Società Italiana di Medicina Veterinaria Preventiva

INQUINAMENTO AMBIENTALE E SICUREZZA ALIMENTARE DEGLI ALIMENTI DI ORIGINE ANIMALE

Senigallia (AN)

27 Maggio 2016

Rischi emergenti in sicurezza alimentare legati all'inquinamento ambientale

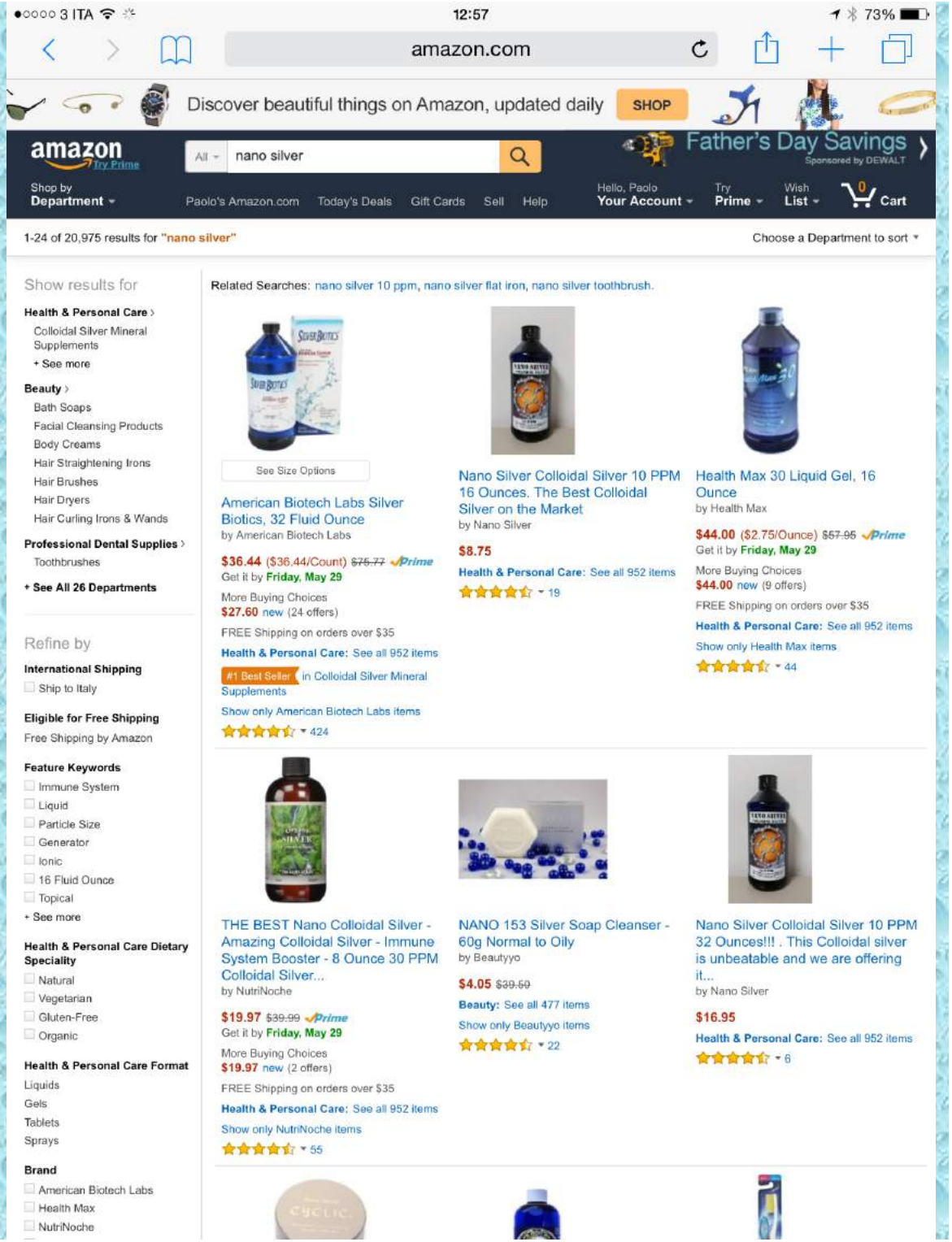
Prof. Paolo Tucci

Dipartimento di Medicina Clinica e Sperimentale

Università degli Studi di Foggia

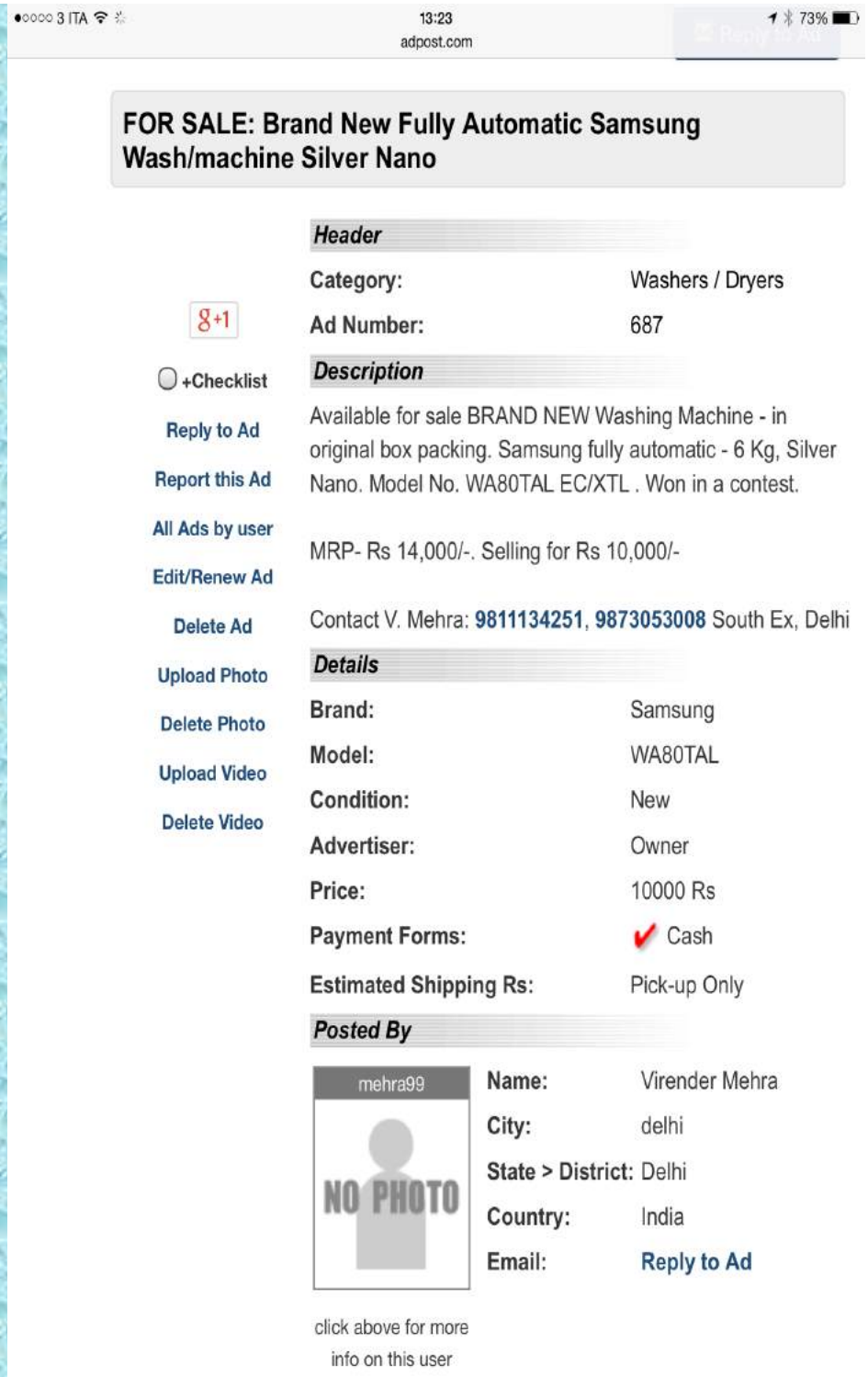
Rischi emergenti:
1. Nanomateriali

Inseriamo il termine “nanoargento su amazon.com : otteniamo migliaia di risultati: dai contenitori alimentari agli integratori



Nel 2006 la Samsung costruisce delle lavatrici in grado di rilasciare ioni argento nell'acqua.

In seguito la produzione viene sospesa per motivi non chiari



Nel 1978 la rivista *Science Digest* affermava che il nanoargento poteva agire su circa 650 tipi di batteri (bibliografia assente)

Extract from Science Digest - March 1978

And now it's silver that is finding wholly new uses as a wonder in modern medicine ...

Perhaps is soon will be recognised as

OUR MIGHTIEST GERM FIGHTER

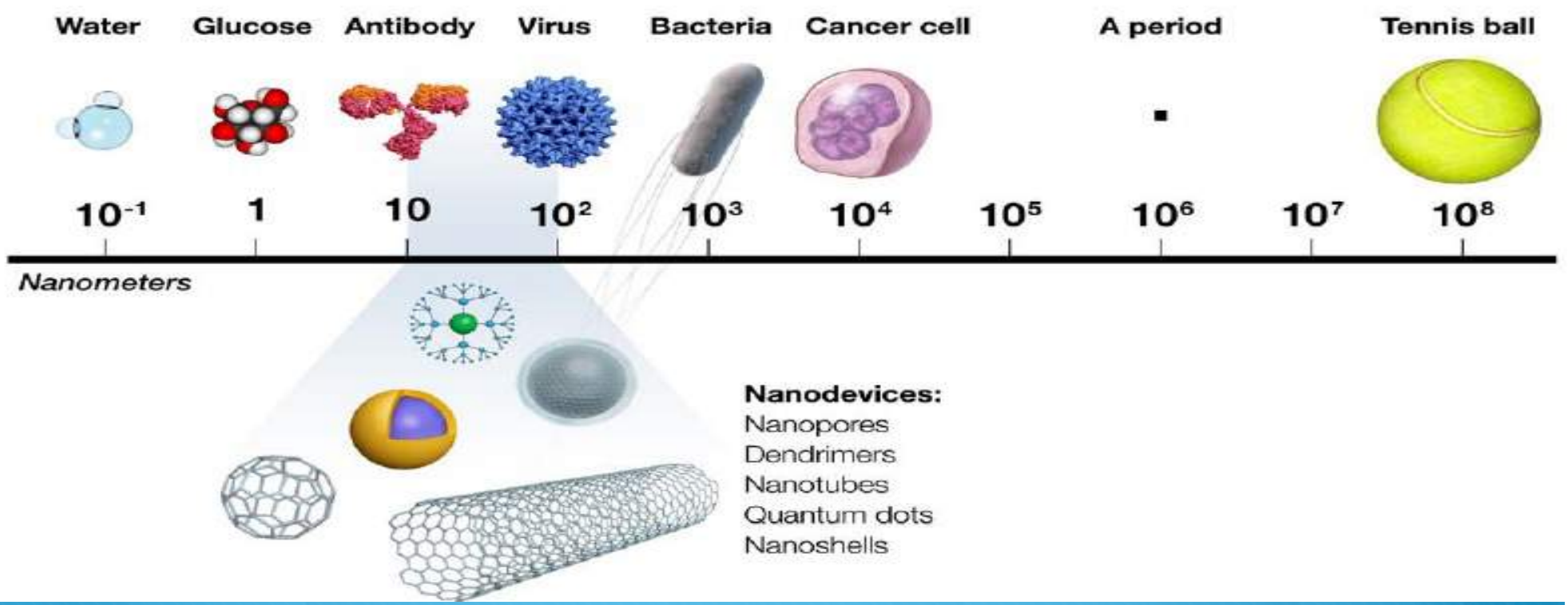
By Jim Powell

Thanks to eye-opening research, silver is emerging as a wonder of modern medicine. An antibiotic kills perhaps half-dozen different disease organisms, but silver kills some 650. Resistant strains fail to develop. Moreover, silver is virtually non-toxic. Says a pioneering silver researcher, Dr Harry Margraf of St Louis: "Silver is the best all around germ-fighter we have."

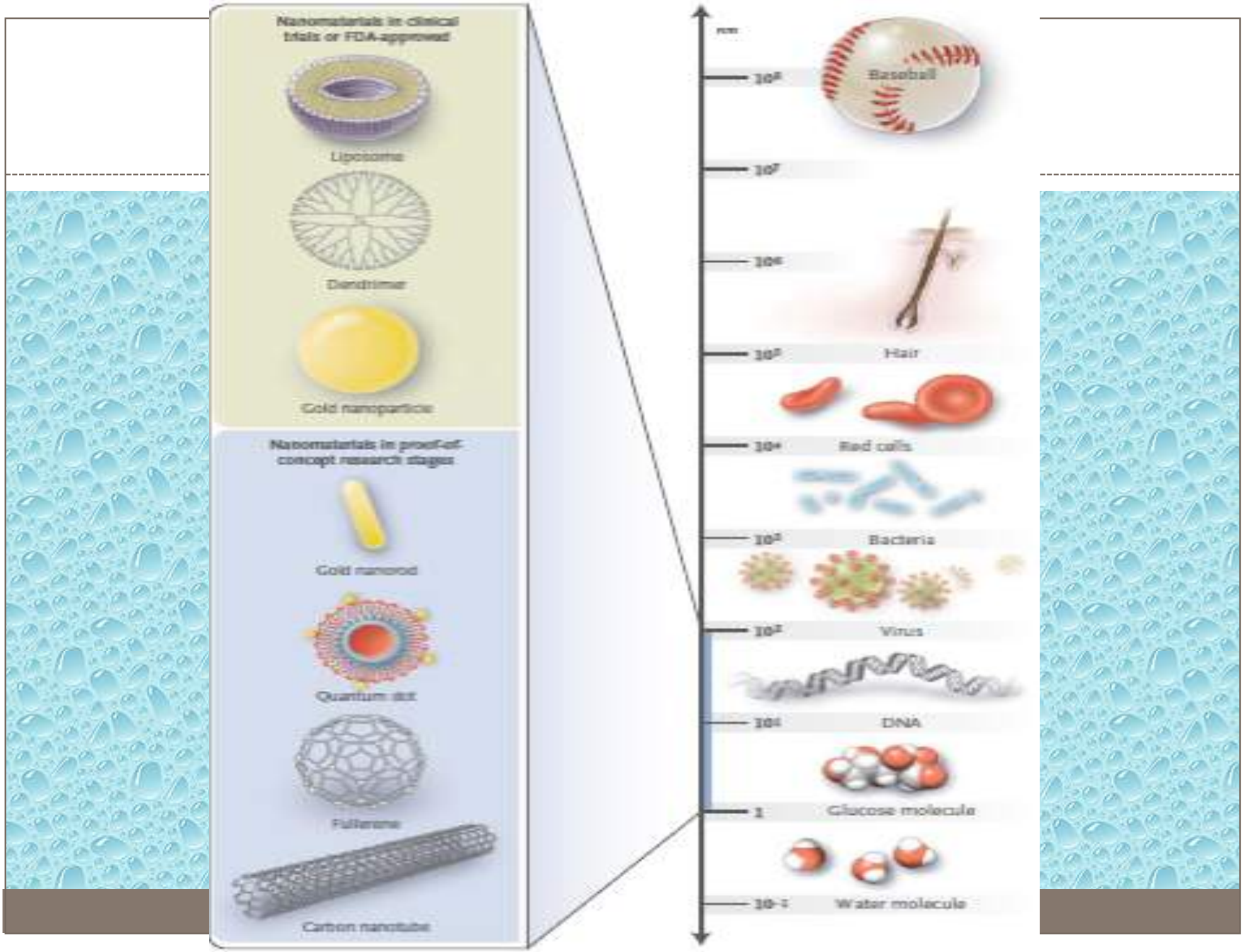
Developed by Dr. Charles Fox of Columbia University, a silver compound known as silver sulfadiazine is used in 70 percent of burn centers in the U.S. It also stops the herpes virus responsible for cold sores and fever blisters. With silver sulfadiazine, Dr Fox scored what properly is acclaimed as a momentous breakthrough, for it was the first new silver compound to win FDA approval and become generally available. A pharmaceutical house, Marion Laboratories, is offering it as an ointment, under the brand name of Silvadene; other companies are making silver sulfadiazine available in several countries from Canada to India.

Doctors are reporting that, taken internally, the compound works against three scourges - syphilis, cholera and malaria. And even tiny amounts of silver wipe out huge quantities of disease organisms in water. Some specific instances of silver's use:

- To guard against such water-borne diseases as dysentery, more than half the world's airlines now use silver water filters. For instance: British Airways, Swissair, Scandinavian Airlines, Lufthansa, Olympic, Air France, Canadian pacific Airlines, Alitalia, KLM, Japan Airlines and Pan Am.
- The Swiss government has approved silver water filters. They're used in homes and offices throughout the country.
- After testing 23 methods of purifying water, NASA selected a silver system for the space



- Sono definiti come nanomateriali quei materiali che hanno componenti strutturali con almeno una dimensione nell'intervallo 1-100 nm.


Nanomaterials in clinical trials or FDA-approved
Liposome
Dendrimer
Gold nanoparticle
Nanomaterials in proof-of-concept research stages
Gold nanorod
Quantum dot
Fullerene
Carbon nanotube
nm
10^8
Baseball
10^7
10^6
10^5
Hair
Red cells
10^4
10^3
Bacteria
10^2
Virus
DNA
10^1
1
Glucose molecule
10^{-1}
Water molecule

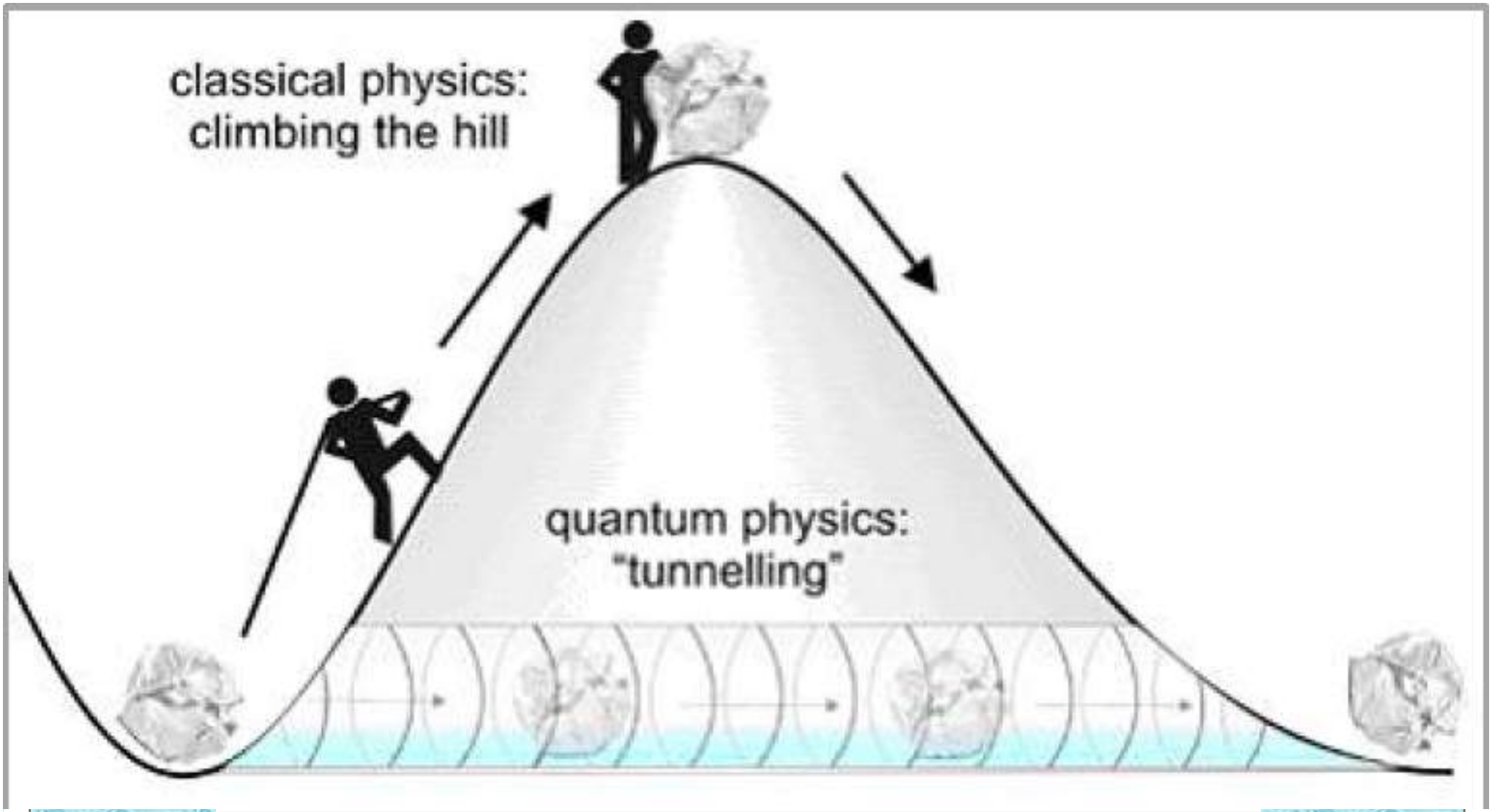


Figure 2: Schematic representation of tunnelling. (Image credit: Copyright Max Planck Institute for Quantum Optics).

Tratto da: Nanoyou teachers training kit

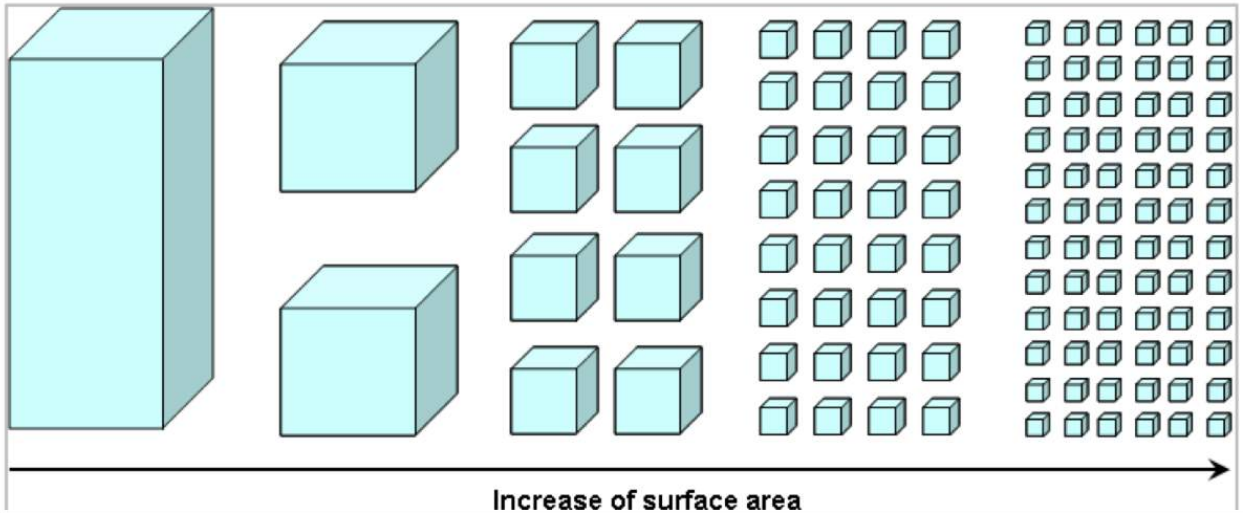
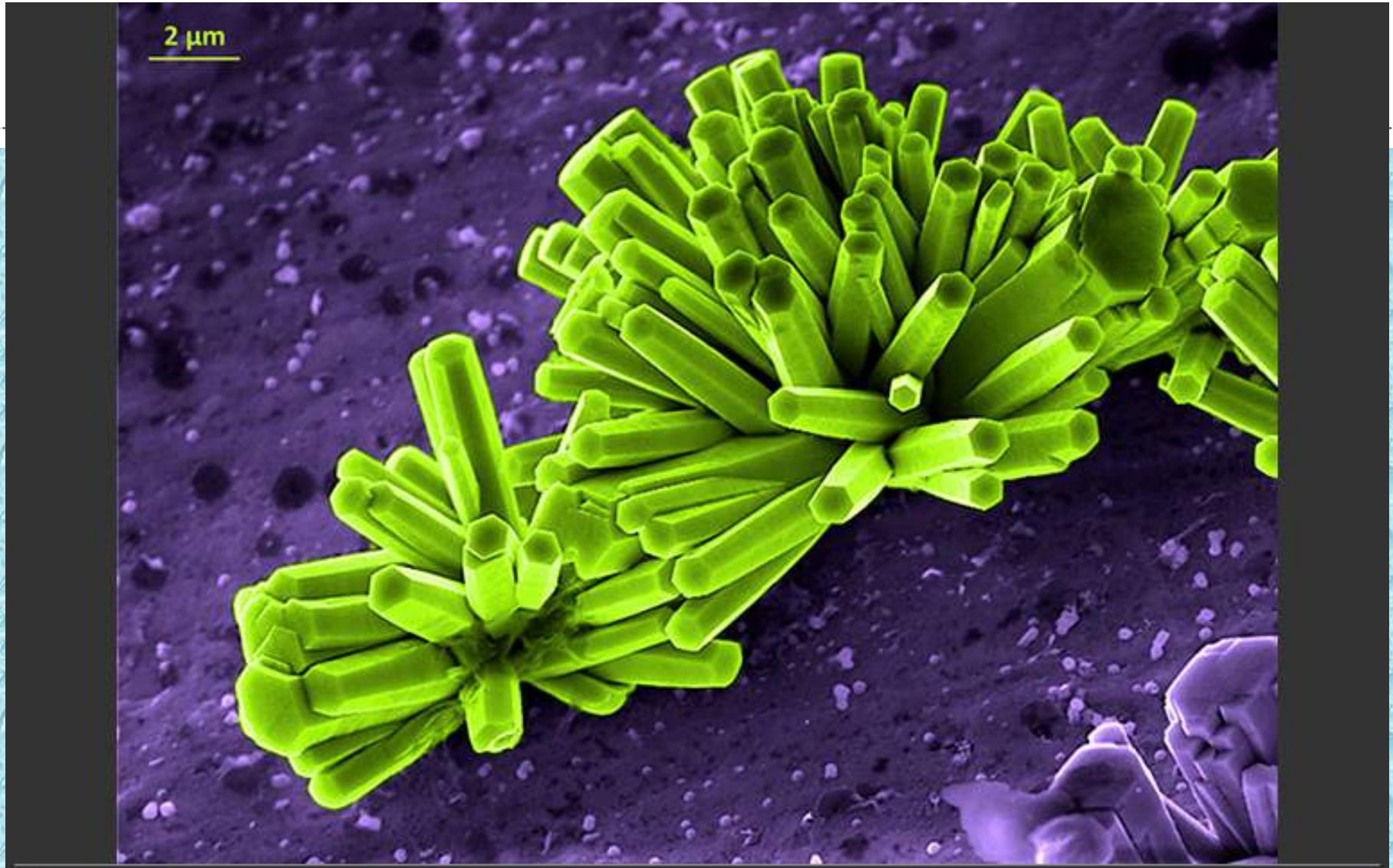


Figure 3. Schematic drawing showing how surface-to-volume increases as size is decreased. Image not to scale. (Image source: L. Filipponi, iNANO, Aarhus University, Creative Commons ShareAlike 3.0)

Size of cube side	Number of cubes	Collective Surface Area
1 m	1	6 m^2
0.1 m	1000	60 m^2
0.01 m = 1cm	10^6 = 1 million	600 m^2
0.001 m = 1mm	10^9 = 1 billion	6000 m^2
10^{-9} m = 1 nm	10^{27}	$6x10^9$= 6000 Km^2

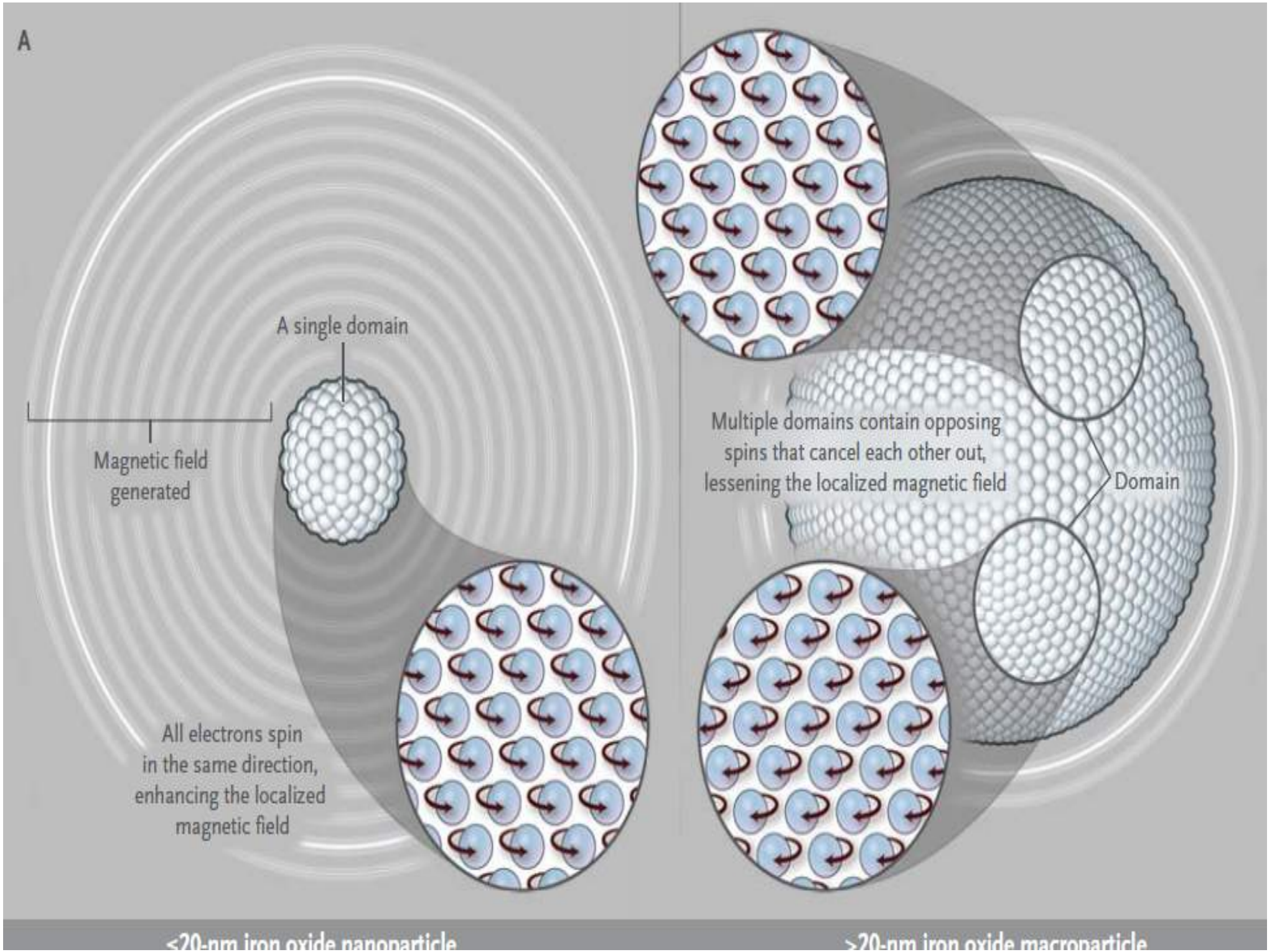


These are one-dimensional zinc oxide (ZnO) nanorods; the high surface-to-volume ratio gives them enhanced optical and electrical properties. They are used in a range of applications in photonics and sensing. The image was captured using the Zeiss Ultra Scanning Electron Microscope in Crann (the Centre for Research on Adaptive Nanostructures and Nanodevices) at Trinity College, Dublin

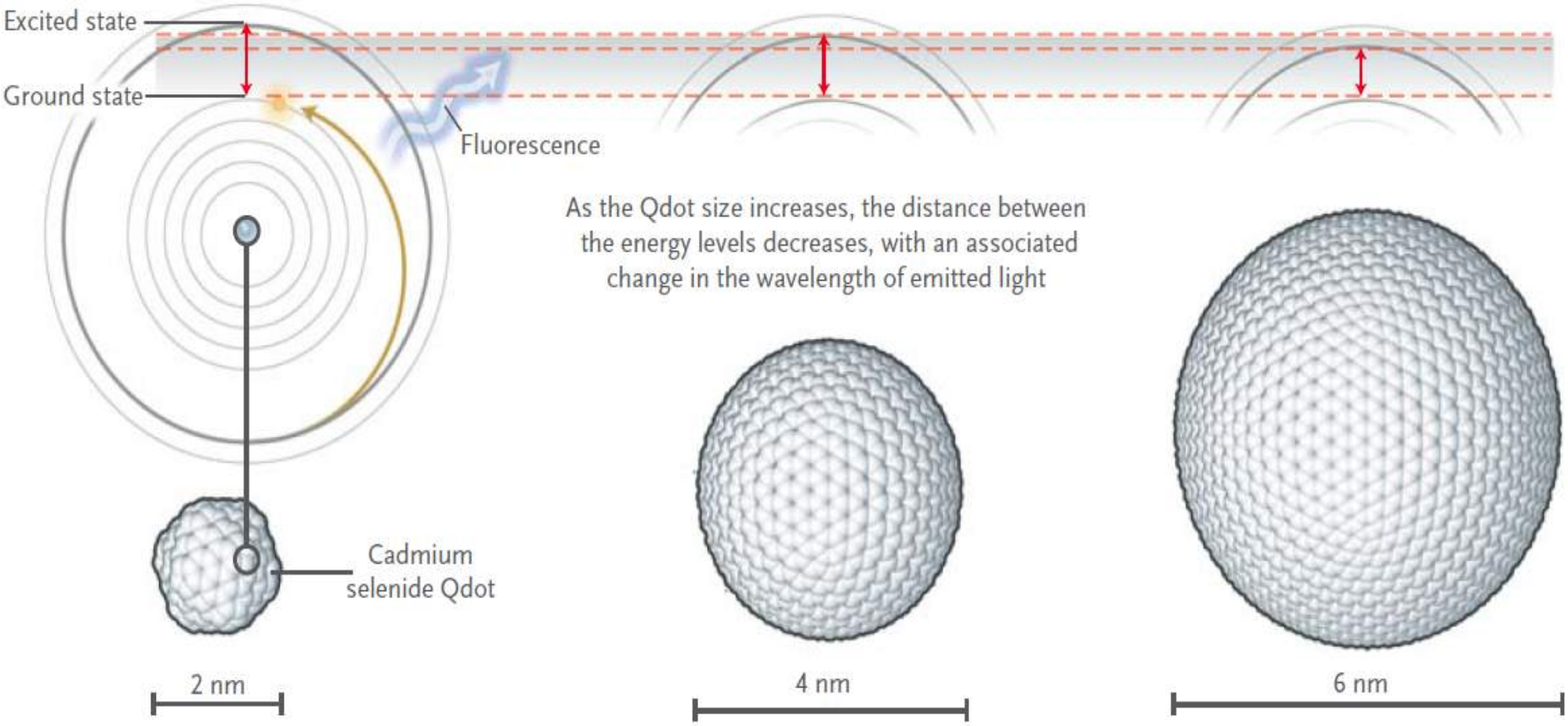
Photograph: Niall McEvoy/Crann/Trinity College Dublin

These 'poppies' are carbon nanotubes (CNTs), bundled together and pulled inwards into tiny pillars. Researchers have proposed the use of CNTs in numerous applications because of their remarkable properties. In biomedical settings, they could be used for a novel transdermal drug delivery system, acting as the scaffolds for microneedles. These have the potential to provide a rapid, self-administered and painless alternative to hypodermic needles. A technique called capillography makes the CNT pillars collapse inwards, increasing their packing density. The greater the packing density, the less pain patients will feel when the needle penetrates their skin

Photograph: Courtesy of Adrianus Aria/California Institute of Technology/Materials Research Society/Science as Art Competition


A
A single domain
Magnetic field generated
All electrons spin in the same direction, enhancing the localized magnetic field
Multiple domains contain opposing spins that cancel each other out, lessening the localized magnetic field
Domain
<20-nm iron oxide nanoparticle
>20-nm iron oxide macroparticle

B


Excited state
Ground state
Fluorescence
As the Qdot size increases, the distance between the energy levels decreases, with an associated change in the wavelength of emitted light
Cadmium selenide Qdot
2 nm
4 nm
6 nm

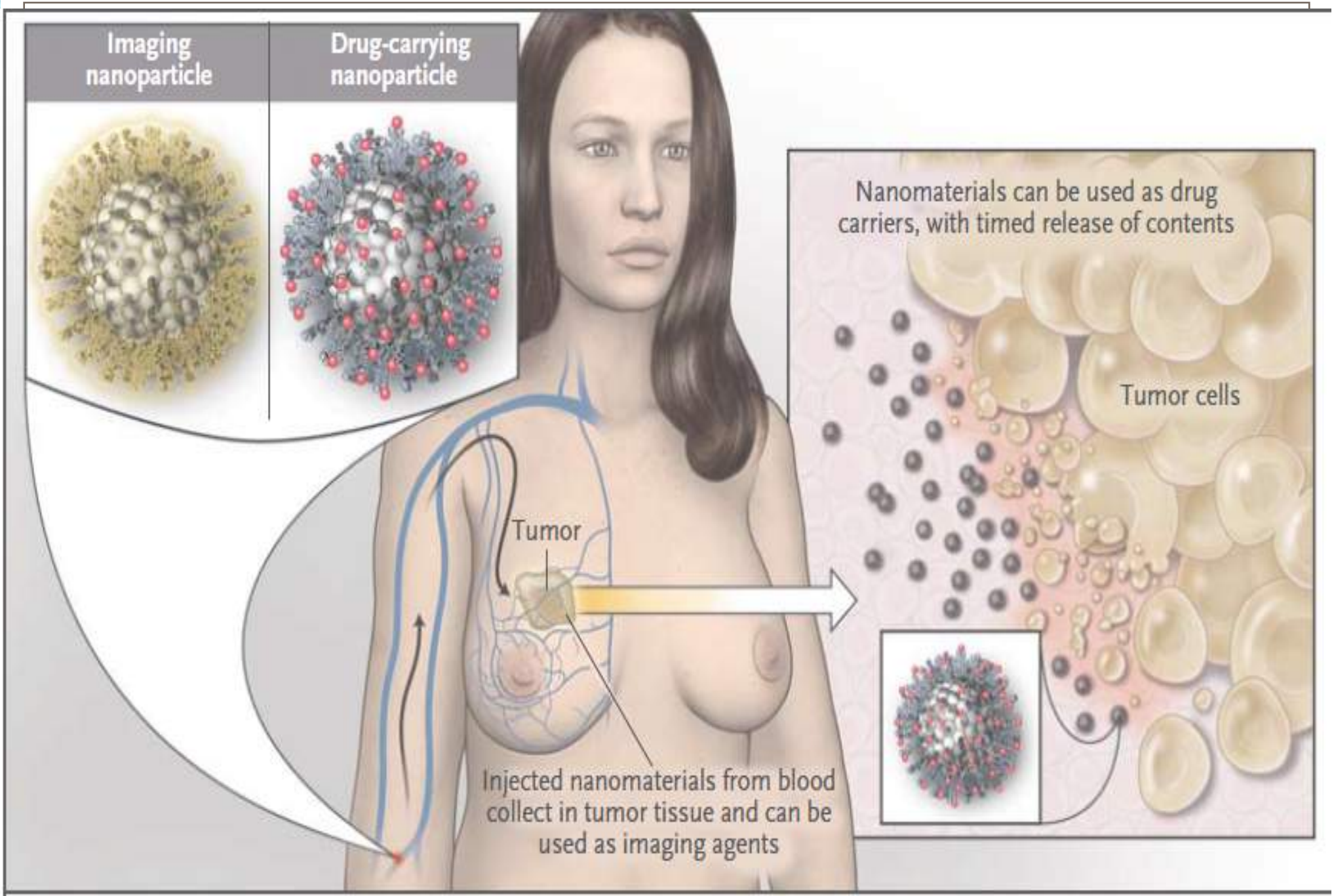
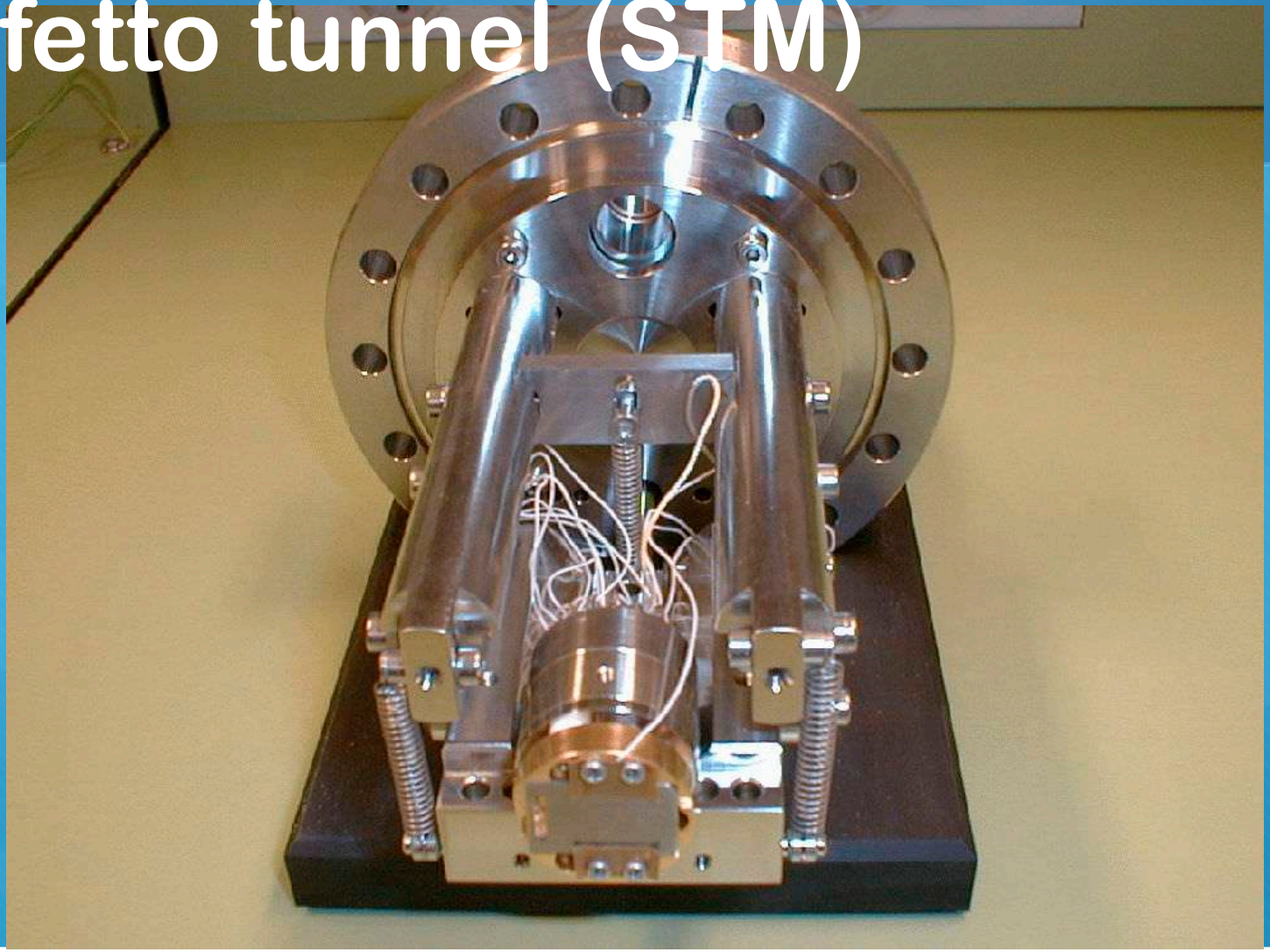
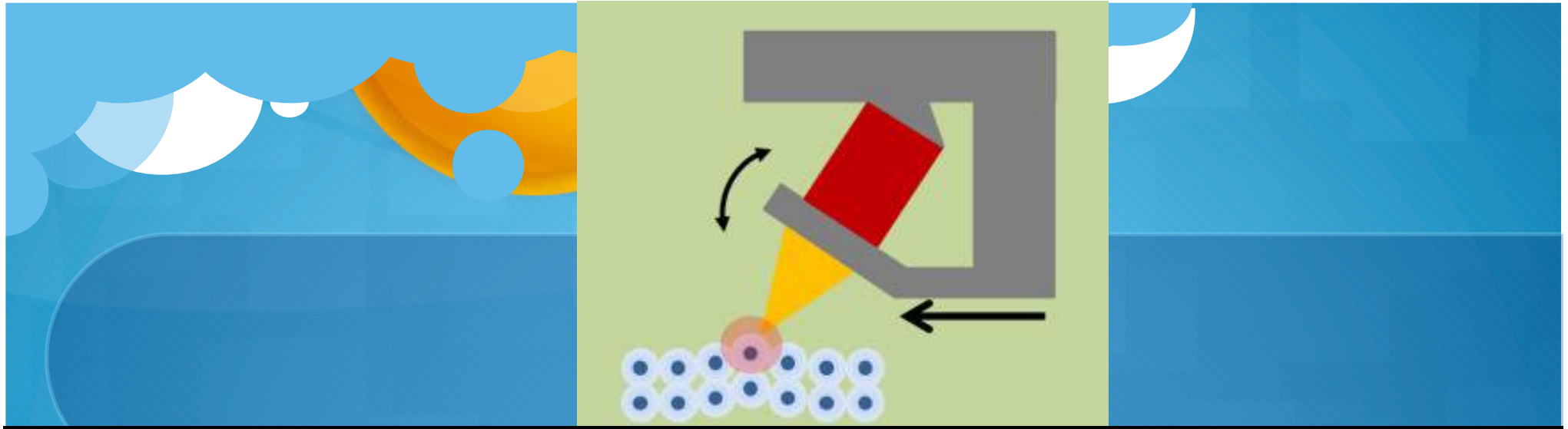
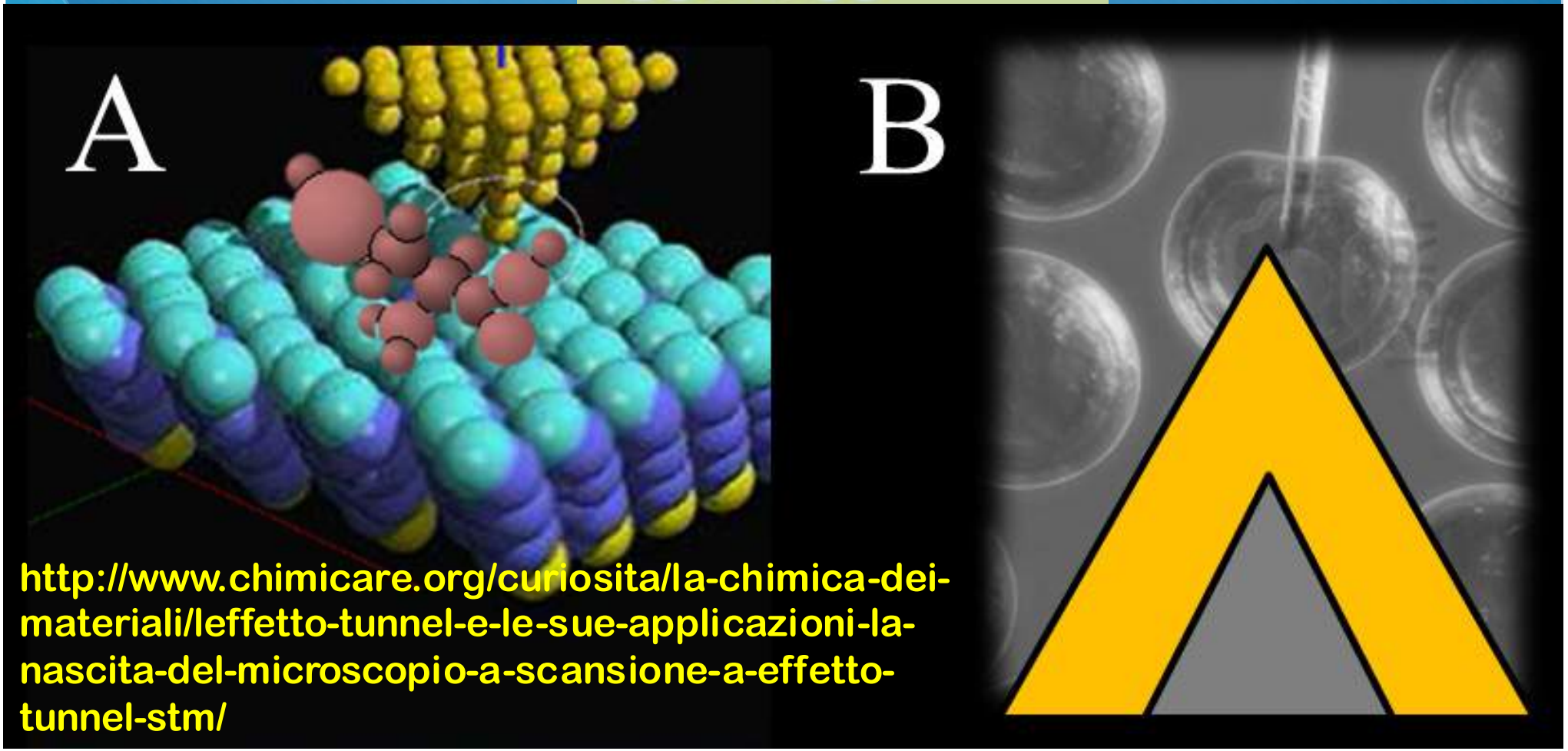


Figure 3. Nanomaterials Used as Drug Carriers or Contrast Agents for In Vivo Cancer Applications.

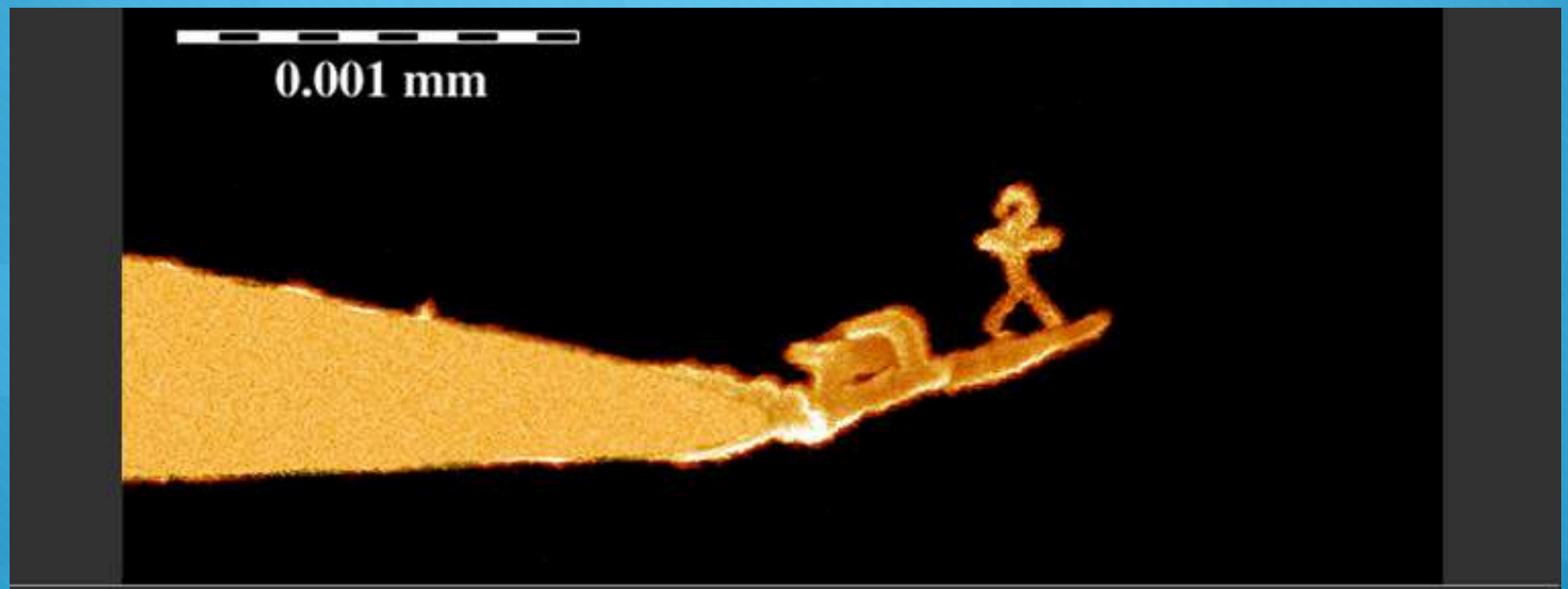
Microscopio a scansione a effetto tunnel (STM)





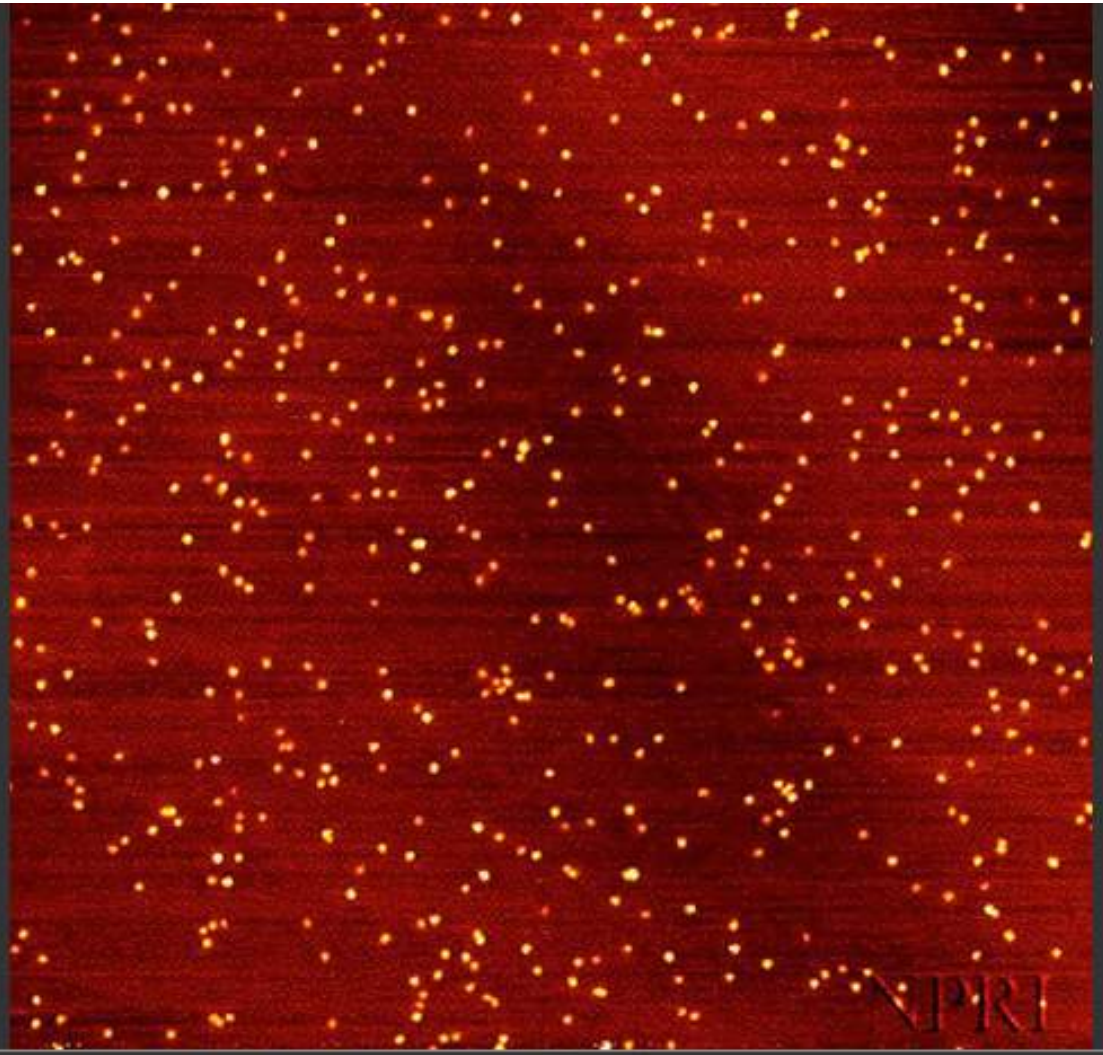


http://www.chimicare.org/curiosita/la-chimica-dei-materiali/leffetto-tunnel-e-le-sue-applicazioni-la-nascita-del-microscopio-a-scansione-a-effetto-tunnel-stm/



This nanoman demonstrates the precision of a scanning tunnelling microscope (STM).
It was created by focused electron beam deposition on the tip of a STM with a
precision of 10nm

Photograph: Richard Palmer/Nanoscale Physics Research Laboratory/University of Birmingham



Researchers have found a way to prepare particles containing anything from a few atoms to thousands. In this image, taken by a scanning tunneling microscope, each gold particle contains just 17 atoms. The particles are also known as nanoclusters, and they have different electrical, mechanical and optical properties depending on their size. They act as anchors and can be used to trap individual protein molecules, enabling the detection of biological markers of disease. One potential application is the early stage detection of prostate cancer

Photograph: Richard Palmer/Nanoscale Physics Research Laboratory/University of Birmingham

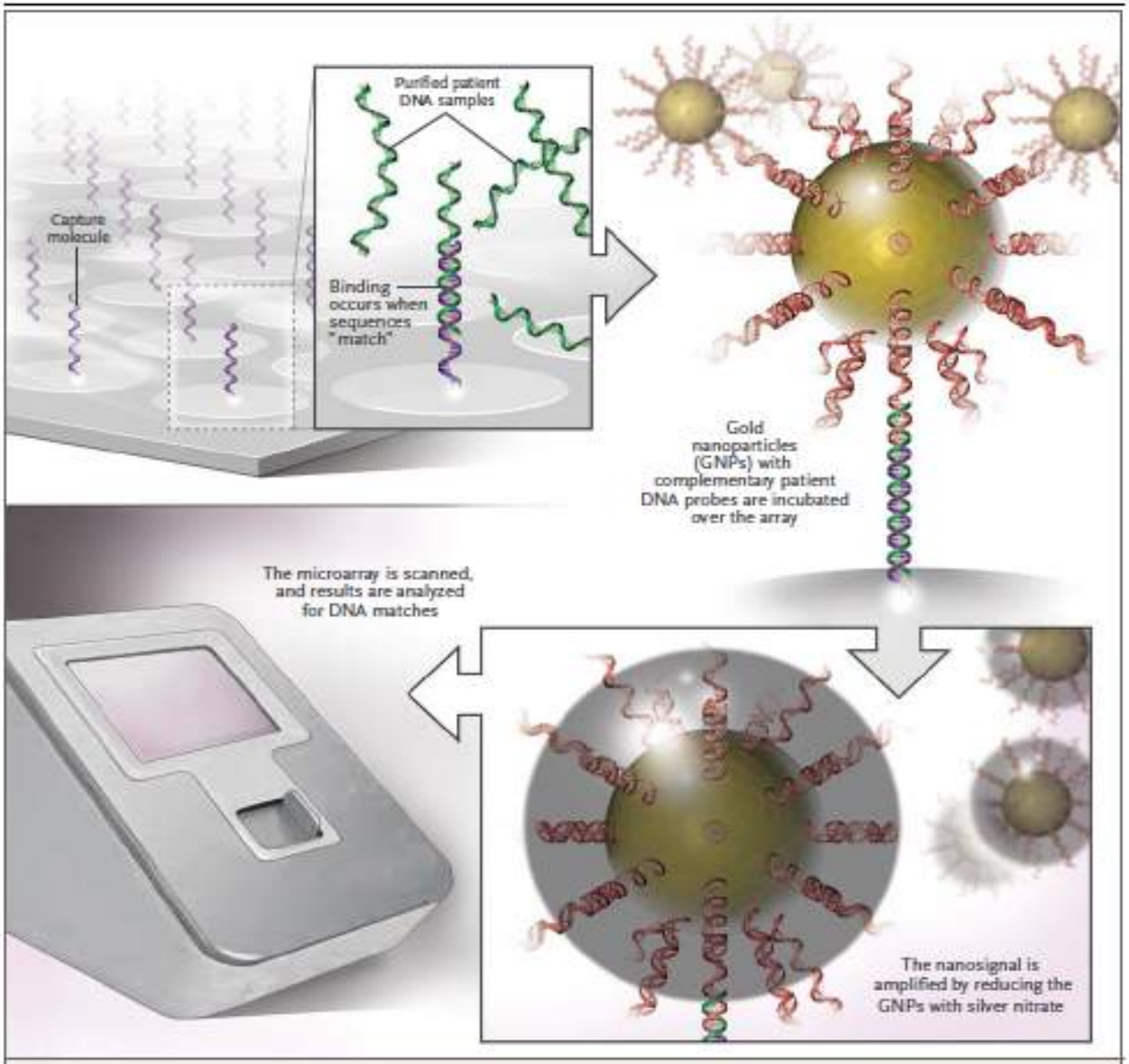


Figure 4. Nanomaterials Used as Labels to Amplify Detection Signals in Diagnostic Devices.

Nanomaterials such as gold nanoparticles can be coated with biorecognition molecules to target either a patient's DNA or a protein sample. Here, gold nanoparticles are coated with a complementary oligonucleotide (single-stranded DNA) that recognizes the variant gene sequence captured on a surface. Once nanoparticles are bound to the surface, the signal is amplified by means of a silver nitrate reduction reaction. This technique has been reported to have sensitivity equivalent to that of the polymerase-chain-reaction assay for genetic analysis.

L'Agenzia statunitense per la protezione dell'ambiente (Environmental Protection Agency – EPA) ordina il ritiro dal commercio di alcuni contenitori alimentari di plastica.

Il motivo è la presenza di nanoparticelle d'argento, presentate dall'azienda produttrice, Pathway Investment Corporation, come rimedio per ridurre la crescita di muffe, funghi e batteri.

Queste affermazioni fanno rientrare i contenitori della Pathway nella categoria dei pesticidi e devono essere testati, registrati e autorizzati dall'EPA, cosa che invece non è

Le nanoparticelle d'argento liberano continuamente ioni che raggiungono i sedimenti acquatici

Quindi possono entrare nella catena alimentare

In questo studio alghe esposte a ioni argento in bassissime concentrazioni entro un quarto d'ora mostrano segni di sofferenza: riduzione fotosintesi, risposte di difesa.

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> Current Issue > vol. 111 no. 9 > Smitha Pillai, 3490–3495, doi: 10.1073/pnas.1319388111

CrossMark

Linking toxicity and adaptive responses across the transcriptome, proteome, and phenotype of *Chlamydomonas reinhardtii* exposed to silver

Smitha Pillai[a,b,1], Renata Behra[a,b], Holger Nestler[a], Marc J.-F. Suter[a,b], Laura Sigg[a,b], and Kristin Schirmer[a,b,c,1]

Author Affiliations

Edited by Holger Hintelman, Trent University, Peterborough, ON, Canada, and accepted by the Editorial Board January 15, 2014 (received for review October 16, 2013)

Abstract | Full Text | Authors & Info | Figures | SI | Metrics | PDF | PDF + SI

Significance

Comprehending the responses of organisms to pollutants by a systems-based approach allows characterization of molecular events and the cellular pathways that have been perturbed. However, mapping only adverse outcomes of a toxicant in an organism falls short of describing the defense response that is mounted to maintain homeostasis and resistance to the toxic insult. Our study provides the understanding of molecular mechanisms of algae in response to silver, which in turn indicates how the algae might behave in a silver contamination scenario. We have used complementary information obtained from the transcriptome, proteome, and physiology to gain mechanistic insights into the responses of *Chlamydomonas reinhardtii*. We show here the importance of stress and adaptive responses, especially at sublethal concentrations of pollutant.

Abstract

Understanding mechanistic and cellular events underlying a toxicological outcome allows the prediction of impact of environmental stressors to organisms living in different habitats. A systems-based approach aids in characterizing molecular events, and thereby the cellular pathways that have been perturbed. However, mapping only adverse outcomes of a toxicant falls short of describing the stress or adaptive response that is mounted to maintain homeostasis on perturbations and may confer resistance to the toxic insult. Silver is a potential threat to aquatic organisms because of the increasing use of silver-based nanomaterials, which release free silver ions. The effects of silver were investigated at the transcriptome, proteome, and cellular levels of *Chlamydomonas reinhardtii*. The cells instigate a fast transcriptome and proteome response, including perturbations in copper transport system and detoxification mechanisms. Silver causes an initial toxic insult, which leads to a plummeting of ATP and photosynthesis and damage because of oxidative stress.

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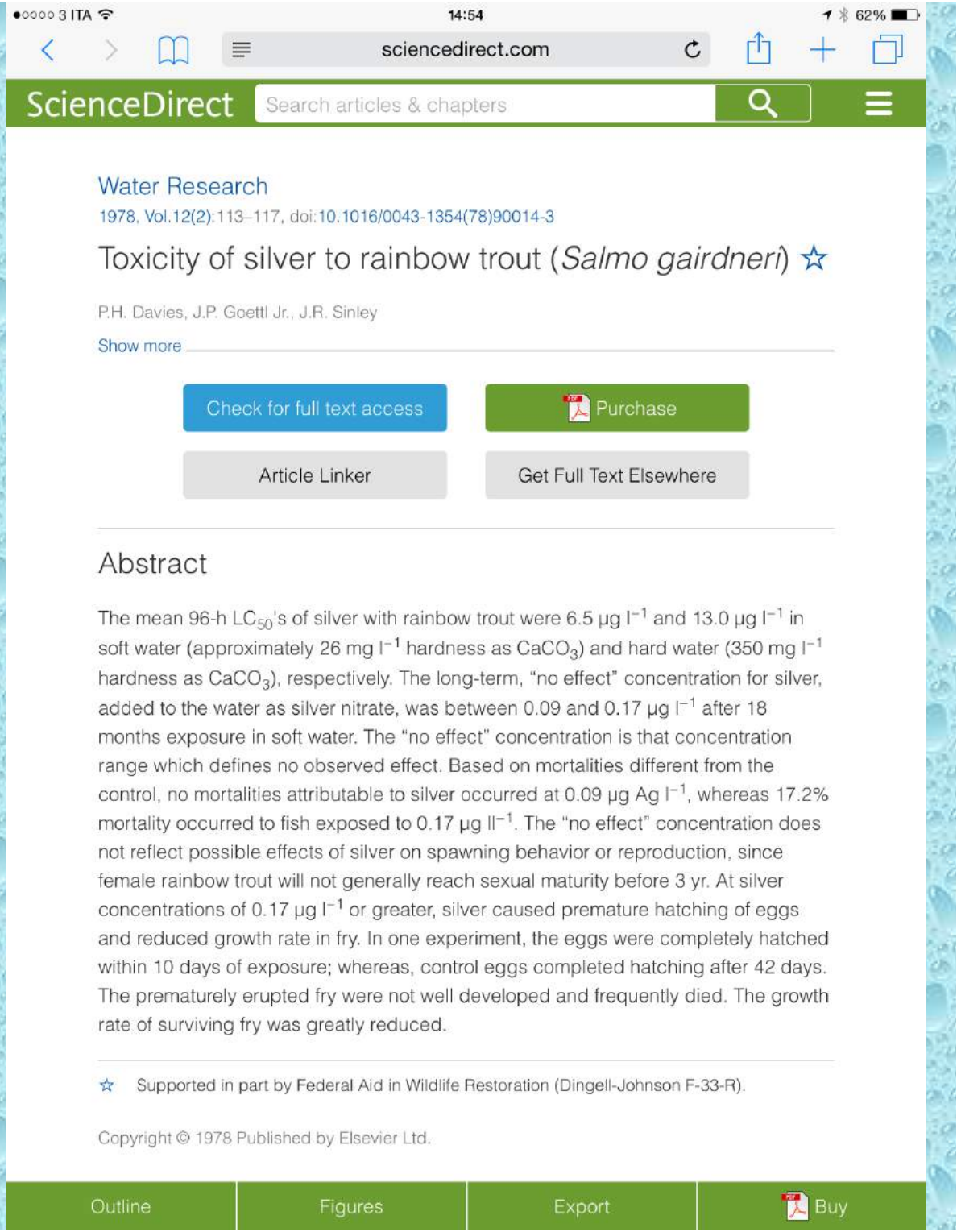
Published online before print February 18, 2014, doi: 10.1073/pnas.1319388111 PNAS March 4, 2014 vol. 111 no. 9 3490-3495

Classifications

Biological Sciences
Environmental Sciences

Precedentemente gli ioni argento sono risultati tossici per le trote arcobaleno (vengono colpite le uova con una forte riduzione della riproduzione)



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Water Research
1978, Vol.12(2):113–117, doi:10.1016/0043-1354(78)90014-3

Toxicity of silver to rainbow trout (*Salmo gairdneri*) ☆

P.H. Davies, J.P. Goettl Jr., J.R. Sinley

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Abstract

The mean 96-h LC_{50}'s of silver with rainbow trout were 6.5 μg l^{-1} and 13.0 μg l^{-1} in soft water (approximately 26 mg l^{-1} hardness as $CaCO_3$) and hard water (350 mg l^{-1} hardness as $CaCO_3$), respectively. The long-term, "no effect" concentration for silver, added to the water as silver nitrate, was between 0.09 and 0.17 μg l^{-1} after 18 months exposure in soft water. The "no effect" concentration is that concentration range which defines no observed effect. Based on mortalities different from the control, no mortalities attributable to silver occurred at 0.09 μg Ag l^{-1}, whereas 17.2% mortality occurred to fish exposed to 0.17 μg ll^{-1}. The "no effect" concentration does not reflect possible effects of silver on spawning behavior or reproduction, since female rainbow trout will not generally reach sexual maturity before 3 yr. At silver concentrations of 0.17 μg l^{-1} or greater, silver caused premature hatching of eggs and reduced growth rate in fry. In one experiment, the eggs were completely hatched within 10 days of exposure; whereas, control eggs completed hatching after 42 days. The prematurely erupted fry were not well developed and frequently died. The growth rate of surviving fry was greatly reduced.

☆ Supported in part by Federal Aid in Wildlife Restoration (Dingell-Johnson F-33-R).

Outline | Figures | Export | Buy

Il nanoargento ha provocato danni al DNA e ha cambiato temporaneamente la produzione di proteine di cellule dell'intestino umano.

Le cellule recuperano il danno grazie alla presenza di sostanze come i cloruri.

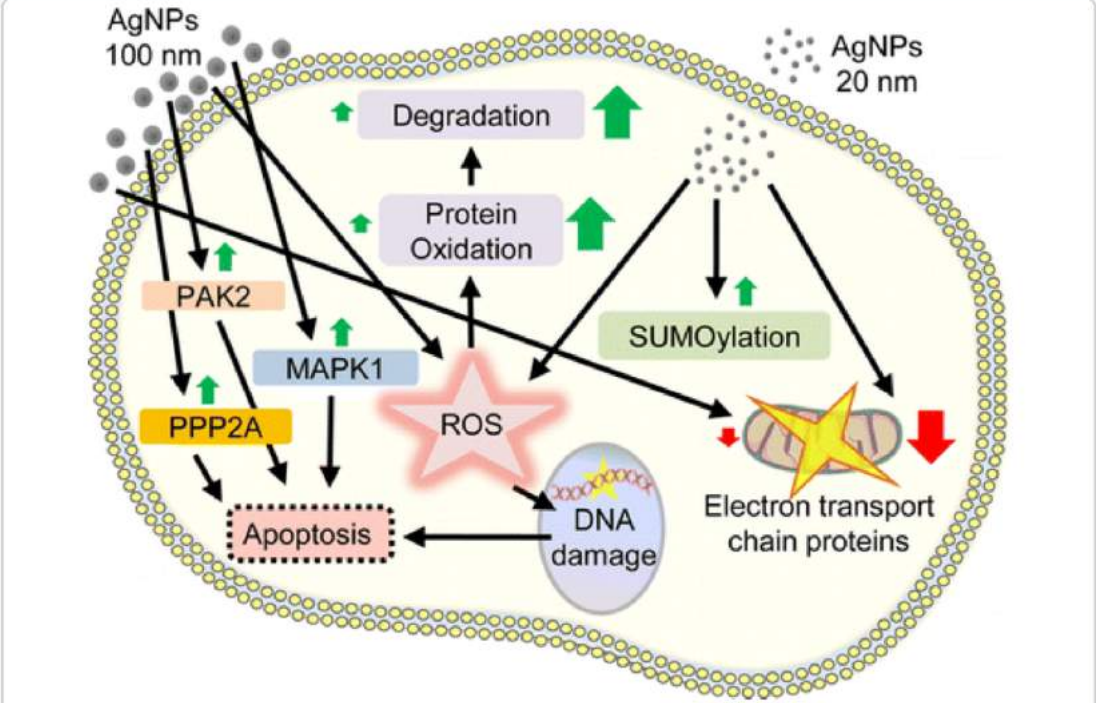
Tuttavia ad alte concentrazioni quest'azione scavenger potrebbe ridursi e le cellule perderebbero la capacità di recuperare.

Le alte concentrazioni si possono raggiungere grazie alla bioaccumulazione

ACS Nano, **2014**, *8* (3), pp 2161–2175
DOI: 10.1021/nn4050744
Publication Date (Web): February 10, 2014

*Address correspondence to frankk@bmb.sdu.dk.

Abstract



The use of nanoparticles in foods, materials, and clinical treatments has increased dramatically in the past decade. Because of the possibility of human exposure to nanoparticles, there is an urgent need to investigate the molecular mechanisms underlying the cellular responses that might be triggered. Such information is necessary to assess potential health risks arising from the use of nanoparticles, and for developing new formulations of next generation nanoparticles for clinical treatments. Using mass spectrometry-based proteomic technologies and complementary techniques (*e.g.*, Western blotting and confocal laser scanning microscopy), we present insights into the silver nanoparticle–protein interaction in the human LoVo cell line. Our

- **Bioaccumulo**
  - sostanze lipofile
  - sostanze persistenti

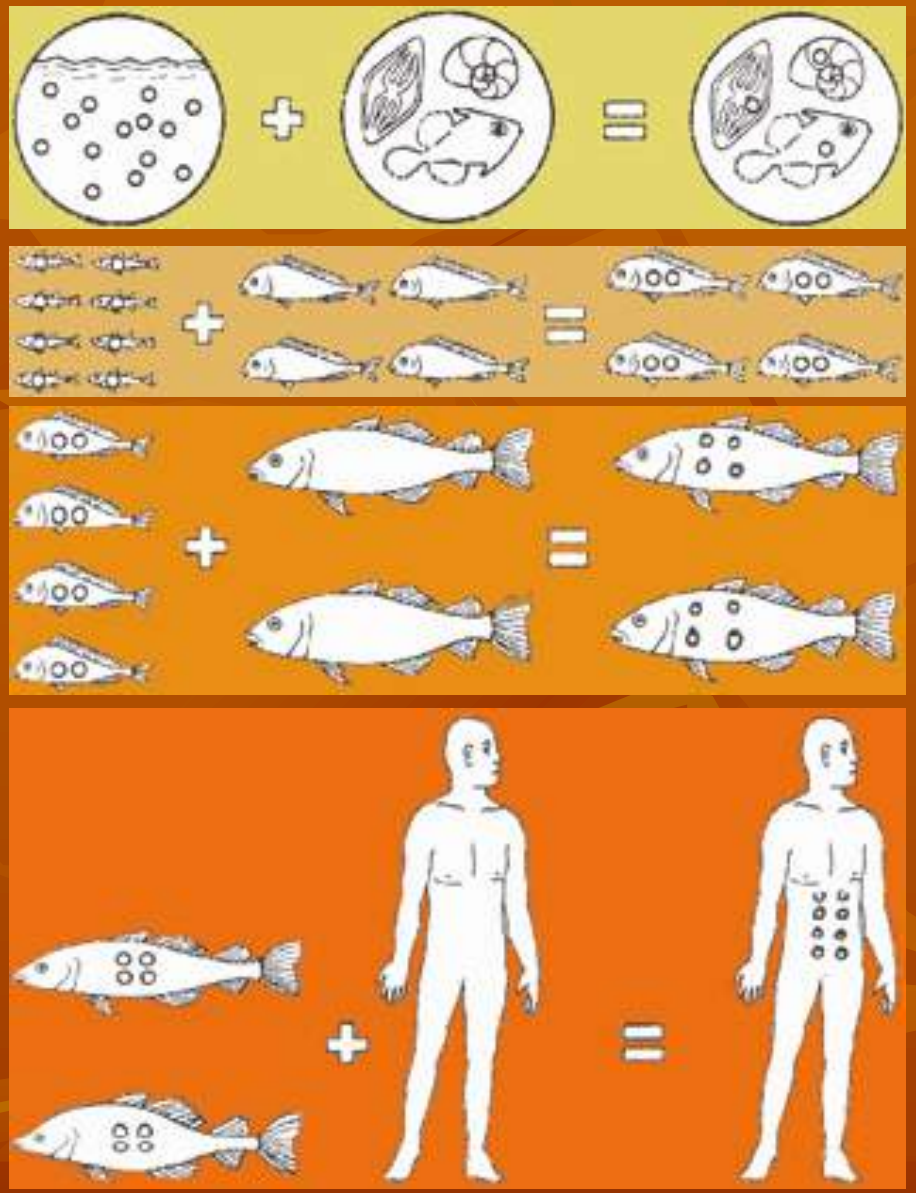
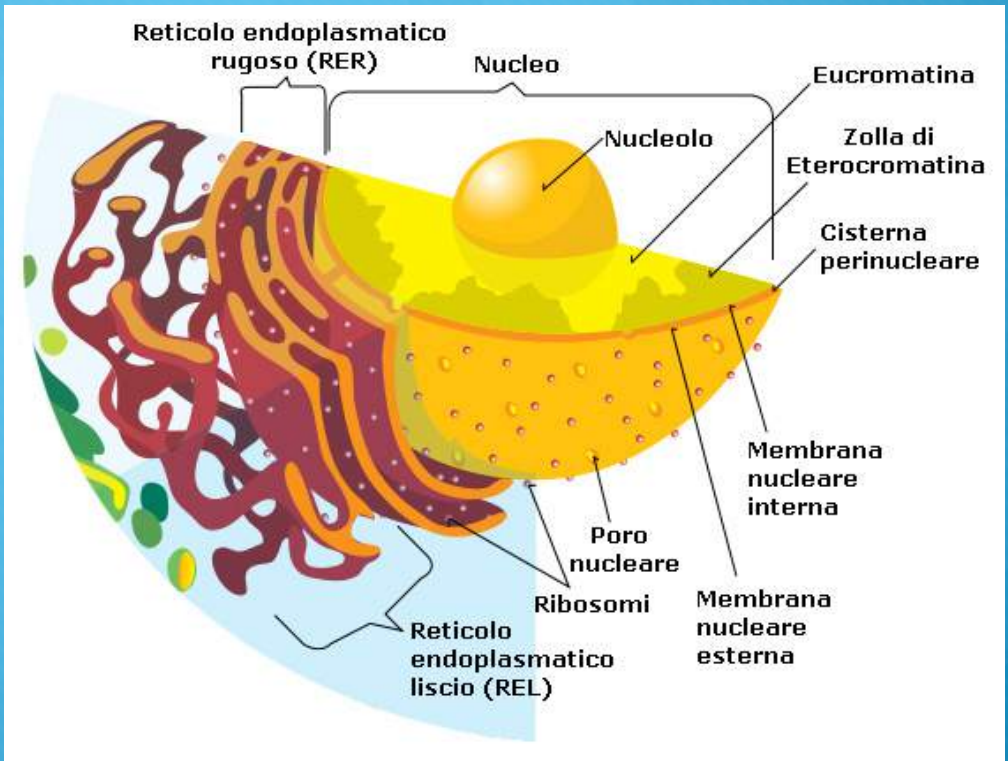


Table 4: Experimental evidence of the ecotoxicity of nanomaterials now in commercial use

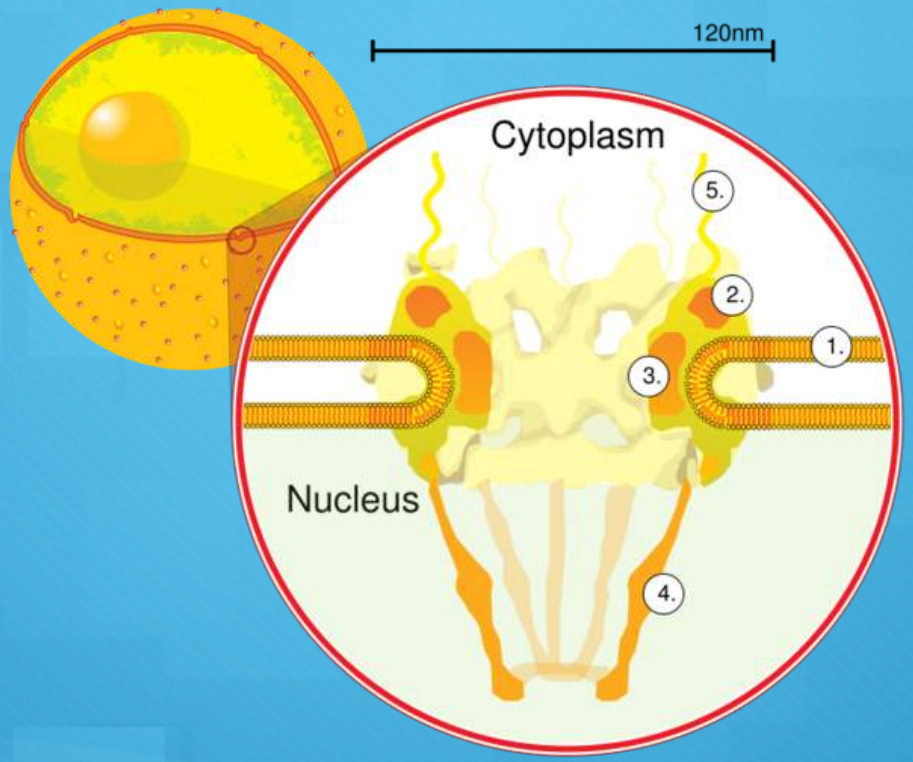
NANOMATERIAL AND CURRENT APPLICATIONS	SIZE AND PHYSICAL DESCRIPTION	EXPERIMENTAL EVIDENCE OF TOXICITY
Titanium dioxide Nano form used in sunscreens, self-cleaning glass, remediation, widely use in small micro form in foods and cosmetics	30nm	Killed water fleas (*Daphnea magna*)[114] which are used by regulators as an ecological indicator species
	25nm anatase	UV-illuminated TiO2 toxic to algae and water fleas[115]
Zinc Used in electronics, optoelectronics, gas sensors, sunscreens, cosmetics, food packaging, paint	Nanoparticle zinc oxide, size unknown	Toxic to algae and water fleas (*Daphnea magna*)[116]
Carbon based nanomaterials Carbon black used in tyres, dyes; carbon nanotubes used in specialist car and aeroplane materials and fabrics, potential use in packaging; fullerenes used in cosmetics, potential use in medicines, batteries and electronics	C60 fullerenes	Water soluble C60 caused brain damage (lipid peroxidation) in juvenile largemouth bass (*Micropterus salmoides*)[117], used by regulators as an ecological indicator. Subsequent study found tetrahydrofuran (THF)-solubilized fullerenes even more toxic than water solubilised fullerenes, with 100% mortality in the THF-C60-exposed fish between 6 and 18 hours of exposure[118]
	Single walled carbon nanotubes	By-products associated with their manufacture cause increased mortality and delayed development of small estuarine invertebrate *Amphiascus tenuiremis*[119]
	Single-walled carbon nanotubes	By-products associated with their manufacture delayed hatching of zebra fish (*Danio rerio*) embryos[120].
	C60 fullerenes	Killed water fleas (*Daphnea magna*)[121,122]
	C60 fullerenes and C60HxC70Hx	Caused behavioural and physiological changes in water fleas that are associated with increased risk of predation and reproductive decline[123]
	C60 fullerenes	Toxic to microbes, inhibits growth and decreases respiration[124]
Aluminium Used in cosmetics, sunscreens, scratch resistant coatings	13nm	High levels of exposure stunted root growth in corn, cucumber, soybean, carrot and cabbage crops[125]

Particelle con dimensioni minori di 300 nm possono essere captate dalle cellule



http://it.wikipedia.org/wiki/Poro_nucleare

Particelle con dimensioni minori di 70 nm possono penetrare nel nucleo



http://it.wikipedia.org/wiki/Poro_nucleare

NANOTOSSICOLOGIA

- Alcuni nanomateriali sono risultati tossici per tessuti umani e cellule in coltura con incremento dello stress ossidativo, accensione dlle proteine proinfiammatorie, mutazioni del DNA, danni al nucleo cellulare, interferenza con attività e crescita cellulare, danni al mitocondrio e morte cellulare

NANOTOSSICOLOGIA

Studi sui ratti hanno dimostrato che:

le nanoparticelle passano attraverso la parete intestinale e si accumulano in diversi organi dando origine a sviluppo di granulomi e lesioni.

NANOTOSSICOLOGIA

- Particelle di biossido di titanio delle dimensioni di 200 nm possono attivare il sistema immunitario e promuovere l'infiammazione.
- Alcuni ricercatori hanno suggerito la possibilità che tali particelle possano aumentare l'incidenza di malattie autoimmuni dell'apparato digerente (sindrome dell'intestino irritabile, morbo di Crohn)

NANOTOSSICOLOGIA

- I meccanismi di difesa del nostro organismo non sembrano in grado di rimuovere le nanoparticelle da polmoni, intestino

SolNanoTox

- In Germania è stata avviata una ricerca franco-tedesca (finisce nel 2017) per studiare gli effetti e l'eventuale tossicità dei nanomateriali presenti nei prodotti alimentari, sul corpo umano, in particolare sul fegato e l'intestino.

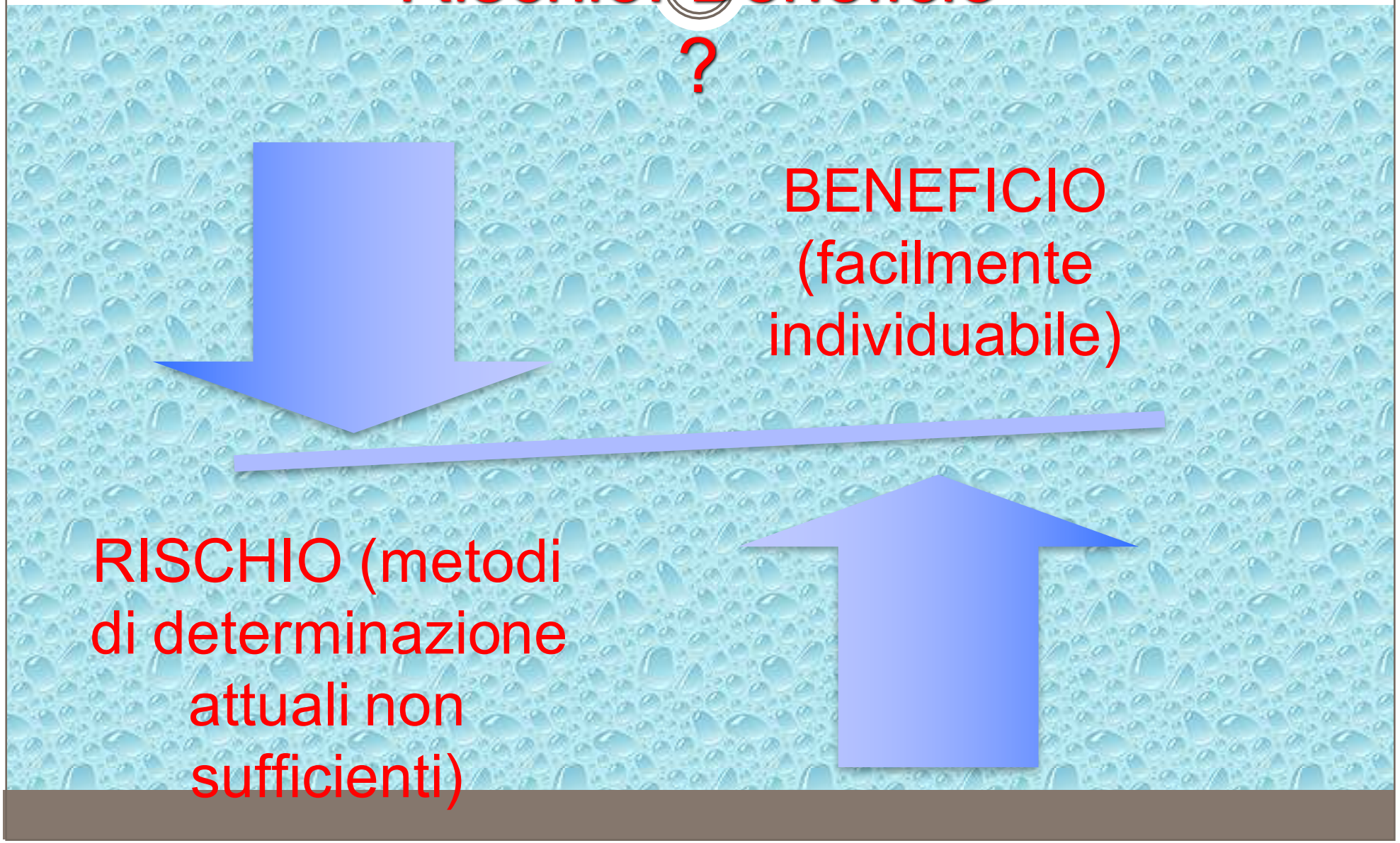
- Lo studio è condotto dal tedesco Federal Institute for Risk Assessment (BfR) e ndall'istituto francese per la sicurezza alimentare Anses

- Non essendo possibile testare le proprietà tossiche dei singoli nanomateriali, a causa del loro gran numero, la ricerca ne ha selezionati due, in base alla loro solubilità:

  il biossido di titanio, insolubile

  l'alluminio, che ha un certo grado di solubilità

Rapporto Rischio: Beneficio ?



TINY INGREDIENTS

BIG RISKS

“Piccoli ingredienti, grandi rischi” è il titolo del nuovo rapporto dell’associazione ambientalista Friends of the Earth sulla diffusione dei nanomateriali negli alimenti.

- **Nel 2008 erano otto i nanomateriali presenti sul mercato statunitense,**
- **Nel 2014 erano 94**

Table 1: A sample of food companies engaged in nanotechnology research and development [85,86,87]

COMPANY	
• Altria (Mondelez)	• H.J. Heinz
• Associated British Foods	• Hershey Foods
• Ajinomoto	• La Doria
• BASF	• Maruha
• Cadbury Schweppes	• McCain Foods
• Campbell Soup	• Mars, Inc.
• Cargill	• Nestle
• DuPont Food Industry Solutions	• Northern Foods
• General Mills	• Nichirei
• Glaxo-SmithKline	• Nippon Suisan Kaisha
• Goodman Fielder	• PepsiCo
• Group Danone	• Sara Lee
• John Lust Group Plc	• Unilever
	• United Foods

ON THE MARKET

Table 2: Food products that may contain manufactured nanomaterials [88]

PRODUCTS	
• Almond beverages	• Milk
• Candy	• Mints
• Cereal	• Oils
• Chocolate	• Pasta
• Chocolate syrup	• Popcorn
• Coffee Creamer	• Pudding
• Cookies	• Rice beverages
• Crackers	• Salad Dressing
• Cream Cheese	• Soy
• Doughnuts	• Soy beverages
• Gum	• Sports Drinks and other beverages
• Mashed Potatoes	• Yogurt
• Mayonnaise	

Many foods Americans eat on a daily basis contain nanomaterial ingredients (see Table 2 for a list of

Table 1: Examples of the current use of nanomaterials in agriculture, foods and food packaging (see Appendix A for a complete referenced list)

Type of product	Product name and manufacturer	Nano content	Purpose
Nutritional supplement	Nanoceuticals 'mycrohydrin' powder, RBC Lifesciences	Molecular cages 1-5 nm diameter made from silica-mineral hydride complex	Nano-sized mycrohydrin has increased potency and bioavailability. Exposure to moisture releases H- ions and acts as a powerful antioxidant.
Nutritional drink	Oat Chocolate Nutritional Drink Mix, Toddler Health	300nm particles of iron (SunActive Fe)	Nano-sized iron particles have increased reactivity and bioavailability.
Food contact material (cooking equipment)	Nano silver cutting board, A-Do Global	Nanoparticles of silver	Nano-sized silver particles have increased antibacterial properties.
Food contact material (crockery)	Nano silver baby mug, Baby Dream	Nanoparticles of silver	Nano-sized silver particles have increased antibacterial properties.
Food contact material (kitchenware)	Antibacterial kitchenware, Nanocaretech/NCT	Nanoparticles of silver	Nano-sized silver particles have increased antibacterial properties.
Food packaging	Adhesive for McDonald's burger containers, Ecosynthetix	50-150nm starch nano-spheres	These nanoparticles have 400 times the surface area of natural starch particles. When used as an adhesive they require less water and thus less time and energy to dry.
Food packaging	Durethan® KU 2-2601 plastic wrapping, Bayer	Nanoparticles of silica in a polymer-based nanocomposite	Nanoparticles of silica in the plastic prevent the penetration of oxygen and gas of the wrapping, extending the product's shelf life.
Food additive	Aquasol preservative, AquaNova	Nanoscale micelle (capsule) of lipophilic or water insoluble substances	Surrounding active ingredients within soluble nanocapsules increases absorption within the body (including individual cells).
Plant growth treatment	PrimoMaxx, Syngenta	100nm particle size emulsion	Using nano-sized particles increases the potency of active ingredients, potentially reducing the quantity to be applied.

Applicazioni delle nanotecnologie in agricoltura

- Rendere più salutari alcuni cibi: meno grassi, aumento proteine, fibre o vitamine
- Intensificazione degli aromi, variazioni di colore, riduzione costi
- Personalizzazione degli alimenti a seconda del tipo di consumatore
- Incremento del tempo di conservazione

Nanofoods

- Le nanotecnologie permettono l'uso di rivestimenti per il cibo dello spessore di 5 nm invisibile all'occhio umano
- Questo rivestimento è commestibile ed utilizzato per carne, formaggio, frutta, vegetali, confetture, prodotti da forno e prodotti fast food
- Hanno il vantaggio di allungare la conservazione dell'alimento dopo l'apertura del confezionamento primario

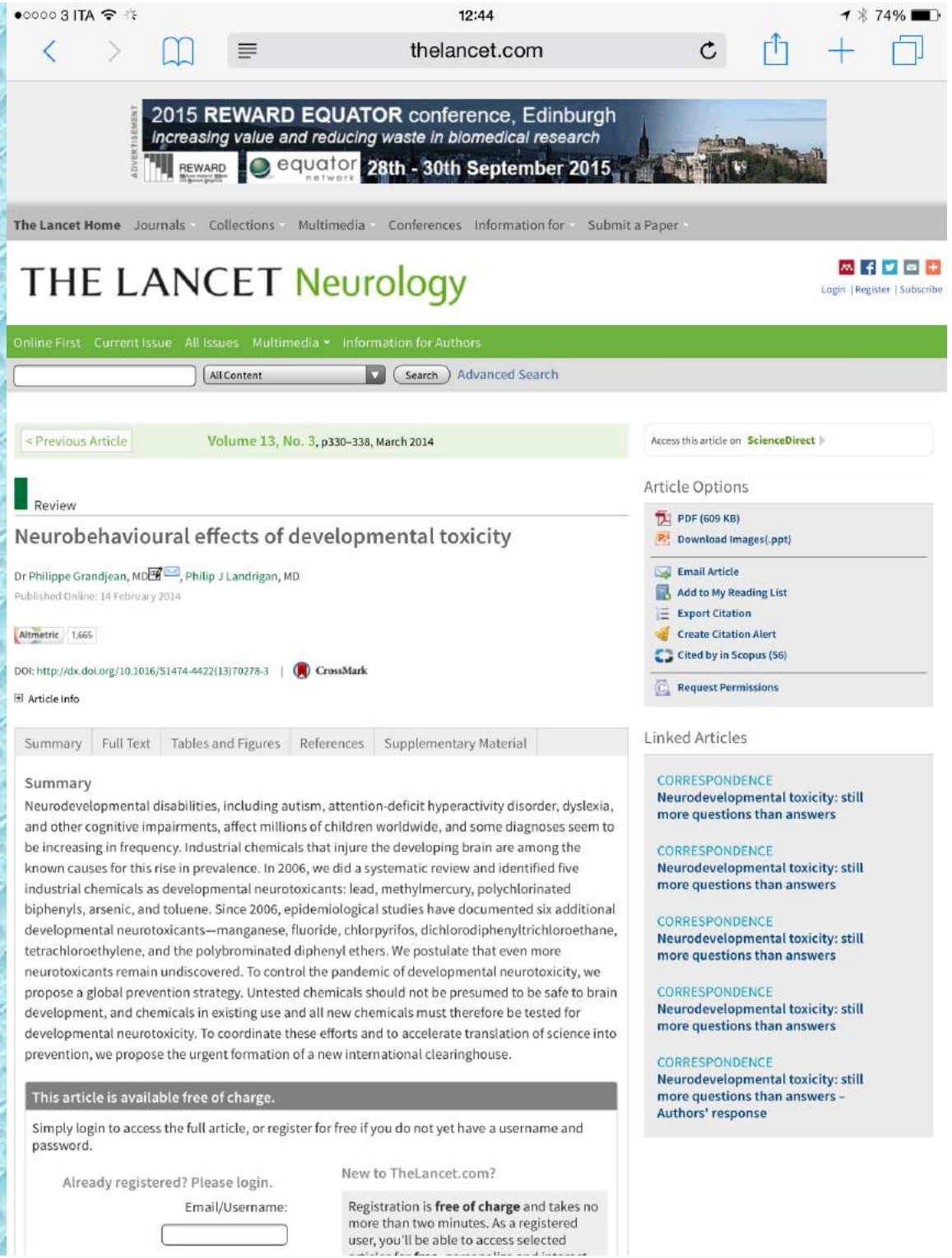
Table 8: Experimental evidence of the toxicity of selected nanomaterials now in commercial use by the food industry

Nanomaterial and current applications	Size and physical description	Experimental evidence of toxicity
Titanium dioxide Small microparticle form widely used as food additive; nanoparticle form used as antimicrobial and U.V. protector in food packaging and storage containers and sold as food additive	20nm	Destroyed DNA (*in vitro*; Donaldson et al. 1996)
	30nm mix of rutile and anatase forms of titanium dioxide (see glossary)	Produced free radicals in brain immune cells (*in vitro*; Long et al. 2006)
	Nanoparticle, size unknown, rutile and anatase forms	DNA damage to human skin cells when exposed to UV light (*in vitro*; Dunford et al. 1997)
	Four sizes 3-20nm, mix of rutile and anatase form	High concentrations interfered with the function of skin and lung cells. Anatase particles 100 times more toxic than rutile particles (*in vitro*; Sayes et al. 2006)
	25nm, 80nm, 155nm	25nm and 80nm particles caused liver and kidney damage in female mice. TiO_2 accumulated in liver, spleen, kidneys and lung tissues (*in vivo*; Wang et al. 2007b)
Silver Used as antimicrobial in food packaging, storage containers, chopping boards and refrigerators, also sold as health supplement	15nm	Highly toxic to mouse germ-line stem cells (*in vitro*; Braydich-Stolle et al. 2005)
	15nm, 100nm	Highly toxic to rat liver cells (*in vitro*; Hussain et al. 2005)
	15nm, ionic form	Toxic to rat brain cells (*in vitro*; Hussain et al. 2006)
Zinc and zinc oxide Sold as nutritional additives and used as antimicrobial in food packaging	20nm, 120nm zinc oxide powder	120nm particles caused dose–effect damage in mice liver, heart and spleen. 20nm particles damaged liver, spleen and pancreas (*in vivo*; Wang et al. 2007a)
	19nm zinc oxide	Toxic to human and rat cells even at very low concentrations (*in vitro*; Brunner et al. 2006)
	58±16 nm, 1.08±0.25μm zinc powder	Test mice showed severe symptoms of lethargy, vomiting and diarrhoea. Nanoparticle dose produced more severe response, killed 2 mice in first week, and caused greater kidney damage and aneamia. Greater liver damage in microparticle treatment (*in vivo*; Wang et al. 2006)
Silicon dioxide Particles a few hundred nm in size used as food additives, nano form touted for use in food packaging	50nm, 70nm, 0.2μm, 0.5 μm, 1μm, 5 μm	50nm and 70nm particles taken up into cell nucleus where they caused aberrant protein formation and inhibited cell growth. Caused the onset of a pathology similar to neurodegenerative disorders (*in vitro*; Chen and von Mickecz 2005)

Rischi emergenti:
2. Inquinanti e alterazioni comportamentali nell'uomo

Sostanze neurotossiche per lo sviluppo cerebrale:

- piombo,
- metilmercurio,
- arsenico,
- policlorobifenili (PCB)
- toluene
- manganese
- fluoruri
- pesticidi chlorpyrifos
- DDT
- solvente tetracloroetilene
- ritardanti di fiamma a base di polibromodifenileteri (PBDE)
- Bisfenoli



Sostanze neurotossiche per lo sviluppo cerebrale

Gli autori riportano i risultati di studi che hanno posto in relazione la riduzione del potenziale intellettivo di una popolazione con la capacità produttiva e il PIL della nazione:

ogni punto di QI perso, corrispondebbe una perdita economica nell'arco della vita lavorativa stimabile in almeno 12.000 euro;

in seguito all'esposizione al metilmercurio nell'Unione Europea vanno perduti circa 600.000 punti QI all'anno;

si devono considerare anche altre 200 sostanze capaci di danneggiare il cervello adulto.

Sostanze neurotossiche per lo sviluppo cerebrale

La maggioranza delle oltre 80.000 sostanze industriali usate negli Stati Uniti non sono mai state testate rispetto a effetti tossici che potrebbero pregiudicare lo sviluppo del cervello del feto o un bambino.

Nuova strategia di prevenzione internazionale che attribuisca ai produttori chimici l'onere di dimostrare che i loro prodotti sono a basso rischio attraverso una serie di test simili a quelli adottati per i farmaci.

Rischi emergenti: 3. Dispersione dei farmaci nell'ambiente

Residui di farmaci nelle acque

- **Diversi studi hanno dimostrato che è possibile ritrovare quantità non trascurabili di farmaci e loro metaboliti nelle acque di superficie, nelle acque di fogna dopo i trattamenti sanitari e persino nell'acqua potabile**

- L'analisi d'acque di fogna trattate, ha evidenziato:
  - fino a 6,3 microg/l di carbamazepina (farmaco antiepilettico), fino a 15 microg/l di iopamidolo e fino a 11 microg /l di iopromide (due farmaci diagnostici) (GERMANIA)
  - si sono ritrovati livelli nell'ordine dei microg /l di acido clofibrico (utilizzato nelle dislipidemie) e alcuni dei suoi principali metaboliti in acque di scolo negli USA
  - in Gran Bretagna in acqua di fogna trattate, sono stati ritrovati farmaci in concentrazioni comprese tra 0,1 e 1 microg/l; le conseguenze sono rappresentate dall'inquinamento delle acque dei fiumi con concentrazioni di farmaci fino a 0,5 microg /l (come per il diclofenac)
  - concentrazioni fino a 0,27 microg /l di acido clofibrico sono state ritrovate nell'acqua da bere in Germania (acquedotto di Berlino)

Quali residui nelle acque?

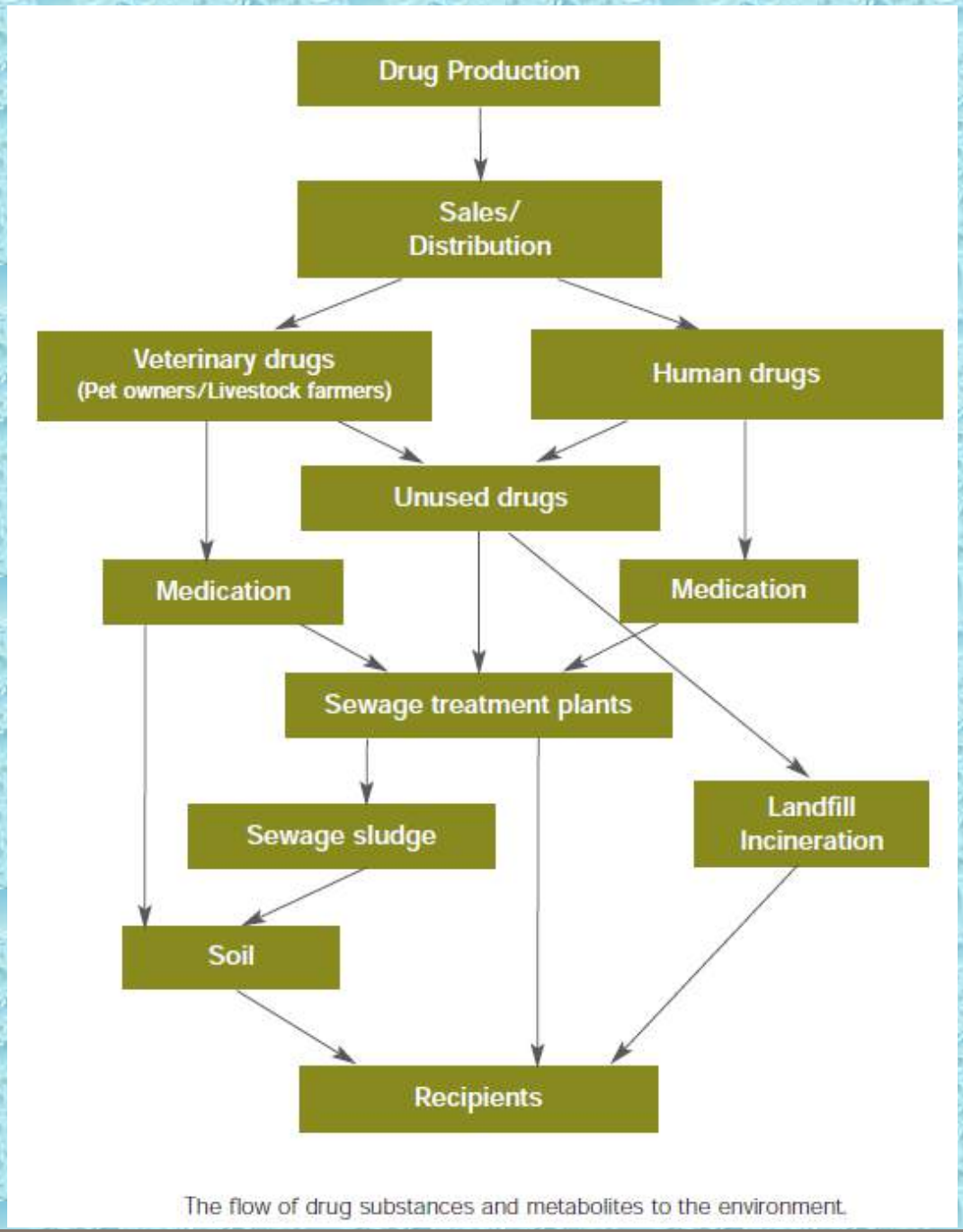
- **In generale sono stati ritrovati fino a 160 tipi di farmaci diversi dispersi in vari tipi di acque e, inaspettatamente, anche nell'Artide**

- **È importante notare che la presenza di metaboliti è un indicatore dei farmaci escreti dopo l'assunzione e non derivano dalla dispersione diretta nell'ambiente**

Come arrivano i farmaci nel sistema fognario?

I farmaci dovrebbero essere eliminati attraverso i contenitori dedicati posti a ridosso delle farmacie ma non sempre è così…..

I farmaci e i loro metaboliti vengono eliminati nelle fogne anche attraverso le deiezioni



The flow of drug substances and metabolites to the environment.

Quali rischi?

CrossMark click for updates

Assessing the exposure risk and impacts of pharmaceuticals in the environment on individuals and ecosystems

Kathryn E. Arnold, Alistair B. A. Boxall, A. Ross Brown, Richard J. Cuthbert, Sally Gaw, Thomas H. Hutchinson, Susan Jobling, Judith C. Madden, Chris D. Metcalfe, Vinny Naidoo, Richard F. Shore, Judit E. Smits, Mark A. Taggart, Helen M. Thompson

DOI: 10.1098/rsbl.2013.0492 . Published 26 June 2013

Veterinary Microbiology
16 July 2014, Vol.171(3):441–447, doi:10.1016/j.vetmic.2014.02.017
Special Issue: ARAE 2013, Antimicrobial Resistance of Bacteria from Animals and the Environment
Open Access, Creative Commons license, Funding information

Functional metagenomic analysis reveals rivers are a reservoir for diverse antibiotic resistance genes

G.C.A. Amos, L. Zhang, P.M. Hawkey, W.H. Gaze, E.M. Wellington

Abstract

The environment harbours a significant diversity of uncultured bacteria and a potential source of novel and extant resistance genes which may recombine with clinically important bacteria disseminated into environmental reservoirs. There is evidence that pollution can select for resistance due to the aggregation of adaptive genes on mobile elements. The aim of this study was to establish the impact of waste water treatment plant (WWTP) effluent disposal to a river by using culture independent methods to study diversity of resistance genes downstream of the WWTP in comparison to upstream. Metagenomic libraries were constructed in *Escherichia coli* and screened for phenotypic resistance to amikacin, gentamicin, neomycin, ampicillin and ciprofloxacin. Resistance genes were identified by using transposon mutagenesis. A significant increase downstream of the WWTP was observed in the number of phenotypic resistant clones recovered in metagenomic libraries. Common β-lactamases such as bla_{TEM} were recovered as well as a diverse range of acetyltransferases and unusual transporter genes, with evidence for newly emerging resistance mechanisms. The similarities of the predicted proteins to known sequences suggested origins of genes from a very diverse range of bacteria. The study suggests that waste water disposal increases the reservoir of resistance mechanisms in the environment either by addition of resistance genes or by input of agents selective for resistant phenotypes.

Keywords

Ecotoxicology and Environmental Safety
June 2014, Vol.104:103–109, doi:10.1016/j.ecoenv.2014.02.020

Occurrence of antidepressant residues in the sewage-impacted Vistula and Utrata rivers and in tap water in Warsaw (Poland)

Joanna Giebułtowicz, Grzegorz Nałęcz-Jawecki

Highlights

- First time antidepressants in waters of Eastern Europe were analysed.
- In surface water 11 antidepressants from 21 analysed were detected.
- Moclobemid, venlafaxine and citalopram were found in highest concentrations.
- First time moclobemid and tianeptine were detected in surface water.
- In tap water 5 antidepressants from 21 analysed were detected.

Abstract

Antidepressants, even at low concentrations, can reveal some adverse effects on aquatic life due to disturbing homeostasis throughout the central and peripheral nervous system both in vertebrates and invertebrates. To date there have not been any reports regarding the presence of these pharmaceuticals in surface and tap waters in Eastern Europe. Therefore the aim of this study was to determine the presence of 21 antidepressant pharmaceuticals at specific points of the main Polish river – the Vistula, a smaller river of the Warsaw region – the Utrata, as well as in tap water samples of Warsaw. Samples were collected twice at one month intervals and analysed using solid-phase extraction (SPE) technique coupled with the liquid chromatography–electrospray ionisation–tandem mass spectrometer (LC–MS/MS) method operated under the multiple reaction monitoring mode (MRM).

This is the first study where active compounds such as moclobemid or trazodone in the environment have been investigated.

Chemosphere
February 2015, Vol.120:108–114, doi:10.1016/j.chemosphere.2014.06.049

Determining the effects of a mixture of an endocrine disrupting compound, 17α-ethinylestradiol, and ammonia on fathead minnow (*Pimephales promelas*) reproduction

Brandon M. Armstrong, James M. Lazorchak, Cheryl A. Murphy, Herman J. Haring, Kathleen M. Jensen, Mark E. Smith

Highlights

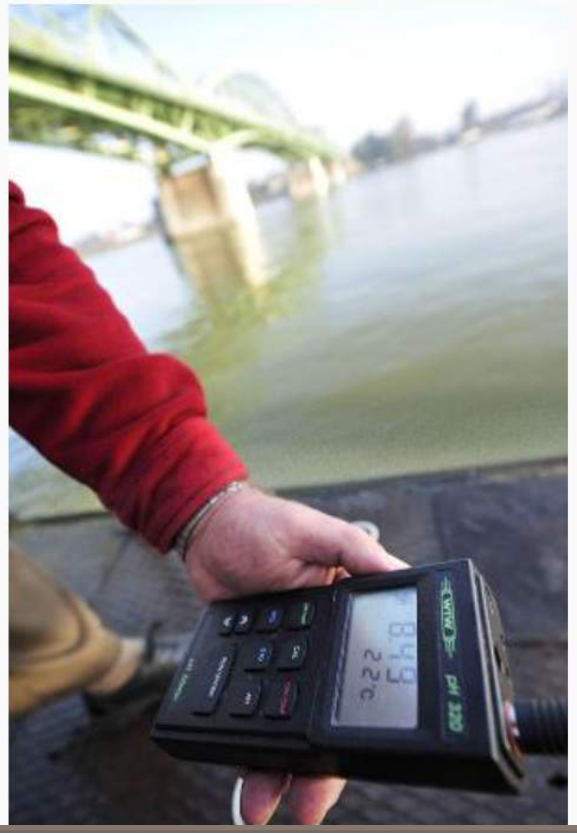
- We utilized a 21D reproduction protocol to determine the effects of EE2 and NH_3.
- Exposure to a mixture of EE2 and NH_3 at their respective NOAEC induced mortality.
- Exposure to EE2, NH_3 and their mixture at their NOAEC did not affect reproduction.

Abstract

Aquatic organisms are exposed to a multitude of contaminants and to fully understand the impact of multiple stressors on fish populations, we must first understand the mechanism of action for each toxicant and how the combined effects manifest at the level of the individual. 17α-ethinylestradiol (EE2) has been known to cause adverse reproductive effects including reduced fecundity and fertility, intersex and skewed sex ratios in fish by mimicking naturally produced estrogen at low concentrations. Ammonia can cause adverse reproductive and mortality effects in individual fish through effects or damage to the central nervous system. Both EE2 and ammonia are found in most municipal effluents in various concentrations. A flow-through diluter system was used to test the individual effects of these two contaminants at their respective no observable adverse effect concentration (NOAEC) as well as their combined effects on fathead minnow, (*Pimephales promelas*) reproduction in a mixture exposure. While neither contaminant nor their mixture altered reproduction in terms of fecundity, their mixture resulted in significant

Surface waters: 12 new controlled chemicals, three pharmaceuticals on watch list

PLENARY SESSION Press release - **Environment / Public health** – 02-07-2013 - 13:04



Twelve new substances will be added to the EU priority list of those known to pose a pollution risk to surface waters under rules endorsed by MEPs on Tuesday. For the first time, three pharmaceuticals will also be included in a "watch list" of emerging pollutants that could one day be placed on the priority list.

"Water policy is a long-term policy. Our citizens should have access to clean water in every form (...). Unfortunately, studies show that we have some way to go to achieve good environmental status for chemicals, particularly in surface waters. The environmental quality standards in this new directive apply to 15 new substances, painstakingly defined with stakeholders", said rapporteur Richard Seeber (EPP, AT), who steered the legislation through Parliament. The agreement he negotiated with Council was endorsed by 646 votes in favour, 51 against and 14 abstentions.

Two hormones and a painkiller

Download press release in PDF format.

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Adopted text will be available here (click on 00.00.2013)

Text of the agreement with Council

Video recording of debate (click on 1.07.2013)

Procedure file

Science of The Total Environment
15 September 2014, Vol.493:392–404, doi:10.1016/j.scitotenv.2014.06.013

Eco-directed sustainable prescribing: feasibility for reducing water contamination by drugs

Christian G. Daughton

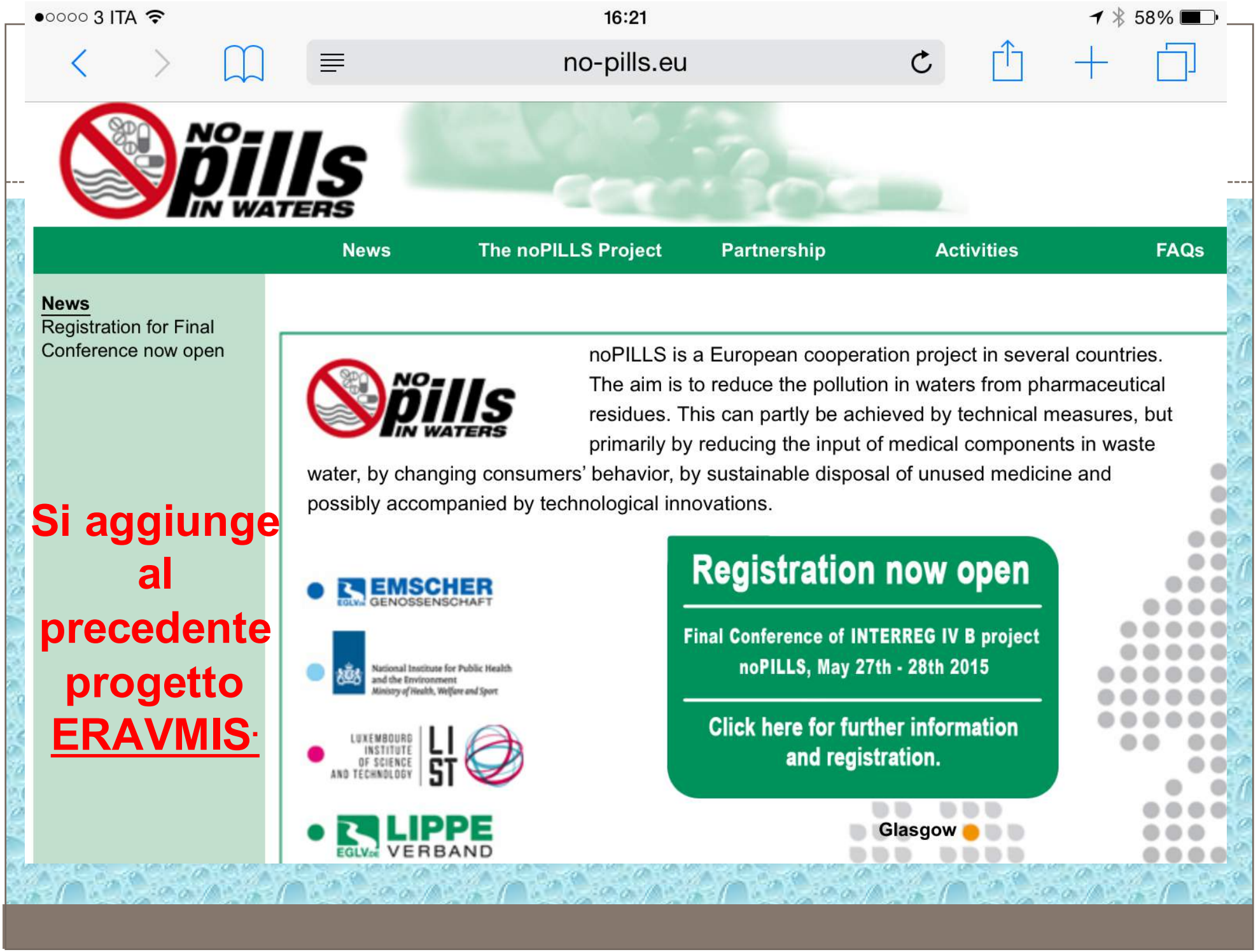
Show more

Highlights

- Role of pollution prevention is examined for reducing drug entry to the environment.
- Eco-directed sustainable prescribing (EDSP) is proposed for reducing drug excretion.
- Drug loadings in environment via sewers are dictated by pharmacokinetics.
- Prescribing could be guided by selecting drugs that are poorly excreted.
- Do empirical environmental occurrence data for drugs correlate with pharmacokinetics?

Abstract

Active pharmaceutical ingredients (APIs) from the purchase and use of medications



Si aggiunge al precedente progetto ERAVMIS·

The 'Wise List' – A Comprehensive Concept to Select, Communicate and Achieve Adherence to Recommendations of Essential Drugs in Ambulatory Care in Stockholm

Lars L. Gustafsson[1,2], Björn Wettermark[1,3], Brian Godman[1], Eva Andersén-Karlsson[3,4], Ulf Bergman[1,2], Jan Hasselström[5], Lars-Olof Hensjö[6], Paul Hjemdahl[2,7], Ingrid Jägre[3], Margaretha Julander[3], Bo Ringertz[8], Daniel Schmidt[9], Susan Sjöberg[3], Folke Sjöqvist[1], Carl-Olav Stiller[2,7], Elisabeth Törnqvist[3], Rolf Tryselius[3], Sigurd Vitols[2,7] and Christer von Bahr[10], for the Regional Drug Expert Consortium*

[1]Division of Clinical Pharmacology, Department of Laboratory Medicine, Karolinska Institutet at Karolinska University Hospital Huddinge, Stockholm, Sweden, [2]Clinical Pharmacology Services, Karolinska University Hospital, Stockholm, Sweden, [3]Regional Drug and Therapeutics Committee, Medical Knowledge Centre, Stockholm County Council (Healthcare Region), Stockholm, Sweden, [4]Department of Internal Medicine, Södersjukhuset, Stockholm, Sweden, [5]Storvreten General Practice Centre, Tumba, Sweden, [6]Inera Ltd, National Information Services for Swedish Healthcare, Stockholm, Sweden, [7]Clinical Pharmacology Unit, Department of Medicine, Karolinska Institutet at Karolinska University Hospital Solna, Stockholm, Sweden, [8]Division of Rheumatology, Department of Medicine, Karolinska Institutet at Karolinska University Hospital Solna, Stockholm, Sweden, [9]Department of Internal Medicine, St Göran Hospital, Stockholm, Sweden, and [10]Section of Clinical Pharmacology, Department of Internal Medicine, Södersjukhuset, Stockholm, Sweden

(Received 12 September 2010; Accepted 4 January 2011)

Abstract: The aim was to present and evaluate the impact of a comprehensive strategy over 10 years to select, communicate and achieve adherence to essential drug recommendations (EDR) in ambulatory care in a metropolitan healthcare region. EDRs were issued and launched as a 'Wise List' by the regional Drug and Therapeutics Committee in Stockholm. This study presents the concept by: (i) documenting the process for selecting, communicating and monitoring the impact of the 'Wise List'; (ii) analysing the variation in the number of drug substances recommended between 2000 and 2010; (iii) assessing the attitudes to the 'Wise List' among prescribers and the public; (iv) evaluating the adherence to recommendations between 2003 and 2009. The 'Wise List' consistently contained 200 drug substances for treating common diseases. The drugs were selected based on their efficacy, safety, suitability and cost-effectiveness. The 'Wise List' was known among one-third of a surveyed sample of the public in 2002 after initial marketing campaigns. All surveyed prescribers knew about the concept and 81% found the recommendations trustworthy in 2005. Adherence to recommendations increased from 69% in 1999 to 77% in 2009. In primary care, adherence increased from 83% to 87% from 2003 to 2009. The coefficient of variation (CV%) decreased from 6.1% to 3.8% for 156 healthcare centres between these years. The acceptance of the 'Wise List' in terms of trust among physicians and among the public and increased adherence may be explained by clear criteria for drug recommendations, a comprehensive communication strategy, electronic access to recommendations, continuous medical education and involvement of professional networks and patients.

Inappropriate use of drugs causes increased morbidity, mortality, adverse drug reactions, therapeutic failures and drug resistance as well as wasting valuable resources [1–6]. This recognition was a driving force behind the birth of Drug and Therapeutics Committees (DTC) [7–9] and the Essential Drug concepts [10] by WHO in the late 1970s. However, adherence to drug recommendations from DTCs varies markedly among prescribers [11–14].

Stockholm Healthcare Region with approximately 2 million inhabitants consists of 209 Primary Healthcare Centres, seven emergency hospitals as well as private specialists, nursing homes and other healthcare providers [15], with all healthcare financed through public taxation with co-pay-

Valutazione del rischio: studio dei parametri chimico-fisici

- **Per valutare l'impatto inquinante degli xenobiotici (e quindi anche dei farmaci) occorre studiare "la resistenza alla degradazione" e "il tempo di permanenza del farmaco"**

  - **La resistenza alla degradazione indica il tempo necessario affinchè una sostanza si degradi**
  - **La persistenza indica il tempo che la sostanza trascorre in un certo ambiente prima di essere eliminata (non importa come viene eliminata e dove va a finire)**

Valutazione del rischio: studio dei parametri chimico-fisici

- **Una forte resistenza alla degradazione indica che la sostanza rimarrà come tale nel compartimento ambientale per molto tempo.**
- **Una lunga persistenza del farmaco indica che quel farmaco potrà agire per molto tempo in un determinato ambiente.**
- **La mobilità è un altro parametro importante per capire la persistenza di un farmaco in un certo ambiente.**

Valutazione del rischio: studio dei parametri chimico-fisici

- **L'altra categoria di sostanze che induce timori è rappresentata dagli ormoni steroidei.**

- **I fattori che li rendono temibili sono costituiti dalla struttura poco degradabile e dall'enorme potenza per cui possono agire a concentrazioni molto basse**

NATURE COMMUNICATIONS | ARTICLE

Coupled reversion and stream-hyporheic exchange processes increase environmental persistence of trenbolone metabolites

Adam S. Ward, David M. Cwiertny, Edward P. Kolodziej & Colleen C. Brehm

Affiliations | **Contributions** | **Corresponding author**

Nature Communications **6**, Article number: 7067 | doi:10.1038/ncomms8067
Received 26 January 2015 | Accepted 27 March 2015 | Published 08 May 2015

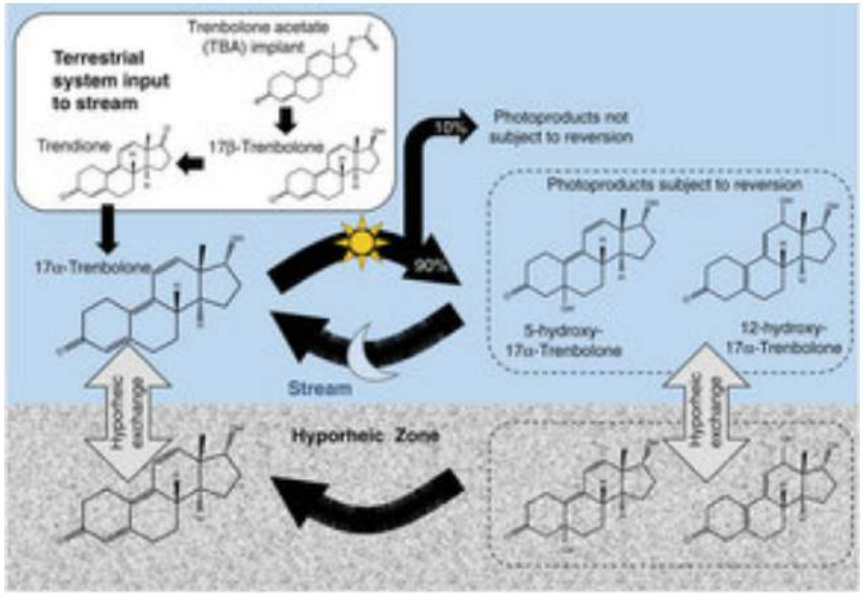
Abstract

Abstract · References · Author information · Supplementary information

Existing regulatory frameworks for aquatic pollutants in the United States are idealized, often lacking mechanisms to account for contaminants characterized by (1) bioactivity of both the parent and transformation products and (2) reversible transformations (that is, metastable products) driven by chemical or physical heterogeneities. Here, we modelled a newly discovered product-to-parent reversion pathway for trenbolone acetate (TBA) metabolites. We show increased exposure to the

Subject terms: Earth sciences · Ecology · Biogeochemistry

Figure 1: Overview of interacting physical and chemical systems.



Structures of TBA (primary component implanted into cattle), metabolites 17β-TBOH (pharmacologically active androgen), trendione, 17α-TBOH (primary product excreted to the environment) and 17α-TBOH photoproducts (5- and 12-hydroxy-17α-T…

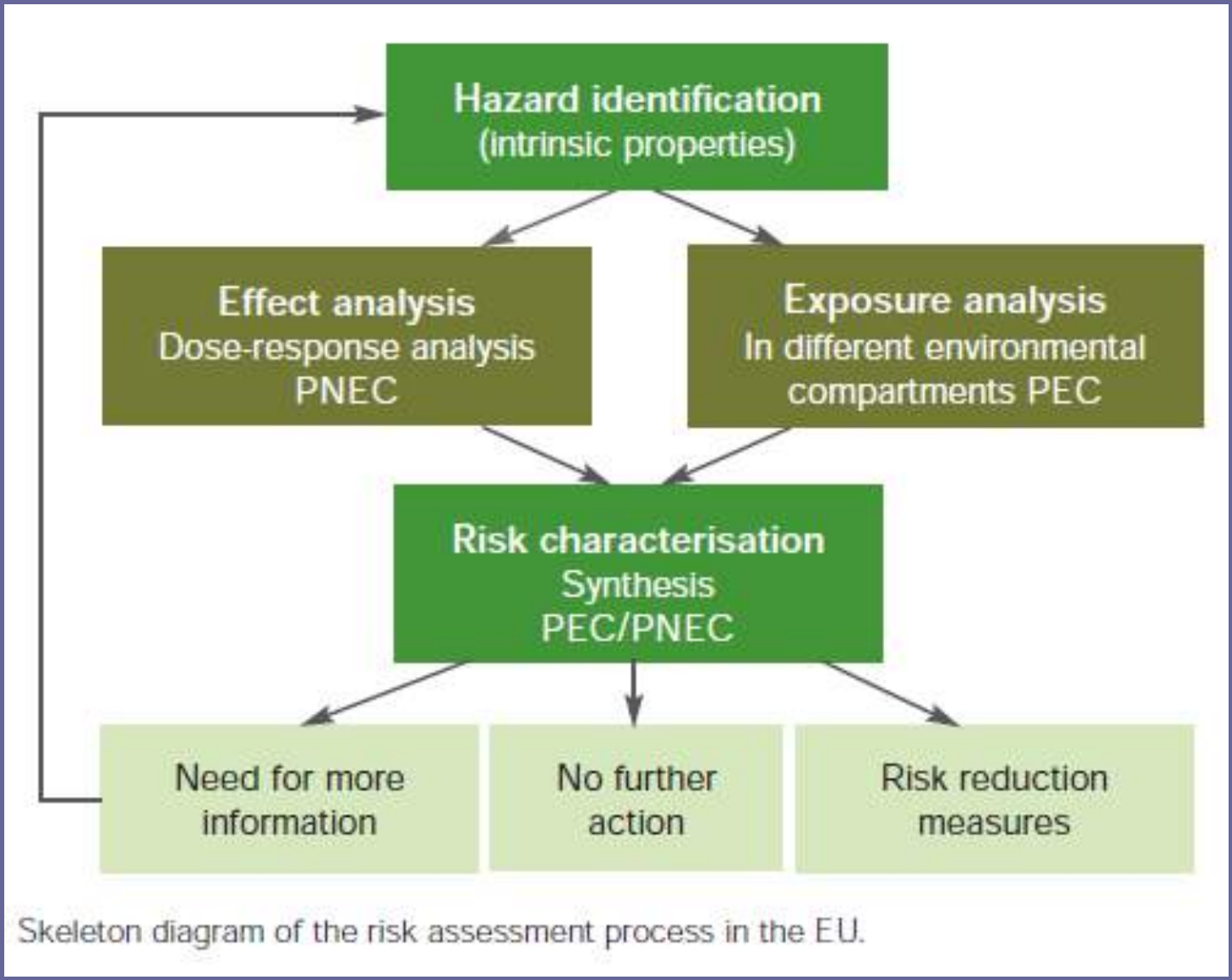
Valutazione del rischio: test biologici

- **Per stabilire il rischio ambientale dei prodotti farmaceutici i target utilizzati sono :**

- **alghe**
- **dafnie**
- **zebra fish**

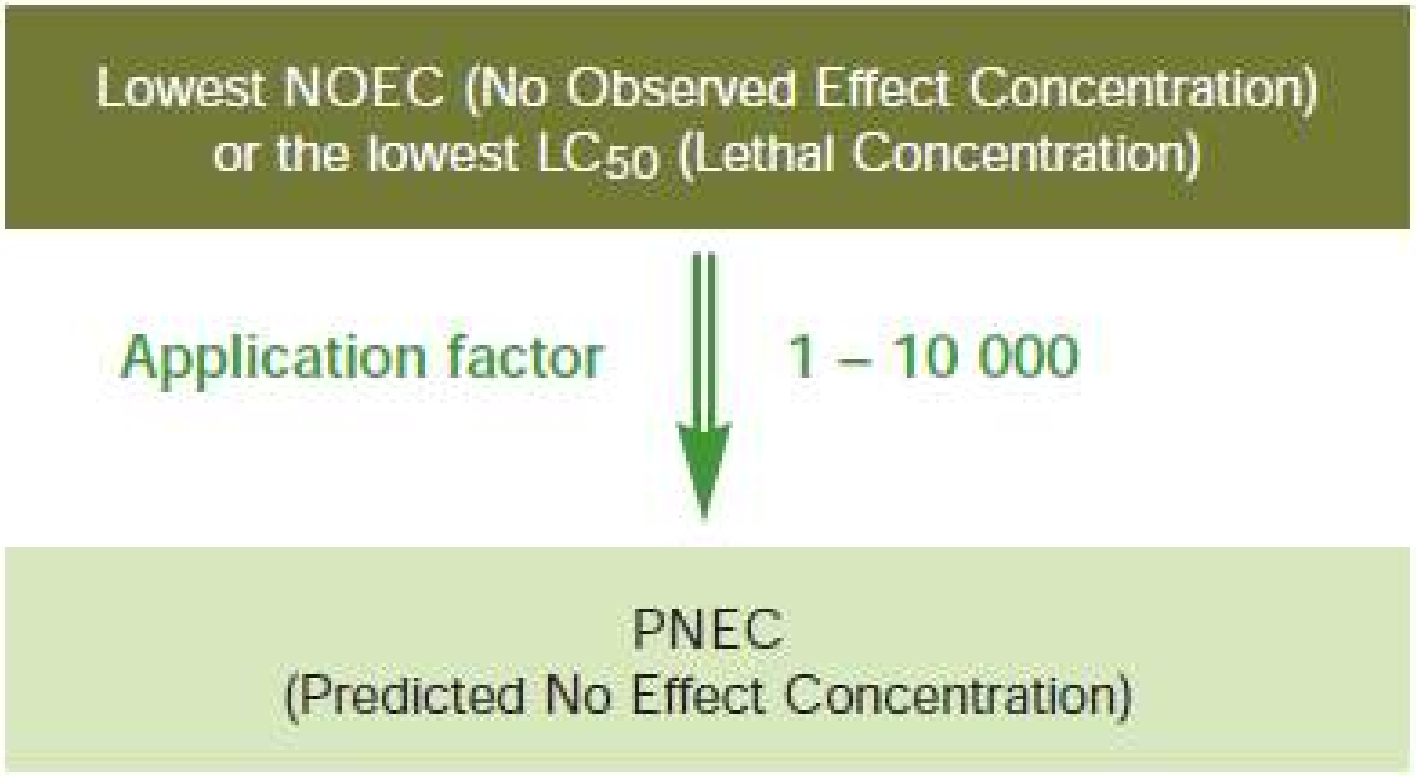
- **Sentinelle ambientali**

Quantificazione del rischio



Skeleton diagram of the risk assessment process in the EU.

Quantificazione del rischio



Procedure for calculating the PNEC of aquatic organisms with the help of application factors.

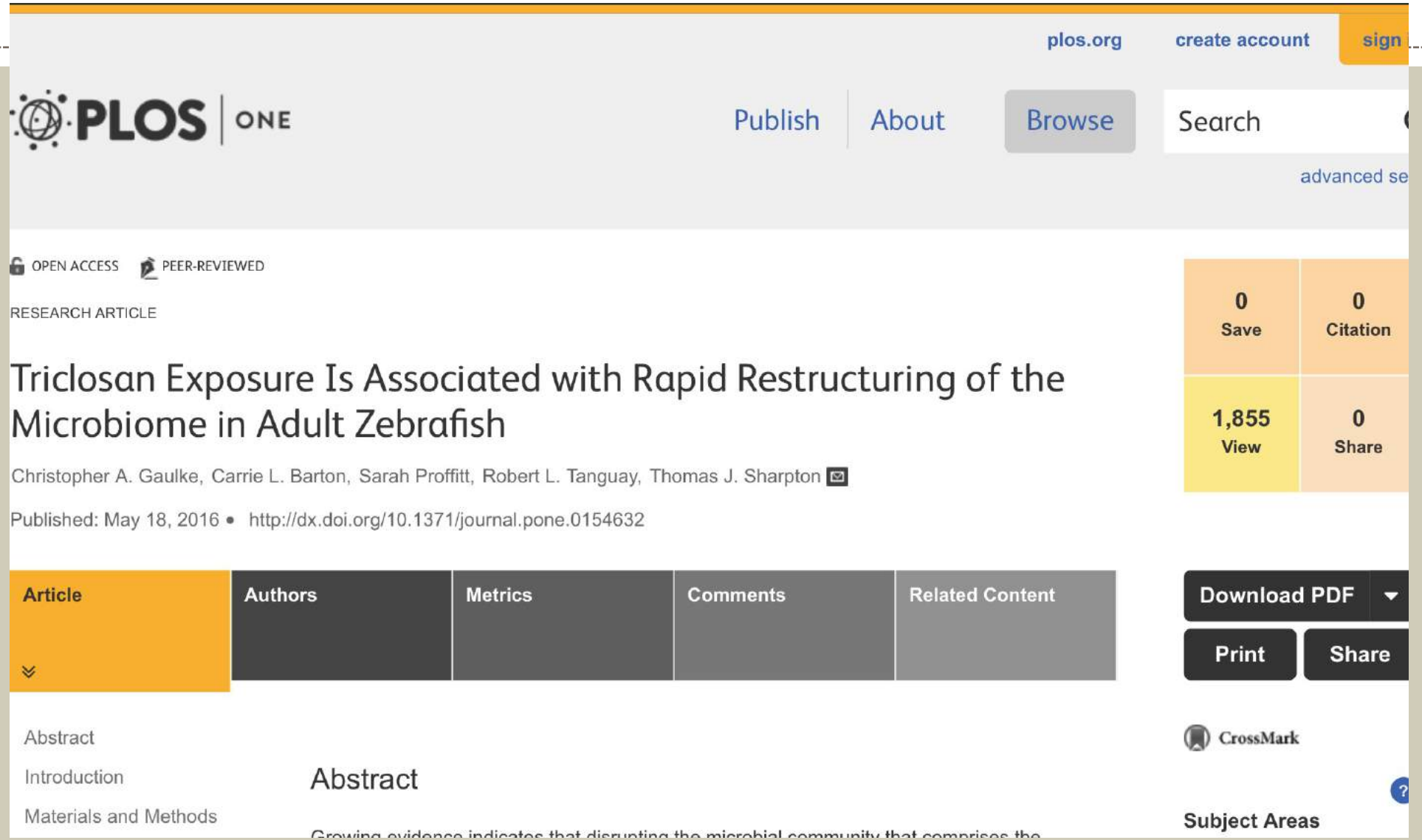
Quantificazione del rischio

- **Secondo alcune simulazione basate sui dati esistenti, nell'ipotesi di bere 2 l di acqua contaminta al giorno per un periodo di 70 anni, introdurremo nel nostro organismo dosi di farmaci molto più basse rispetto a quelle in grado di svolgere un'azione biologica**

Quantificazione del rischio

- **L'esposizione a basse concentrazioni di farmaci dispersi nell'ambiente può comportare una sensibilizzazione involontaria (che sfugge all'anamnesi) in grado di scatenare una reazione allergica (potenzialmente fatale) quando la stessa persona sarà esposta, per motivi terapeutici, allo stesso farmaco**

- **L'ingestione di quantità sub-terapeutiche di antibatterici, antivirali, antifungini favorisce lo sviluppo di ceppi resistenti con notevoli danni nella gestione terapeutica di molte patologie e delle comunità ospedaliere**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RESEARCH ARTICLE
Triclosan Exposure Is Associated with Rapid Restructuring of the Microbiome in Adult Zebrafish
Christopher A. Gaulke, Carrie L. Barton, Sarah Proffitt, Robert L. Tanguay, Thomas J. Sharpton
Published: May 18, 2016 • http://dx.doi.org/10.1371/journal.pone.0154632
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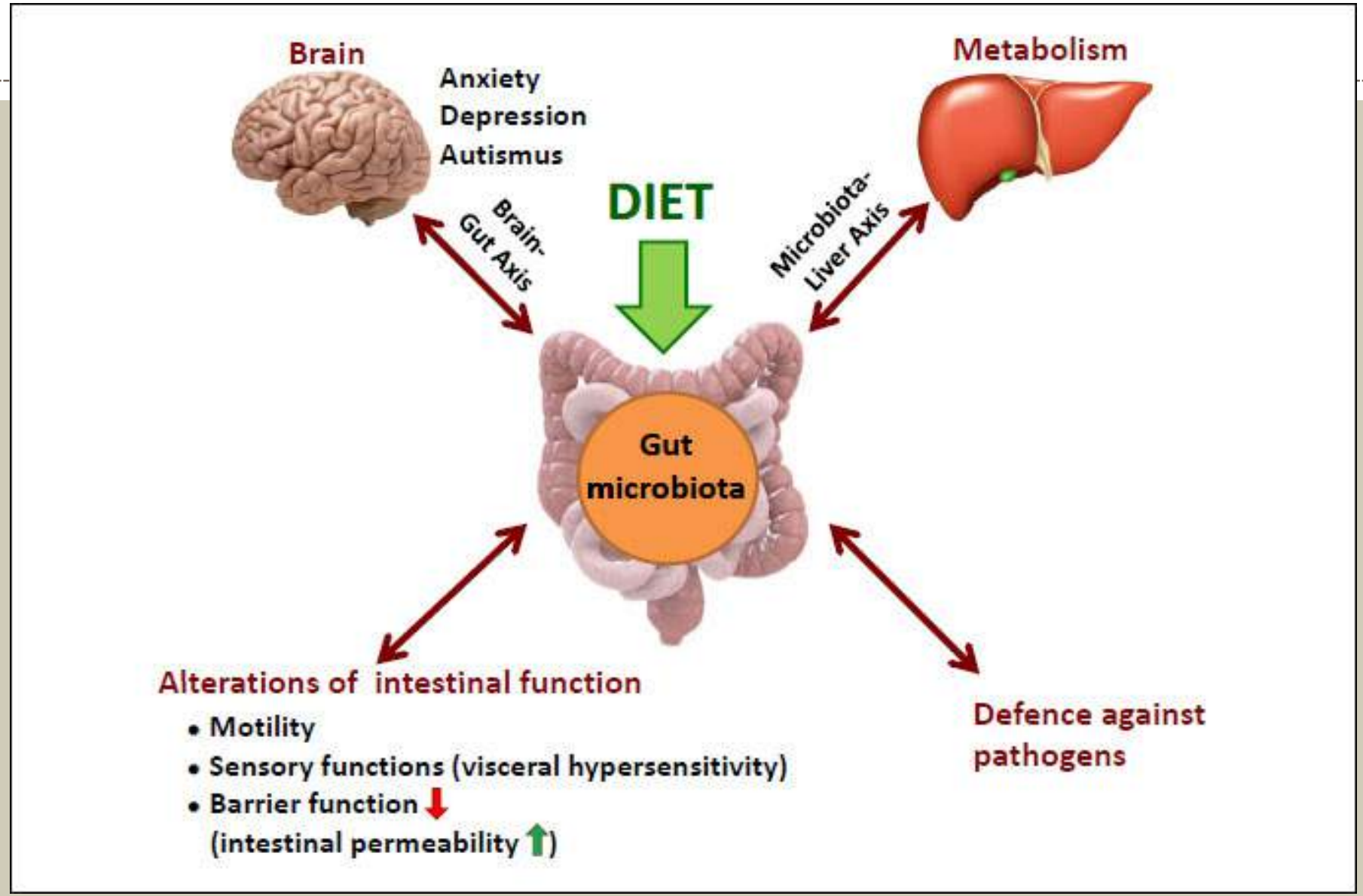
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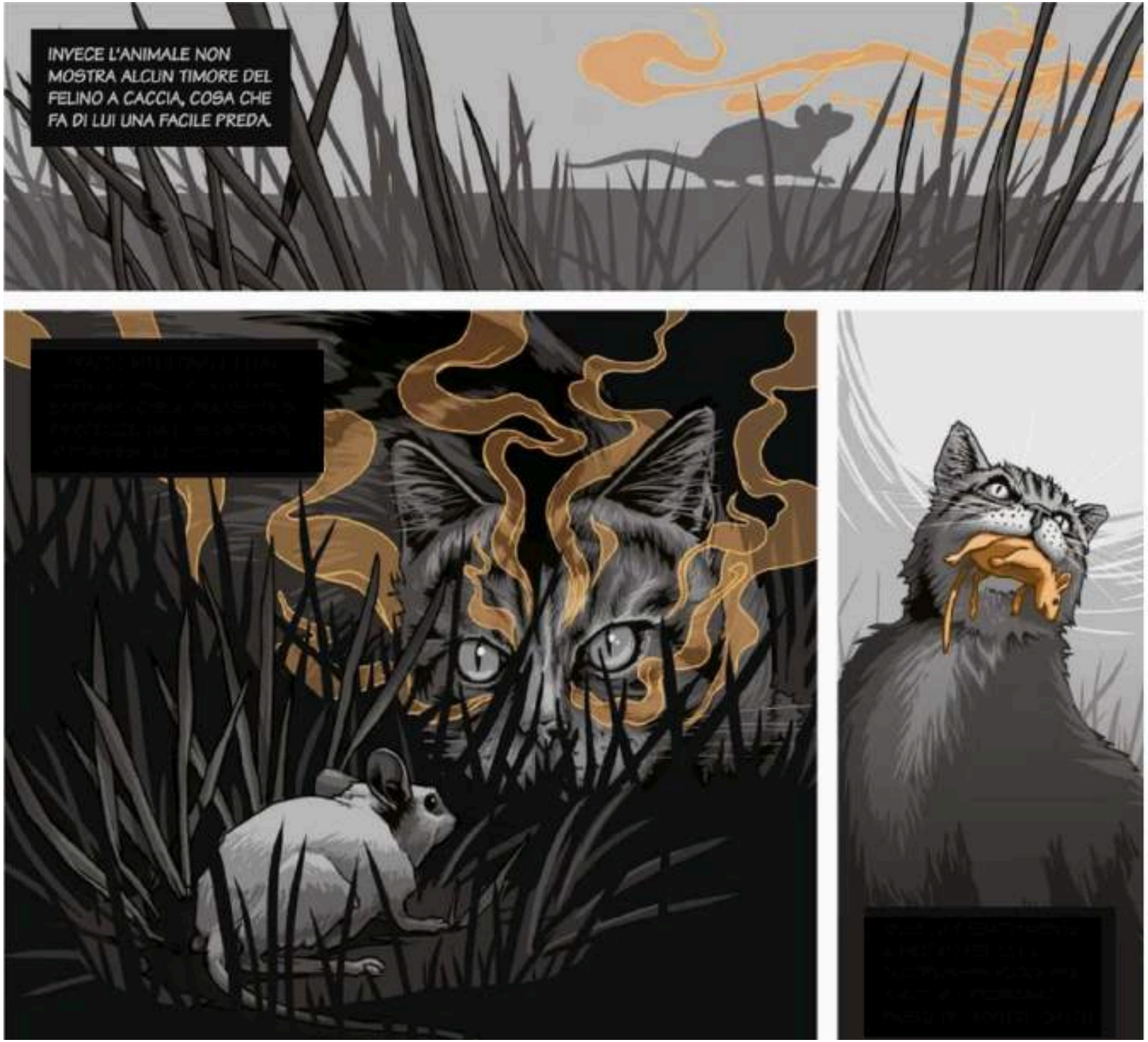
Anxiety
Depression
Autismus
Metabolism
DIET
Brain-
Gut Axis
Microbiota-
Liver Axis
Gut
microbiota
Alterations of intestinal function
• Motility
• Sensory functions (visceral hypersensitivity)
• Barrier function ↓
(intestinal permeability ↑)
Defence against
pathogens

FONTE: ROBERT M. SAPOLSKY AND PATRICK HOUSE, STANFORD UNIVERSITY

Tratto da:
National Geographic Italia, novembre 2014



Tratto da:
National Geographic Italia, novembre 2014

Birds The Observer

Europe's vultures under threat from drug that killed millions of birds in Asia

After an ecological disaster in India, wildlife groups call for ban on vets using diclofenac in Italy and Spain

A Spanish griffon vulture. Vultures in Europe could be under threat from approval of the use of the drug diclofenac in Italy and Spain. Photograph: Chris Hellier/CORBIS

Robin McKie Science Editor

Saturday 7 June 2014 12.06 BST

- A partire dal 1990 la popolazione di tre specie di avvoltoi (*Gyps bengalensis, Gyps tenuirostris, Gyps indicus*) è drasticamente diminuita in India, Pakistan e Nepal.
- Secondo alcune stime le tre popolazioni di avvoltoio si riducevano al ritmo del 30% anno
- Le tre specie furono quindi inserite tra le specie a rischio estinzione dalla BirdLife International.

BirdLife INTERNATIONAL

- L’85% di 259 avvoltoi esaminati erano morti a causa di una insufficienza renale

- Le necropsie mostrarono segni di “gotta viscerale” una tipica complicazione dell’insufficienza renale negli uccelli. NATURE ,VOL 427 | 12 FEBRUARY 2004

Diclofenac sodico

- **I ricercatori condussero una breve indagine tra 74 veterinari e farmacisti pakistani per capire se esisteva un farmaco usato in veterinaria tossico per il rene e assorbito per via orale**

- **Un farmaco rispondeva a questi criteri: il diclofenac sodico**

Diclofenac sodico

- **Il diclofenac è letale nell'avvoltoio ad una dose pari al 10% di quella utilizzata nel mammifero**

- **I residui presenti nelle carcasse erano ancora attivi per l'avvoltoio**

Diclofenac sodico

- I cani, non avendo più la concorrenza degli avvoltoi, a causa dell'abbondanza di cibo sono aumentati
- I cani sono sensibili al diclofenac ma a dosi molto elevate e non compatibili con quelle presenti nelle carcasse
- L'aumento dei cani ha comportato un aumento delle morsicature e dei casi di rabbia nell'uomo
- Contemporaneamente anche i ratti sono aumentati

Diclofenac sodico

- **L'ambiente molto acido dello stomaco degli avvoltoi distrugge la maggior parte dei patogeni potenzialmente presenti nella carcassa (ad esempio quelli della tubercolosi bovina o dell'antrace)**

- **I ratti e i cani che accedono alla carcassa degli animali (prima degli avvoltoi) non svolgono la stessa funzione di filtro**

- **Nel campo della ecotossicologia, questo rappresenta uno dei pochissimi esempi di dimostrazione univoca e documentata sperimentalmente degli effetti sull'ecosistema dei residui di farmaci**

- **Un altro esempio è fornito dai neonicotinoidi:**
  - **Api**
  - **Uccelli**
  - **Uomo**

Quali residui nelle acque?

- **Phthalates are a class of high-production-volume industrial chemicals that are ubiquitously used in commerce. High-molecular-weight phthalates, such as di(2-ethylhexyl) phthalate (DEHP), are used as plasticizers to impart flexibility in polyvinyl chloride (PVC) materials such as food packaging, flooring, and medical devices (US Environmental Protection Agency 2012). In recent years, other phthalates, including diisononyl phthalate (DiNP), have been replacing DEHP in these applications due, in part, to legislation limiting the use of DEHP in certain applications (European Chemicals Agency 2012). Bisphenol A (BPA) is a high-production-volume chemical used to make polycarbonate plastics and epoxy resins, found in food and beverage cans as well as thermal receipt paper (Calafat et al. 2008).**

POP dispersi nelle acque

- Inquinanti organici persistenti (POP): prodotti chimici artificiali che perdurano nell'ambiente e tendono ad accumularsi negli animali.

- La loro persistenza ambientale deriva dalla proprietà quali alogenazione e idrofobia che rallentano il degrado e promuovono la distribuzione negli organismi animali.

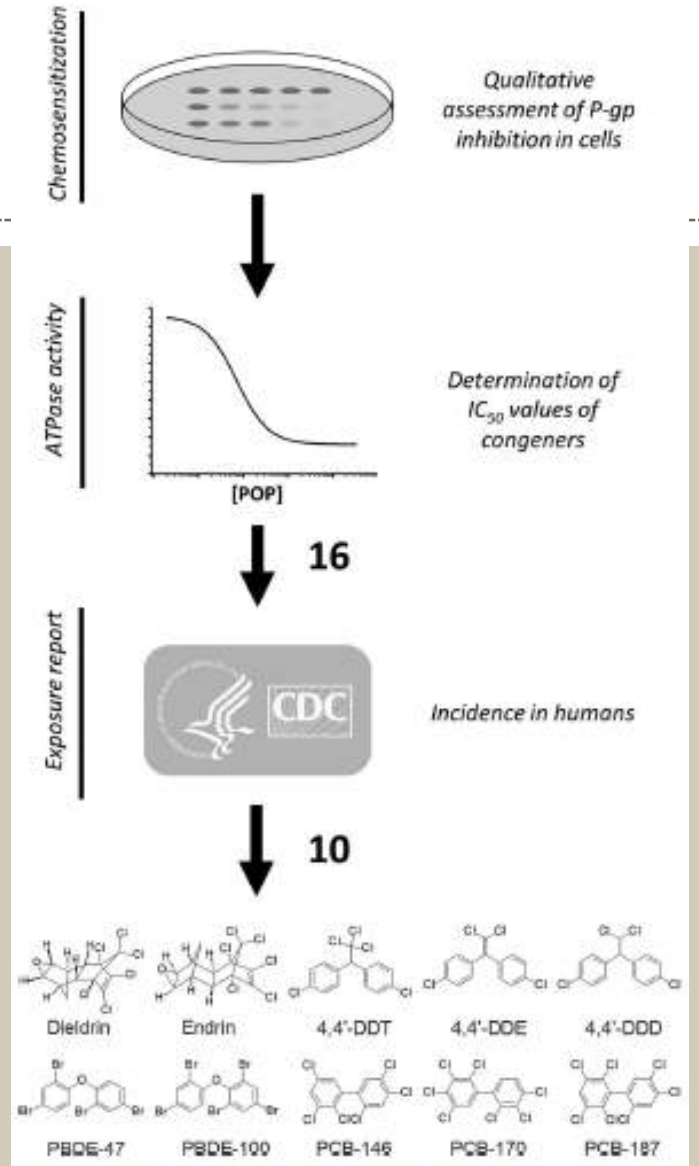


Fig. 1. Identification of P-gp–inhibiting POPs. Thirty-seven pollutants were tested for interactions with mouse P-gp using two independent assays (see Table 1). Sixteen compounds were identified as inhibitors in both assays. We focused on 10 congeners reported in humans on the basis of the literature (*86*, *87*) and the *Fourth National Report on Human Exposure to Environmental Chemicals* of the U.S. Centers for Disease Control and Prevention (*88*). DDD, dichlorodiphenyldichloroethane; DDE, dichlorodiphenyldichloroethylene; DDT, dichlorodiphenyltrichloroethane; PCB, polychlorinated biphenyl; PBDE, polybrominated diphenyl ether.

From:
Nicklisch, Sascha CT, et al. *Science Advances* 2.4 (2016): e1600001.

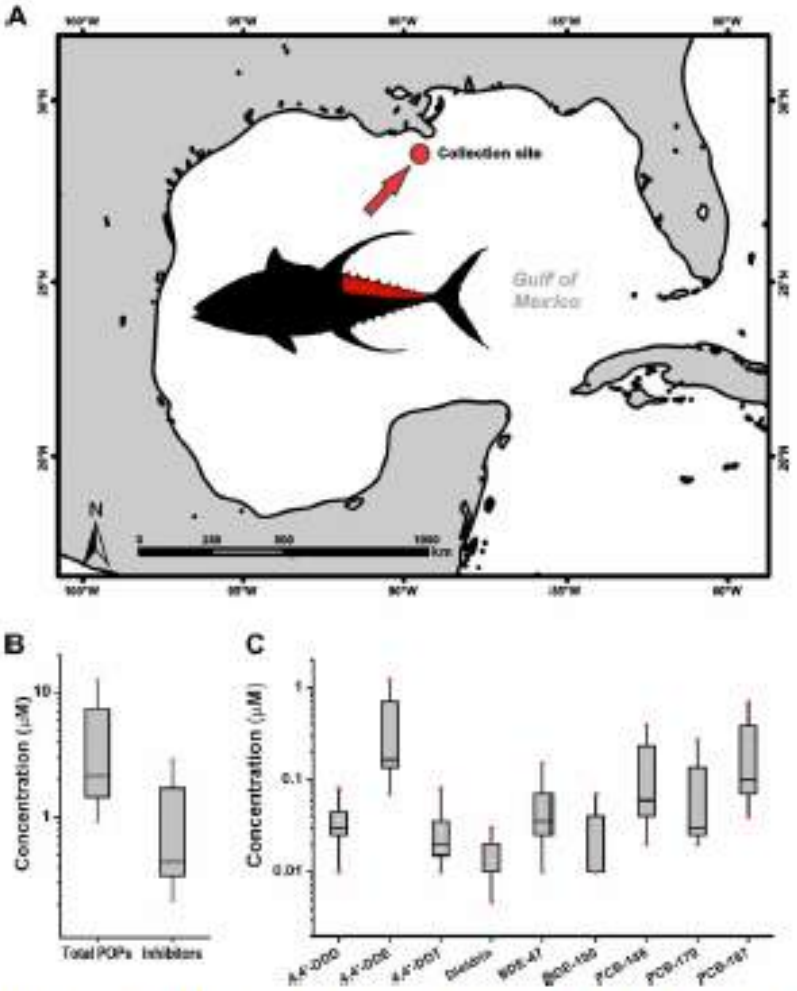
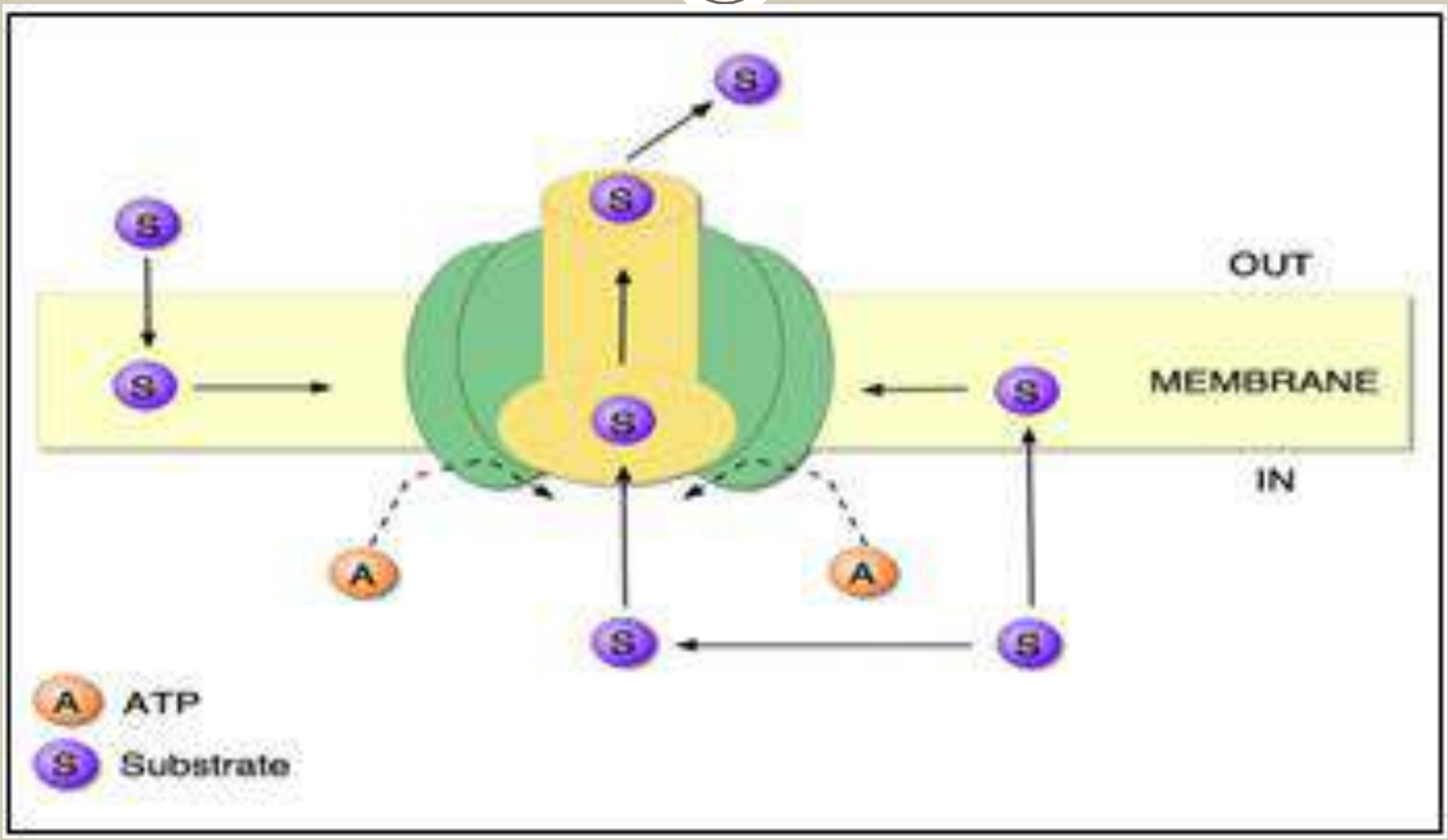


Fig. 4. Levels of P-gp inhibitors in yellowfin tuna (*T. albacares*). (A) Sampling site for the eight yellowfin tunas (*T. albacares*) caught in the GOM. The inset shows a yellowfin tuna with the sampled dorsal muscle tissue marked in red. **(B)** Lipid-normalized concentrations of the total POPs and the 10 P-gp inhibitors. The red-filled circles represent the minimum and maximum values. The white diamonds represent the mean value. The horizontal lines represent the 50th percentile, and the boxes represent the 25th and 75th percentiles. **(C)** Range of concentrations of nine inhibitory POPs measured in yellowfin tuna muscle from the GOM.

From:
Nicklisch, Sascha CT, et al. *Science Advances* 2.4 (2016): e1600001.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P-gp Tissue Distribution

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Intestine

Kidney

Blood-Organ Barrier Sites

Lymphocytes

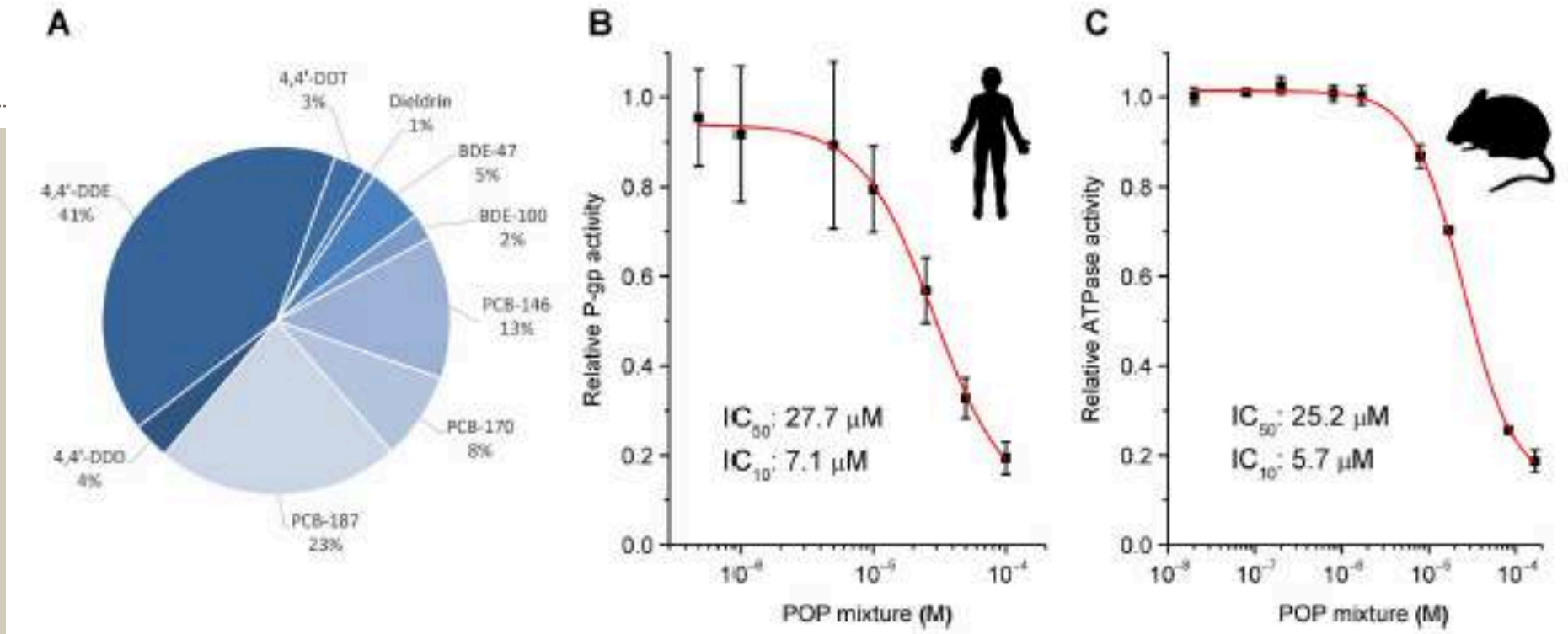


Fig. 5. An environmentally relevant POP mixture inhibits the transport function of human and mouse P-gp. (**A**) Relative ratio of the mean concentrations of P-gp inhibitors found in yellowfin tuna. (**B**) Inhibition of human P-gp by the POP mixture. Points represent the average percentage of NMQ uptake ± SD relative to the control from nine different experiments and with increasing concentration of the POP mixture. (**C**) Inhibition of verapamil-stimulated ATPase activity of mouse P-gp by the POP mixture. Shown is the respective dose-response curve as ATPase activity relative to 100 μM verapamil stimulation. The ATPase activity of the purified protein was measured in the presence of increasing concentrations of the POP mixture on the basis of the relative concentration of nine inhibitory POPs identified in this study. All data were fitted using a Hill function [$y = v_1 + (v_2 - v_1) * x^n/(K^n + x^n)$]. The R^2 value was >0.99.

- Nicklisch, Sascha CT, et al. *Science Advances* 2.4 (2016): e1600001.

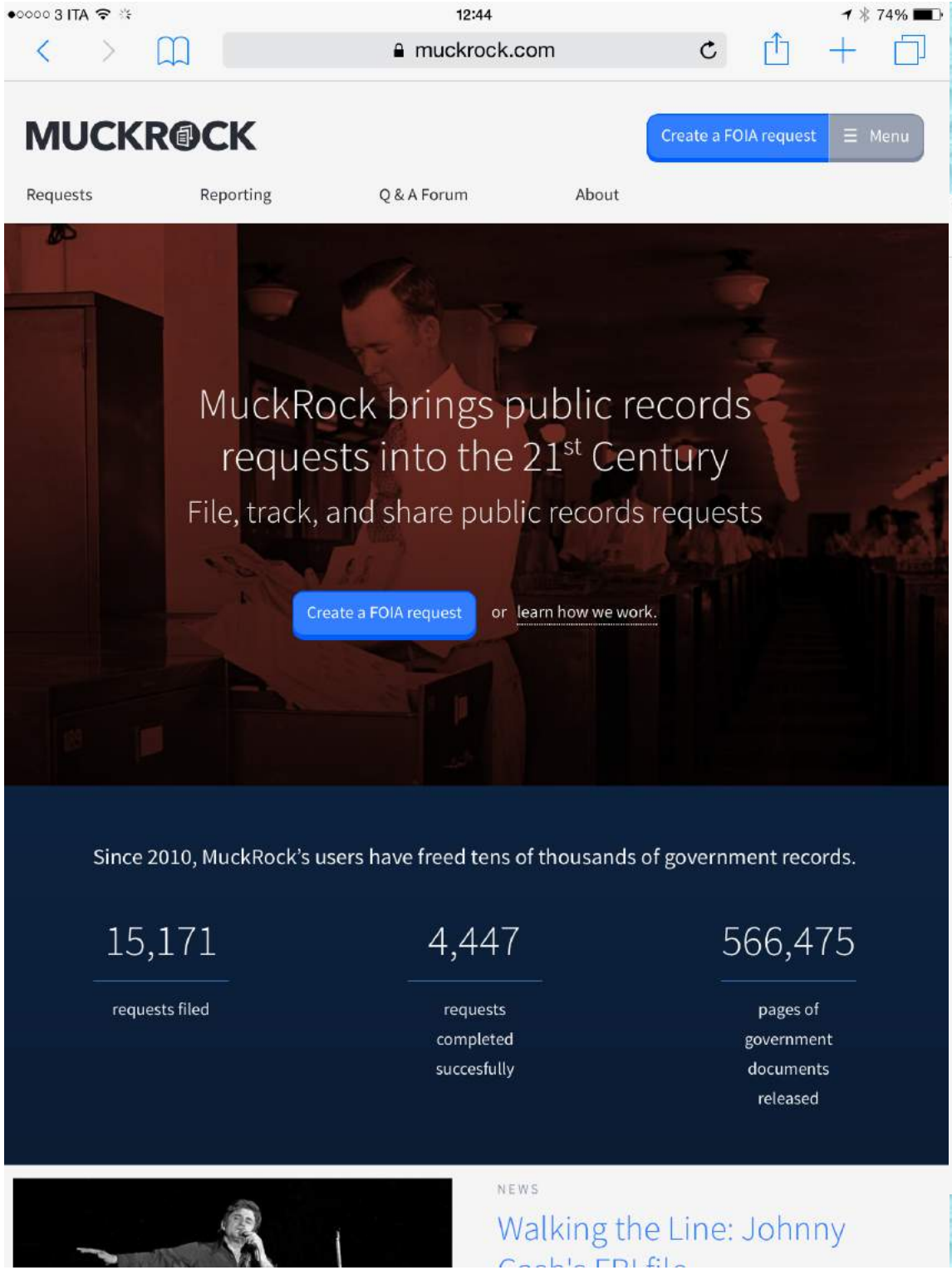
Rischi emergenti:
4. La coltivazione di Cannabis (?)

The Washington Post

Wonkblog

DEA warns of stoned rabbits if Utah passes medical marijuana

By Christopher Ingraham March 2 Follow @_cingraham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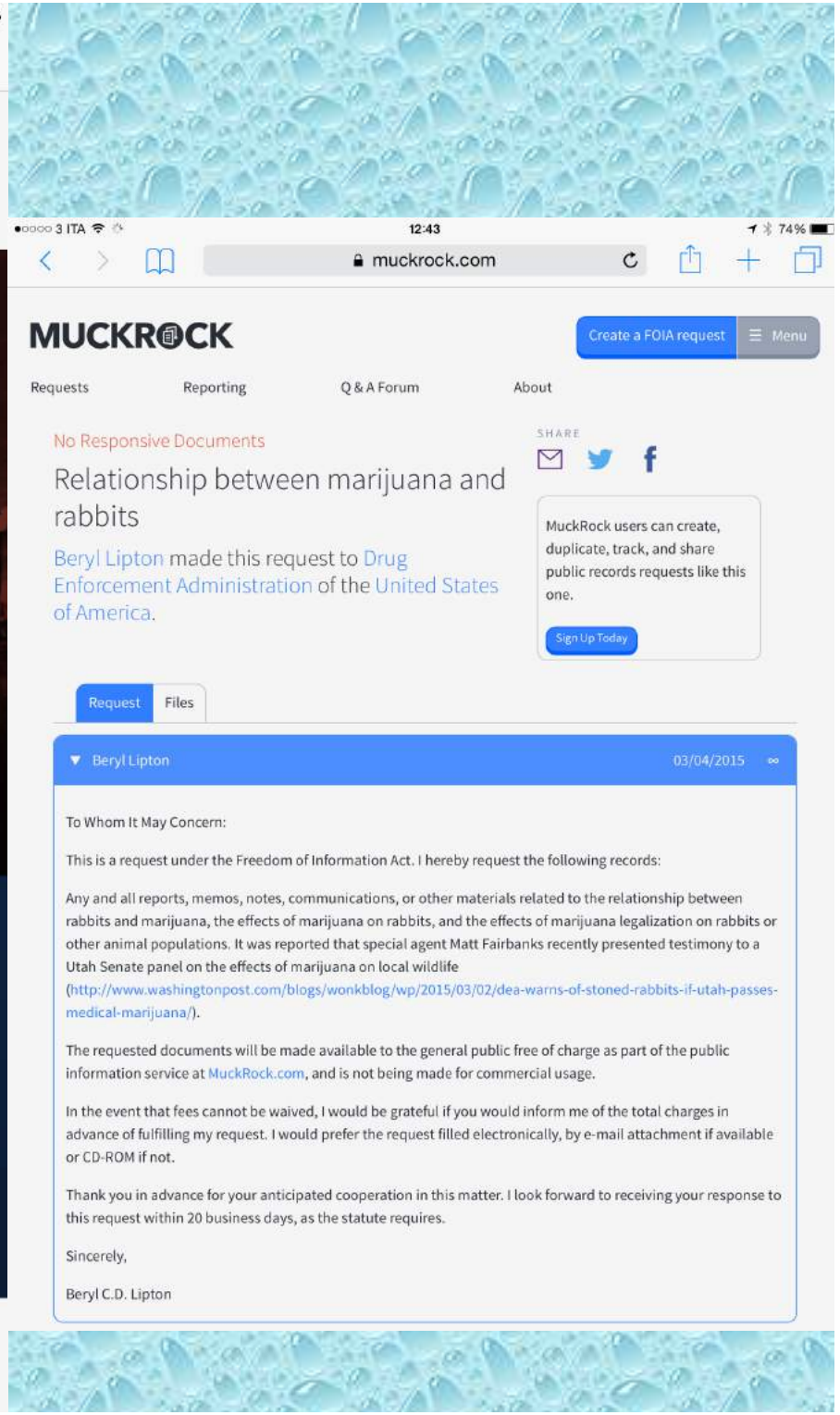
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03/04/2015
To Whom It May Concern:
This is a request under the Freedom of Information Act. I hereby request the following records:
Any and all reports, memos, notes, communications, or other materials related to the relationship between rabbits and marijuana, the effects of marijuana on rabbits, and the effects of marijuana legalization on rabbits or other animal populations. It was reported that special agent Matt Fairbanks recently presented testimony to a Utah Senate panel on the effects of marijuana on local wildlife (http://www.washingtonpost.com/blogs/wonkblog/wp/2015/03/02/dea-warns-of-stoned-rabbits-if-utah-passes-medical-marijuana/).
The requested documents will be made available to the general public free of charge as part of the public information service at MuckRock.com, and is not being made for commercial usage.
In the event that fees cannot be waived, I would be grateful if you would inform me of the total charges in advance of fulfilling my request. I would prefer the request filled electronically, by e-mail attachment if available or CD-ROM if not.
Thank you in advance for your anticipated cooperation in this matter. I look forward to receiving your response to this request within 20 business days, as the statute requires.
Sincerely,
Beryl C.D. Lipton

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Cannabis farming in California using so much water it could wipe out salmon population, biologists warn

Species already listed as threatened in the region

AGENCY Sunday 05 October 2014

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Water use and other actions by the marijuana industry in the Emerald Triangle of Northern California and Southern Oregon are threatening salmon already in danger of extinction, US biologists have said.

Concerns about the impact of pot farming were raised by the NOAA Fisheries Service in its final recovery plan for coho salmon in the region. The full plan was to be posted on the agency's website.A copy obtained in advance calls for determining then decreasing the amount of water that pot growers illegally

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nmfs.noaa.gov

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29. Mattole River Population

Southern Coastal Stratum

Non-Core 1, Functionally Independent Population

High Extinction Risk

1,000 Spawners Required for ESU Viability

Population likely below depensation threshold

296 mi² (21 % Federal ownership)

250 IP-km (155 IP-mi) (24% High)

Dominant Land Uses are Timber Harvest and Rural Residential

Key Limiting Stresses are 'Lack of Floodplain and Channel Structure' and 'Altered Hydrologic Function'

Key Limiting Threats are 'Dams/Diversions' and 'Urban/Residential/Industrial Development'

Highest Priority Recovery Actions

• Implement an enhancement program (e.g. captive broodstock, rescue rearing, or conservation hatchery) • Construct off-channel habitats, alcoves, backwater habitat, and old oxbows • Secure and maintain sufficient instream flows	• Determine effects of marijuana cultivation and reduce if necessary • Increase water retention (i.e. storage and recharge) • Increase large woody debris (LWD), boulders, or other instream structure