Nano Safety

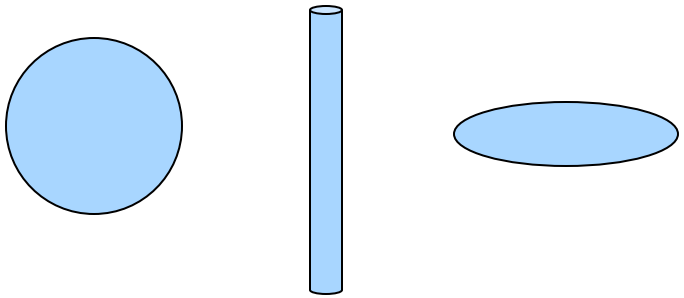
Interaction between living matter and nanoscale particles.

Nanotoxicology and biocompatibility.

Nanosafety:

Risk = Exposure x Toxicity

Nanoparticles (1nm ≤ size ≤100 nm)



Manufactured

- -Semi-conductor nanoparticles (quantum dots)
- - Polymer nanoparticles
- - Nanowires
- -Carbon nanotubes
- - Metal nanoparticles

Combustion byproducts

- - Diesel particles
- - Wood, candles…

Nanoparticles from combustion and industrial processes

https://whatcanjifdoforyou.wordpress.com


Nanoparticles from combustion

Nanoparticles from combustion

Nanoparticles from combustion

https://toxicnj.com/

Diesel particles

Nanoparticles from combustion

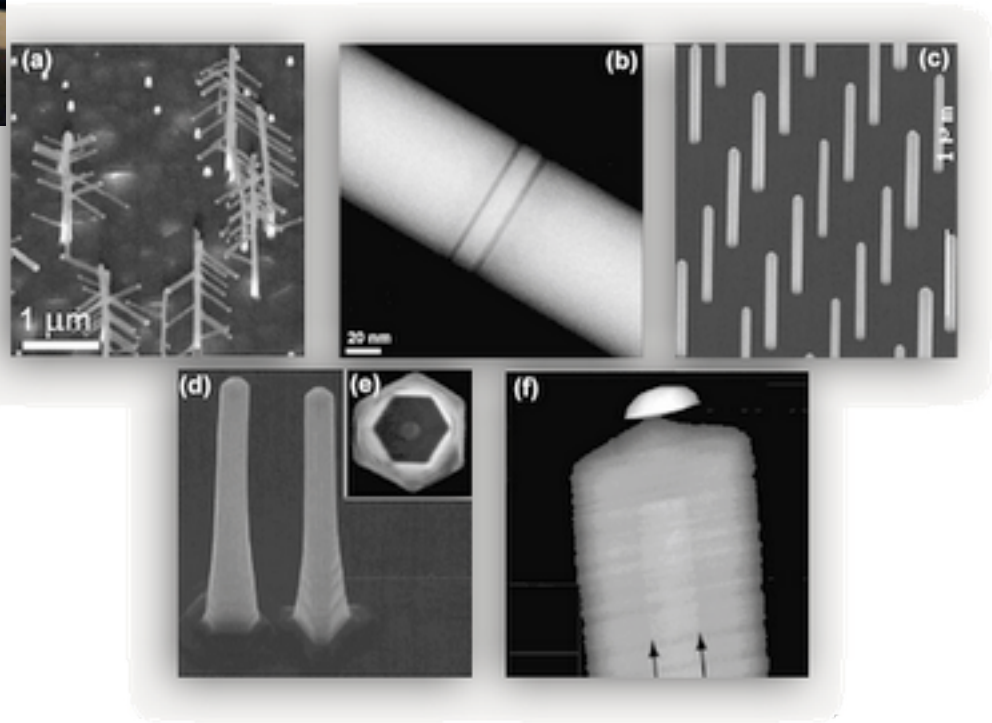
Getty images

Nanoparticles from combustion

No nanoparticles

Nanoparticles from volcanic eruptions

High-tech nanoparticles

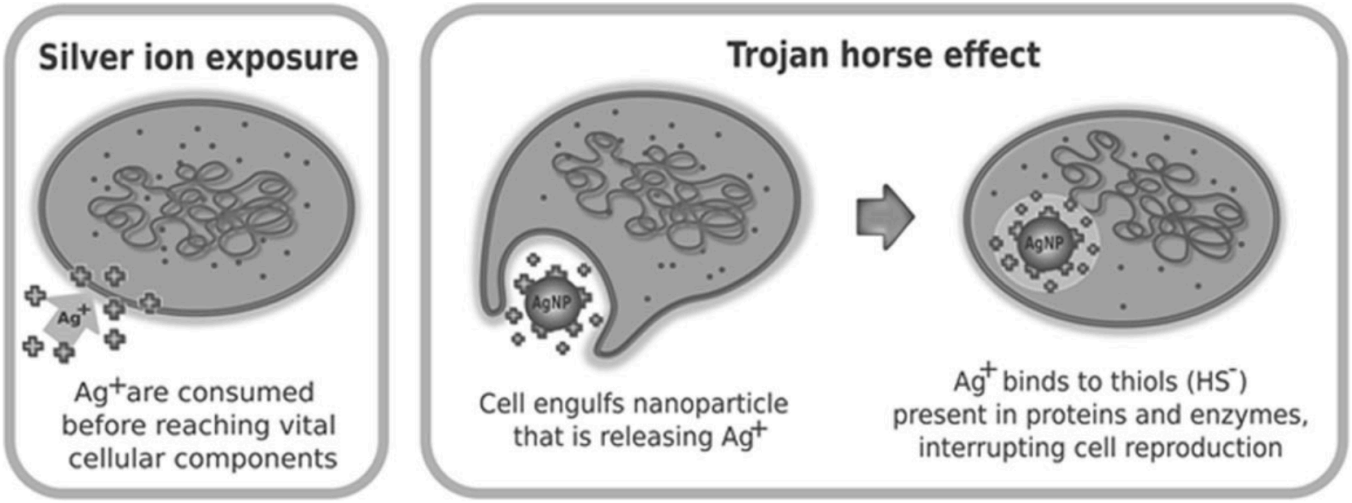


Why investigate their possible toxicity?

Why investigate their possible toxicity?

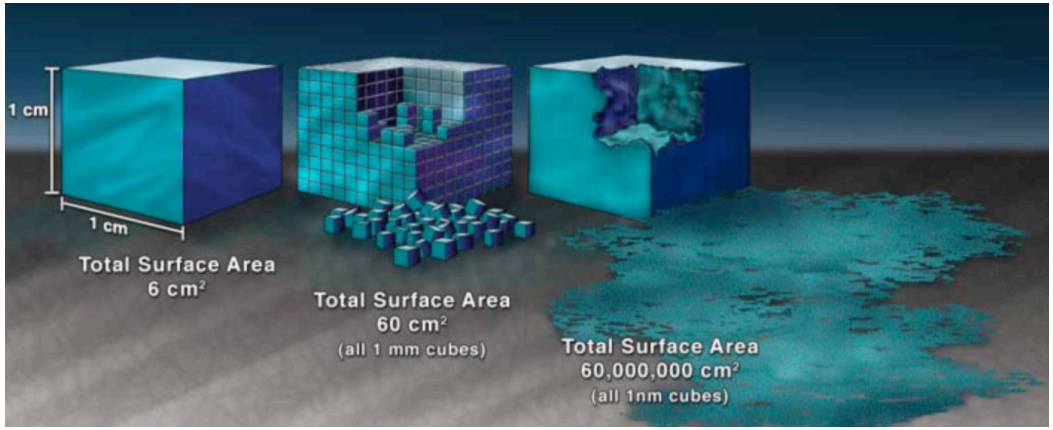
1) Nanoparticles can easily penetrate cells and tissue

Example:
Ag nanoparticles



https://doi.org/10.3155/1047-3289.60.7.770

General issue with nanoparticles:
Large surface to volume ratio i.e. more area for interactions/reactions.



https://www.nano.gov/

Why investigate their possible toxicity?

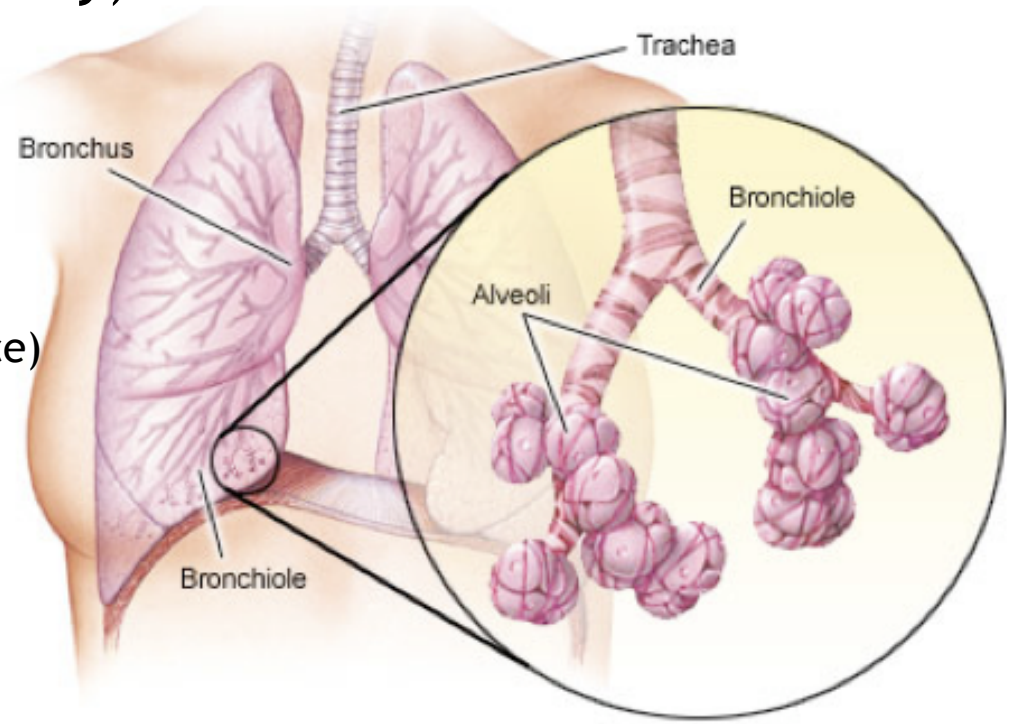
2) Previous knowledge of toxicity from ”old” nanoparticles

Silicosis (since ancient Greek and Roman period)

Asbestosis (since 20th century)

Small Particles deposited
Deep in the lung
(Alveoli, where gas exchange takes place)

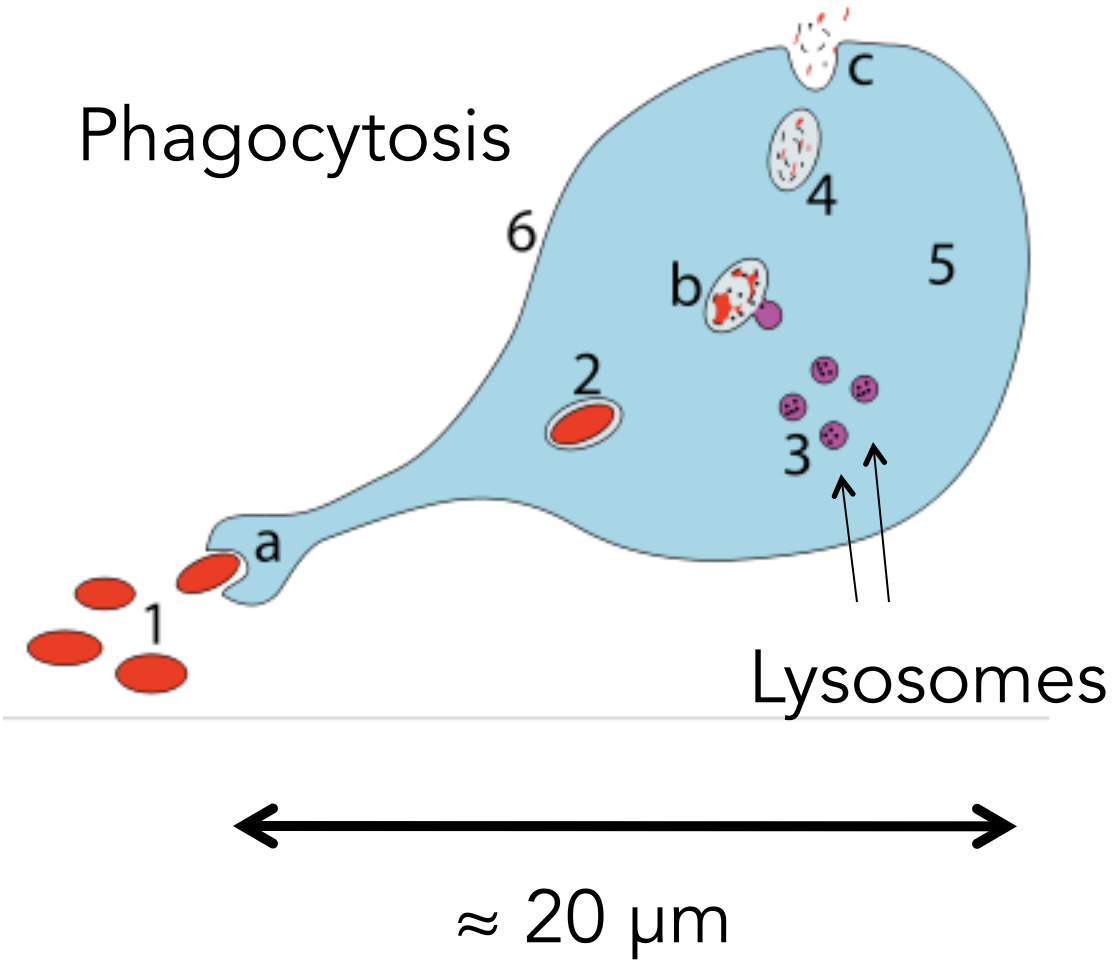
Chronic inflammation,
Fibrosis



Macrophages

+ H_2O_2

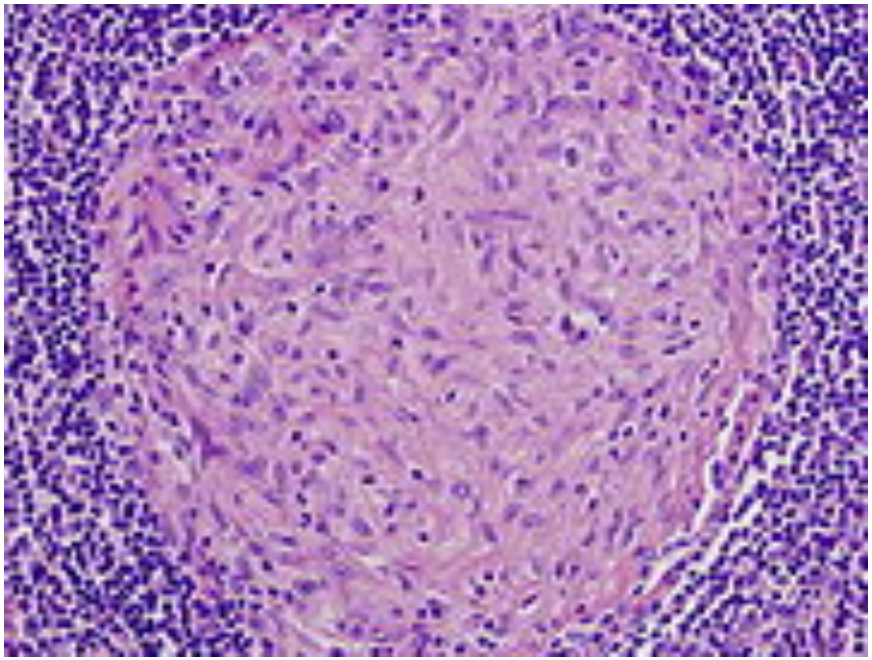
+NO



Lysosomes: Spherical organelles that contain enzymes
Granuloma: organized collection of macrophages

Source: wikipedia

Granuloma

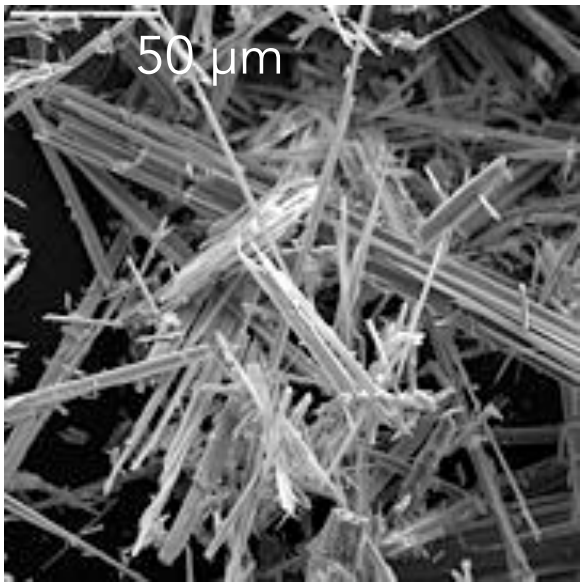


Organization of immune cells (macrophages) when they can not get rid of a substance.

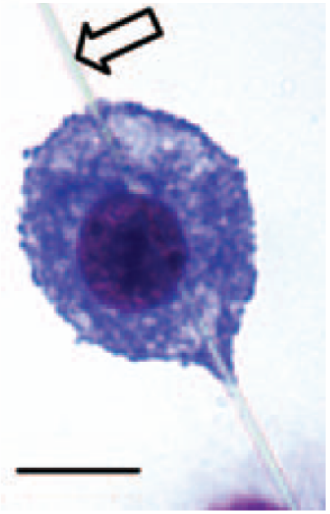
Ex: Bacteria (tuberculosis, leprosis…), Asbestos

Source: wikipedia

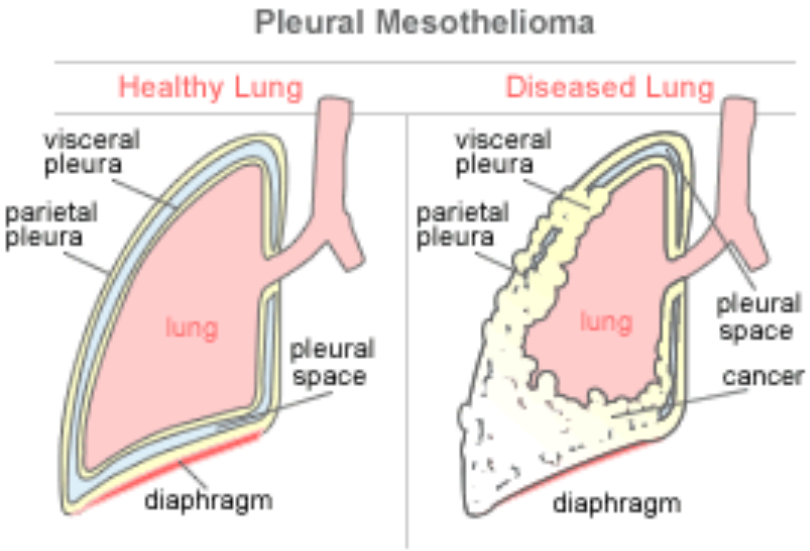
Asbestos



Frustrated phagocytosis



Mesothelioma



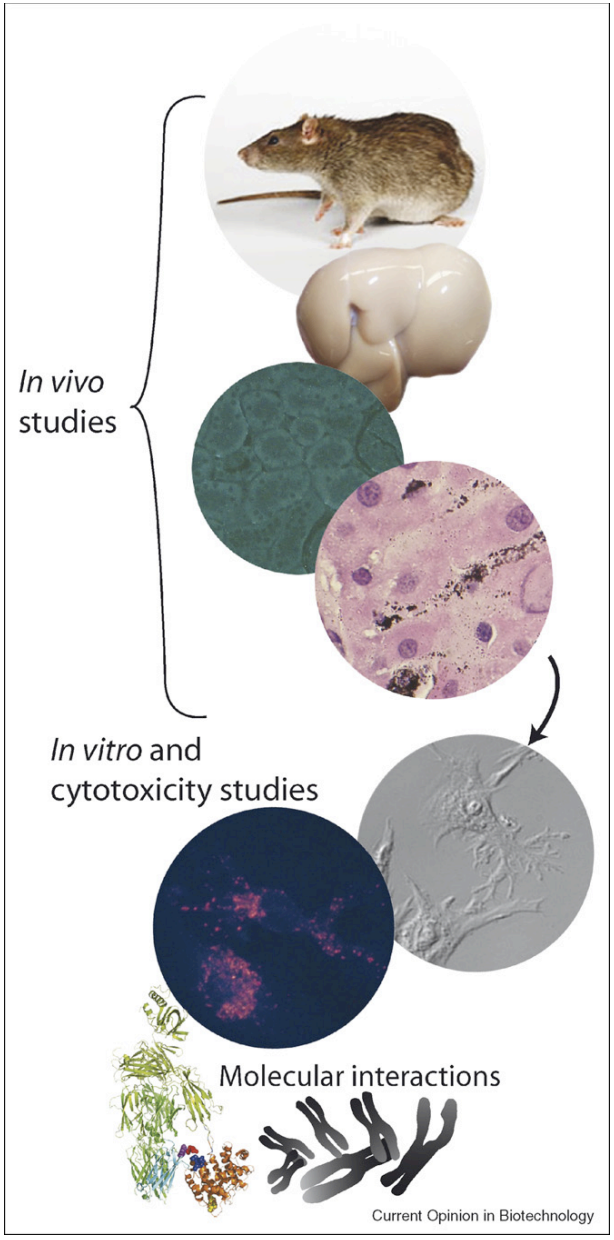
Cancer of the mesothelium which is a protective sac that covers most of the body's internal organs.

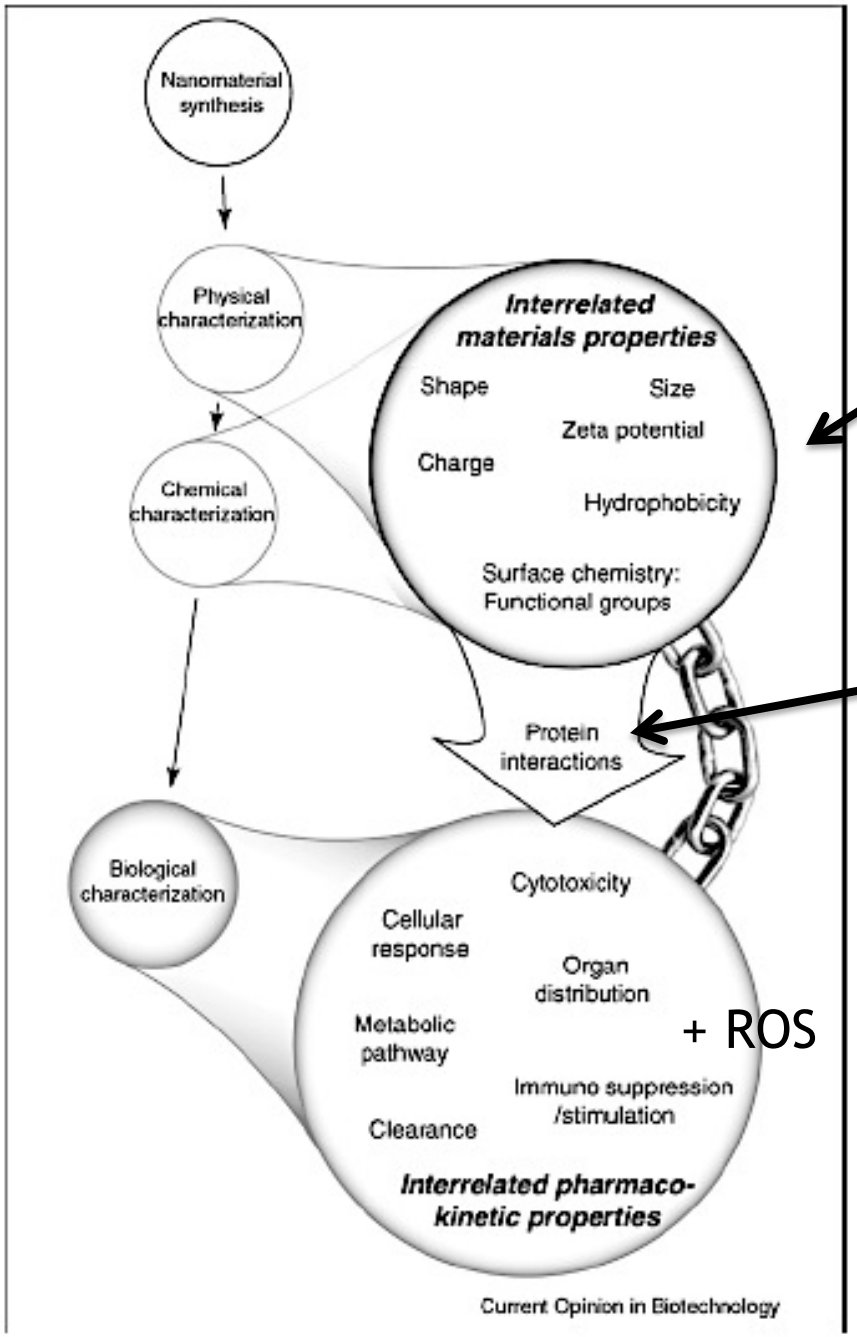
Fibre pathogenicity paradigm: Length > immune cells
Durability
Stiffness

Do CNT and nanowires comply with this paradigm?

Nanoparticles studies

What do we need to know about the nanoparticle in order to understand the effects of a particular nanoparticle?



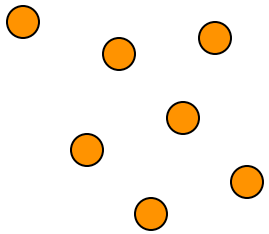


Aggregation?

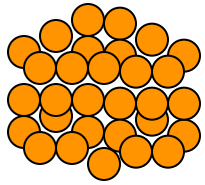
Protein corona ?

Aggregation – surface area

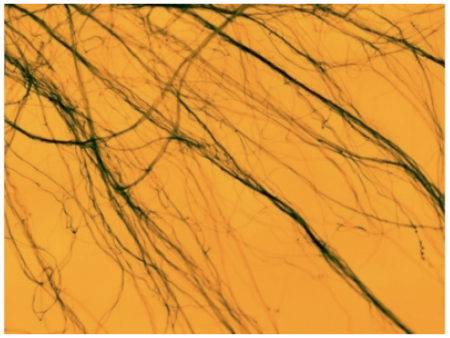
In air, blood, water, food….



or

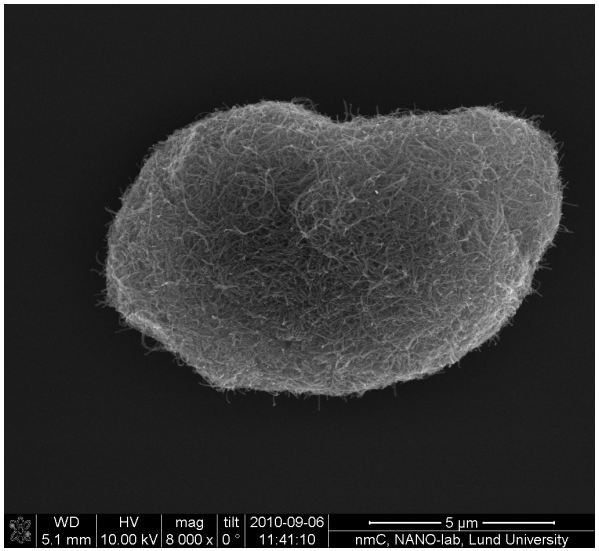


Carbon nanotubes



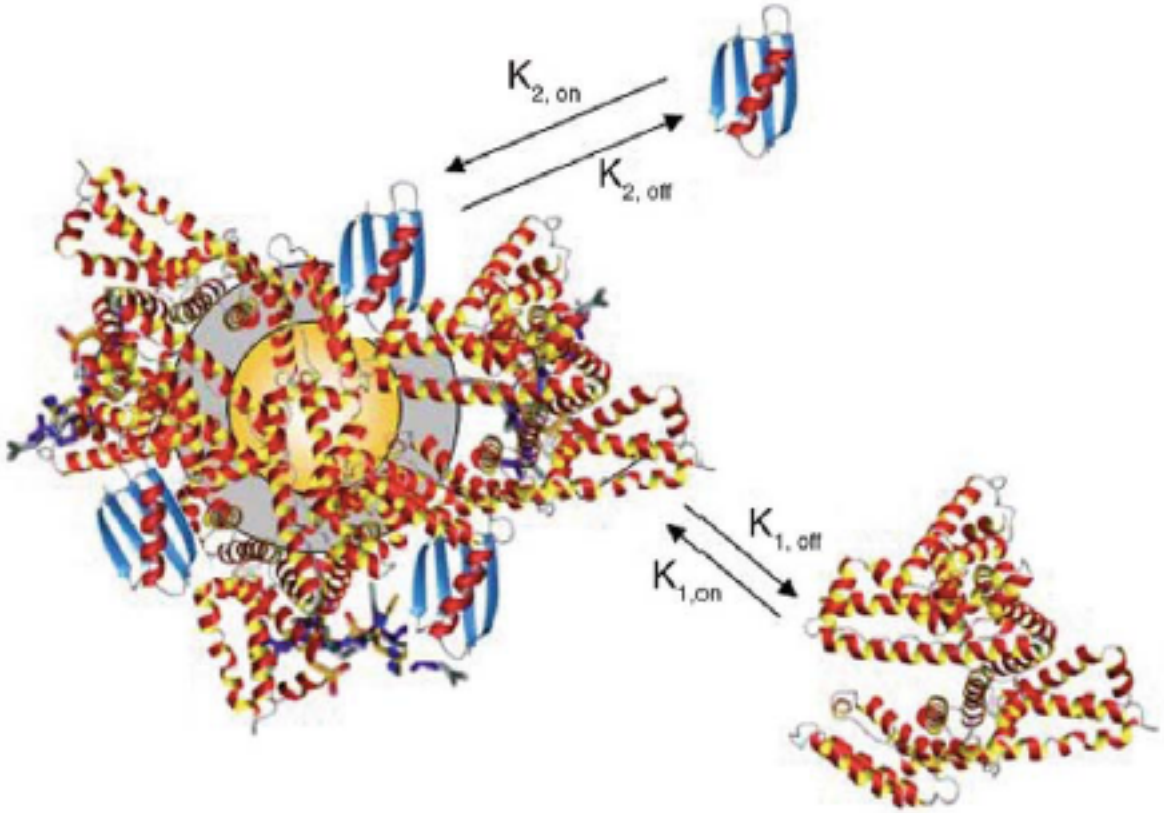
www.gizmag.com

or



Protein corona

In biological fluid

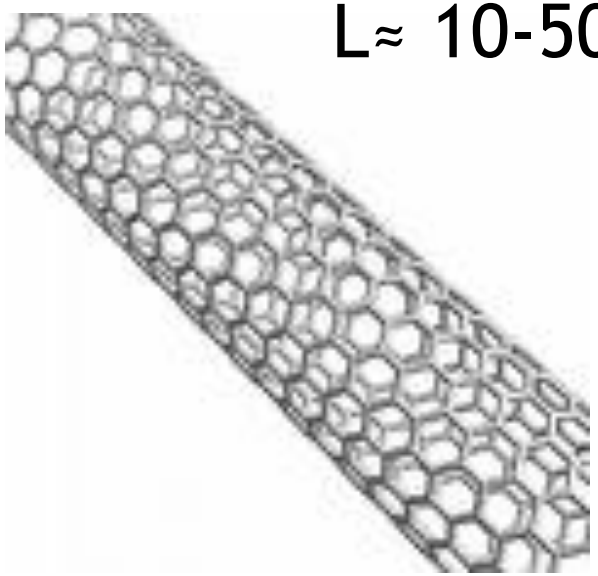


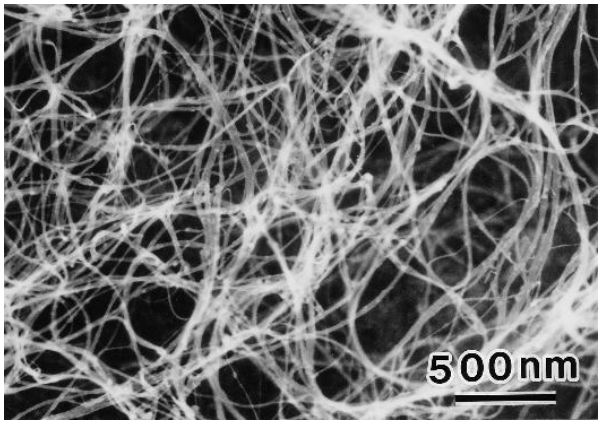
Protein corona: defines the biological identity of the particle

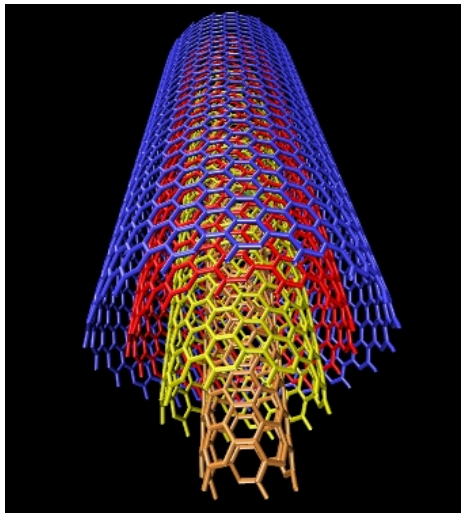
(ref Prof Sara Linse, Lund University)

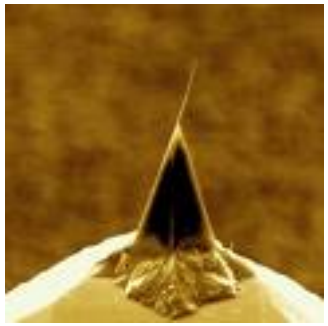
Carbon Nanotubes

D≈nm
L≈ 10-50 μm









Carbon Nanotube study: example 1

-Inhaled CNT reach the subpleural tissue in mice (Ryman-Rasmussen et al., Nature Nanotech 2009)

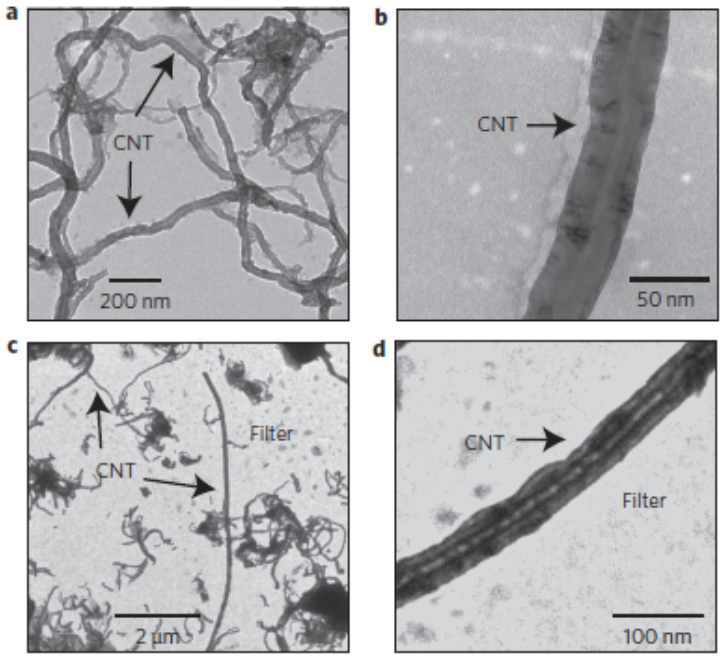


Figure 1 | Aerosolization of carbon nanotubes. a, TEM image of bulk MWCNTs before aerosolization. **b**, Higher magnification of an individual CNT in the bulk sample. **c**, Aerosolized CNTs captured by electrostatic precipitation on a filter located within the inhalation tower port (see Supplementary Information). **d**, Higher magnification of an aerosolized precipitated CNT on filter.

Characteristic		Manufacturer (Helix)	Independent (MRL)
Purity	(TGA)	>95%	>94%
Amorphous Carbon	(TGA)	<2%	ND
Ash	(TGA)	<0.2 wt %	ND
C	(EDX)	93.4%	93.75 ± 3.93 %
O	(EDX)	6.4%	0.71 ± 0.19 %
Ni	(EDX)	0.12%	5.53 ± 3.92%
La	(EDX)	0.06%	ND
C	(ICP-AES)	ND	99.00%
O	(ICP-AES)	ND	0.63%
Ni	(ICP-AES)	ND	0.34%
La	(ICP-AES)	ND	0.03%
Avg. Diameter	(TEM)	10-30 nm	30-50 nm
Length	(TEM, SEM)	0.5-40 µm	0.3-50 µm
Surface Area	(BET)	40-300 m^2/g	109.29 m^2/g

Dose: 1mg/m^3 and 30 mg/m^3

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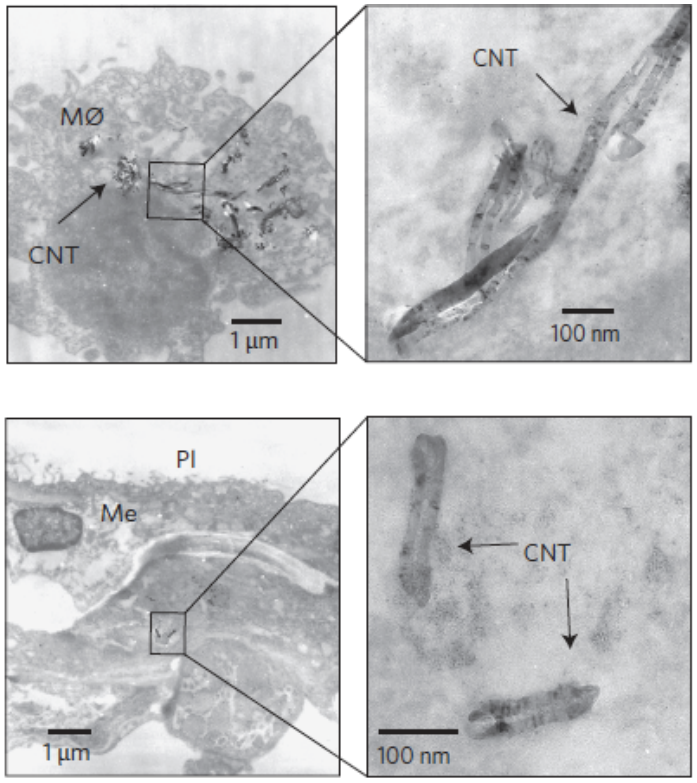
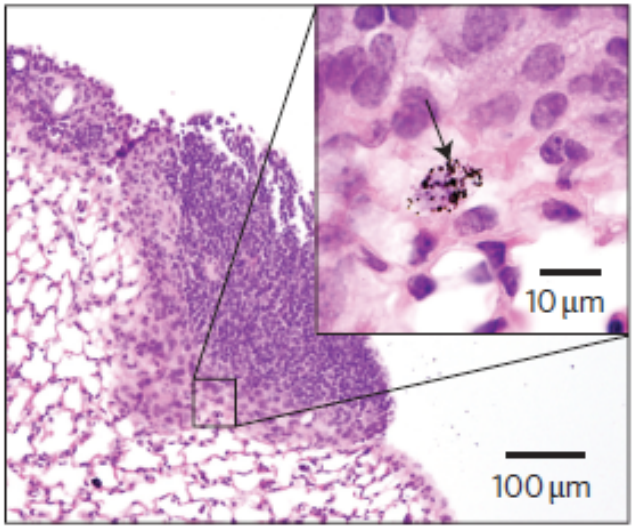
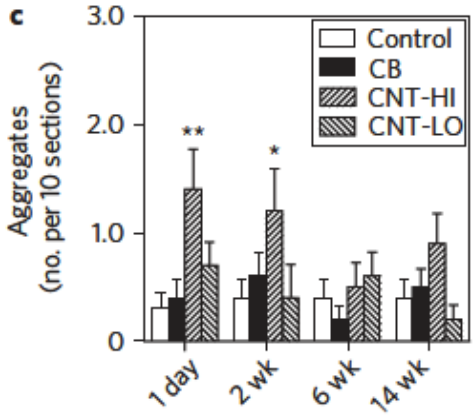






-formation of mononuclear cell aggregates (immune reactions)

Carbon Nanotube study: example 2

-CNT introduced in the abdominal cavity of mice show asbestos pathogenicity (Poland et al.,Nature Nanotech 2008)

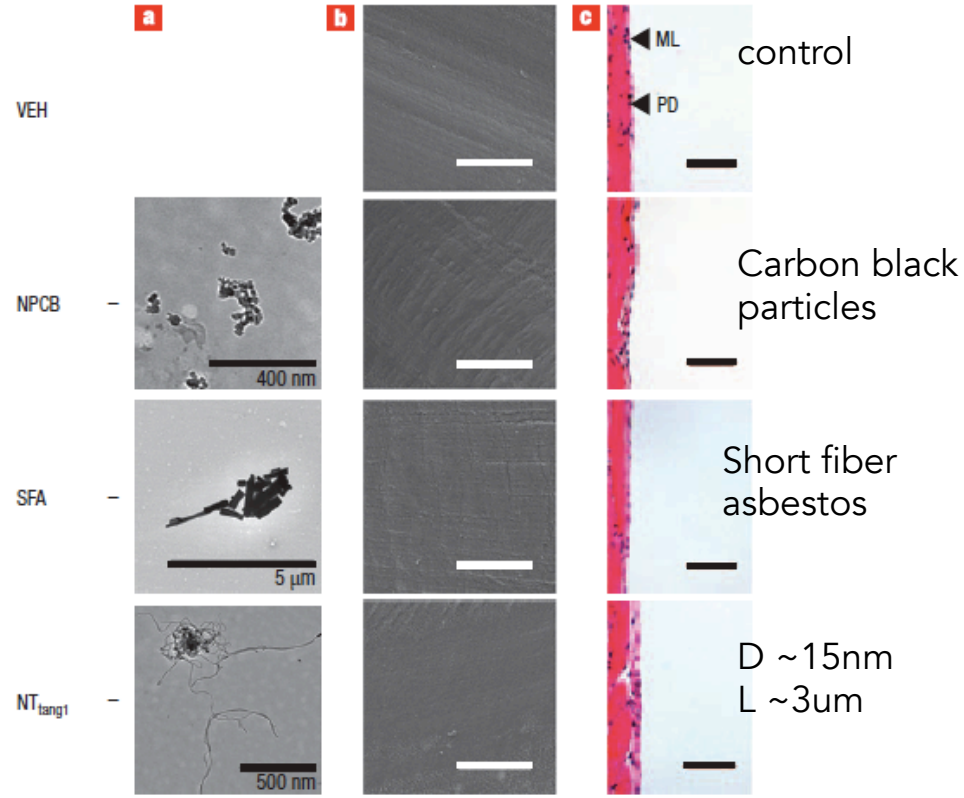
	NT_{tang1}	NT_{tang2}	NT_{long1}	NT_{long2}
Source	NanoLab, Inc.	NanoLab, Inc.	Mitsui & Co.	Dr Ian Kinloch (University of Manchester)
Description of morphology (from SEM, TEM and light microscopy)	Short MWNTs forming tightly packed spherical agglomerates, a large proportion of which are in the respirable size range <5 μm, with frayed edges of singlet nanotubes.	Bundles of intermediate-length MWNTs. Often stellate in form with longer fibres protruding from the central tangled agglomerate, a large proportion of which are in respirable size range <5 μm.	Dispersed bundles and singlets of long and intermediate-length MWNTs, many in the range 10–20 μm and longer. Many very short fibres often decorate the long fibres.	Regular bundles and ropes of MWNTs with a fairly constant length and diameter. Typically, single ropes of tubes are more than 20 μm in length.
Diameter as supplied by the manufacturer (nm, mean ± s.e.m.)	15 ± 5	15 ± 5	40–50	20–100
Diameter as determined by authors (nm, mean ± s.e.m.)	14.84 ± 0.50	10.40 ± 0.32	84.89 ± 1.9	165.02 ± 4.68
Length as supplied by the manufacturer (μm)	1–5	5–20	Mean 13	Max 56
Percentage fibres greater than 15 μm (see Supplementary Information, Methods, for methodology)	‡	‡	24.04	84.26
Percentage fibres greater than 20 μm (see Supplementary Information, Methods, for methodology)	‡	‡	11.54	76.85
Endotoxin ($pg\ ml^{-1}$)*	ND	ND	ND	ND
Soluble metals ($\mu g\ g^{-1}$)† (see Supplementary Information, Fig. S2, for a full analysis)				
Fe	7.9	13.4	ND†	37.3
Cu	5.1	1	1.2	1.2
V	ND†	ND†	0.8	ND
Ni	9.7	5	6.2	6.2
Zn	5.5	7.5	0.7	ND†
Co	3.7	ND†	1.9	3.4

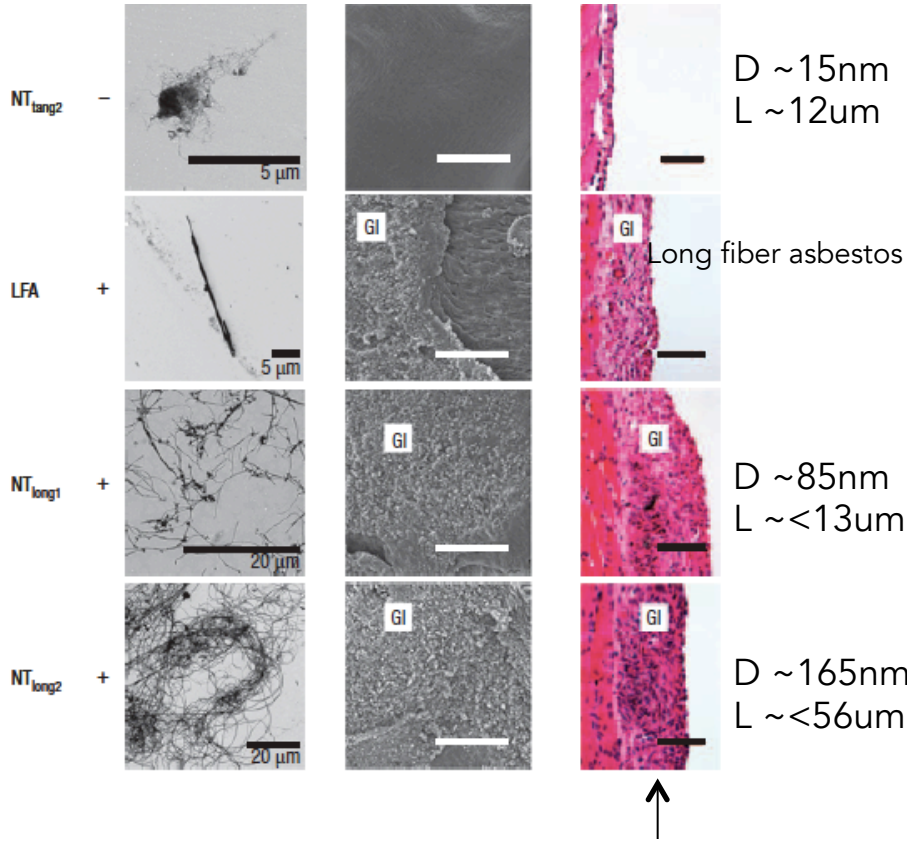
ND = not detectable.
*Endotoxin detection limit $<10\ pg\ ml^{-1}$
†Metal analysis detection limit $<0.1\ \mu g\ g^{-1}$.
‡The presence of long fibres could not be reliably determined.

Carbon Nanotube study: example 2

-CNT introduced in the abdominal cavity of mice show asbestos pathogenicity (Poland et al.,Nature Nanotech 2008)

peritoneal diaphragm (PD) mesothelial layer (ML)



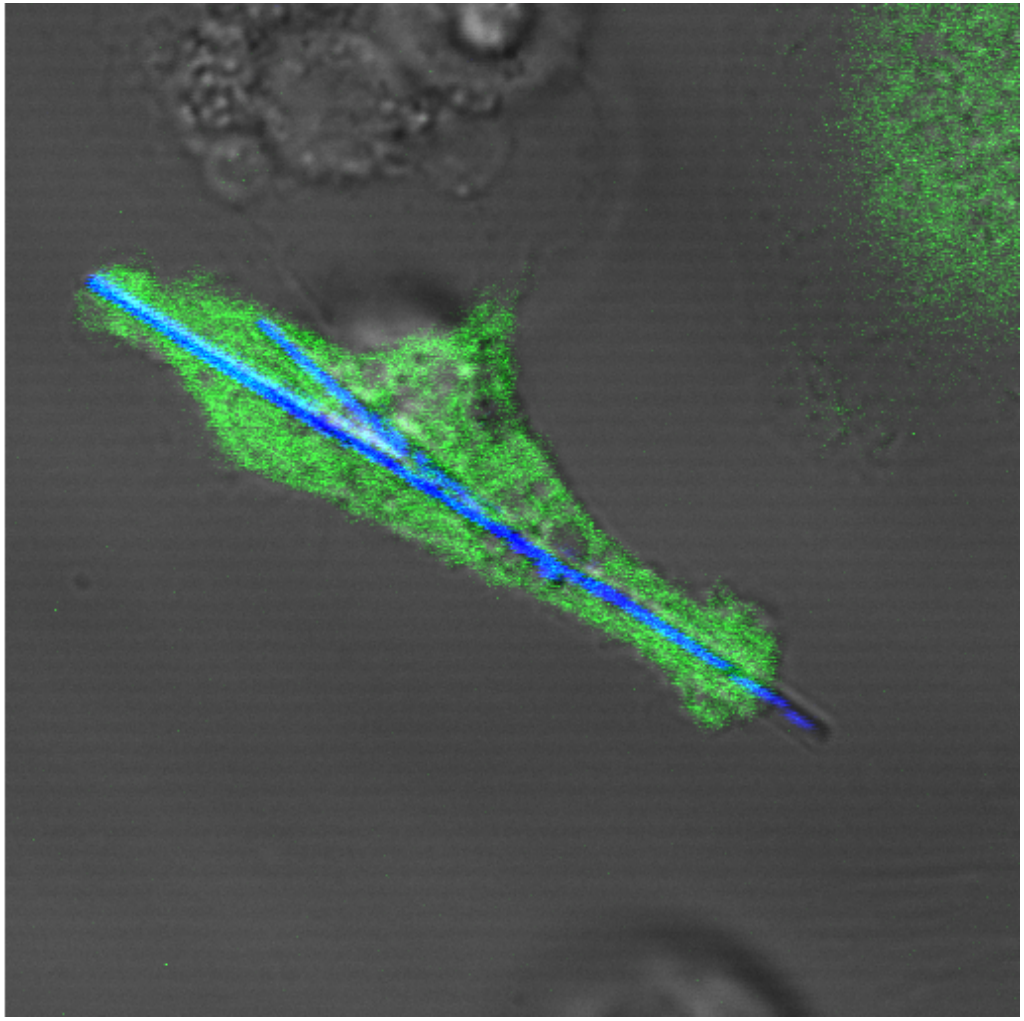


After 7 days

GI: granulamatous inflammation

Fiber pathogenicity paradigm

Macrophage having problem engulfing long PS nanowire

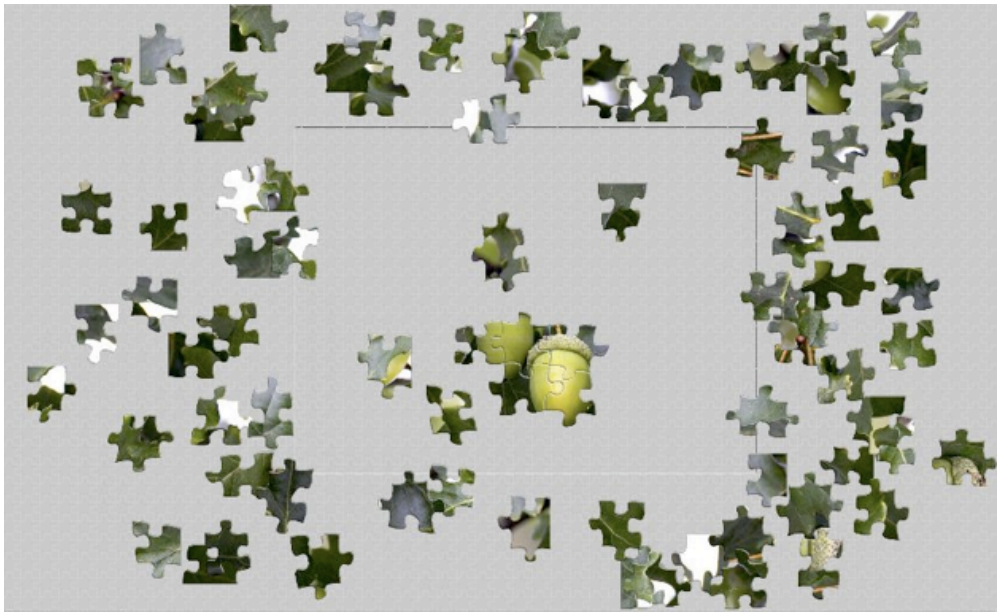


Filename:
Macrophage.avi

Fredrik Johansson (Biology)

Biocompatibility of Nanoparticles depends on:

-size
-shape
-surface chemistry
-surface charges
-surface reactivity
-protein corona
-dose
-route of exposure
- method used and biological “host”
- etc….



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