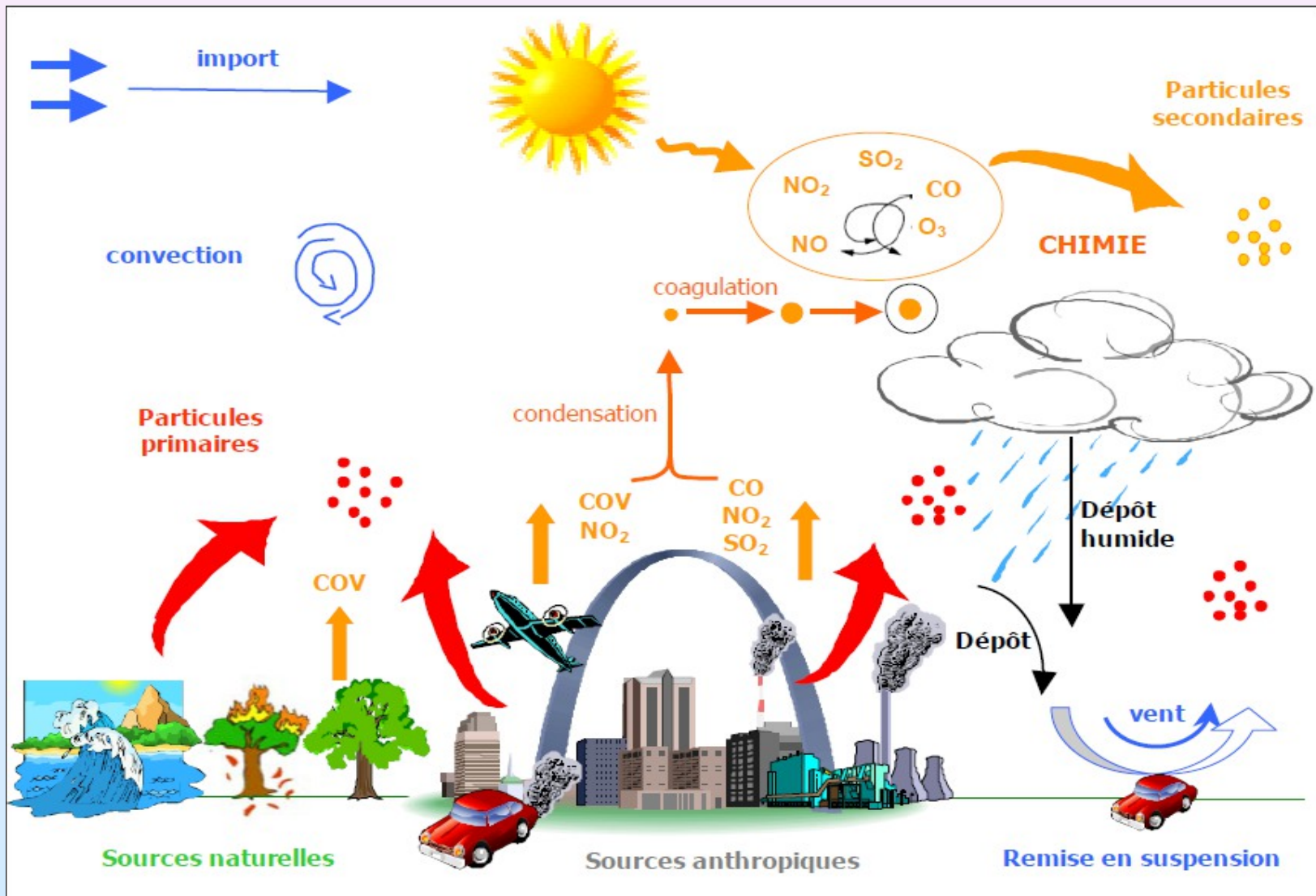
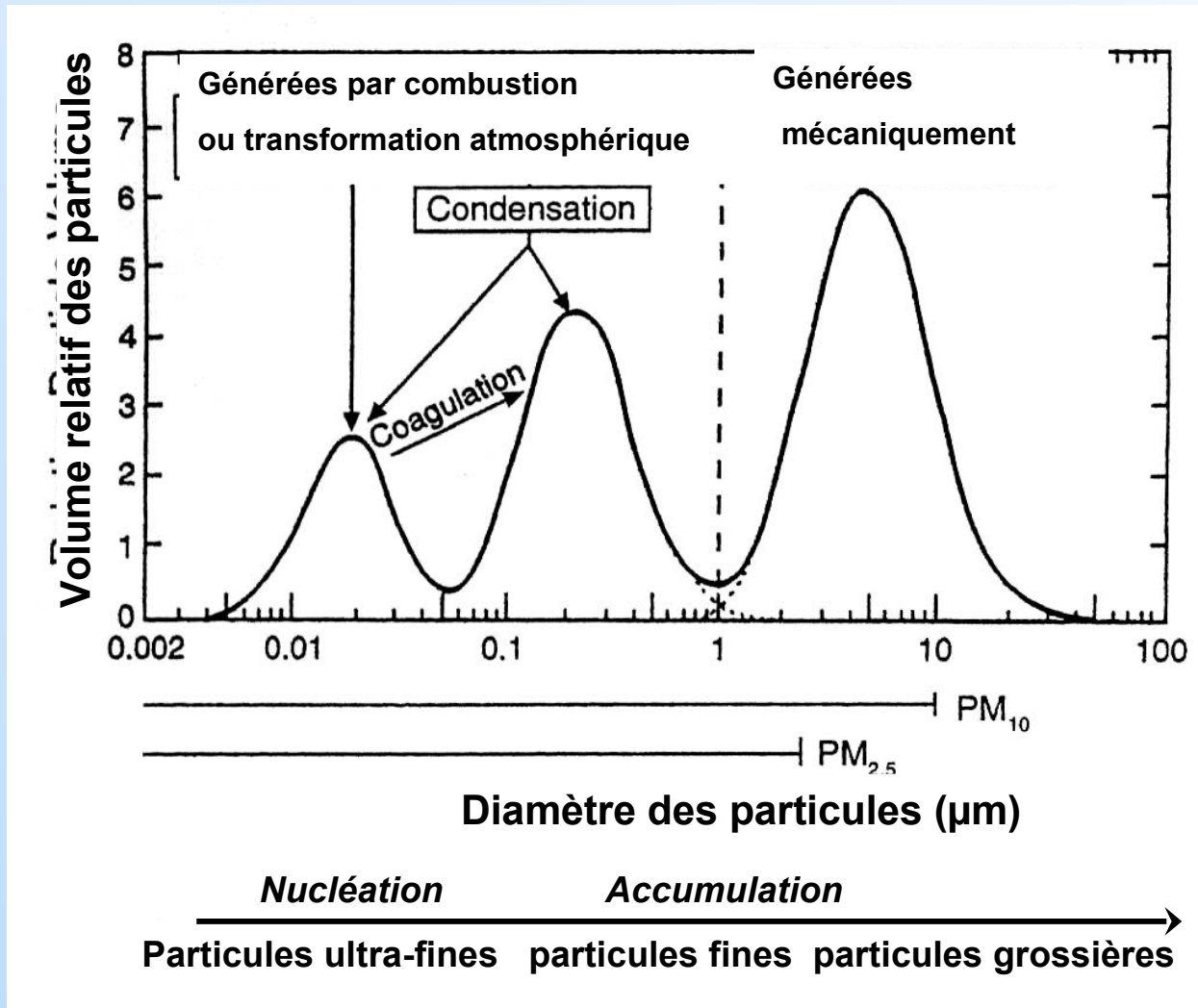


Effets sur la santé des particules et leurs mécanismes d'action

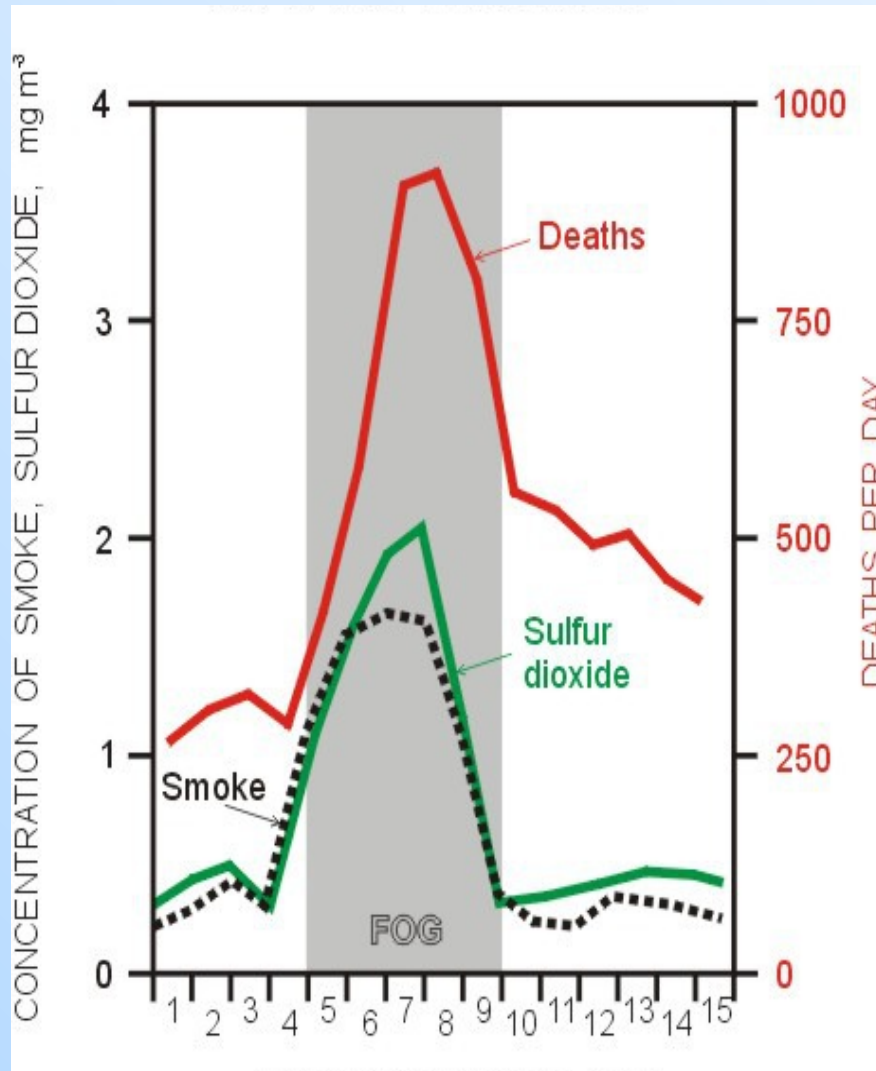
Origine des particules atmosphériques



FORMATION DES PARTICULES AMOSPHERIQUES TYPIQUES D'UN AEROSOL URBAIN



Le SMOG londonien: le « great smog » de 1952



Décembre 1952

Effets de la pollution particulaire sur la santé: Etudes épidémiologiques, effets court terme

Augmentation de la mortalité et de la morbidité pour cause cardiorespiratoire lors d'épisodes de pics de pollution particulaire

(Katsouyanni 1997, Zanobetti 2000, Schwartz 2000)

 + 15% des manifestations allergiques
(Medina et coll., 1997)

Association entre particules ultrafines dans l'air ambiant et santé respiratoire d'un groupe d'adultes asthmatiques
(Penttinen et coll 2001)

Association entre l'augmentation de la prise de médicament pour l'asthme et les particules fines et ultrafines
(Von Klot et coll 2002)

Extrapol 33, 2007, Pollution atmosphérique: particules ultrafines et santé

Etude ACS « American Cancer Society »

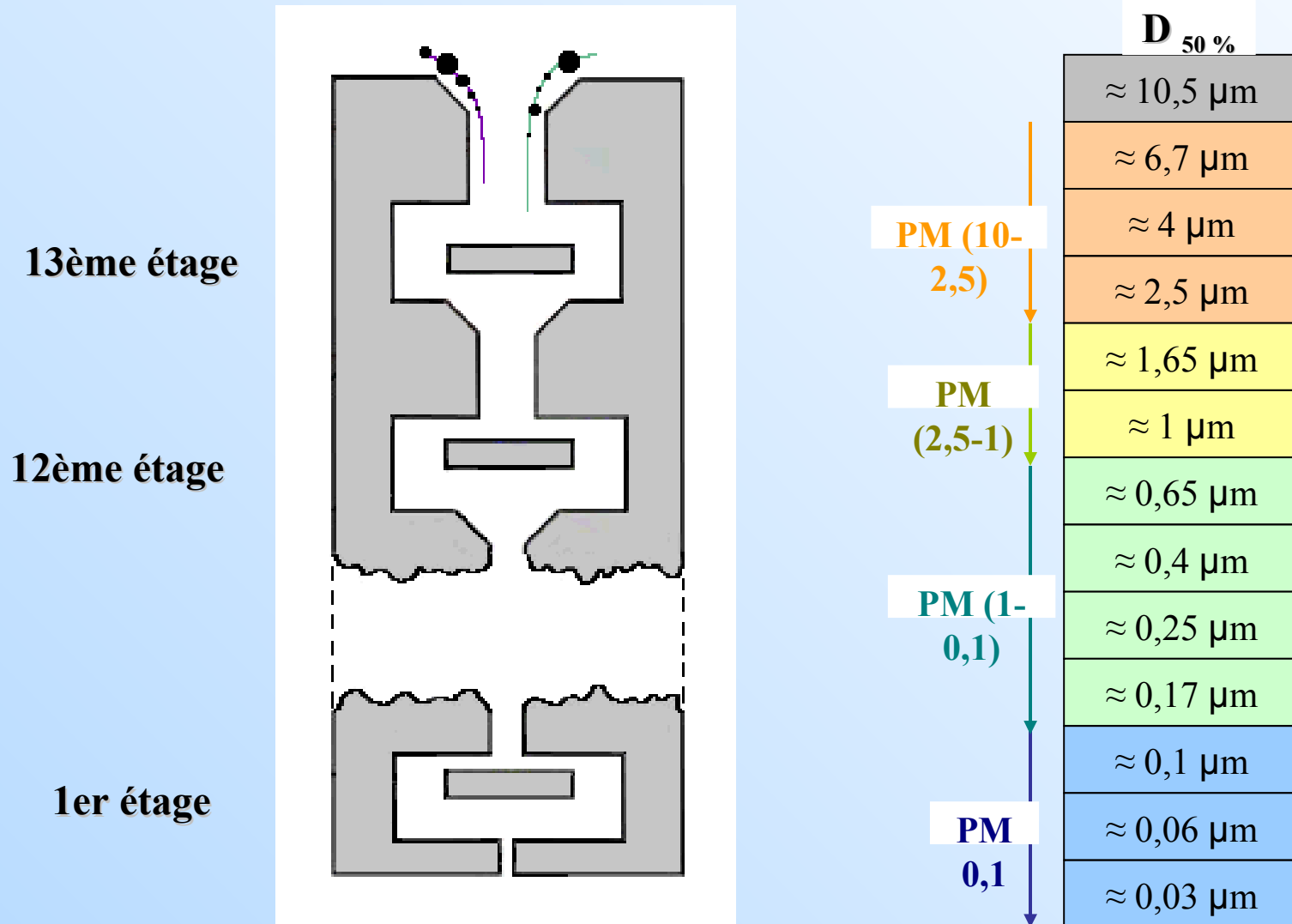
Pope et al 2002

➤ 500 000 sujets âgés de plus de 30 ans suivis pendant 16 ans

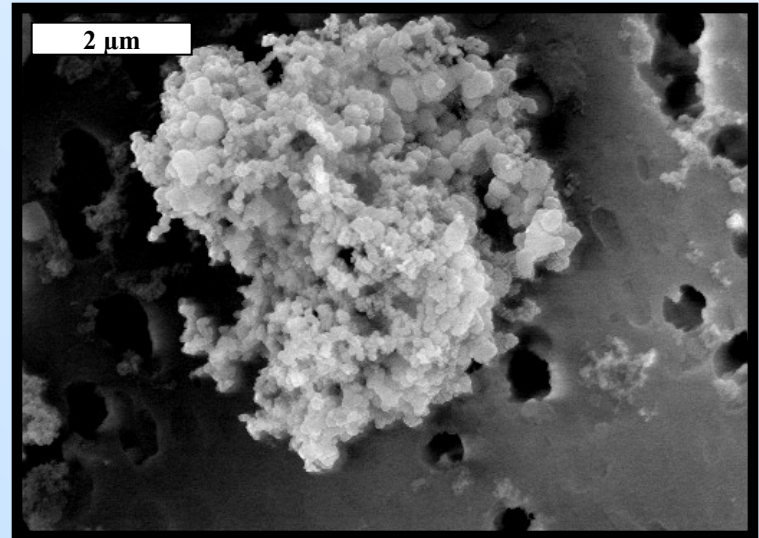
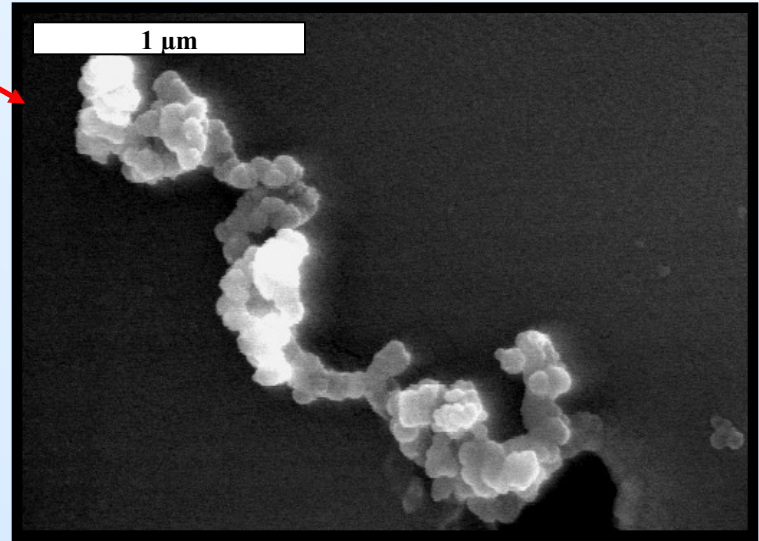
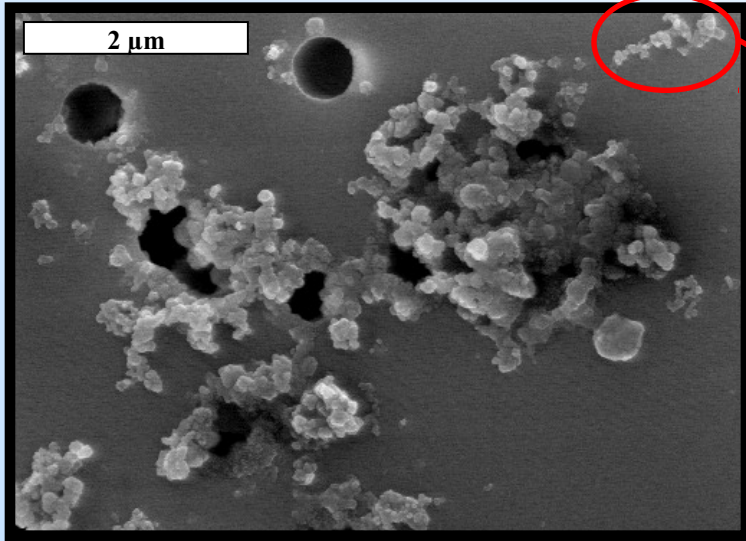
➤ Augmentation de $10\mu\text{g}/\text{m}^3$ du niveau de $\text{PM}_{2.5}$ associée à une augmentation du risque de décès

- toutes causes : + 6 %
- pour causes cardio-pulmonaires : + 9 %
- par cancer du poumon : + 8 %

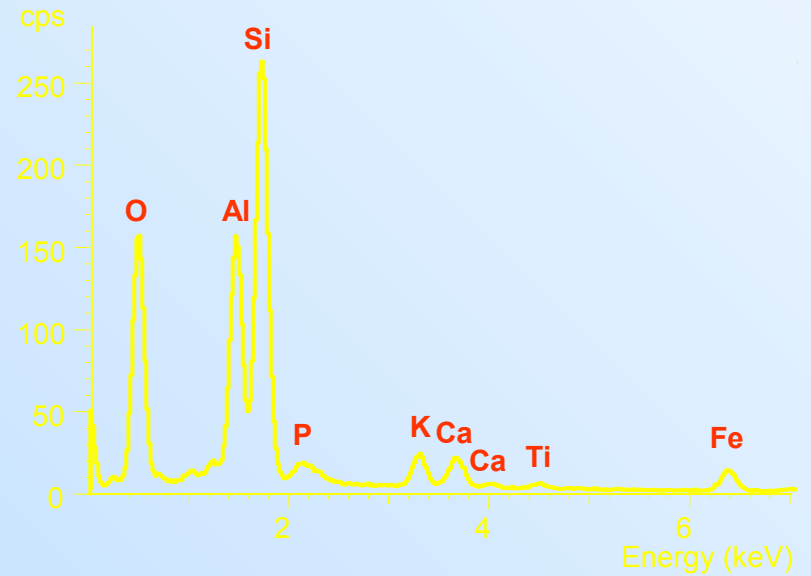
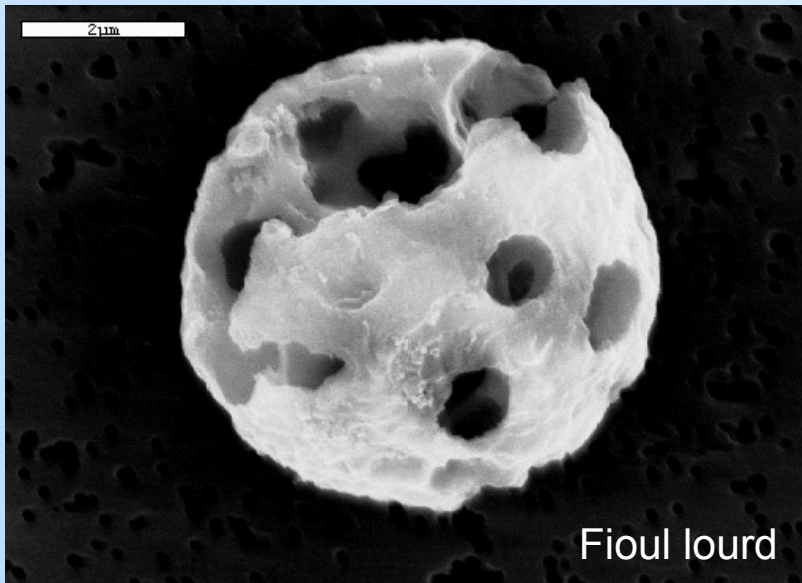
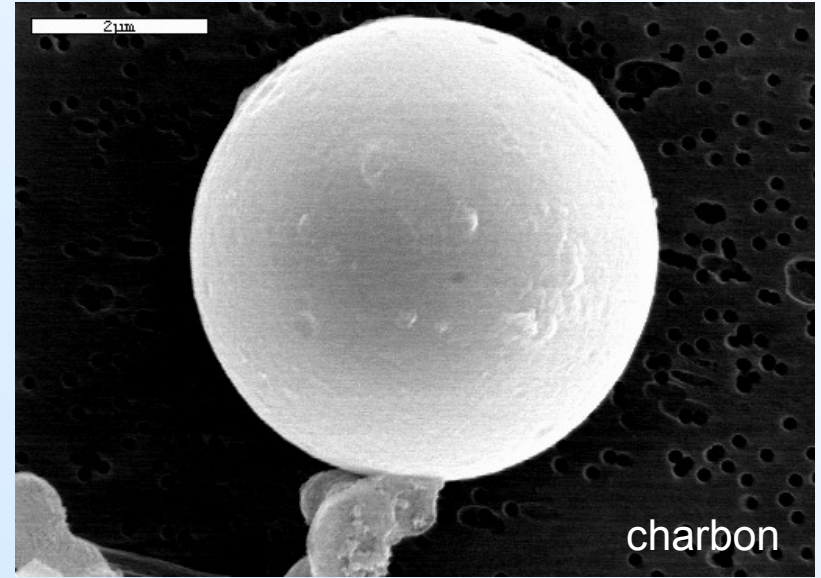
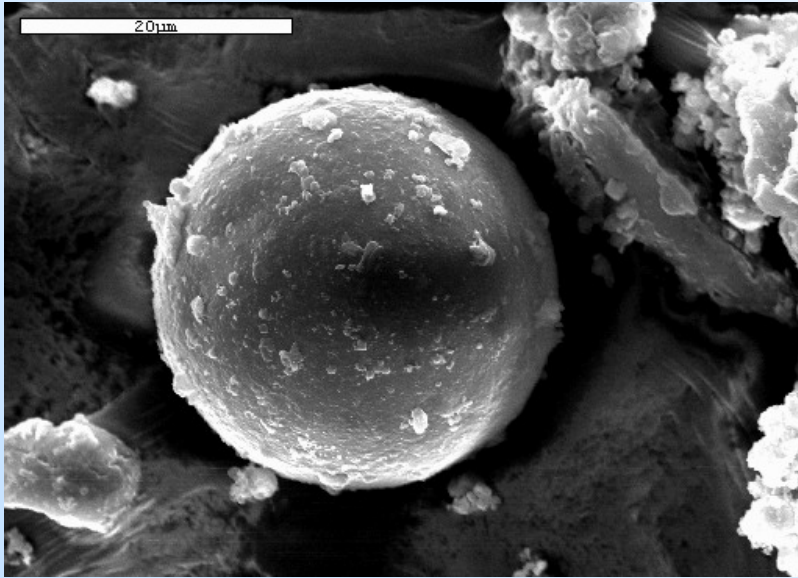
Impacteur 13 étages



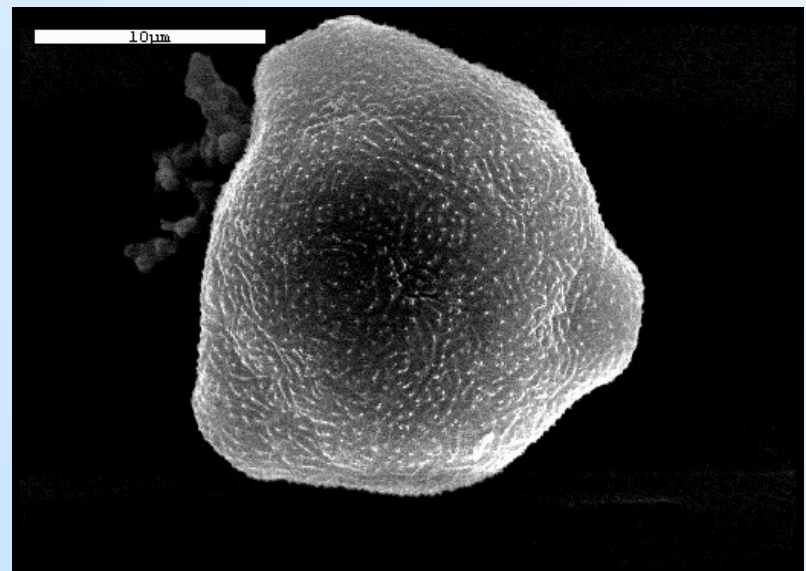
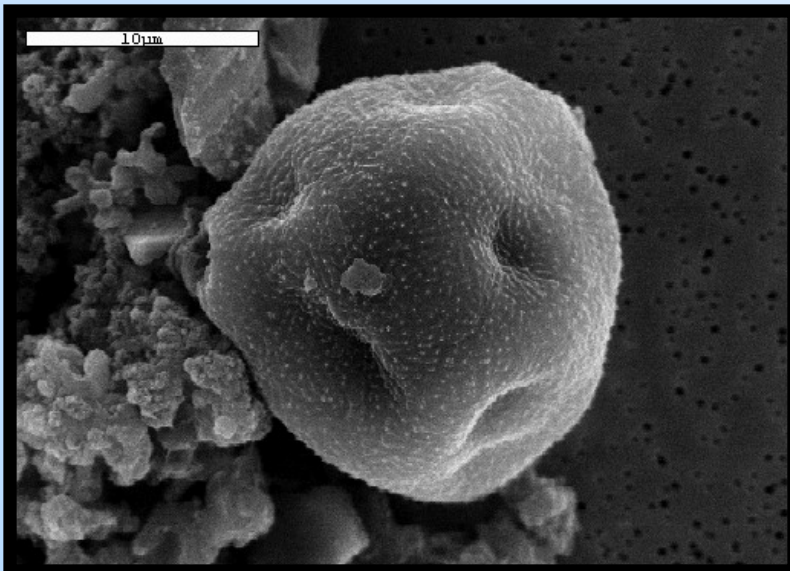
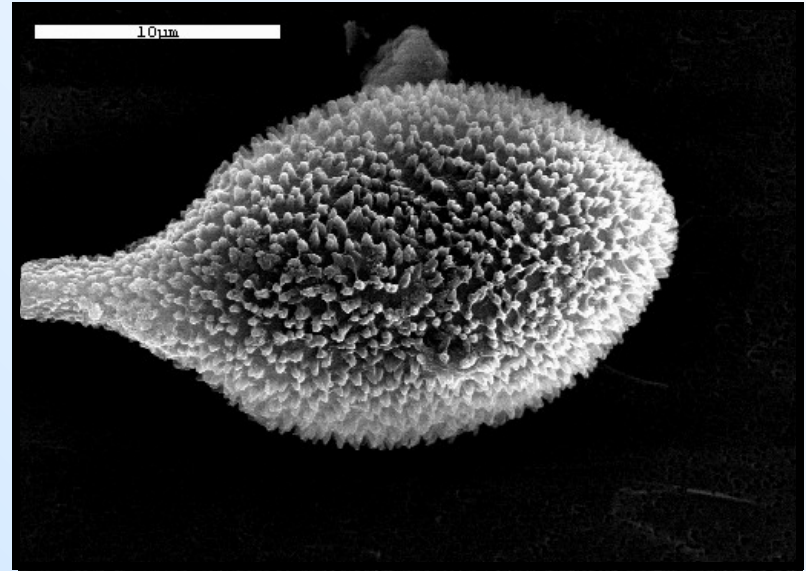
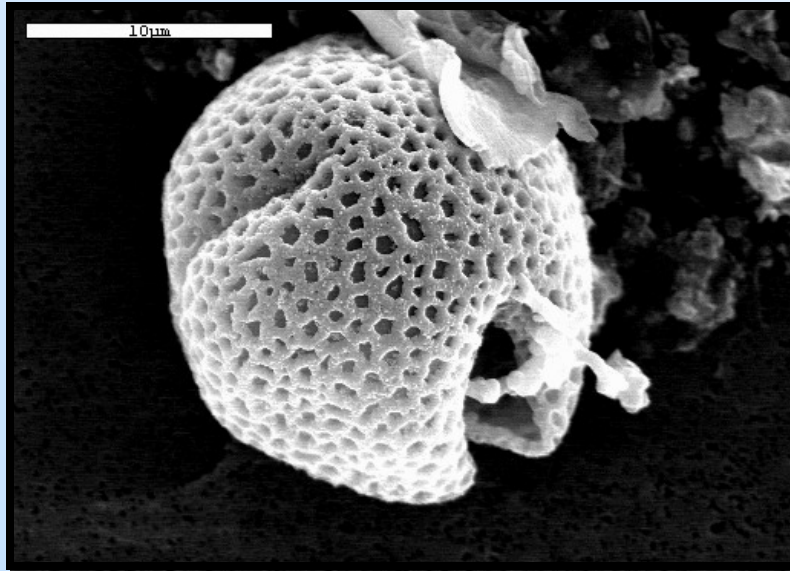
Les suies



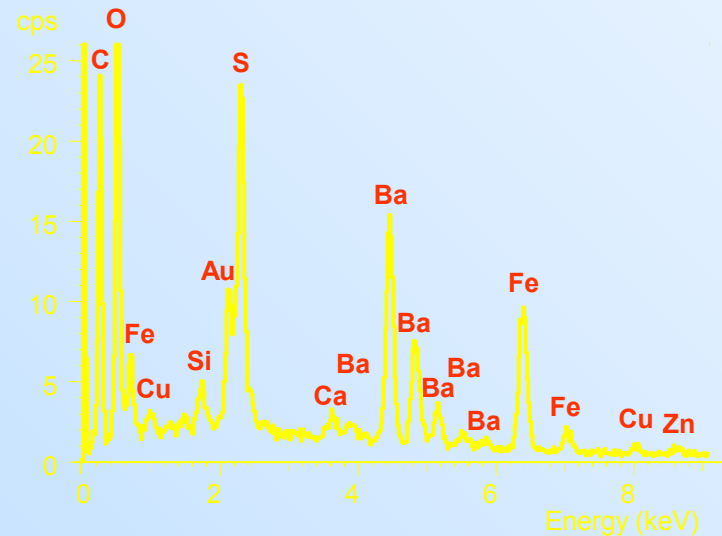
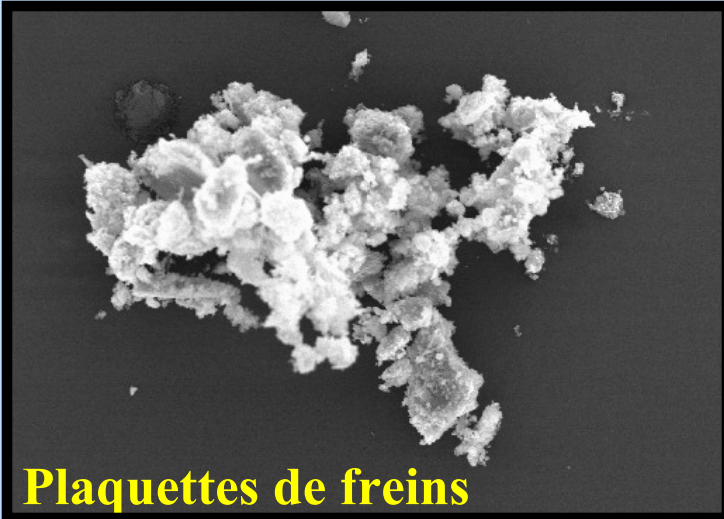
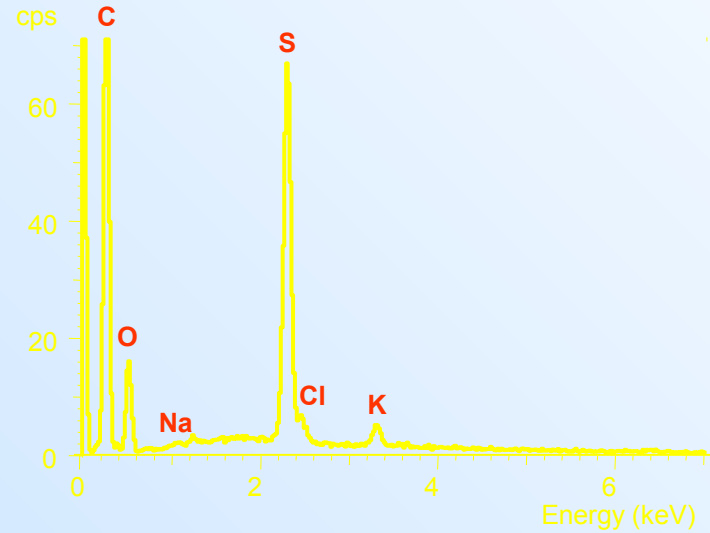
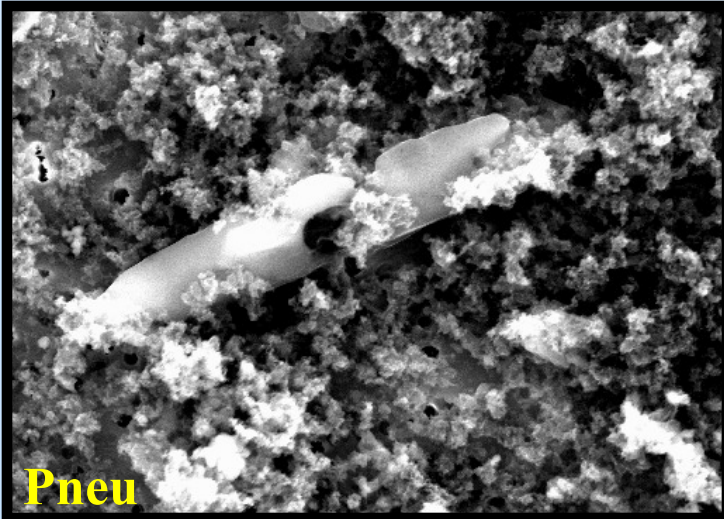
Les Fly-ash: cenaires volantes



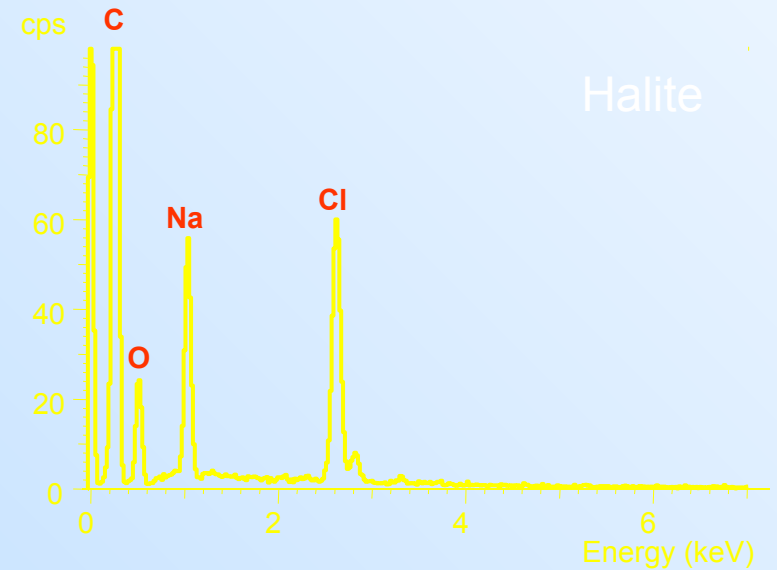
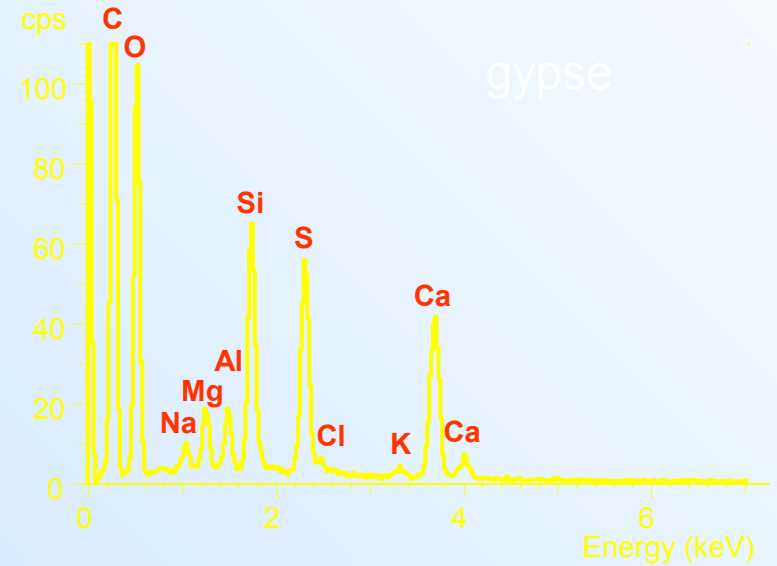
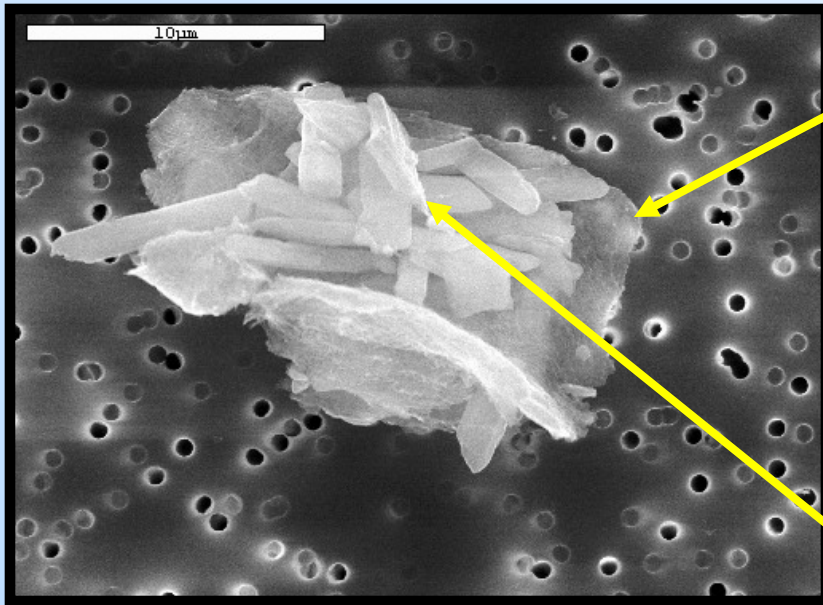
Les pollens



Les particules d'usure

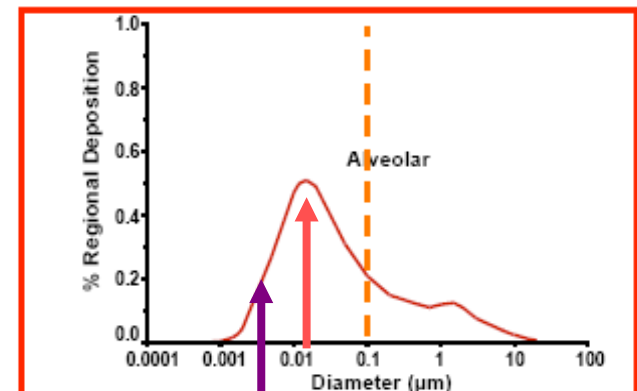
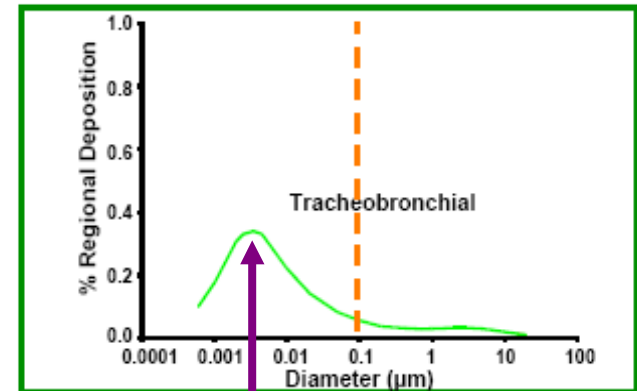
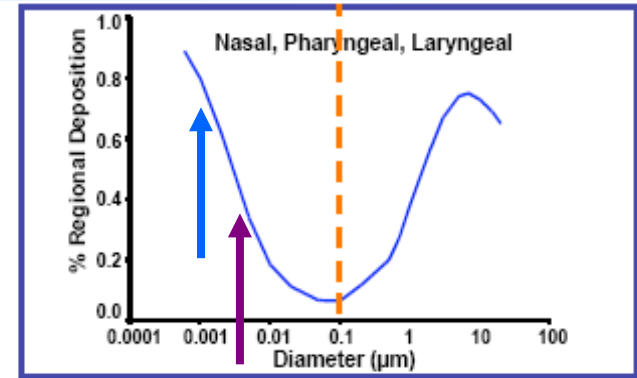
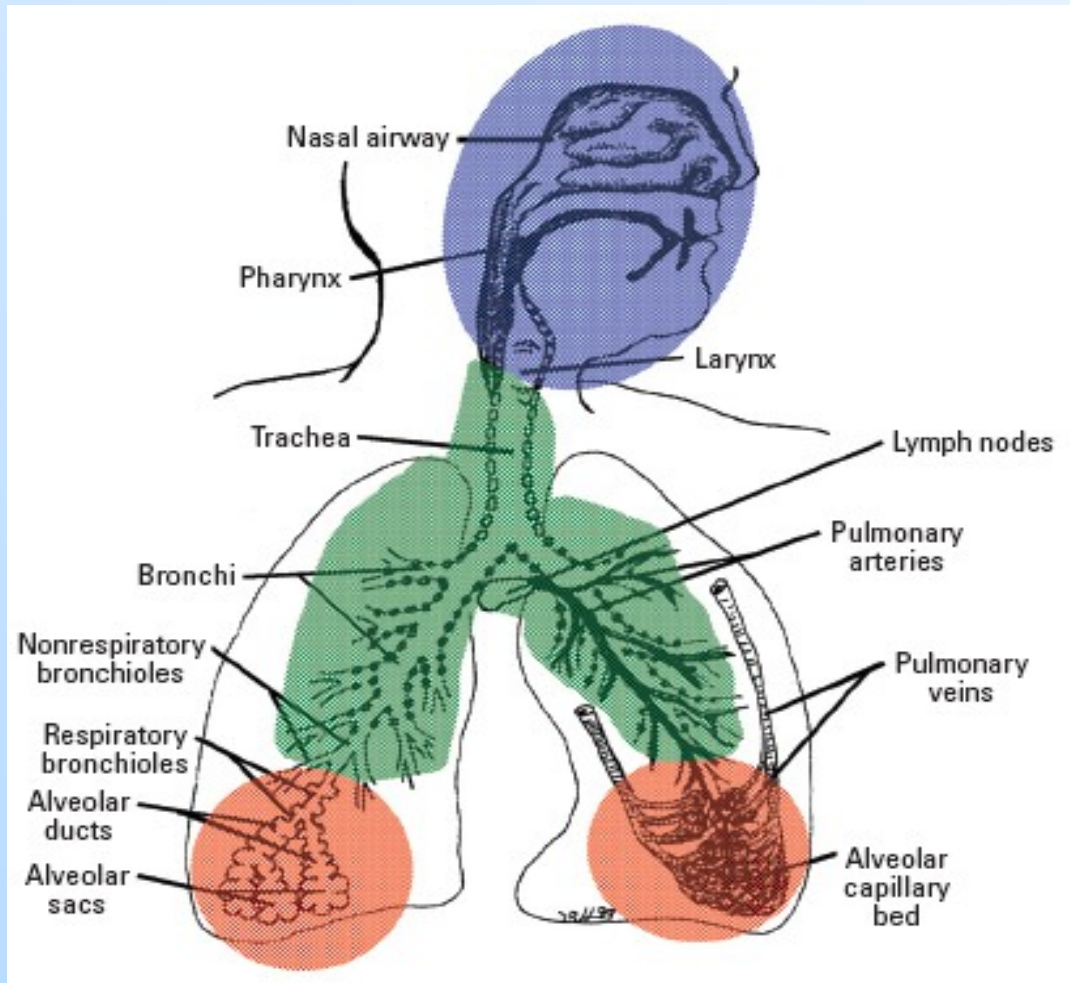


Les particules terrigènes



Déposition des PM dans l'appareil respiratoire en fonction de leur taille

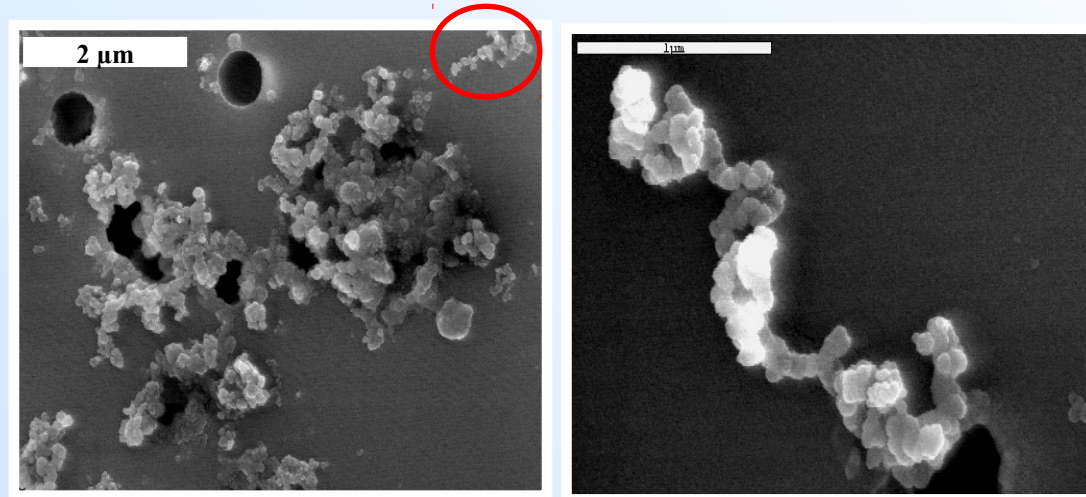
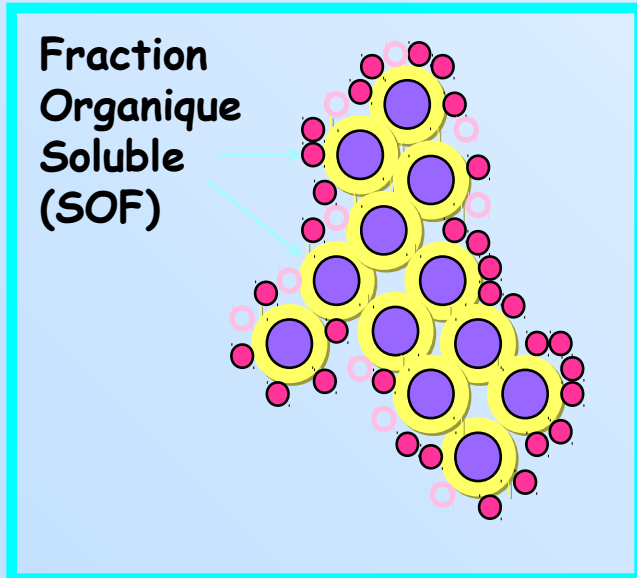
Surface 140 m²



Structure des particules fines et ultrafines

Particules Diesel

Suies (60- 90% PM2.5 trafic)



● sphères de carbone
(0.01-0.08 μm)
qui forment des agglomérats (0.05- 1 μm)

○ hydrocarbures adsorbés

● hydrocarbures condensés

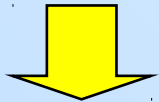
○ Sulfates hydratés

- Composés organiques
- Métaux
- Endotoxines
- Allergènes

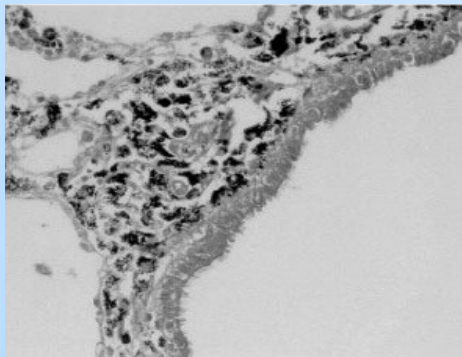
Caractéristiques des particules impliquées dans leurs effets biologiques

Taille

- Pénétration
- Déposition
- Epuration



Rétention (*Churg, 2000*)



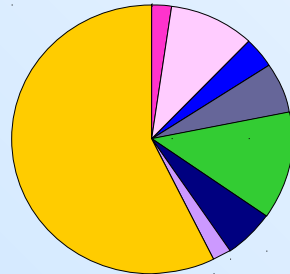
réactivité
de surface

Composition

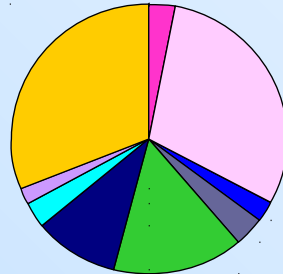
- Métaux
- Composés organiques
- Endotoxines
- Allergènes

Composition chimique en fonction de la taille

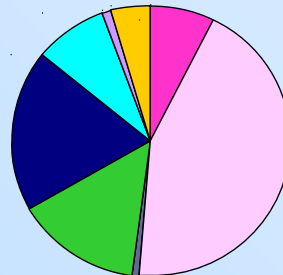
PM [10-2,5]



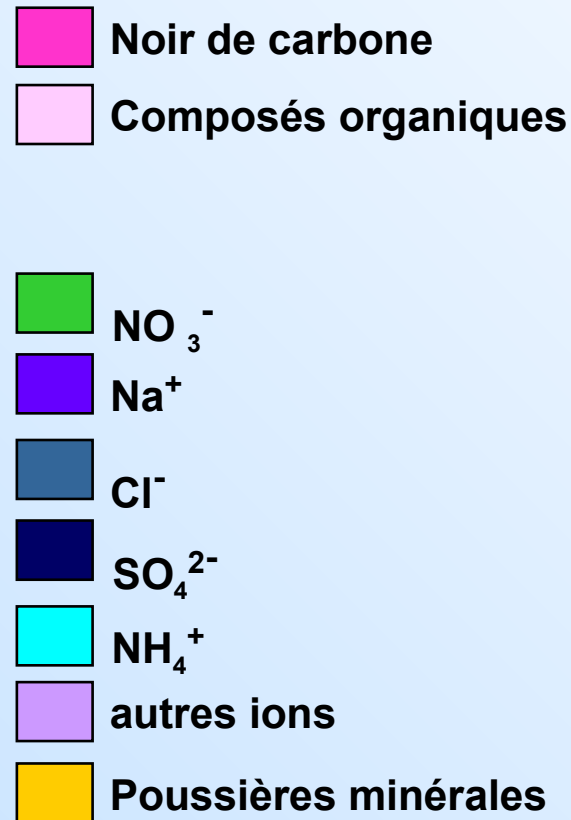
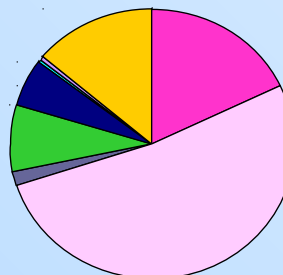
PM [2,5-1]



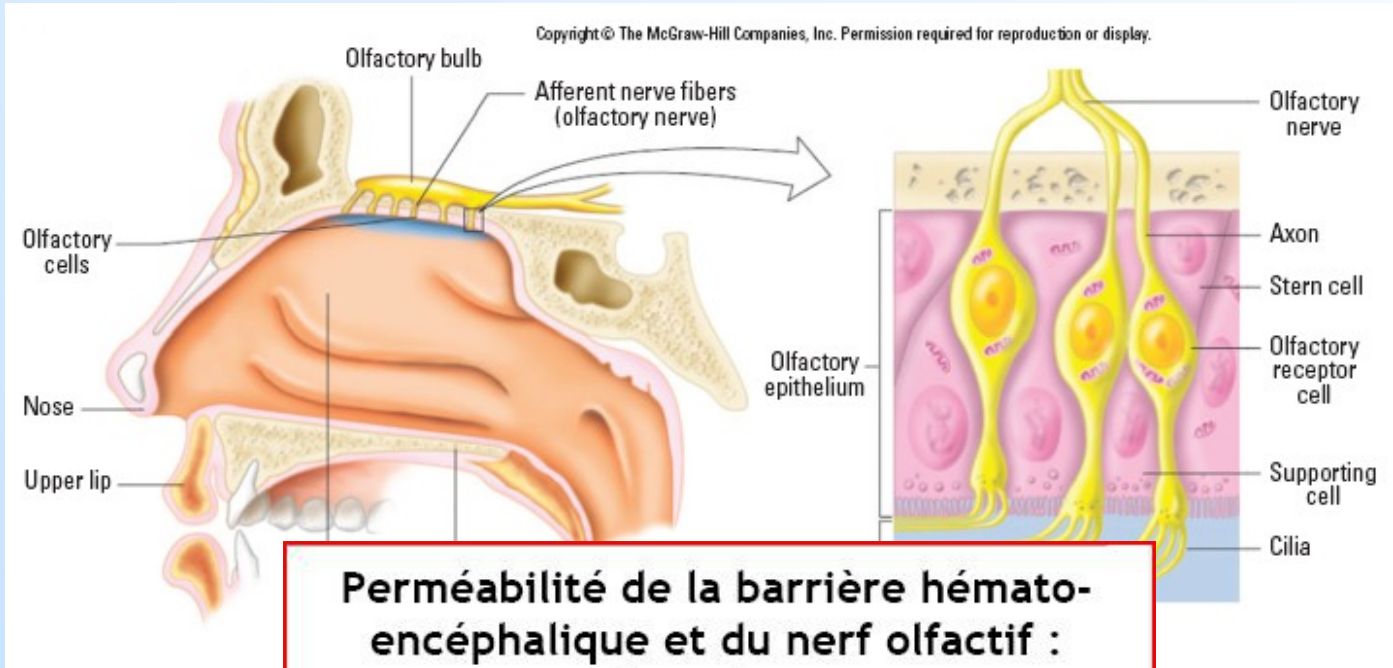
PM fines [1-0,1]



PM Ultrafines 0,1
PUF

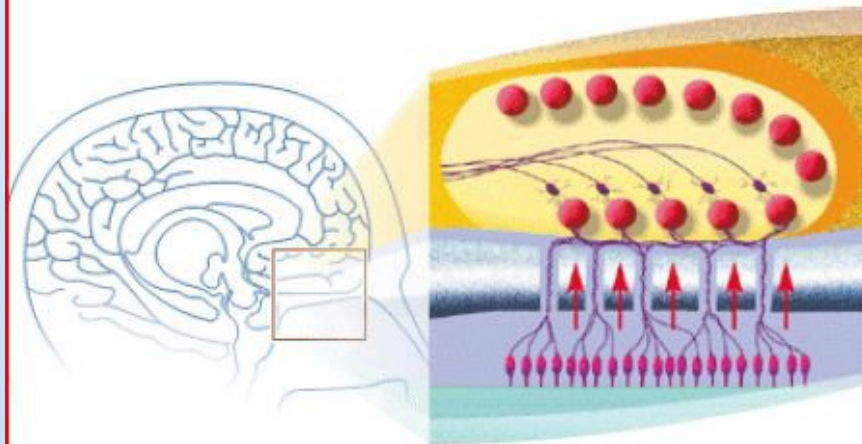


Translocation neuronale ?



Perméabilité de la barrière hémato-encéphalique et du nerf olfactif :

$$\varnothing_{NP} < 4 \text{ nm}$$



dörster et al, 2004)

kert et al, 2004)

al, 2007)

Les NPs peuvent atteindre le cerveau

Table 1 Translocation of various ENPs via respiratory pathways or via injection to blood and/or CNS

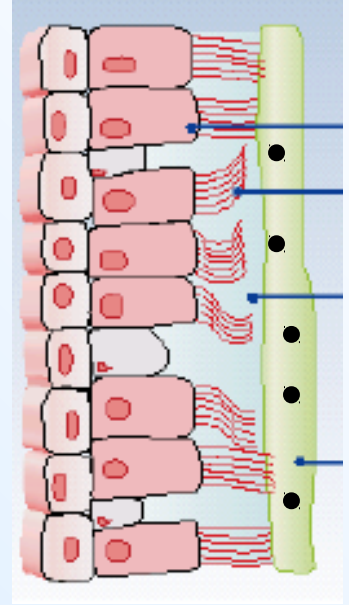
Material	Administration			ENP size (nm)**	Translocation to blood	Translocation to CNS
	Inhalation	Nasal instillation	Injection			
Carbon particles	X			4-20	X	
	X			100	X	
		X		36		X
Cu	X			23.5	X	
Ir	X			2-4	X	X
MnO ₂	X			30	X	X
	X			23	X	X
Polystyrene	X			56.4	X	X
	X			202	X	X
TiO ₂	X			20	X	
		X		80, 155 (very high doses)		X
			X	25-70 (s.c.)		X
			X	25-70 (i.v.)		X
			X	5 (i.p.)		X
Latex particles		X		20-200		X
Ag		X		70-110		X

Neurotoxicité et exposition humaine?

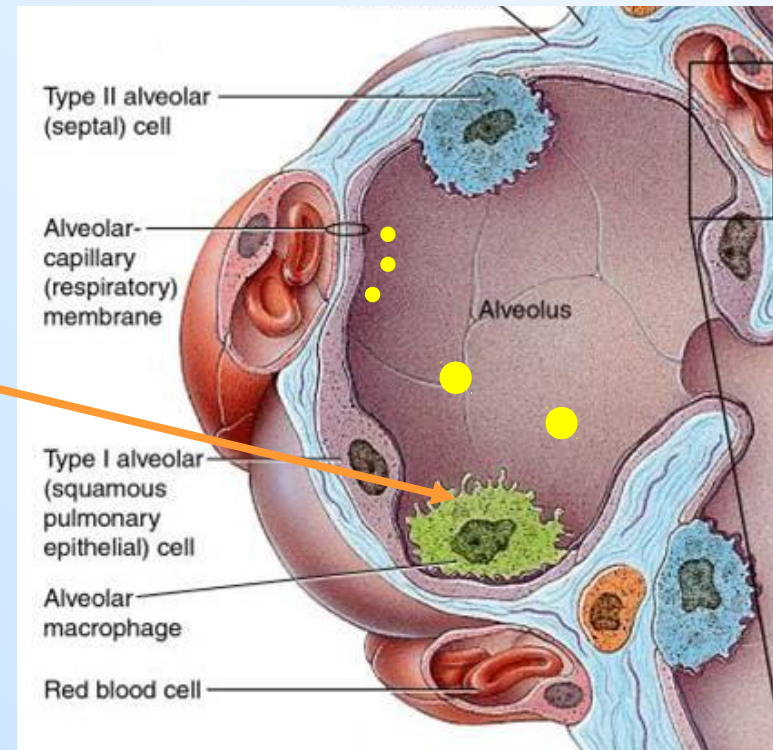
1. Inflammation du bulbe olfactif et lésions neurologiques chez des enfants de Mexico en relation avec la pollution atmosphérique particulaire fine et ultrafine (signes précoces de maladie de Parkinson)
(Calderon-Garciduenas et al 2010, 2011)
2. Mn NPs neurotoxicité chez les enfants (11-14 ans) et personnes âgées à Valcamonica (Italie) :
Troubles olfactifs et moteurs.
Augmentation de la prévalence de la maladie de Parkinson.
(Lucchini et al 2007, 2012)
3. "Early Alzheimer's and Parkinson's Disease Pathology in Urban Children: Friend versus Foe Responses—It Is Time to Face the Evidence »
(Calderon-Guarciduenas et al Biomed. Res.Int. 2013)

Interactions dans l'appareil respiratoire

Mucus dans les voies aériennes



Surfactant dans les alvéoles



PDi et REPONSE INFLAMMATOIRE

Expositions humaines contrôlées

Instillation nasale de PDi ,
Exposition à des échappements Diesel :

- ✦ cellules inflammatoires
- ✦ cytokines et chimiokines
- ✦ IgE

Instillation nasale de
PDi + allergènes :

- ✦ IgE spécifiques de l'allergène
- ☛ effet adjuvant des PDi

Hypothèse

AIR INHALE

Particules

Allergènes



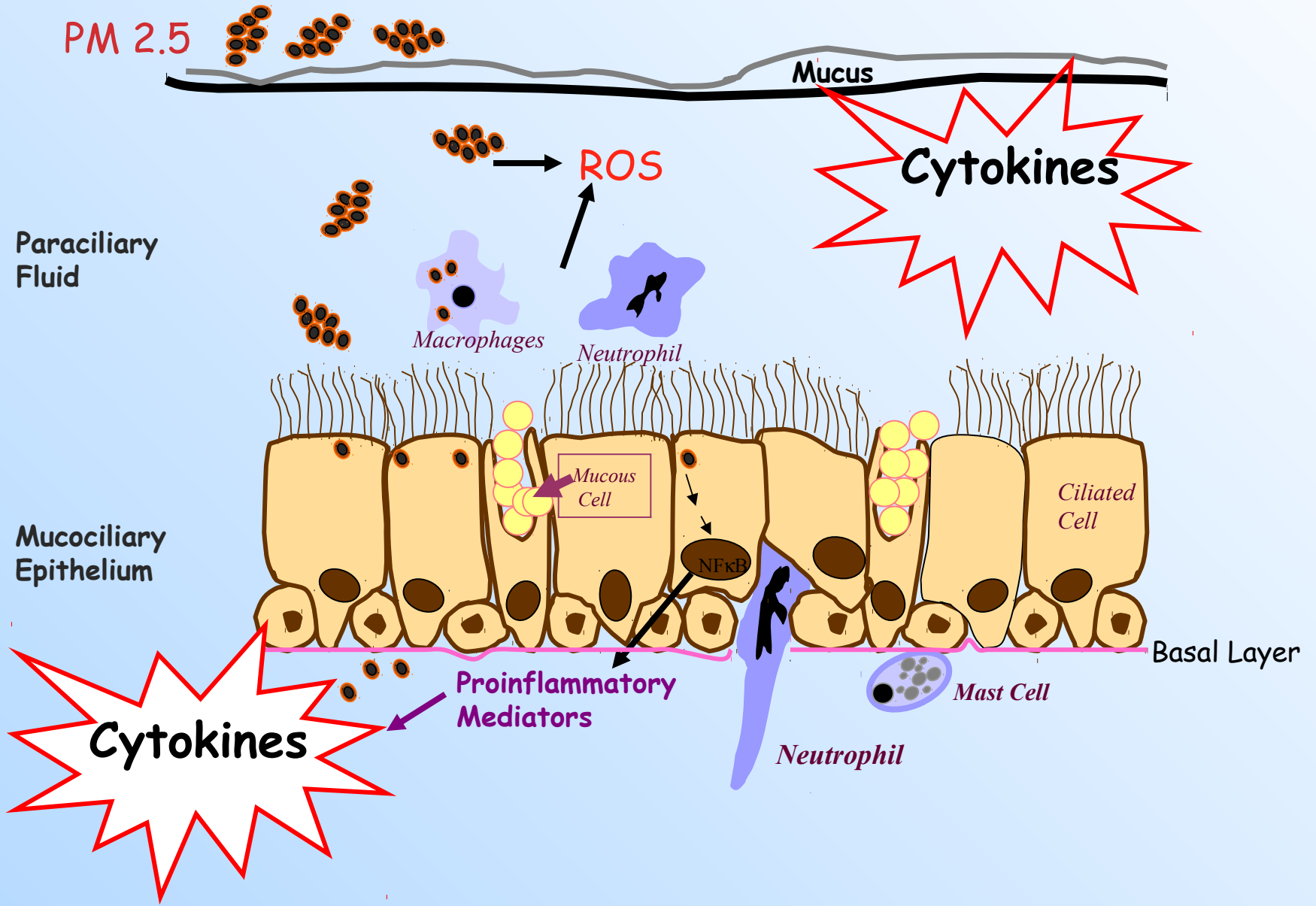
Epithélium bronchique

REPONSE INFLAMMATOIRE:
CYTOKINES

*activation des
cellules immunitaires*

REPONSE ALLERGIQUE
PRODUCTION d'IgE

Inflammation



Role de l'inflammation dans la toxicologie des particules

Combustion-derived nanoparticles

This also represents the dominant hypothesis for new nanoparticles

Free radicals / oxidative stress

Inflammation

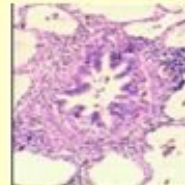
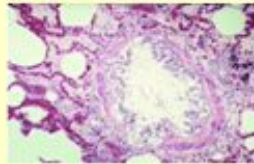
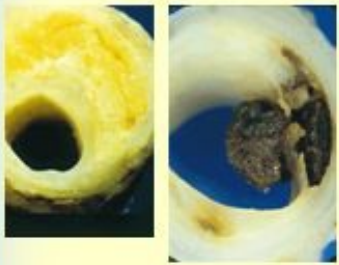
Cardiovascular disease

Asthma

COPD

Scarring

Cancer

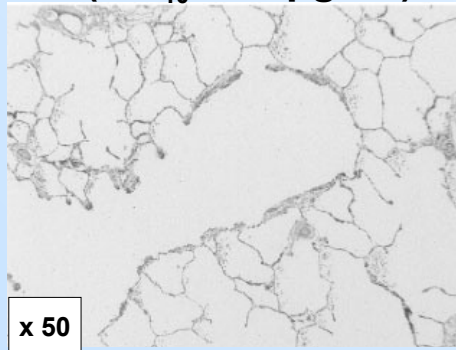


lungs

Effets sanitaires des PM: à long terme

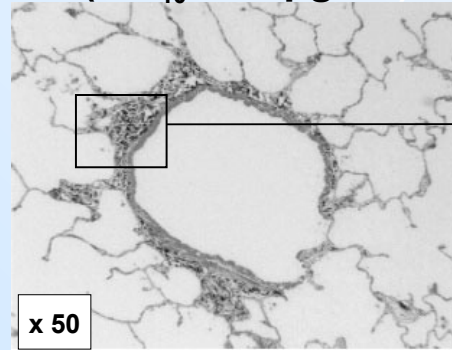
Vancouver

(PM₁₀ : 14 µg/m³)

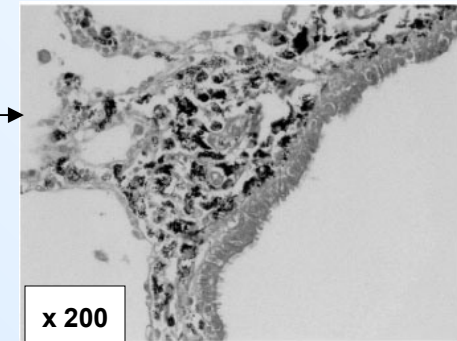


Mexico

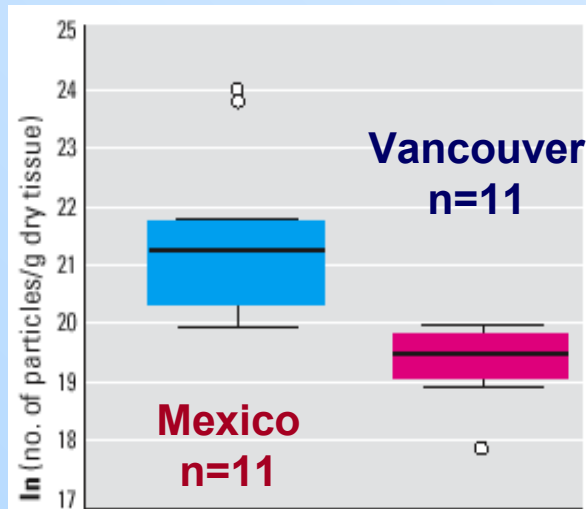
(PM₁₀ : 66 µg/m³)



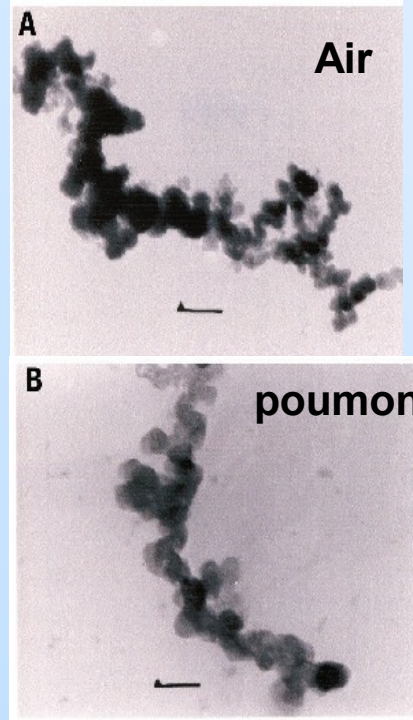
Churg et coll, 2003



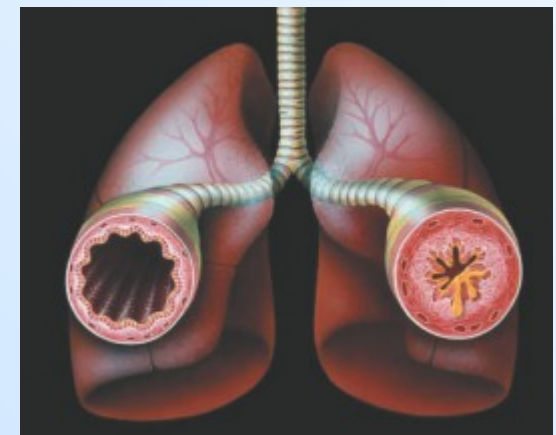
Coupes de parenchymes pulmonaires



Brauer et al, 2001



➤ persistance de particules atmosphériques (Ø : 0,4 µm)



➤ remodelage des parois des voies respiratoires

PARTICULES DIESEL et CANCEROGENESE

- Etudes de mutagenèse
 - ✦ extraits organiques de PDi +
- Etudes chez l'animal:
 - ✦ induction de tumeurs varie selon l'animal:
 - rat +
 - hamster—

MECANISMES ?

Génétique

HAP: adduits

EAO

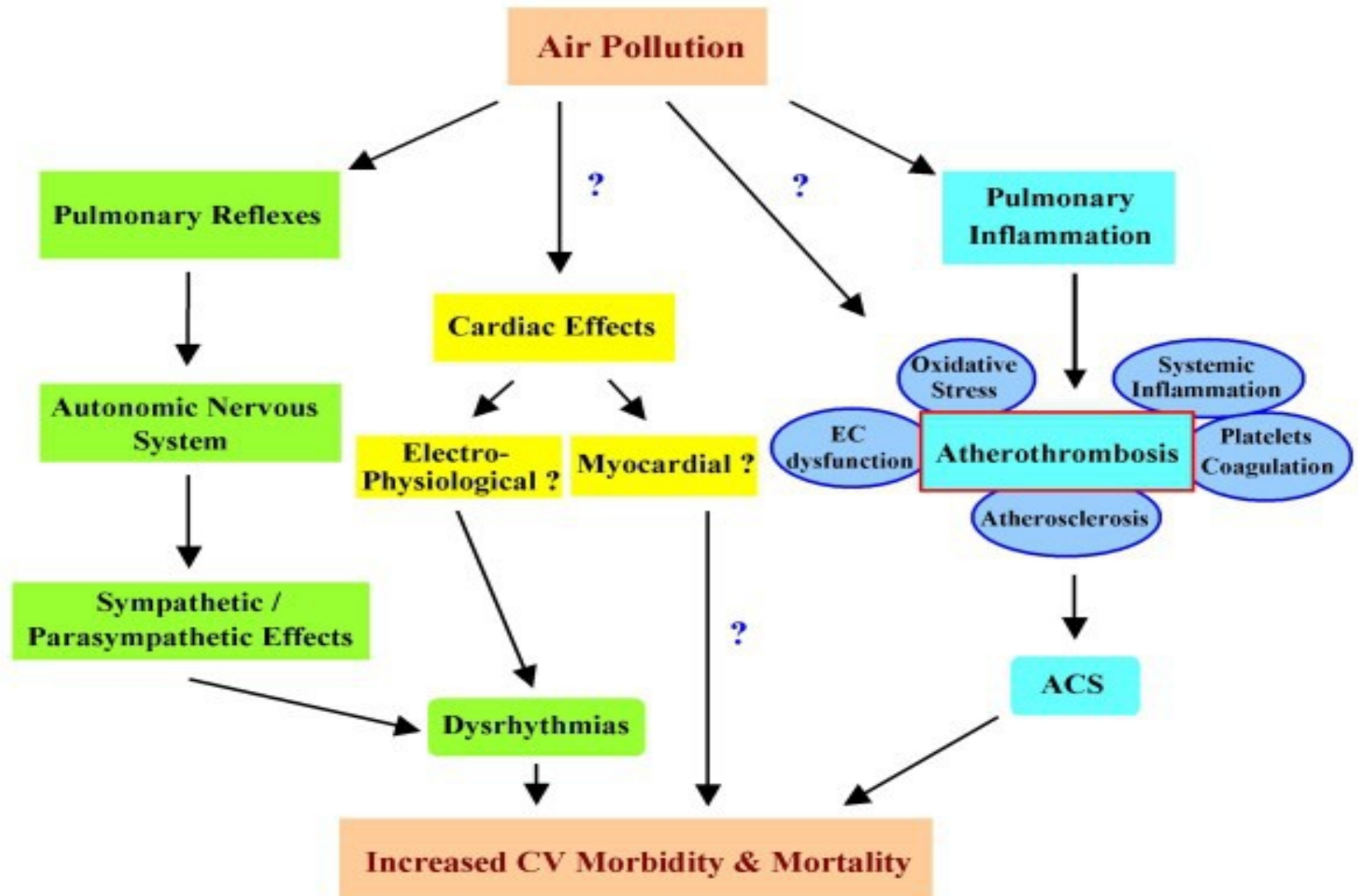
Epigénétique

réponse inflammatoire

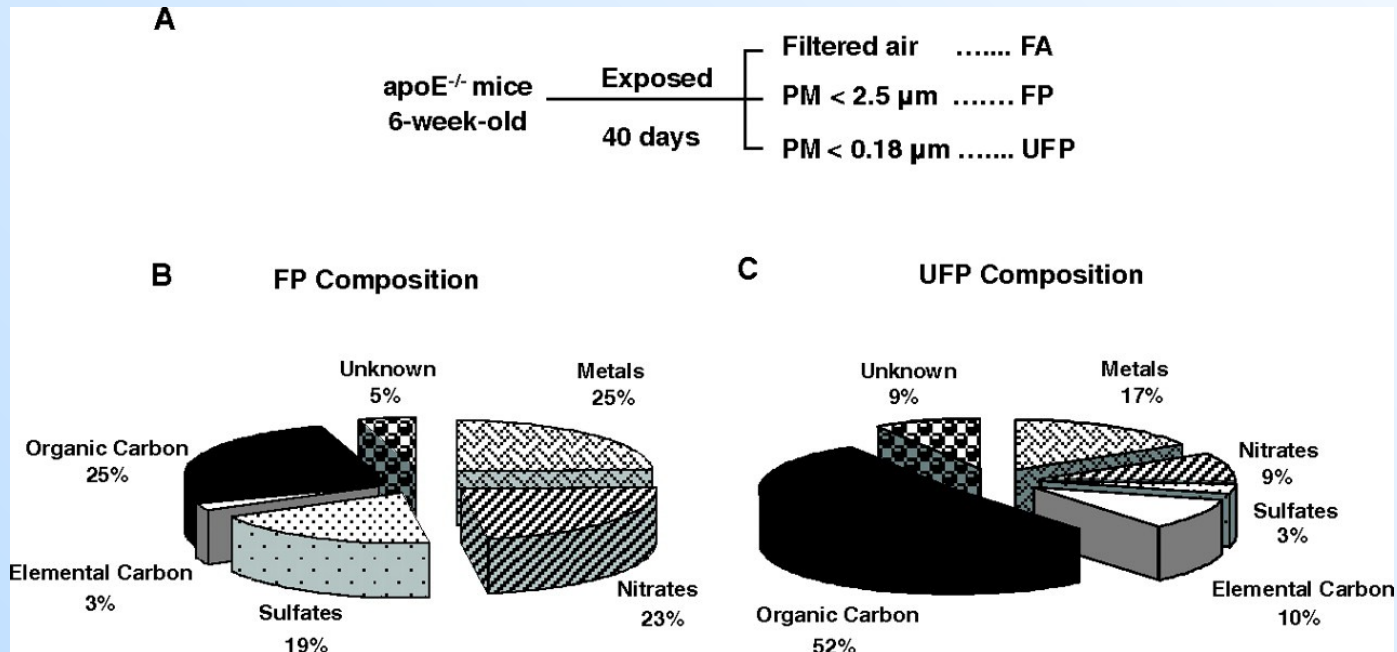
prolifération épithéliale

➤ **Groupe 1: cancérigène certain (IARC)**

PM, Inflammation pulmonaire et athérotrombose: quels mécanismes?

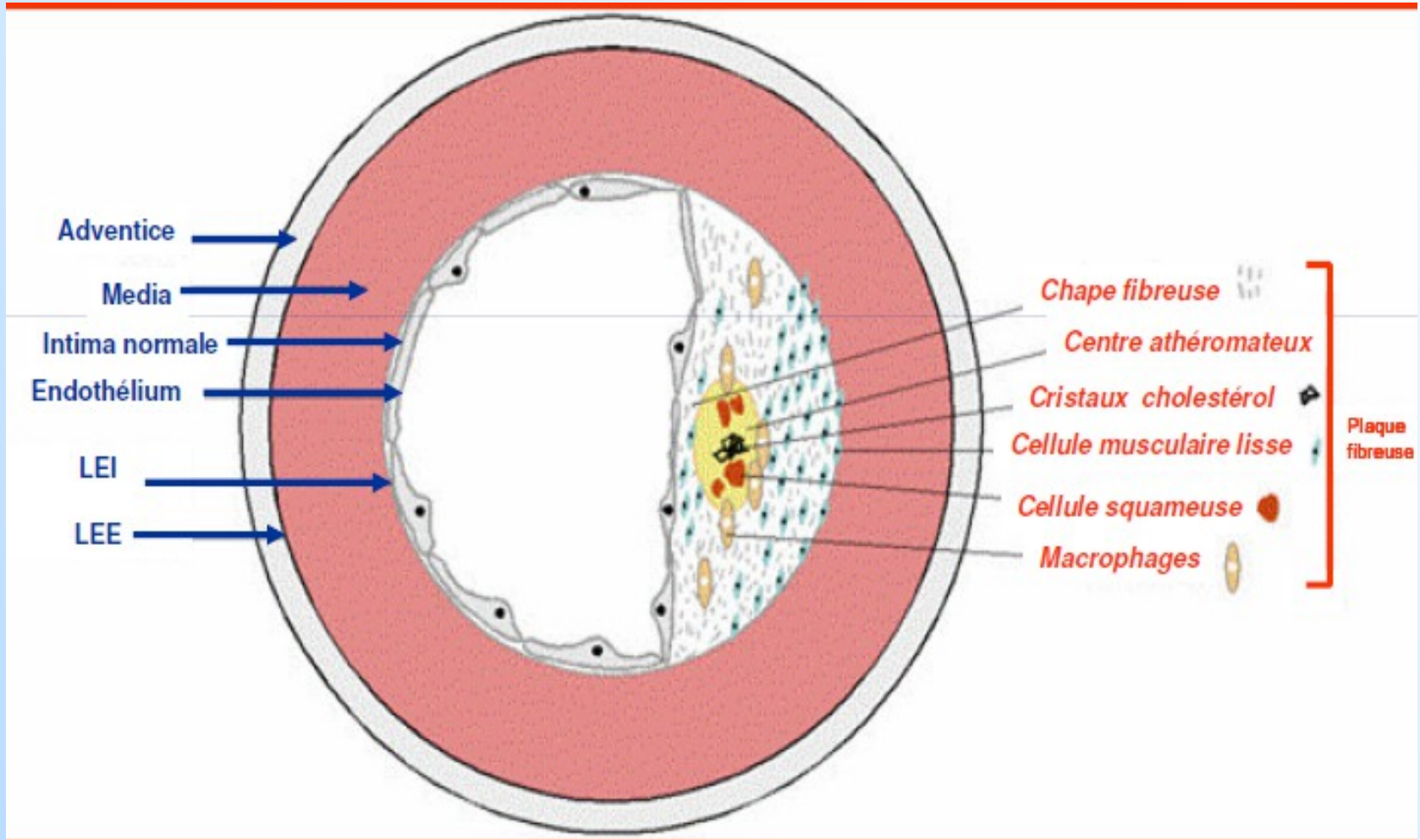


Effet des grosses (FA) fines (FP) et ultrafines (UFP) particules sur des souris sensibles aux pathologies cardiovasculaires (apoE^{-/-})

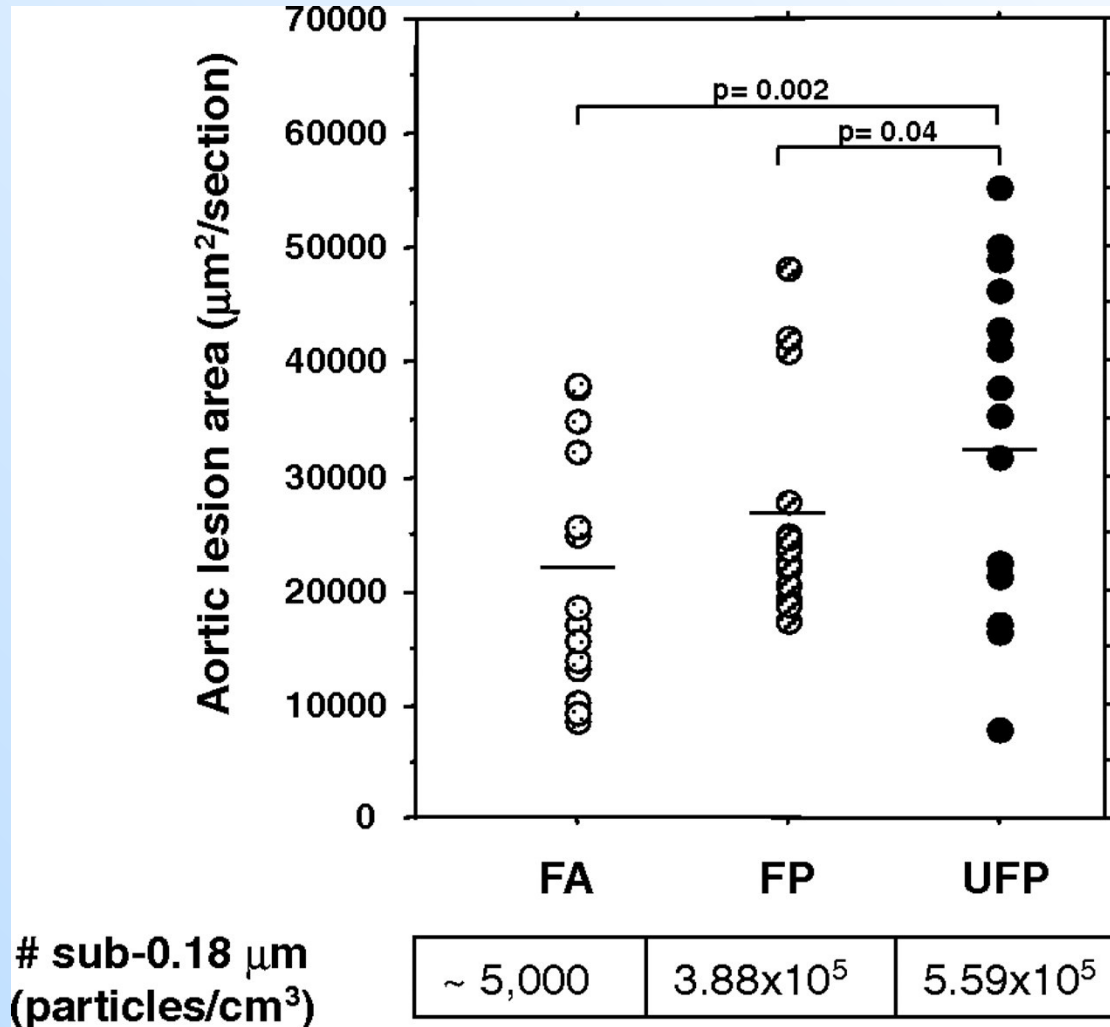


Araujo, J. A. et al. Circ Res 2008;102:589-596

Schéma de la plaque d'athérome dans une artère



UFP is the most proatherogenic PM fraction



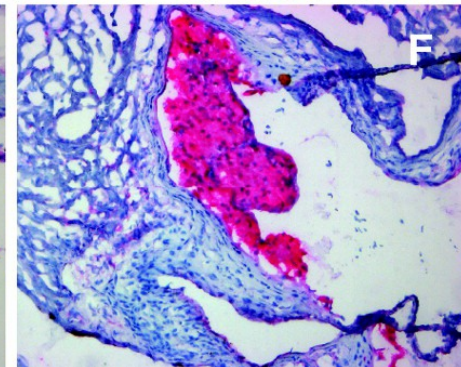
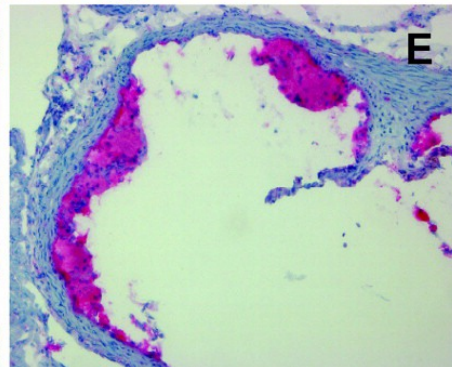
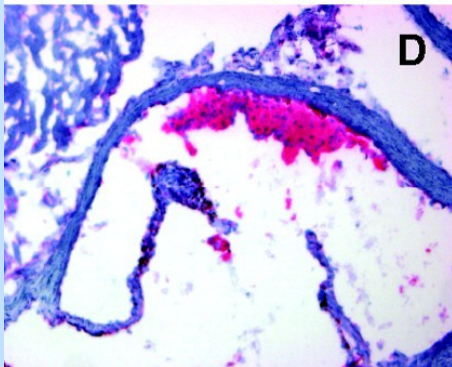
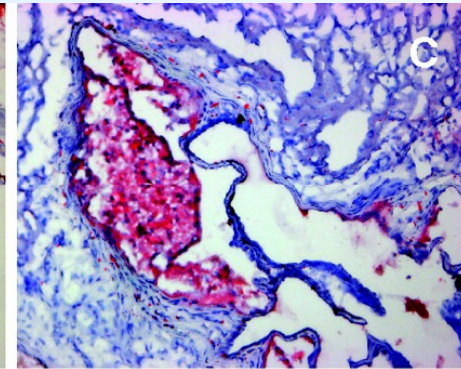
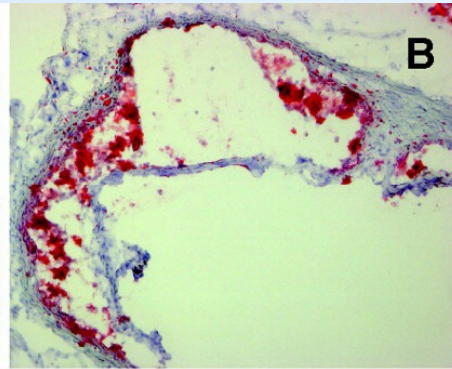
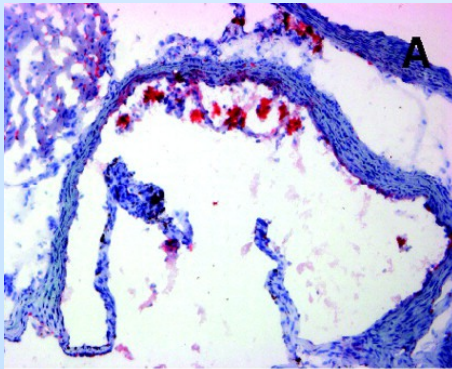
Araujo, J. A. et al. Circ Res 2008;102:589-596

Representative histological photomicrographs of aorta with atherosclerotic lesions

Coarse PM

Fine PM

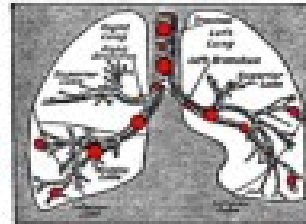
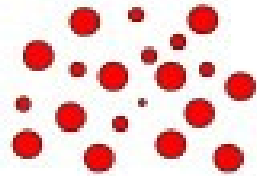
Ultrafine PM



Araujo, J. A. et al. *Circ Res* 2008;102:589-596

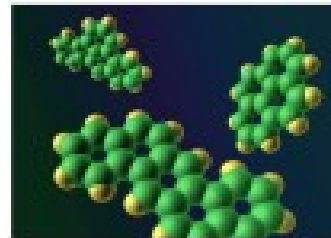
Why are the smallest particles more proatherogenic ?

Greater particle number and lung retention



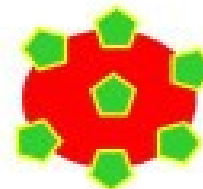
Greater content of prooxidant compounds

↑ 2X



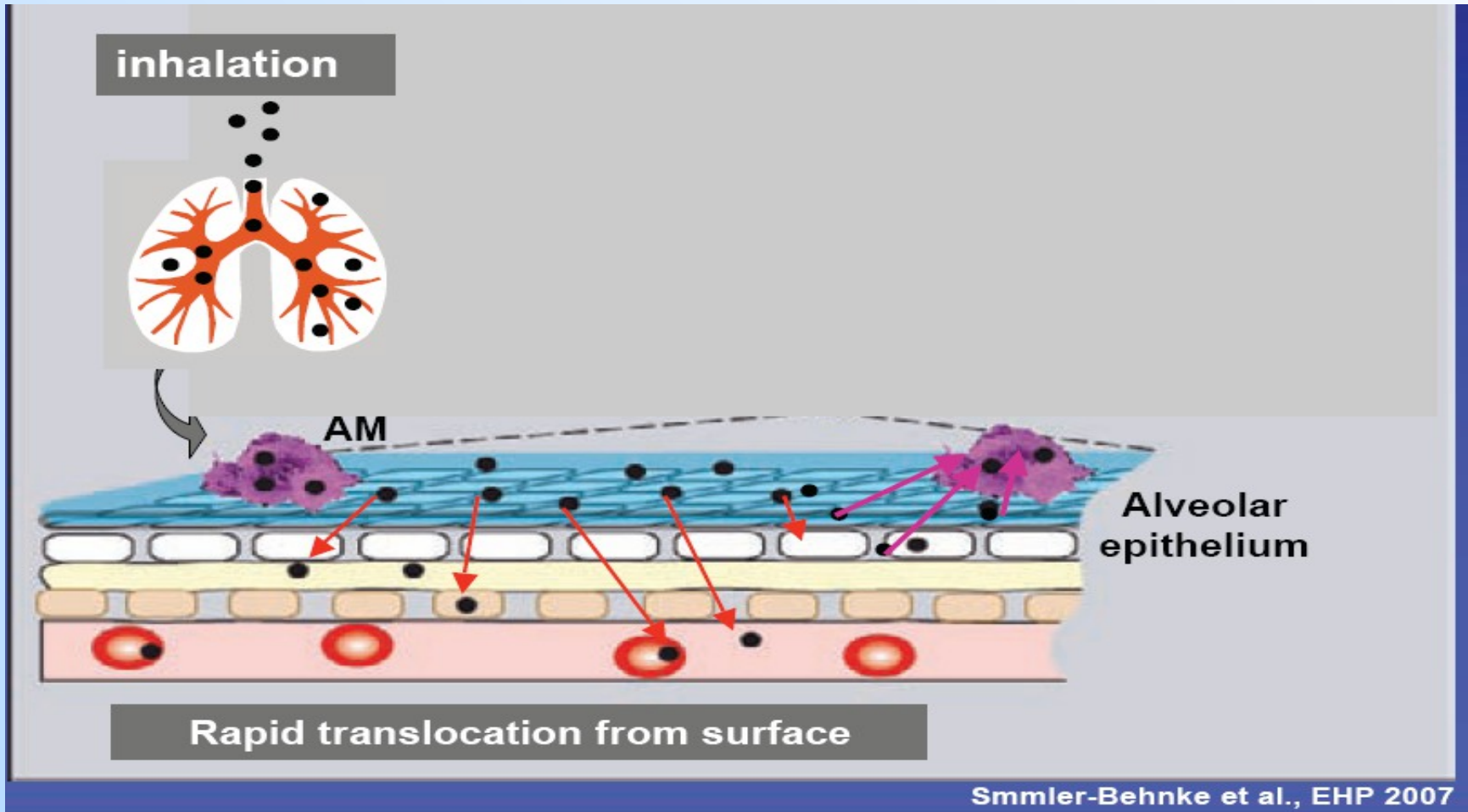
Greater bioavailability of reactive compounds

↑ 2X

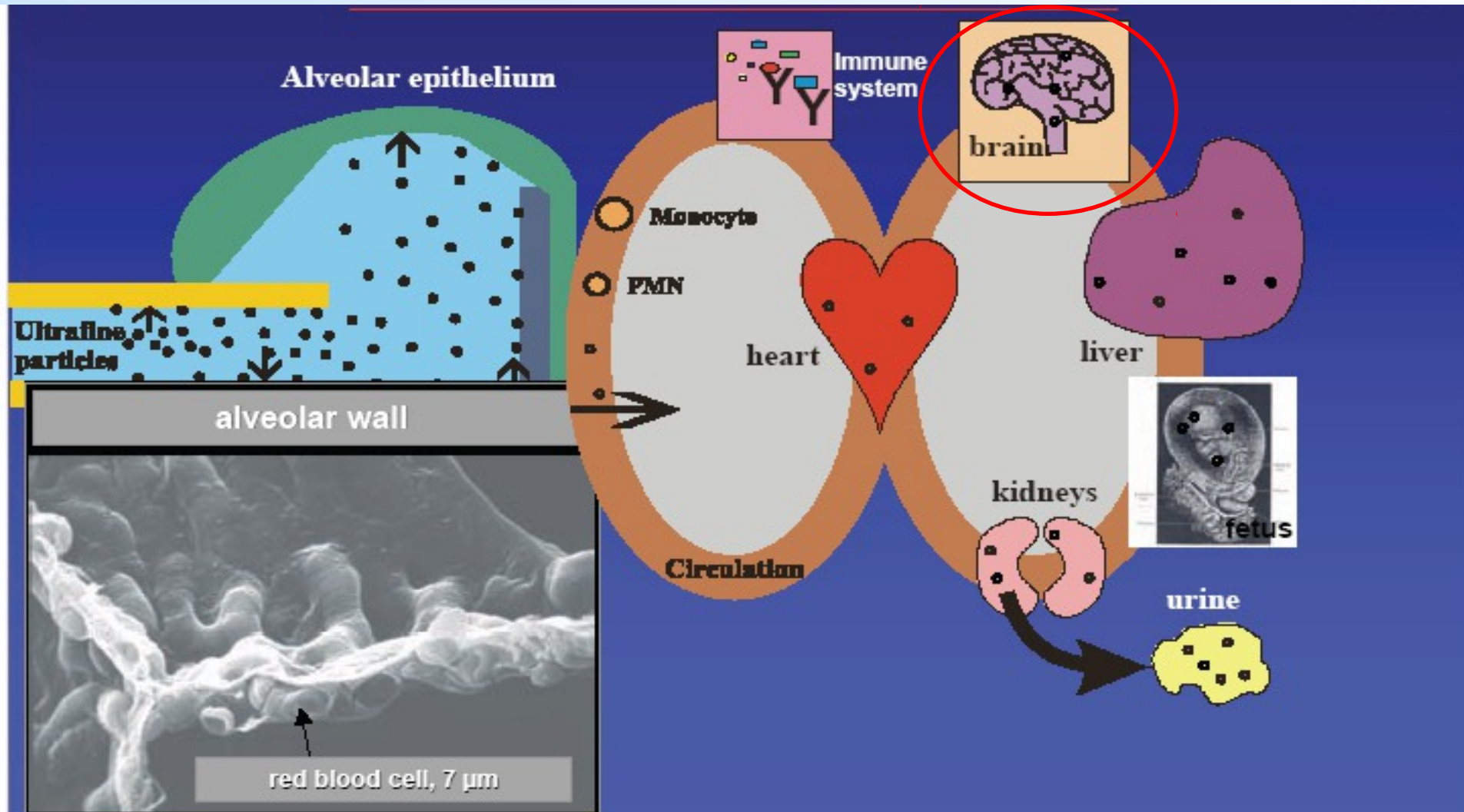


Surface-to-mass ratio

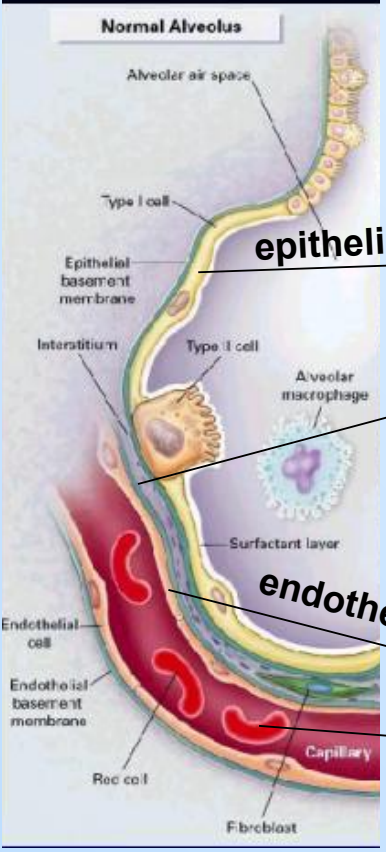
Transport des PM à travers la barrière pulmonaire?



Hypothèse de transfert des NPs à partir du poumon



Localisation de TiO₂ NP (22 nm) 1h après l' inhalation par le rat

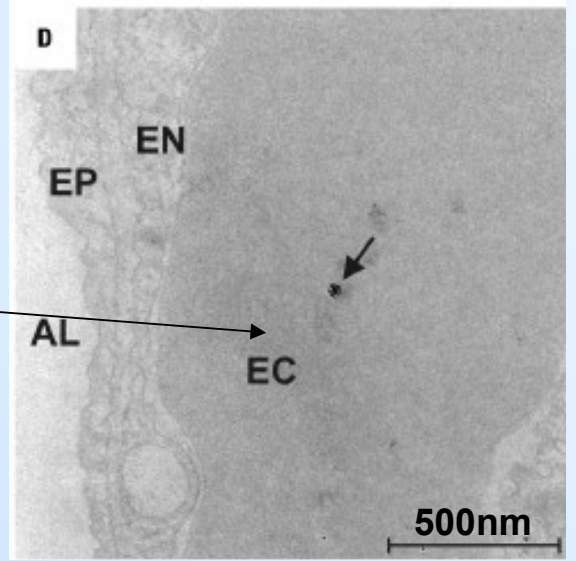
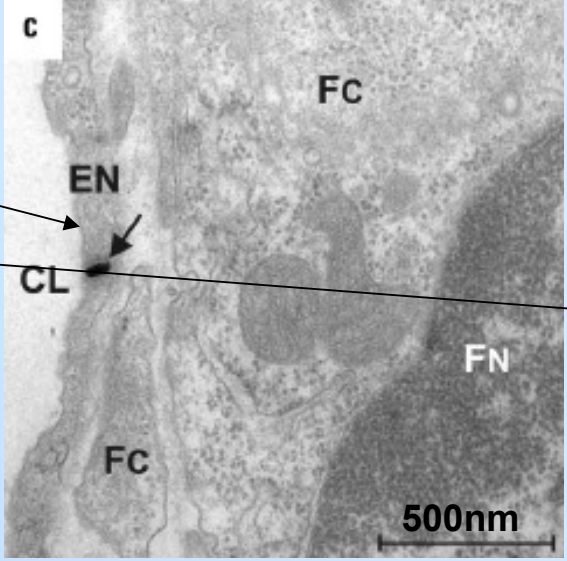
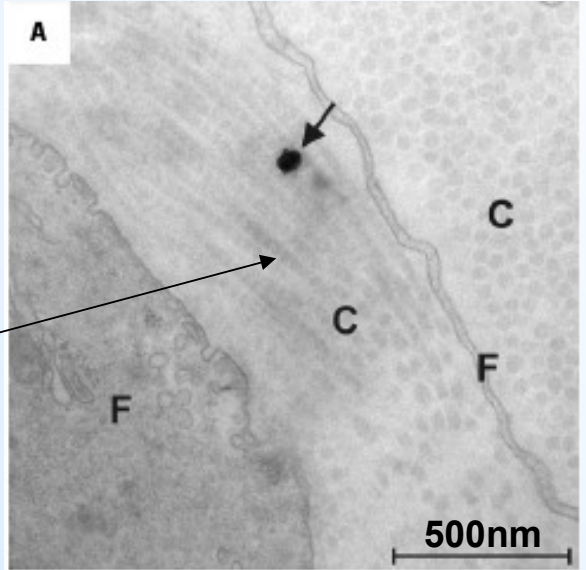
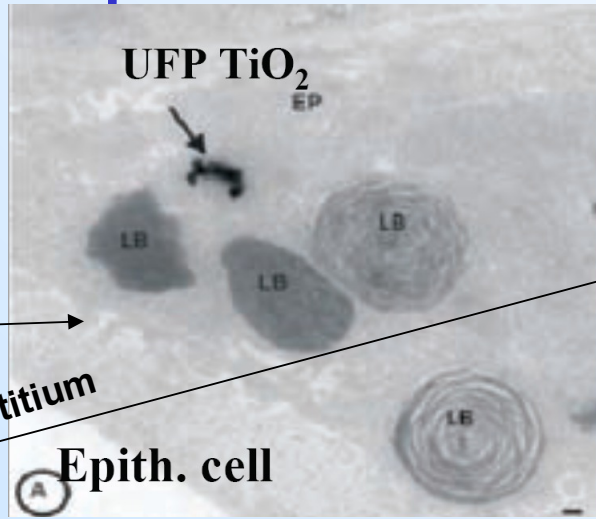


epithelial cell

interstitium

endothelial cell

red cells

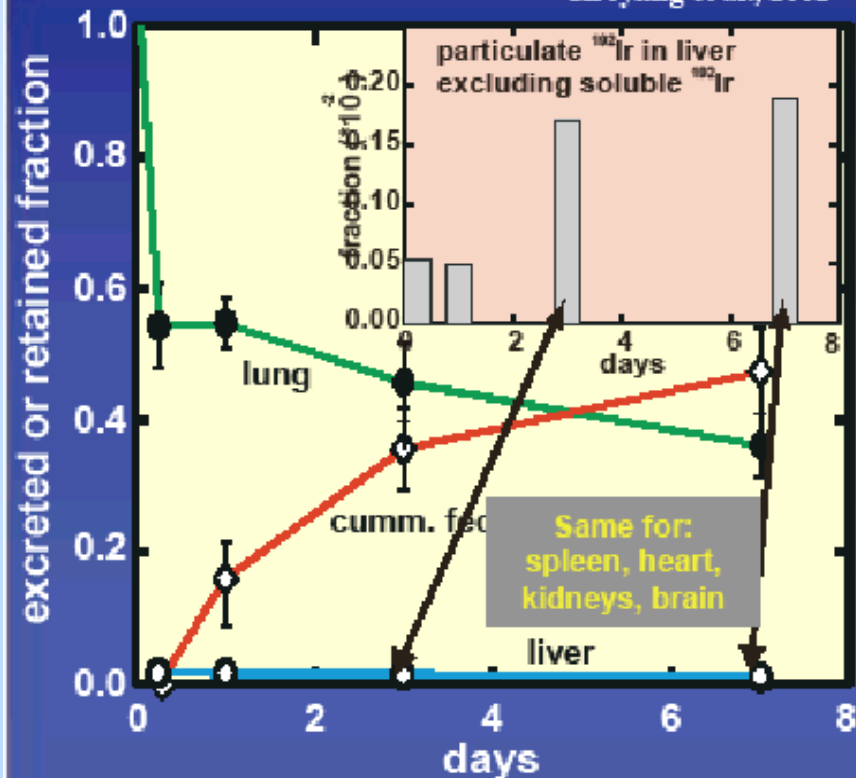


Electron microscopy

Translocation systémique des NP vers des organes secondaires

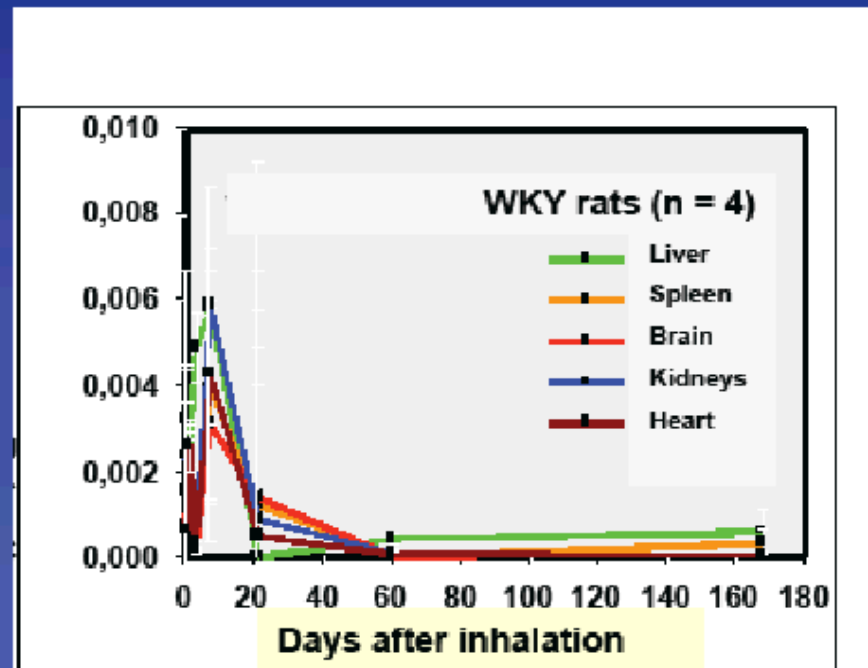
WKY rat, ^{192}Ir NP, 1 hr exposure
15 nm CMD, 10^7 cm^{-3} , 0.2 mg/m^3

Kreyling et al., 2002



Long-term translocation kinetics
same exposure

Semmler et al., 2004



There is little but persistent translocation of Ir-NP towards secondary target organs

Conclusions

- Les fractions fine et ultrafine des PM sont essentiellement responsables des effets pro inflammatoires
- Les composés organiques (HAP, quinones) sont fortement impliqués
- Ils jouent un rôle central dans le potentiel rédox des PM et génèrent un stress oxydant
- Les PM ultrafines sont responsables de l'effet « adjuvant » dans la sensibilisation allergique (via leur potentiel pro-oxidant ?)

An aerial photograph of Paris, France, featuring the Eiffel Tower in the foreground. The city's skyline, including several skyscrapers, is visible in the background under a hazy, blue-tinted sky. The word "MERCI" is overlaid in the center-right of the image.

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