

Le méthotrexate dans le traitement de l'arthropathie hémophilique

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

UR-4609 | Hém^ostase & Thr^omb^ose

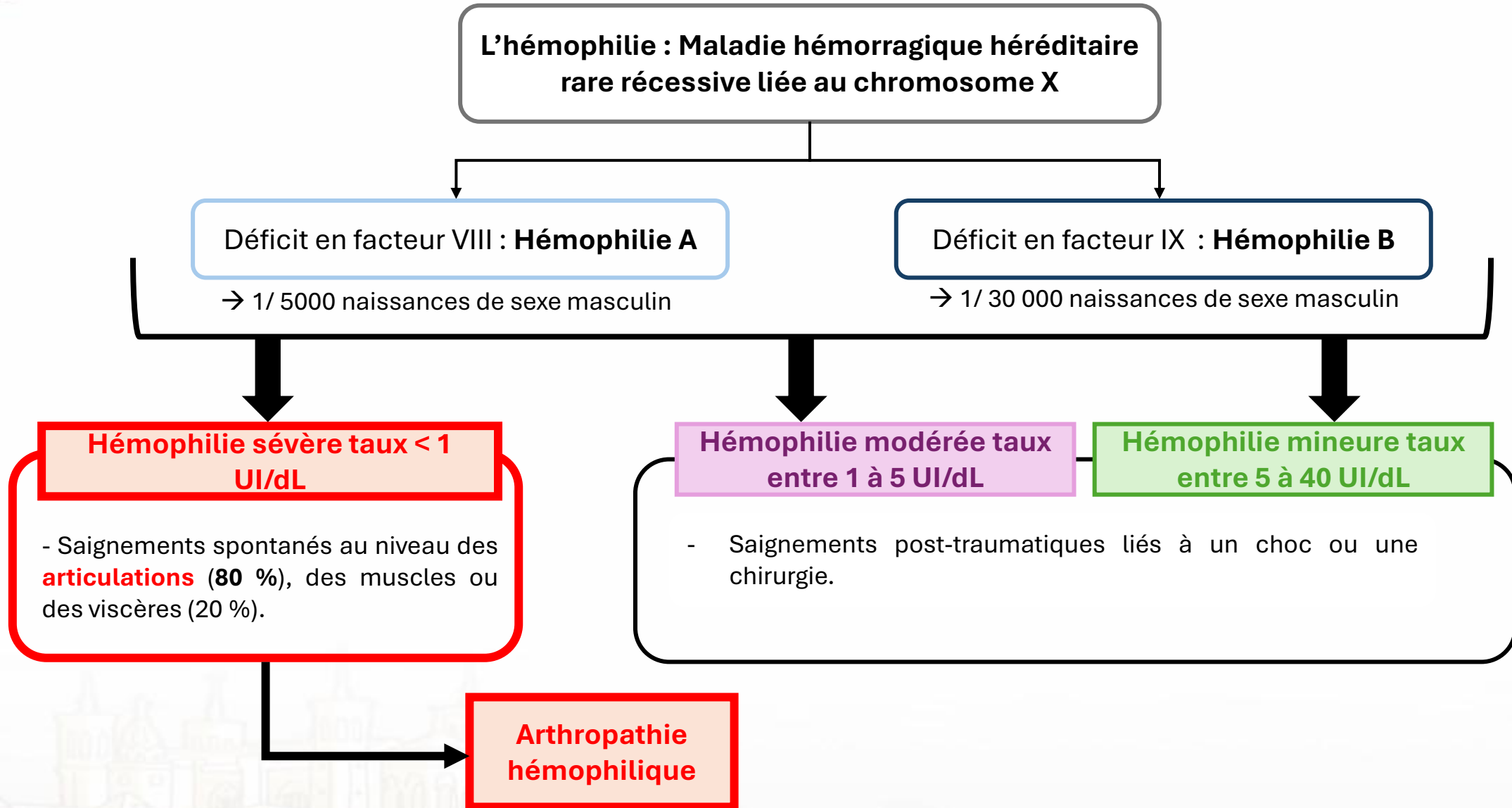


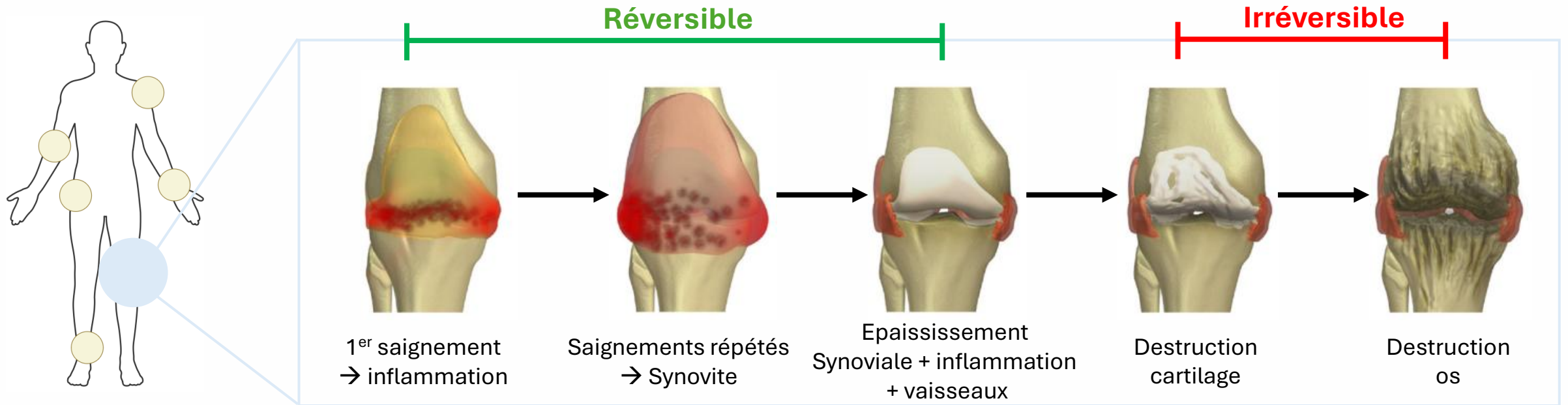
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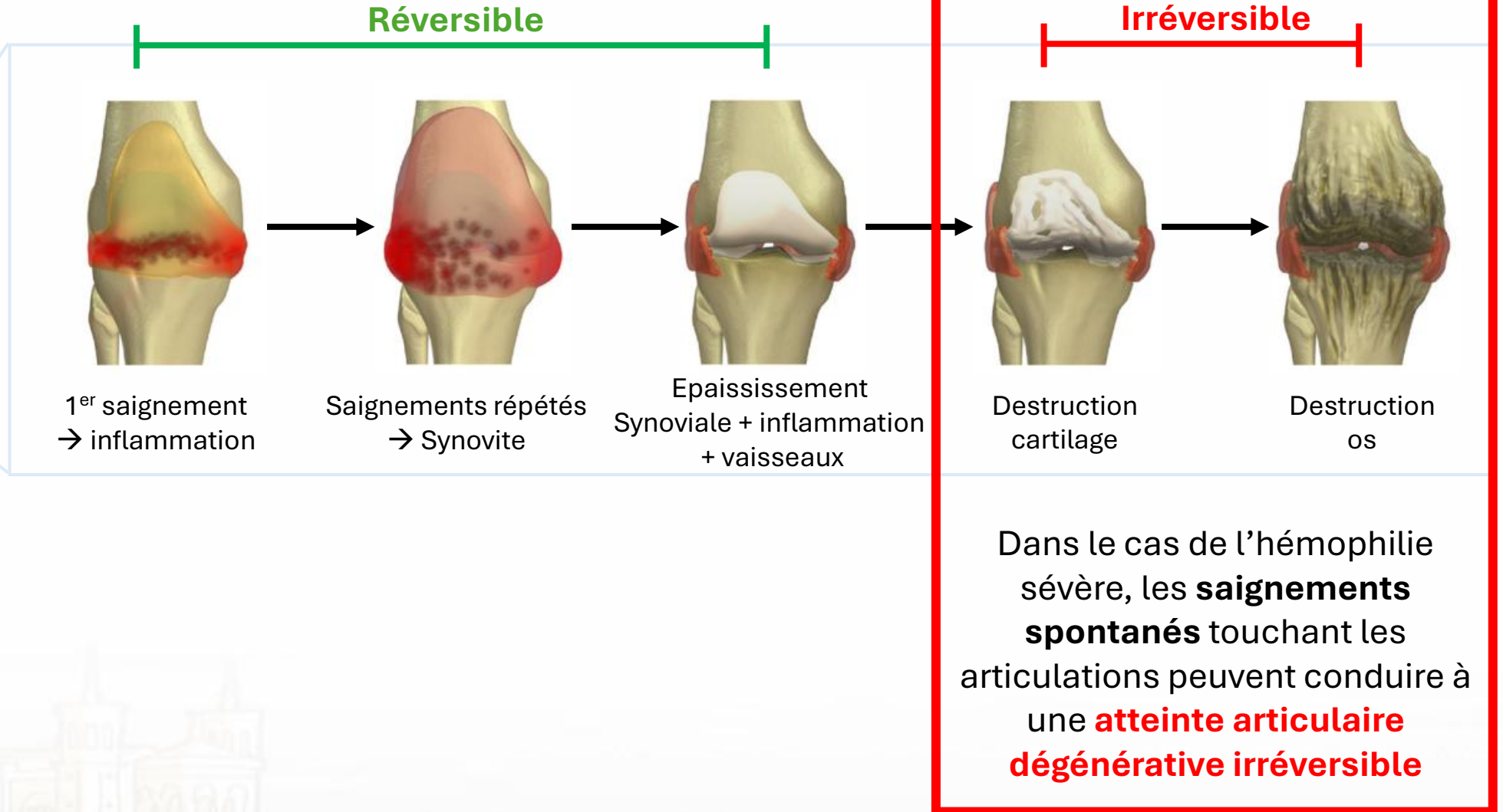
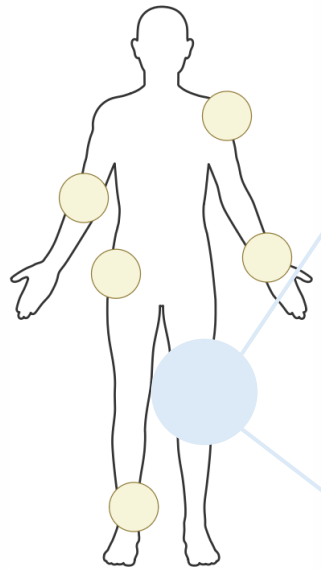


Lyon 1









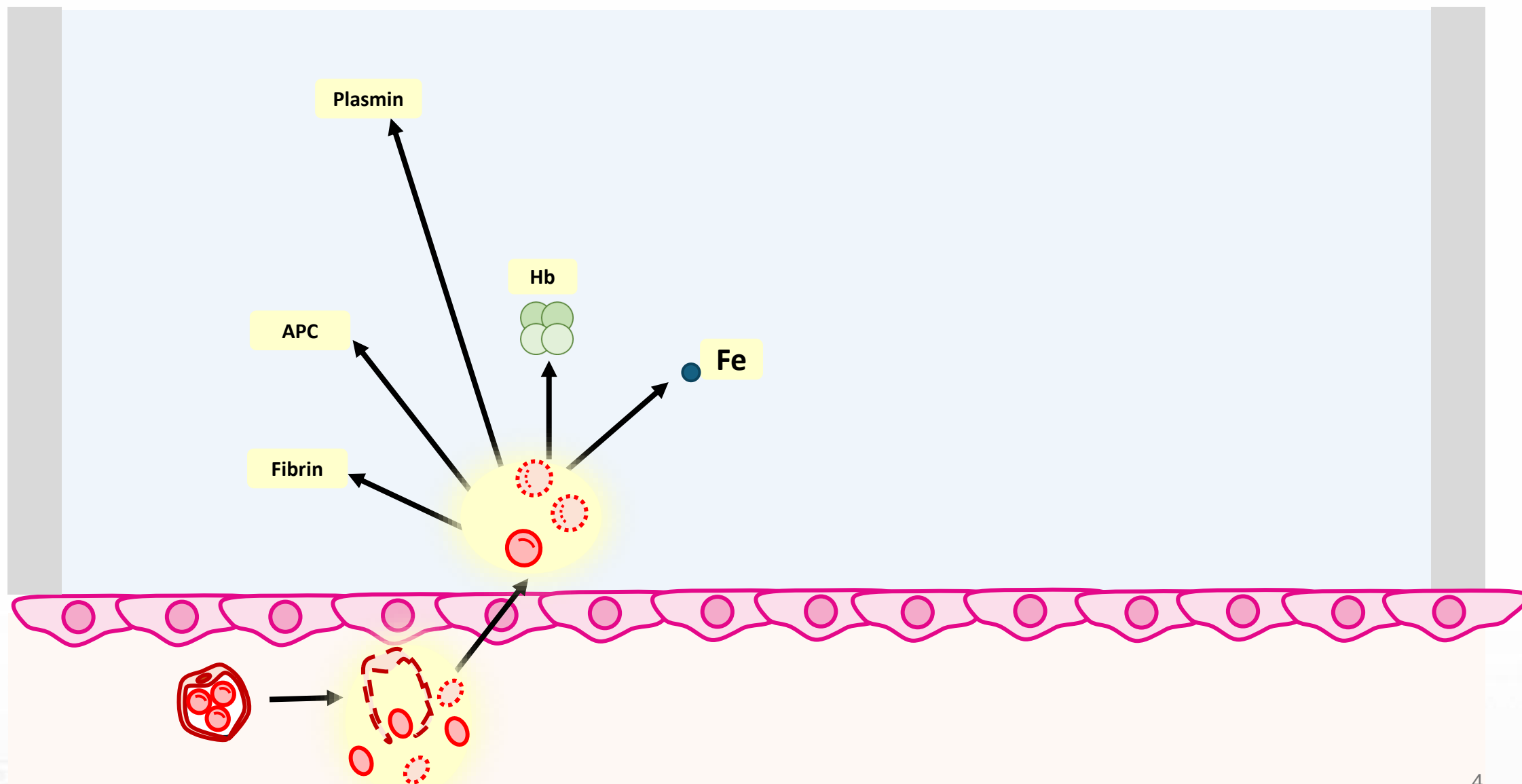
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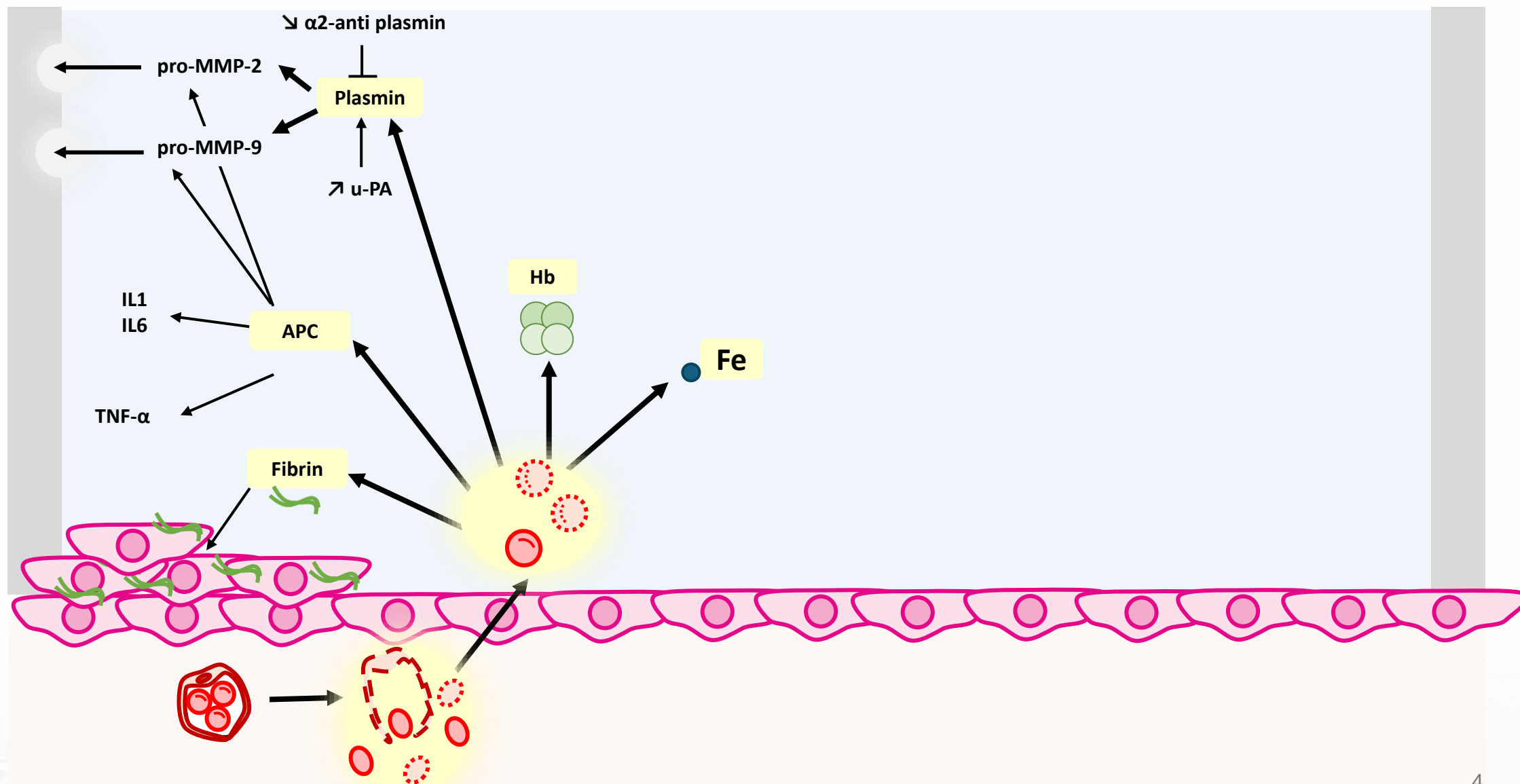
Liquide articulaire

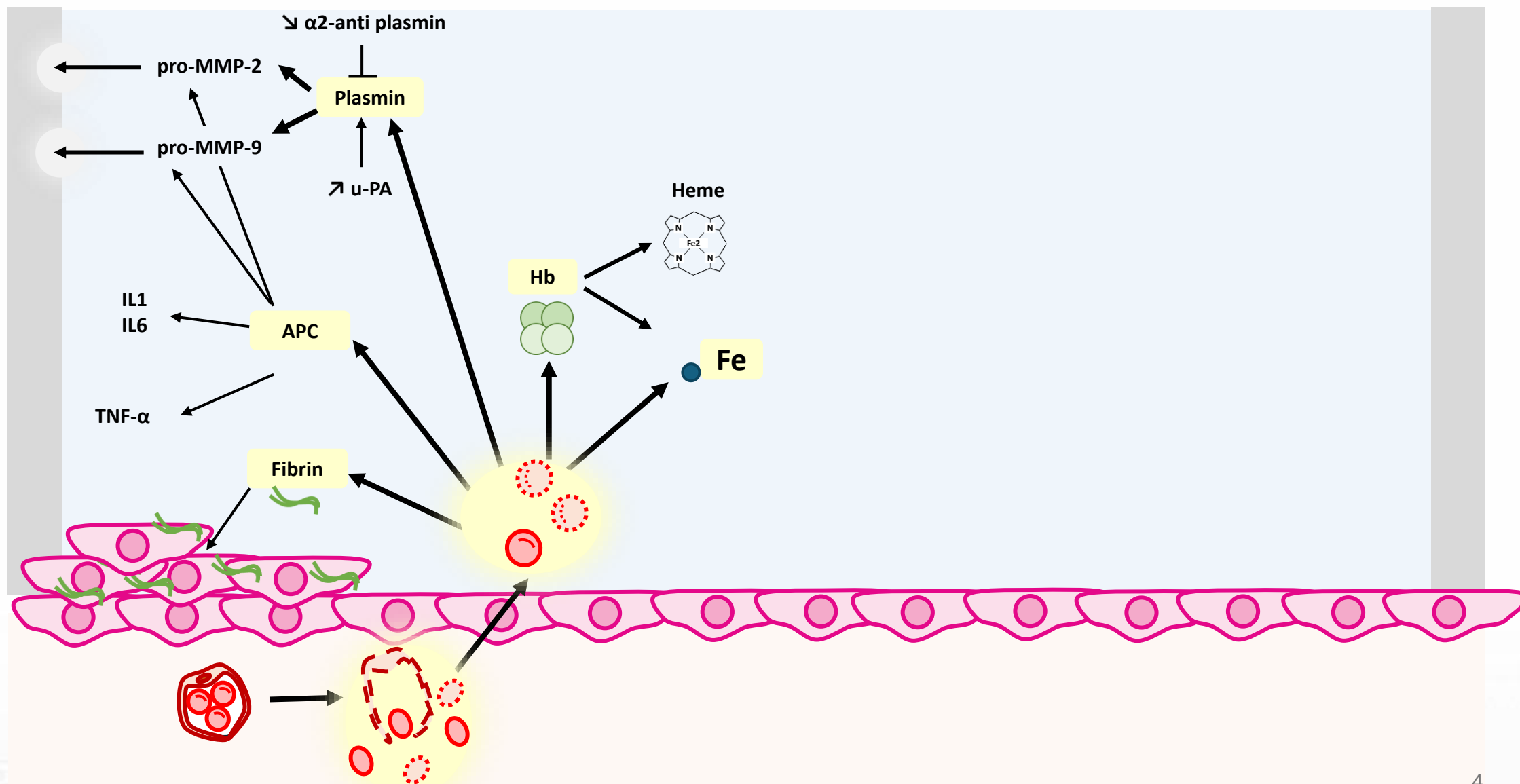


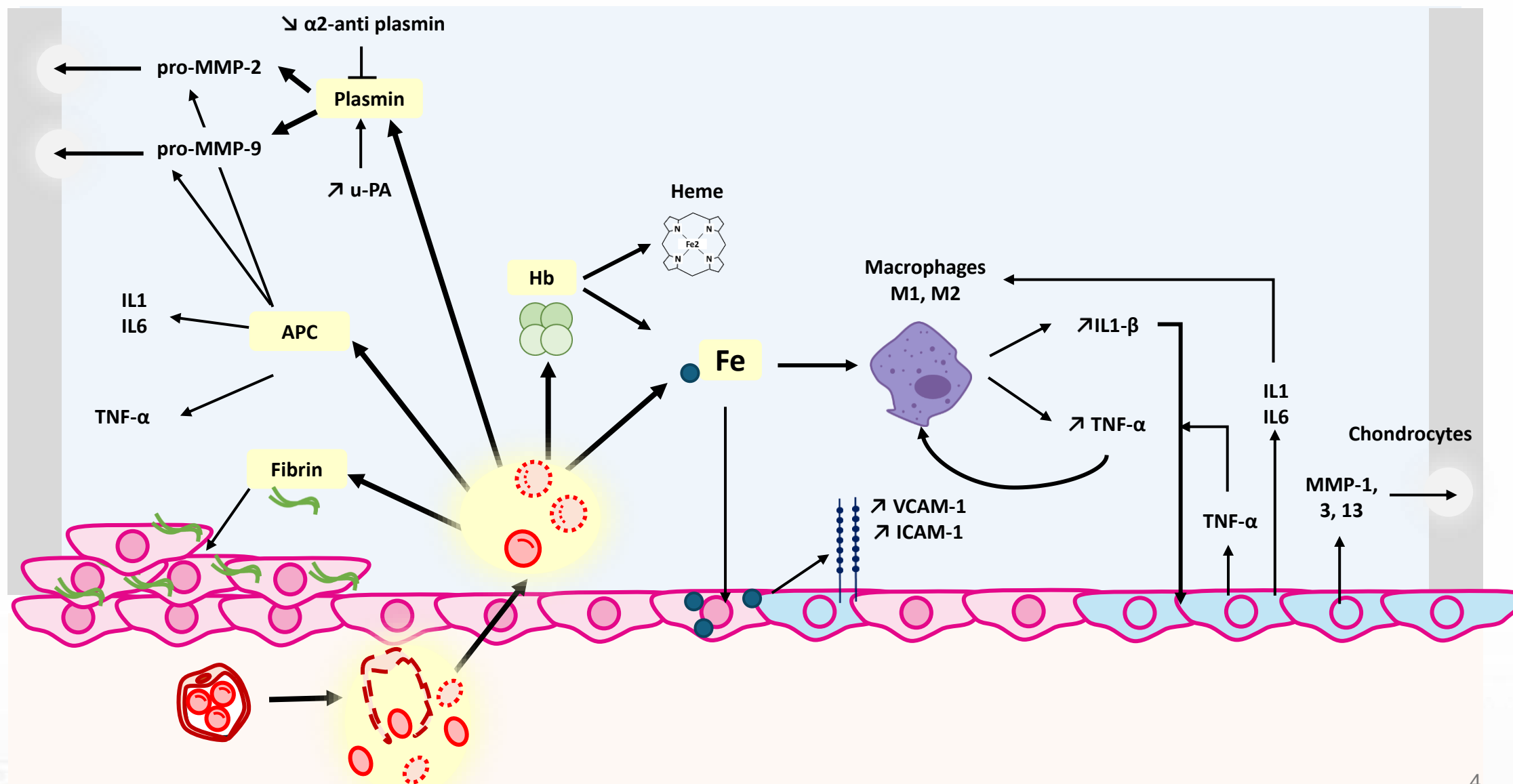
Synoviocyte

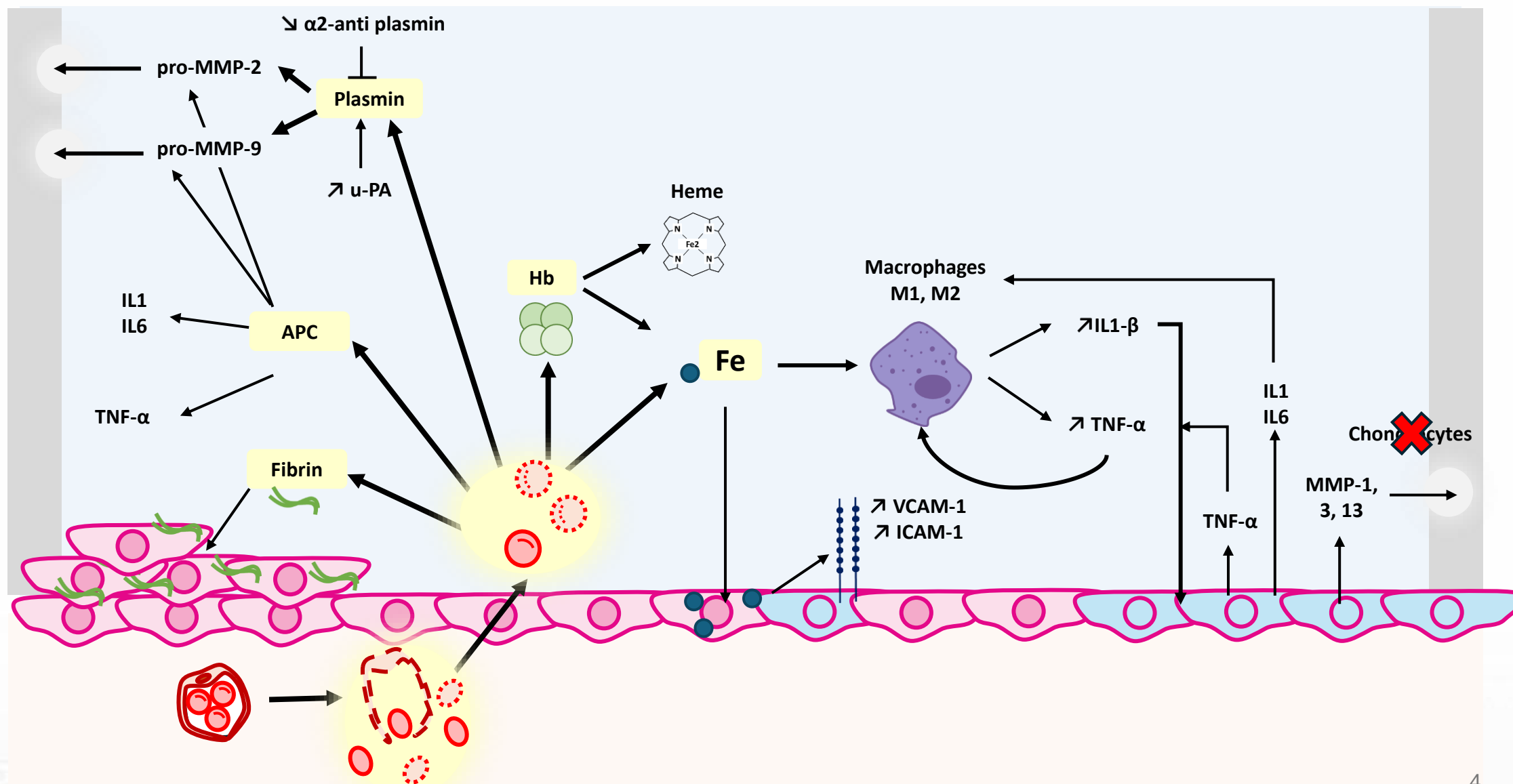


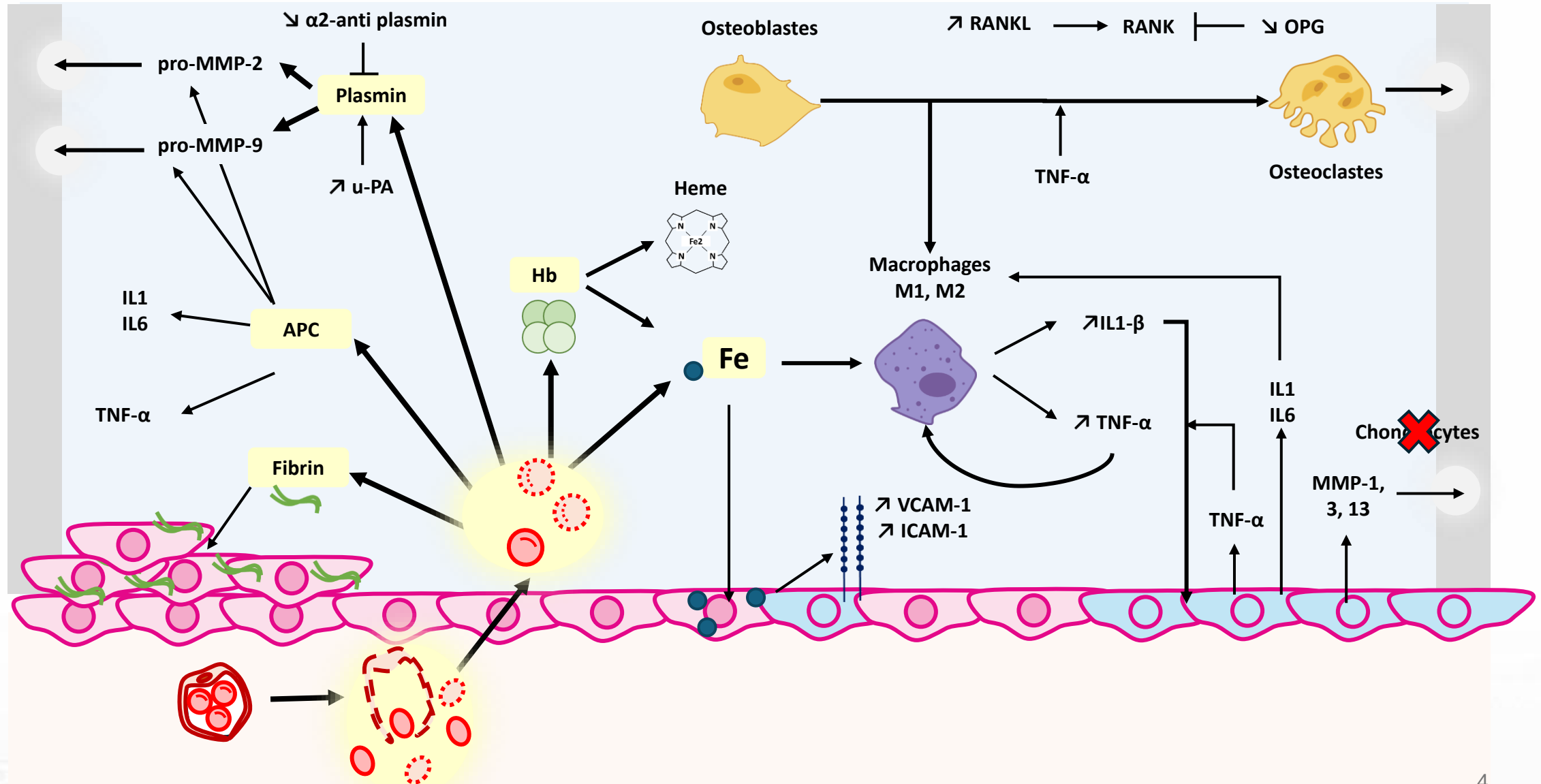


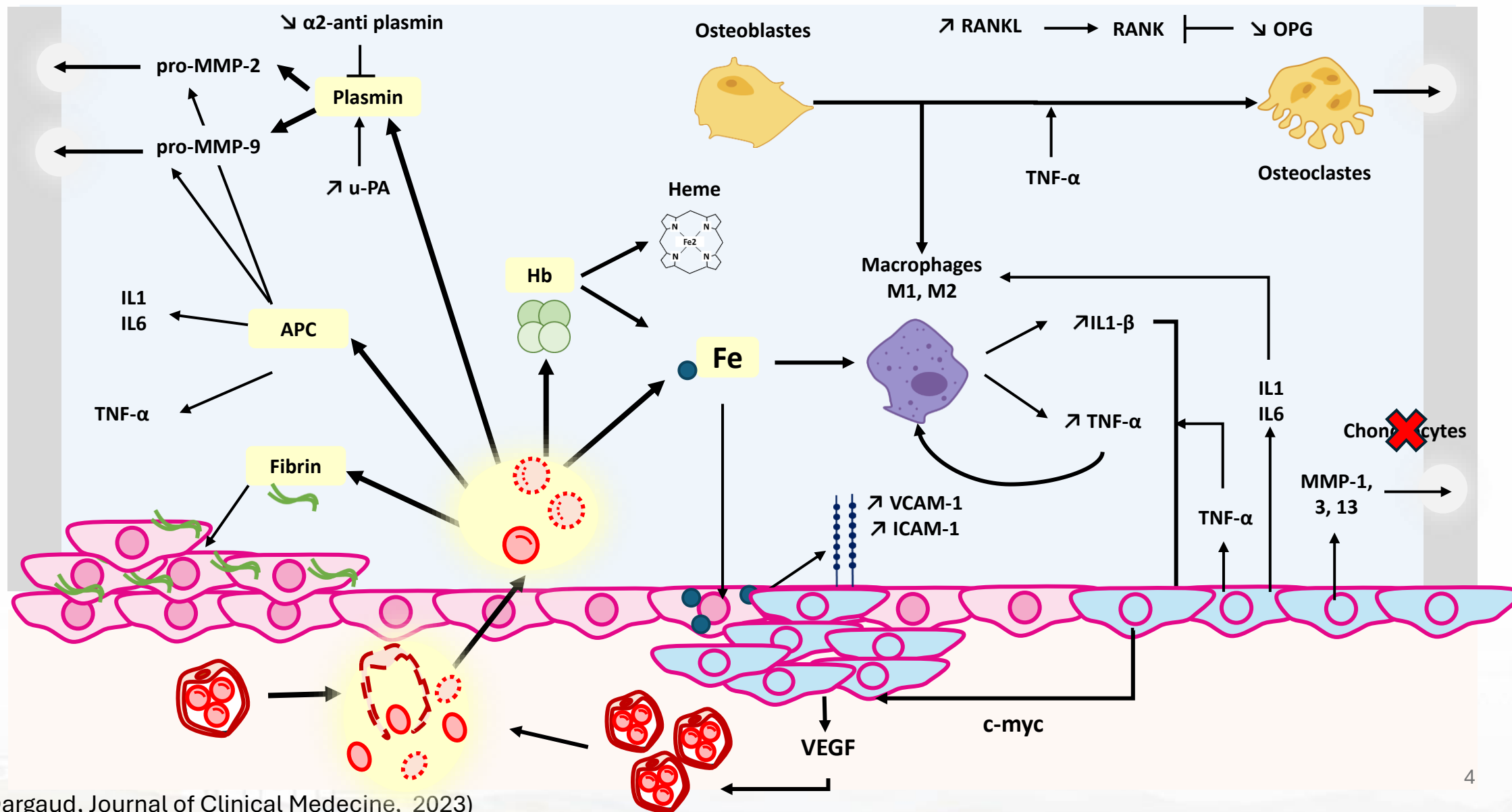














Arthropathie hémophilique (ArtH)



- Hémarthroses

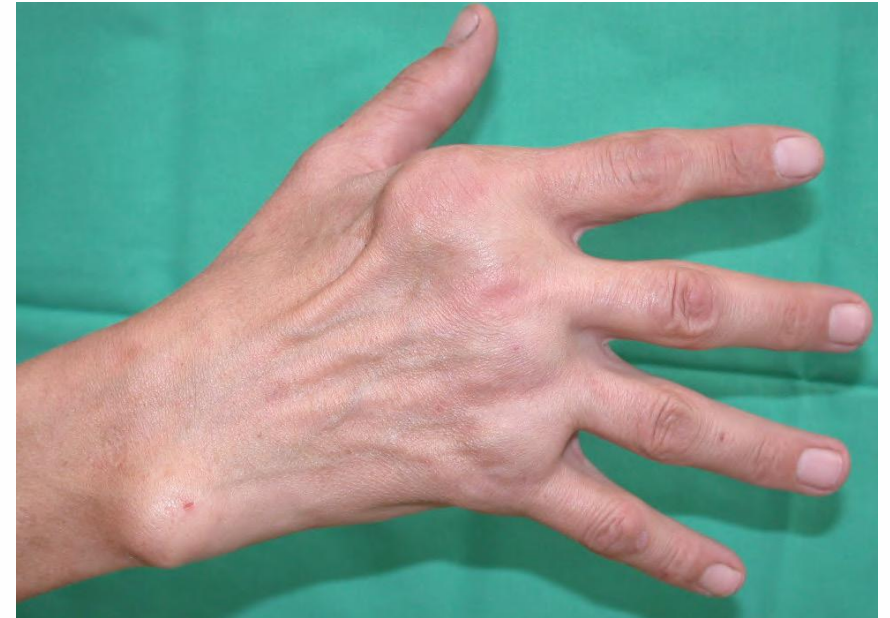


Arthropathie hémophilique (ArtH)



- Hémarthroses

Polyarthrite Rhumatoïde (PR)



- Maladie auto-immune



Arthropathie hémophilique (ArtH)



- Hémarthroses

- Similitude physiopathologique des mécanismes inflammatoires
- Similitude de lésions dégénératives

- **Traitements à visé hémostatique (FVIII/FIX)**

Polyarthrite Rhumatoïde (PR)



- Maladie auto-immune

- Traitement : agent immunomodulateur → **Méthotrexate**





Arthropathie hémophilique (ArtH)

Polyarthrite Rhumatoïde (PR)

Besoin d'un traitement pour l'arthropathie hémophilique



- Hémarthroses



- Maladie auto-immune

- Similitude physiopathologique des mécanismes inflammatoires
- Similitude de lésions dégénératives

- **Traitements à visé hémostatique (FVIII/FIX)**

- Traitement : agent immunomodulateur → **Méthotrexate**

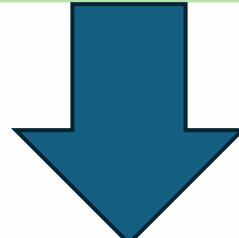




Arthropathie hémophilique (ArtH)

Polyarthrite Rhumatoïde (PR)

Besoin d'un traitement pour l'arthropathie hémophilique



Utilisation du MTX comme adjuvant au FIX

- Hémarthroses

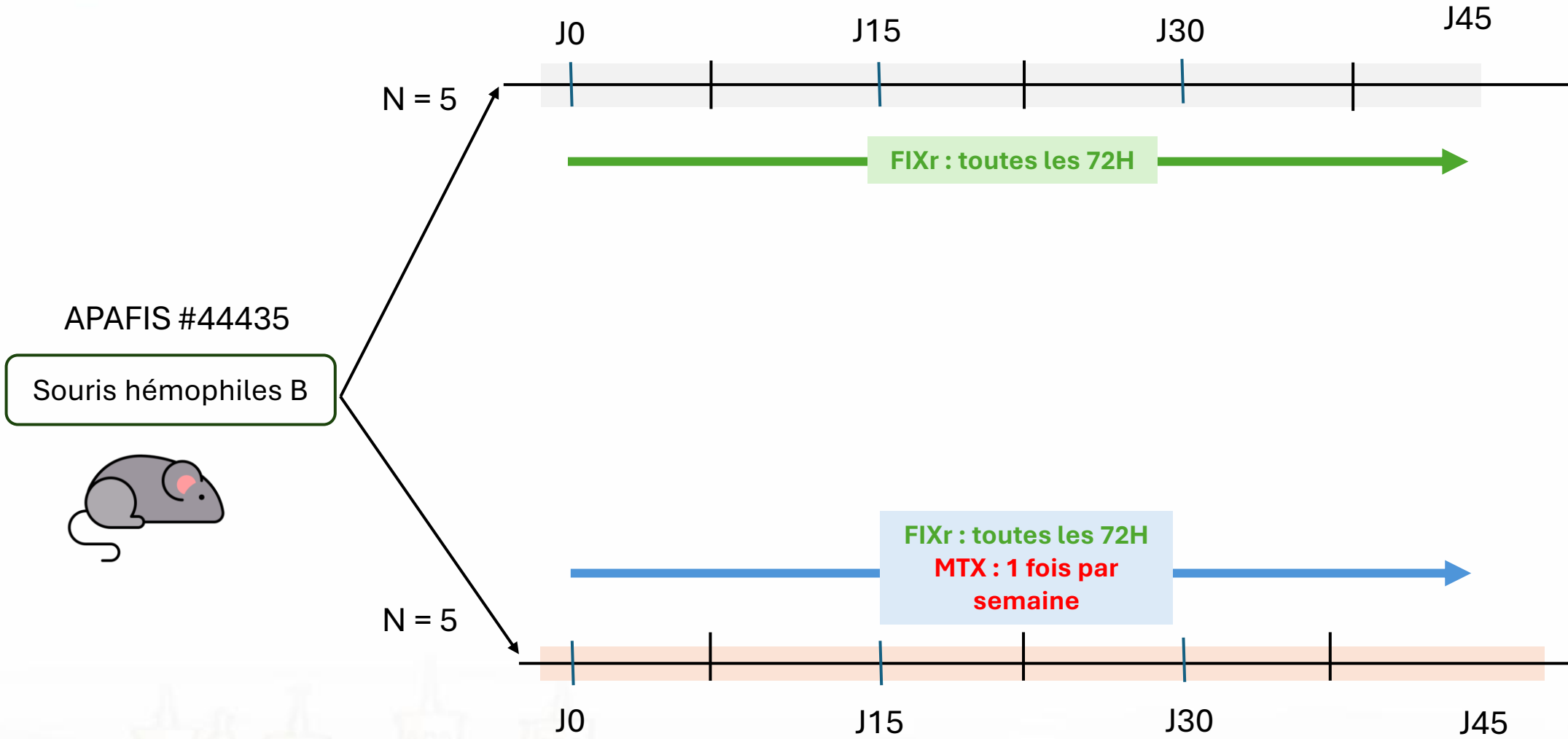
- Maladie auto-immune

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- **Traitements à visé hémostatique (FVIII/FIX)**

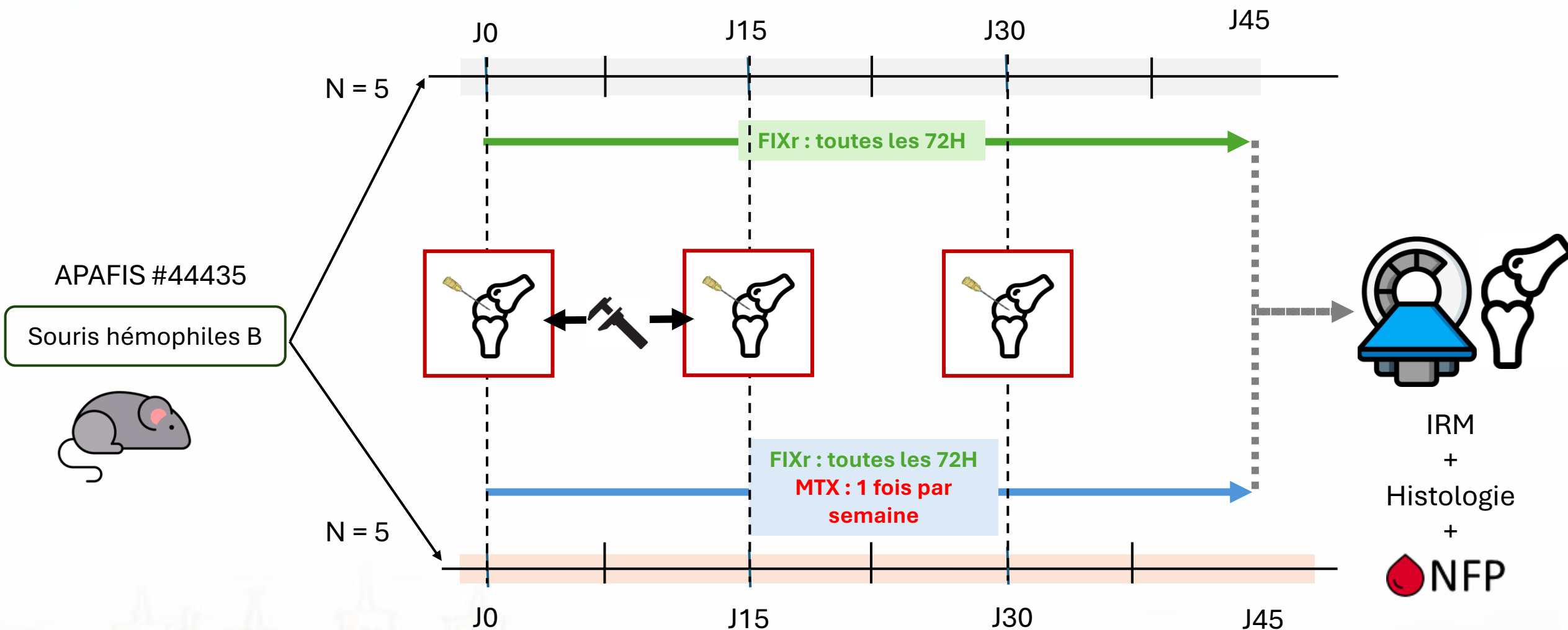
- Traitement : agent immunomodulateur → **Méthotrexate**





MTX : 20 mg/Kg/semaine

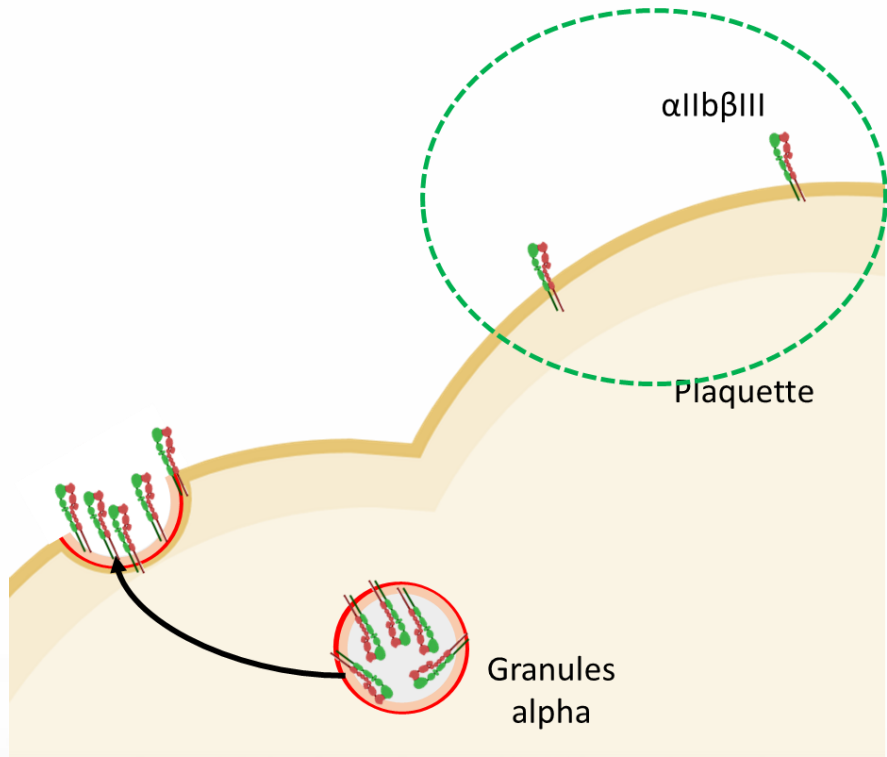
FIXr-FP : 50 UI/Kg



MTX : 20 mg/Kg/semaine

FIXr-FP : 50 UI/Kg

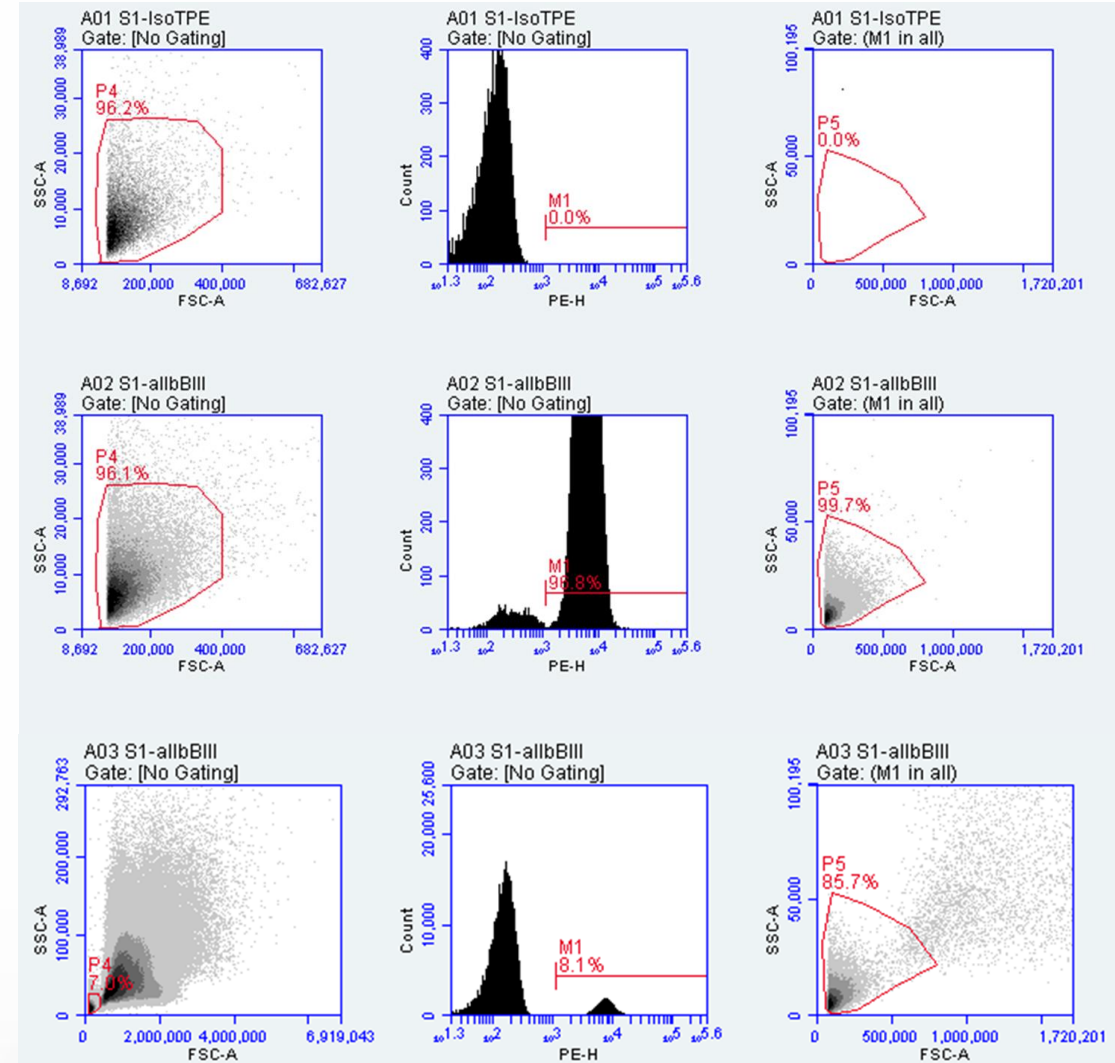
MTX : peut induire une baisse des plaquettes par suppression médullaire → **thrombopénie = surrisque hémorragique !**



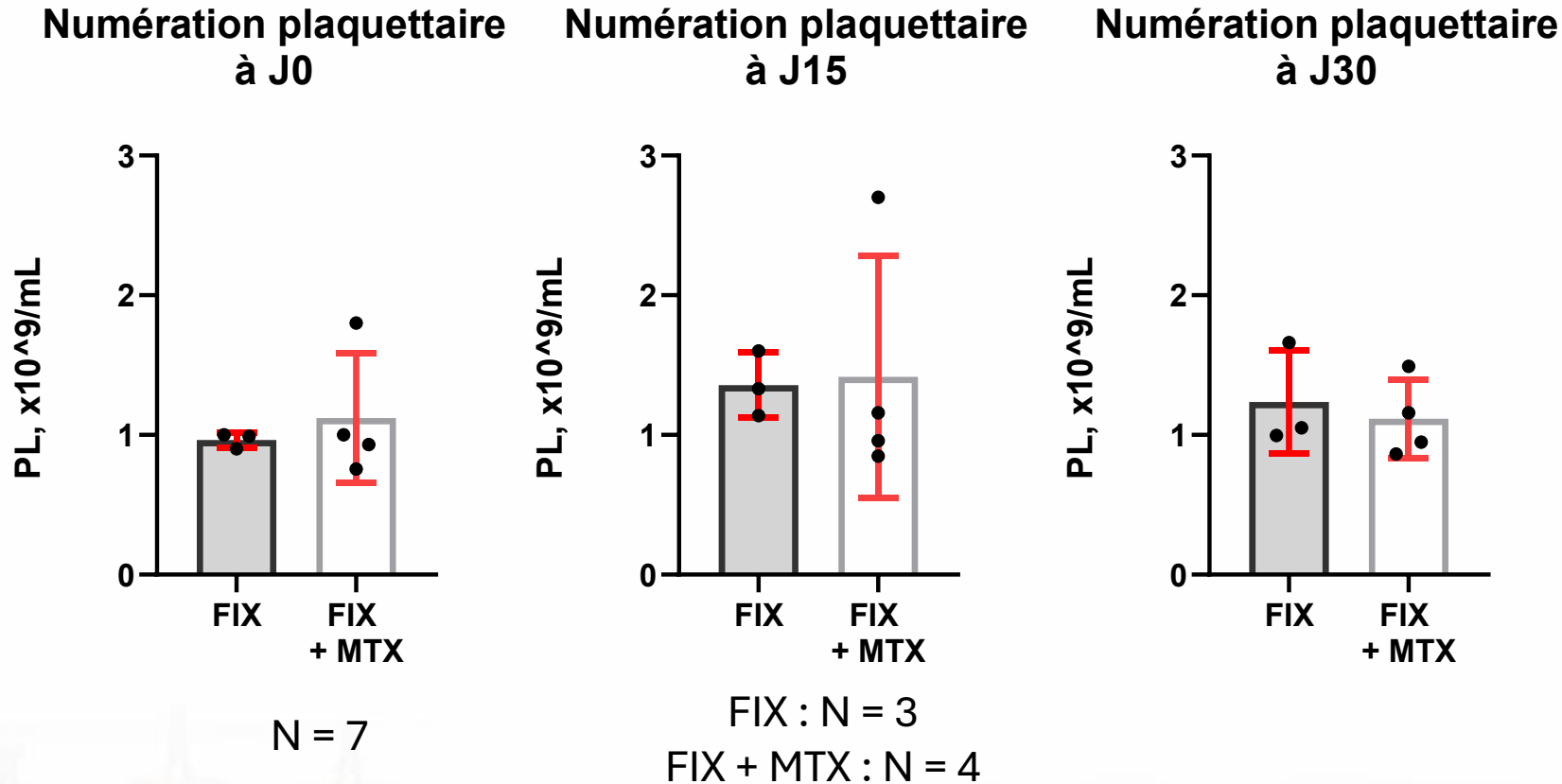
Non-immun
+ sang total

Ac anti- α IIb β III
+ PRP

Ac anti- α IIb β III
+ sang total



MTX : peut induire une baisse des plaquettes par suppression médullaire → **thrombopénie = surrisque hémorragique !**



Pas de thrombopénie
→ Pas de surrisque hémorragique induit par le MTX

Genou sain



Genou arthropathique non traité



Genou FIX

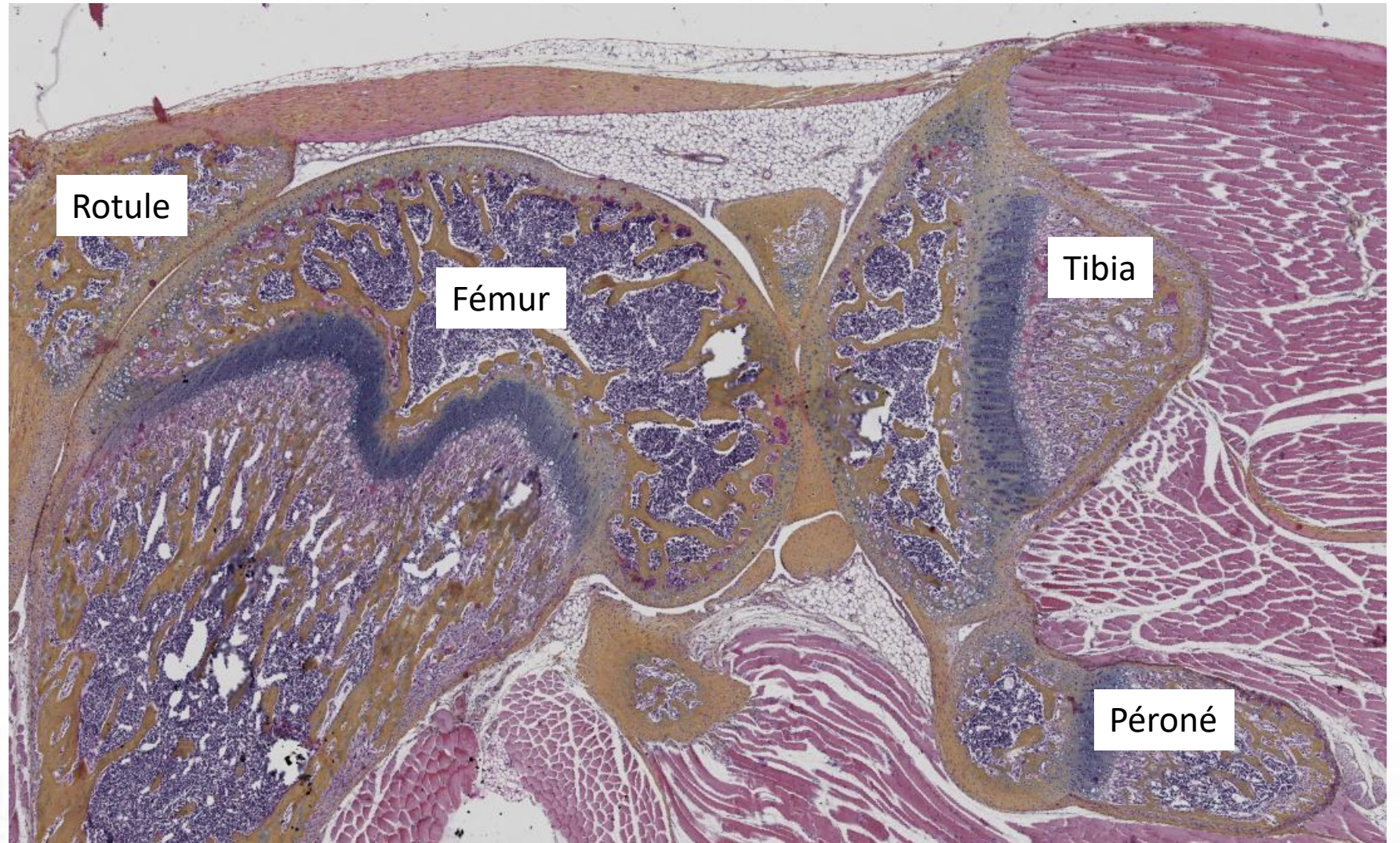
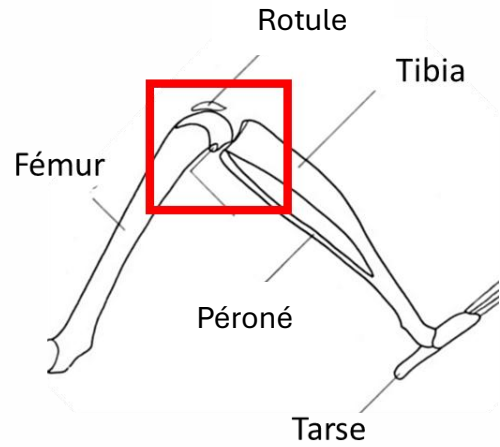


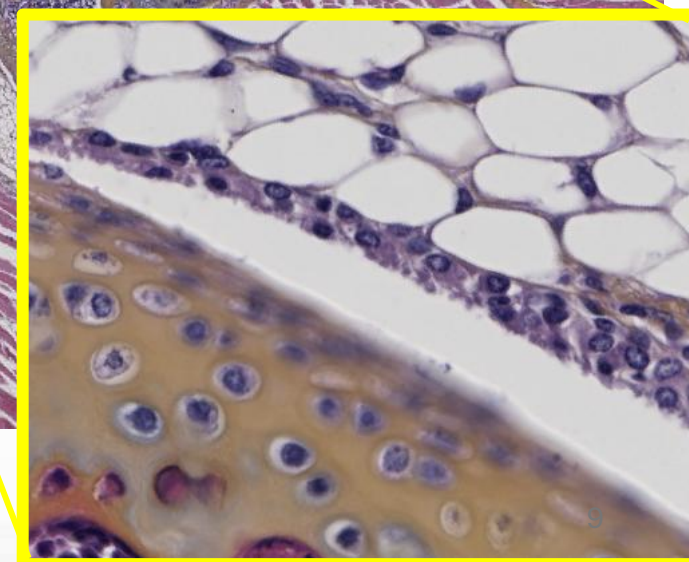
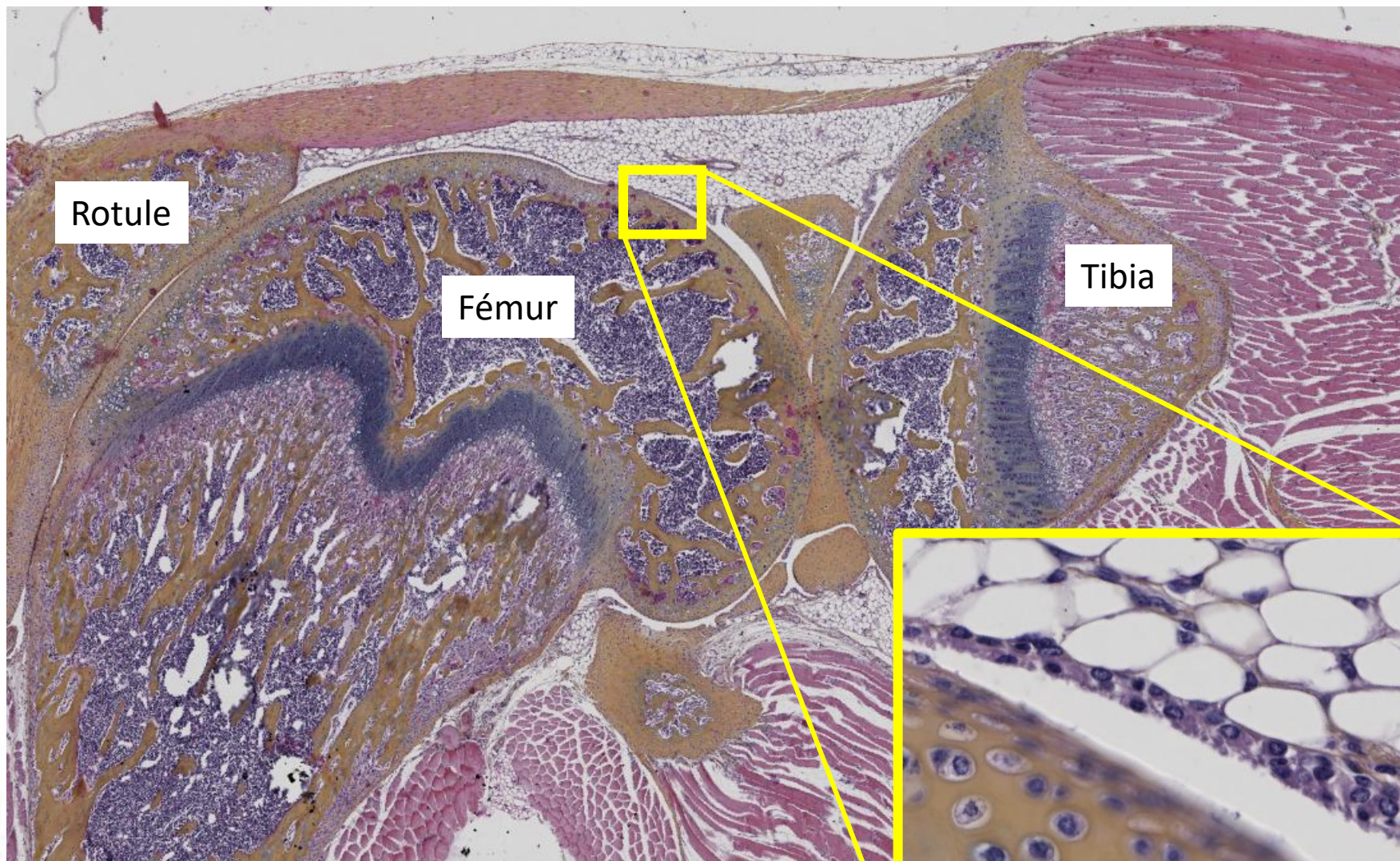
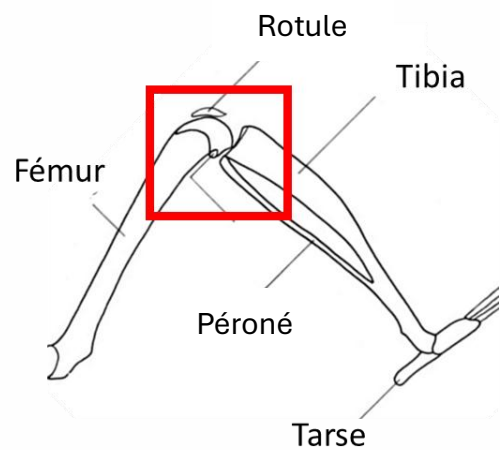
Genou FIX + MTX



Ponction

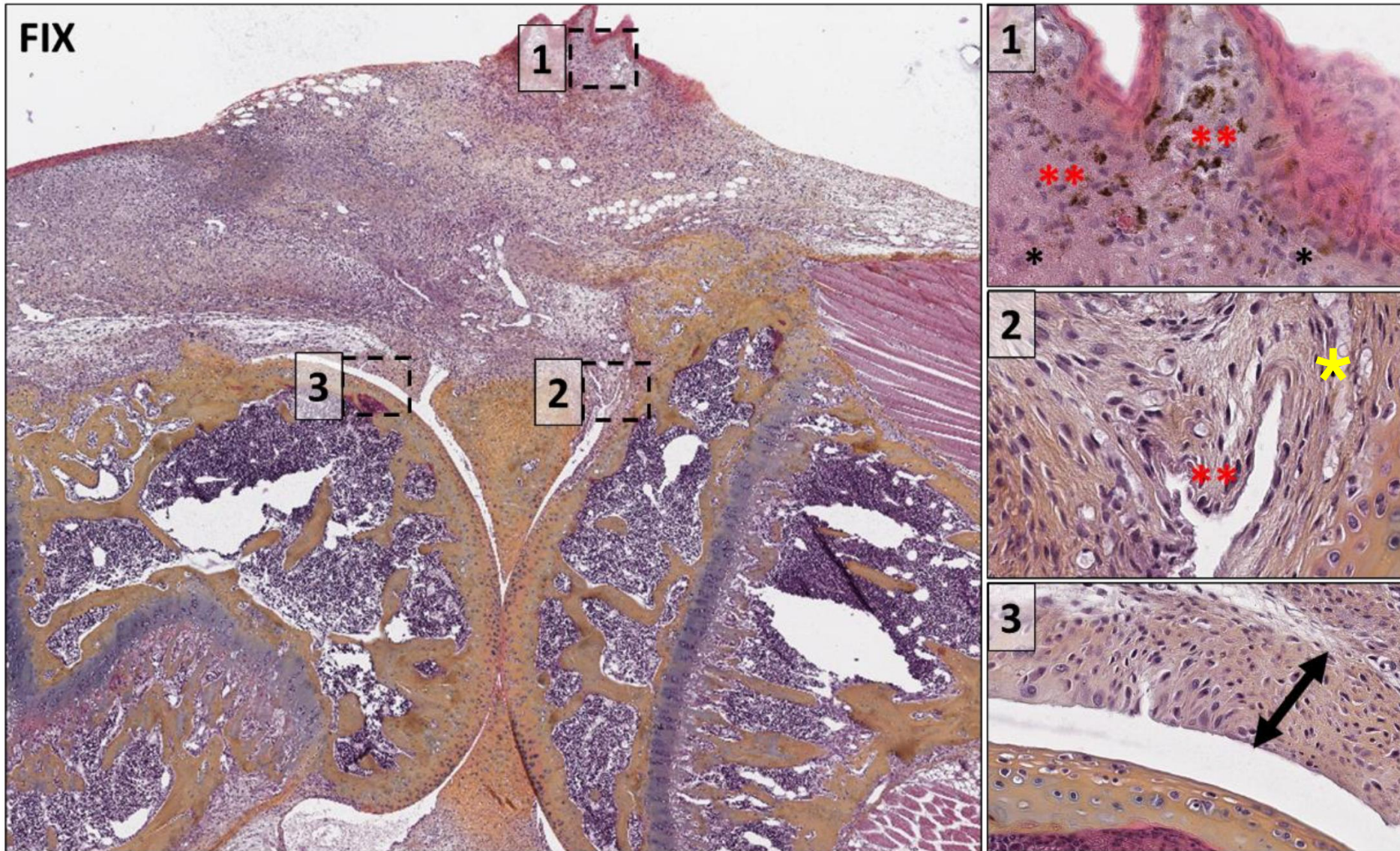
Diminution de l'hypersignal (présence de sang) dans le genou traité par FIX + MTX





Score histologique selon Valentino

Caractéristiques	Score	Description
Hyperplasie synoviale	0	Normal, moins de 4 couches
	1	4 à 5 couches
	2	6 à 7 couches
	3	Plus de 7 couches
Hémosidérine	0	Absent
	1	Présent
Sang	0	Absent
	1	Présent
Villosité	0	Absent
	1	Présent
Erosion du cartilage	0	Absent
	1	Présent

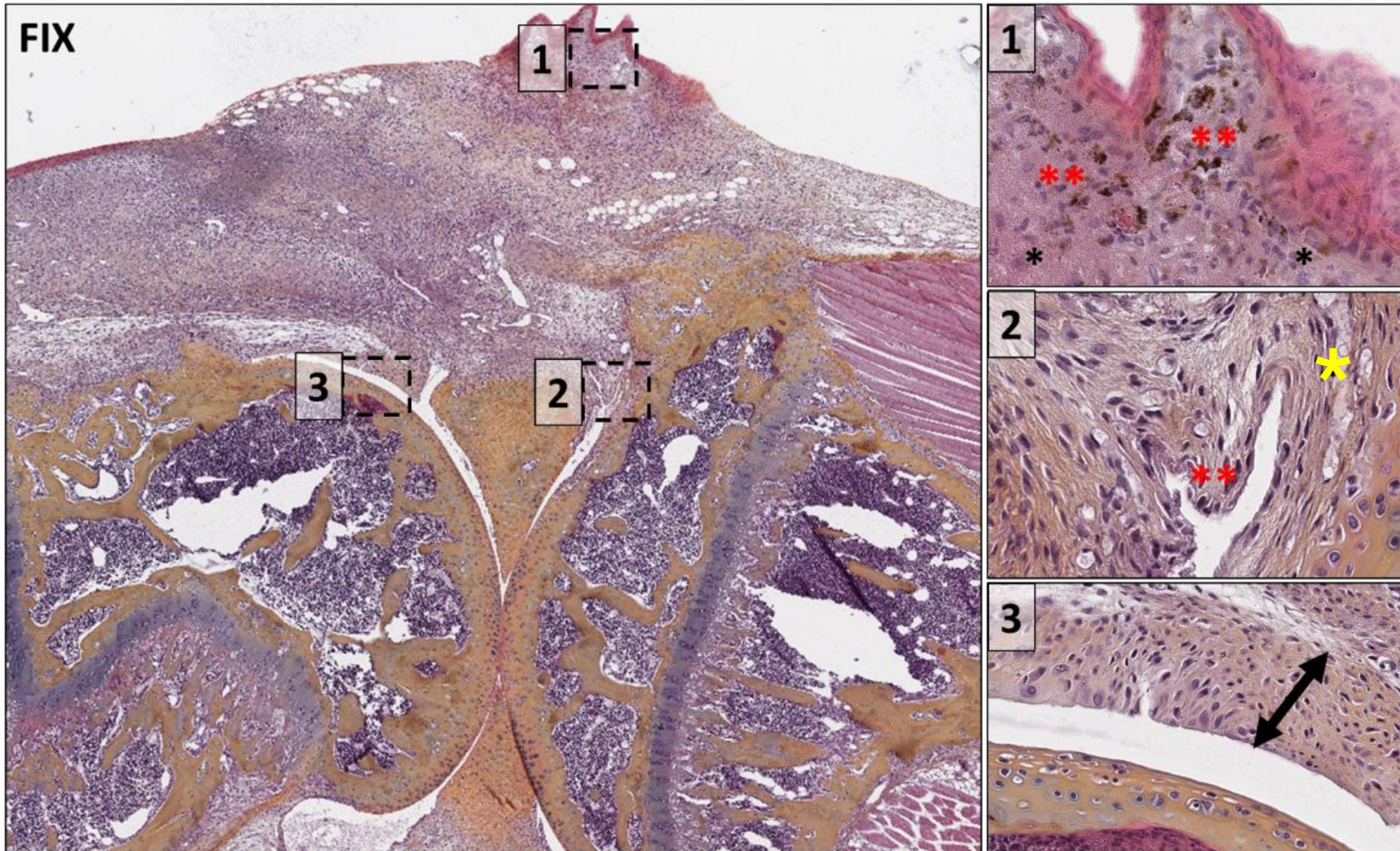


1: ** Présence d'hemosidérine

2: ** Expansion de cellules
* villosités et de vaisseaux

3: ↔ Epaississement de la
synovial

Coloration HES



1: ** Présence d'hémosidérine

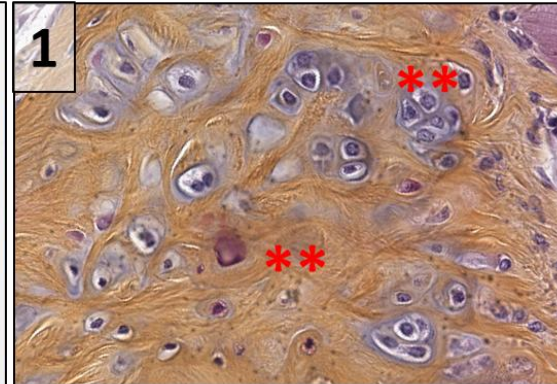
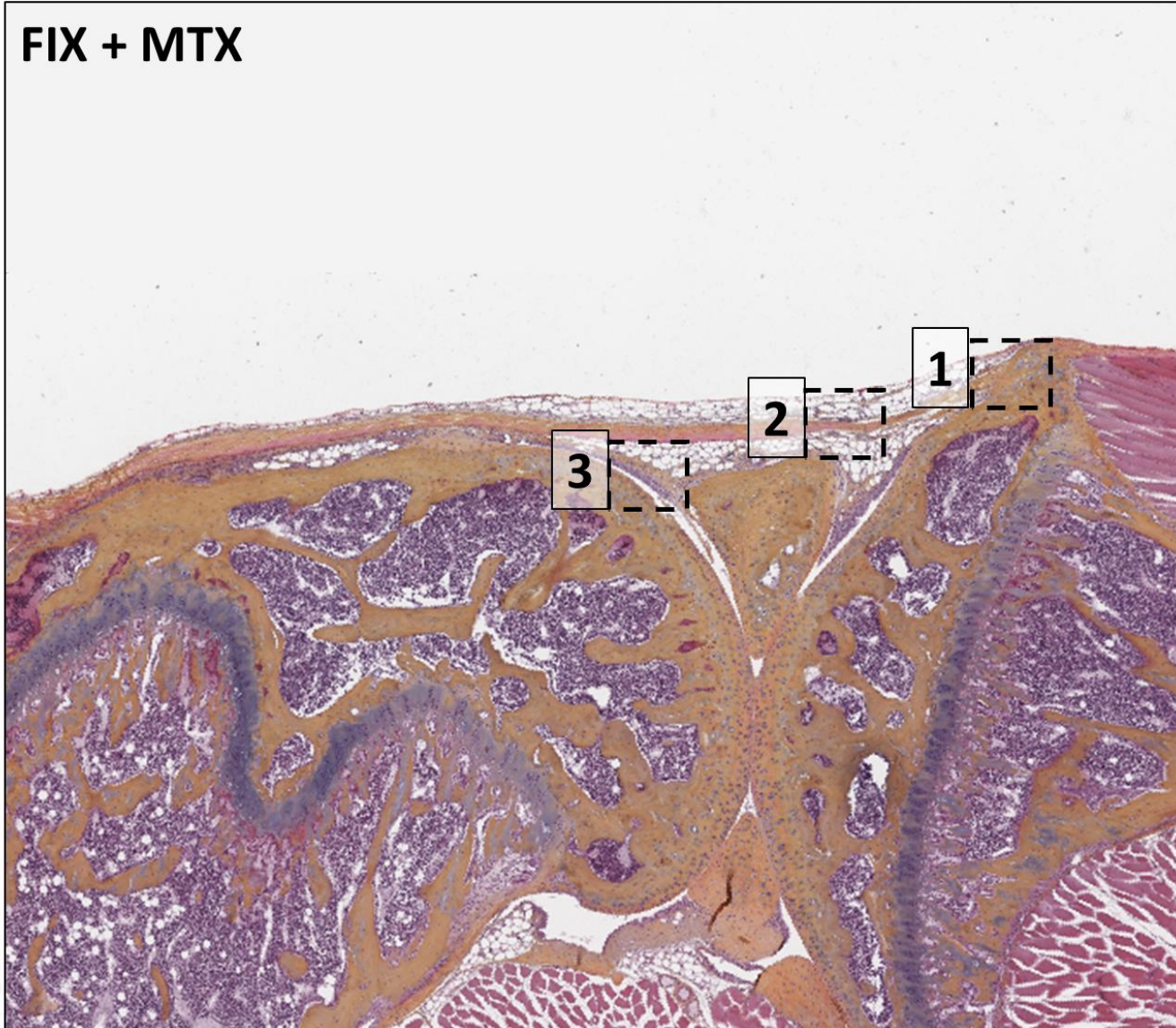
2: ** Expansion de cellules
* villosités et de vaisseaux

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synovial

= Synovite

Coloration HES

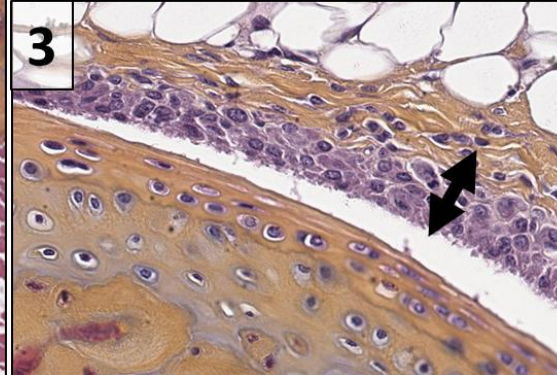
FIX + MTX



1: ** Inclusion d'hémosidérine



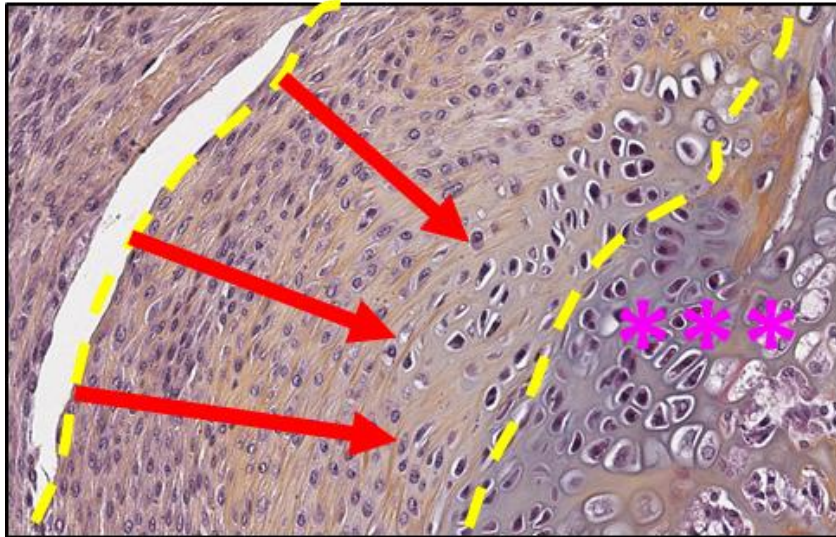
2: * Absence d'infiltration



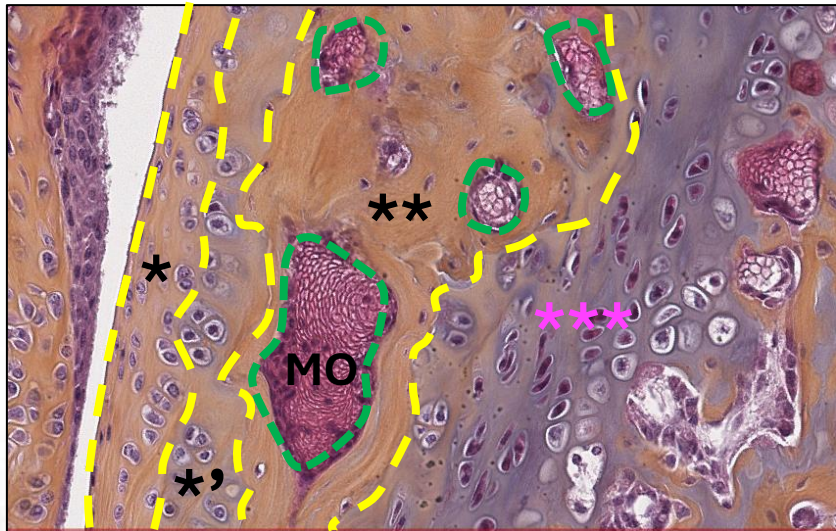
3: ↔ Epaississement de la synovial

Coloration HES

FIX



FIX + MTX



Coloration HES



Moelle osseuse



Zone d'infiltration du cartilage et de l'os atteint

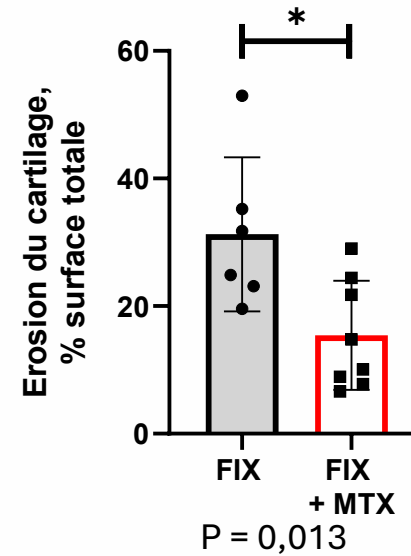
* Cartilage de conjugaison

*' Cartilage calcifié

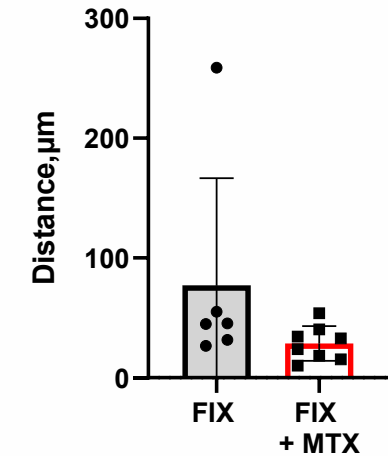
** Os sous chondral

*** Cartilage de croissance

Erosion du cartilage



Invasion oostocartilagineuse de la synoviale

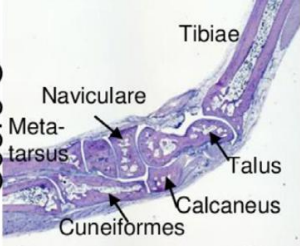
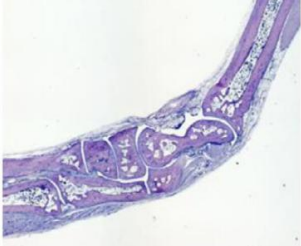
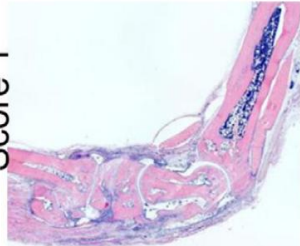
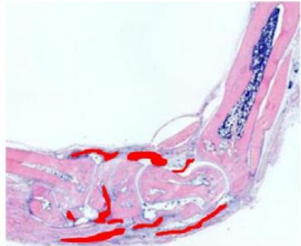
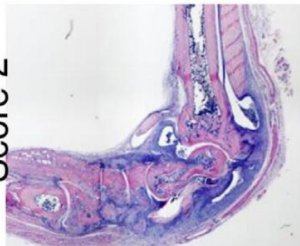
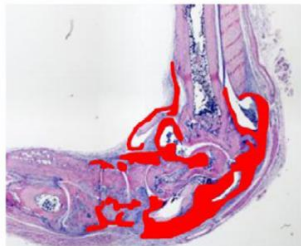
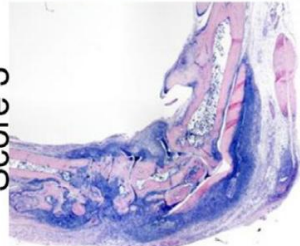
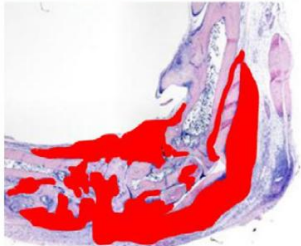
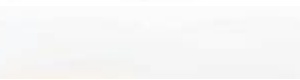
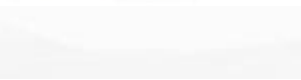


Le MTX en préventif permet de limiter l'invasion synoviale

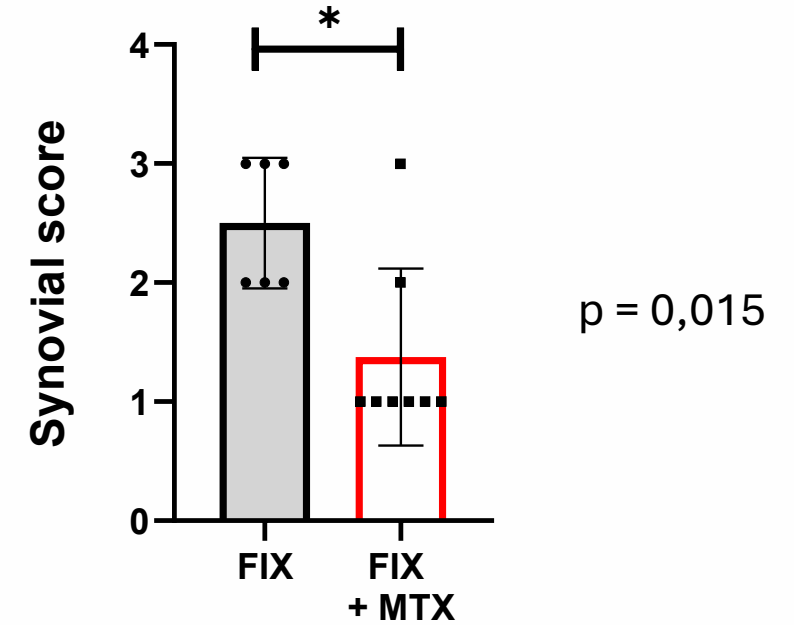
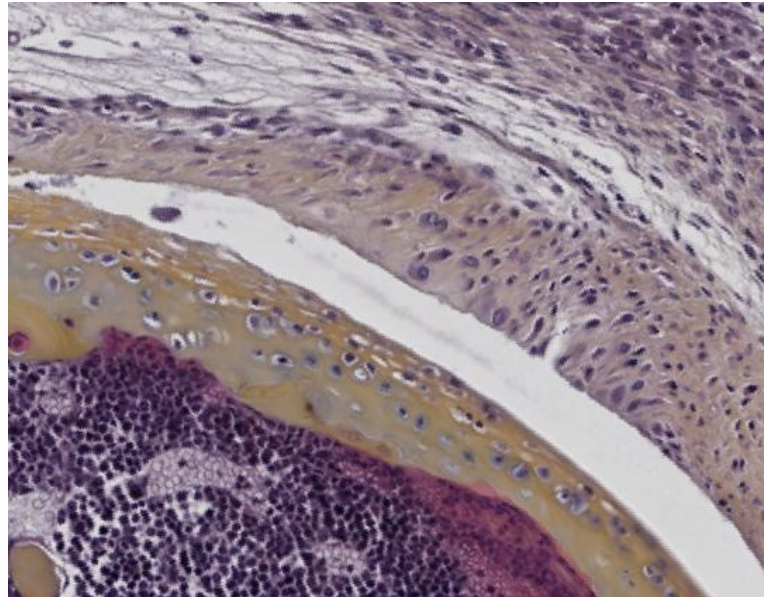
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	1	Présent
Sang	0	Absent
	1	Présent
Villosité	0	Absent
	1	Présent
Erosion du cartilage	0	Absent
	1	Présent

Score histologique selon les recommandations SMASH

Score 0			SYNOVIAL INFLAMMATION (CIA, CAIA) healthy, 1-2 cell layers of synovial membrane, no inflammatory infiltrates
			
Score 1			3-5 layered synovial membranes, mild cellular infiltrates into synovium and exudate in joint cavity, low cell density
			
Score 2			Multi-layered synovial cell membranes, enhanced cellular infiltrates and increased cell density throughout the joints
Score 3			Maximal expanded inflammation filling all joint cavities, hyperplastic synovial tissue, high cell density

FIX



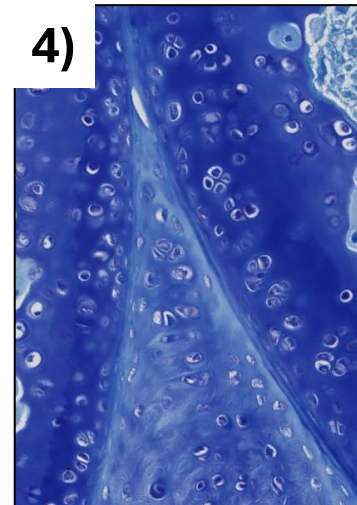
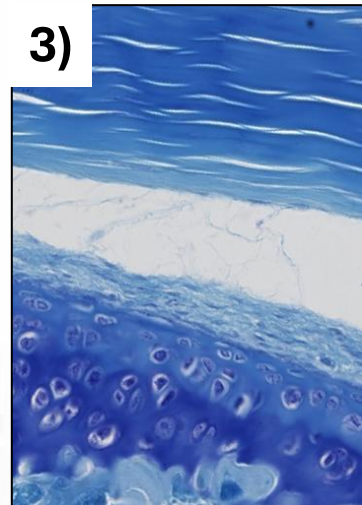
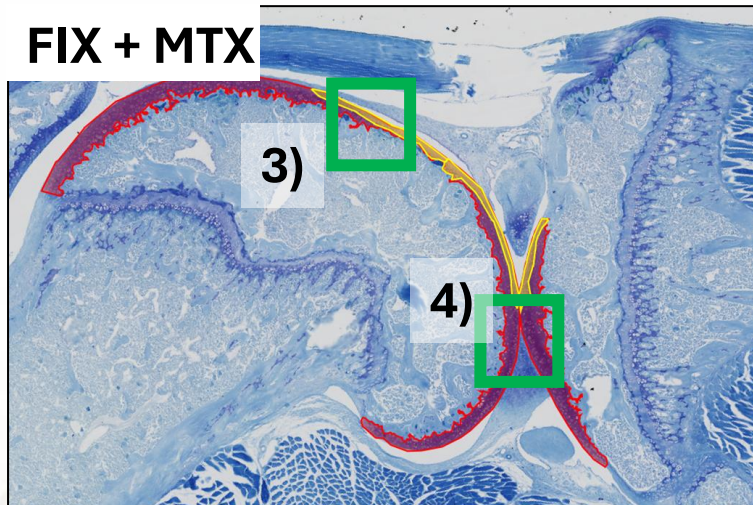
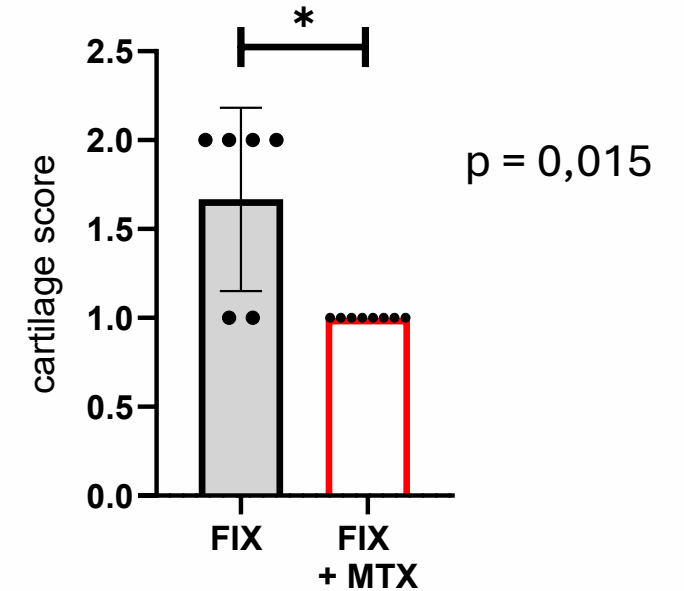
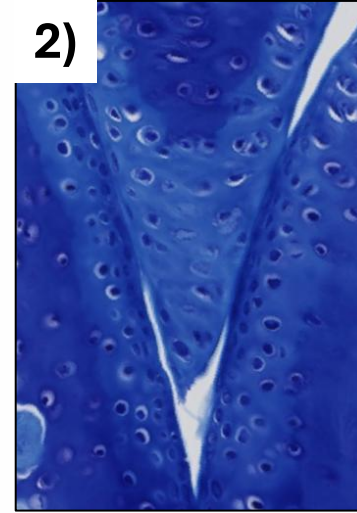
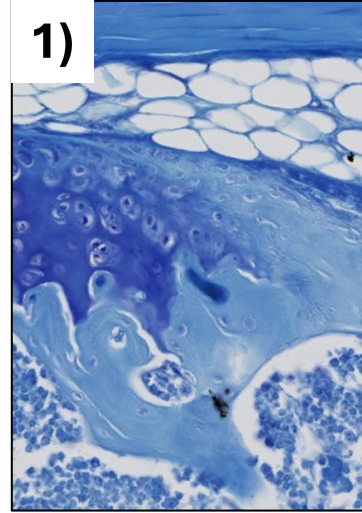
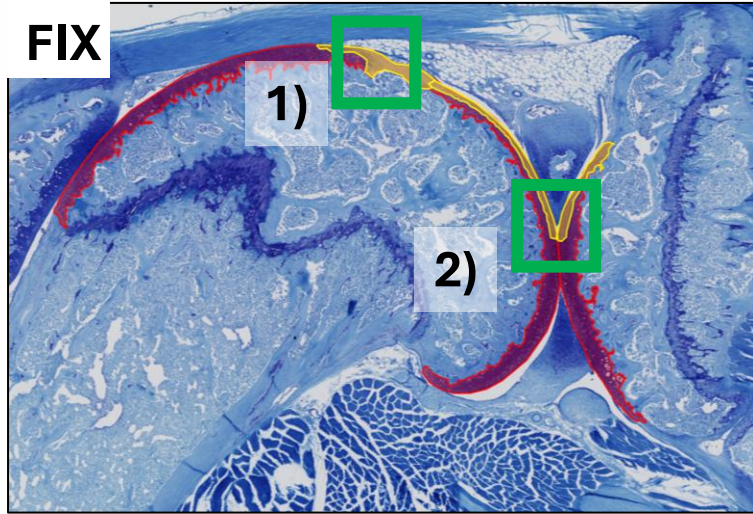
Score 0 _ couches cellules : 1-2 couches

Score 1 _ couches cellules : 3-5 couches

Score 2 _ couches cellules : multi prolifération

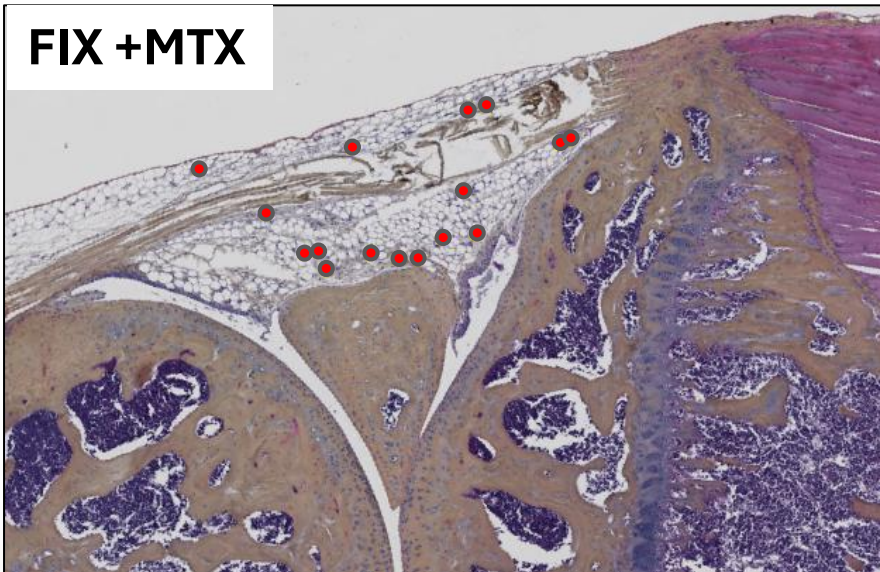
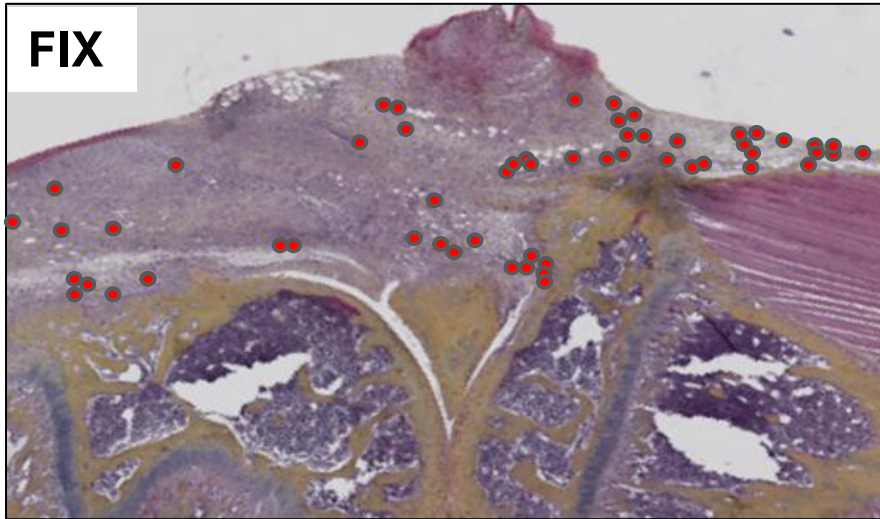
Score 3 _ couches cellules : Hyper prolifération

Le MTX préventif réduit le développement de la synovite

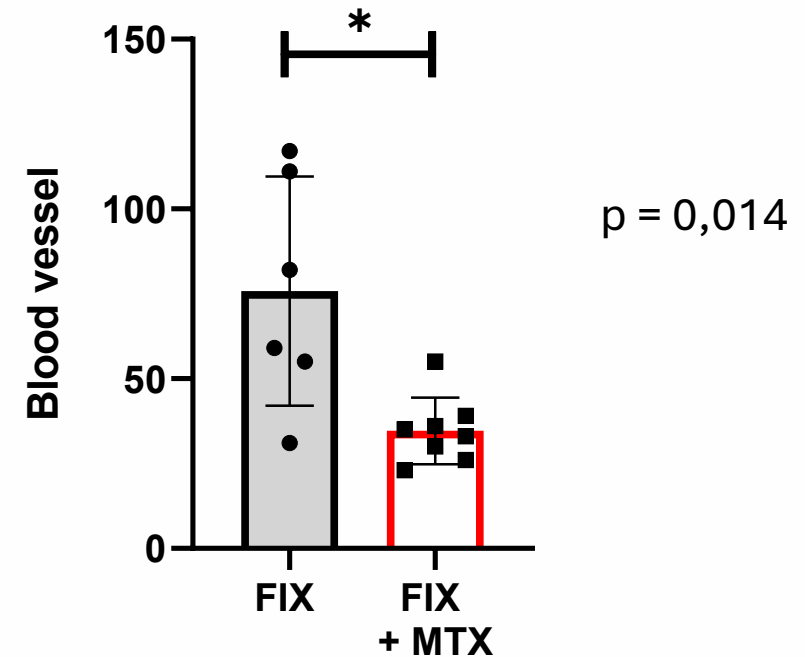


0 _ intact : bleu homogène
1 _ perte coloration ≤ 1/3
2 _ perte modérée 1/3 - 2/3
3 _ perte complète > 2/3

Le MTX préventif limite l'érosion du cartilage

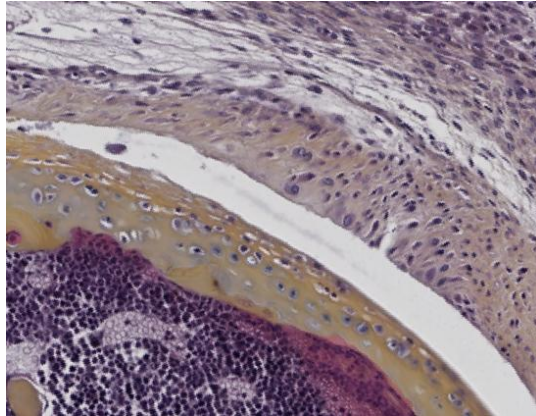


Coloration HES

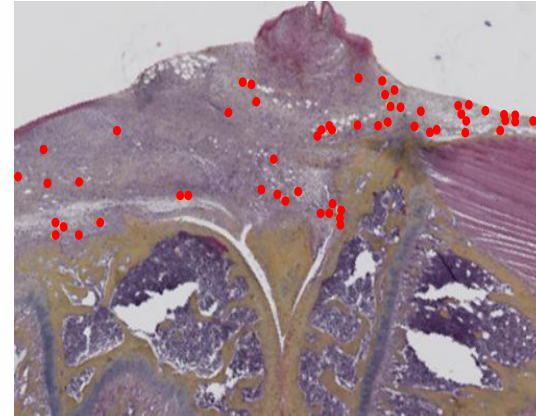


Le MTX préventif limite la
néovascularisation

FIX

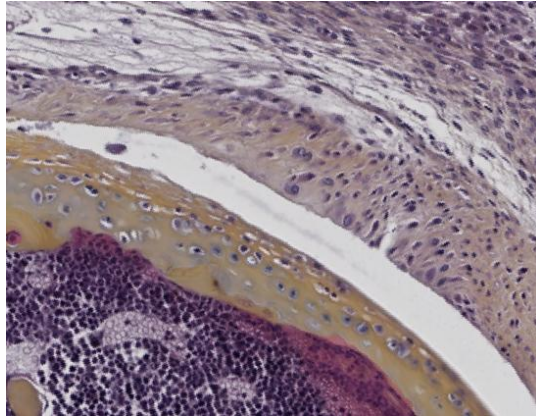


Hyperplasie synoviale

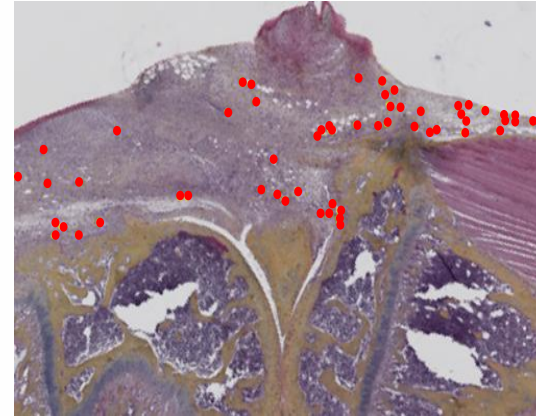


Hyper vascularisation

FIX

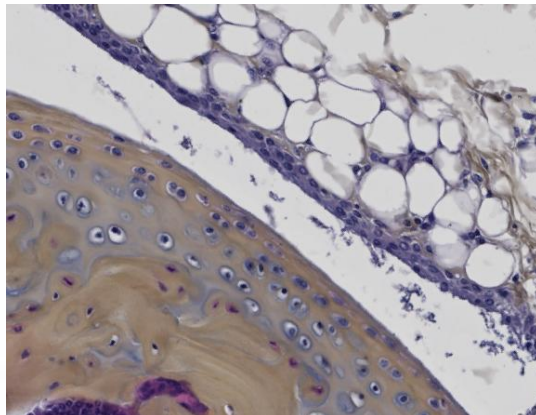


Hyperplasie synoviale

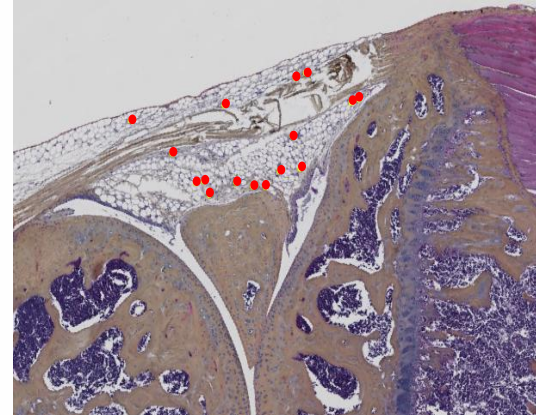


Hyper vascularisation

FIX + MTX



Hyperplasie synoviale



Hyper vascularisation

Effets bénéfiques du MTX préventif sur la synovite chez le modèle murin avec arthropathie

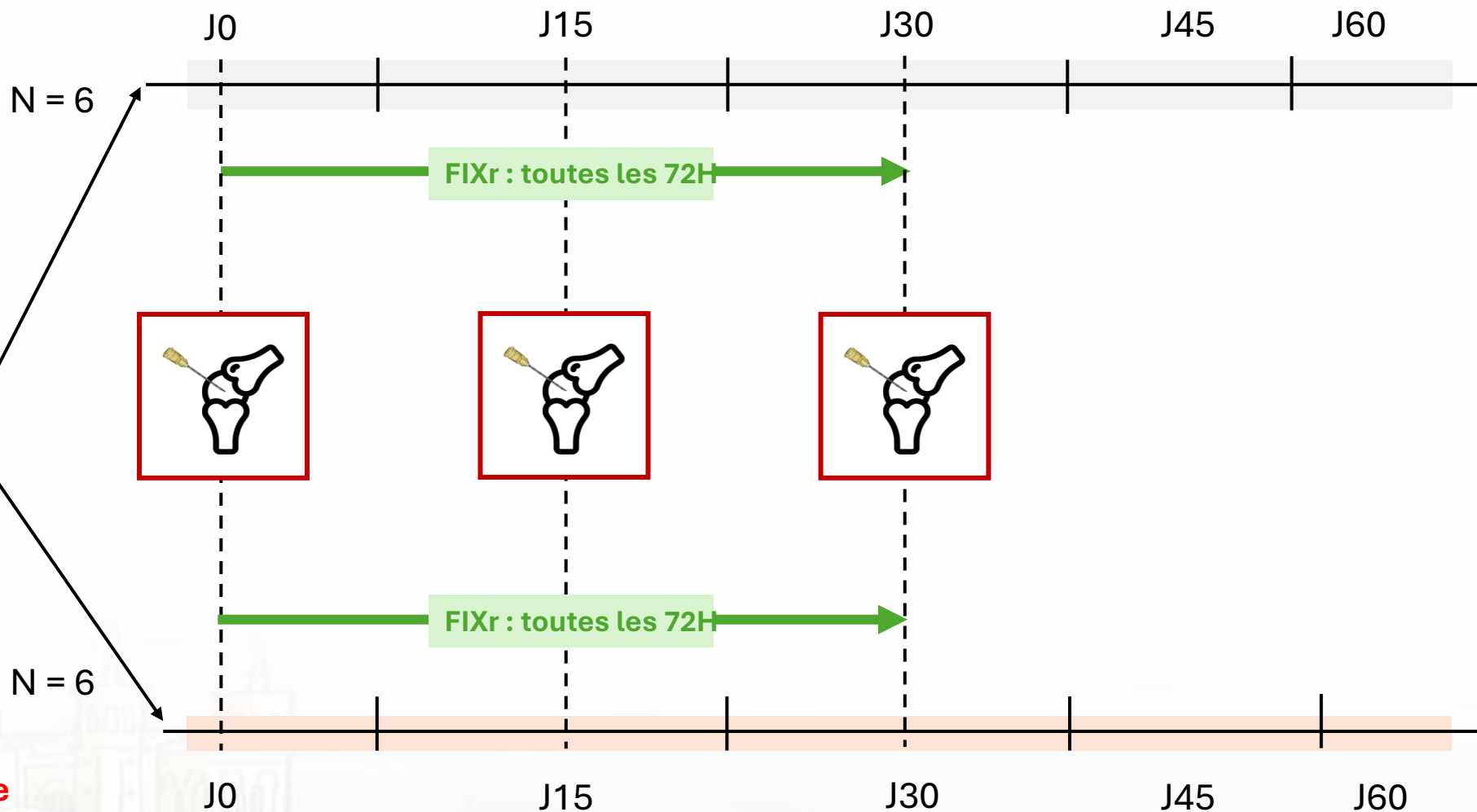
MTX curatif 

APAFIS #52507

MTX curatif



APAFIS #52507



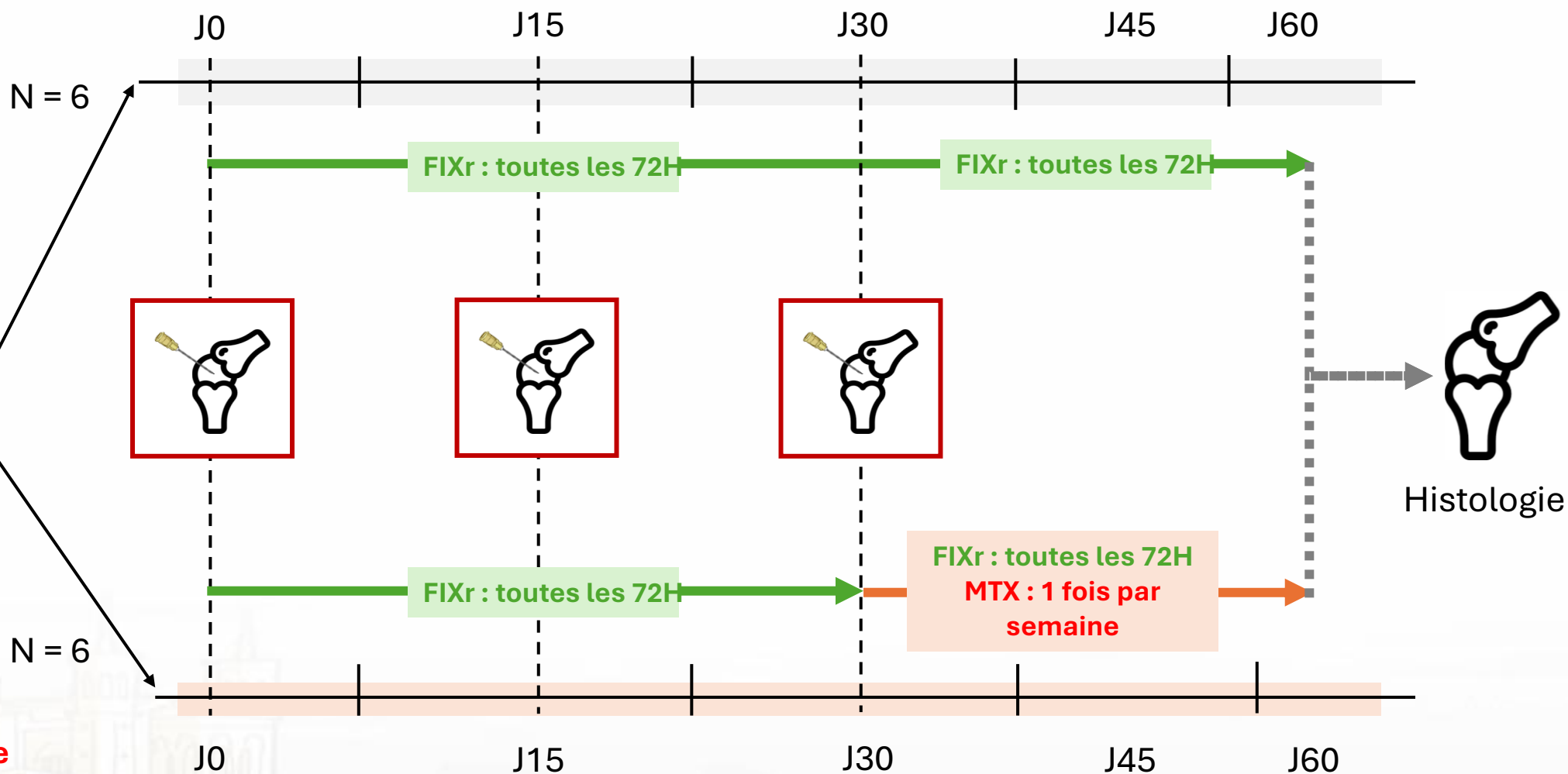
MTX : 20 mg/Kg/semaine

FIXr-FP : 50 UI/Kg

MTX curatif



APAFIS #52507





SFTH
SOCIÉTÉ FRANÇAISE
DE THROMBOSE
ET D'HÉMOSTASE

CONGRÈS de LA SOCIÉTÉ FRANÇAISE de THROMBOSE ET d'HÉMOSTASE

1^{ER}-3 OCTOBRE 2025



Université Claude Bernard Lyon 1



UR-4609

Hémostase & Thrombose



Bruno Chapuis

**ALECS : animalerie Lyon 1 Est
Conventionnel et SPF ALECS**

Angèle Chamousset

cermap
imagerie du vivant

Dr. Radu Bolbos



Dr. Martine Melin

octapharma

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