The Geoscience paradigm
Resources, Risk and future perspectives
Potenza, 19-21 settembre 2023

S24. Asbestos and hazardous dust in geomaterials in the frame of European green economy: new strategies for monitoring, treatment, and reuse in view of exposure assessment - Giovanna Rizzo, Rosalda Punturo, Jasmine Rita Petriglieri, Matteo Giordani, Laura Fornasini e Alessandro Pacella

PRIN 2017 Fibres - A Multidisciplinary Mineralogical, Crystal-Chemical and Biological Project. What have we learned after four years of research?

Gualtieri A.F., Fantone S., Di Valerio S., Tossetta G., Procopio A.D., Marzioni D., Pugnaloni A., Bassi A.M., Almonti V., Mirata S., Vernazza S., Tirendi S., Marengo B., Traverso N., Passalacqua M., Scarfì S., Raneri S., Fornasini L., Bersani D., Perchiazzi N., Ballirano P., Pacella A., Bloise A., Ottaviani M.F., Mattioli M., Giordani M. & Della Ventura G.

UNIMORE Università degli Studi di Modena e Reggio Emilia — Dipartimento di Scienze Chimiche e Geologiche

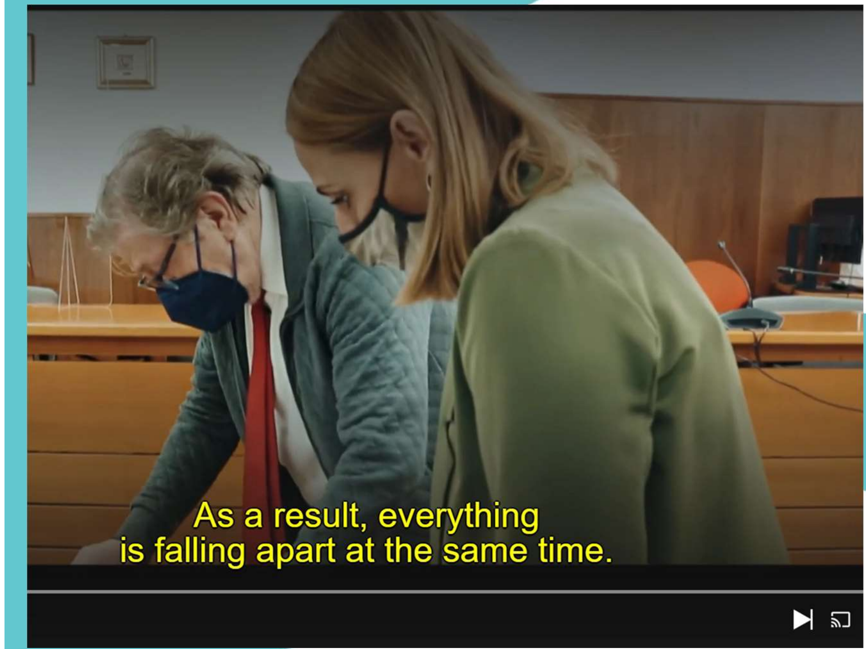
Mineral fibres and asbestos - the global scenario

Global «asbestos» awareness and polarization

- Prevention
- Ban
- Site remediation
- Naturally Occurring Asbestos

- Negationism
- Mining
- Export
- No global convention

Global «asbestos» awareness and polarization



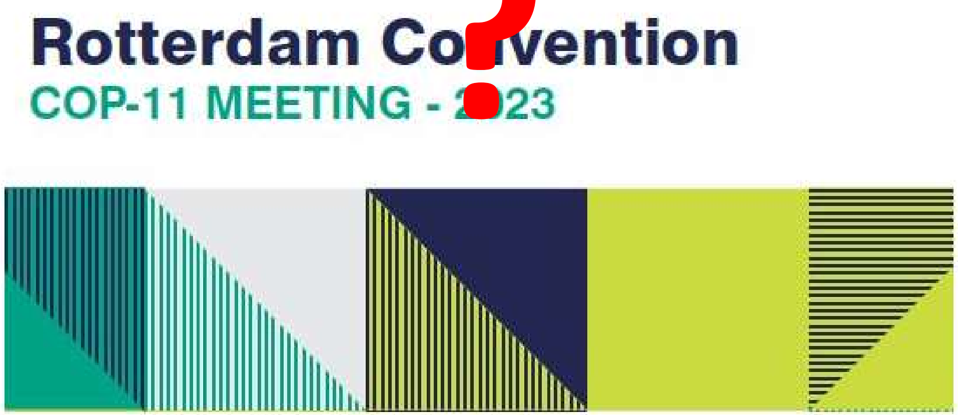
Global chrysotile issue and failure of globalization

- A globally harmonized system is lacking due to disagreement regarding the use of chrysotile and concentration limits of asbestos fibres.

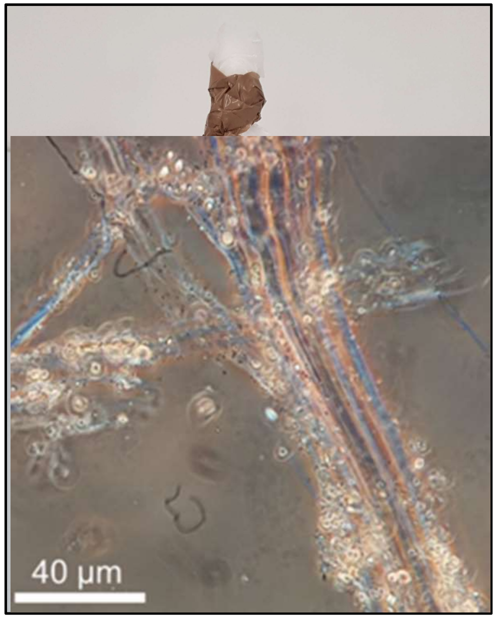
The governing body of the **Rotterdam Convention** for Hazardous Chemicals has not yet managed to reach consensus for listing Chrysotile in **Annex III** and compel producers to label chrysotile.

ICA
International Chrysotile Association

For environmental
occupational health
safe and responsible use



Breach in the global system: Italy imports out-of-law ACMs



PRIN 2017 *"Fibres: a multidisciplinary mineralogical, crystal-chemical and biological project to amend the paradigm of toxicity and cancerogenicity of mineral fibres"* (Prot. 20173X8WA4)

RESEARCH UNITS – Legend:

UNIMORE = University of Modena and Reggio Emilia (P.I. **Alessandro Gualtieri**)

SAPIENZA = University La Sapienza, Roma (L.R. **Paolo Ballirano**)

UNIGE = University of Genova (L.R. **Anna Bassi**)

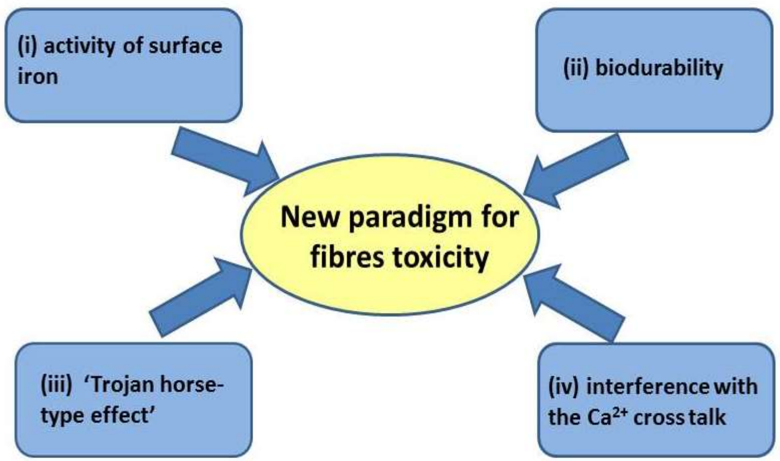
UNIPI = University of Pisa (L.R. **Simona Raneri, under 40**)

UNIURB = University of Urbino (L.R. **Maria Francesca Ottaviani**)

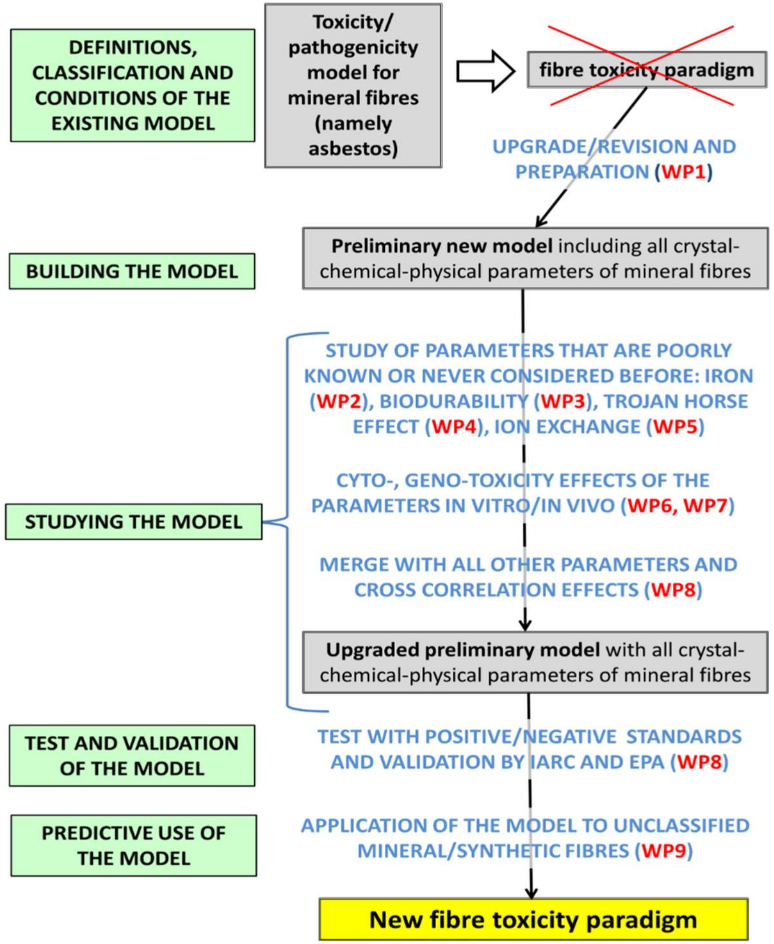
UNIVPM = Università Politecnica delle Marche (L.R. **Antonio Procopio**)

Characterization of the fibres

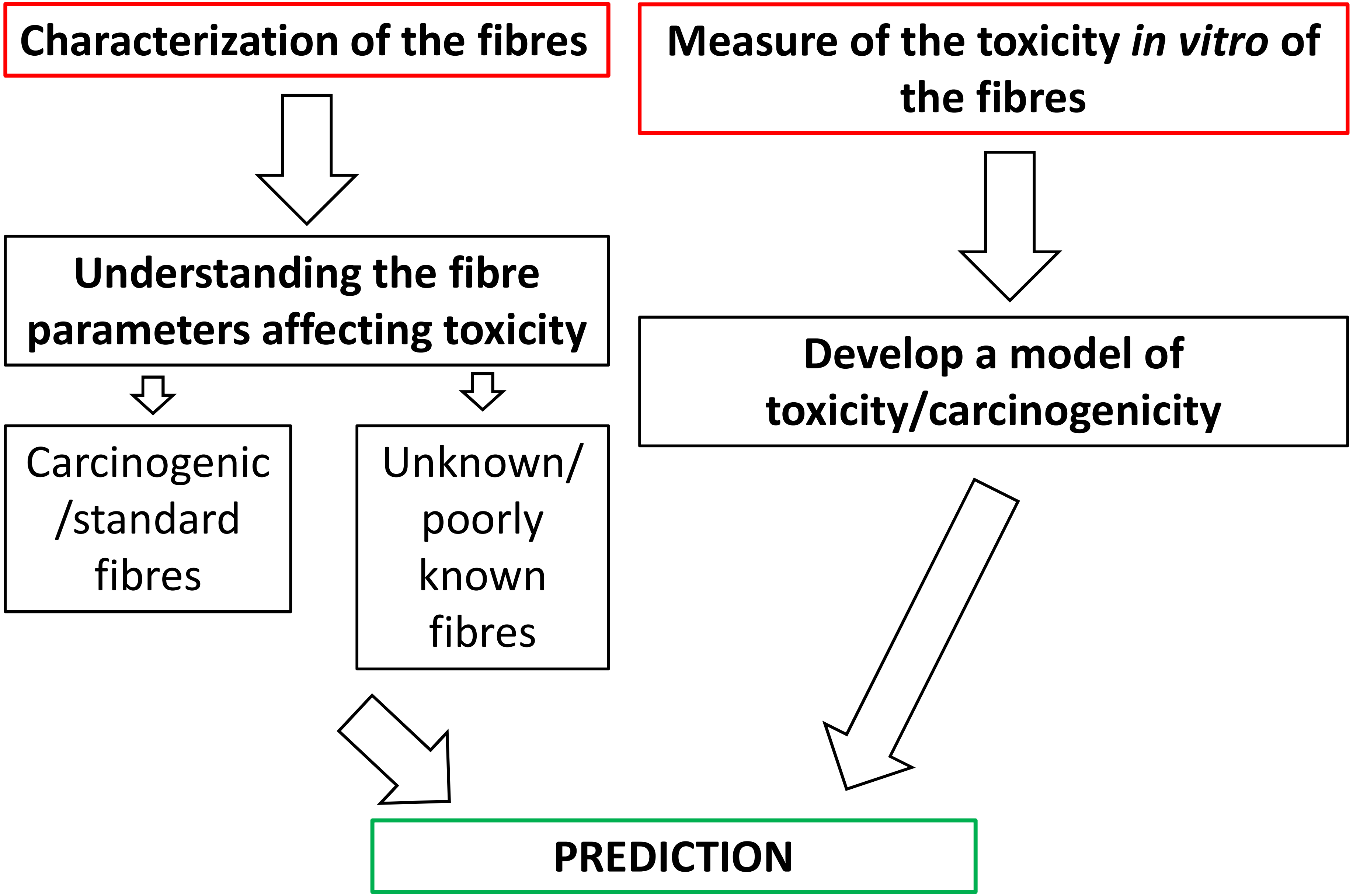
Critical parameters affecting fibres toxicity



Measure of the toxicity of the fibres

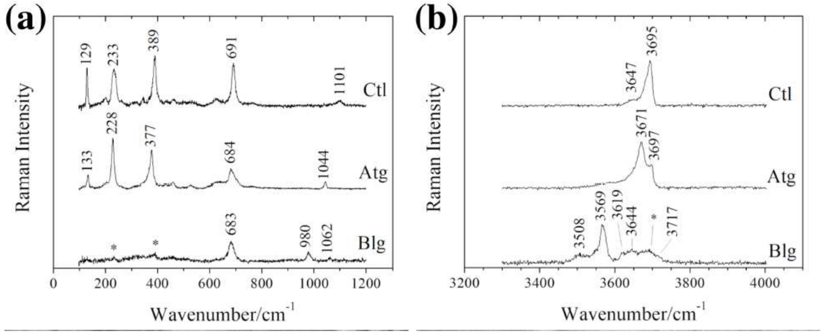


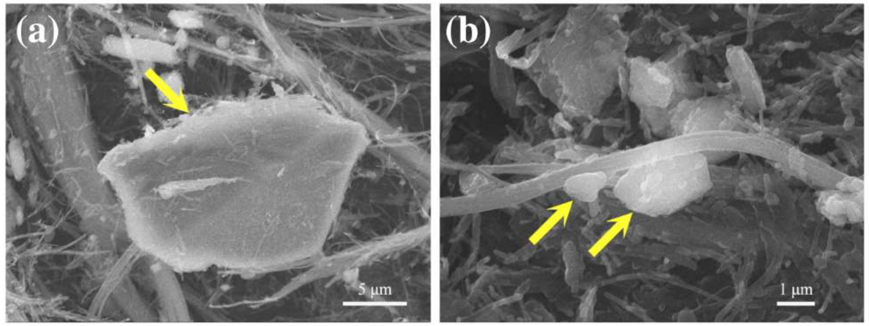
Intro PRIN 2017

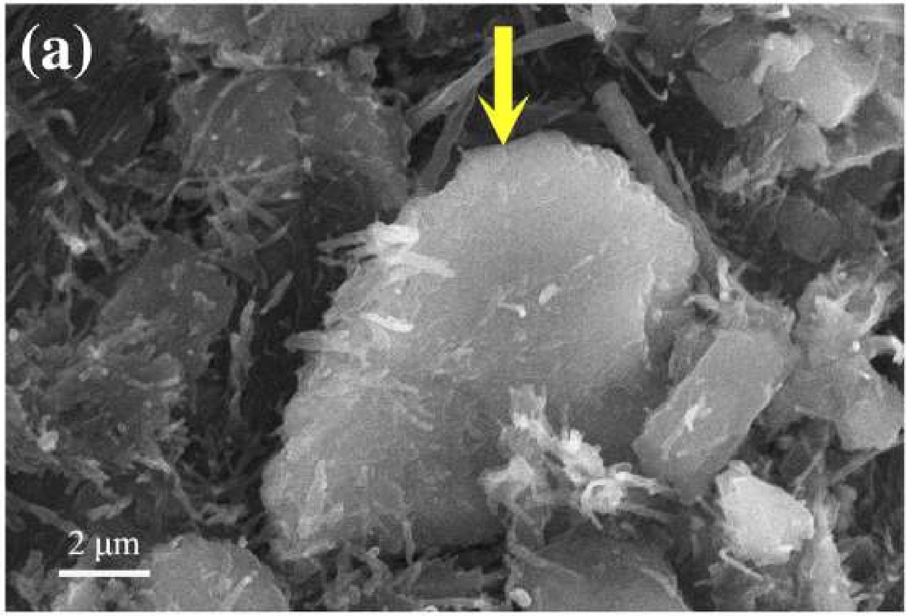


PRIN 2017 - Pisa-Parma Research Unit

1. Micro-Raman characterization of mineral fibres







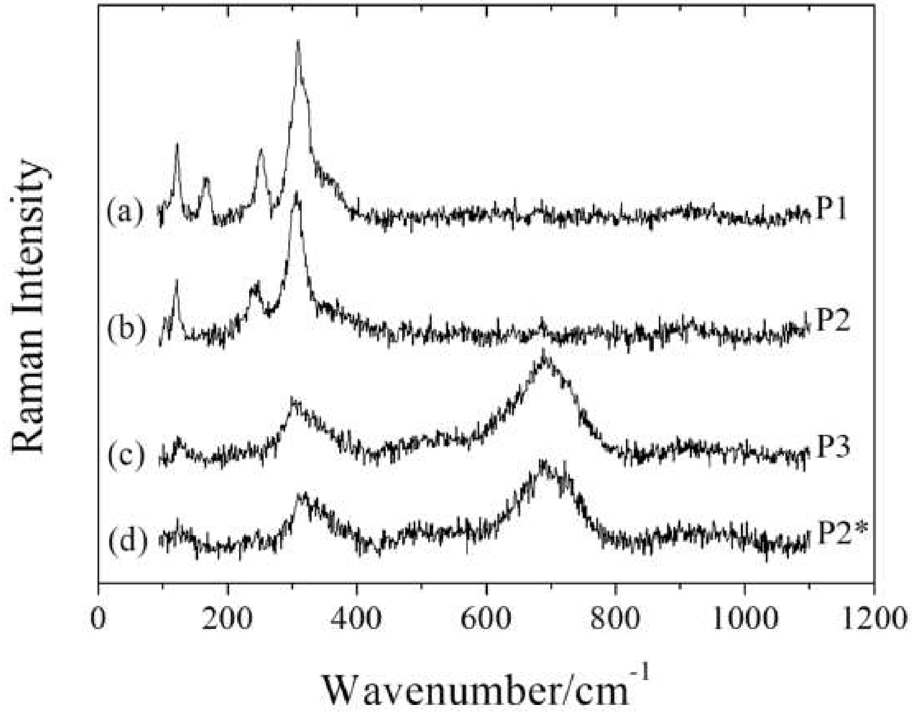
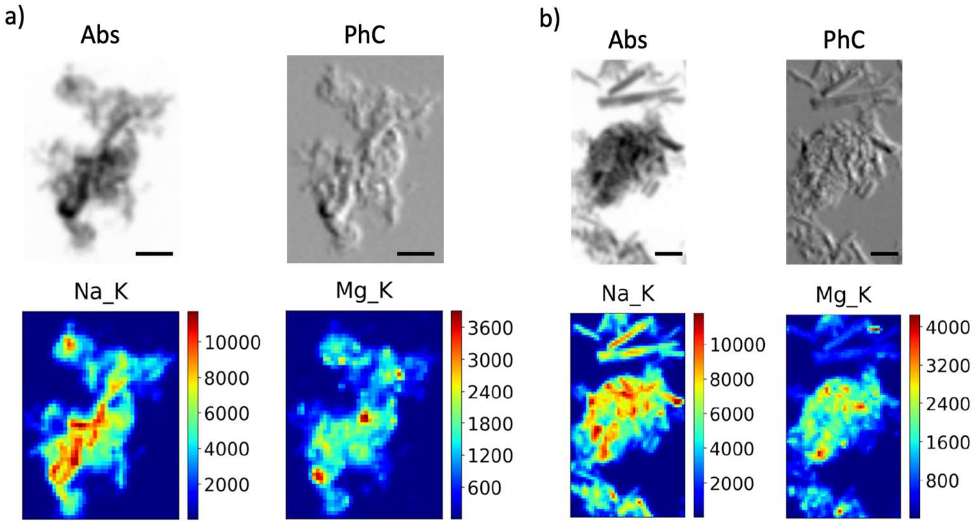
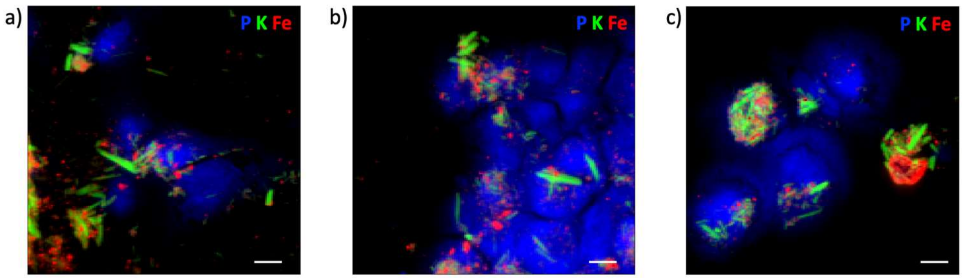


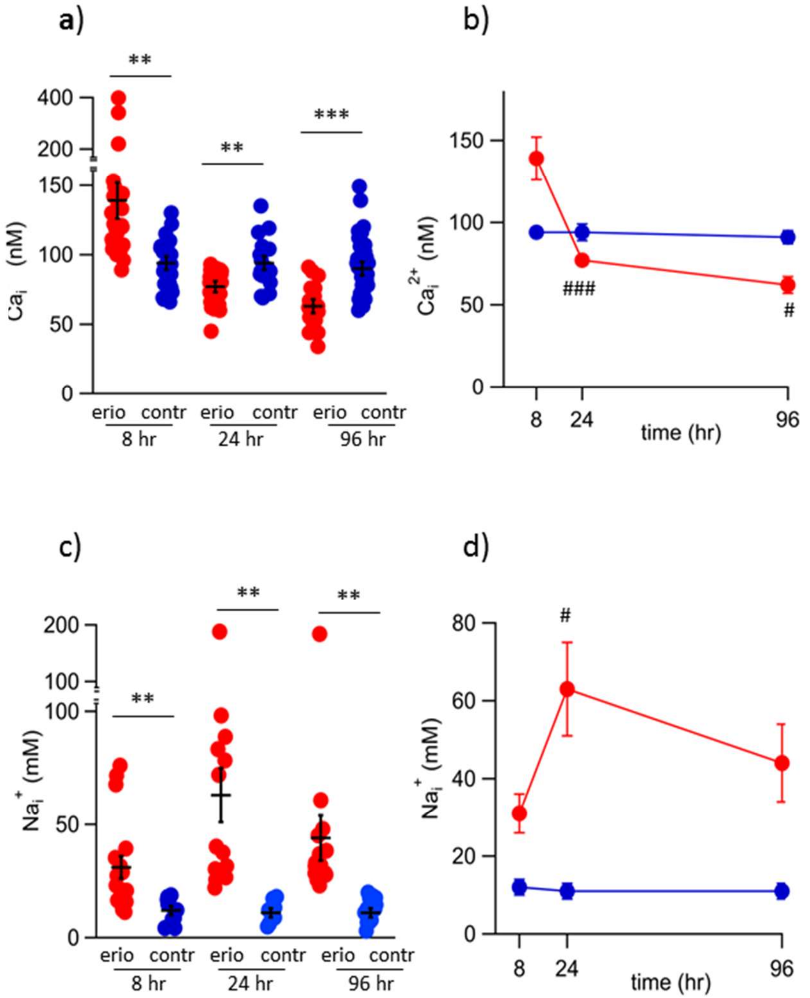
FIGURE 7 Raman spectra on a partially oxidized mackinawite crystal in Balangero chrysotile obtained at 632.8 nm at different laser powers with P1 < P2 < P3: (a) acquisition at P1.

PRIN 2017 - Pisa-Parma Research Unit

2. Synchrotron-based studies on macrophage THP-1 cell-lines exposed to mineral fibres







PRIN 2017 - Roma «La Sapienza» - Calabria Research Unit

Erionite: scambi cationici in MGS

Incubazione di fibre di erionite in MGS a pH 4,5.

minerals MDPI

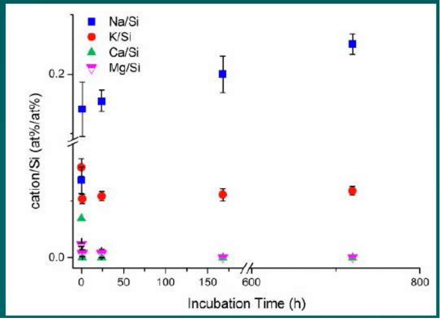
Article

Surface and Bulk Modifications of Fibrous Erionite in Mimicked Gamble's Solution at Acidic pH

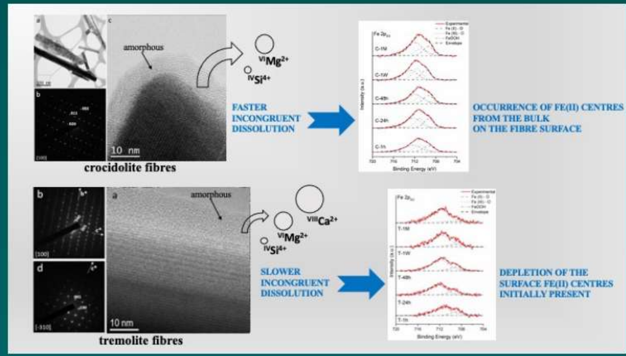
Alessandro Pacella [1,*], Paolo Ballirano [1], Marzia Fantauzzi [2,*], Antonella Rossi [2], Cecilia Viti [3], Lorenzo Arrizza [4], Elisa Nardi [5], Raffaela Caprioli [6] and Maria Rita Montereali [6]

Fibre fissano Na, principalmente nelle prime 24h, mediante scambio ionico con rilascio di cationi EF, in particolare Ca.

Uptake di Na causa modifiche strutturali, come migrazione di Na verso Ca2 che si associa a riarrangiamenti del contenuto della gabbia erionitica.



Modifiche del *bulk* e della superficie di anfiboli incubati in MGS



Rapida dissoluzione crocidolite (20x) espone in superficie centri Fe(II).

Tremolite comportamento opposto: lenta dissoluzione che impedisce esposizione dei cationi del *bulk* e rapida ossidazione del Fe che rimuove dalla superficie i centri Fe(II) inizialmente presenti.

Elementi potenzialmente tossici (PTEs) associati a crisotilo, tremolite e actinolite nella regione Calabria

Chemical Geology 558 (2020) 119896

Contents lists available at ScienceDirect

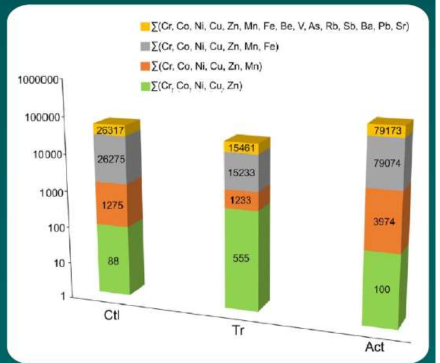
Chemical Geology

journal homepage: www.elsevier.com/locate/chemgeo

Potentially toxic elements (PTEs) associated with asbestos chrysotile, tremolite and actinolite in the Calabria region (Italy)

Andrea Bloise[a,*], Claudia Ricchiuti[b], Rosalda Punturo[b], Dolores Pereira[c,d]

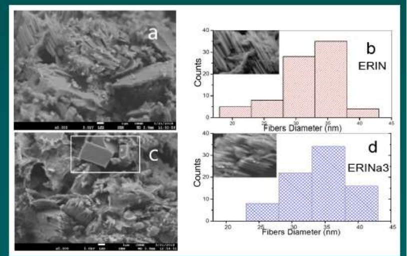
Il ruolo di Mn e Fe nel bilancio totale dei metalli tossici nei campioni studiati è cruciale



PTEs
Actinolite > Crisotilo > Tremolite

Caratterizzazione NONA

Caratterizzazione di campioni di erionite-Na di Agua Prieta, Sonora, Messico sia tal quale che Na-, Ca-, e Mg- scambiati.



minerals MDPI

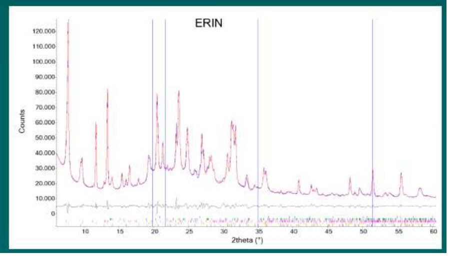
Article

Crystal Chemical and Structural Characterization of Natural and Cation-Exchanged Mexican Erionite

Karla Quiroz-Estrada [1,*], Alessandro Pacella [2,*], Paolo Ballirano [2], Miguel Ángel Hernández-Espinosa [3], Carlos Felipe [4] and Marcos Esparza-Schulz [5]

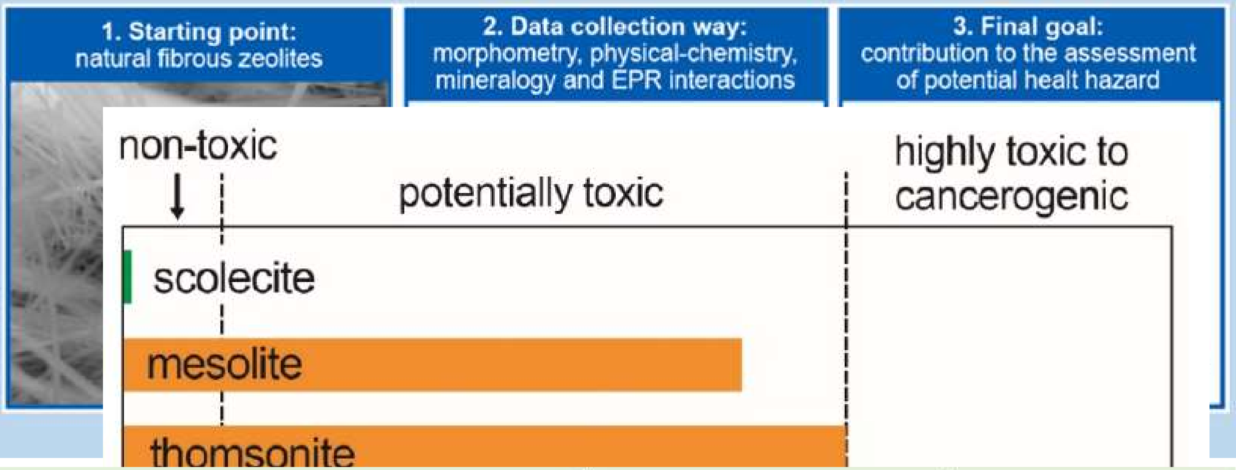
Osservato piccolo scambio cationico di Ca e Mg al posto di Na.

Analisi Rietveld indica che il processo di scambio avviene principalmente a livello del sito Ca1.

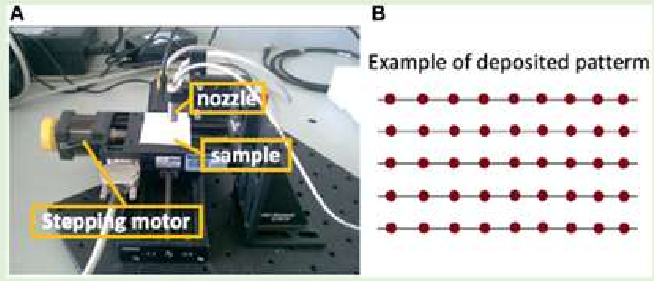


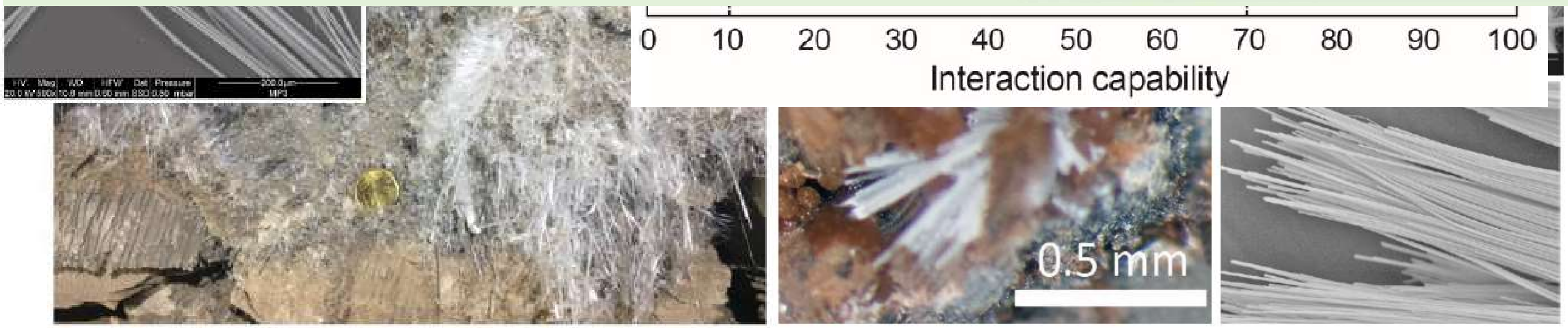
PRIN 2017 – Urbino – Roma Tre Research Unit

1. Investigation of morphological, mineralogical, and physico-chemical features of potentially toxic natural fibrous zeolites and other possibly hazardous mineral fibres*



2. Design of a novel method to prepare fibres depositions to be used for toxicological experiments (Giancarlo Della Ventura)

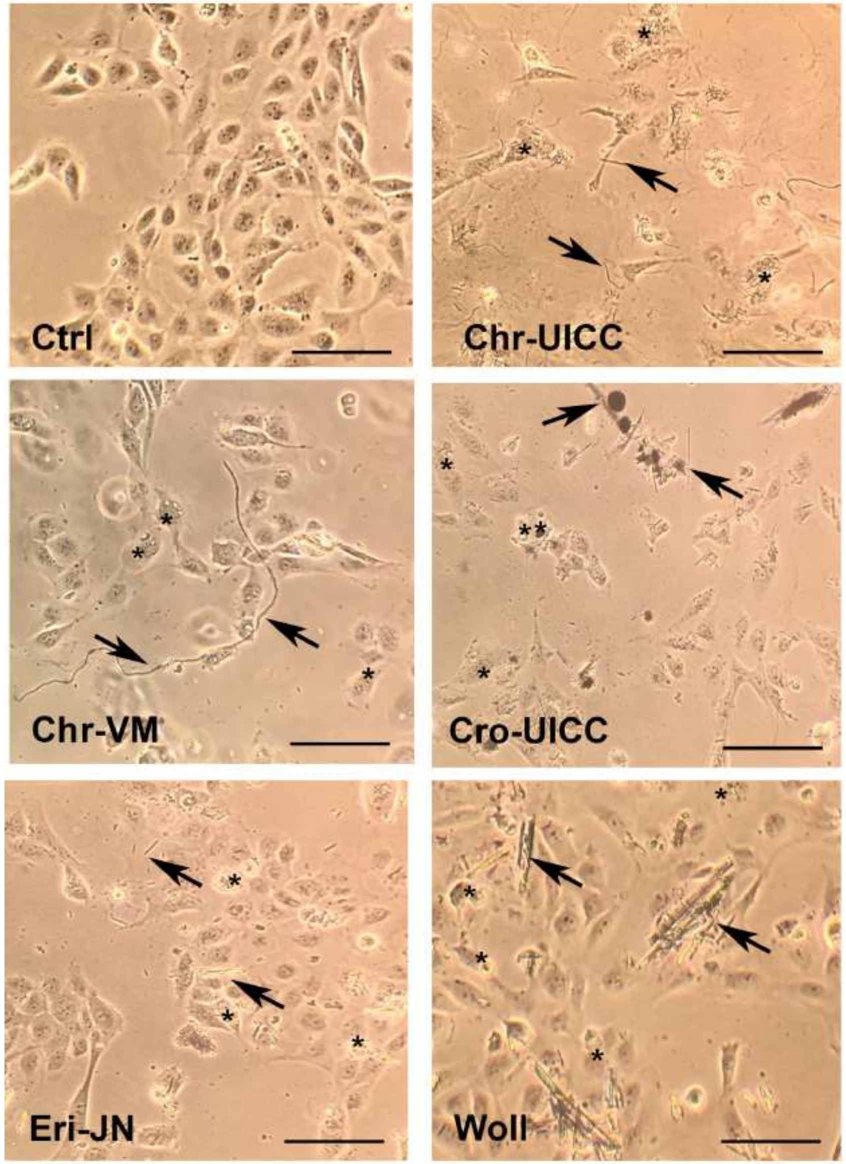


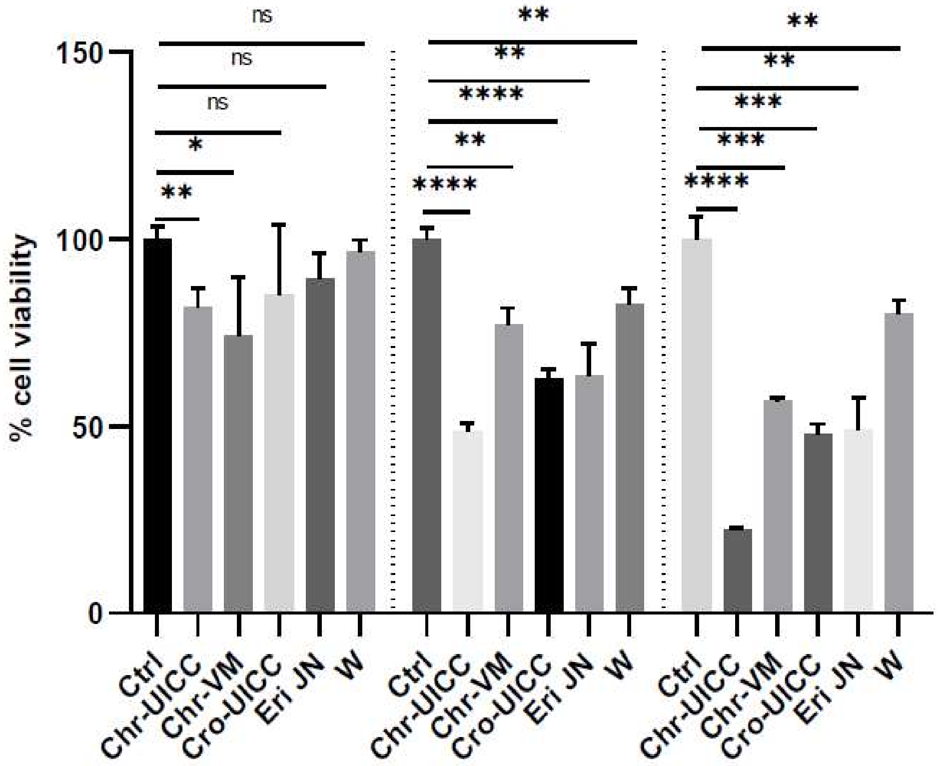


epsomite **erionite**

PRIN 2017 - Ancona Research Unit

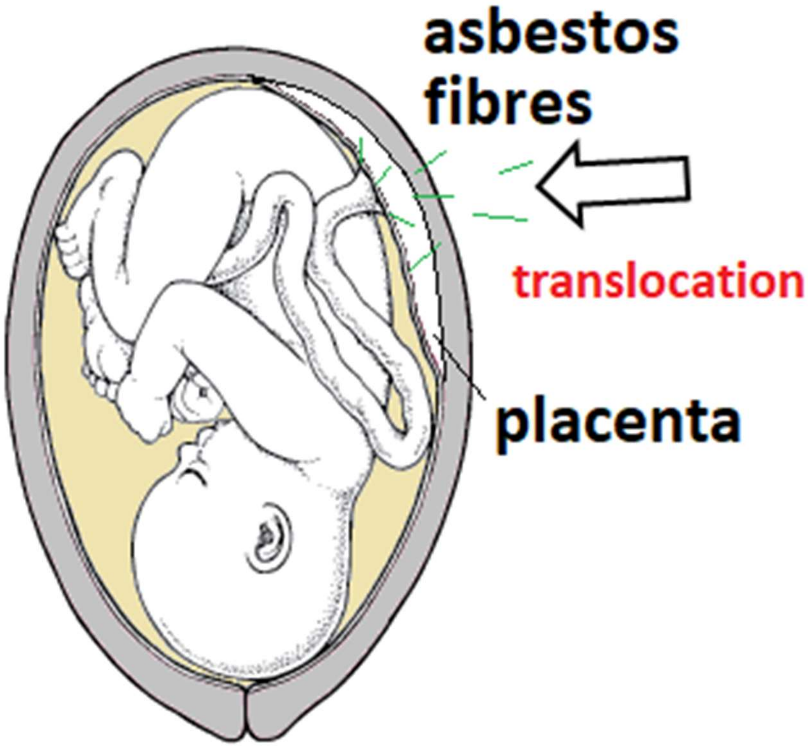
1. Systematic *in vitro* toxicity tests with Met 5a and A549 cells

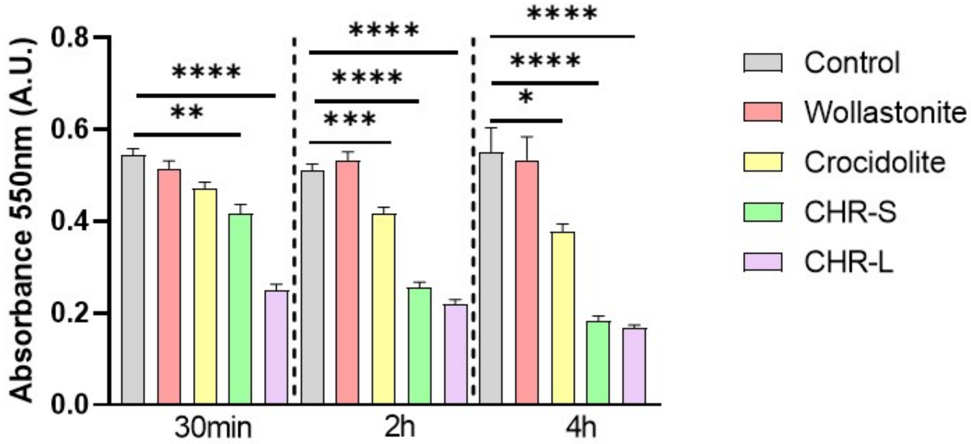


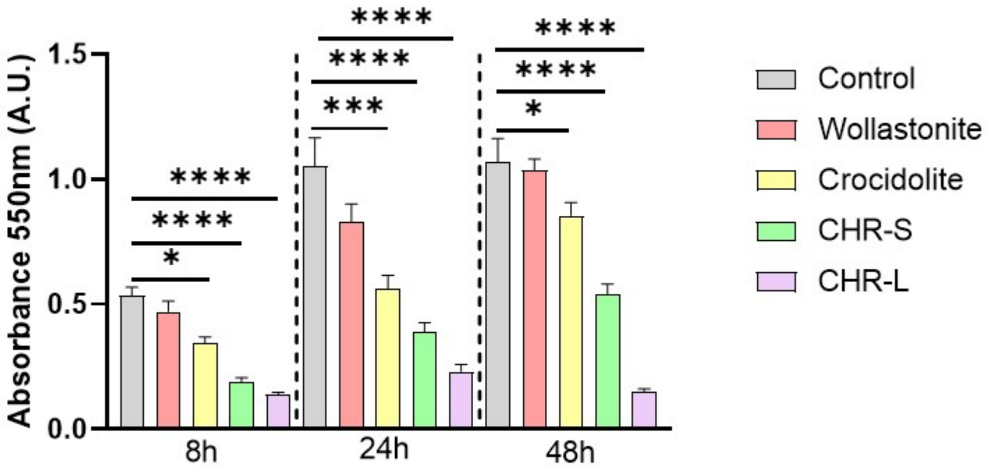


PRIN 2017 - Ancona Research Unit

2. In vitro toxicity of mineral fibres: a possible role in placental development

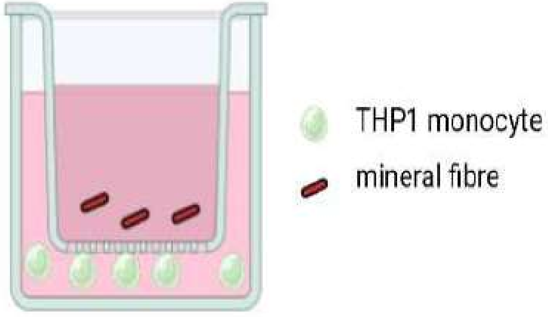




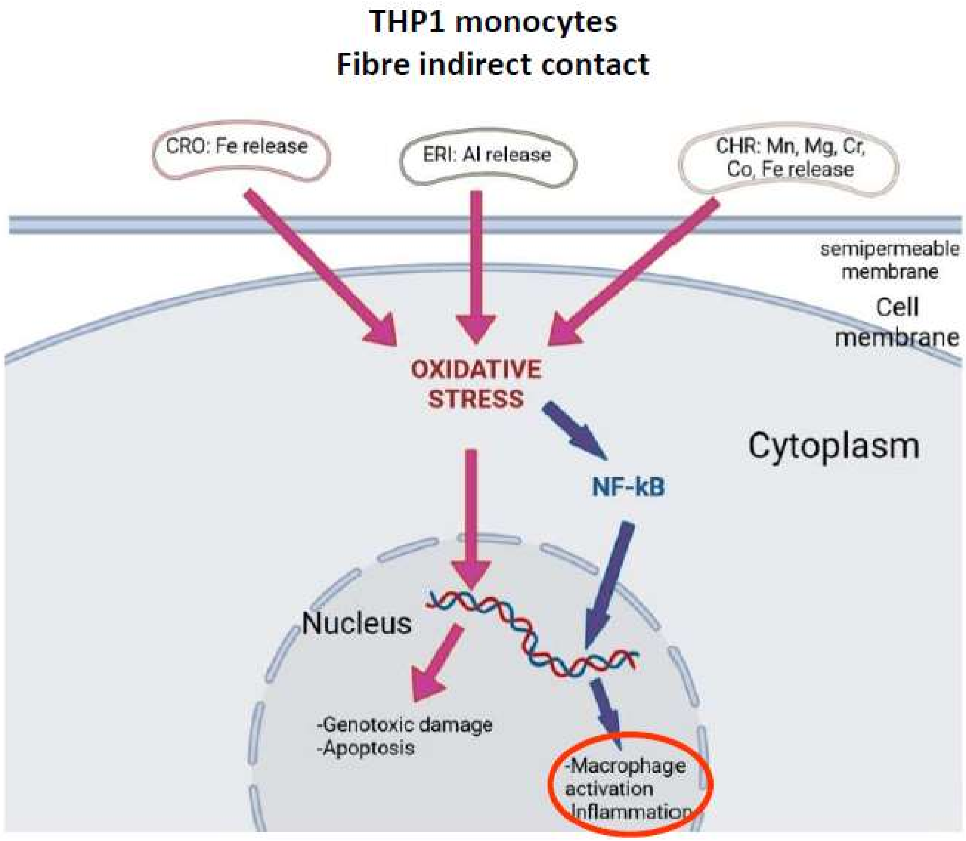


PRIN 2017 – Genova Research Unit

First part: evaluate how direct or indirect exposure to mineral fibres (Crocidolite, Chrysotile and Erionite) affects human cells belonging to the lung environment.

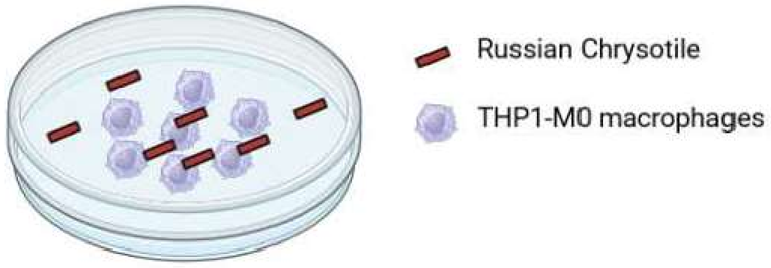


	CRO	CHR-B	ERI
Cell proliferation		- -	
Apoptosis: -Early -Late	 ++ ++++	 ++++ +++	
M0 -CD163 -CXCL10	+	+	
ROS - 4hrs - 24hrs	 +++ +	 +++ ++	 +++ +++
NF-kB		++	
Genotoxicity	++++	++++	++++

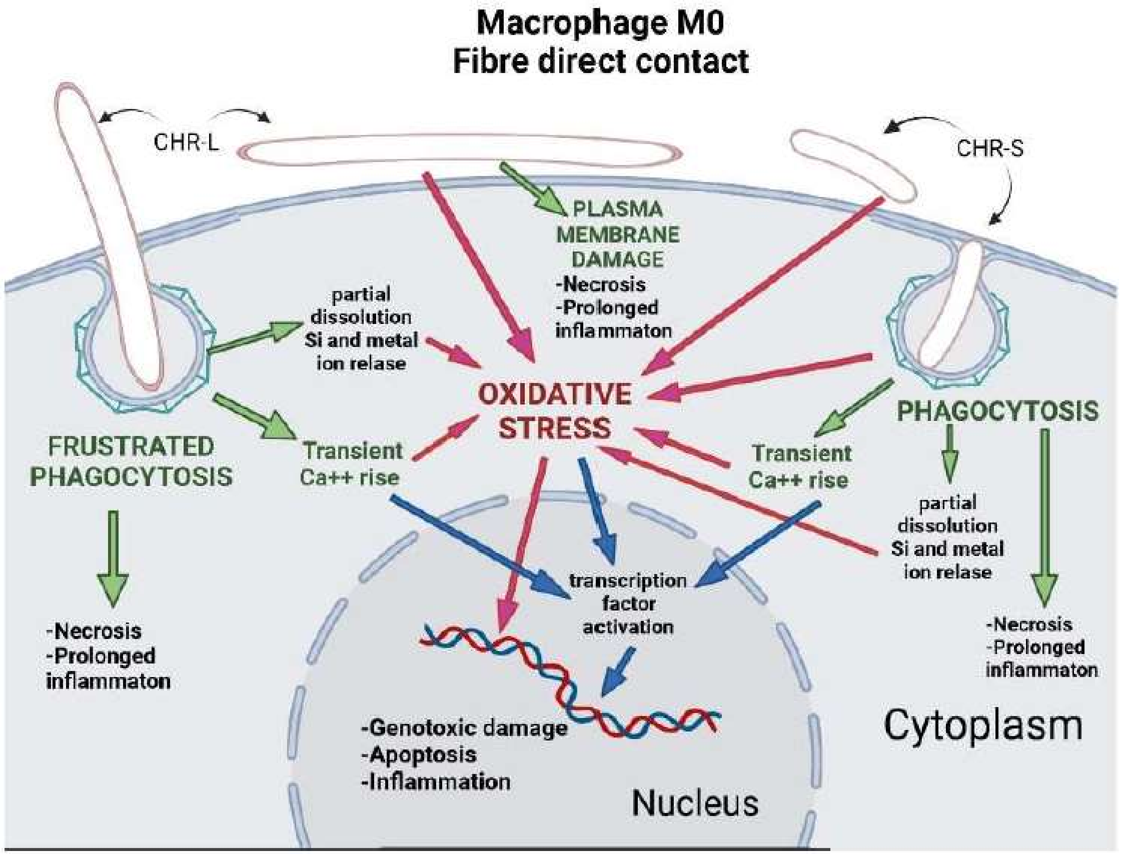


PRIN 2017 – Genova Research Unit

Second part: evaluate how direct exposure to a Russian Chrysotile, divided in two different fractions (< and > 5µm), affects human cells belonging to the lung environment. Compare the results to carcinogenic crocidolite and non-carcinogenic wollastonite



	CRO	CHR-L	CHR-S	WOLL
Biodurability	+++ (66 yrs)	+ (0.3 yrs)	+(0.3 yrs)	+(0.1 yrs)
Cell death	Apoptosis	Apoptosis and cell lysis	Apoptosis	Low effect
ROS production	+++	++++	++++	++++
Genotoxicity	+++	+++	++	no
Acute Inflammatory gene upregulation	+	+++	+	+
Chronic Inflammatory gene upregulation	no	++	no	no



PRIN 2017 unità UNIMORE: model of toxicity/carcinogenicity

- Correlate the **crystal-chemical-physical parameters of mineral fibres** (chrysotile, crocidolite and wollastonite) → **adverse effects *in vitro*** → **10 IARC *key characteristics (KCs) of carcinogens*'**: properties of a cancer-causing agent (Guyton et al. 2018)

1. Electrophilicity
2. Genotoxicity
3. Alteration of DNA repair or genomic instability
4. Epigenetic alteration
5. Oxidative stress
6. Chronic inflammation
7. Immunosuppression
8. Modulation of receptor-mediated effects
9. Immortalization
10. Alteration of cell cycle, growth factors and signaling pathways

Model of toxicity/carcinogenicity: fibre to carcinogenesis

Alessandro F. Gualtieri Current Research in Toxicology 2 (2021) 42–52

Parameter	Element	Major adverse effect
Morphometric		
length L	(1,1)	frustrated phagocytosis
diameter D	(1,2)	frustrated phagocytosis
crystal curvature	(1,3)	reduced surface adhesion of proteins/cells
crystal habit	(1,4)	airways deposition depth
fiber density	(1,5)	airways deposition depth
hydrophobic character of the surface	(1,6)	Interaction with biopolymers, phagocytosis
surface area	(1,7)	airways deposition depth, frustrated phagocytosis
Chemical		
Total iron content	(1,8)	Production of ROS
ferrous iron	(1,9)	Production of ROS
Surface ferrous iron/iron nuclearity	(1,10)	Production of ROS
content of metals other than iron	(1,11)	Production of ROS
Biodurability		
dissolution rate log(R)	(1,12)	frustrated phagocytosis ...
velocity of iron release	(1,13)	production of ROS
velocity of silica dissolution	(1,14)	production of ROS?
velocity of release of metals	(1,15)	ROS production
Surface activity		
ξ potential	(1,16)	production of ROS and hemolysis
fibers' aggregation	(1,17)	frustrated phagocytosis
Cation exchange in zeolites	(1,18)	interference with ER cross-talk?

1. Electrophilicity
2. Genotoxicity
3. Alteration of DNA repair or genomic instability
4. Epigenetic alteration
5. Oxidative stress
6. Chronic inflammation
7. Immunosuppression
8. Modulation of receptor-mediated effects
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Model of toxicity/carcinogenicity: fibre to carcinogenesis

Alessandro F. Gualtieri Current Research in Toxicology 2 (2021) 42–52

Table 3

Key characteristics/pathological process known to cause cancer in humans. For each patho-biological process featuring the 10 IARC key characteristics (Smith et al., 2016), the major adverse effects induced by specific fibre' parameters (see the list in Table 1) are reported.

Fibre parameter	Major adverse effect	Key characteristic of carcinogenicity (patho-biological process)
length (1,1)	Prompts indirect production of electrophilic species like hydroxyl radicals (ROS) due to alveolar macrophages (AM) frustrated phagocytosis	1. electrophilicity
surface area (1,7)	Rules the overall size of the fibre *in vivo* with indirect production of ROS if the fibre is long enough to cause frustrated phagocytosis	
total iron content (1,8)	Prompt direct production of electrophilic species like hydroxyl radicals ROS by metal-mediated Fenton type reaction at the fibre' surface	
ferrous iron (1,9)		
surface ferrous iron (1,10)		
content of metals other than iron (1,11)		
dissolution rate (1,12)	Rules the length of the fibre *in vivo* with indirect production of ROS if the fibre is long enough to cause frustrated phagocytosis	
velocity of iron release (1,13)	Rule the rate of (direct) production of ROS at the fibre' surface or at the surface of newly-formed silica relicts (e.g. after dissolution of chrysotile: Gualtieri et al., 2019c)	
velocity of silica release/formation (1,14)		
velocity of release of metals (1,15)		
length (1,1)	Prompts indirect production of genotoxic ROS/RNS (reactive nitrogen species) during AM frustrated phagocytosis	2. genotoxicity
surface area (1,7)	Rules the overall size of the fibre *in vivo* with indirect production of genotoxic ROS/RNS if the fibre is long enough to cause frustrated phagocytosis	
total iron content (1,8)	Prompt direct production of genotoxic ROS by metal-mediated Fenton type reaction at the fibre' surface	
ferrous iron (1,9)		
surface ferrous iron (1,10)		
content of metals other than iron (1,11)		
dissolution rate (1,12)	Rules the length of the fibre *in vivo* with indirect production of genotoxic ROS/RNS if the fibre is long enough to cause frustrated phagocytosis	
velocity of iron release (1,13)	Rule the rate of (direct) production of genotoxic ROS/RNS at the fibre' surface or at the surface of newly-formed silica metastable products	
velocity of silica release/formation (1,14)		
velocity of release of metals (1,15)		
zeta potential (1,16)	Rules the production of genotoxic ROS/RNS at the fibre' surface	

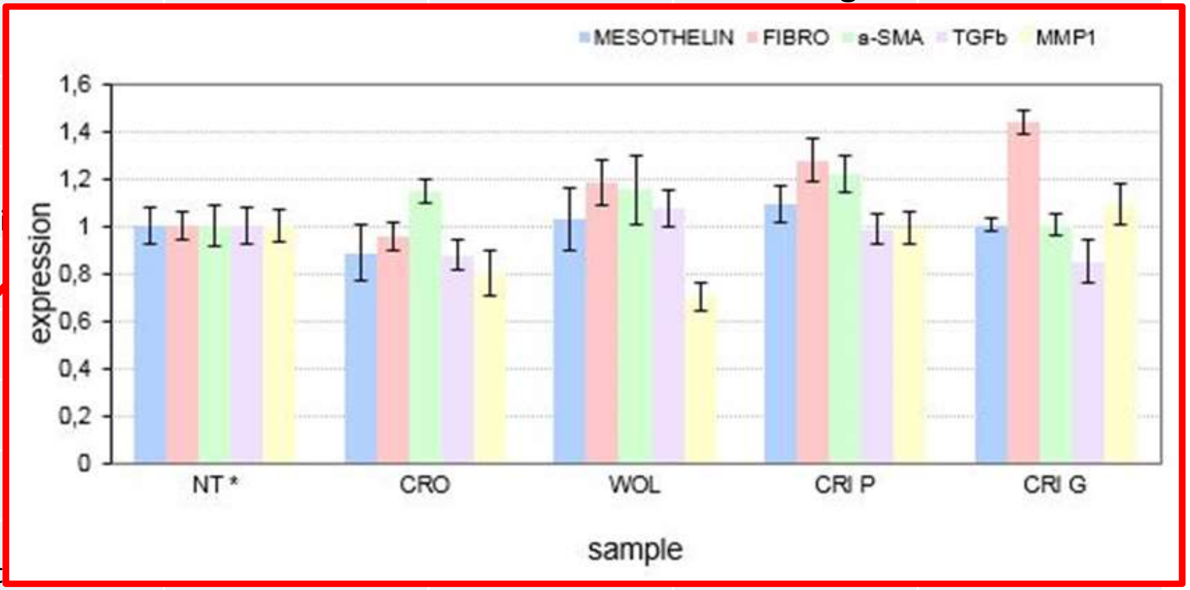
⋮

Major patho-biological process ≡ key characteristic of cancer

Model of toxicity/carcinogenicity: fibre to carcinogenesis

Specific *in vitro* tests for all the KCs of wol, chr, and cro

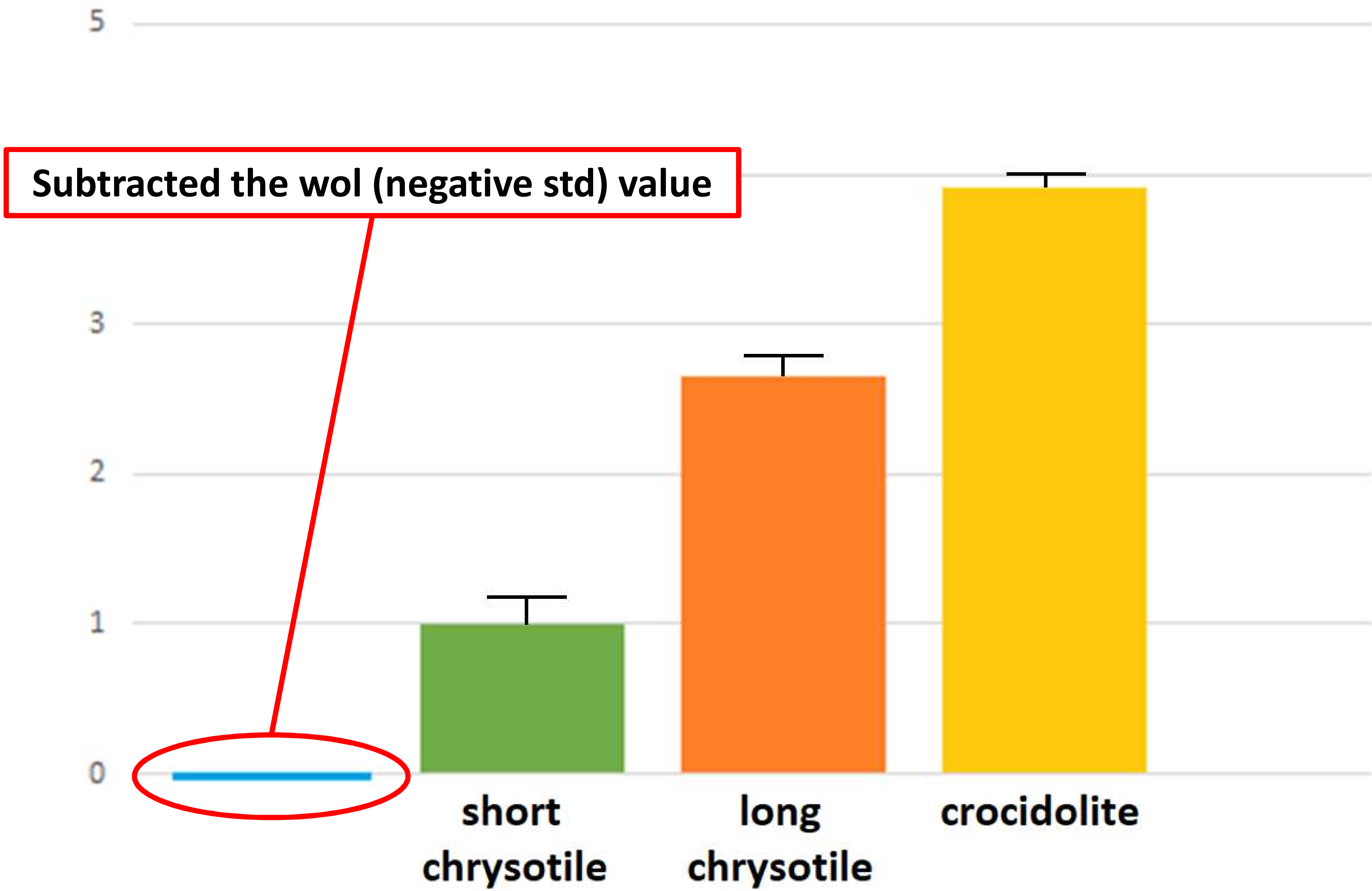
	Values normalized with respect to the maximum			
IARC 10 Key Characteristics	wol	chr short	chr long	cro
1. Electrophilicity				
2. Genotoxicity				
3.DNA repair alteration or genomic instabili				
4.Epigenetic alteration				
5.Oxidative stress				
6.Chronic inflammation				
7.Immunosuppression				
8.Modulation of receptor-mediated effect				
9.Immortalization	0,8313725	1	0,680392	0,845752



Difference vs ctr → sum all results for that KCs → normalization vs highest value

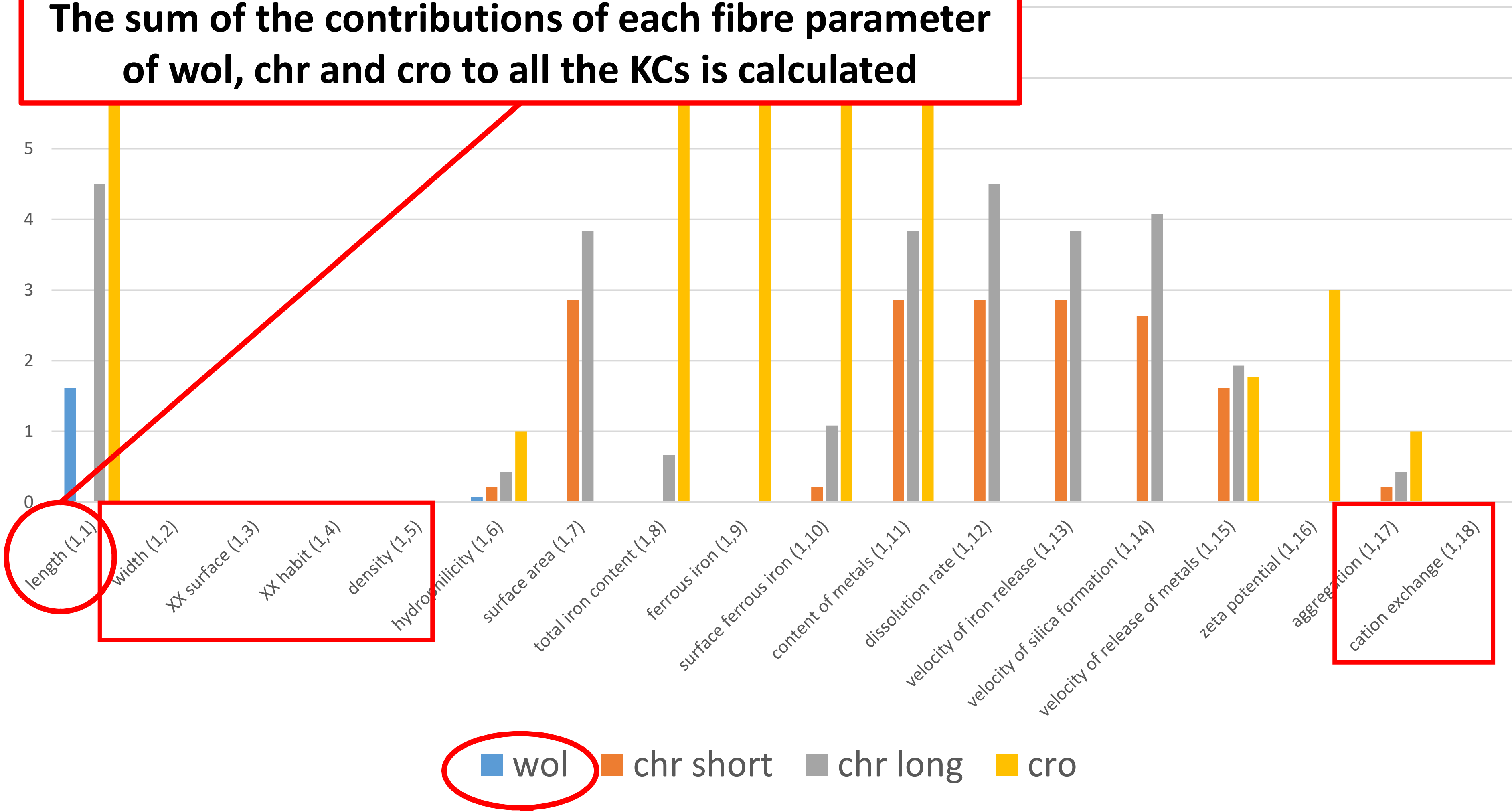
	wol	chr short	chr long	cro
tot	5,433695	6,809099	8,078518	9,29321
media	0,5433695	0,68091	0,807852	0,929321
sum of the squared	1,2534441	0,945114	0,377107	0,065905
dev std	0,3731911	0,324057	0,204697	0,085573

Model of toxicity/carcinogenicity: fibre to carcinogenesis



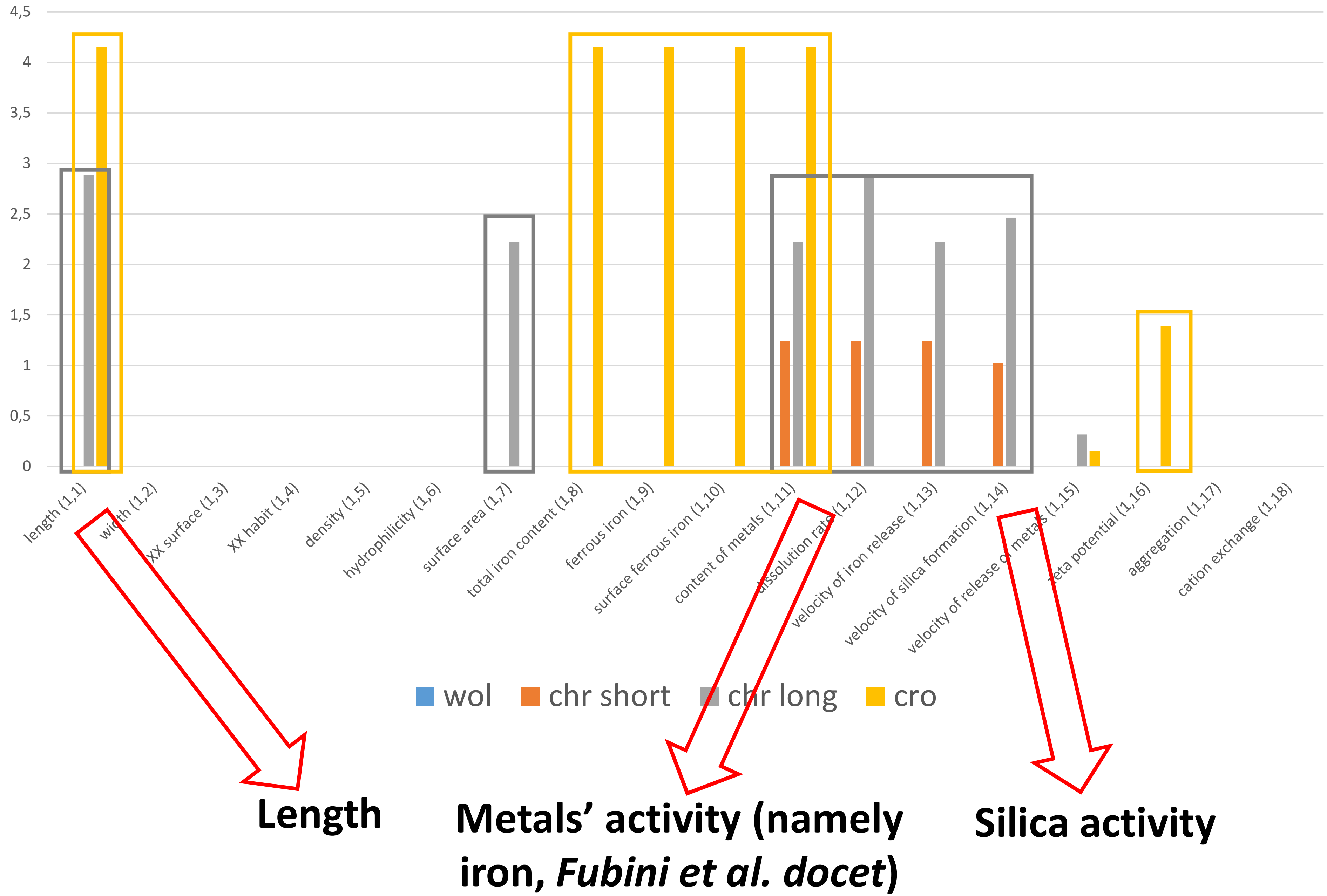
Model of toxicity/carcinogenicity: fibre to carcinogenesis

The sum of the contributions of each fibre parameter of wol, chr and cro to all the KCs is calculated



Subtracted the wol (negative std) value bck threshold

Model of toxicity/carcinogenicity: fibre to carcinogenesis



Model of toxicity/carcinogenicity: the ultimate goal → support cancer prevention

Massive data analysis in progress (preliminary results!)

Discuss our results with the MM medical doctors

Free Radical Biology and Medicine 133 (2019) 206–215

Contents lists available at ScienceDirect

Free Radical Biology and Medicine

journal homepage: www.elsevier.com/locate/freeradbiomed

ELSEVIER

Review Article

Iron addiction with ferroptosis-resistance in asbestos-induced mesothelial carcinogenesis: Toward the era of mesothelioma prevention

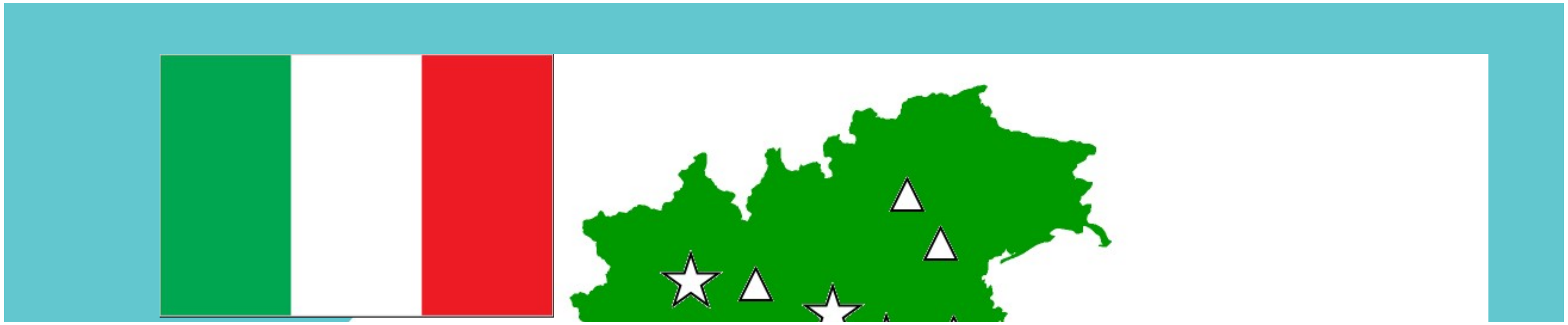
Shinya Toyokuni[a,b]

[a] *Department of Pathology and Biological Responses, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan*
[b] *Sydney Medical School, The University of Sydney, NSW, Australia*

Support specific prevention protocols

- **a redox-inactive iron chelator, deferasirox, as a preventive agent**
- **intraperitoneal use of a redox-inactive iron chelator, desferal**
- **phlebotomy once a month**

There's plenty of asbestos at the bottom…



The key role of Italy in:

- Hazard and risk assessment models
- Identification, mapping and monitoring of NOA all over the world (erionite, antigorite, ferrierite …)
- Prevention

- We are top in this field!

- It is our responsibility *to keep fighting together*!

There’s plenty of asbestos at the bottom

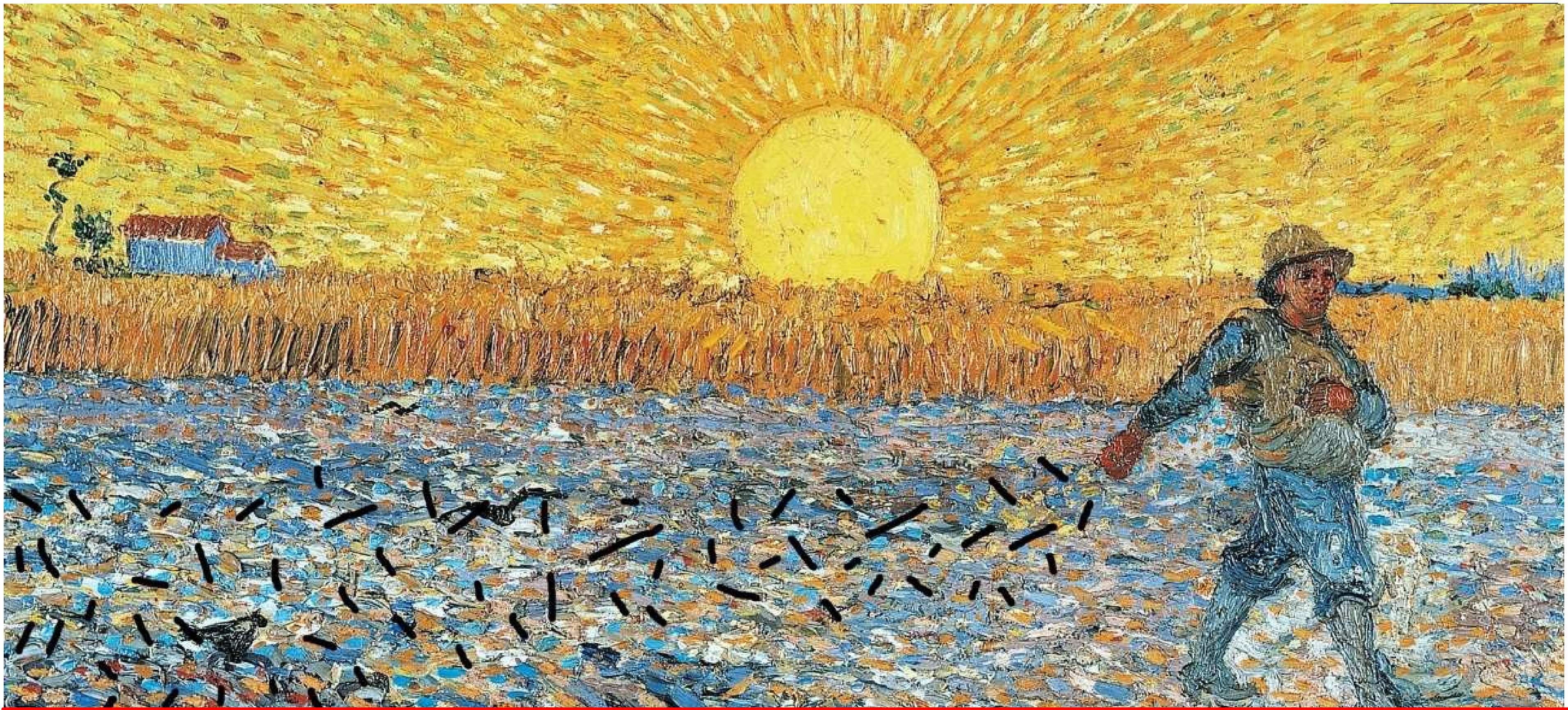
- Naturally occurring asbestos (NOA) is a threat to the public health that transforms from local to geographically widespread when the fibres are present as impurity in industrial minerals that may freely circulate among states

- We must continue the intensive screening of natural materials in search of asbestos for predictive purposes to avoid *ex post* discovering of the exposure of the population or workers through the observation of malignant mesothelioma morbidity peaks (e.g. fluoro-edenite case in Biancavilla!)

Our key role/mission :
target possible asbestos-contaminated natural raw materials or NO materials

brucite **diopside** **olivine** **talc** **vermiculite** **wollastonite**

There's plenty of asbestos at the bottom (and there will be even more...)



"The findings of this work open a new avenue for sustainable heavy metals remediation in groundwater and soils."

A heartfelt thank to all the crew of the PRIN 2017 project!

Thank you all for your attention!

TOXICITY AND CARCINOGENICITY OF MINERAL FIBRES:

AN UPDATE. WHAT HAVE WE LEARNED AFTER FOUR YEARS OF PRIN?

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