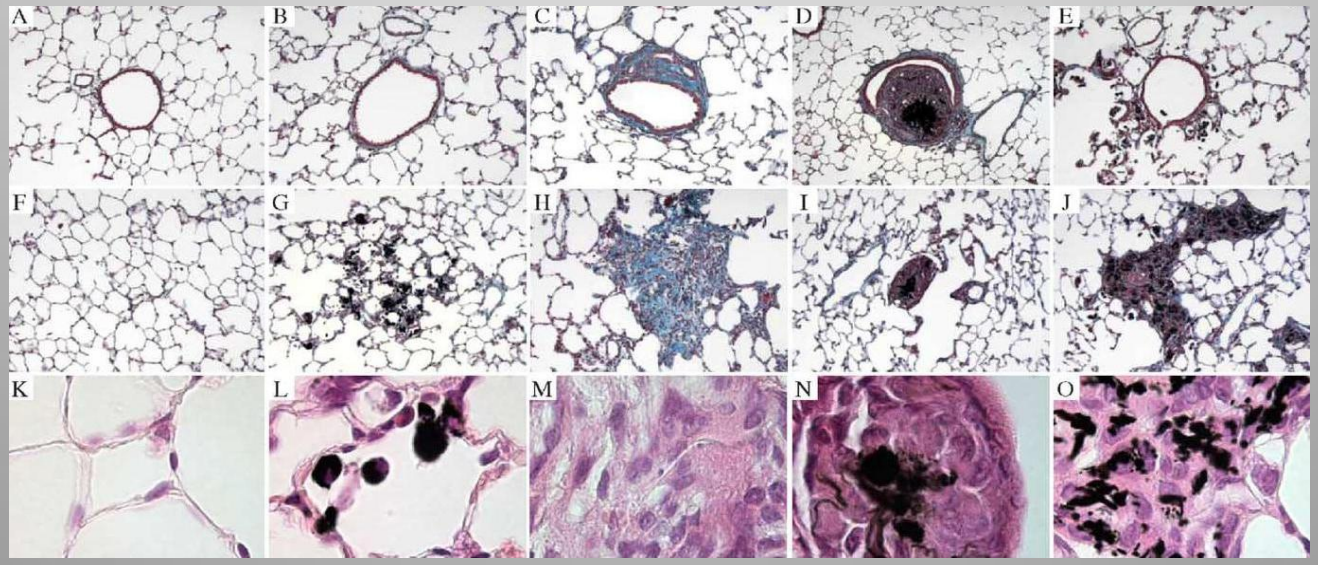
Respiratory toxicity of multi-wall carbon nanotubes



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Synopsis

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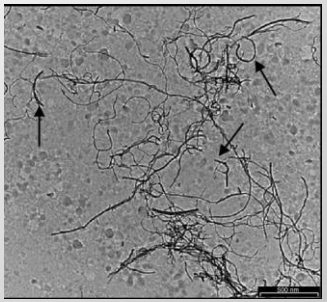
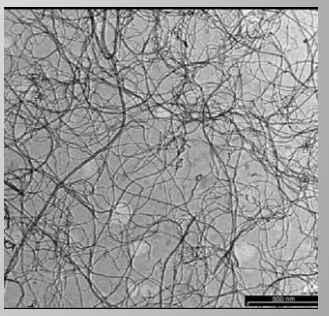
I. Introduction

- Why are the carbon nanotubes so interesting?
- Are they potentially dangerous for health or for the environment ?
- How to determine their toxicity?

II. Experiments





- The animals and the Particles

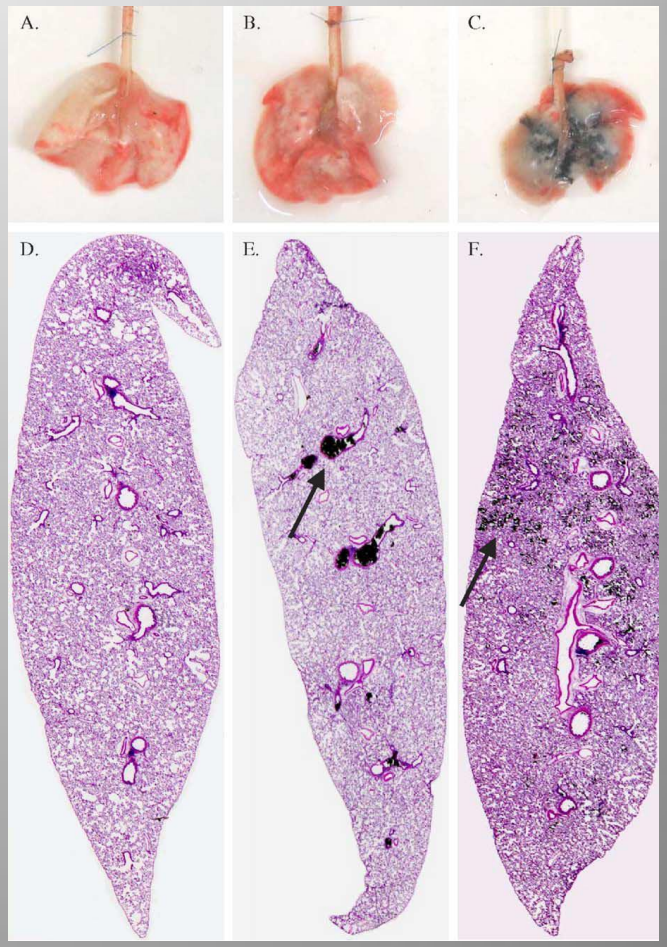
- Experiments in vivo
  - Determination of Biopersistence
  - Determination of Inflammatory response
  - Determination of Fibrotic response
  - Determination of Tumor-Necrosis-Factor-α production

- Experiments in vitro
  - Detemination of the effects induced by CNT on peritoneal macrophages

III. Results

- Grinding of Nanotubes

	CNT	Ground CNT
Length (μm)	5.9 ± 0.05	0.7 ± 0.07
Average inner diameter (nm)	5.2 ± 1.5	5.1 ± 2.1
Average outer diameter (nm)	9.7 ± 2.1	11.3 ± 3.9
Specific surface area (m^2/g)	378 ± 20	307 ± 15
Oxidized forms (atomic %)	13.7 ± 0.7	13.1 ± 0.7
Carbon content (%)	97.8 ± 0.2	98.0 ± 0.2



- Morphology of nanotubes were modified by grinding
- Ground CNT were much better dispersed

III. Results

- In vivo: Biopersistence

Single i.t. dose	Time after particle administration		
	Day 0	Day 28	Day 60
NaCl 0.9%	ND	ND	ND
0.5 mg CNT	0.4 ± 0.1	0.3 ± 0.1 (78.4% ± 15.3)	0.4 ± 0.1 (81.2% ± 26.4)
0.5 mg ground CNT	0.5 ± 0.1	0.4 ± 0.1 (78.4% ± 12.4)	0.2 ± 0.1 (36.0% ± 13.2)

- CNT: not or slowly eliminated
- Ground CNT: more rapidly cleared particularly during the 2nd month

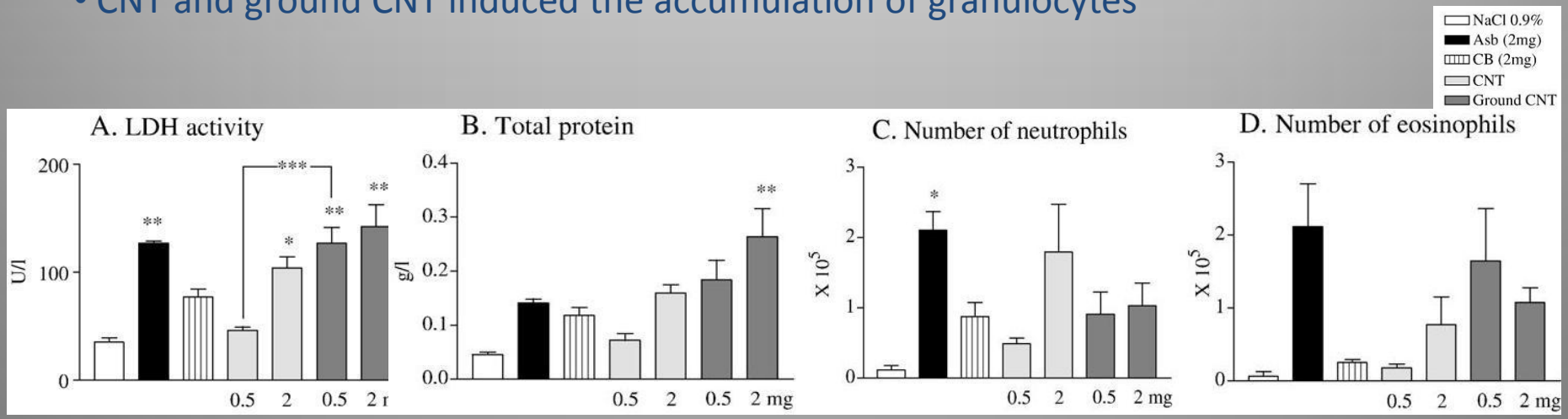
III. Results

- In vivo: Pulmonary inflammation

• LDH activity increased in BALF after administration of Asb, CNT or ground CNT
→ marker of cell toxicity

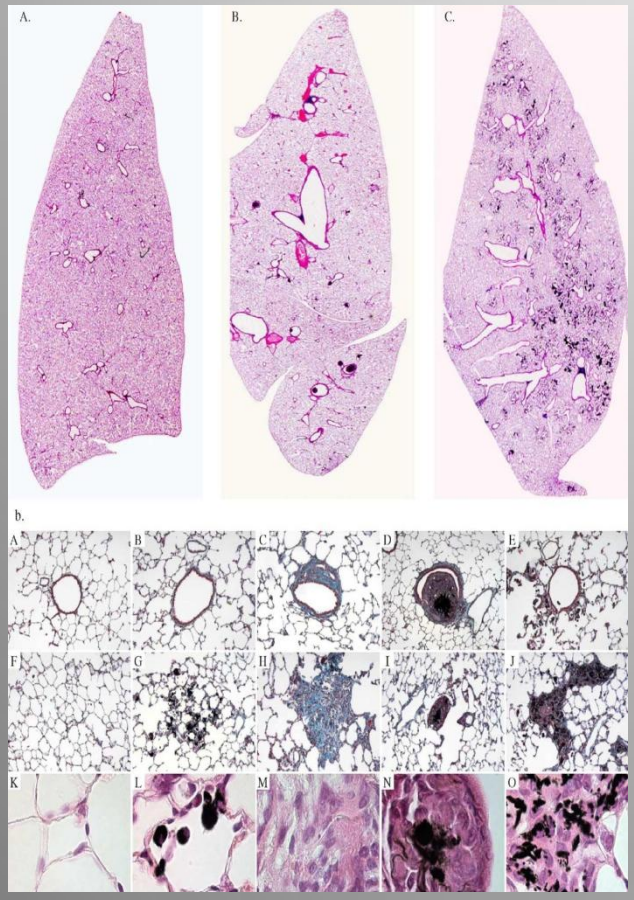
• Protein concentration increased in BALF after administration of CNT or ground CNT
→ reflects alveolo-capillar permeability and/ or alveolitis

• CNT and ground CNT induced the accumulation of granulocytes

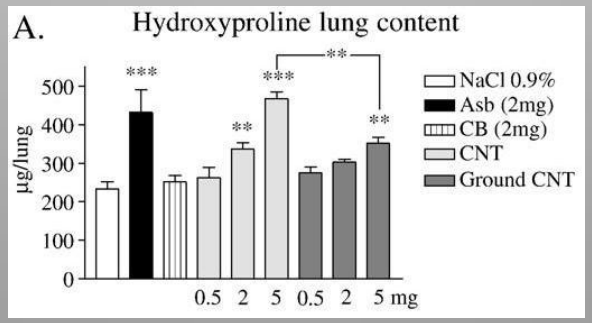


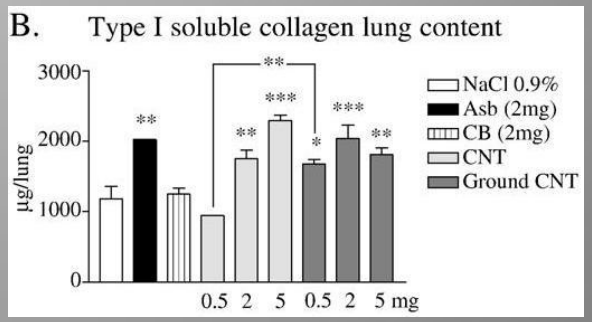
III. Results

- In vivo: Pulmonary fibrosis



- OH-proline levels were dose dependently increased
- Type I collagen levels were increased
- Presence of collagen rich granulomas in the bronchi of animals instilled with CNT → blocked the bronchial lumen
- Ground CNT were better dispersed → granulomas in the interstitium tissue



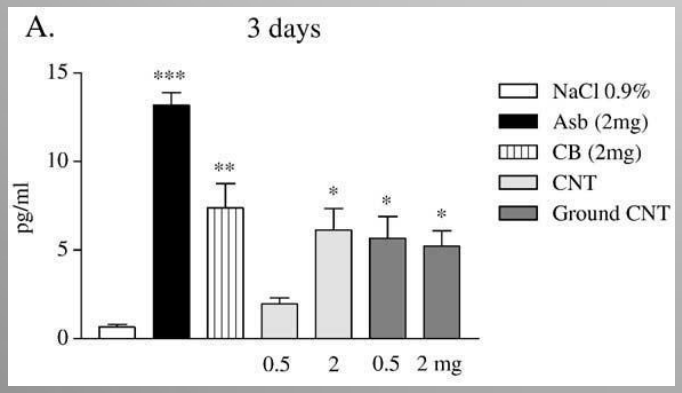


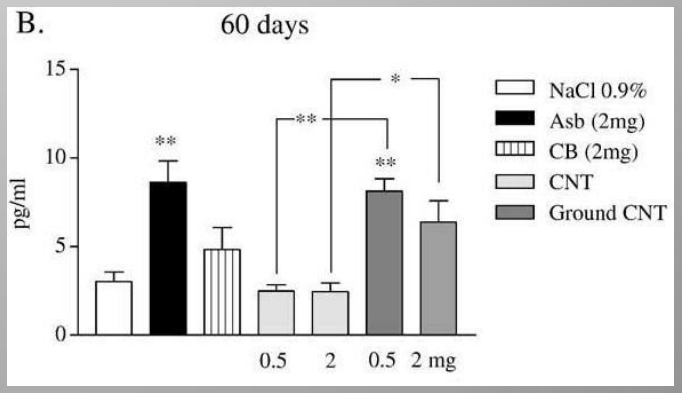
III. Results

- In vivo: TNF-α

  - At inflammatory stage (day 3) : BAL levels of TNF-α were increased

  - At fibrotic stage (day 60) : TNF-α production increased only after instillation of Asb or ground CNT





III. Results

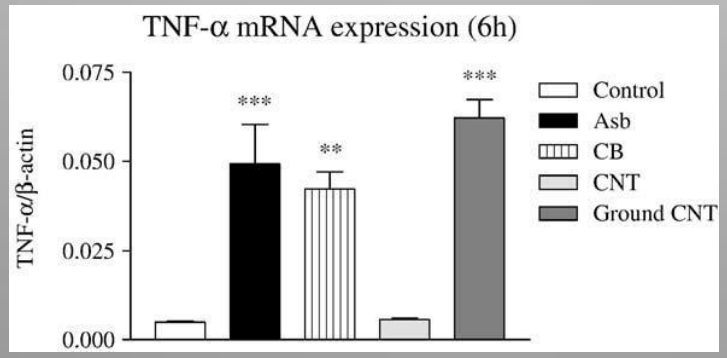
- In vitro

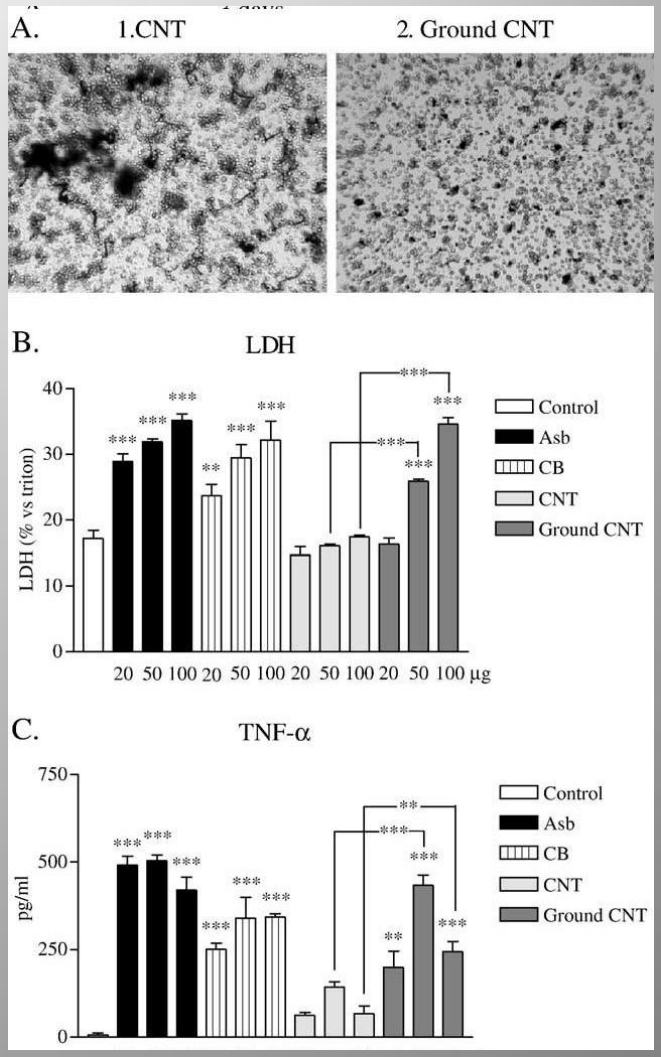
• Ground CNT were well dispersed in medium whereas CNT formed large aggregates and were not in contact with cultured cells

• Level of LDH was dose dependently increased

• Level of TNF-α was only increased by treatment by Abs, CB or ground CNT

•TNF-α mRNA was upregulated after exposure to Abs, CB or ground CNT





IV. Conclusion

- Multi-wall carbon nanotubes are not rapidly eliminated when they reach the lung.
- Intact or ground CNT have the potential to cause inflammatory and fibrotic reactions.
- These data support the idea that carbon nanotubes are toxic to the lung.

IV. Bibliography

- J.Muller, F. Huaux, N. Moreau, P. Misson, J.-F. Heilier, M. Delos, M. Arras, A. Fonseca, J. B. Nagy, D. Lison. 2005. Respiratory toxicity of multi-wall carbon nanotubes. Toxicol. Appl. Pharmacol. 207, 221-231