Plaques carotidiennes vulnérables : où en sont les études ?

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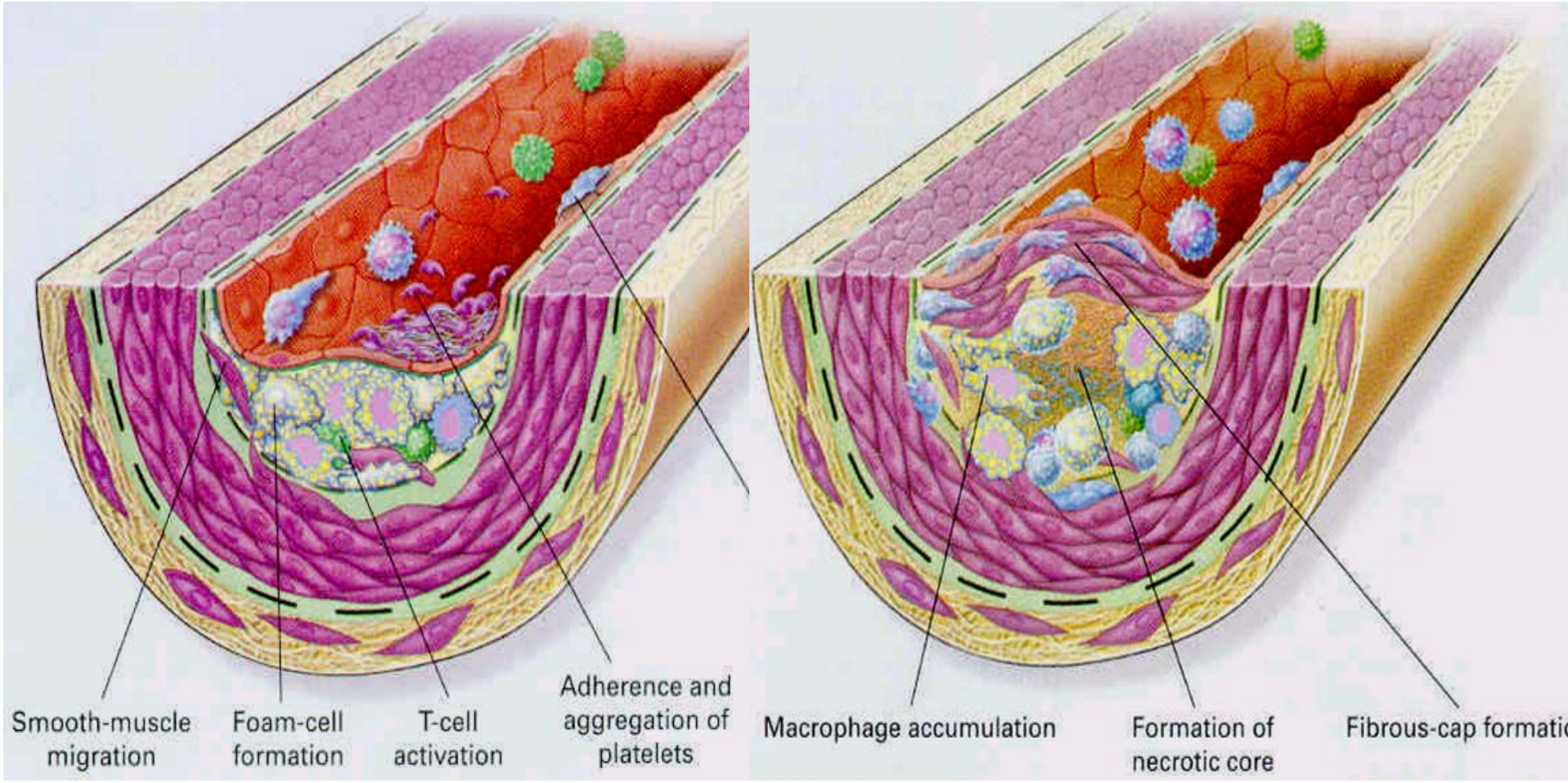
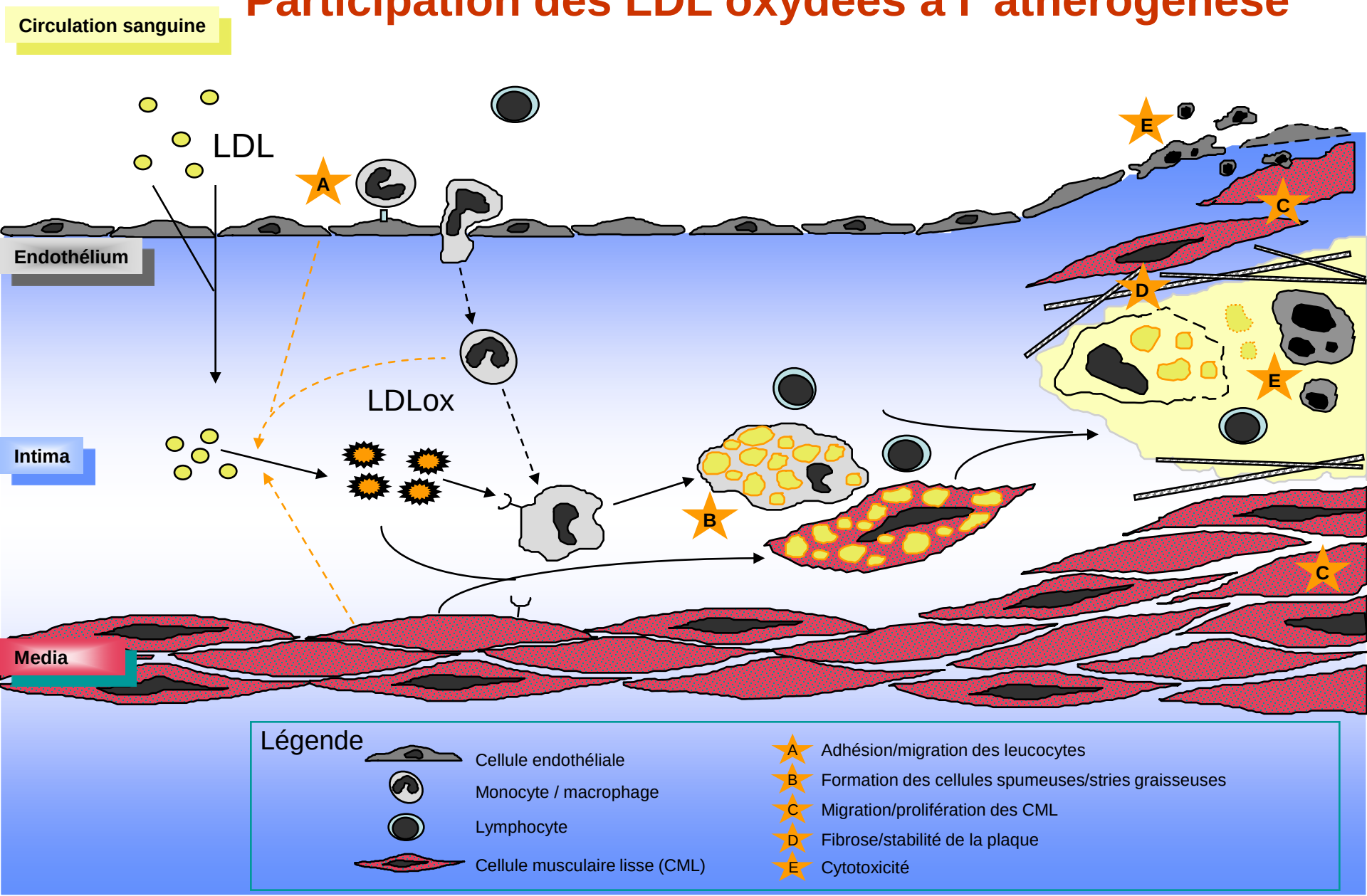
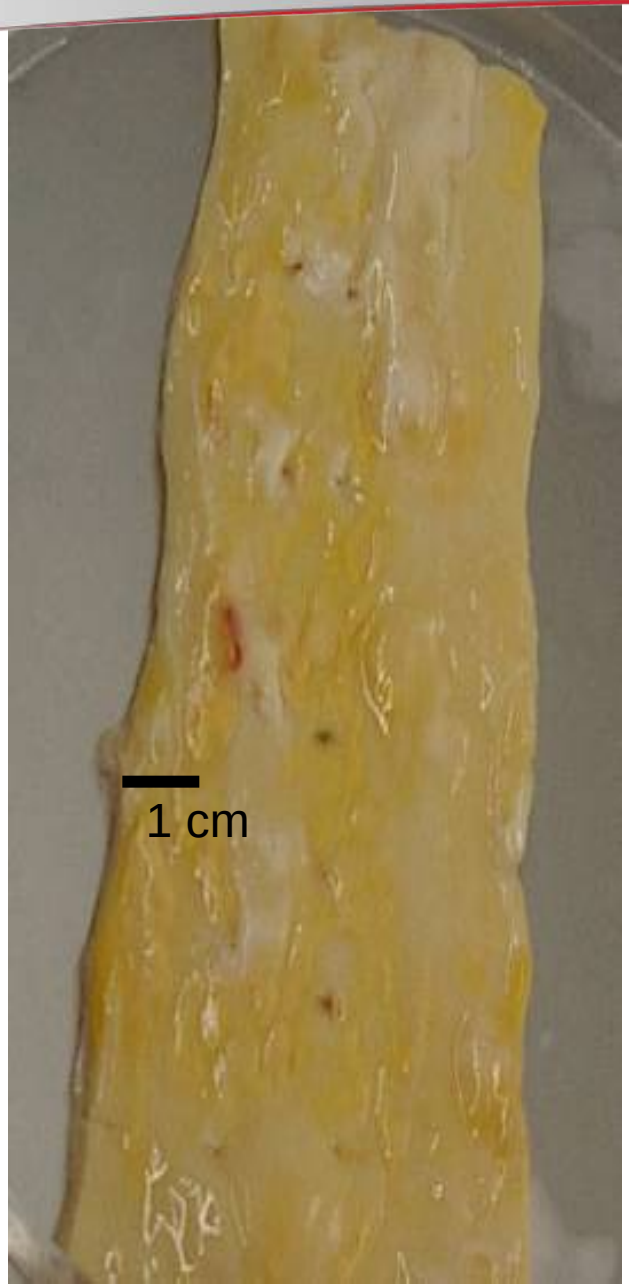
Athérosclérose



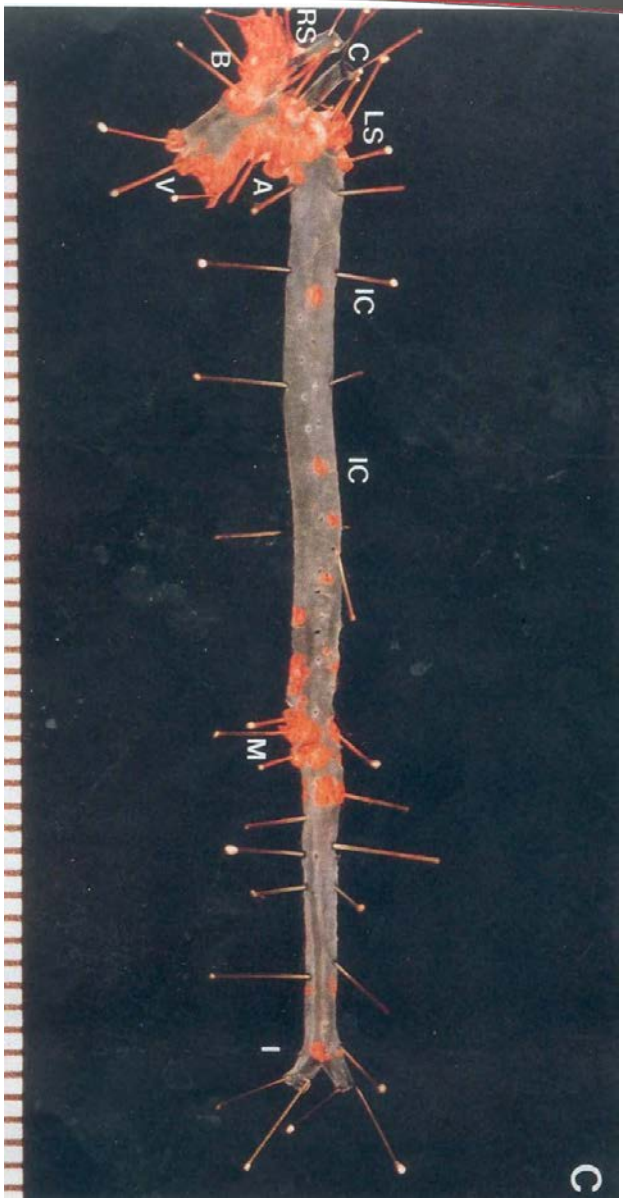
Atherosclerosis: an inflammatory disease. Ross R. NEJM 1999

Participation des LDL oxydées à l'athérogenèse

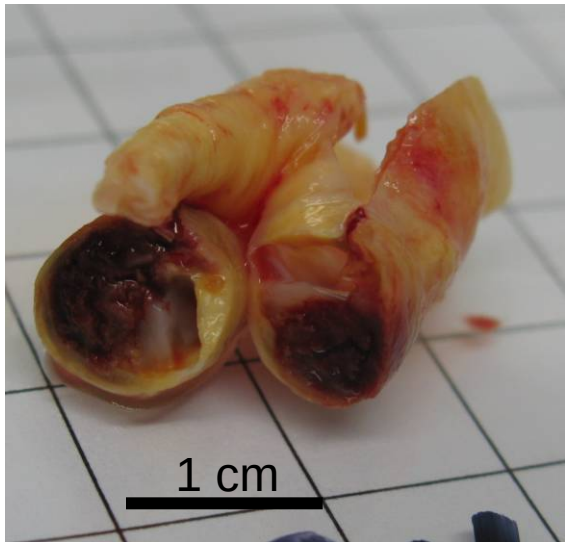


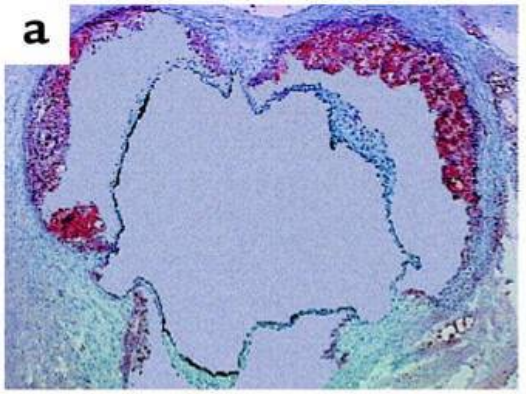


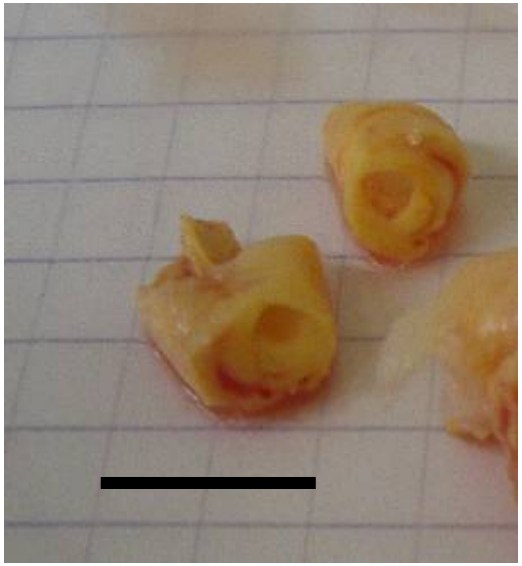
1 cm

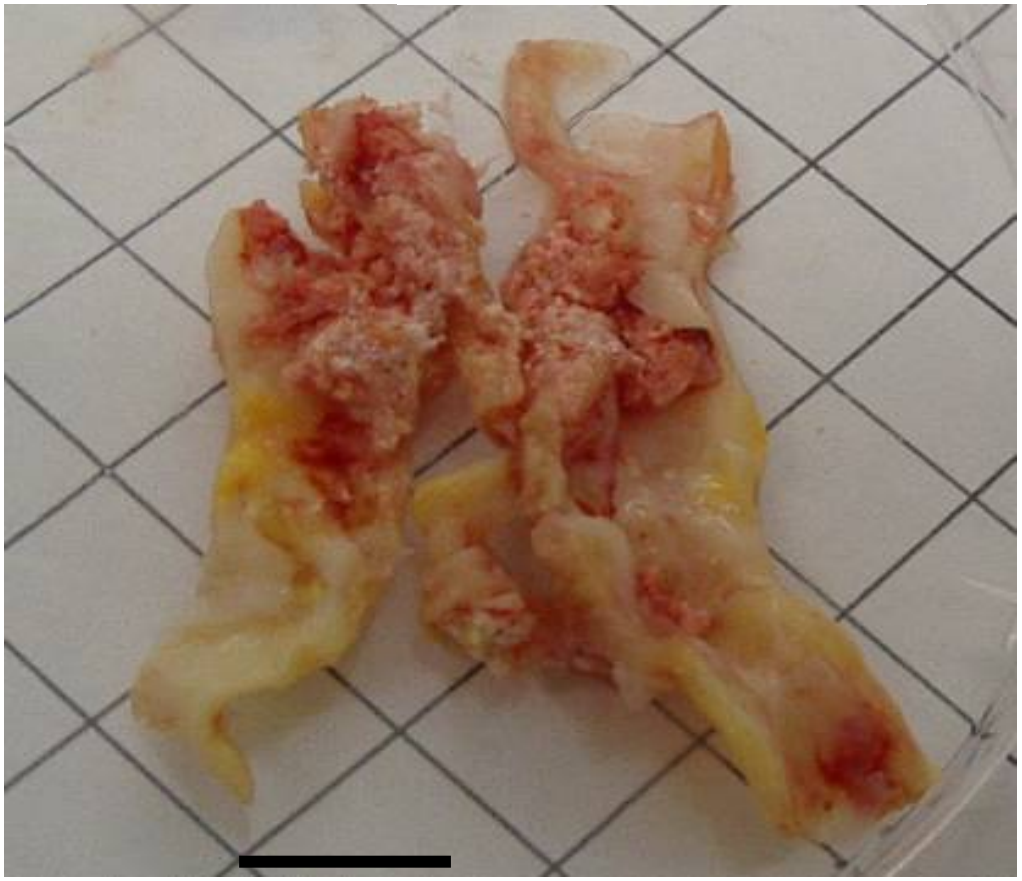


Athérosclérose = athérée (bouillie) + skléros (dur)



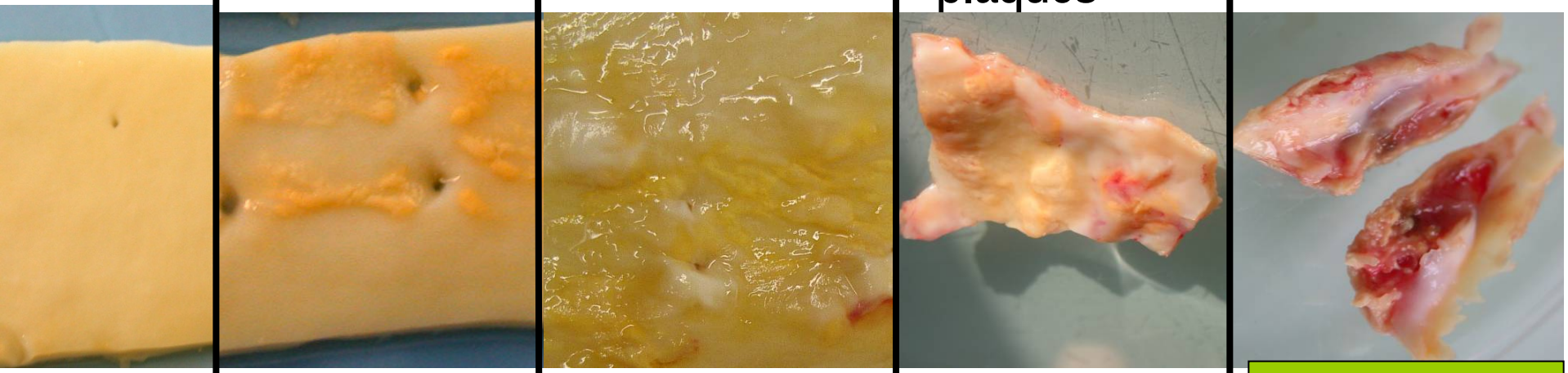






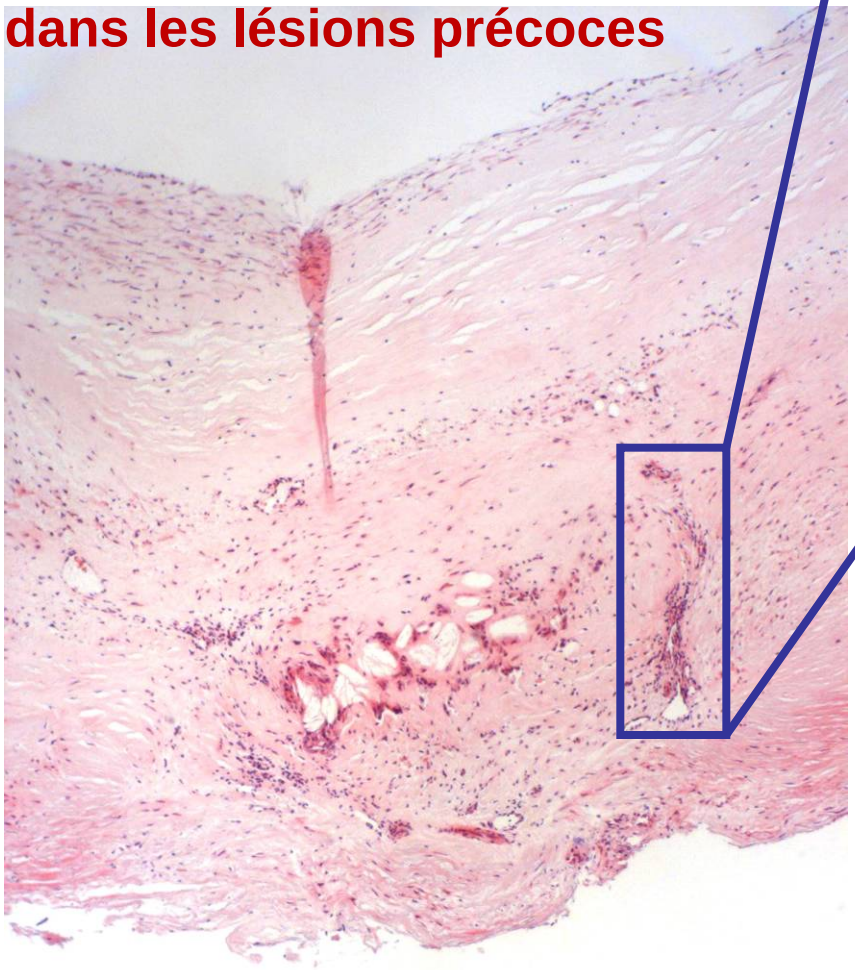
Différentes étapes de l'athérome humain

Normal artery	Fatty streaks	Fibrolipidic streaks	Non-complicated plaques	Vulnerable plaques

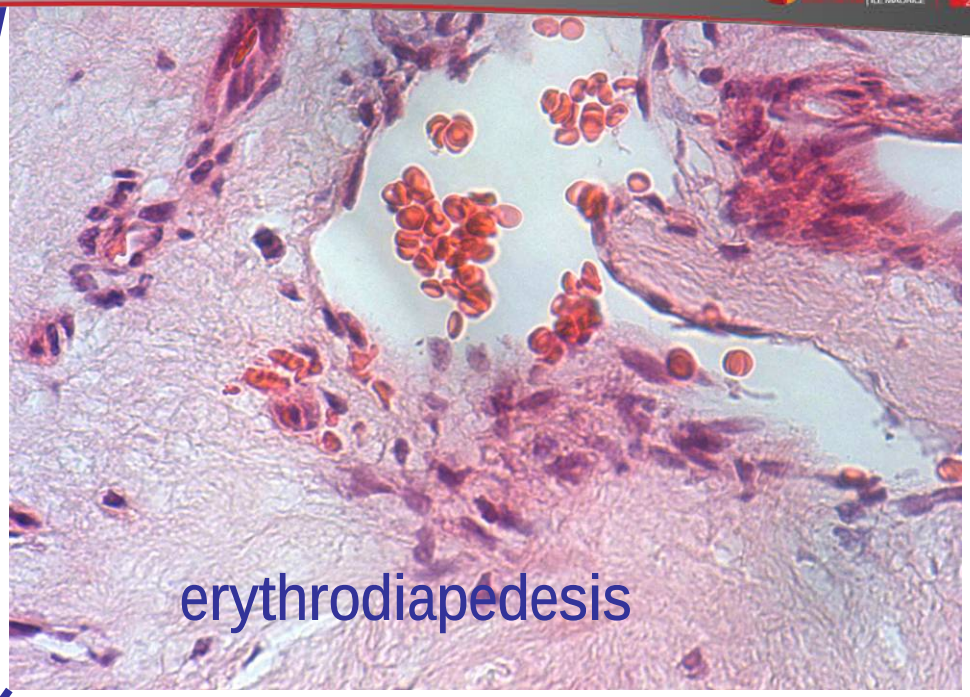


Clinical complications

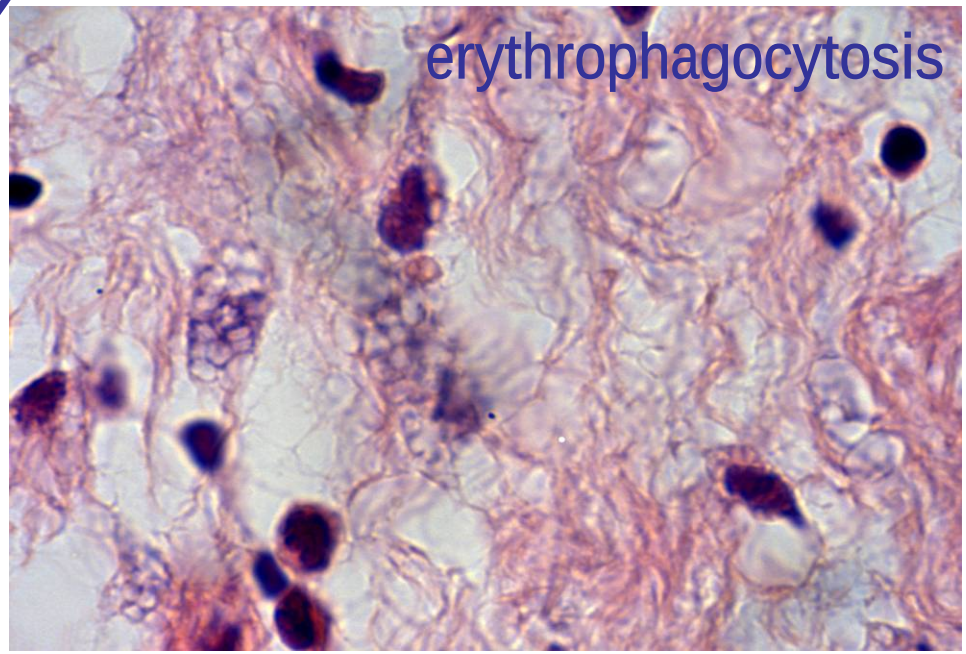
Angiogenèse et globules rouges dans les lésions précoces



angiogenesis

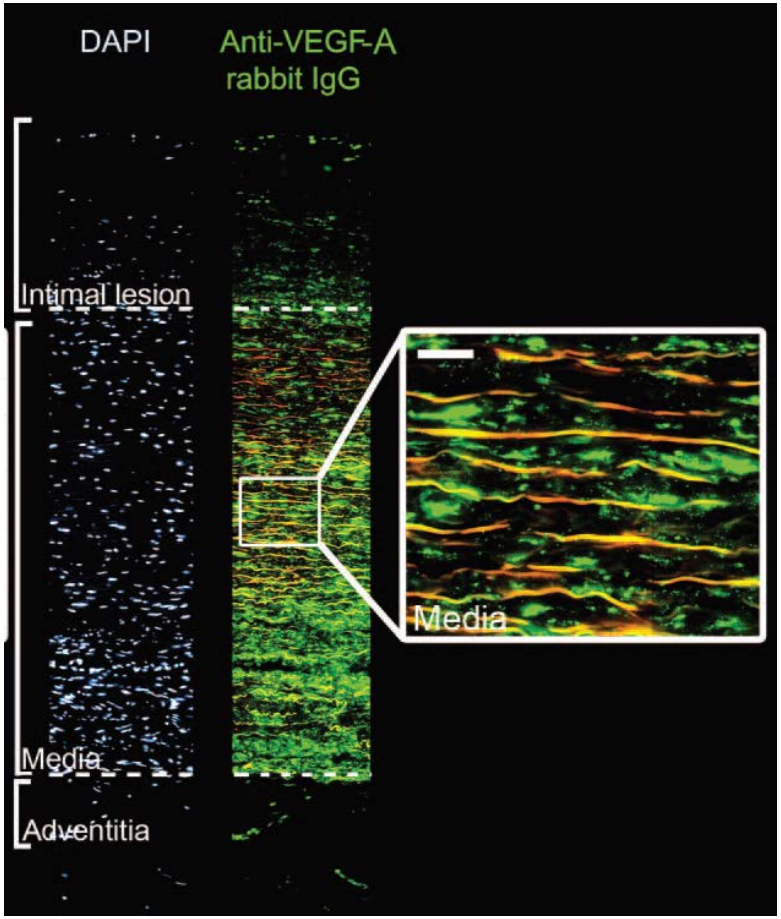


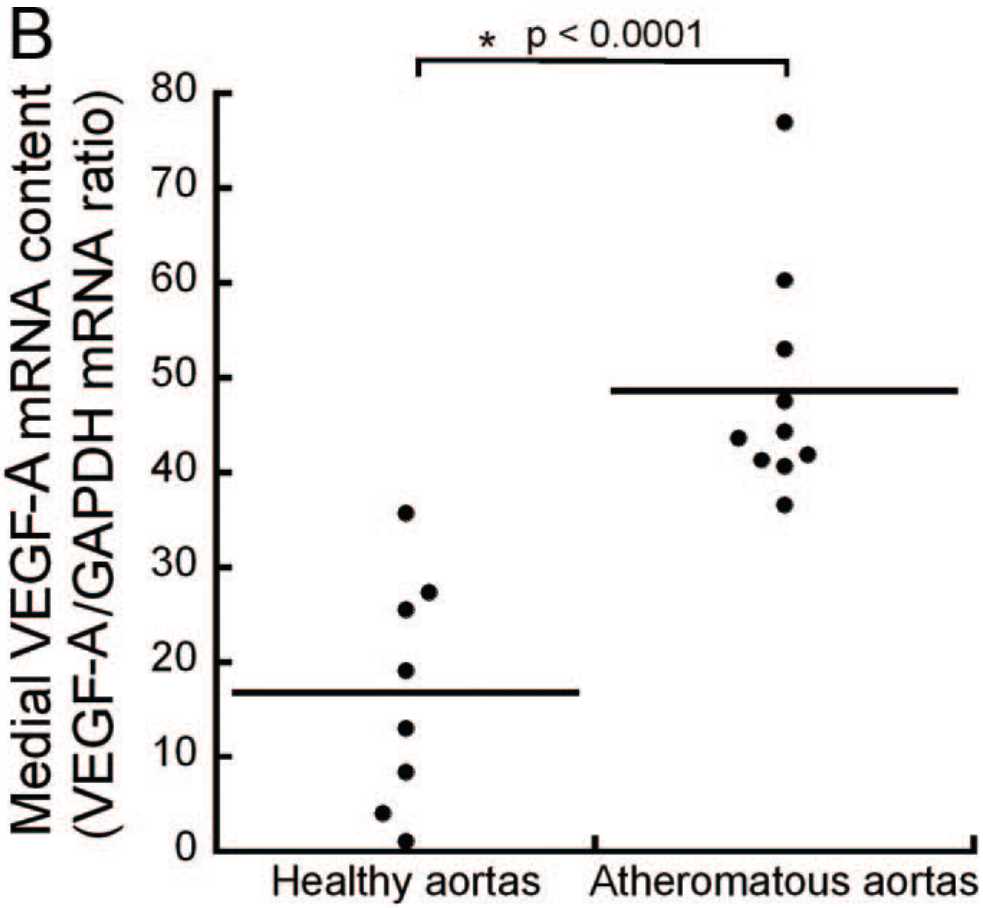
erythrodiapedesis



erythrophagocytosis

Angiogenèse dans les lésions précoces : rôle des CML

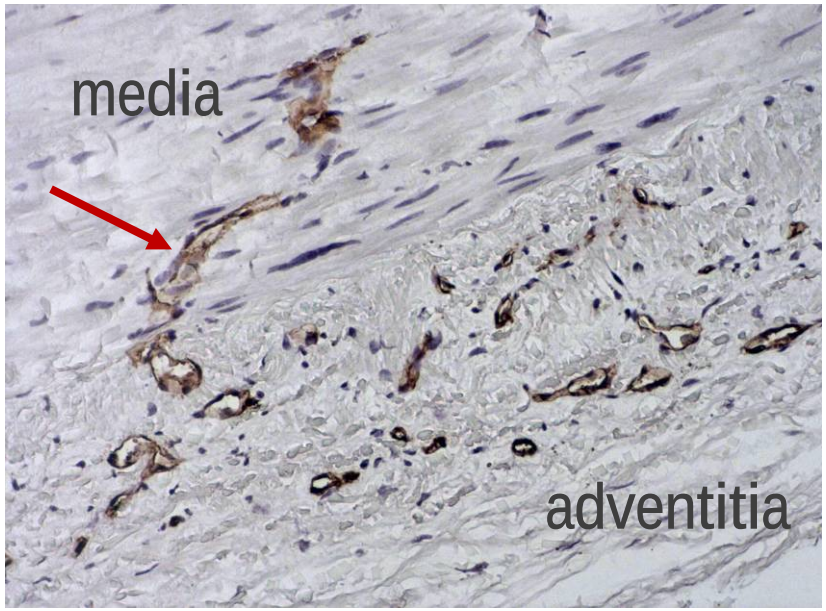




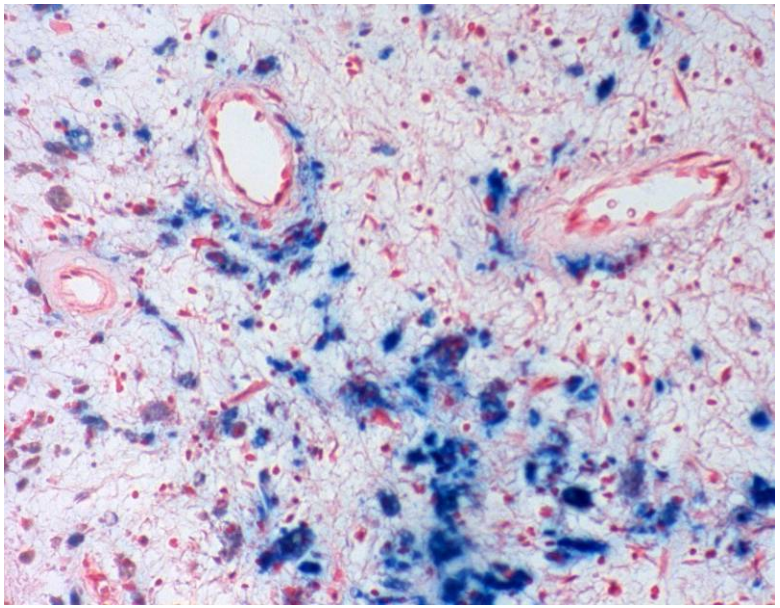
Ho-Tin-Noé et al Atheroma Lipids Trigger Intramural Angiogenesis (*Circ Res*. 2011;109:00-00.)

Néo-angiogenèse : principale source d'hémorragies

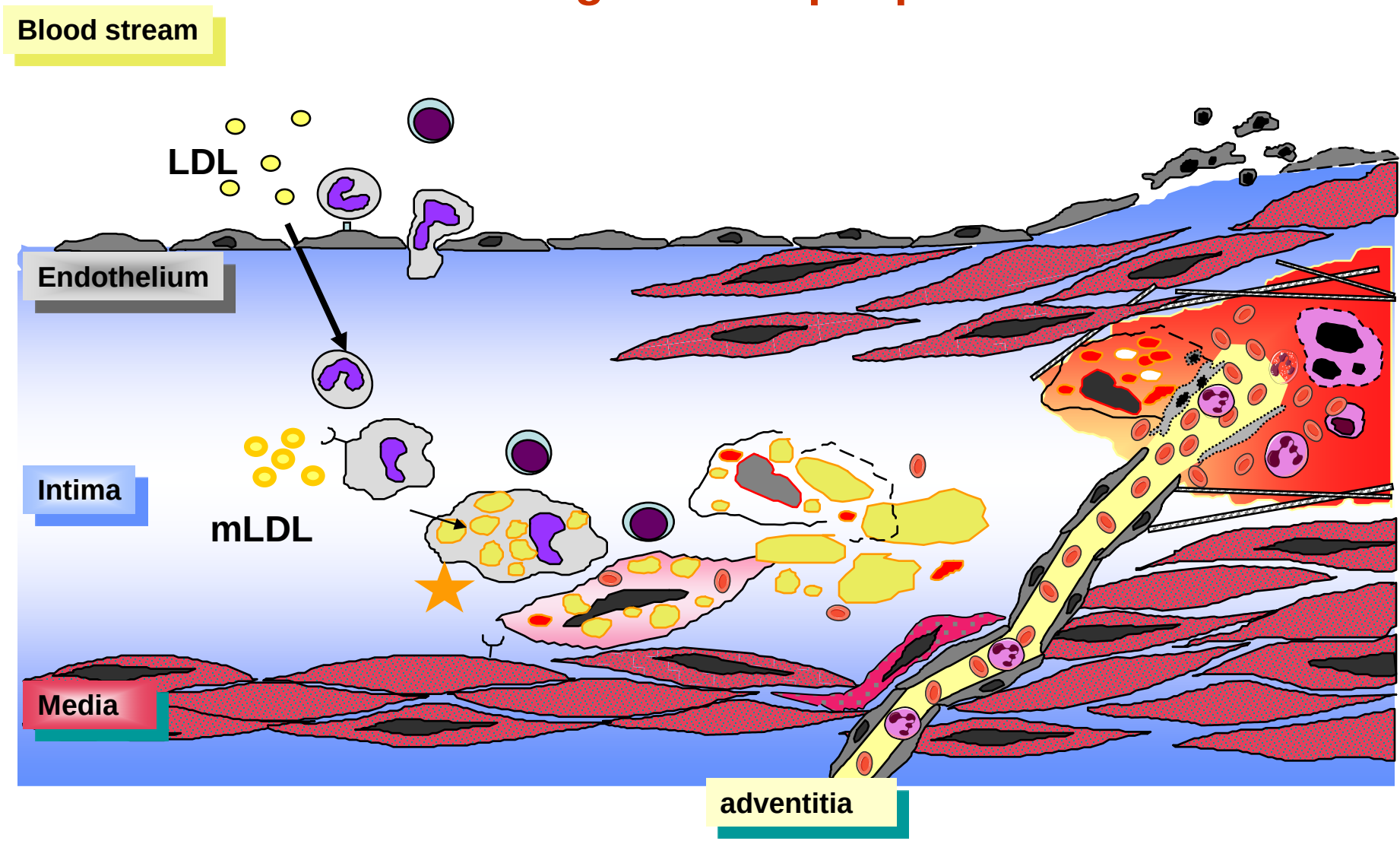
CD 31 (PECAM)



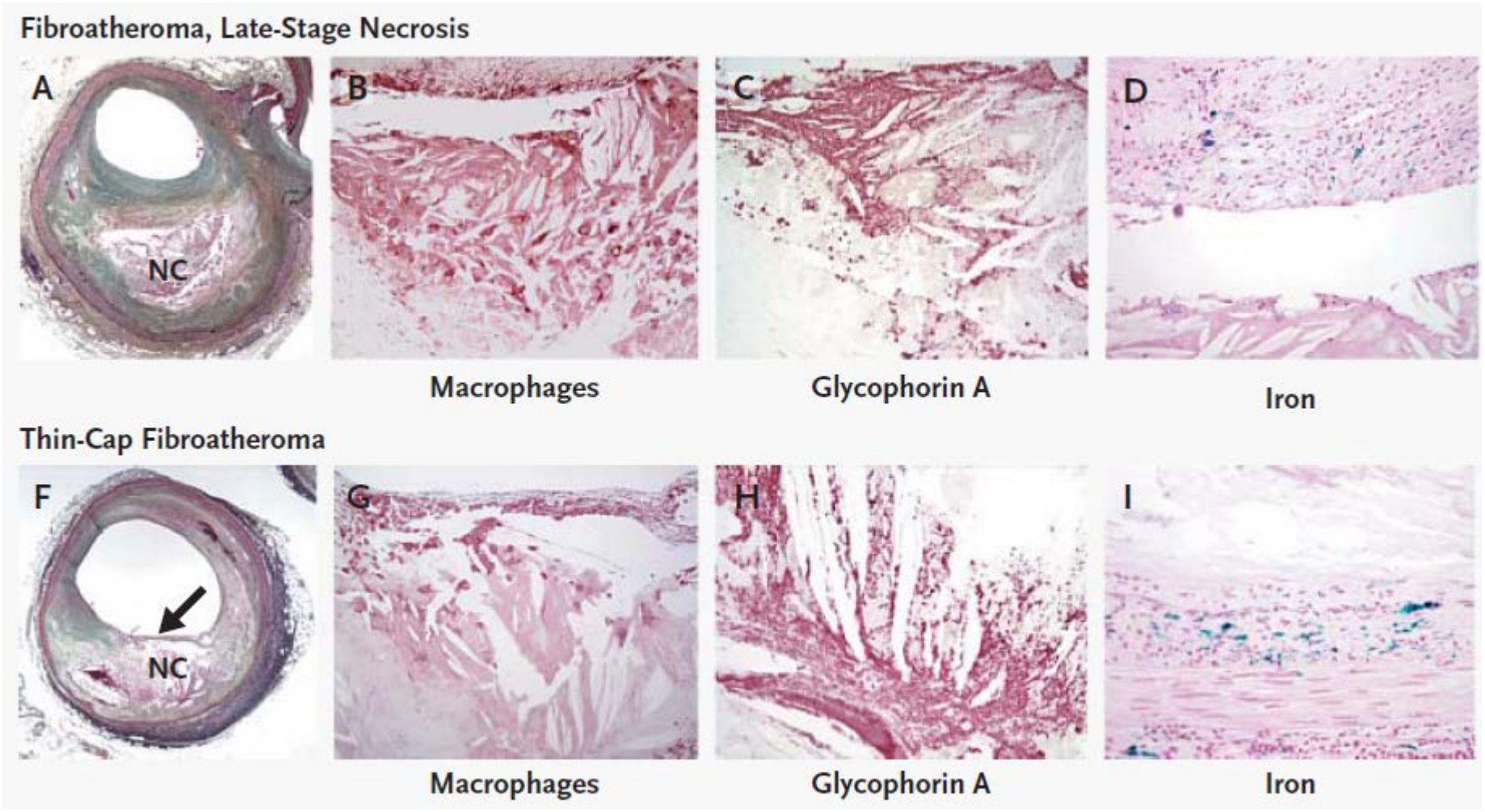
Hémosidérine (Perls)



Hémorragies intra-plaque



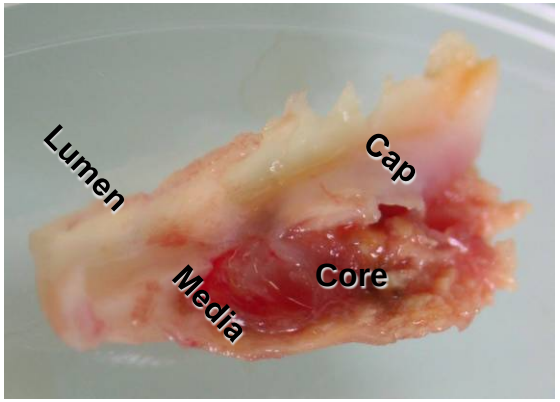
Globules rouges comme source de cholestérol



Frank D. Kolodgie, N ENGL J MED 349;24 DECEMBER 11, 2003

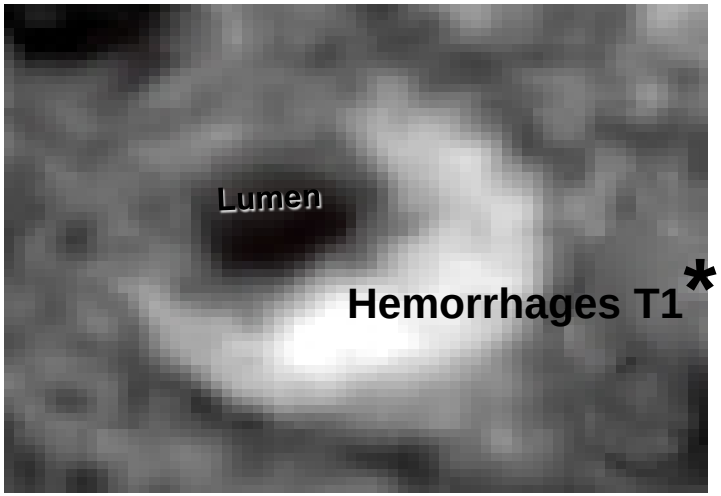
Hémorragies intra-plaque et vulnérabilité à la rupture

Galien 131-201 A.D.



anapath (***Virmani R 2005***)

Histologie

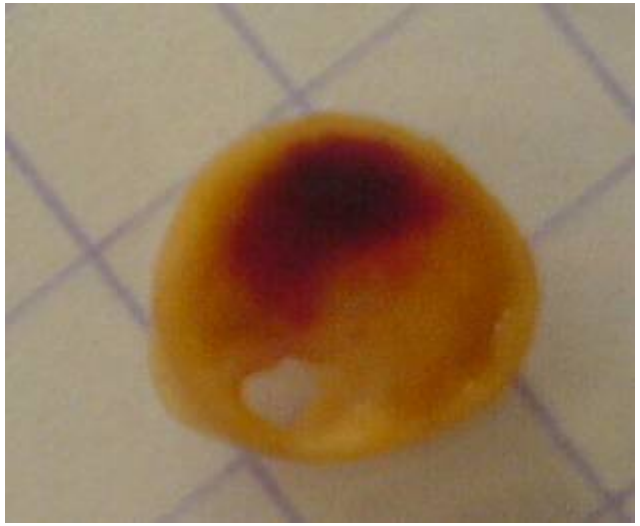


IRM

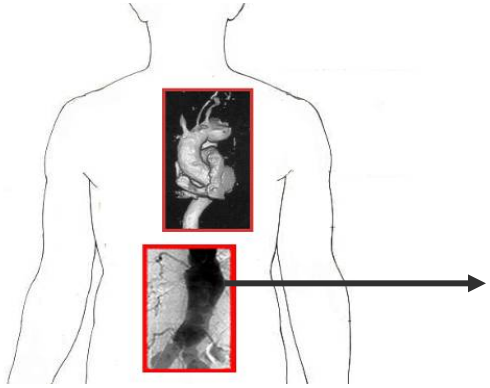
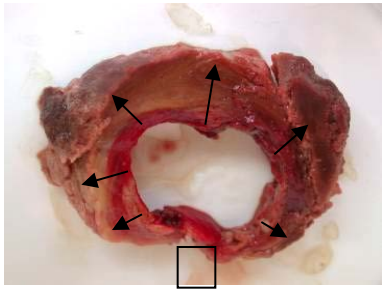
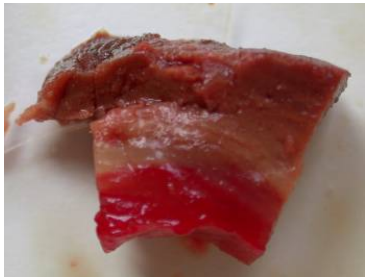
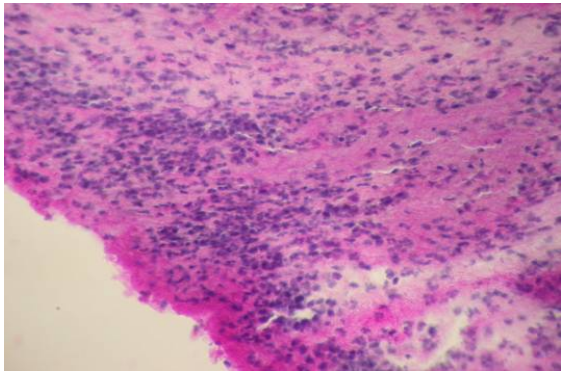
(Takaya N & Hatsukami TS 2005)

Athérothrombose sténosante vs dilatante

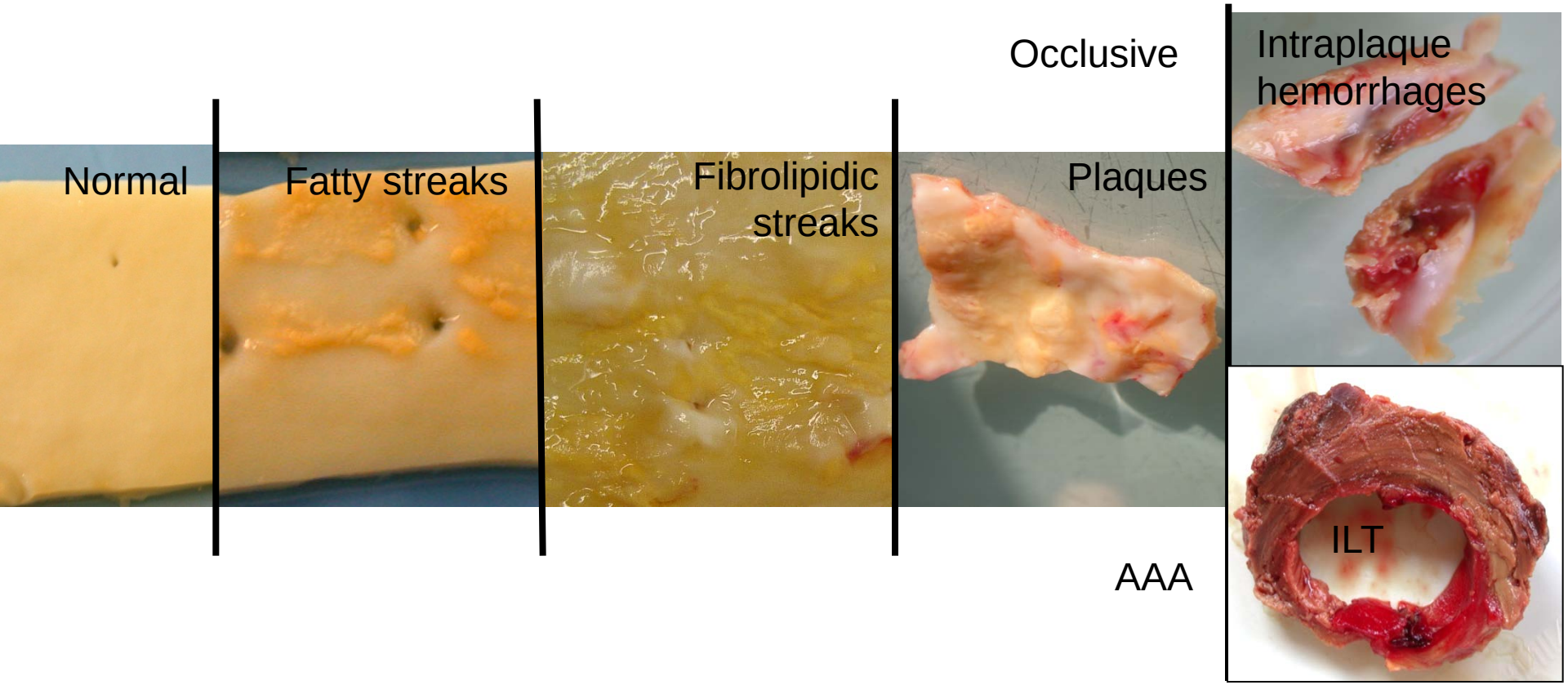
Athérosclérose carotidienne


Anévrysmes de l'aorte abdominale (AAA)

De l'artère normale aux complications cliniques



Stary classification

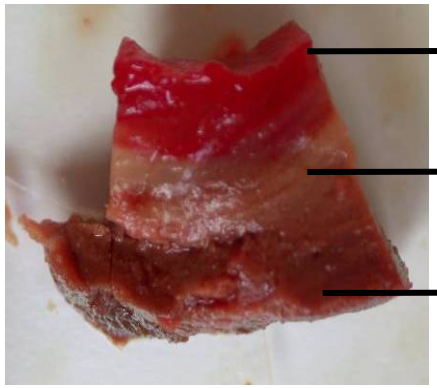
Clinical complications

Athérothrombose : activités protéases

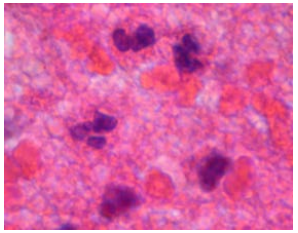
carotide

RPMI, 24h, 37°C

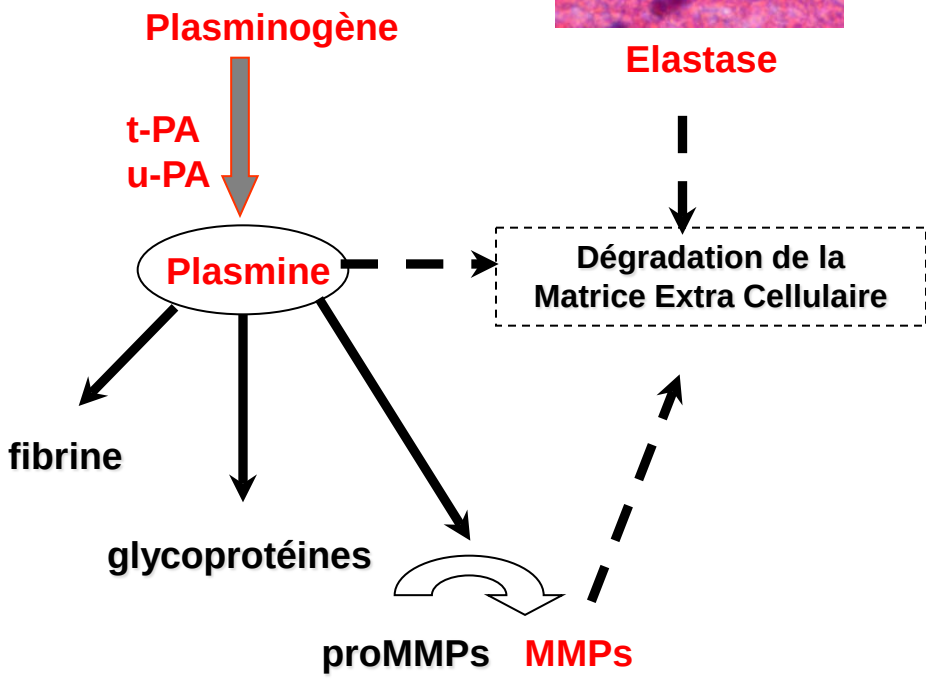
anévrysme



Approche ciblant les protéases :



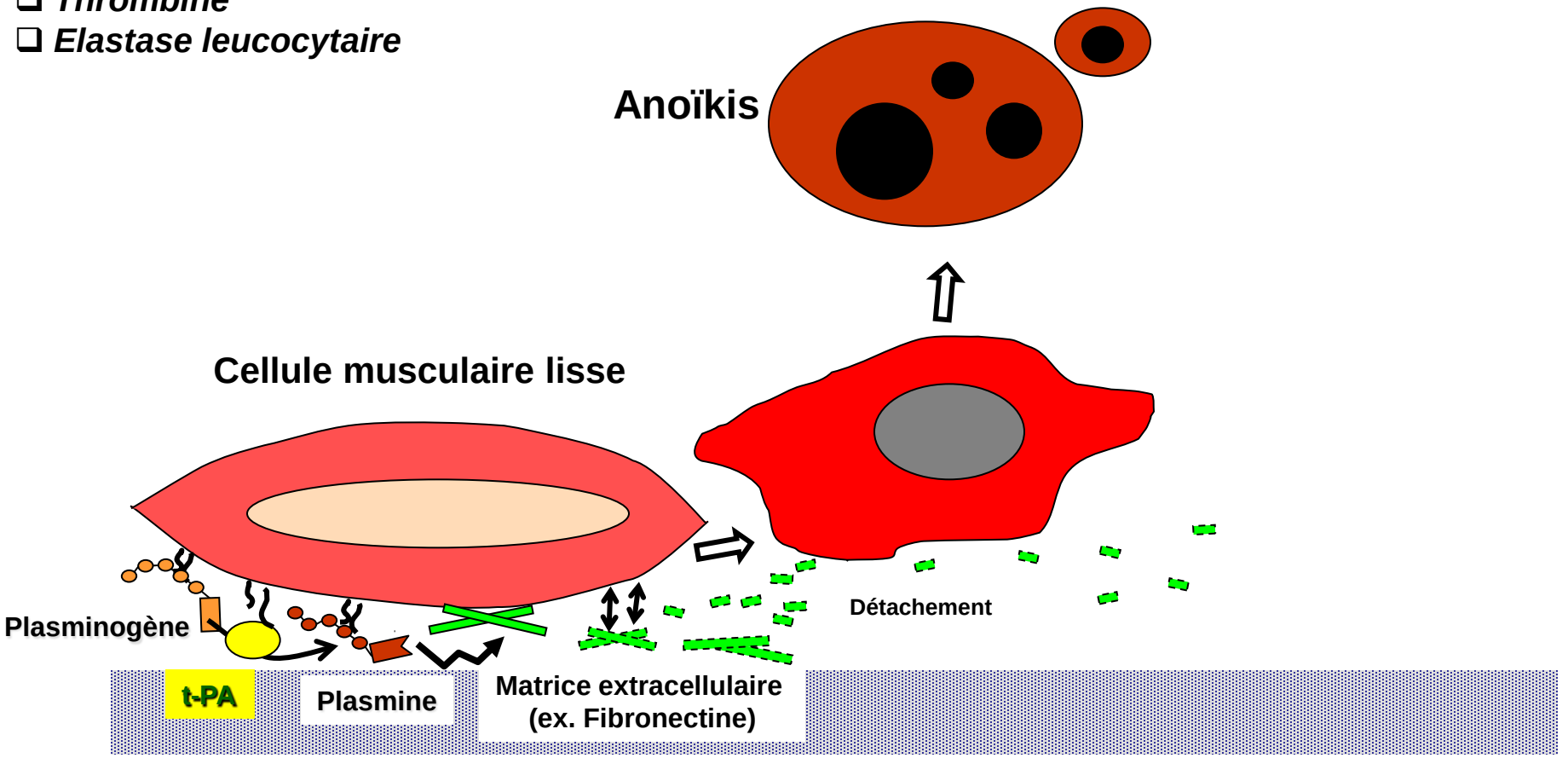
Elastase



Fontaine et al. Am. J. Pathol. 2004
Martin-Ventura JL, Atherosclerosis 2006
Martin-Ventura JL, ATVB 2006
Leclercq A et al. J. Leukocyte Biol. 2007
Leclercq A et al. Atherosclerosis 2007

Protéolyse péricellulaire = mort par apoptose

- ***Plasminogène → plasmine***
- ***Thrombine***
- ***Elastase leucocytaire***

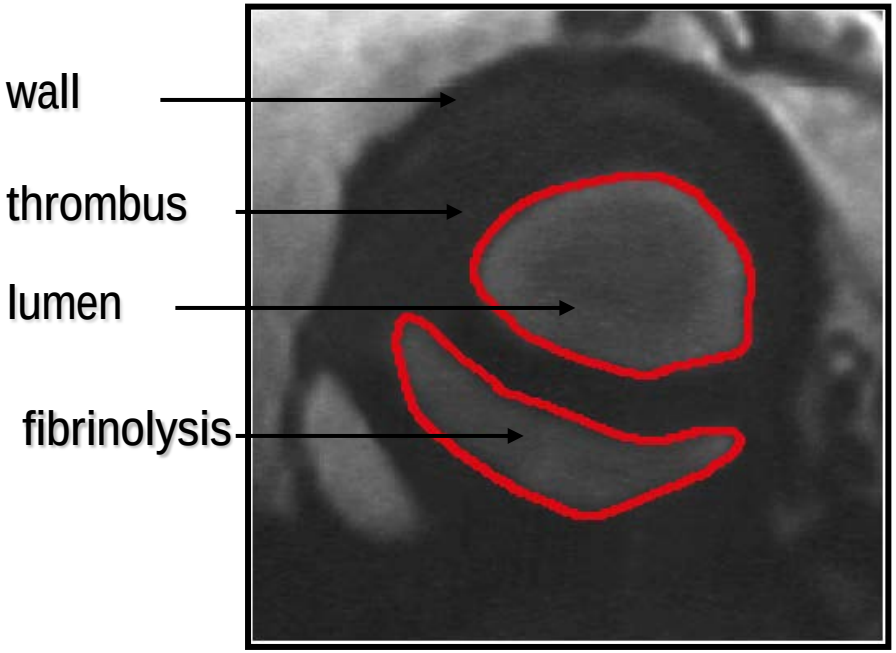


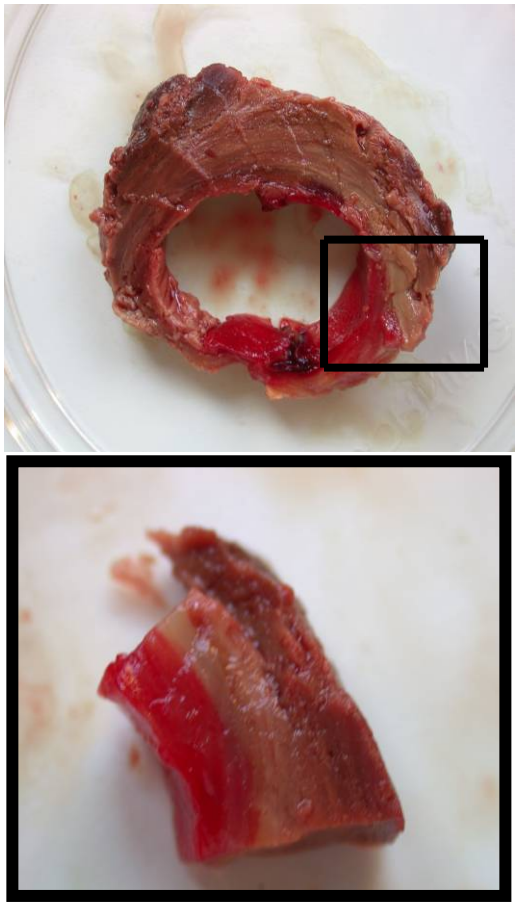
Meilhac et al. FASEB J. 2003

Rossignol et al. Exp Cell Res 2004

Mtairag et al. ATVB 2002

AAA et thrombus mural

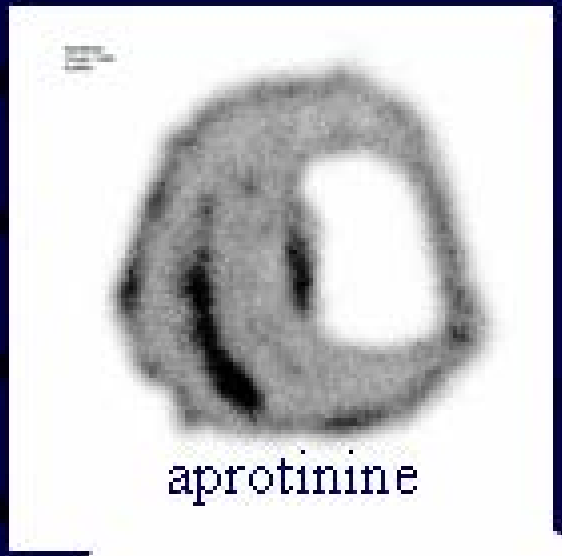


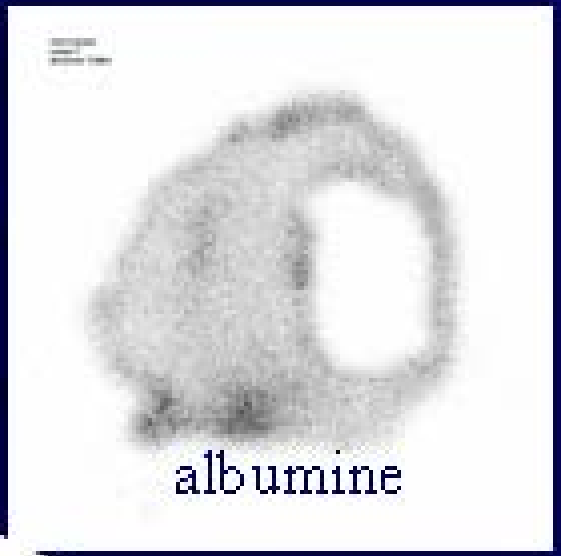


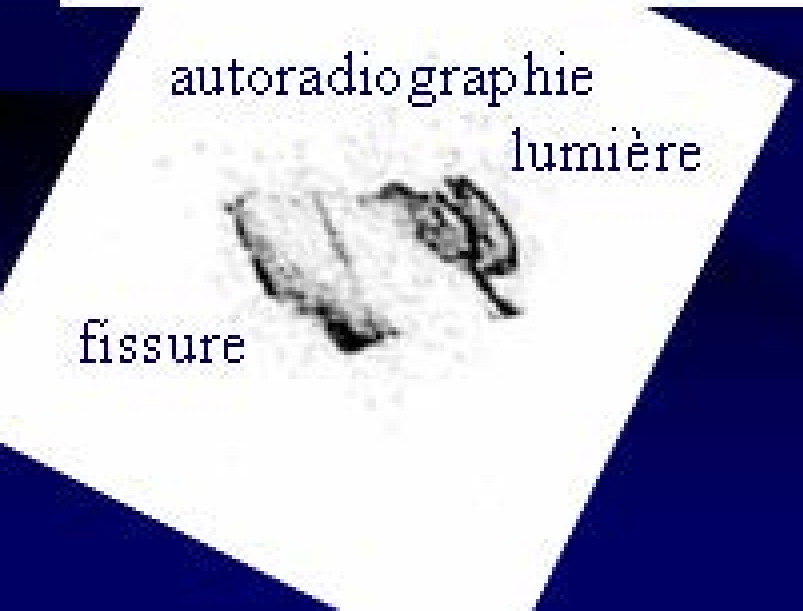
Hypothèse

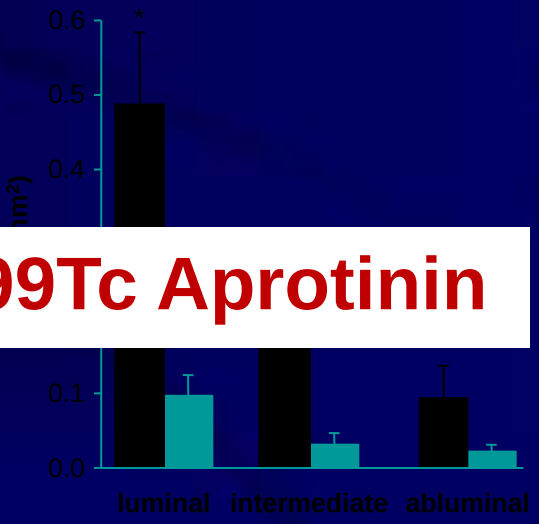
- thrombus d'AAA contient des protéases (système fibrinolytique + autres)
- neutrophiles : sources de protéases

Humain, *ex vivo*





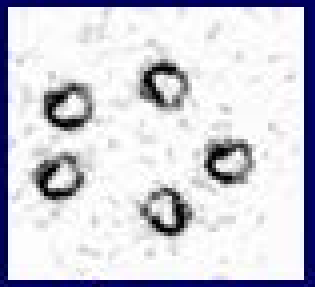




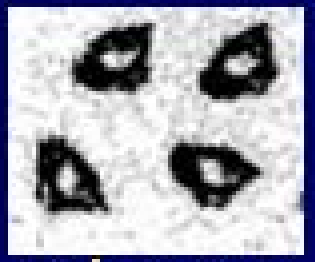
99Tc Aprotinin

In vivo, rat autoradiographie

aorte normale



anévrysme



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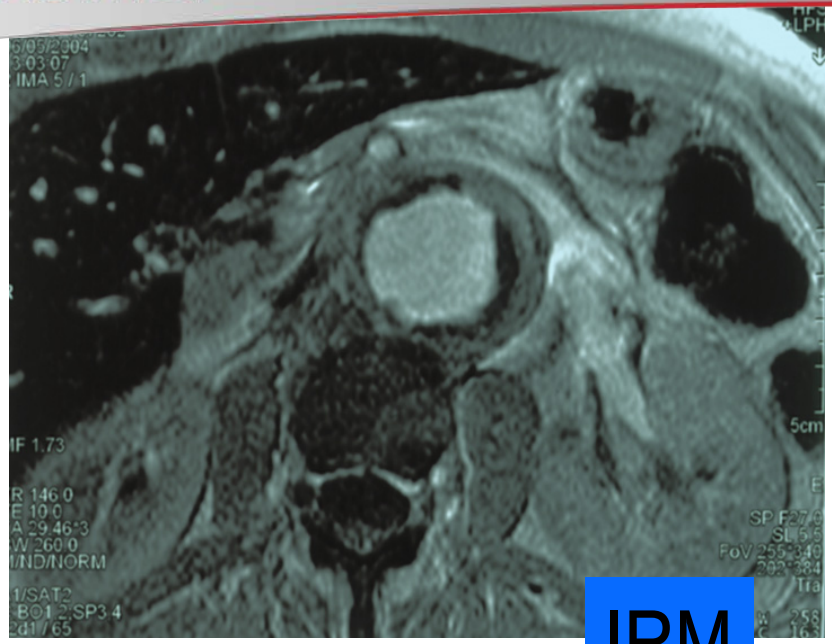
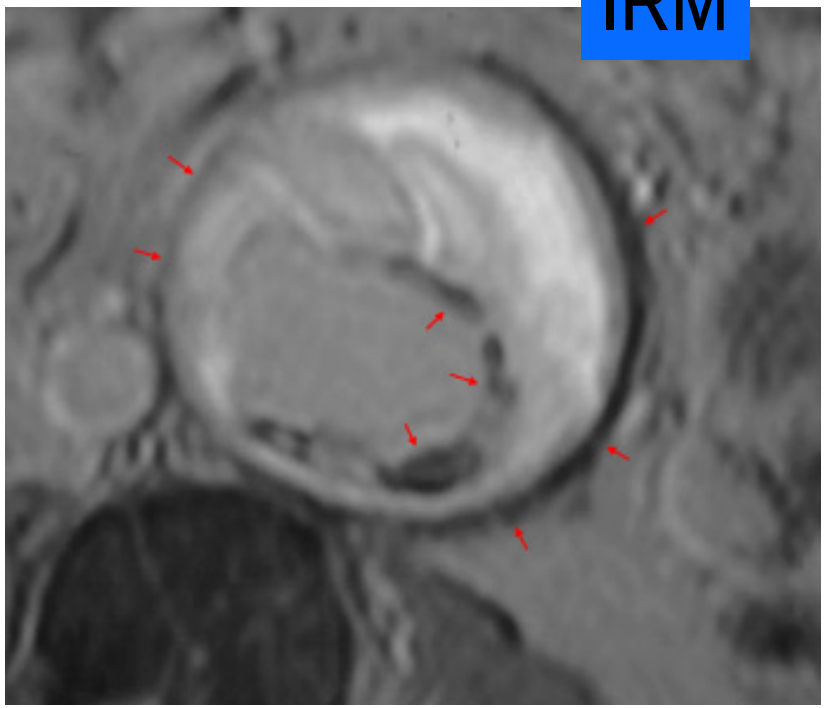
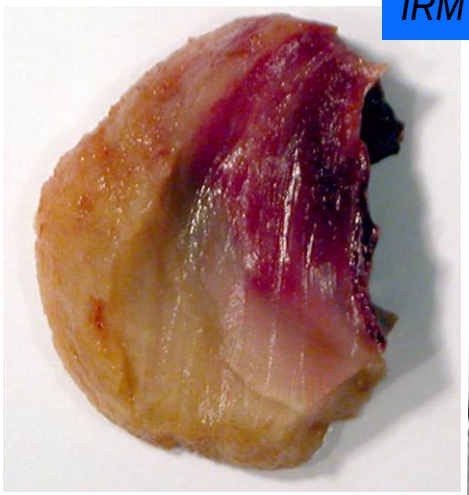
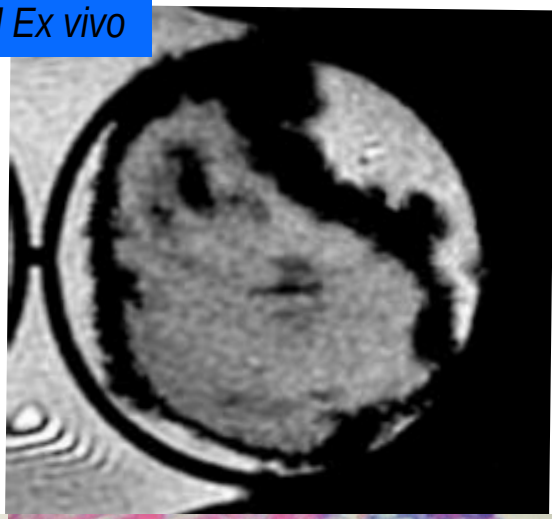


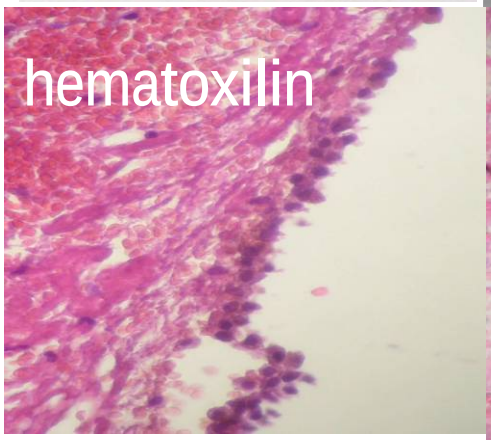
IRM

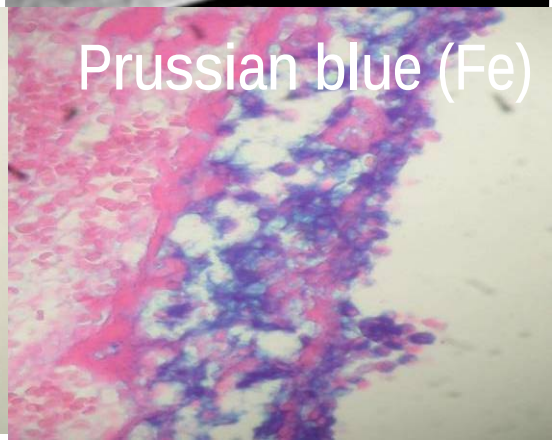


IRM Ex vivo



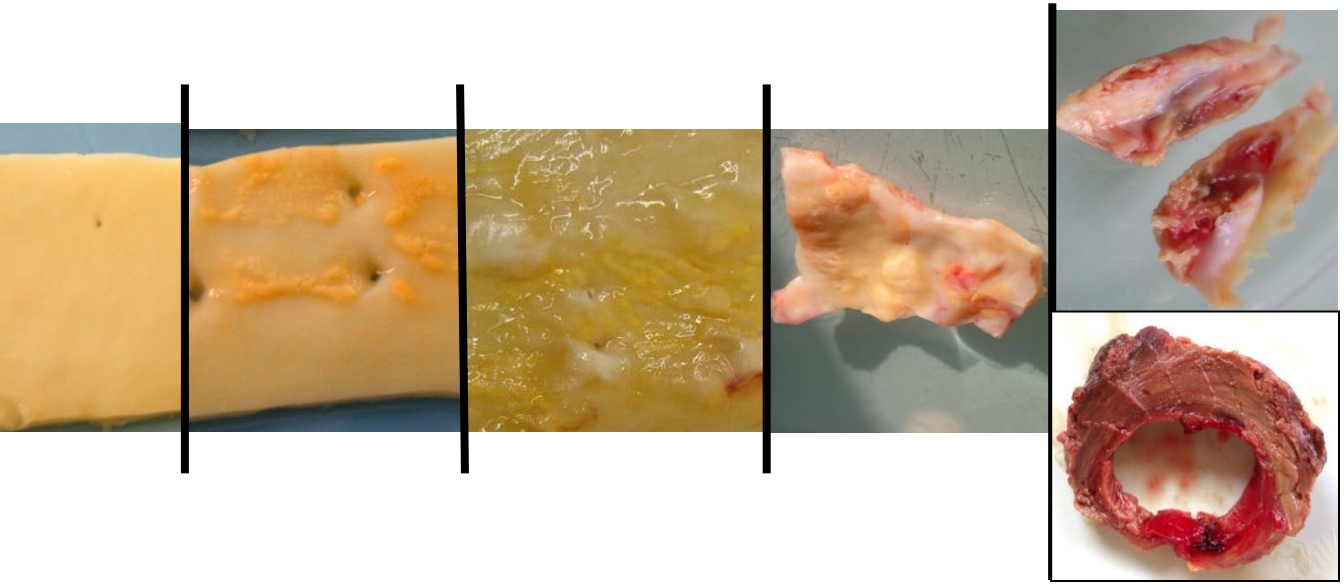


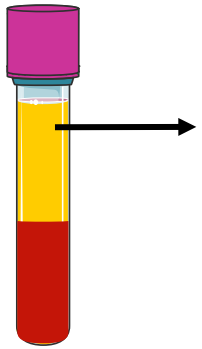




Imagerie fonctionnelle de la phagocytose : SPIO + IRM

Biomarqueurs circulants de vulnérabilité ?





CD163 : scavenger de l'hémoglobine

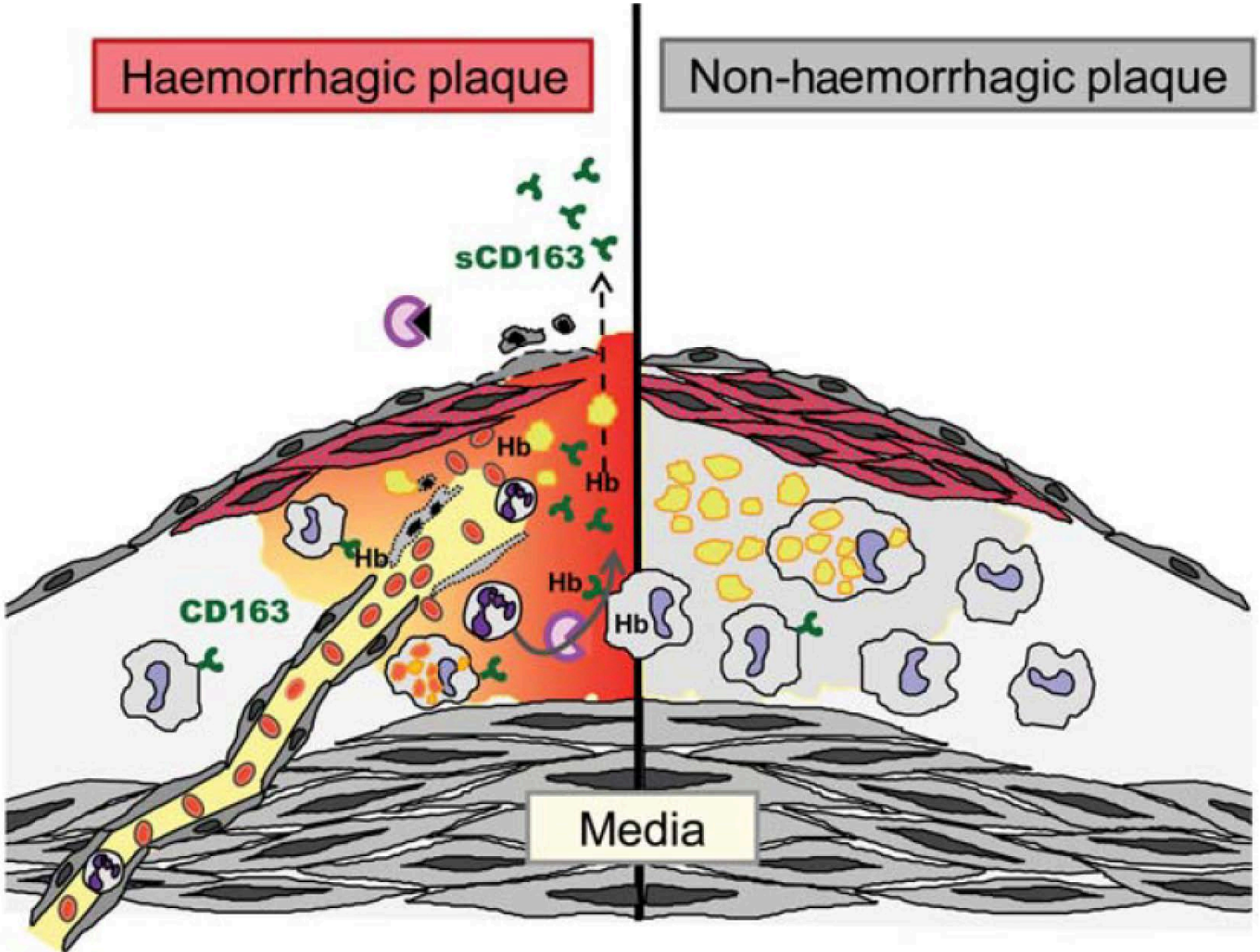
EUROPEAN SOCIETY OF CARDIOLOGY®

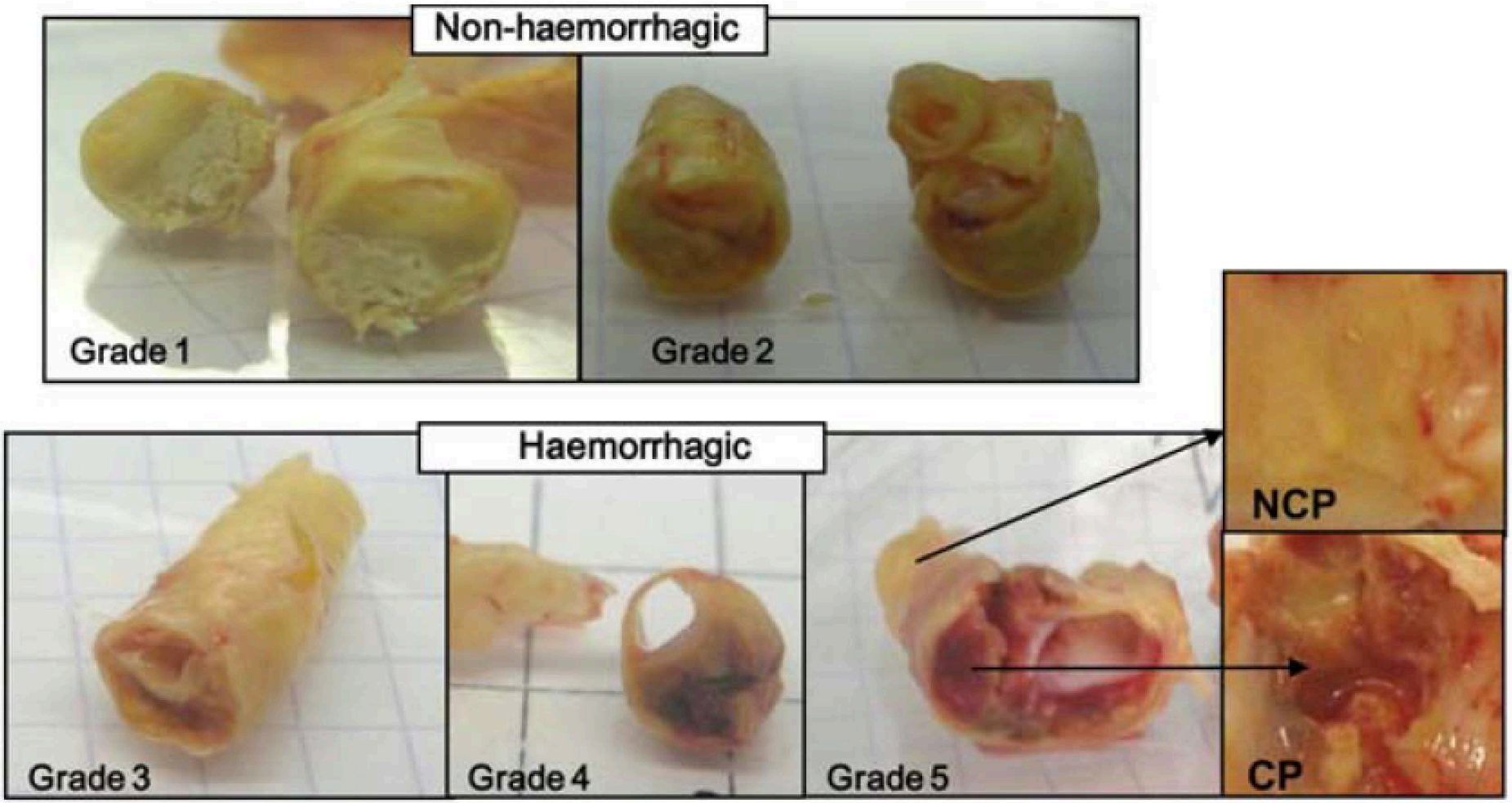
European Heart Journal (2012) **33**, 252–263
doi:10.1093/eurheartj/ehr123

BASIC SCIENCE

In vitro and *in vivo* evidence for the role of elastase shedding of CD163 in human atherothrombosis

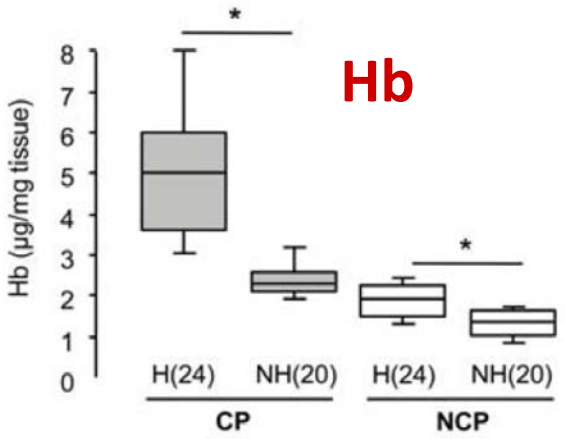
Juan Antonio Moreno[1], Almudena Ortega-Gómez[1], Sandrine Delbosc[1], Nathalie Beaufort[1], Emmanuel Sorbets[1,2], Liliane Louedec[1], Marina Esposito-Farèse[3,4], Florence Tubach[3,4,5], Antonino Nicoletti[1,5], Philippe Gabriel Steg[1,2,5], Jean-Baptiste Michel[1,2,5], Laurent Feldman[1,2,5], and Olivier Meilhac[1,5,6*]

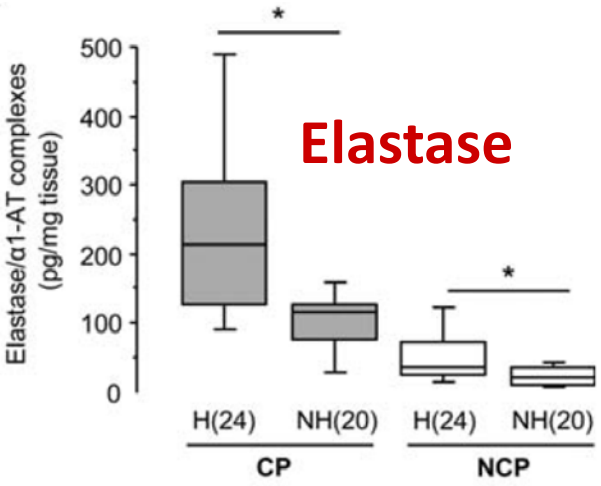

Haemorrhagic plaque
Non-haemorrhagic plaque
sCD163
Hb
Hb
Hb
Hb
Hb
CD163
Media

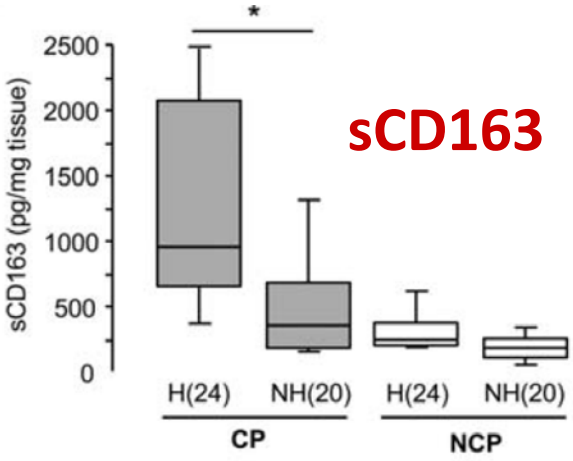

Non-haemorrhagic
Grade 1
Grade 2
Haemorrhagic
Grade 3
Grade 4
Grade 5
NCP
CP

Milieux conditionnés d'endartériectomies carotidiennes

RPMI, 24h, 37°C







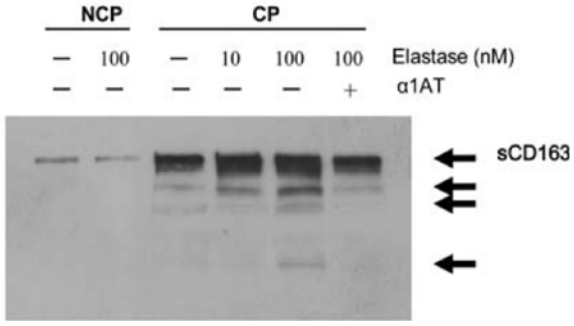


Table 2 Plasma concentration of sCD163 and α1-AT/HLE

	ACS ($n = 42$)	SAP ($n = 28$)	NA ($n = 21$)	*P*-value[a]
sCD163 (ng/mL)	593.2 (264.6)*	543.4 (205.9)**	396.8 (159.6)	0.01
α1-AT/HLE (ng/mL)	51.8 (40.5)	44.6 (27.4)	33 (17)	0.146

Results are expressed as mean; standard deviation is indicated in parentheses.
[a]Global comparison assessed by ANOVA. Non-parametric Kruskal–Wallis test was used for comparisons of sCD163 levels: ACS vs. NA.
*$P = 0.02$ (ACS vs NA) after adjustment by Hochberg's method for multiple comparisons.
**$P = 0.02$ (SAP vs NA), after adjustment by Hochberg's method for multiple comparisons.

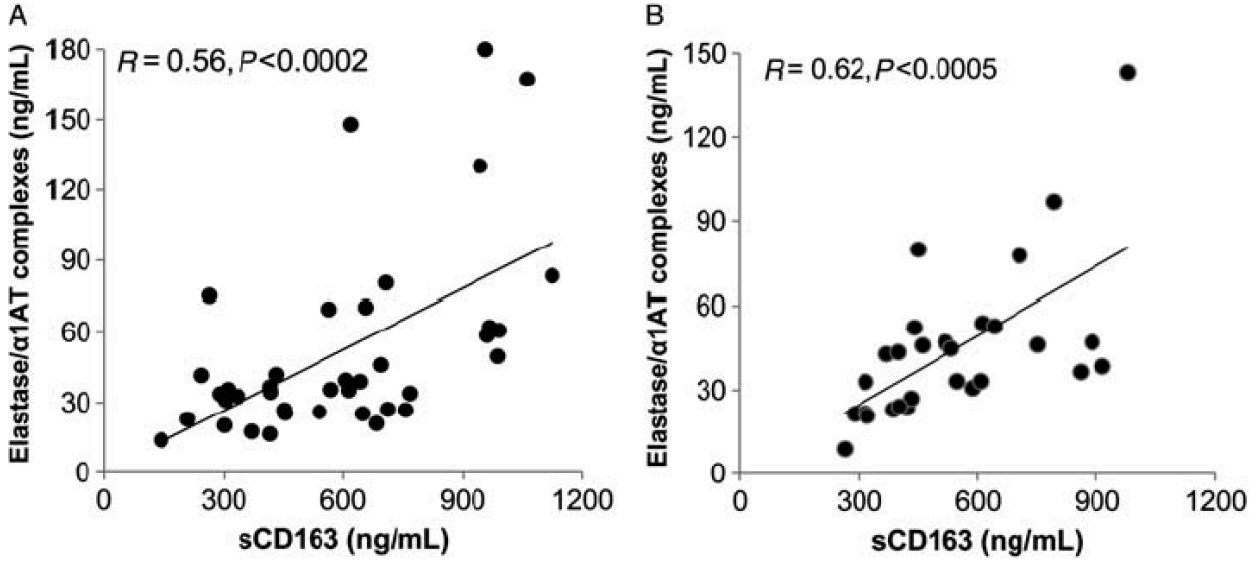
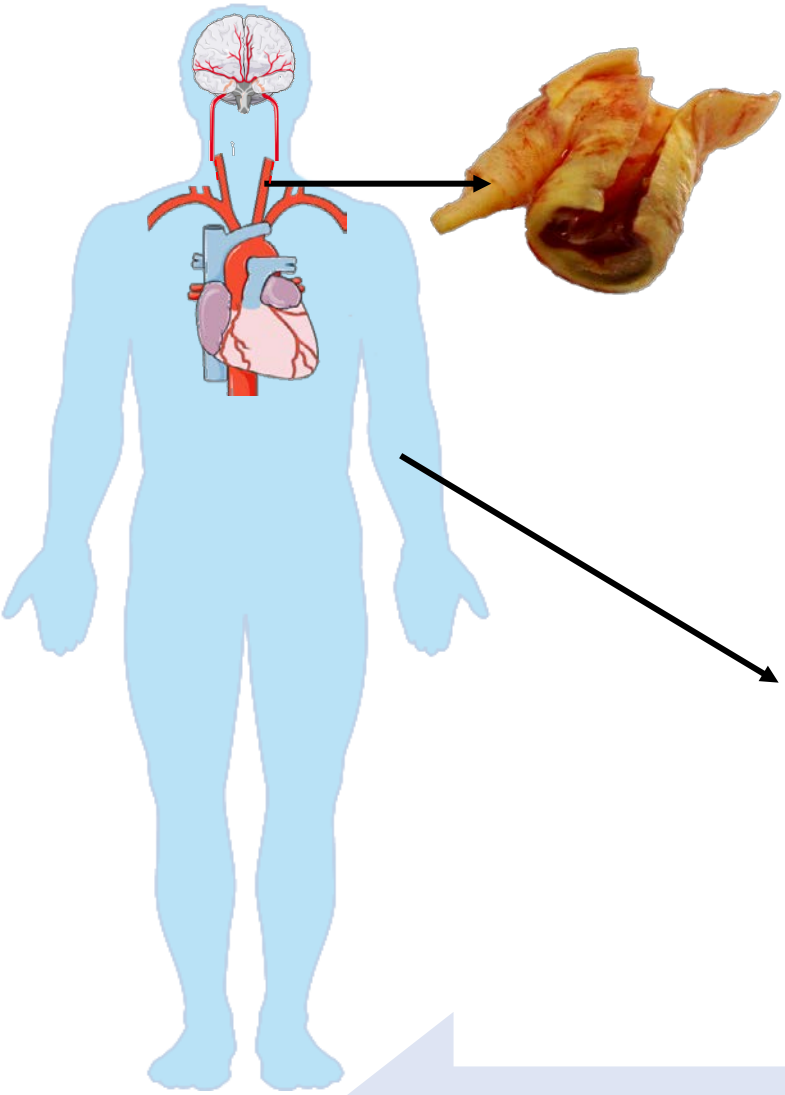
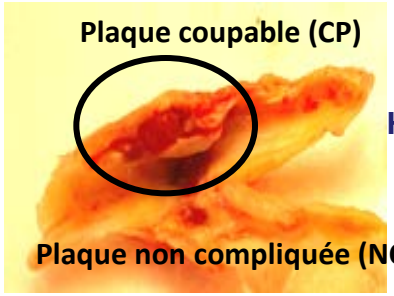


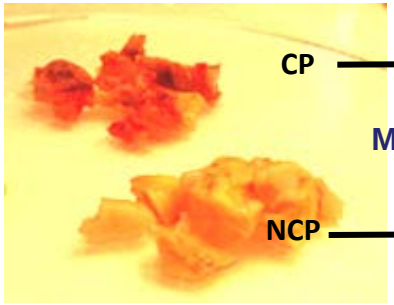
Figure 6 Positive correlation between elastase/α1-AT complexes and sCD163 in patients with acute coronary syndrome (ACS, $n = 42$) (*A*) and in patients with stable angina pectoris (SAP, $n = 28$) (*B*).

Marqueurs d'Athérothrombose chez le Diabétique (MADI)

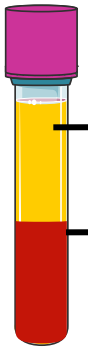




Histologie → **Caractérisation morphologique et biochimique**



Milieux conditionnés → **Protéomique différentielle**

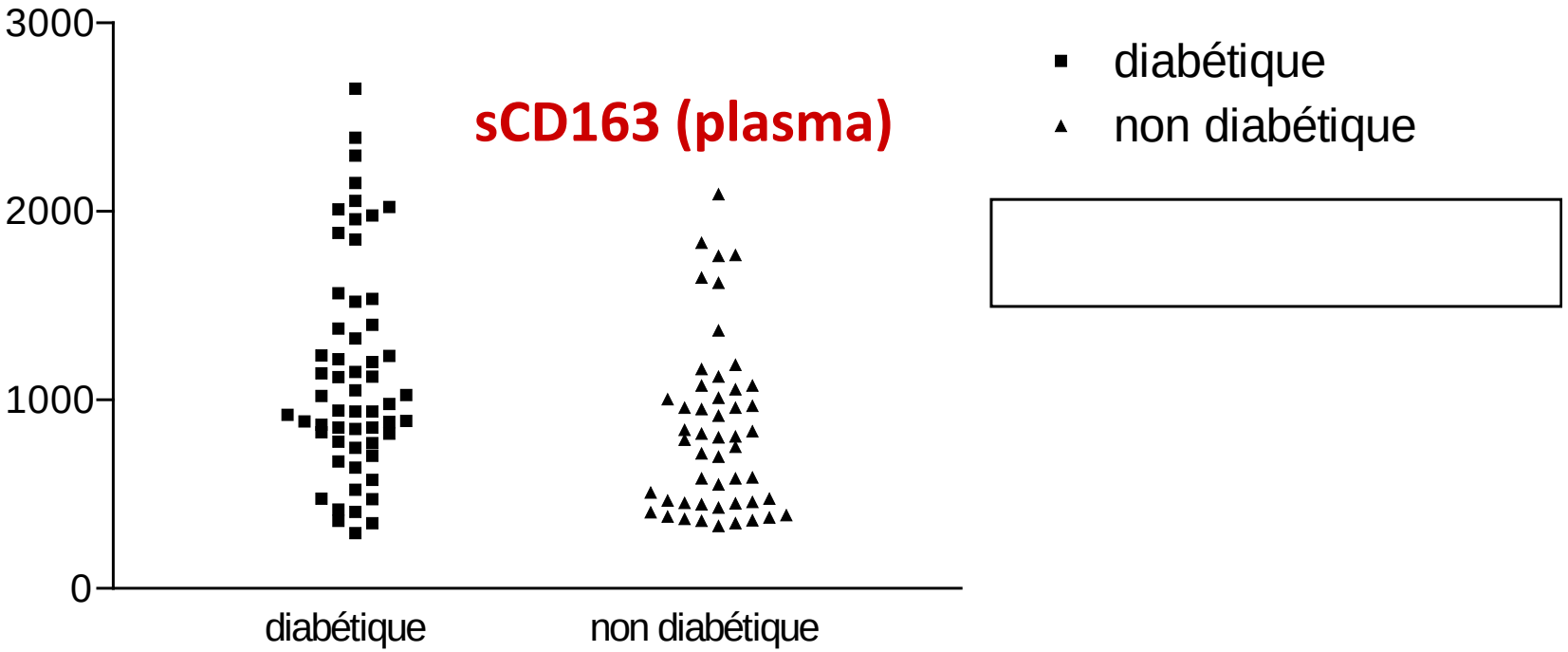


Plasma
Sérum

Cellules → **Extraction d'ADN**

Dosages ELISA: CD163 soluble, myéloperoxydase, MMP-9,
Dosages ADN libre, protéines carbonylées, albumine glyquée
Complexes MPO/DNA (NETs)
Anti-Porphyromonas gingivalis
Isolement des HDL et tests de fonctionnalité

Corrélations avec les données cliniques et dosages de routine



- **pourquoi plus d'hémorragie chez le diabétique ?**
- **hypothèse du microbiote parodontal**
- **détection in situ des parodonto-pathogènes (PCR)**
- **quantification des anticorps anti-bactéries parodontales**

Take home message

- grande hétérogénéité des plaques
- macrophages ou cellules musculaires lisses, quels coupables ?
- globules rouges comme source de cholestérol
- inflammation chronique ou aiguë ?
- microbiote : déclencheur de rupture ?