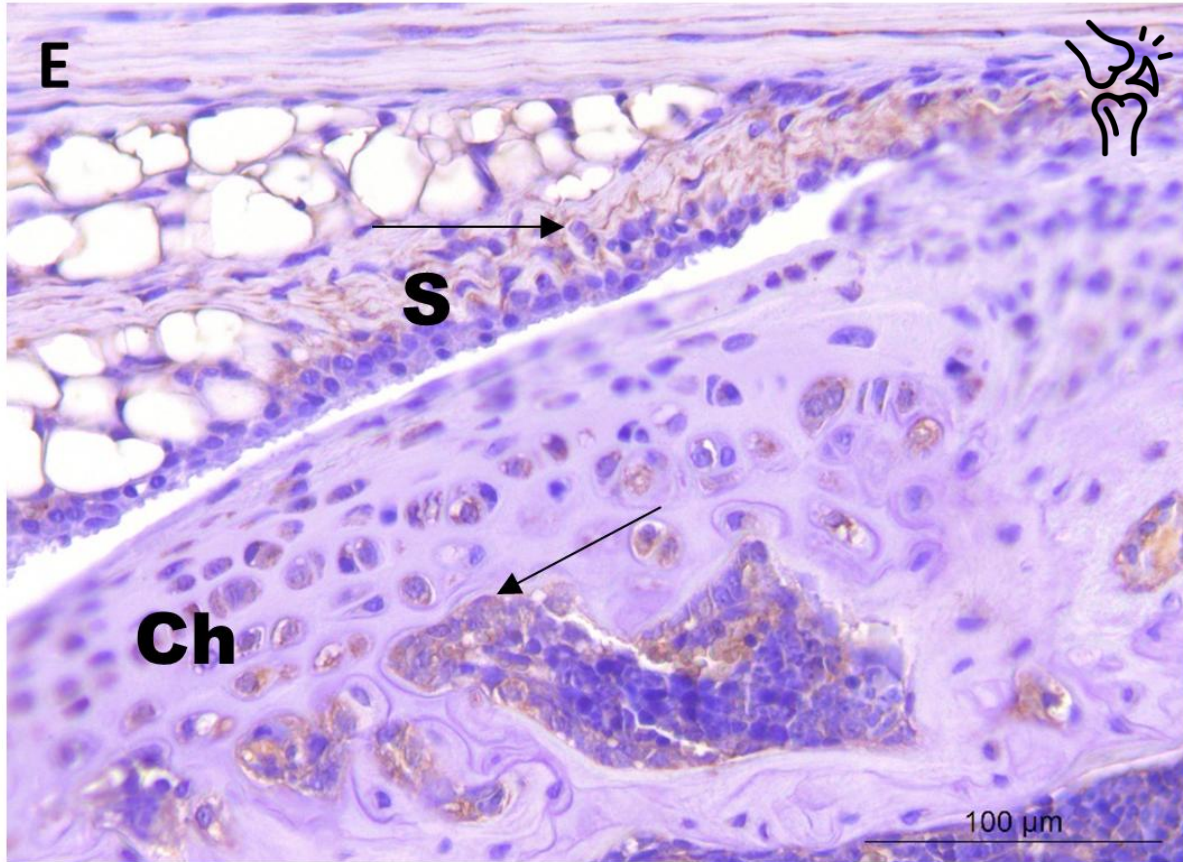




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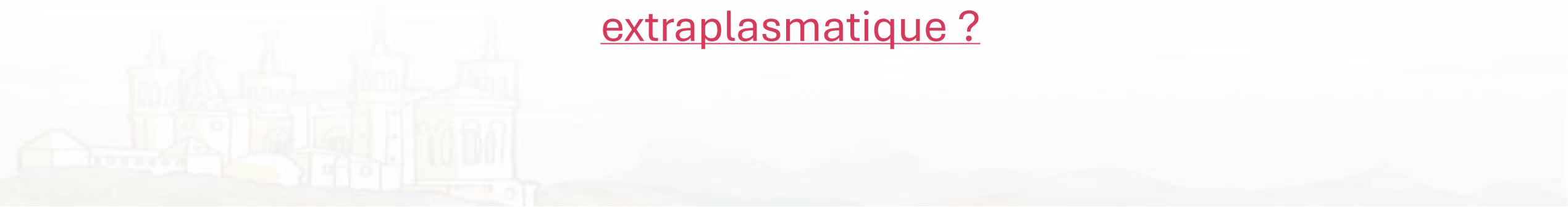
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La prophylaxie par FIX permet de constituer un réservoir autour des vaisseaux

Le FIX reste hémostatiquement actif pour contrôler un saignement

Le FIX lié au Coll-IV le seul réservoir
extraplasmatique ?

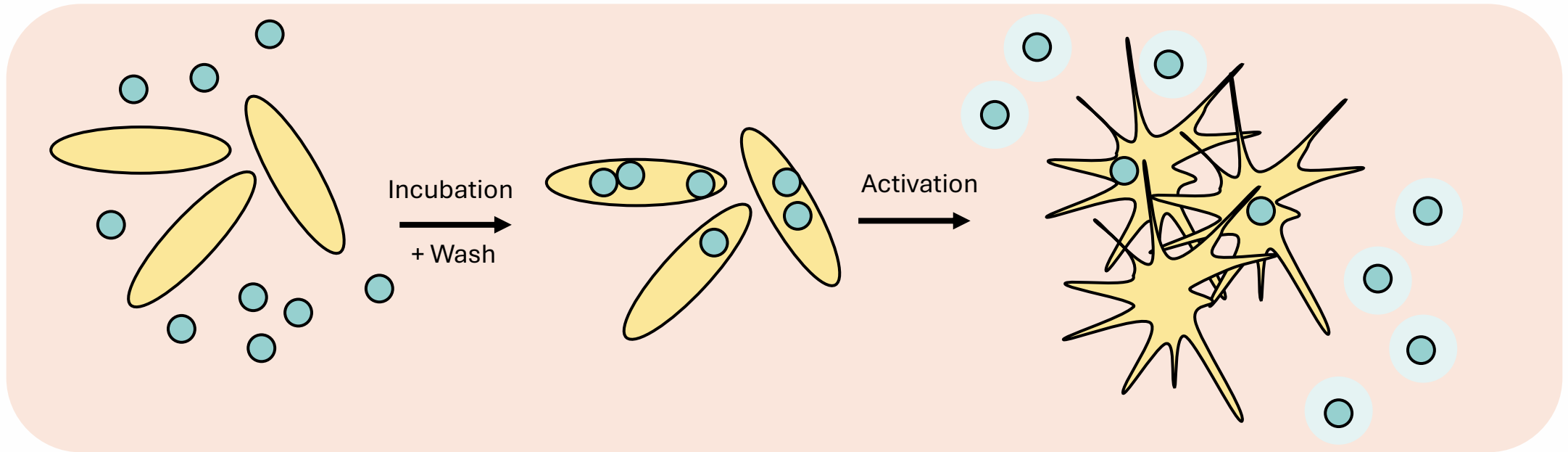


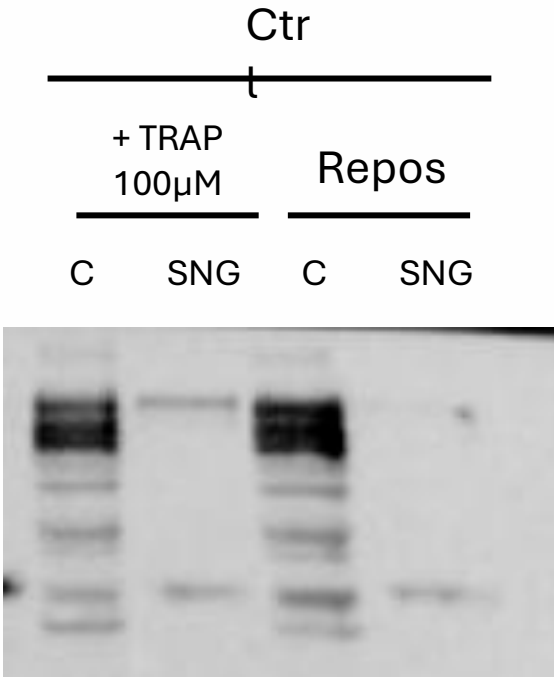


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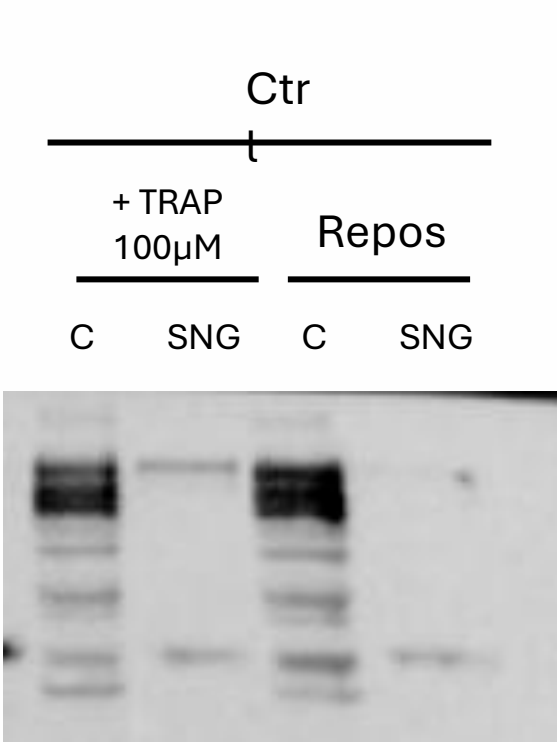
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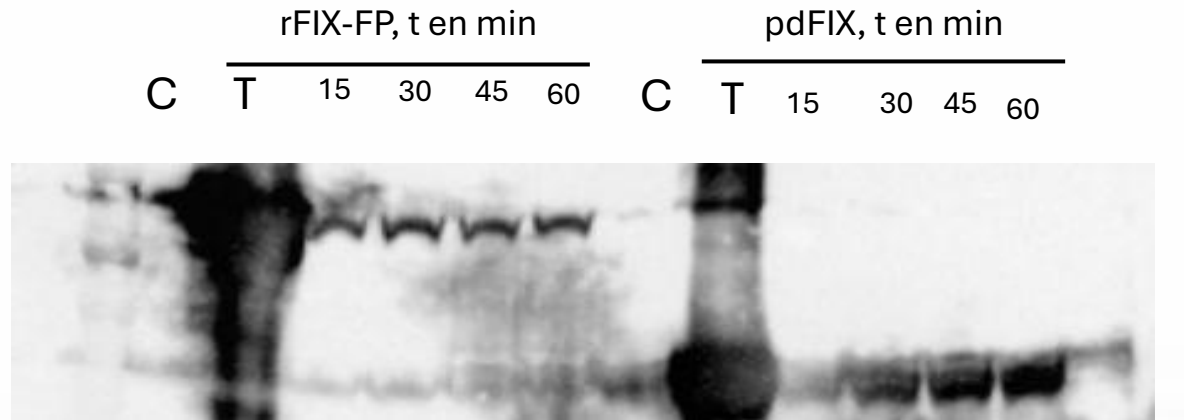
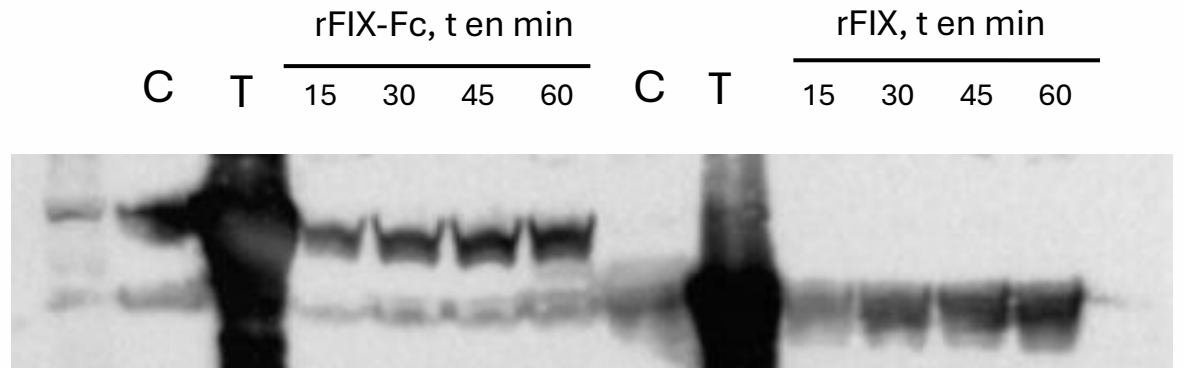


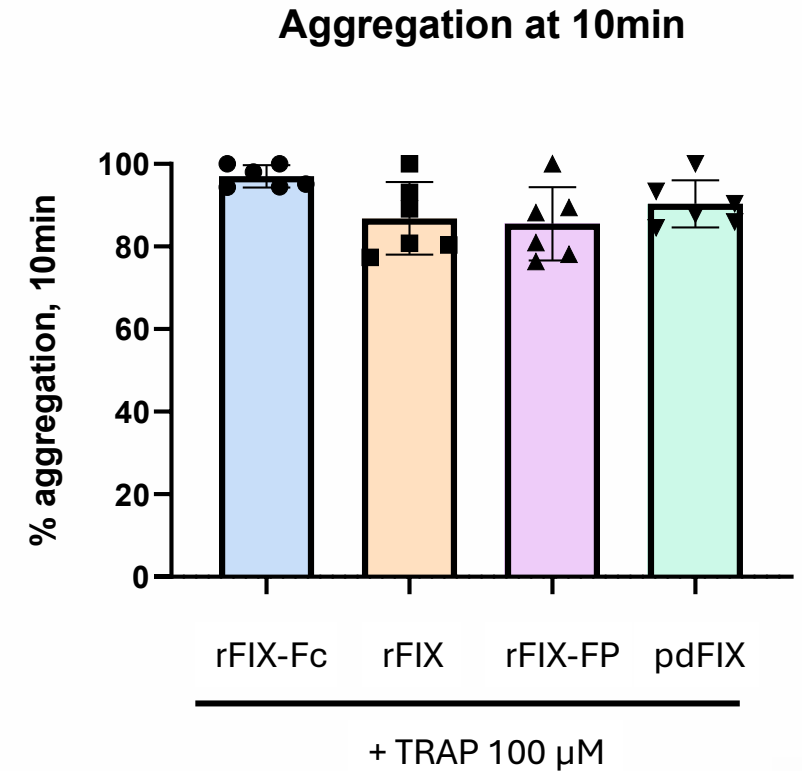
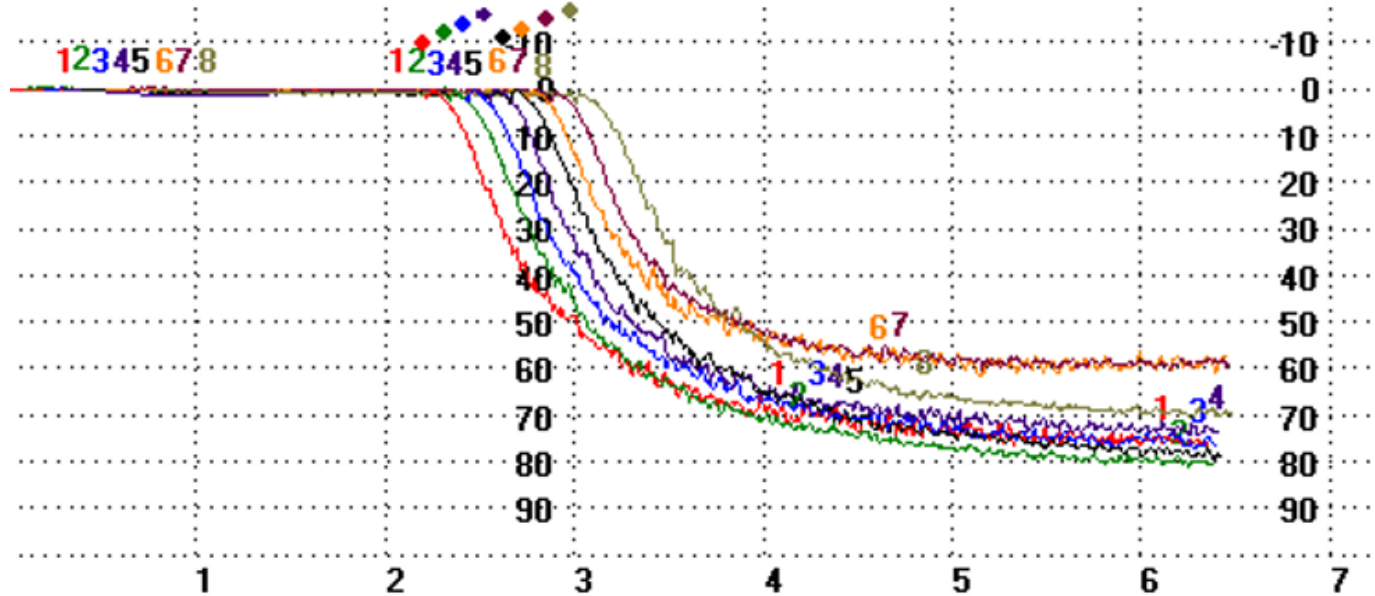


Présence d'une faible quantité de FIX
dans les plaquettes de donneurs sains
FIX sécrété après activation

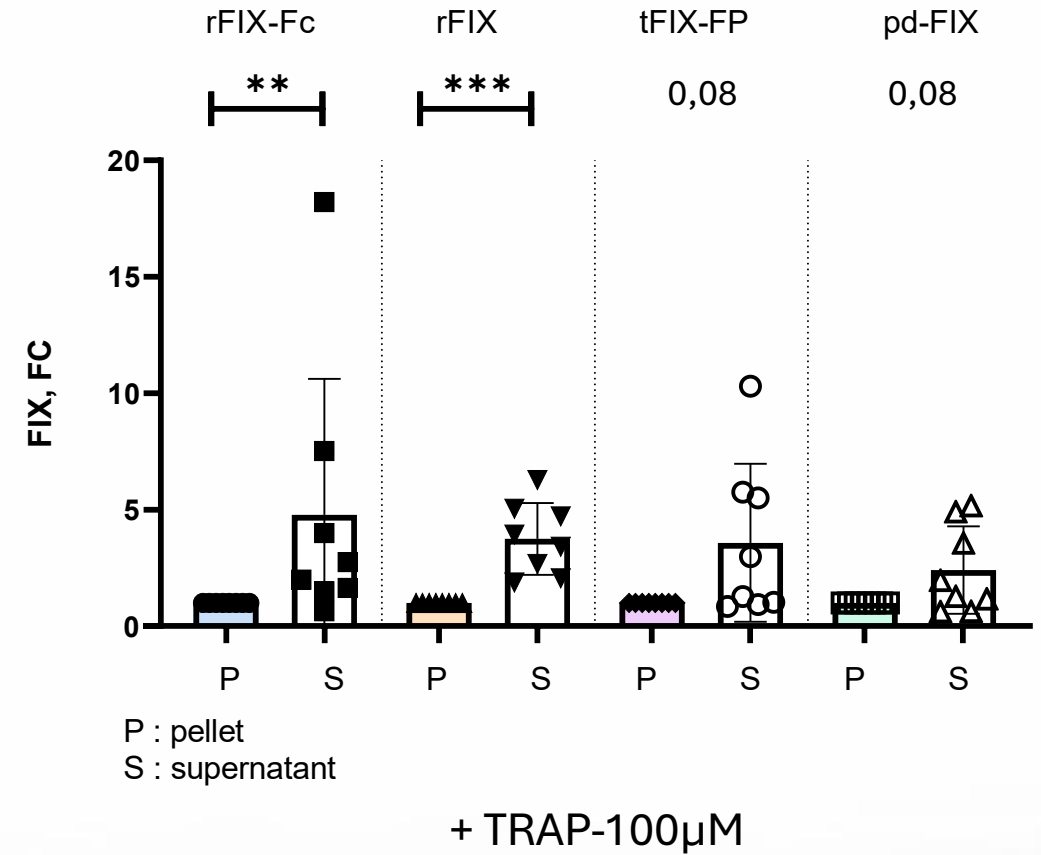
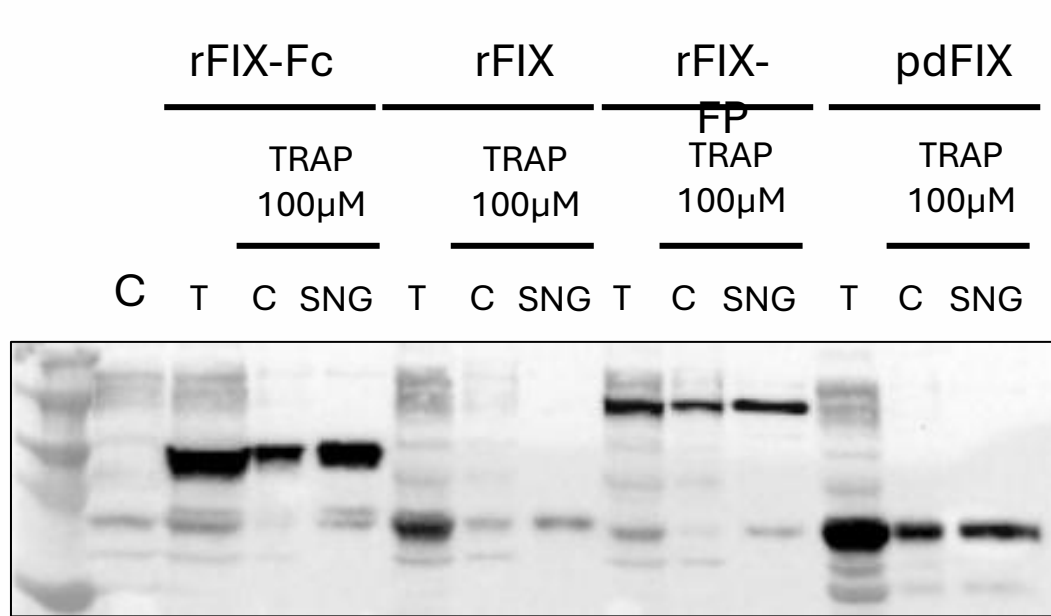


Internalisation du FIX atteinte
pour 30 min





L'internalisation de pdFIX ou de rFIX ne modifie l'agrégation plaquettaire

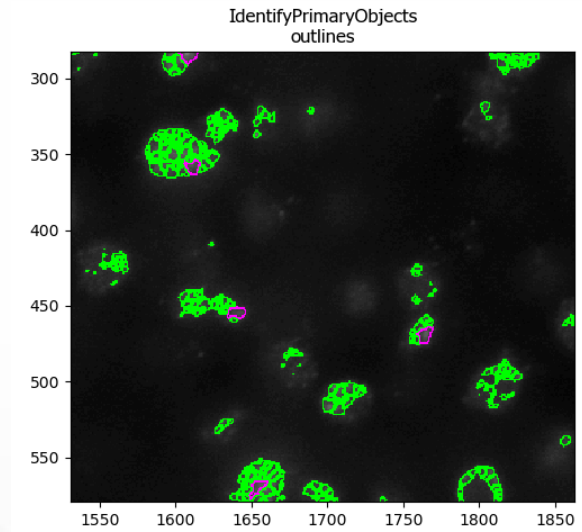
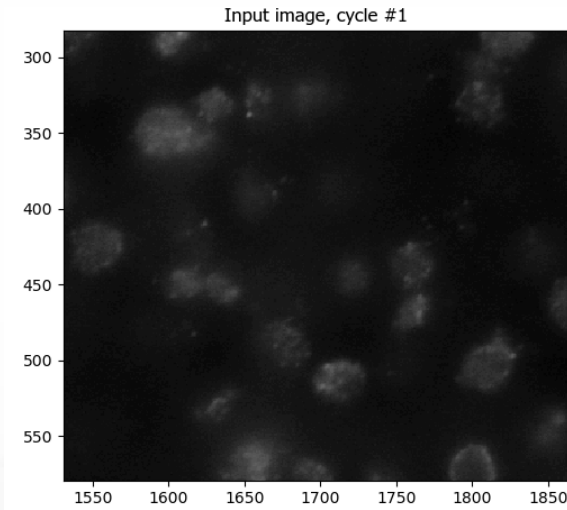
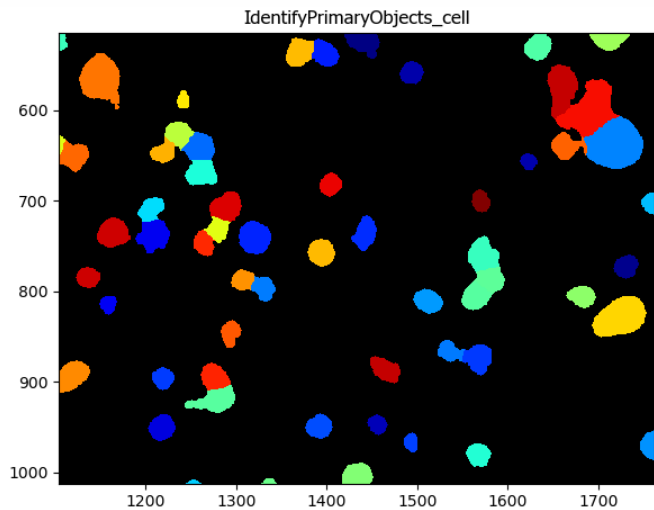
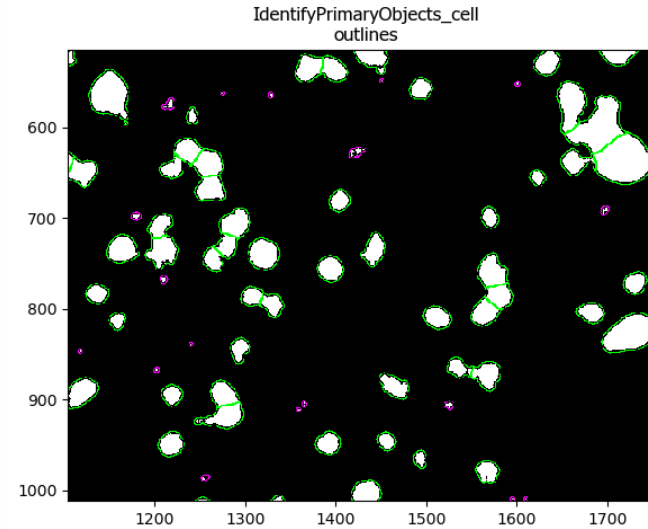
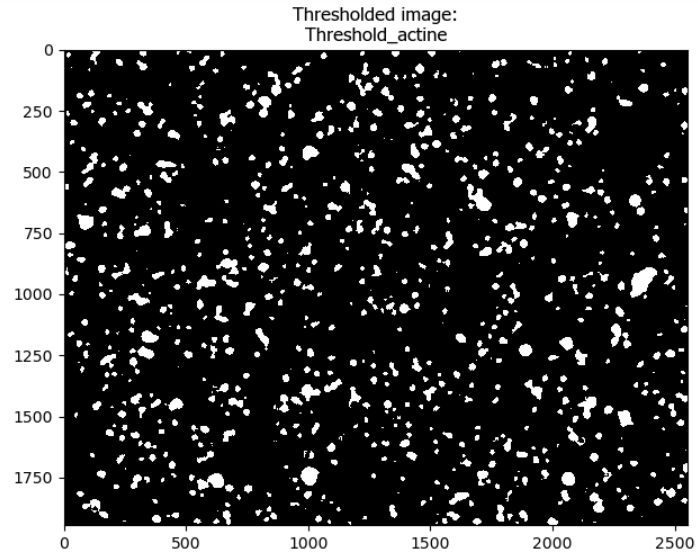


Le pdFIX ou le rFIX internalisé est retrouvé en partie dans le surnageant d'activation des plaquettes



CellProfiler

<https://cellprofiler.org/>

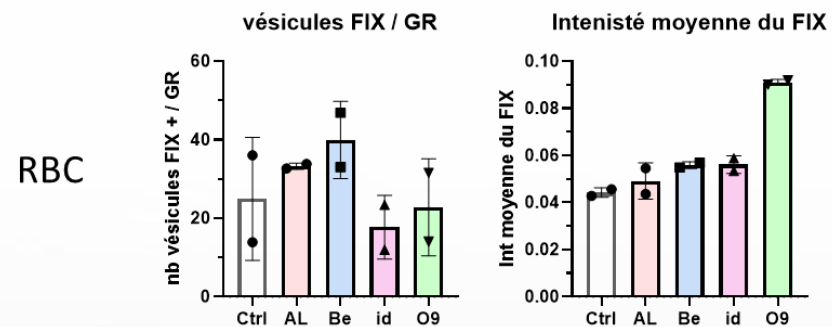
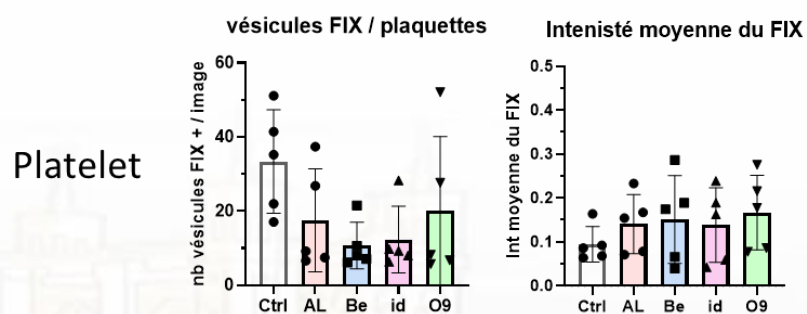
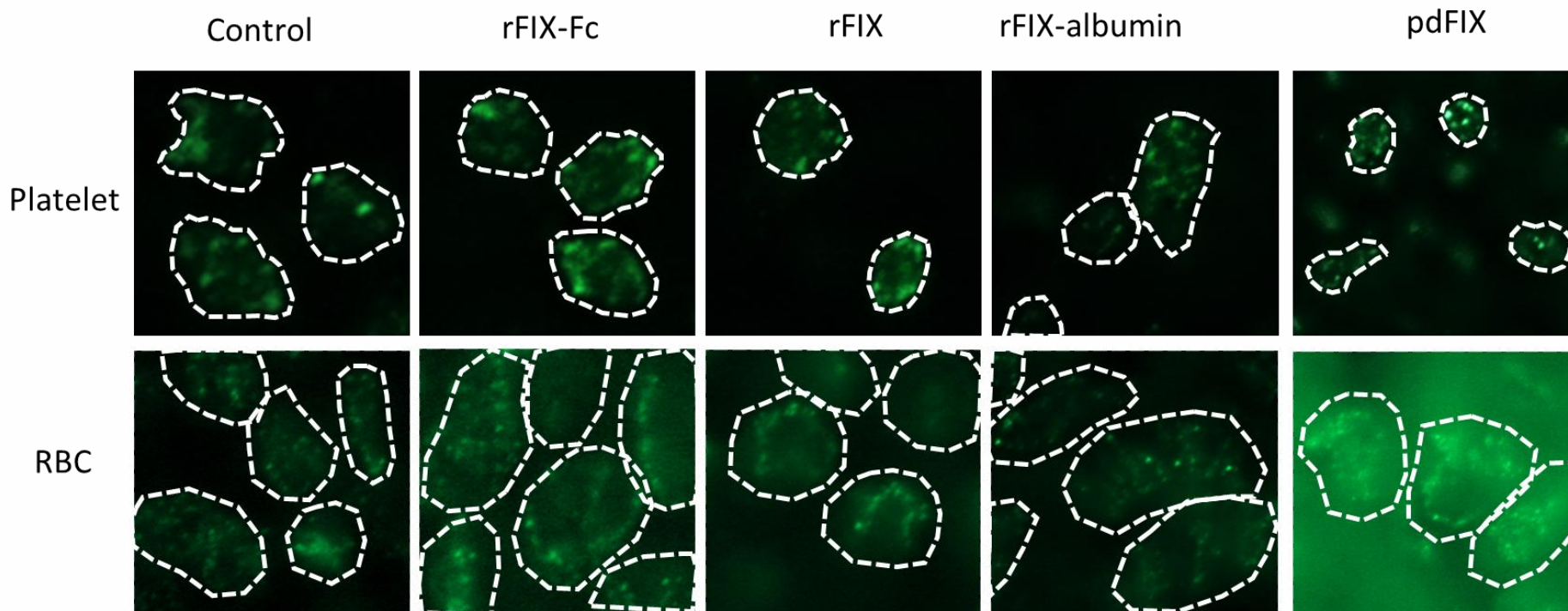




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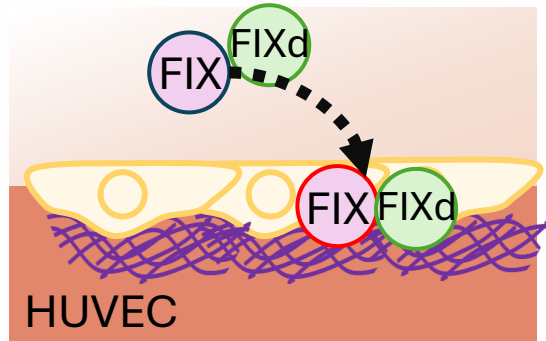
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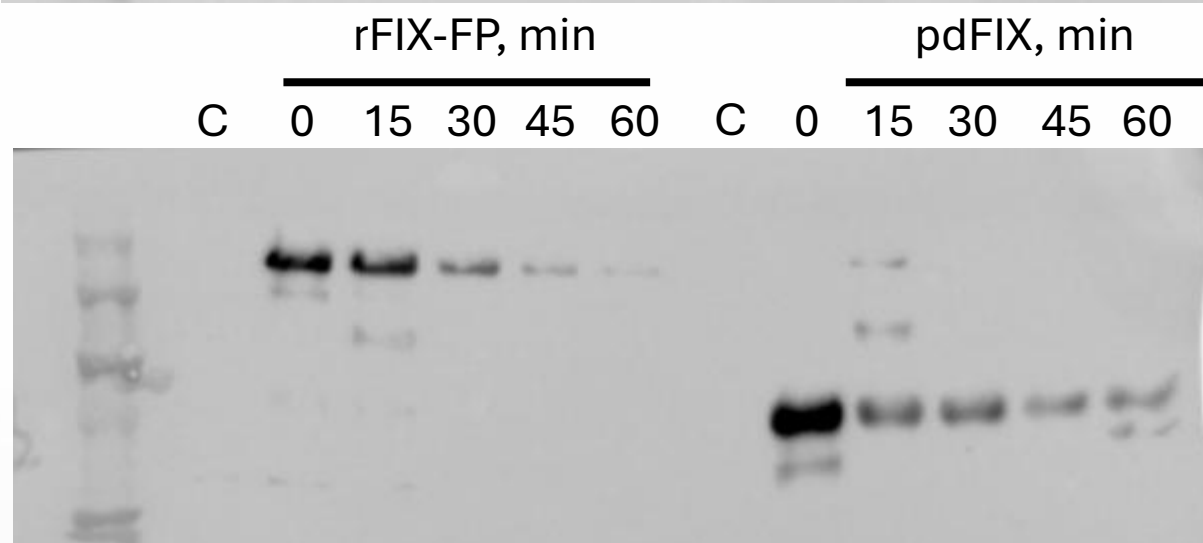
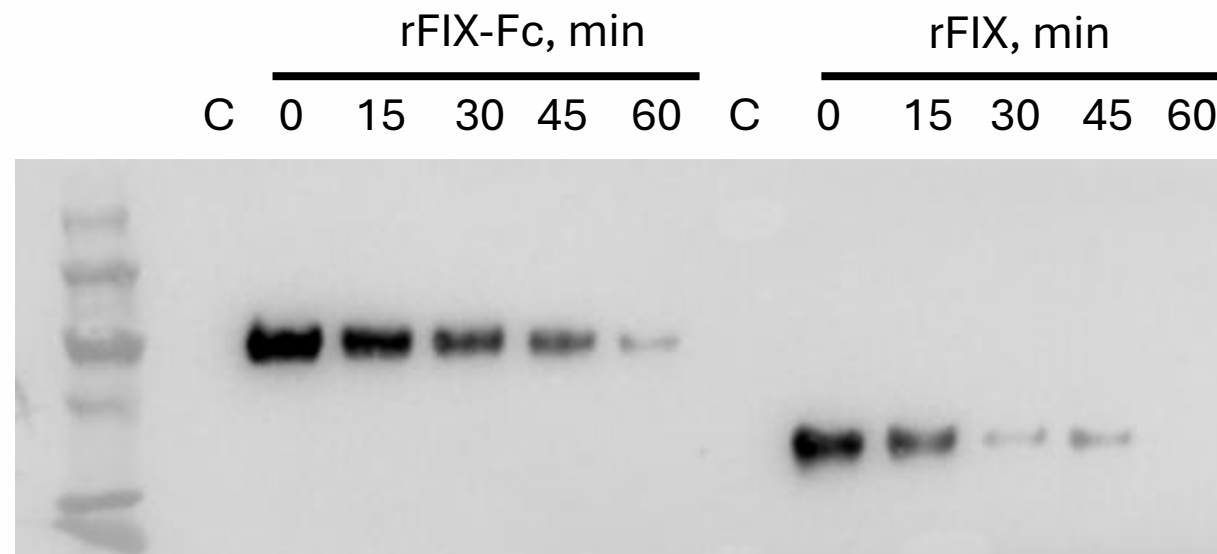
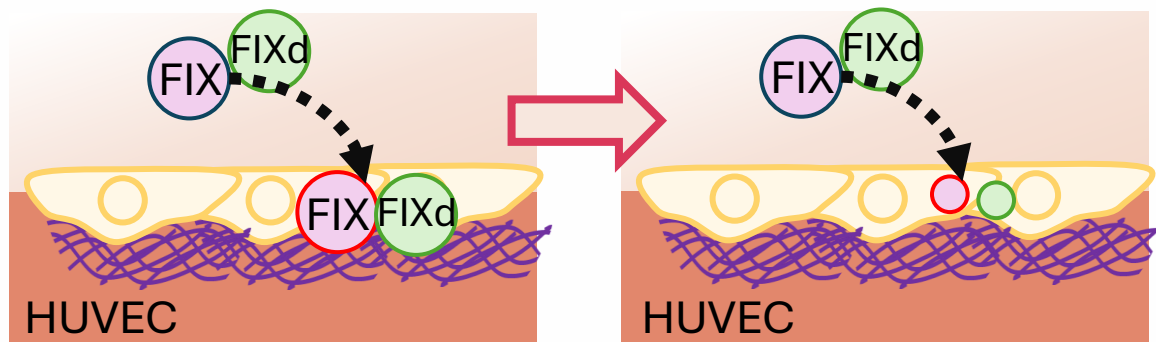
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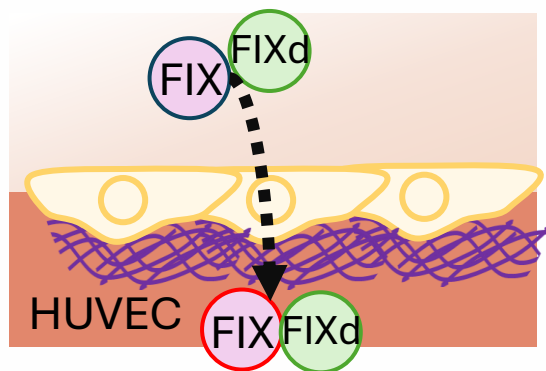
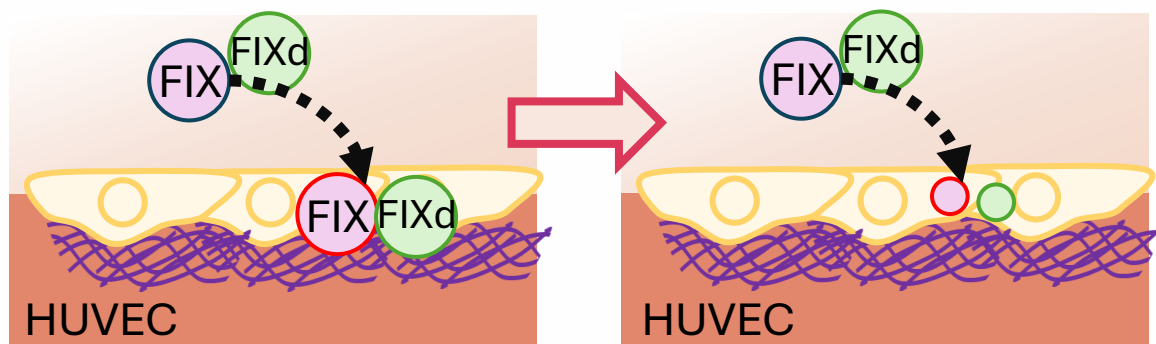
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Données personnelles non publiées



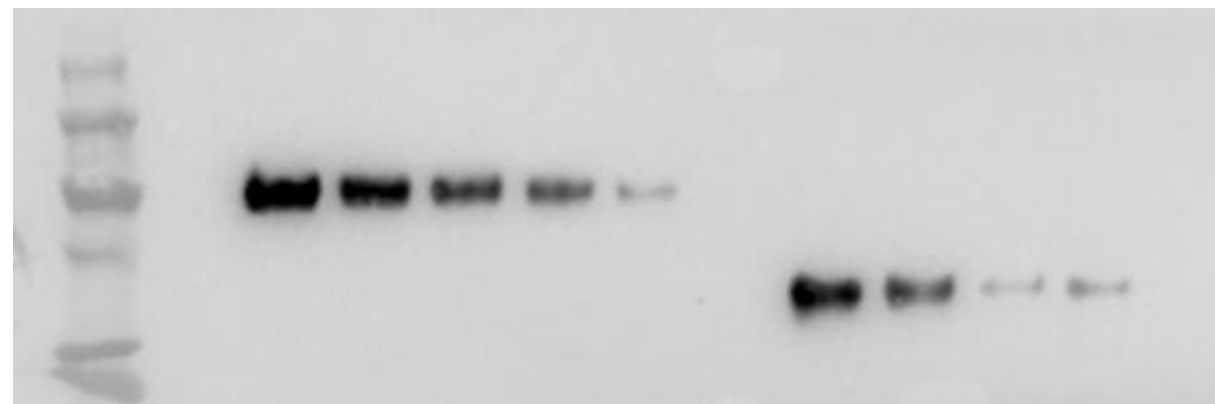


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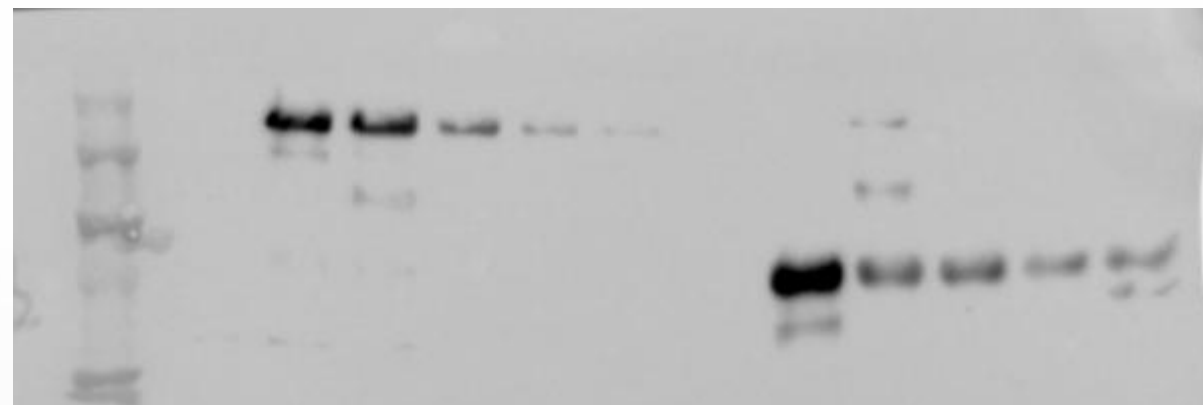


Temps de résidence court dans les HUVECs
Transit vers le sous endothélium?*

rFIX-Fc, min							rFIX, min						
C	0	15	30	45	60		C	0	15	30	45	60	



rFIX-FP, min							pdFIX, min						
C	0	15	30	45	60		C	0	15	30	45	60	



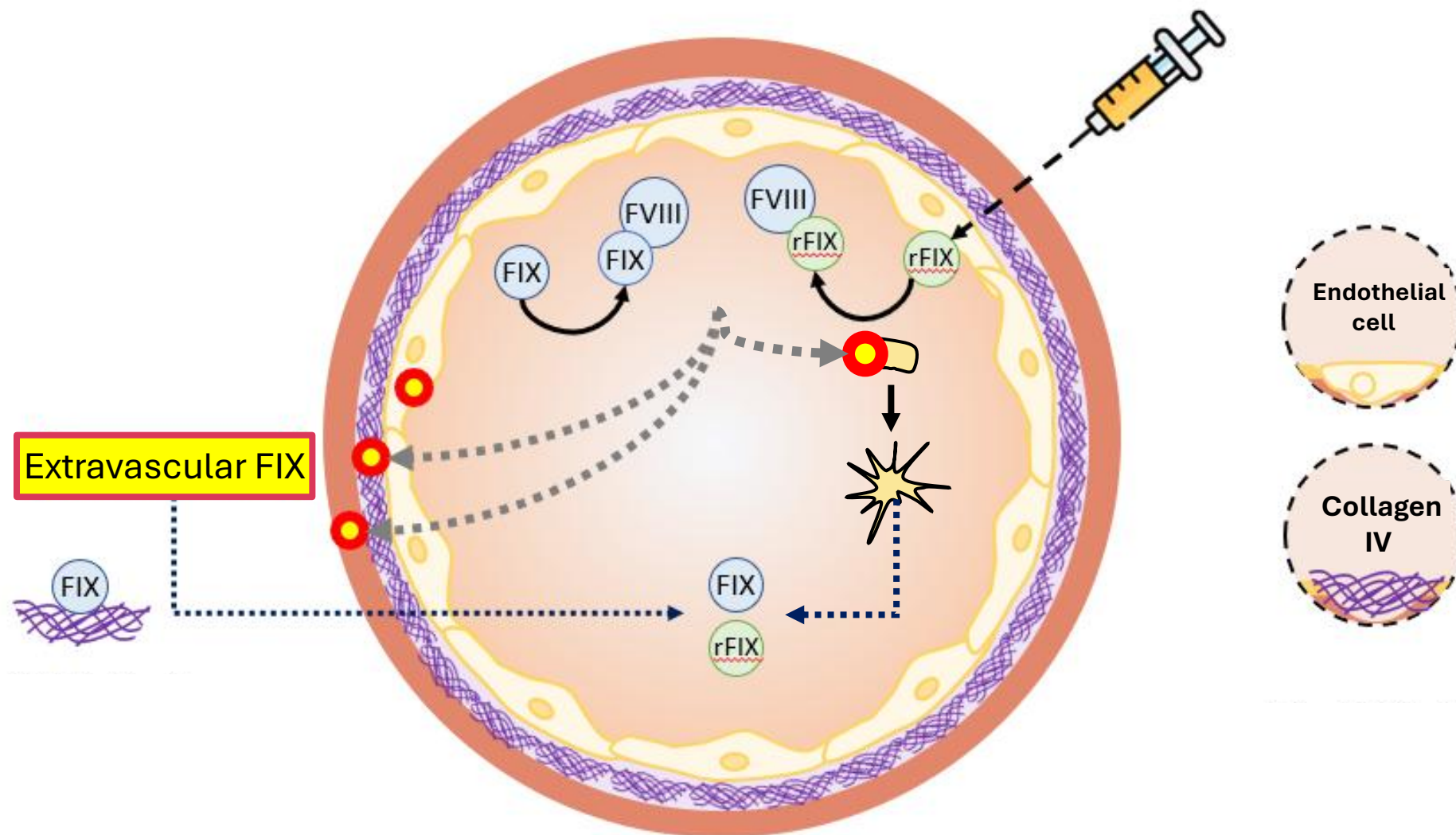
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- La prophylaxie permet de constituer un réservoir de FIX
- Le **FIX fixé au Coll-IV hémostatiquement actif.**
- Les **plaquettes** pourraient également jouer un rôle de **réserve vasculaire**, augmentant la demi-vie du FIX thérapeutique
- Perspectives pour la thérapie génique



Merci de votre attention

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octapharma

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European Association for Haemophilia
and Allied Disorders

CSL Behring

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ECM ANTIBODY PRODUCER • TISSUE ANALYSIS

Martine Melin


CRH **HCL**
Centre de Référence Hémophilie et autres déficits
constitutionnels en protéines de la coagulation
HOSPICES CIVILS
DE LYON

Médecins et infirmières du
CRH



Université Claude Bernard  Lyon 1

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