



European Commission

**University of Modena and Reggio Emilia
LABORATORY OF BIOMATERIALS**



Nanoparticles and nanosafety

By

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ICNT2005, S.Francisco

Consortium



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LABORATORY of BIOMATERIALS



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per la Fisica della Materia



Johannes Gutenberg University
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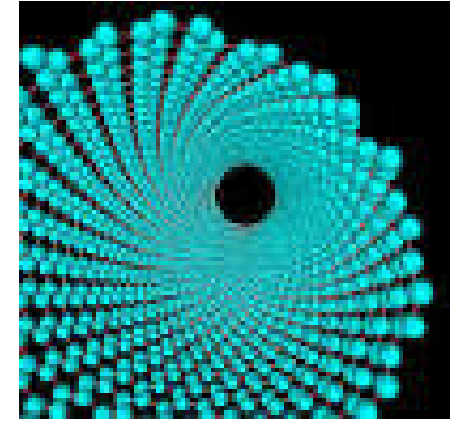
An RTD project funded by
the European Commission

Nano pathology

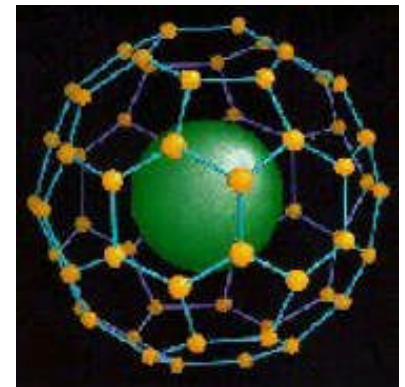
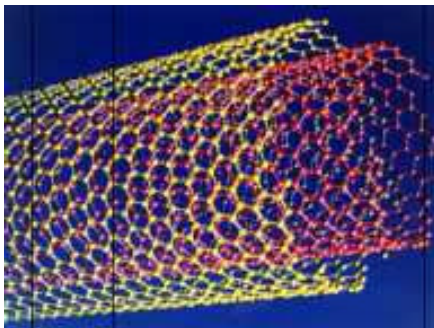
The Role of Micro
and Nanoparticles in
Biomaterial-Induced
Pathology

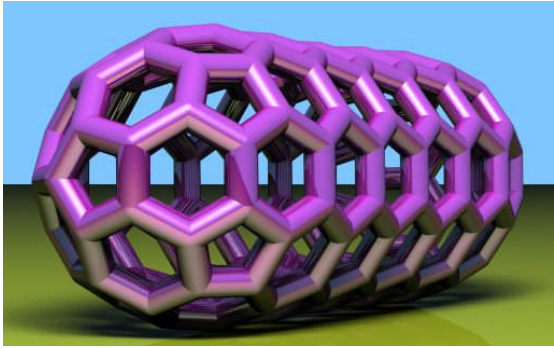
Project
QLRT-2002-147
(2002-2005)

Nanopathology

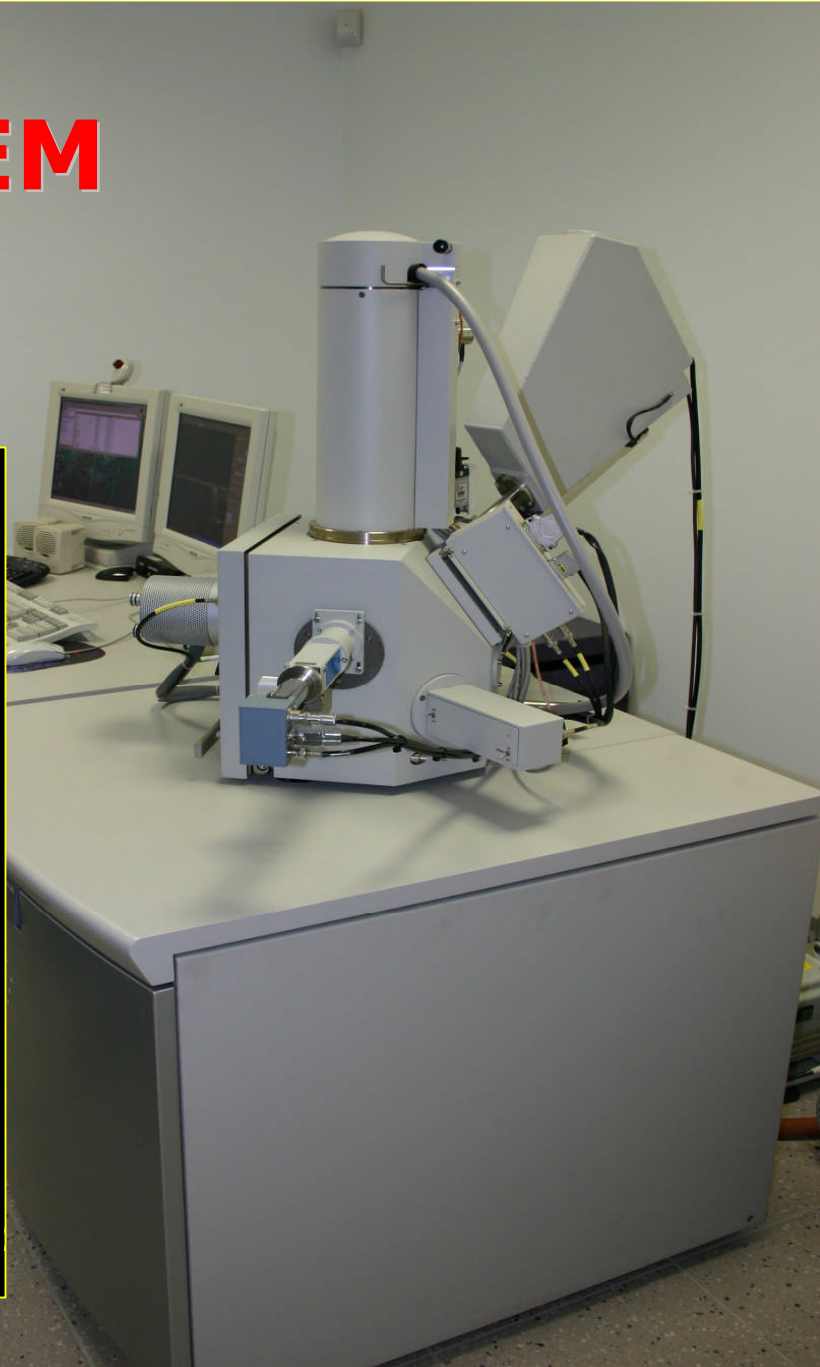


is the branch of learning that deals with how the organism reacts to the presence of micro- and nano-particles

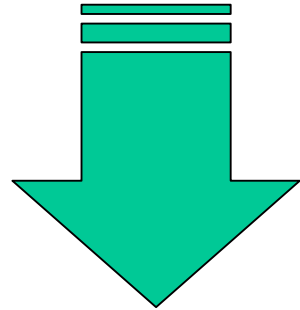




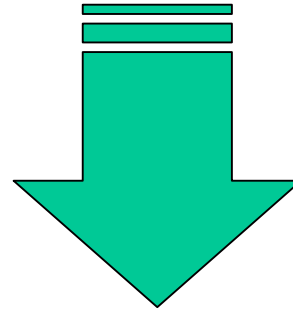
ESEM



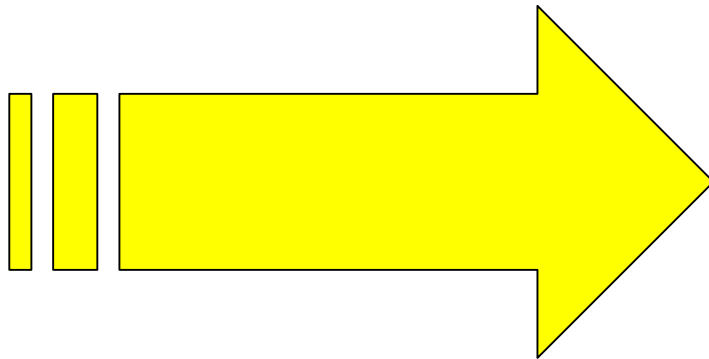
Nano-toxicity of Co, Ni, SiO₂, ZrO₂ and PVC has already been evaluated from different standpoints :



In-vitro tests



In-vivo tests



Clinical results

Nanoparticles

Sizes ranging from 40 up to 200nm

- - Cobalt (Co)

- - Nickel (Ni)

- - PVC

- - Titanium Oxide (TiO_2)

- - Silicon Oxide (SiO_2)

- - Zirconium Oxide (ZrO_2)

} Metals

Polymer

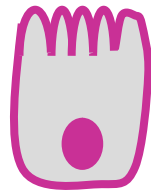
} Ceramics



In-vitro tests



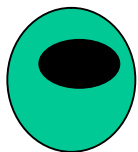
U937



Caco-2



HepG2

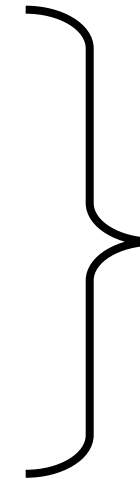


Monocyte/Macrophages

Gut Epithelial cells

Liver Epithelial cells

**3-dimensional angiogenesis cell
cultures** 

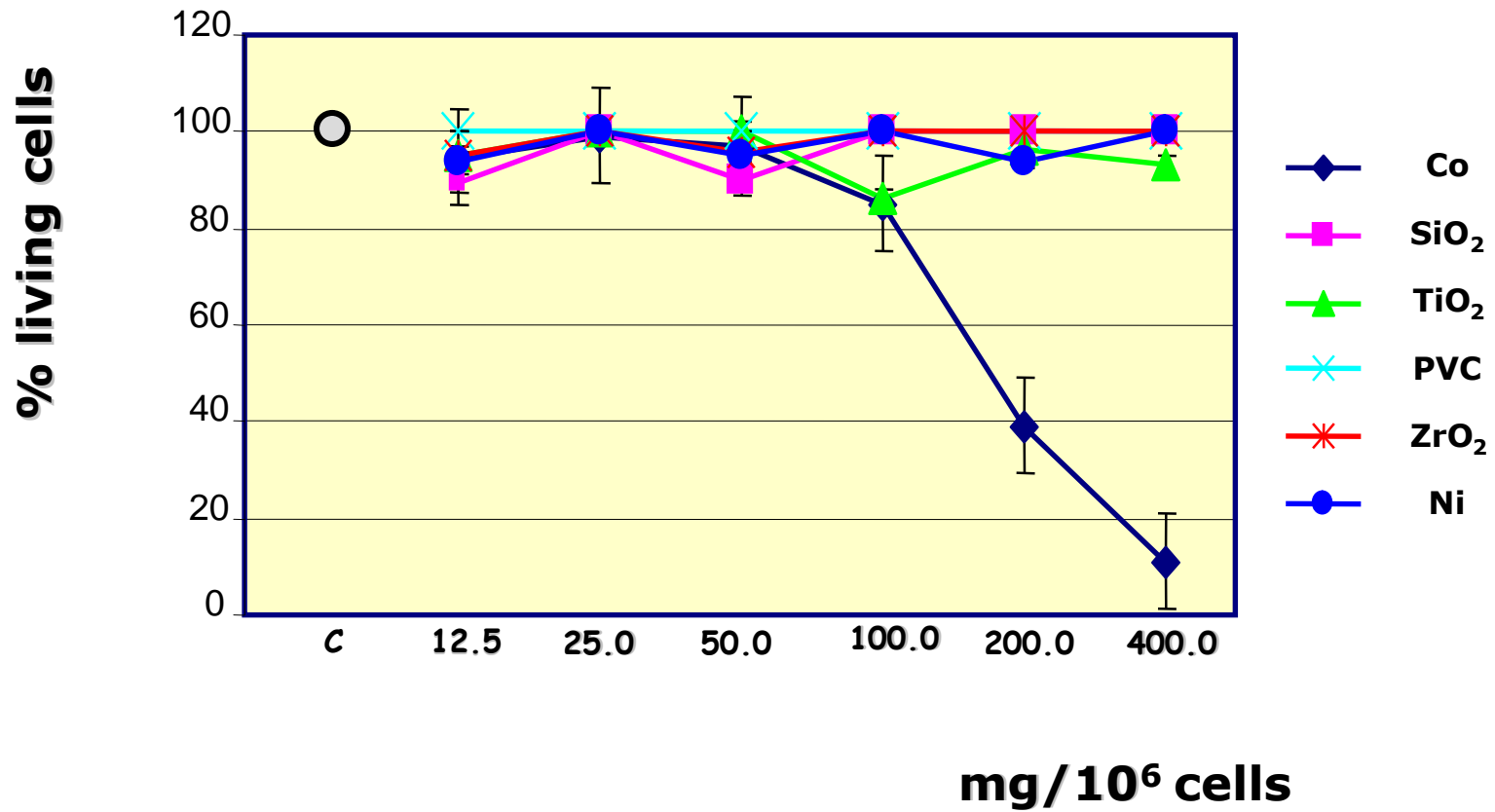


CONSIGLIO
NAZIONALE
DELLE
RICERCHE

Univ. of Mainz, D

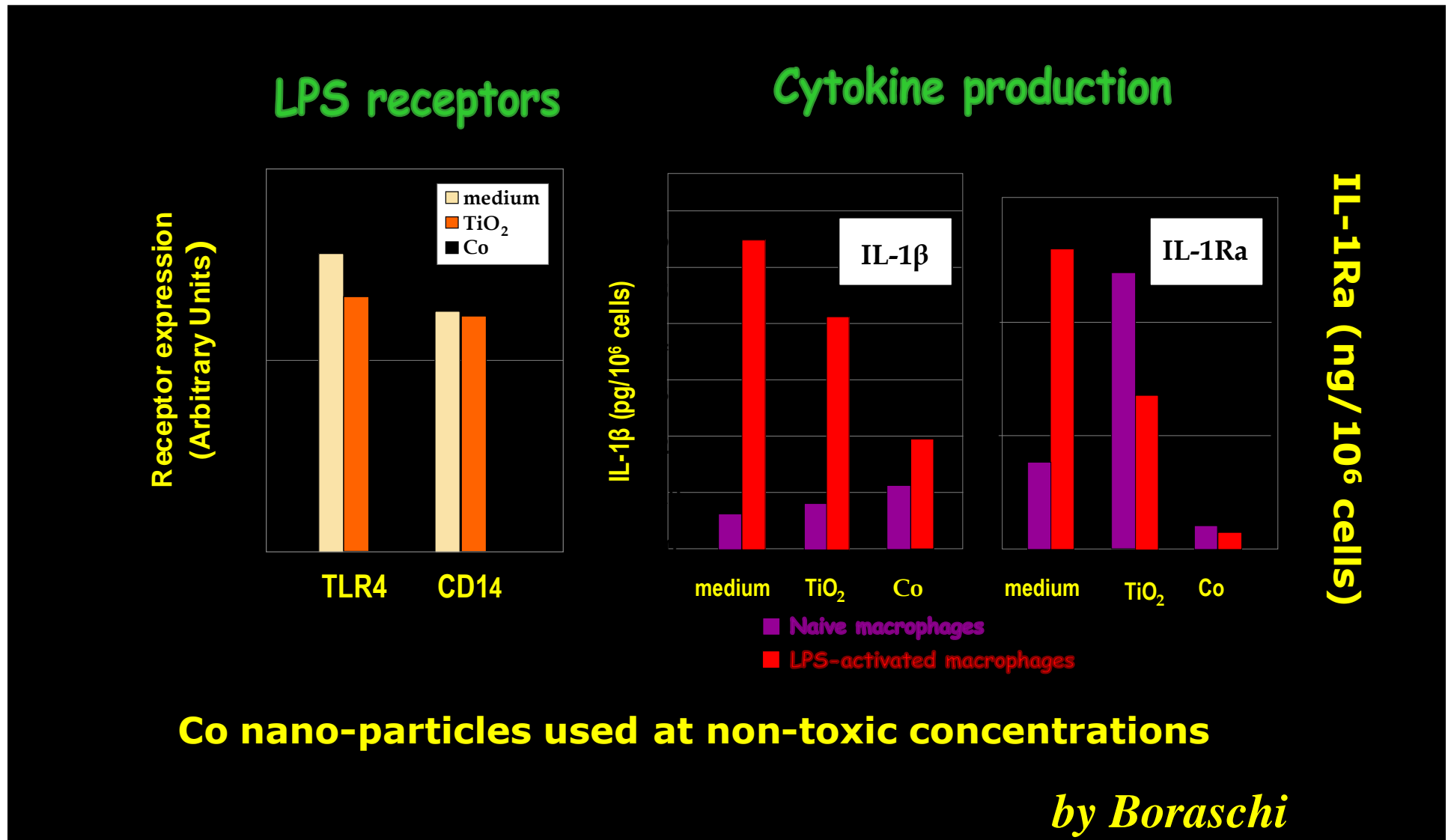
Macrophage Survival

U937

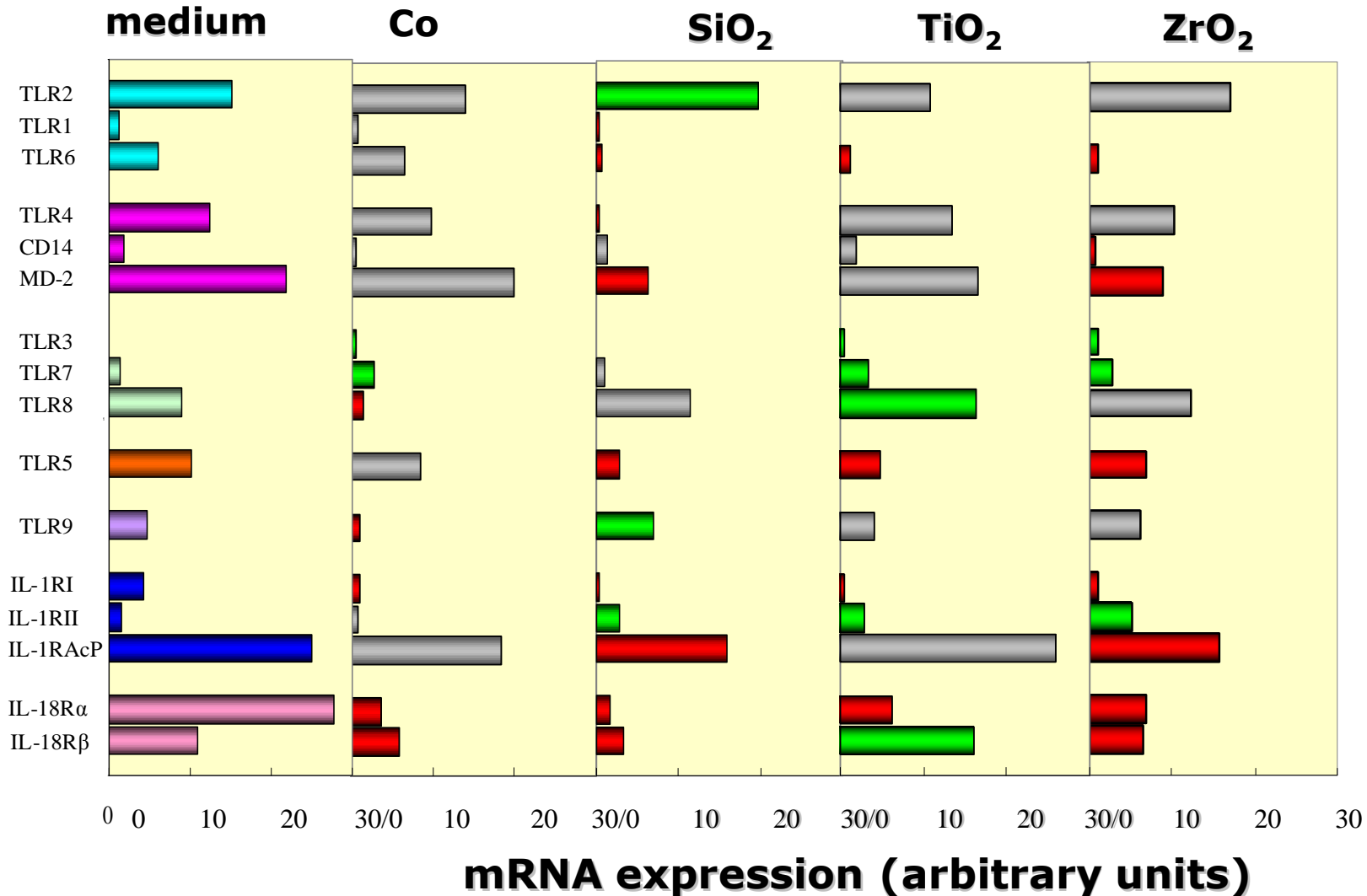


by Boraschi

Co nanoparticles inhibit macrophage reactivity to bacterial challenge



Modulation of TLR expression in U937 by nano-particles



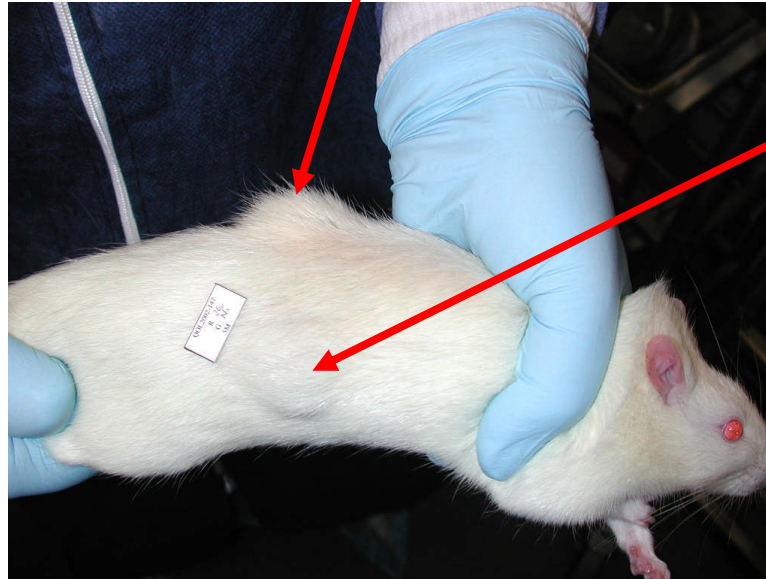
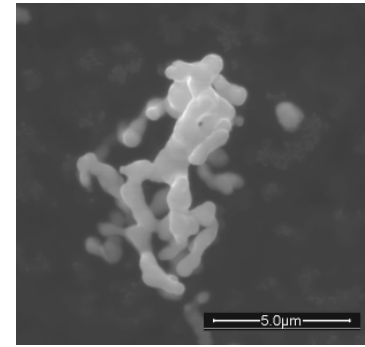
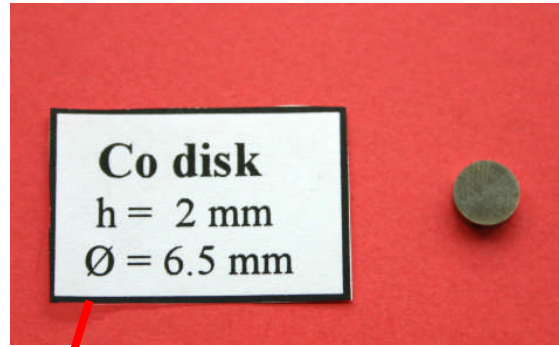
by Boraschi

Conclusions

- **Nano-particles do not affect cell survival or proliferation**
only Co nano-particles are toxic at $>100 \text{ mg}/10^6 \text{ cells}$
- **Co nano-particles inhibit expression of LPS receptors TLR4 and CD14 -** *down-regulation of mRNA expression for TLR4 and CD14, the two receptor chains which recognise bacterial lipopolysaccharide and activate macrophage defence functions*
- **Co nano-particles impair macrophages activation by bacterial LPS -** *negligible cytokine production*

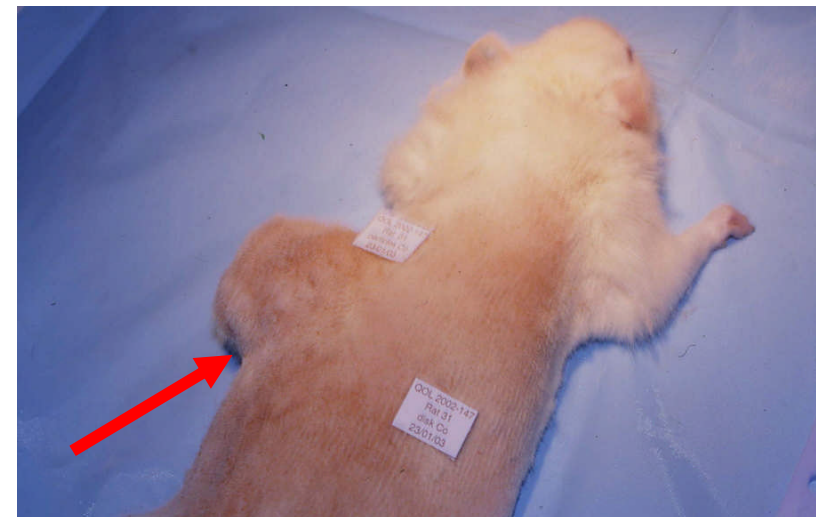
THUS:

- **IN THE PRESENCE OF CO NANO-PARTICLES, MACROPHAGES BECOME UNABLE TO MOUNT APPROPRIATE DEFENCE TO BACTERIAL CHALLENGE**
- **DANGER OF INCREASED SUSCEPTIBILITY TO INFECTIONS**



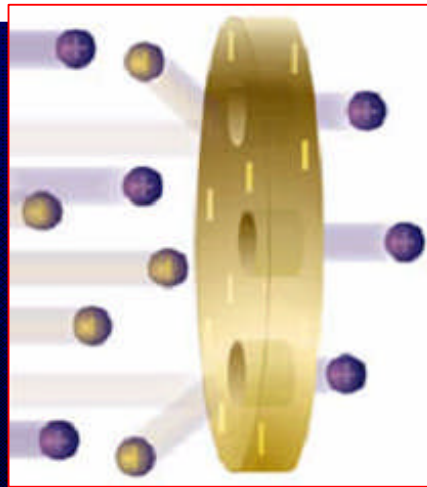
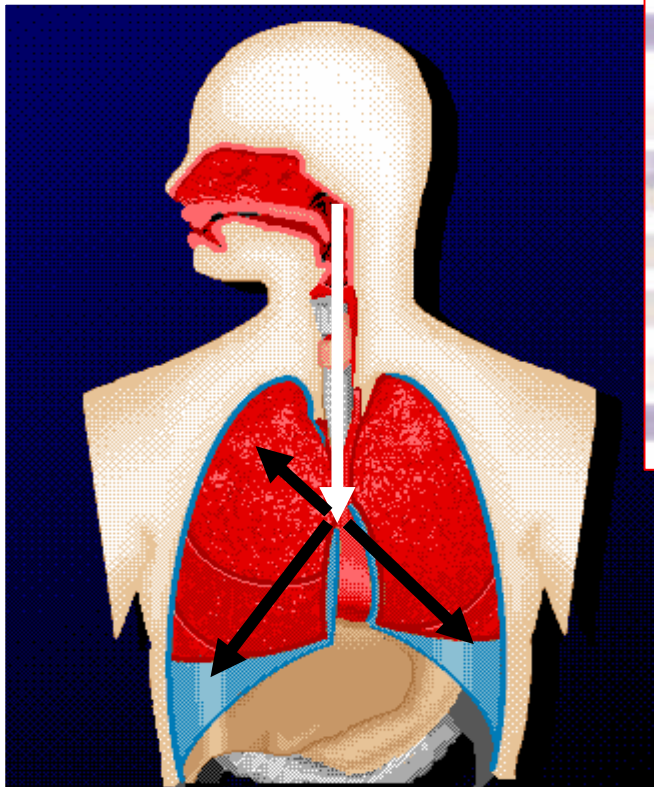
Ni Group :
nodules observed on both sides
(particles + bulk material) in all
animals 6 months after
implantation

Co Group :
Nodules observed on the left
side (nanoparticles IM) in all
cases 8 months after
implantation
– nothing on the right side (bulk
material implanted SC)

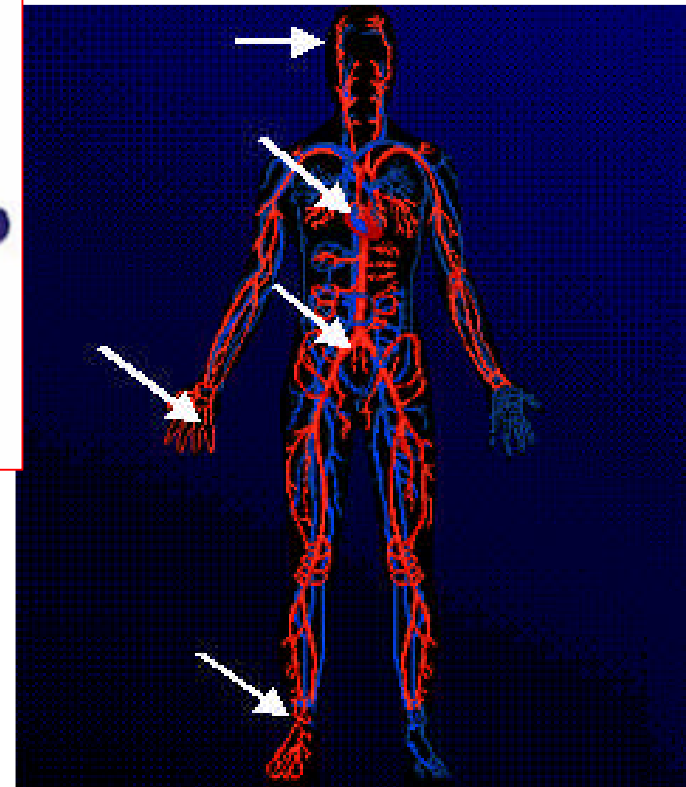


Mechanisms of entrance of nanoparticles into the human body

Respiratory system

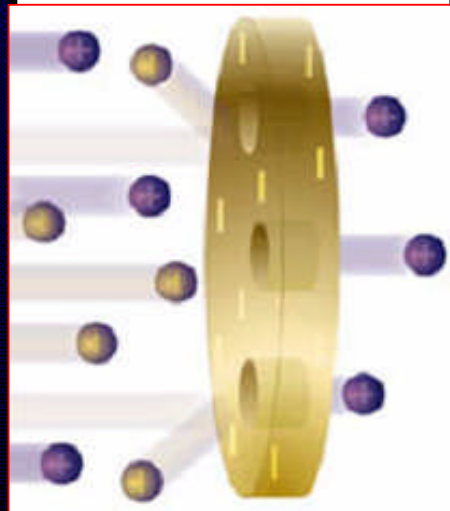
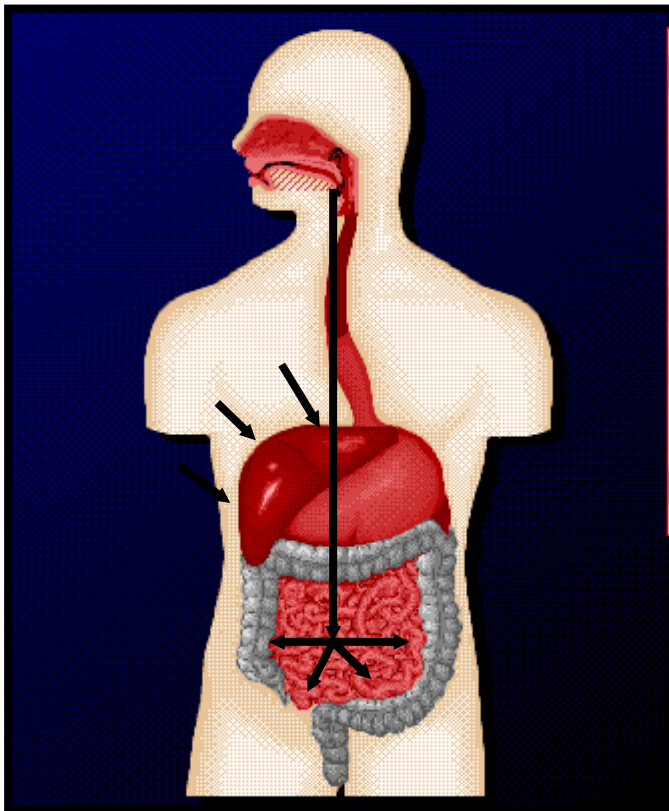


Blood circulation



Mechanisms of entrance of nanoparticles into the human body

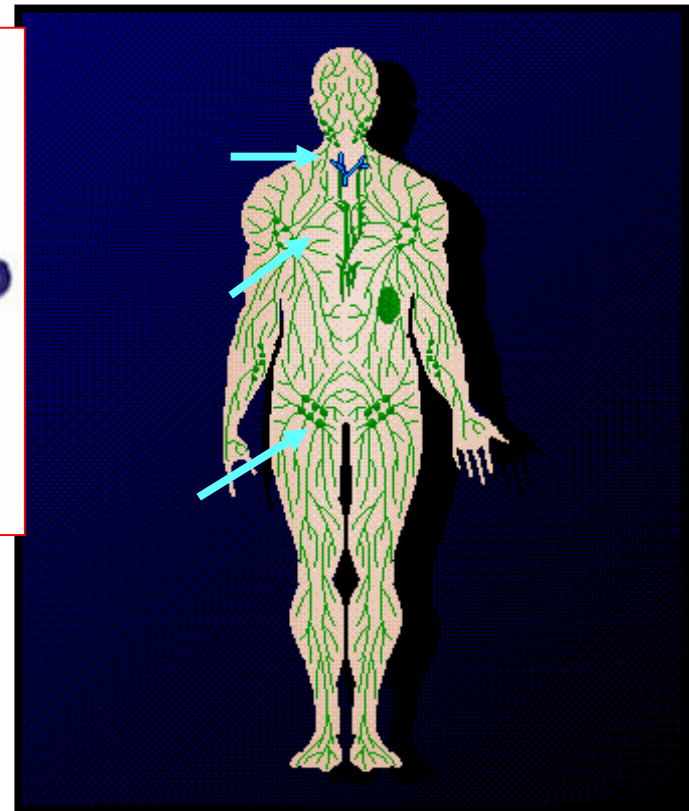
Digestive system



Size $< 20\mu\text{m}$

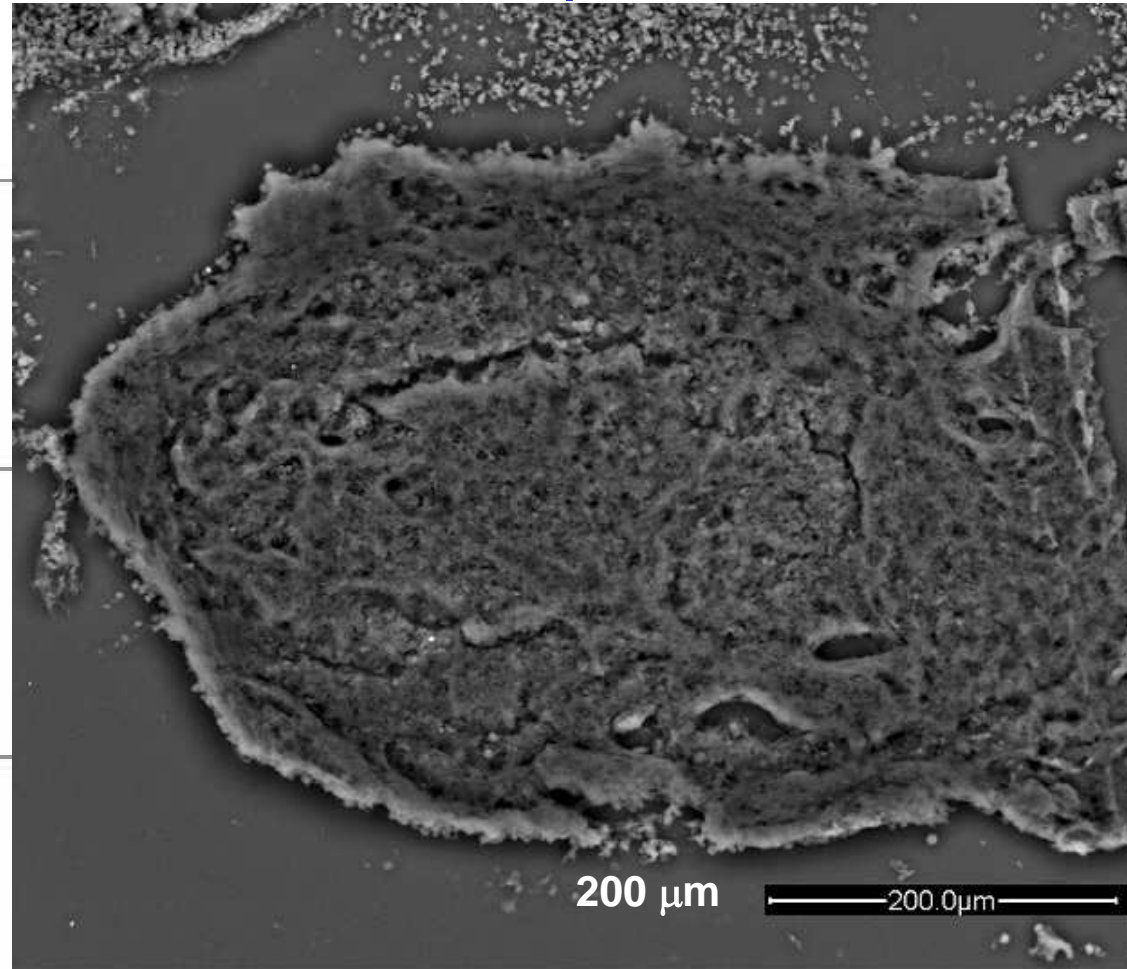
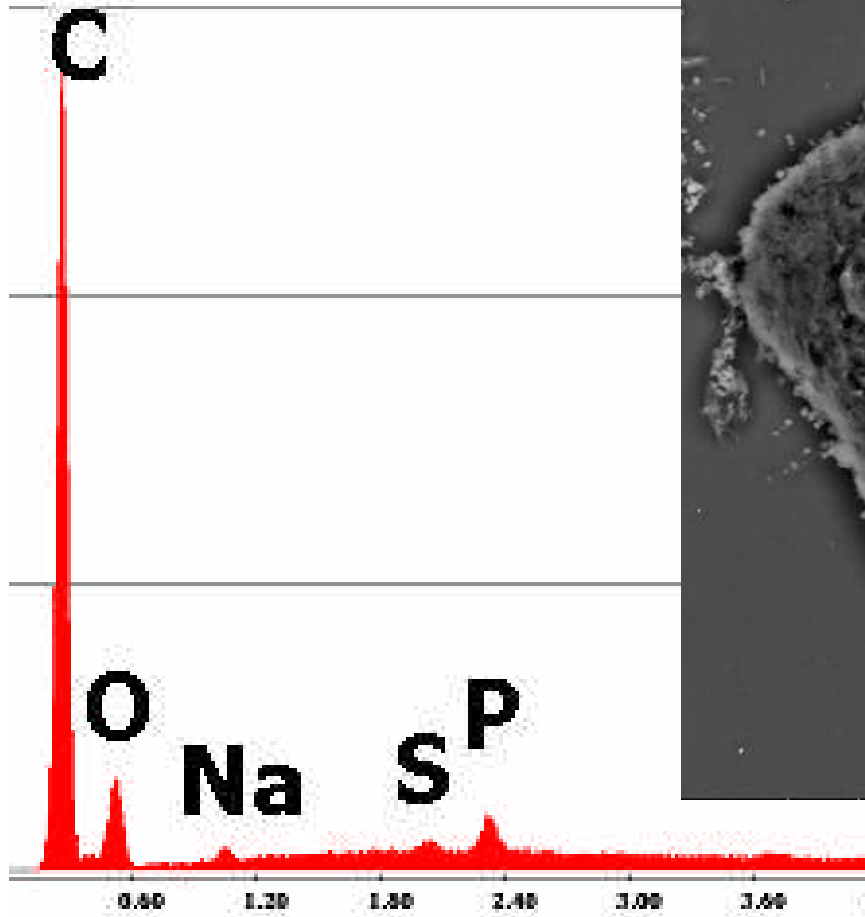


Lymph circulation



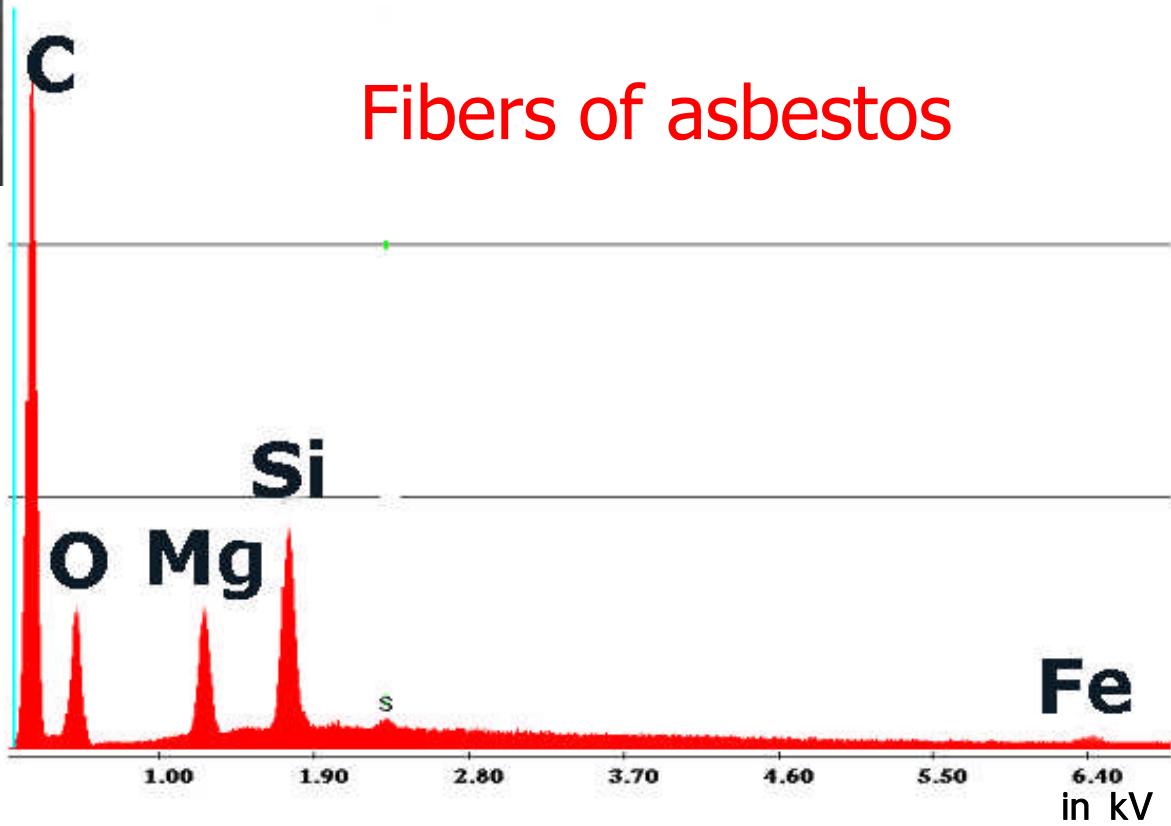
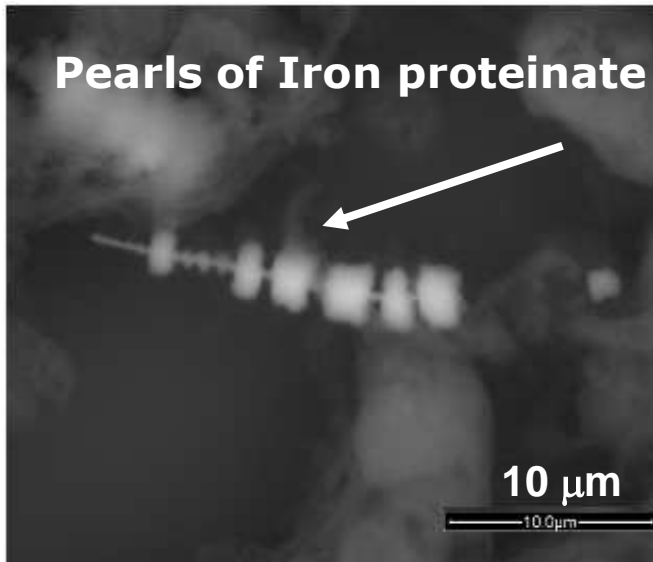
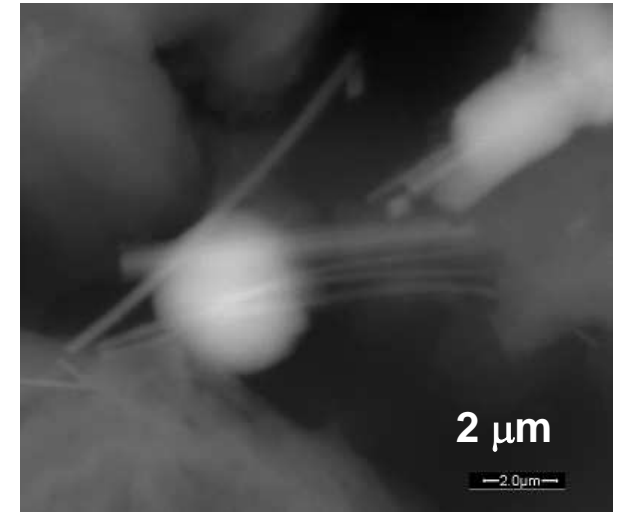
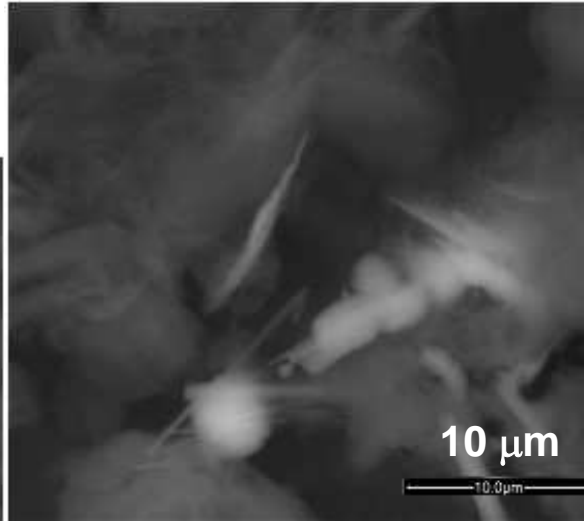
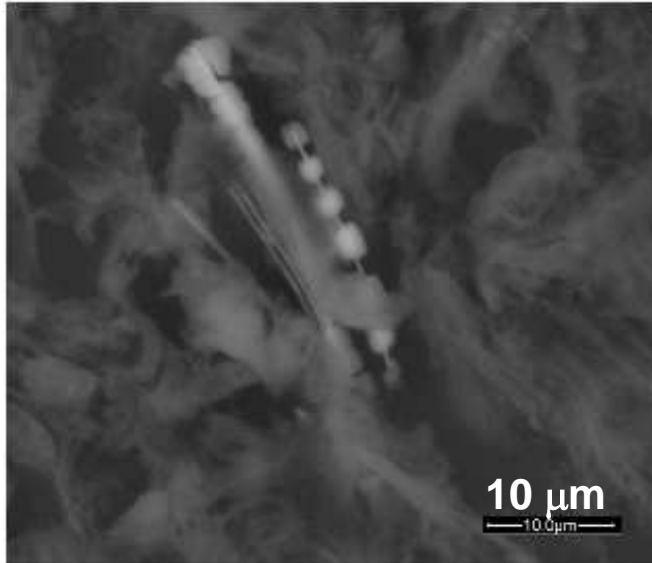
Polluted food

Cross section of a thrombus formed in vivo at low magnification with the EDS spectrum of the elements

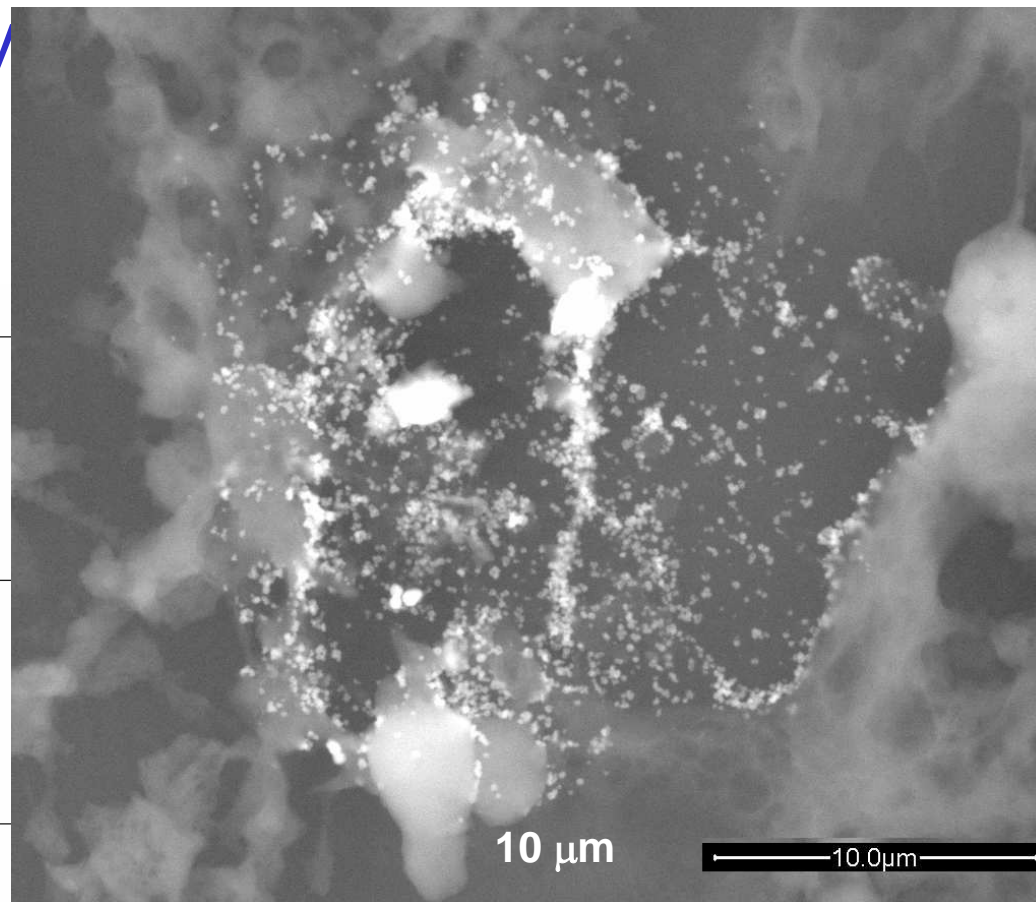
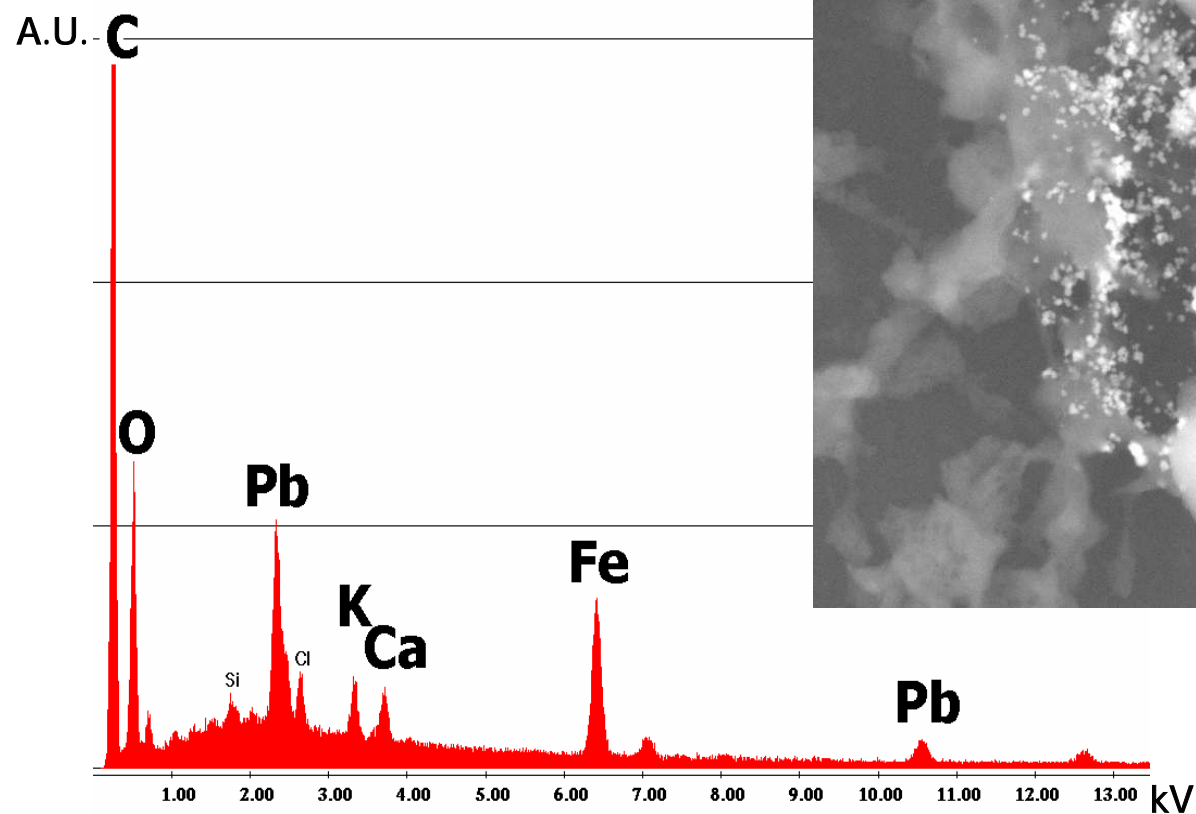


Reference sample

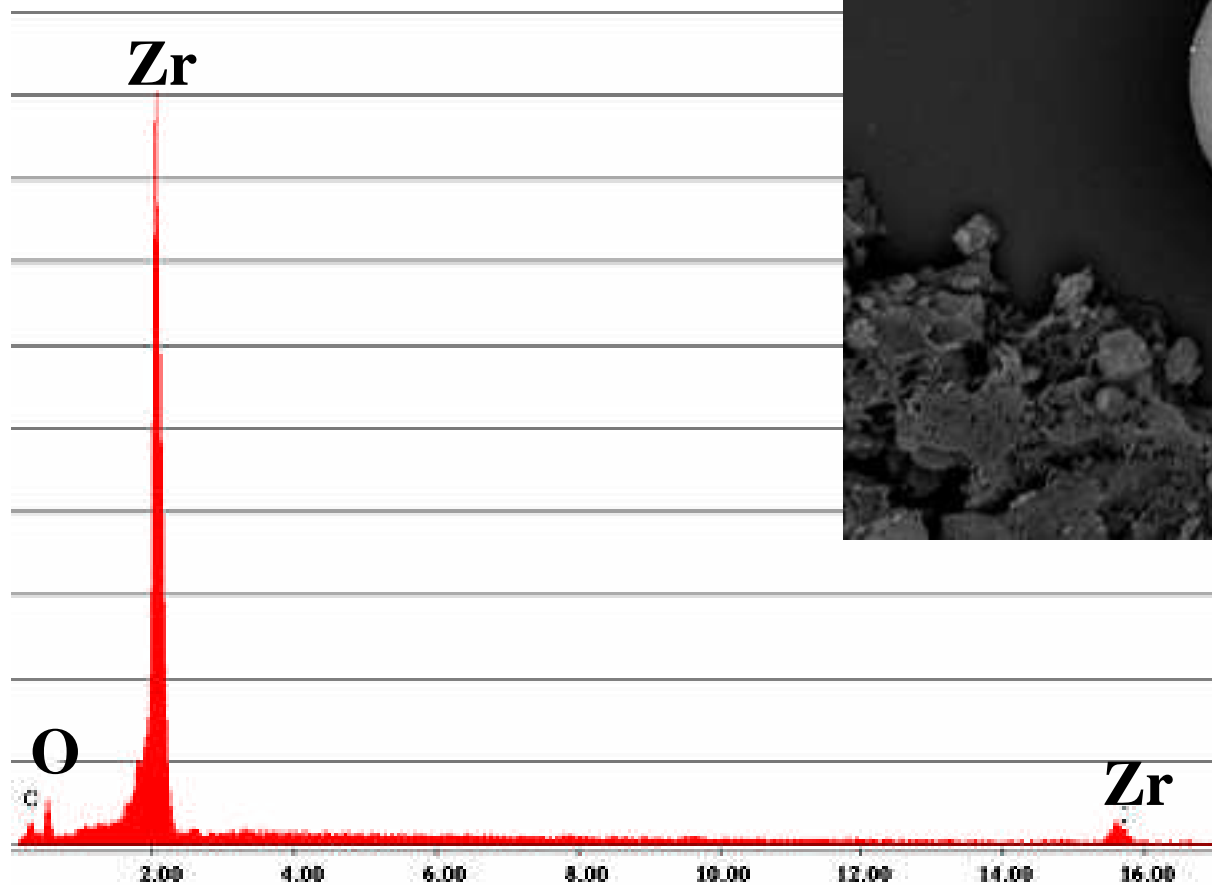
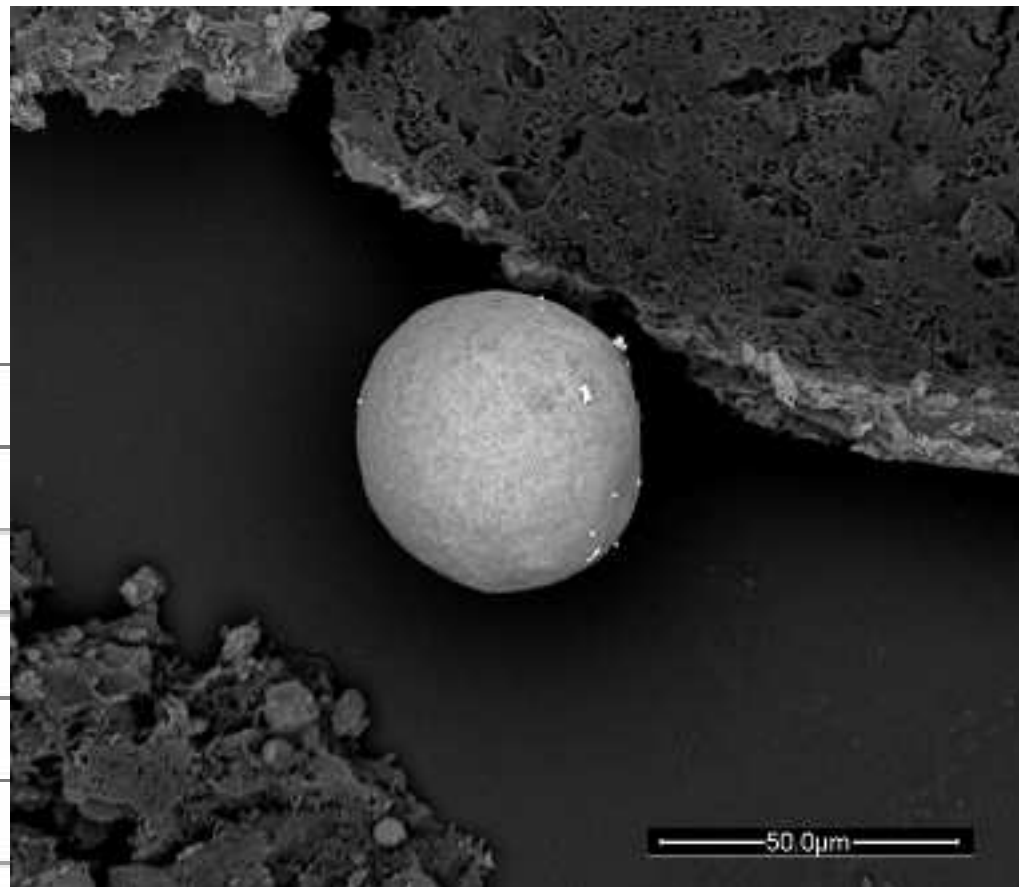
Pulmonary Mesothelioma



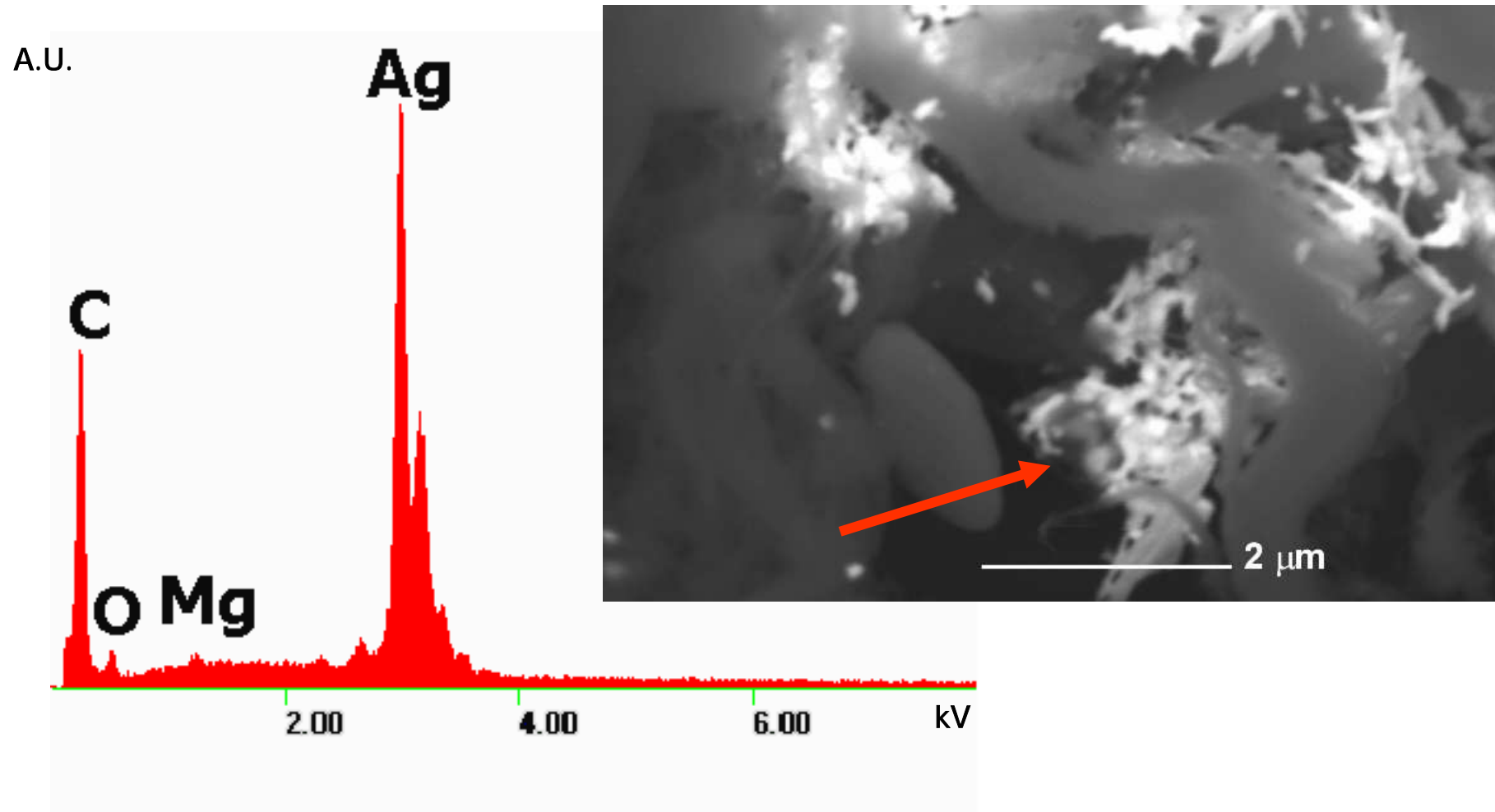
Nanoparticles of a Lead compound in the lung. The patient was affected by a multiorgan granulomatosis



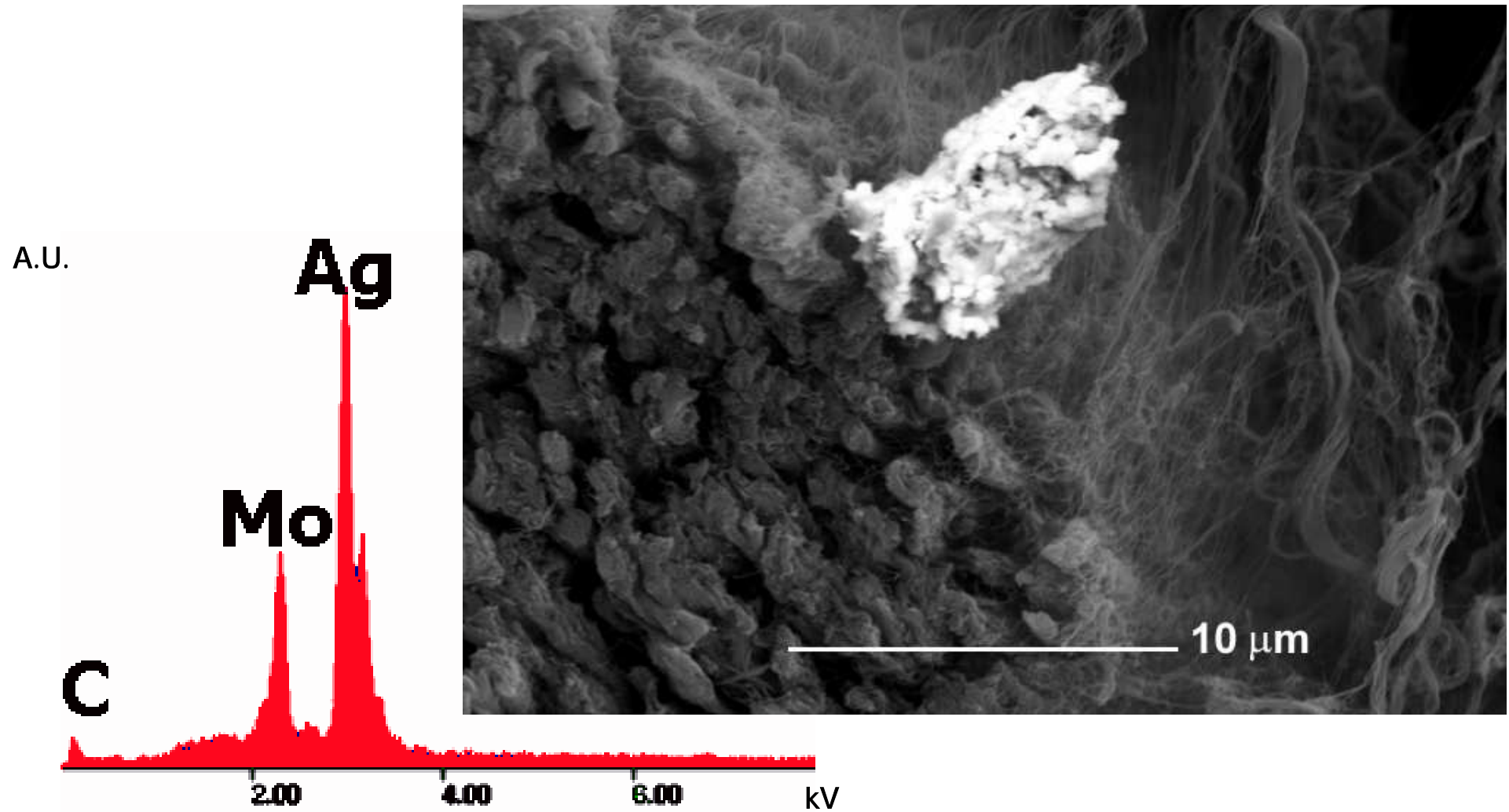
Gastric adenocarcinoma Stomach biopsy



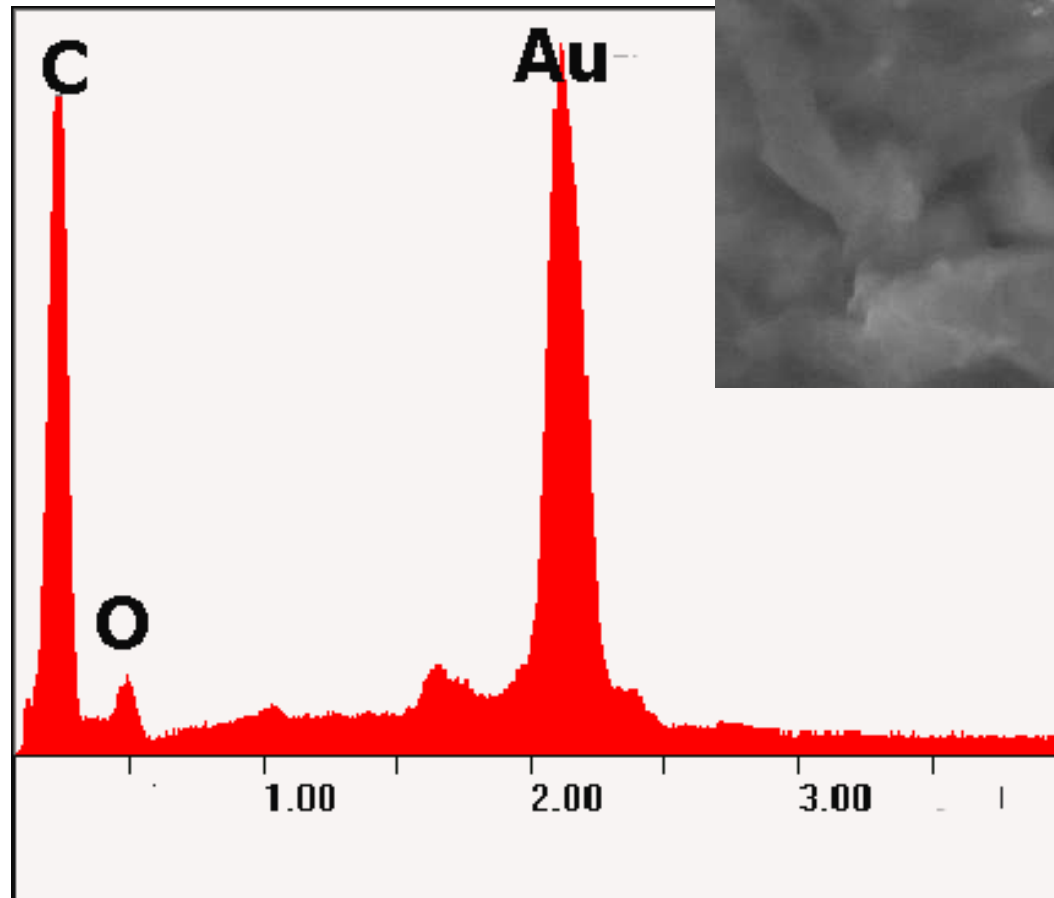
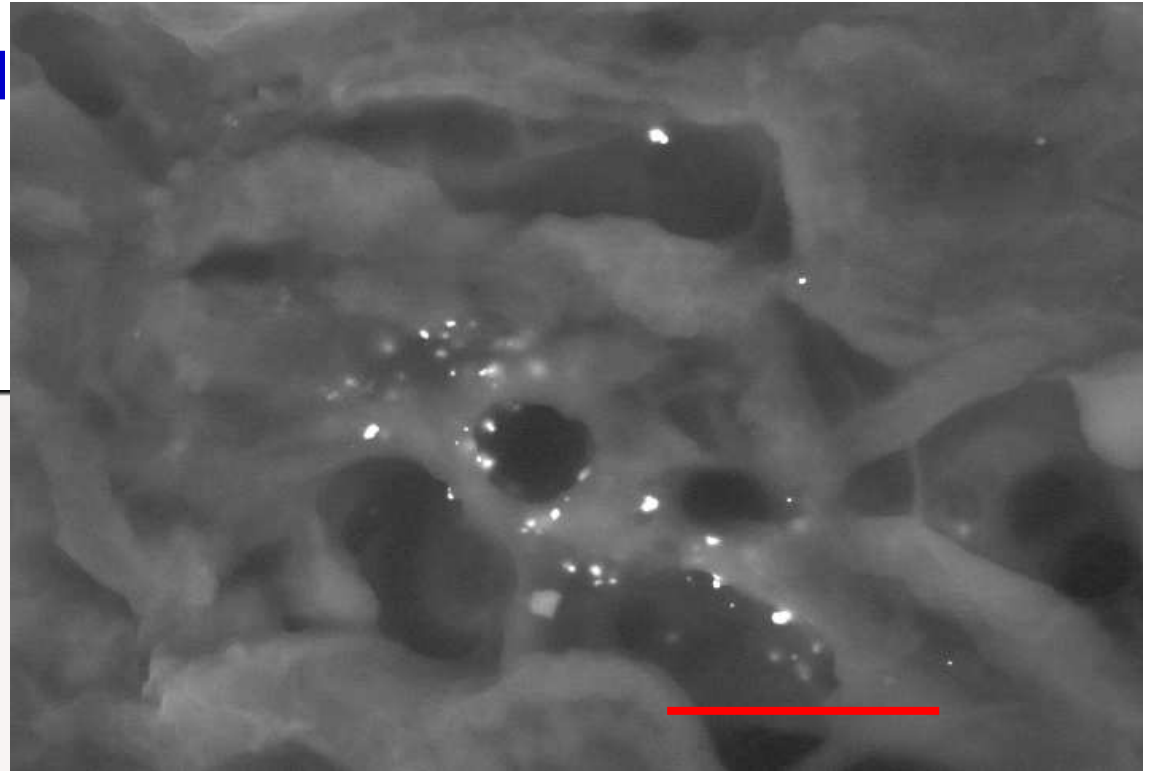
Cancerogenic tissue of the colon with aggregates of nanoparticles of Silver-Magnesium



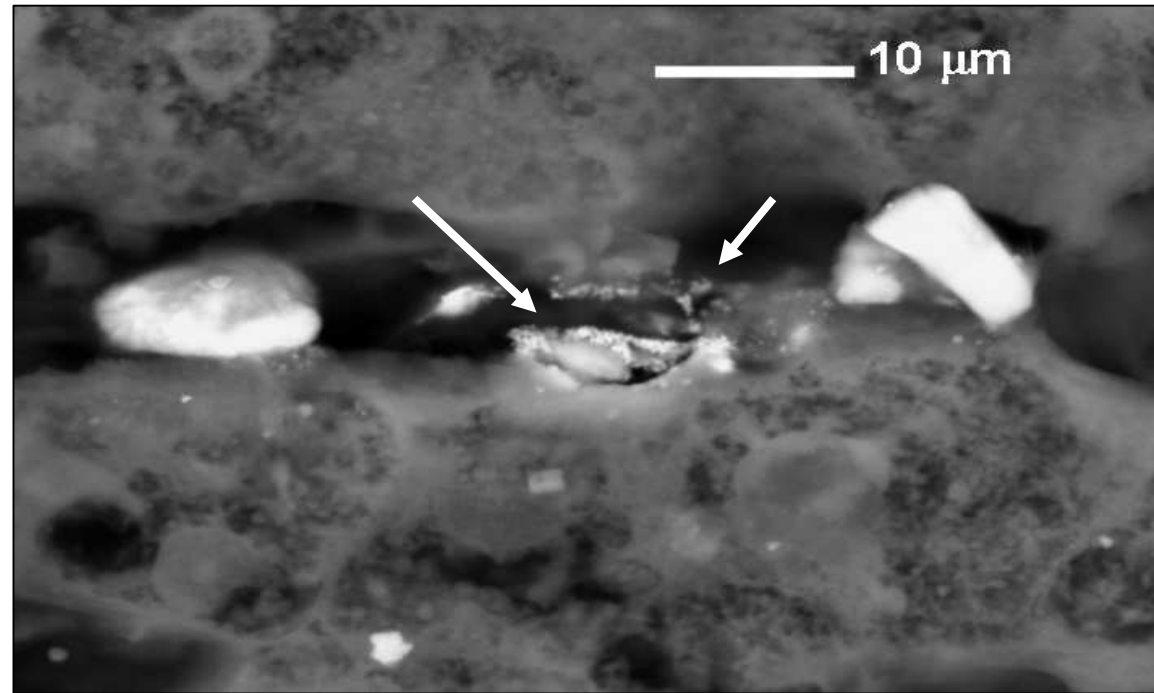
Cancerogenic tissue of colon with an aggregate of particles of Silver-Molibdenum



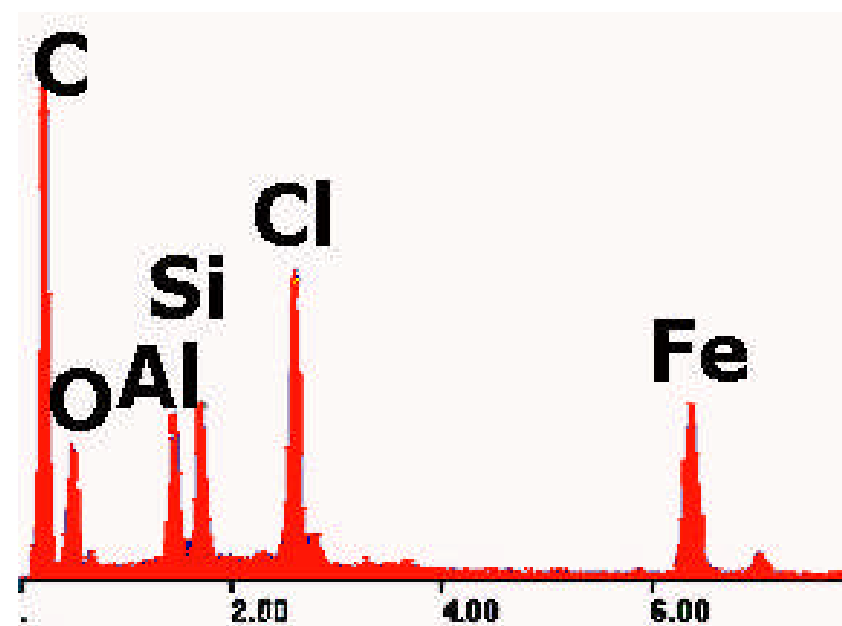
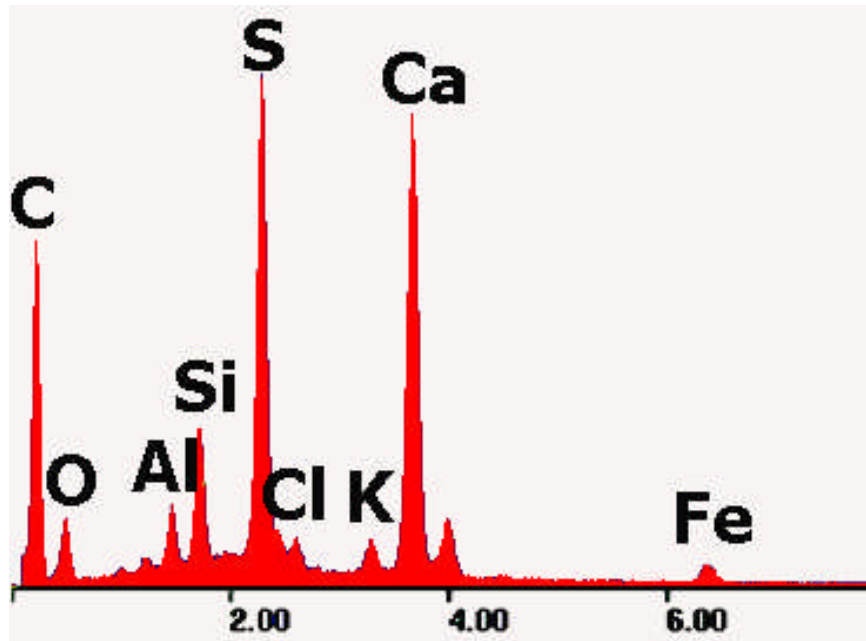
**Nanoparticles of Gold in a liver granuloma.
The patient was treated with colloidal gold particles for knee arthrosis**



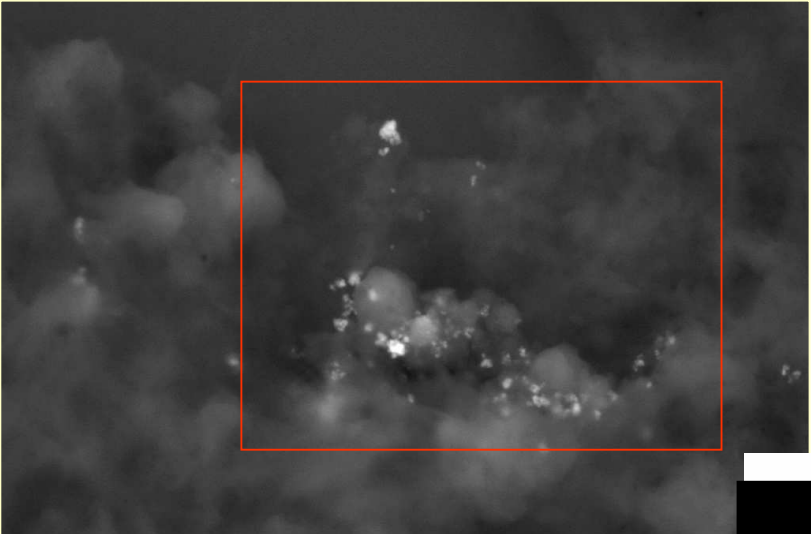
Liver affected by cryptogenic granuloma with micro debris of calcium-sulphate and clusters of nanoparticles of a silicate



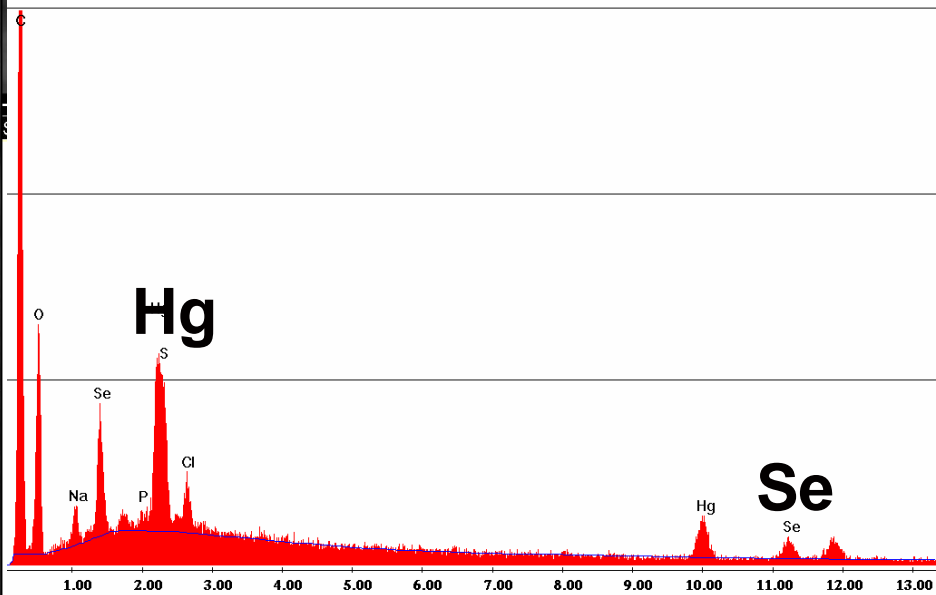
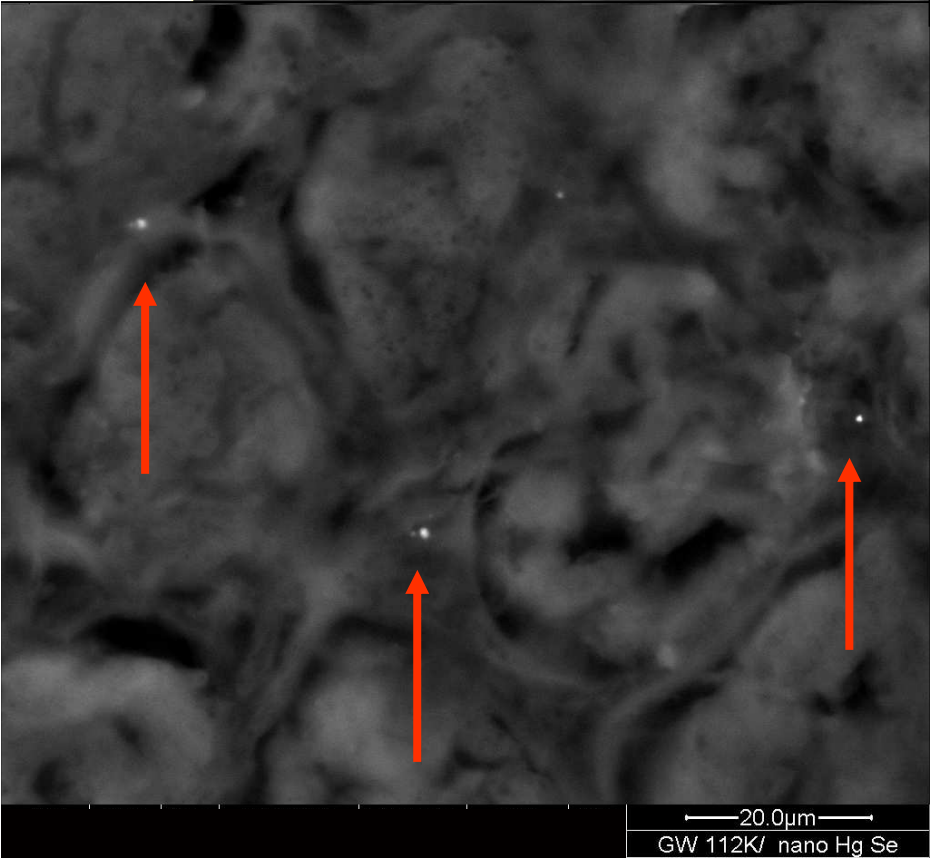
AP 6

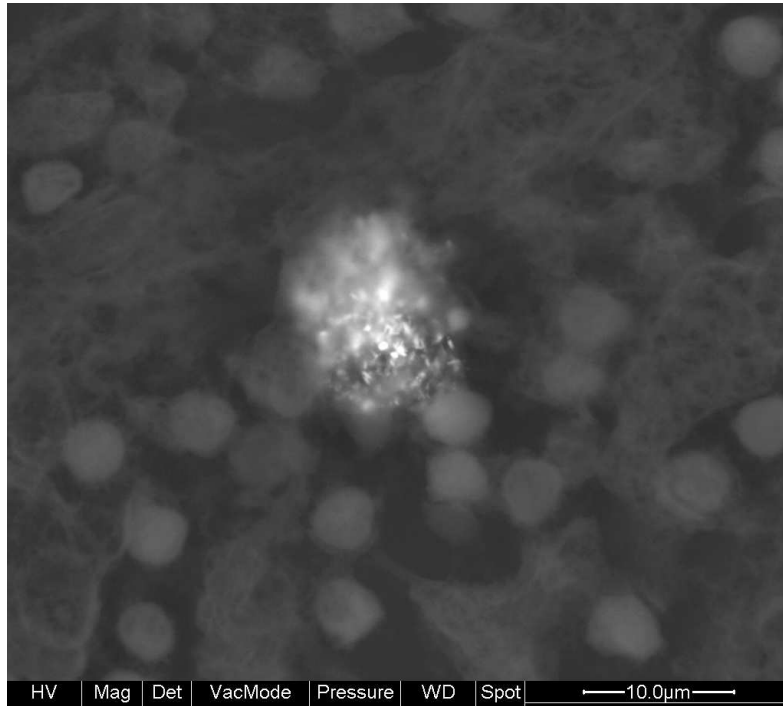


Nanoparticles in a soldier's kidney affected by the Gulf-War Syndrome

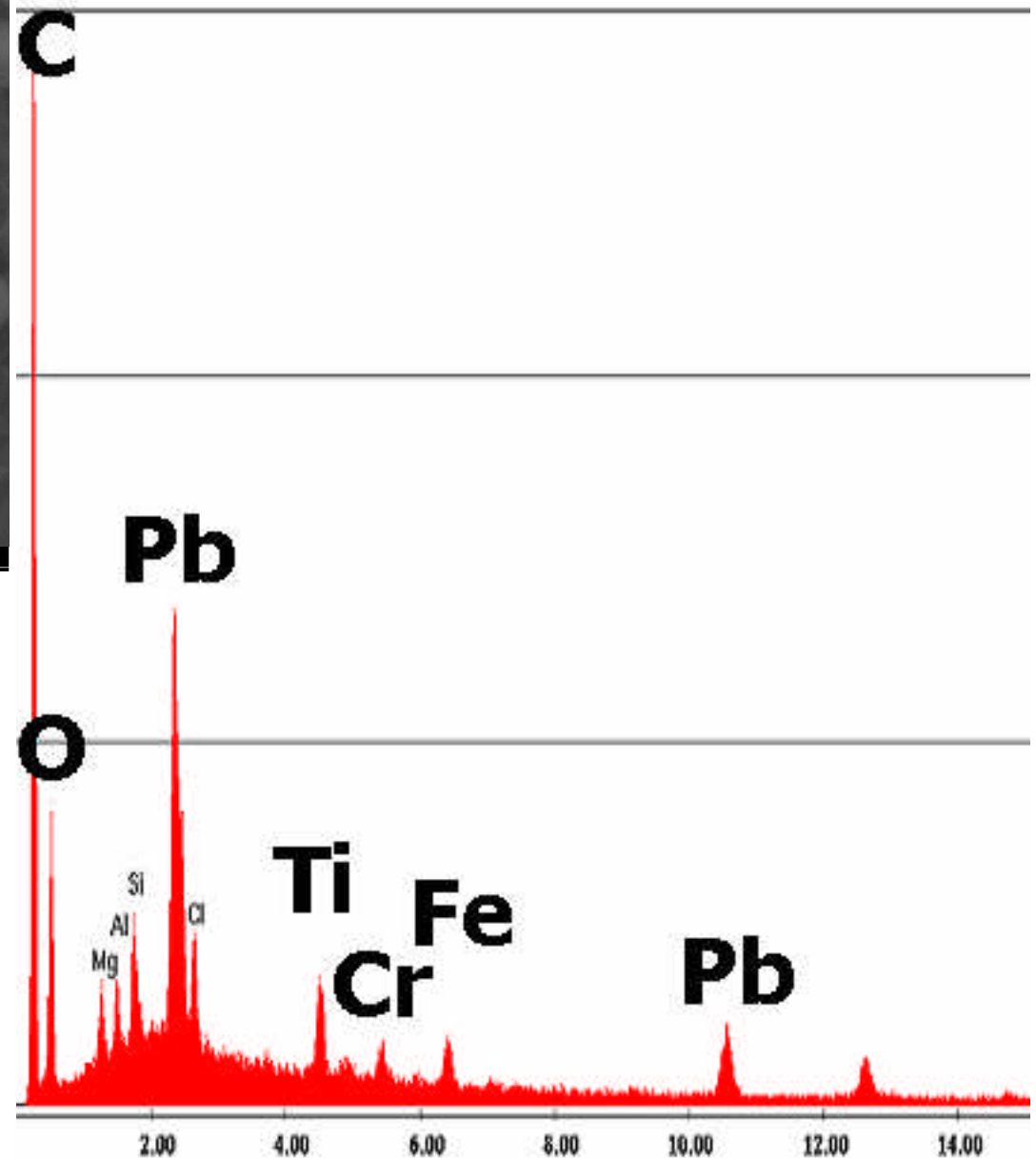


Cluster of nano Hg-Se

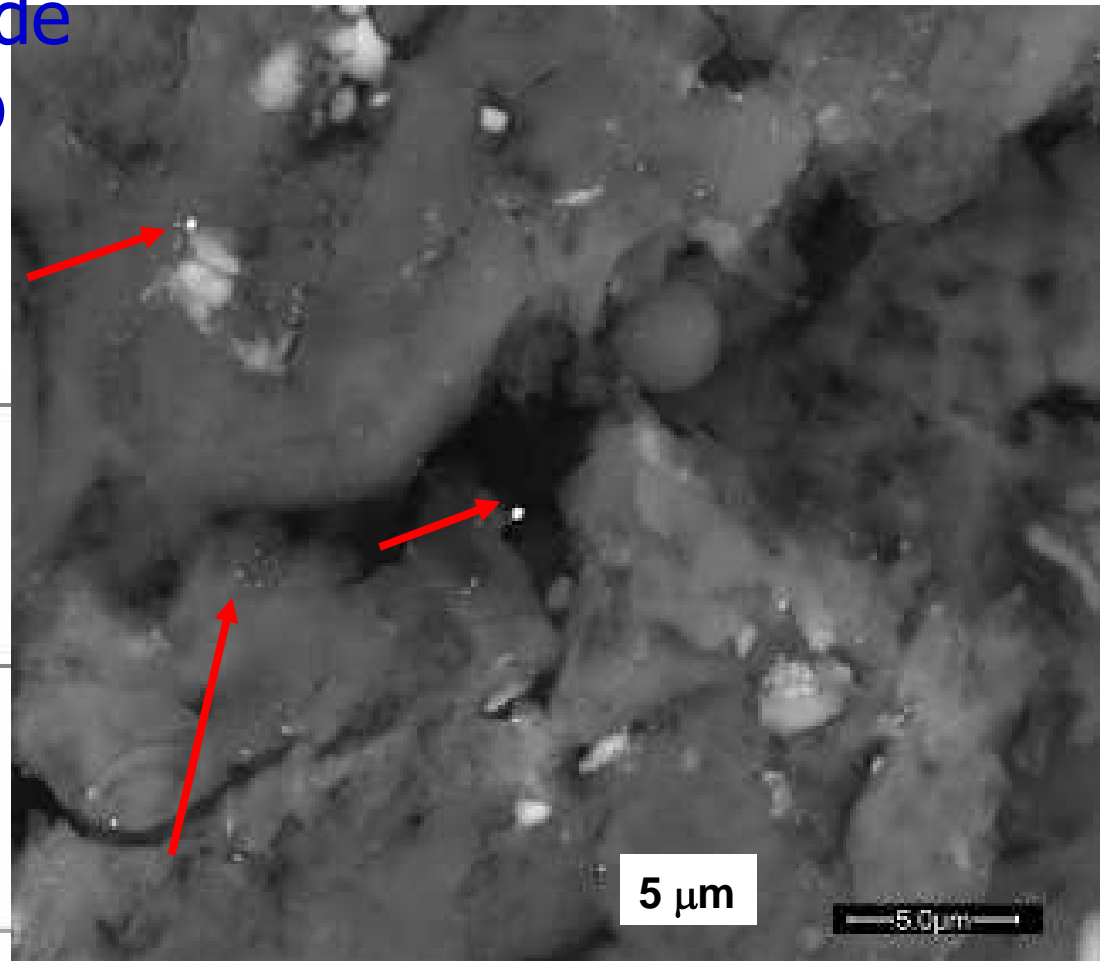
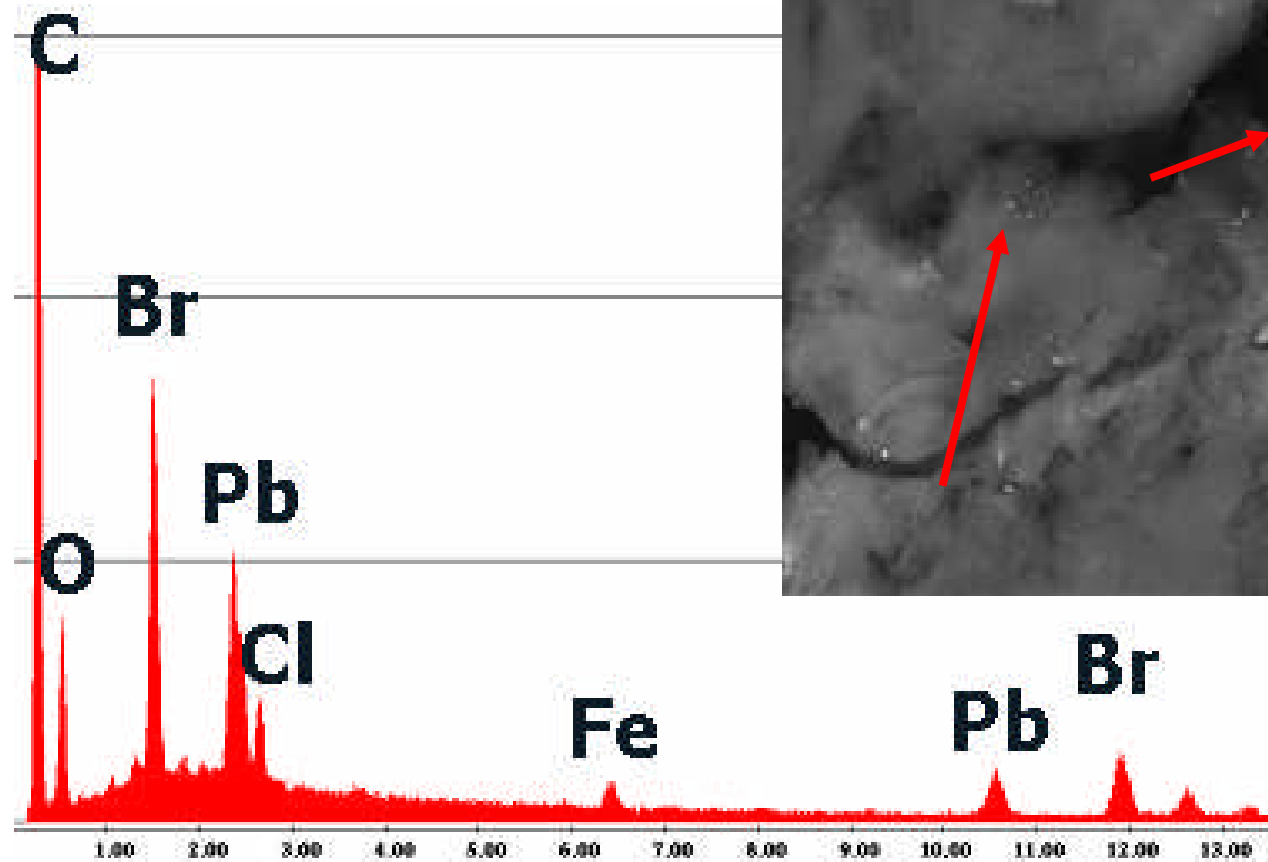




Cluster of nanoparticles of a Lead compound found in a lymph node in a non- Hodgkin lymphoma

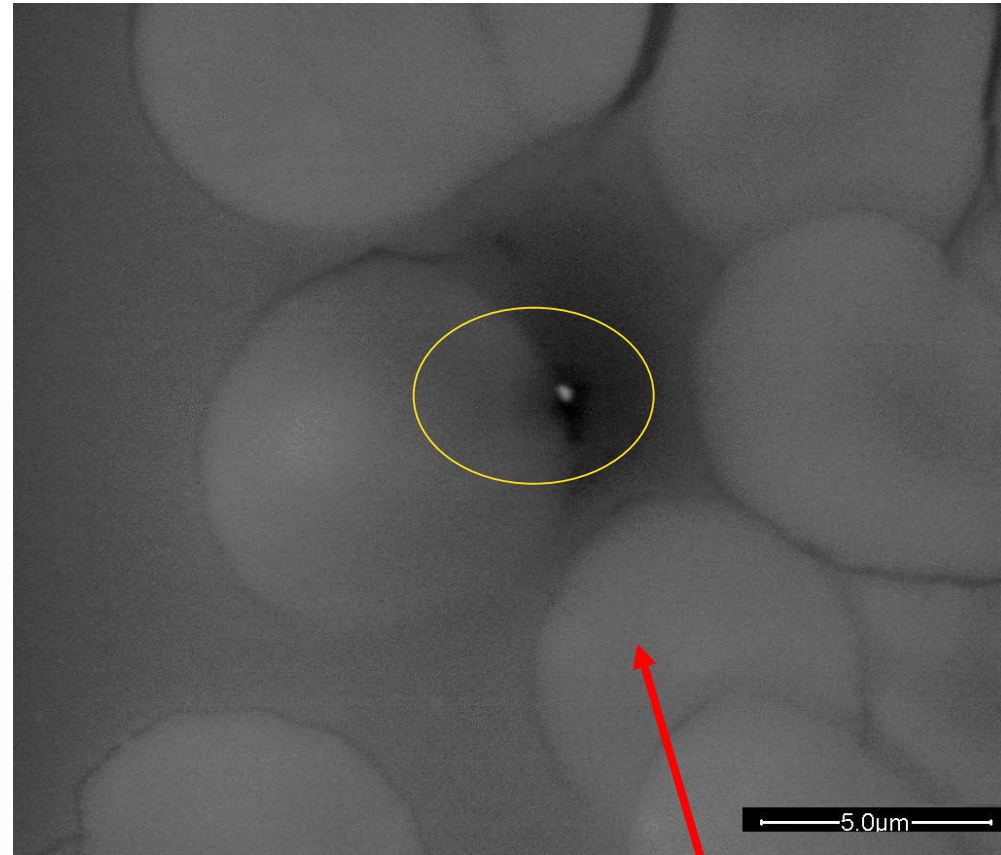
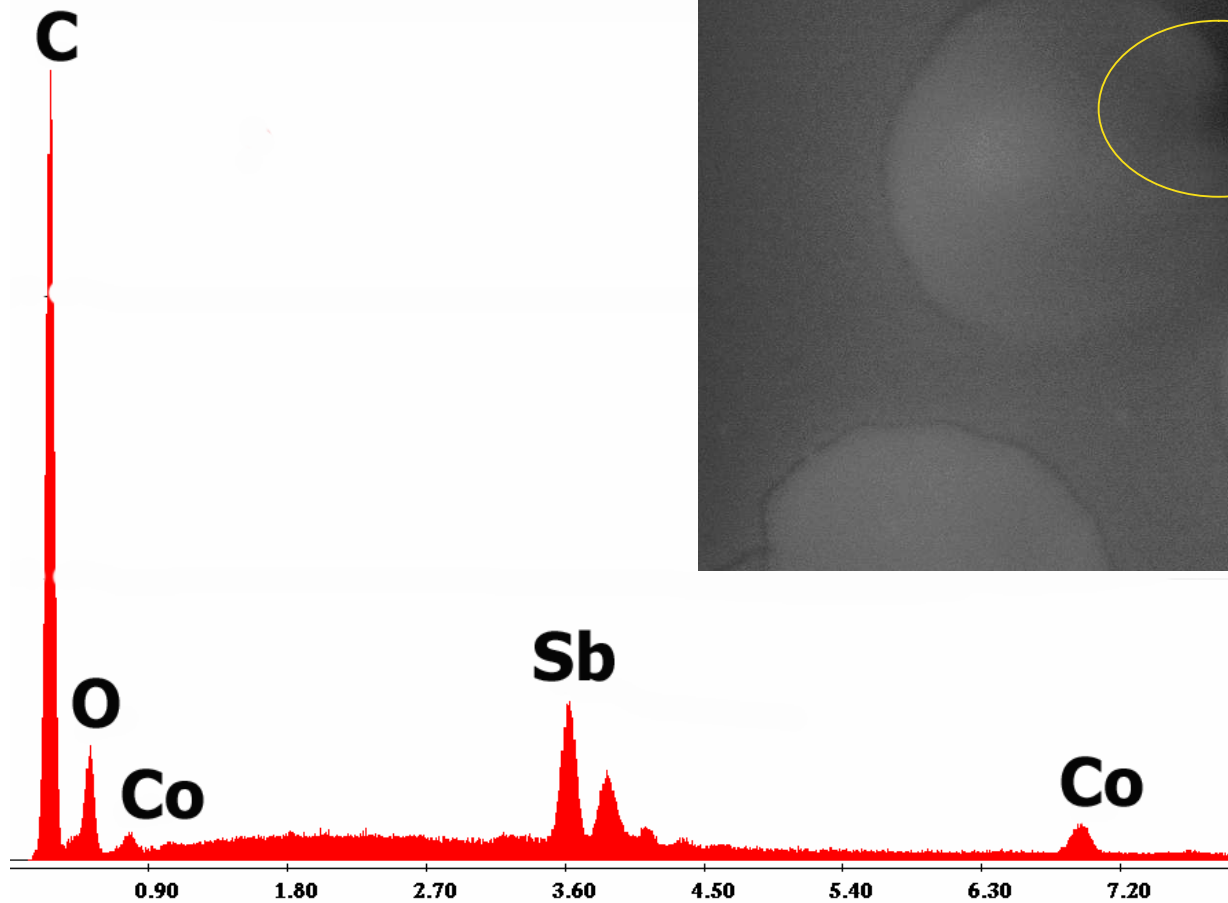


Section of a lymph- node
in a civilian of Sarajevo
affected by Hodgkin
Disease (FEG-Quanta)

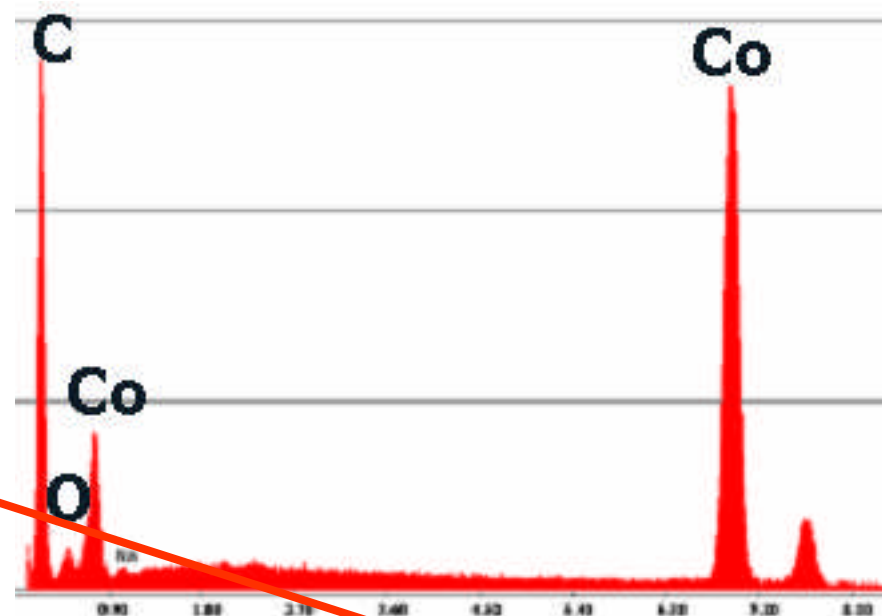
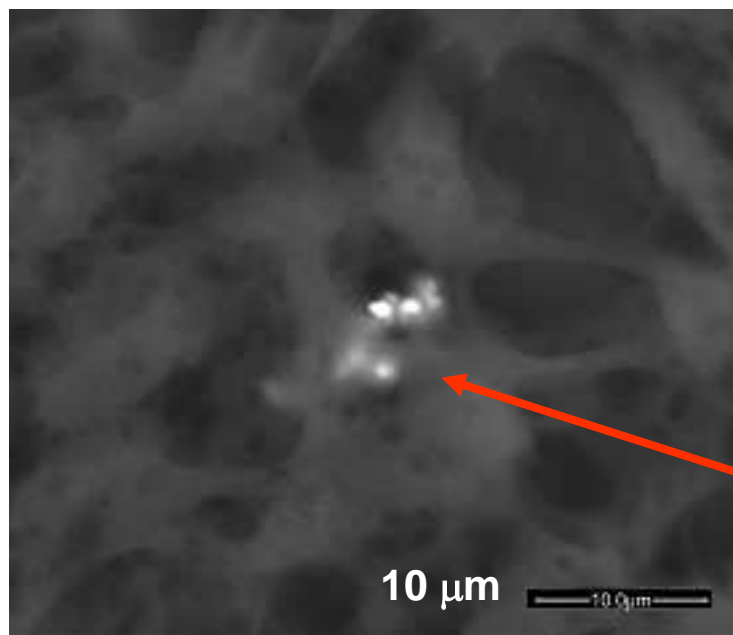


BLOOD

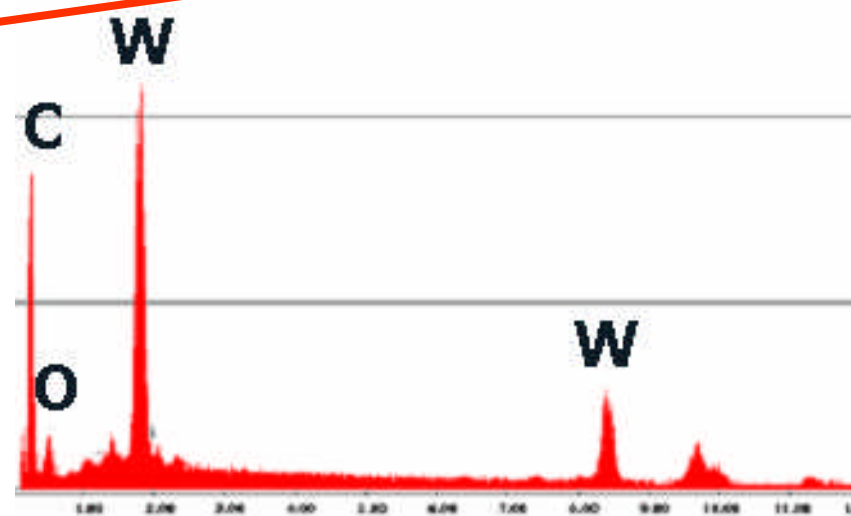
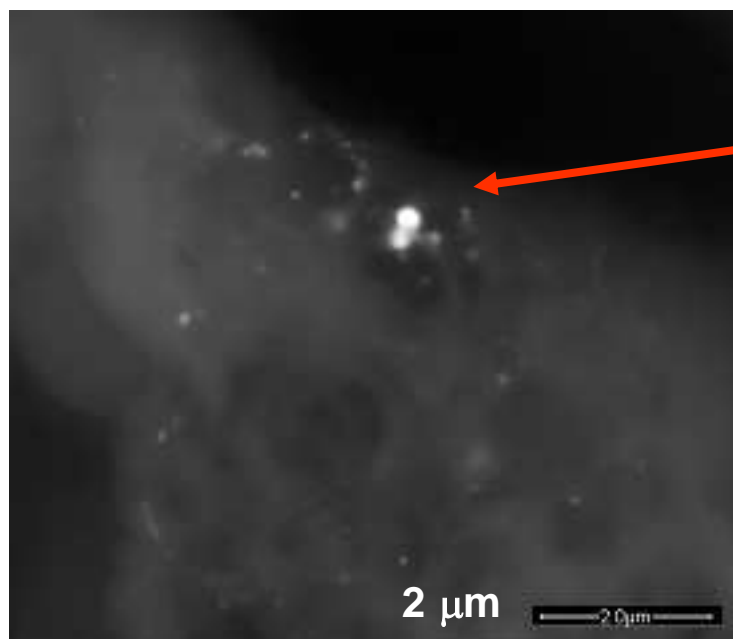
**Soldier's wife
affected by Burning
Semen disease**



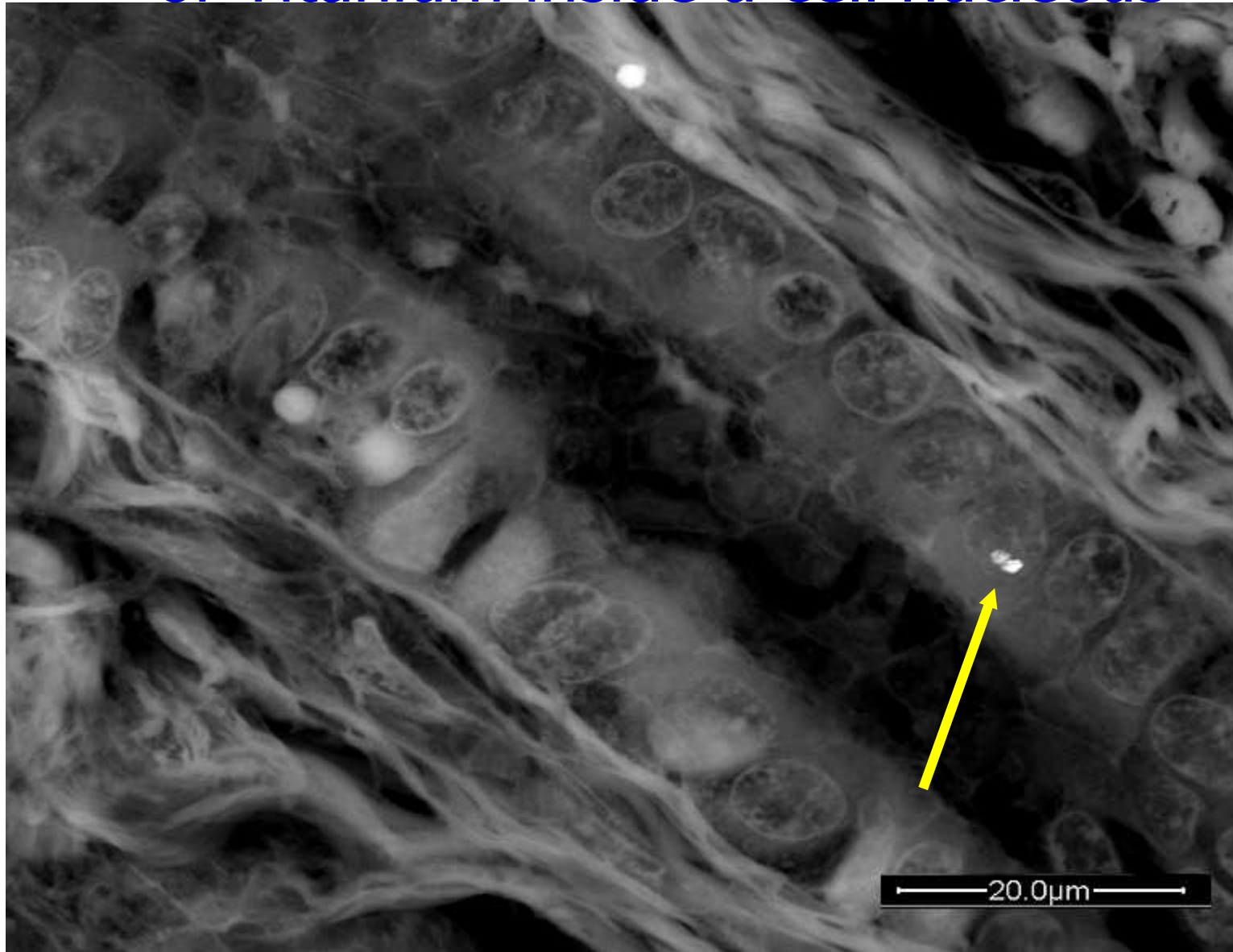
Red cells



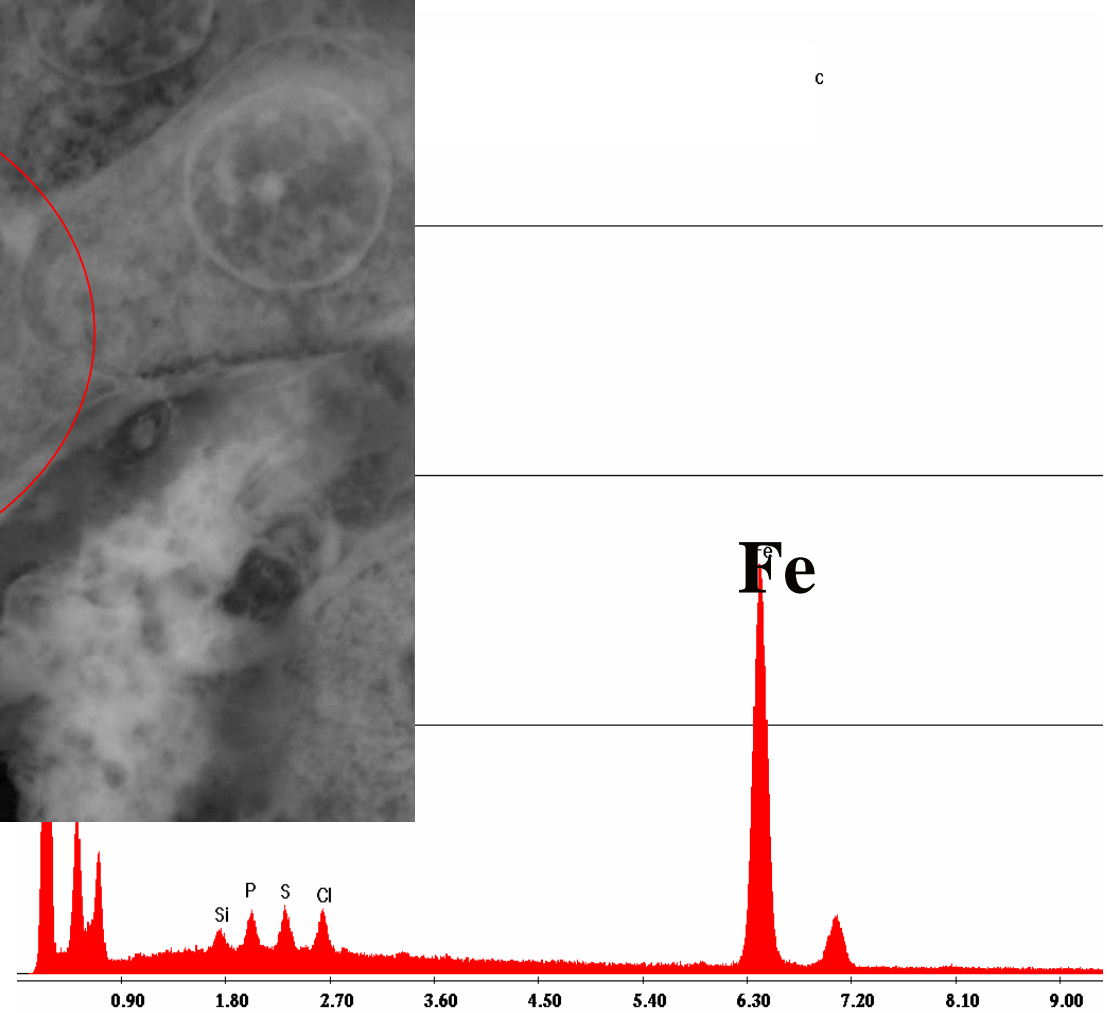
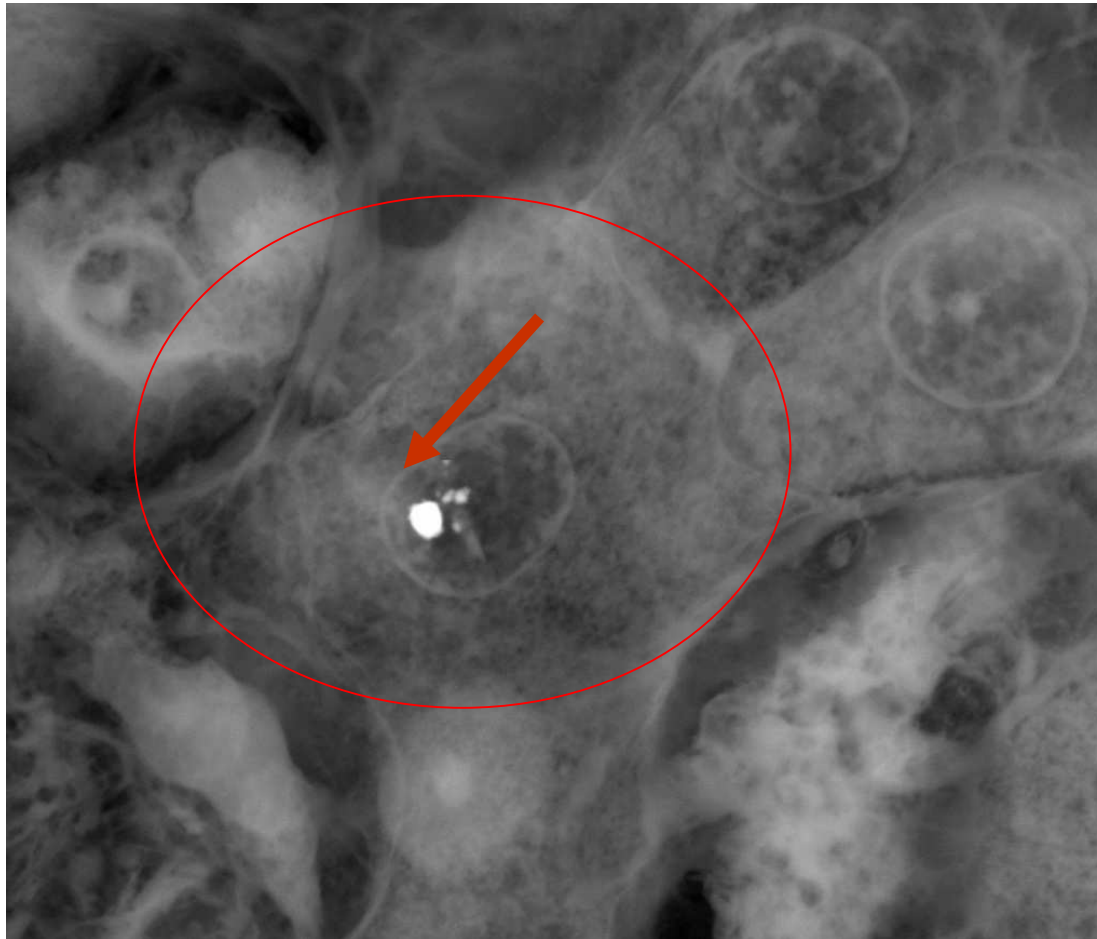
Bladder cancer with Cobalt & Tungsten



Cancerogenic liver tissue with nanoparticles of Titanium inside a cell nucleous



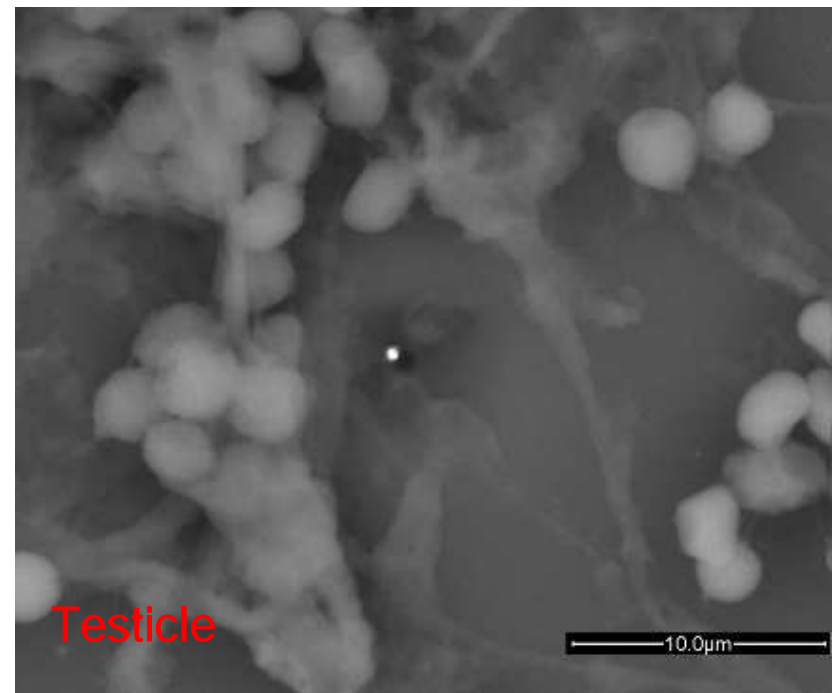
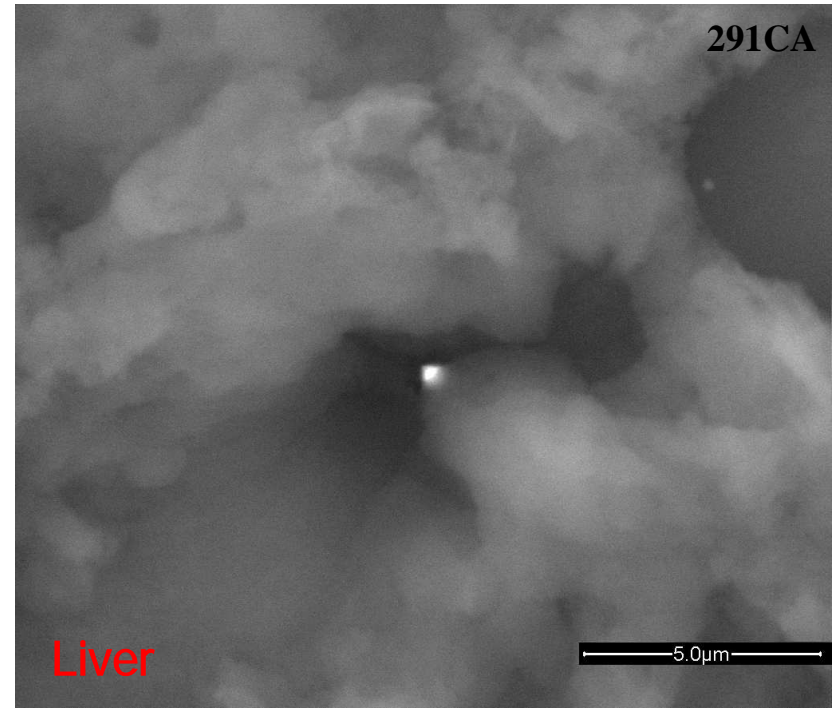
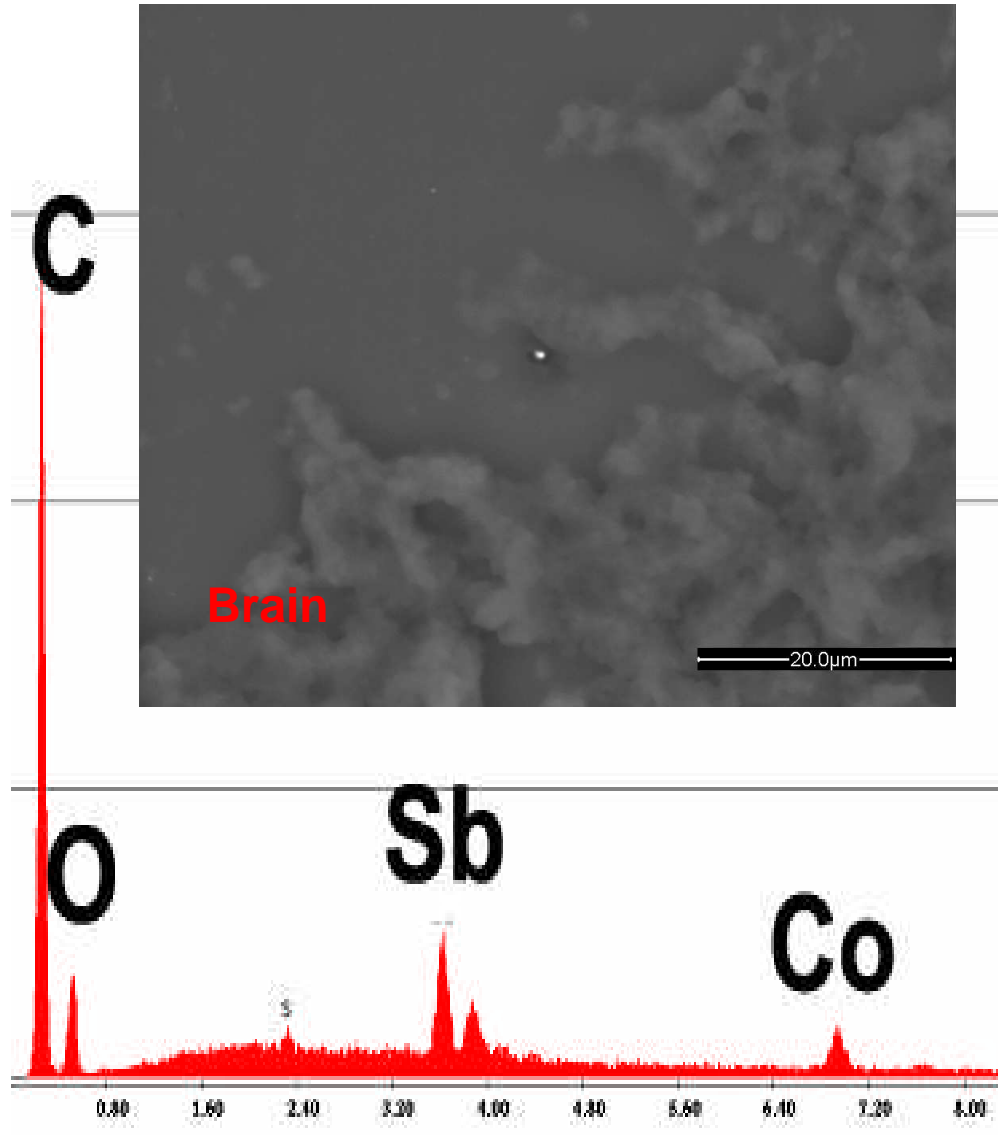
Liver cancer



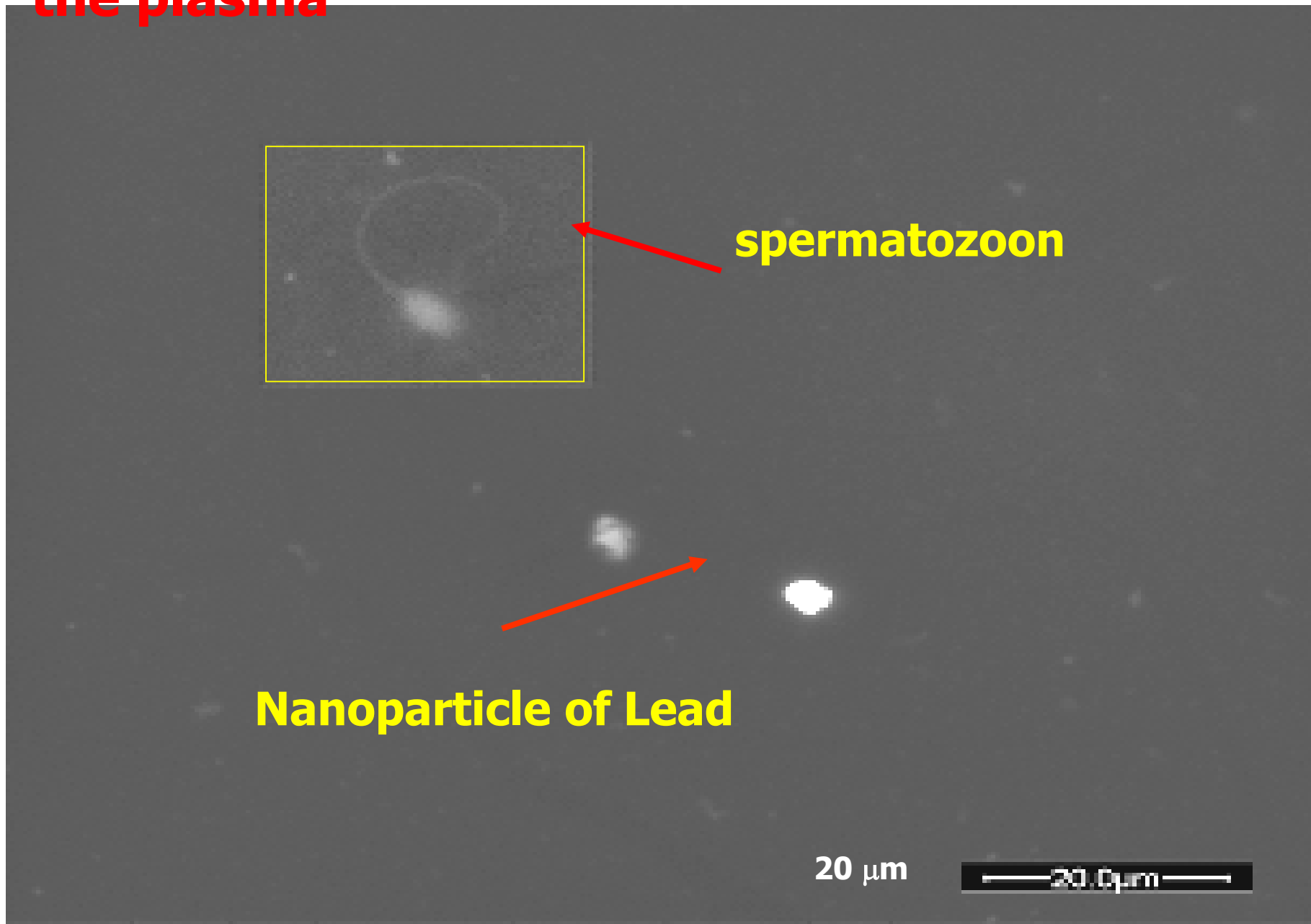
Malformed lamb born inside a
groundfire in Sardinia, 2003



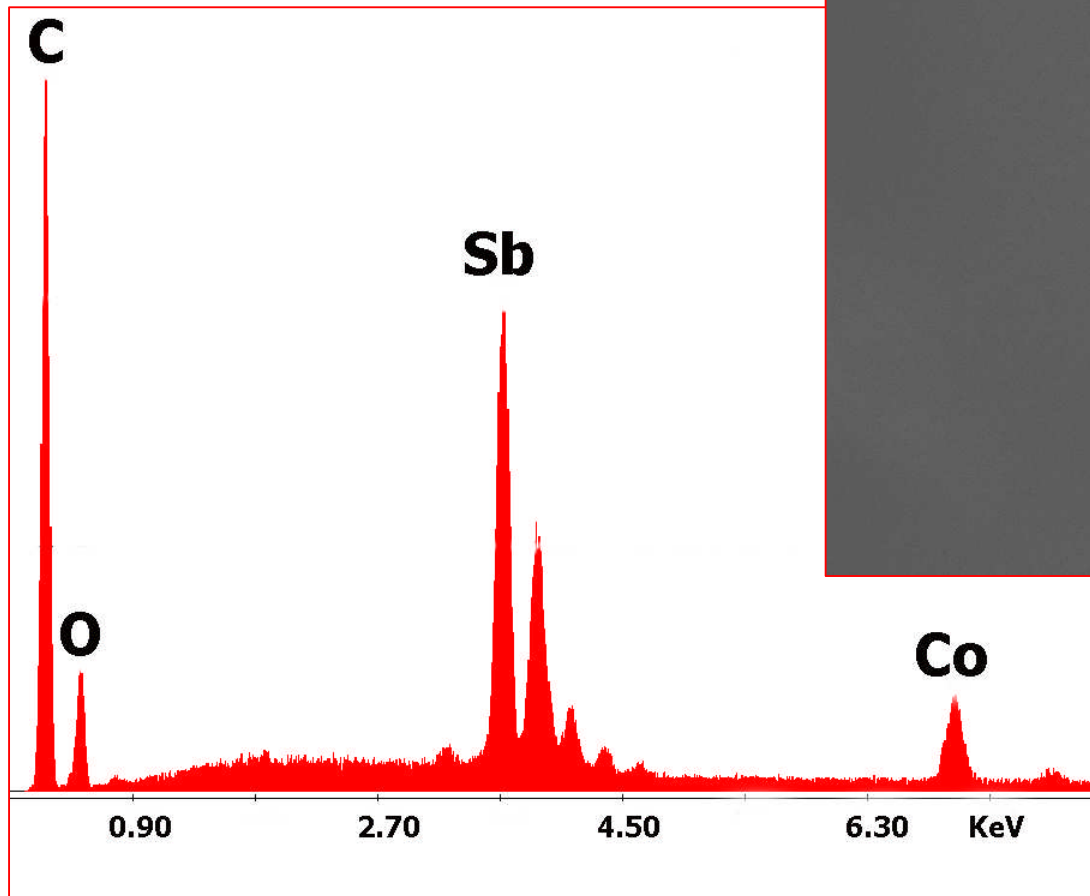
Internal organs of the malformaed foetus



ESEM analysis of an alive spermatozoon inside the plasma



Particle of Antimony- Cobalt found in a soldier's sperm



After an experience of 400 cases of human cancer analyzed we can state:

Can nanoparticles have a pathological meaning to the human health ?

Evidence says: YES

Are the normal cell defence reactions still valid?

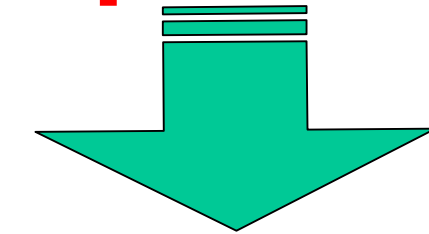
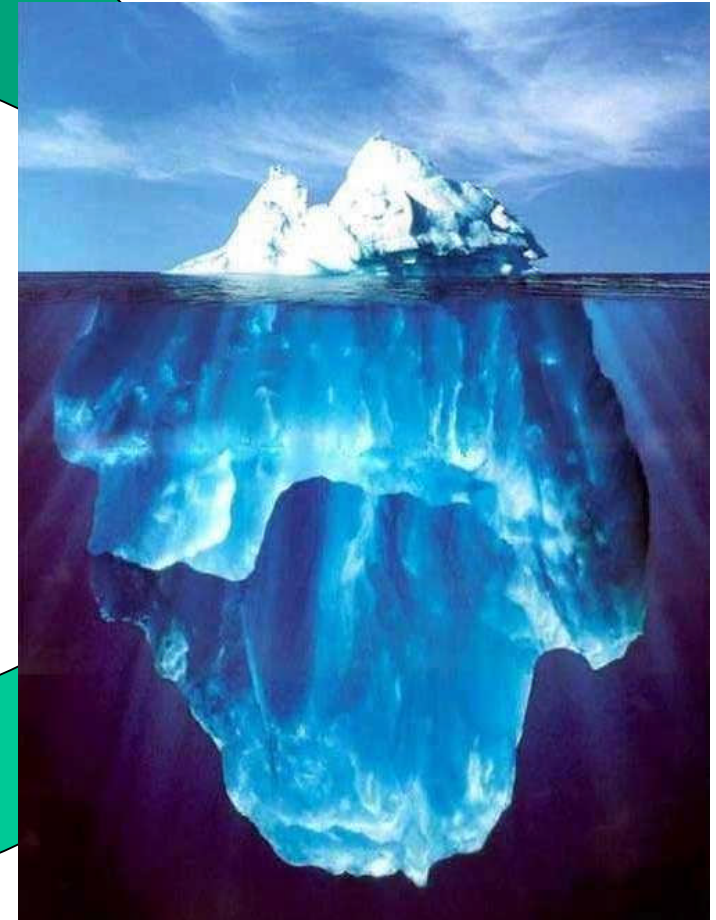
Evidence says: NO

What is the interaction nanodust/organism
(humans, animals,
bacteria, proteins, viruses)?

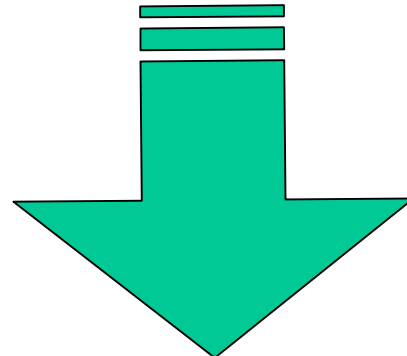
????

Environmental pollution

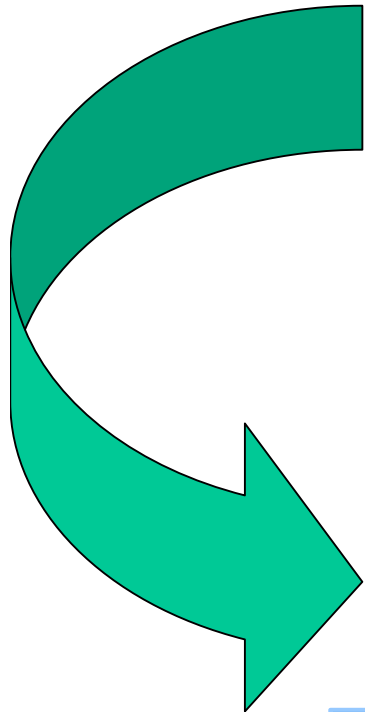
Industrial pollution



Food



Disease





Thanks

The ability to think differently today from yesterday distinguishes the wise man from the stubborn.

J. Steinbeck (Nobel Prize 1962)