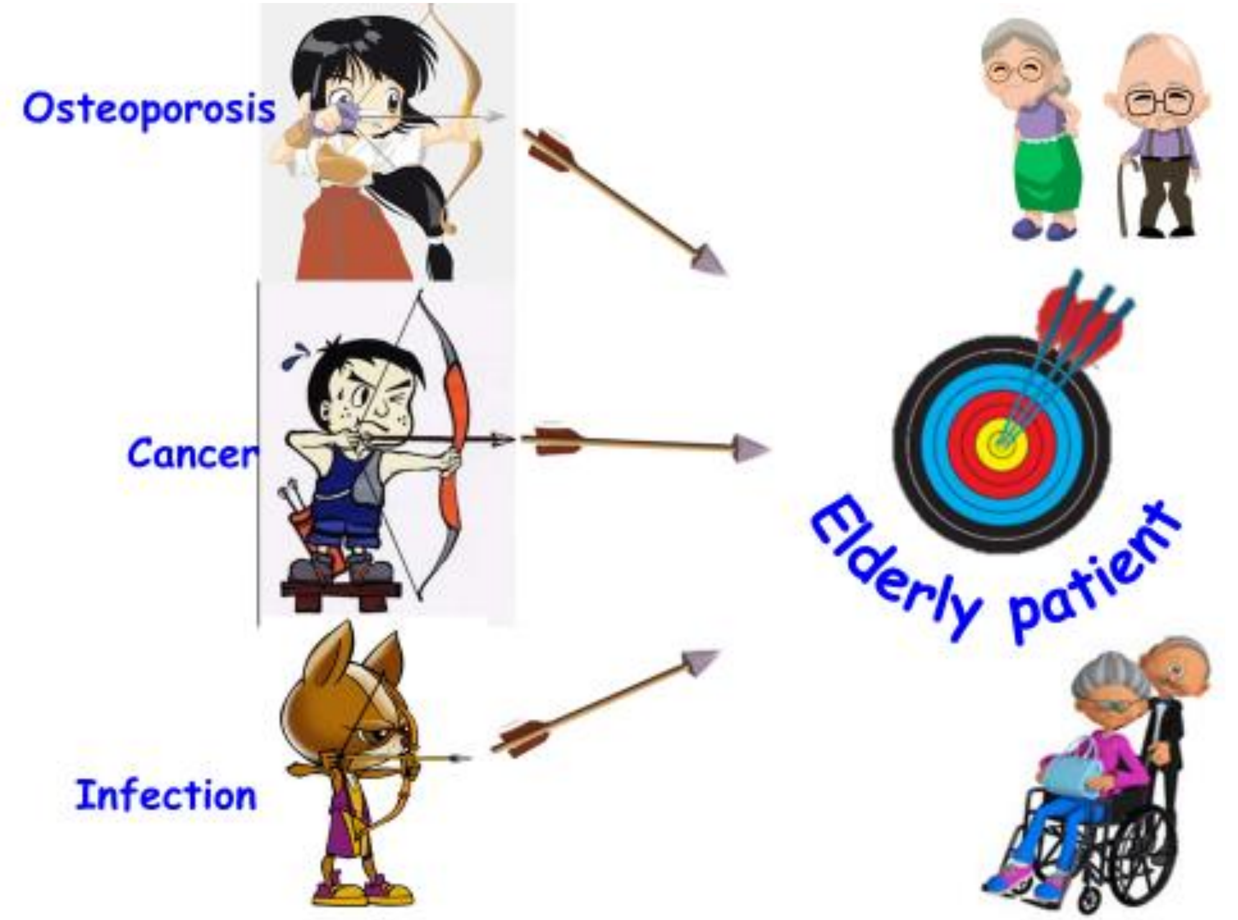
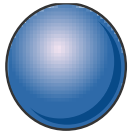
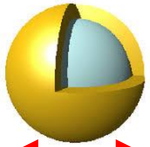
"Infecciones, osteoporosis y cáncer: alternativas para curar huesos "

María Vallet-Regí
https://www.ucm.es/valletregigroup

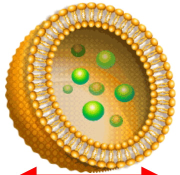


Nanotransportadores clásicos

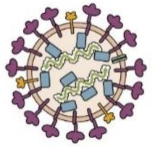
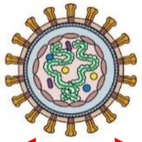
Nanoparticles nanoshells

2 - 100 nm



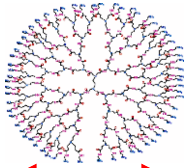
Liposomes

30 - 1000 nm

Viral articles

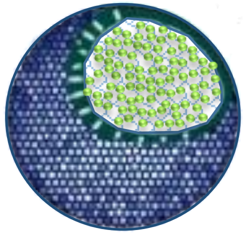
30 - 150 nm



Dendrimers

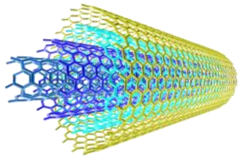
2 - 50 nm

Nuevos nanotransportadores



Mesoporous silica nanoparticles

75 - 150 nm

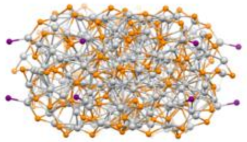


Nanotubes

0,4 - 100 nm

Fullerenes

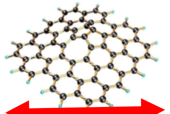
0,4 - 10 nm



Nanocrystals

2 - 50 nm

Graphene



1 nm thick

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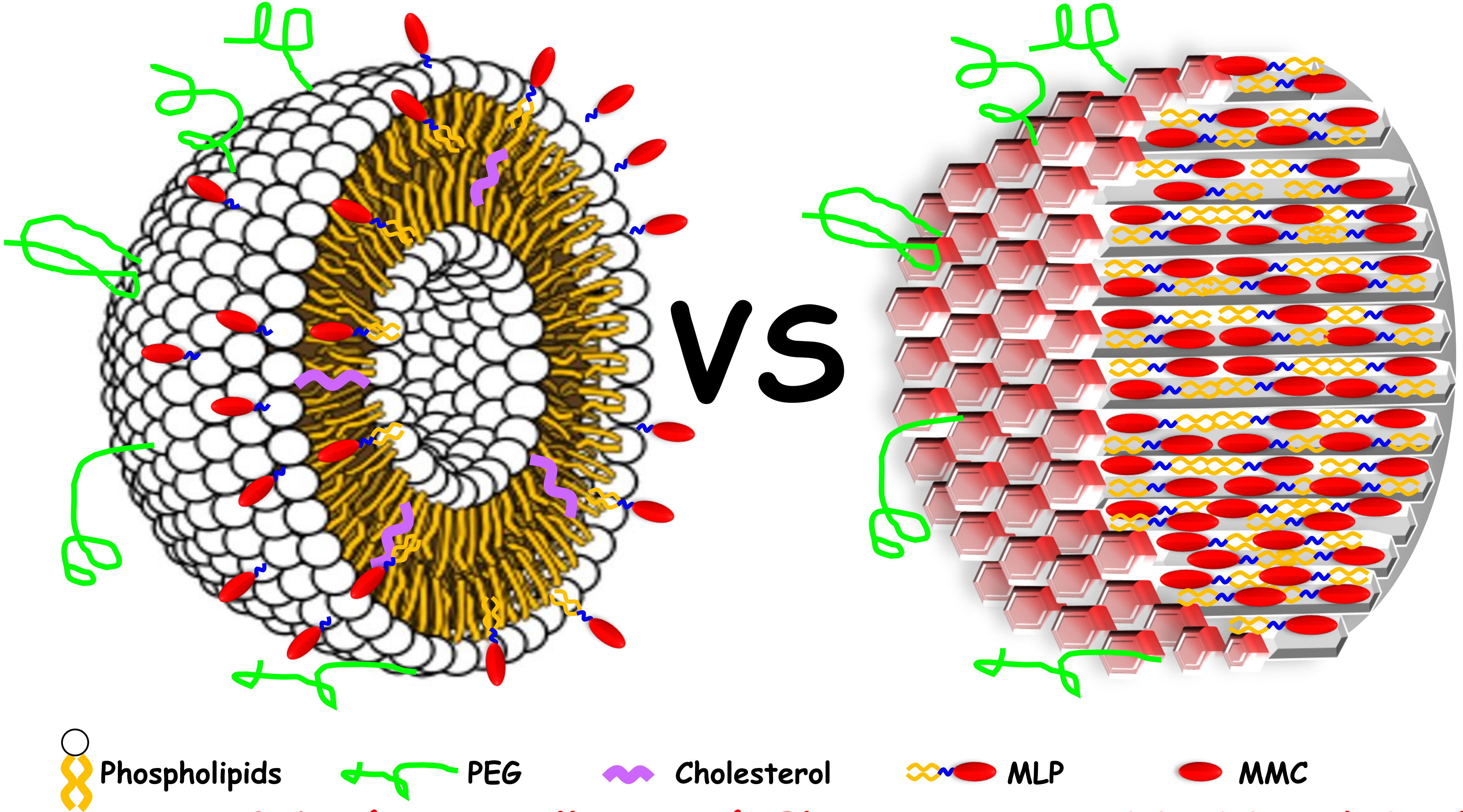
Pegylated Liposomes loaded with MLP

Mesoporous Silica Nanoparticles loaded with MLP



M.Manzano, A.Gabizón, M.Vallet-Regí. Pharmaceutics. 14, 1483 (2022).

2-Estabilidad

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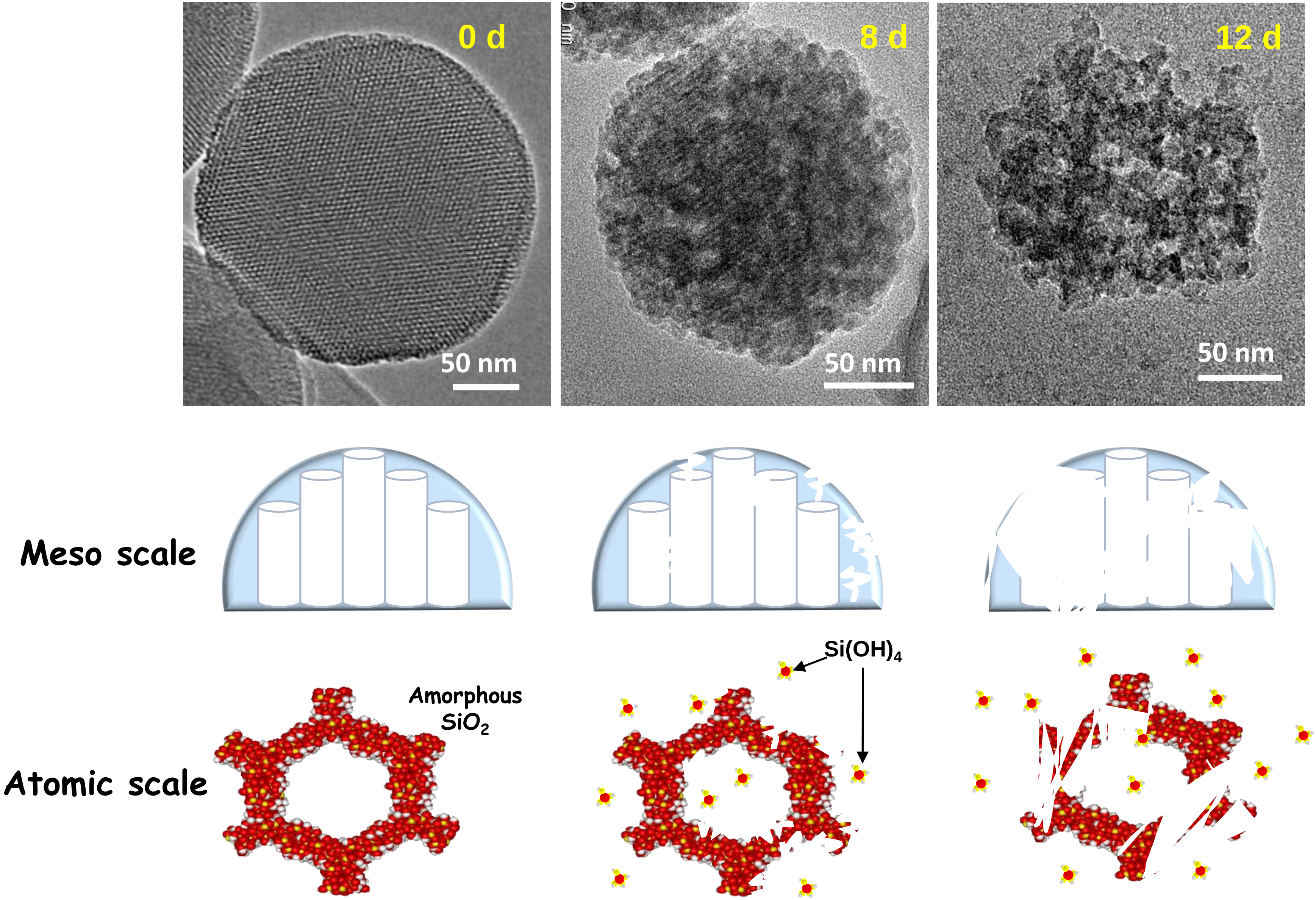
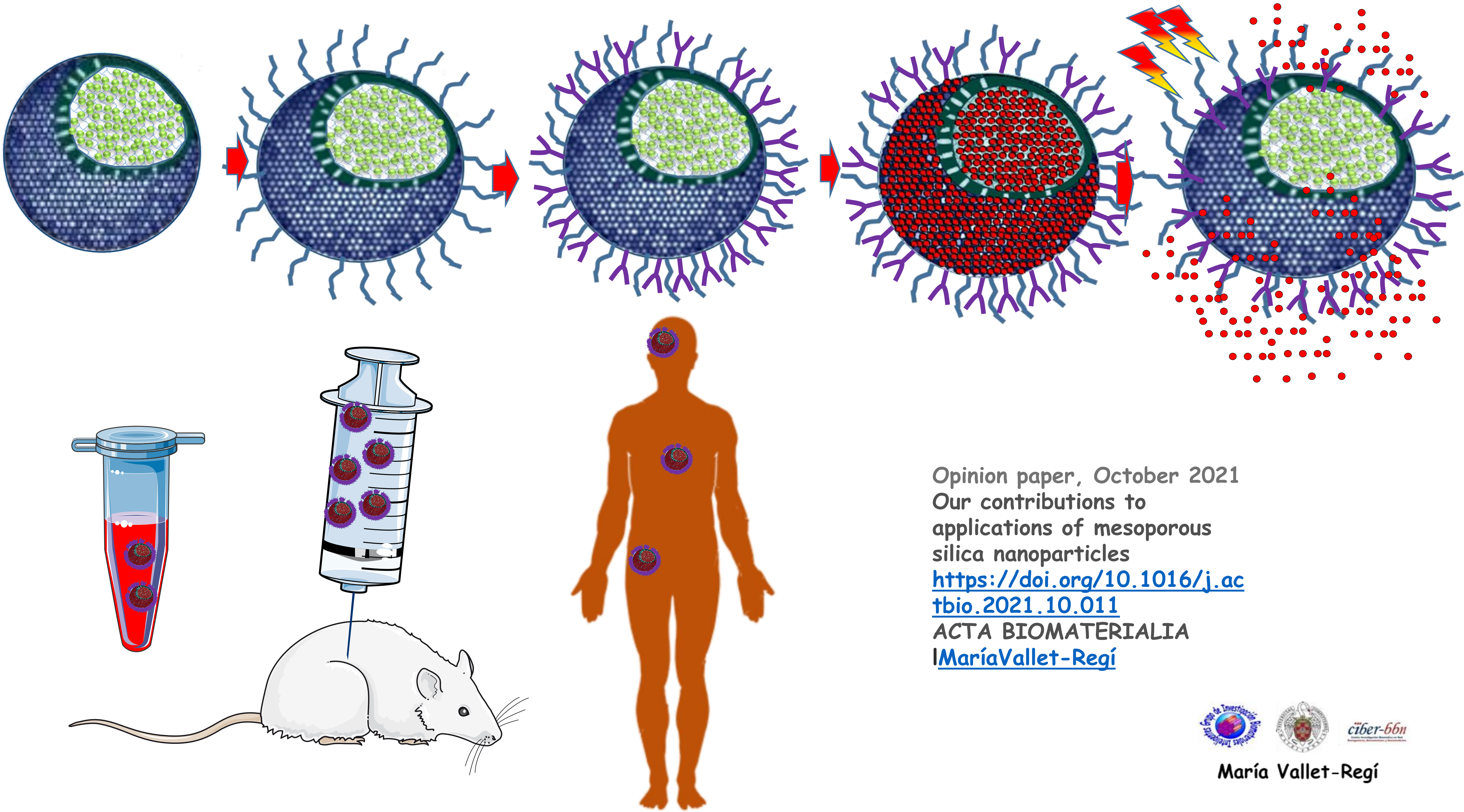


María Vallet-Regí, M.Colilla, I.Izquierdo and M.Manzano, Molecules, 23, 47, 2018

[redacted]



Opinion paper, October 2021
Our contributions to applications of mesoporous silica nanoparticles
https://doi.org/10.1016/j.actbio.2021.10.011
ACTA BIOMATERIALIA
lMaríaVallet-Regí

María Vallet-Regí

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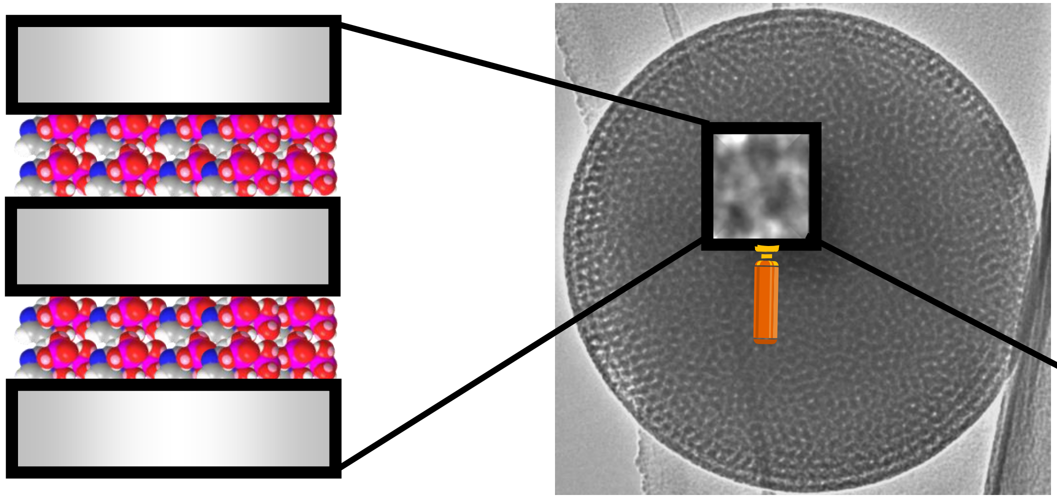
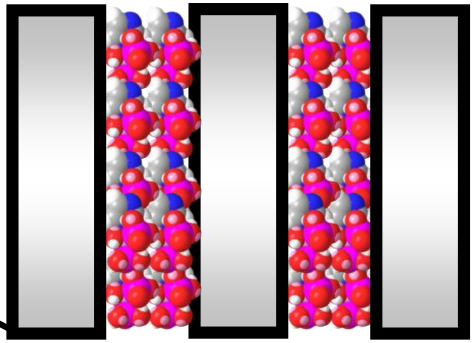
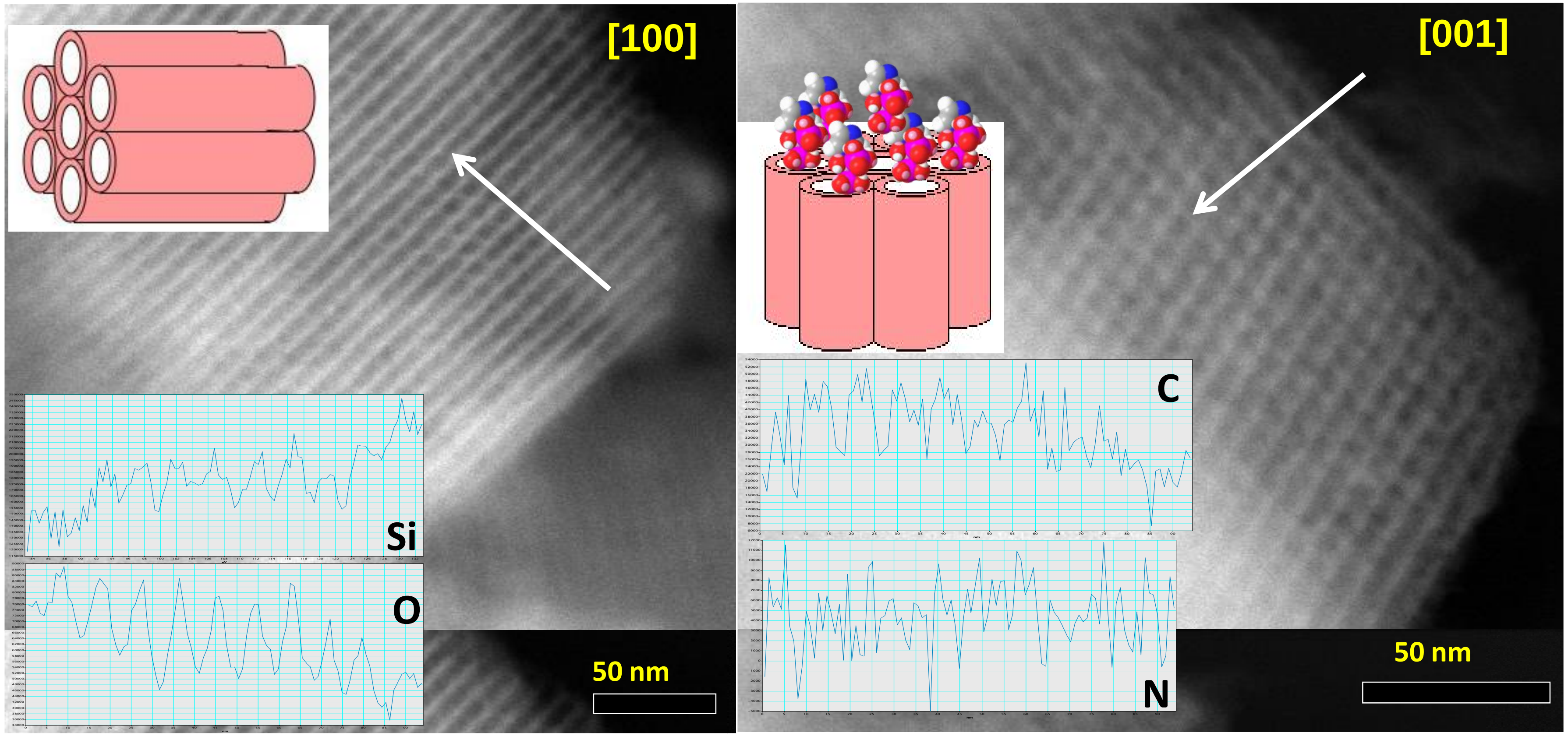
3-Cargar

Vallet-Regí, Manzano, González-Calbet, Okunishi.Chem.Comm., 2010, 46, 2956







4-Inteligentes

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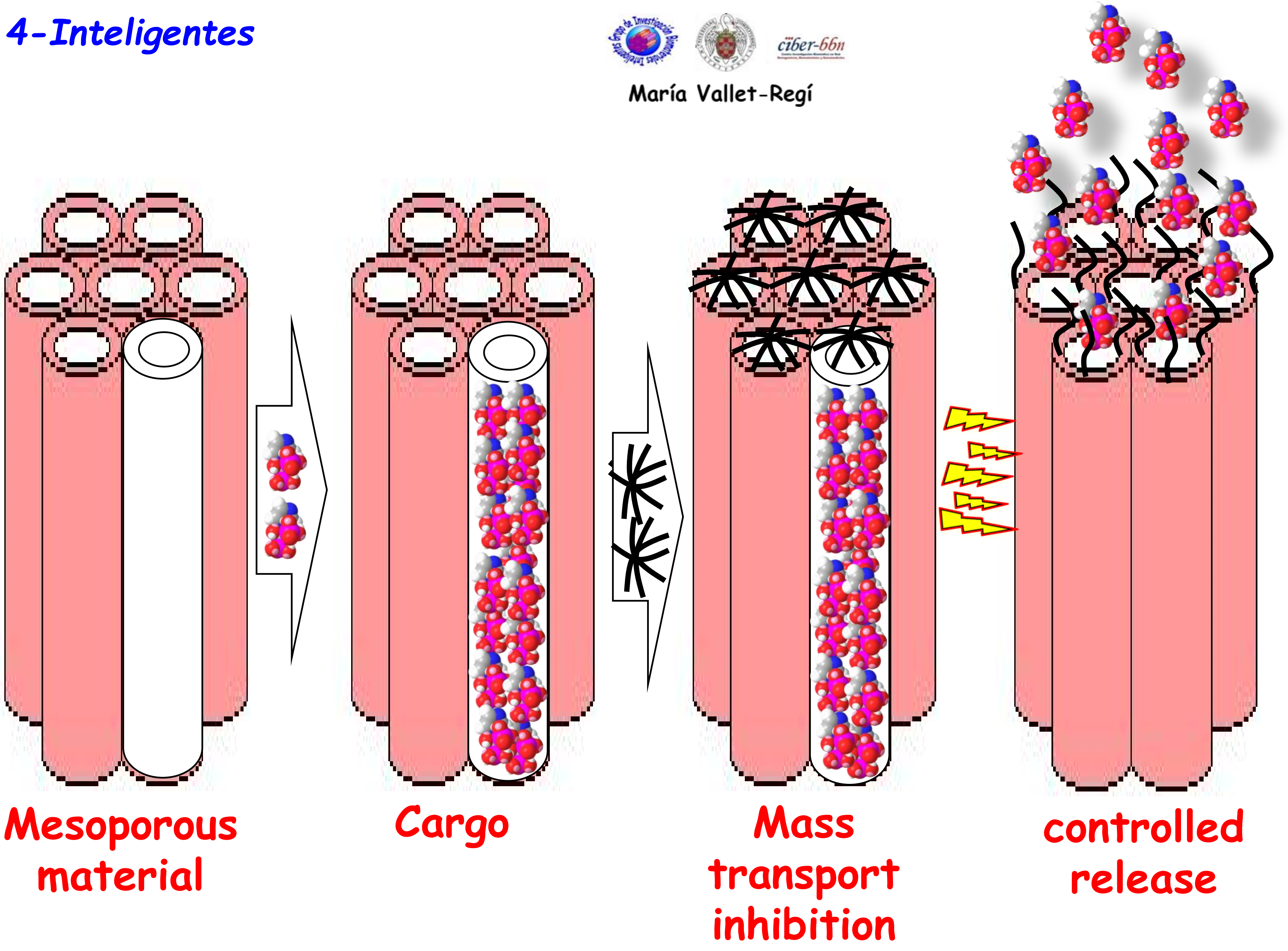

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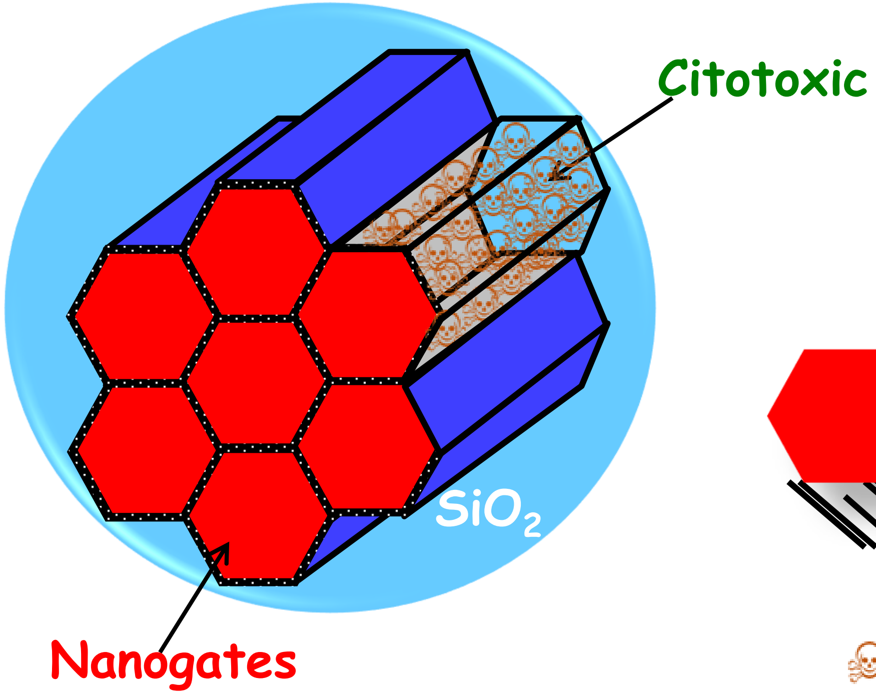
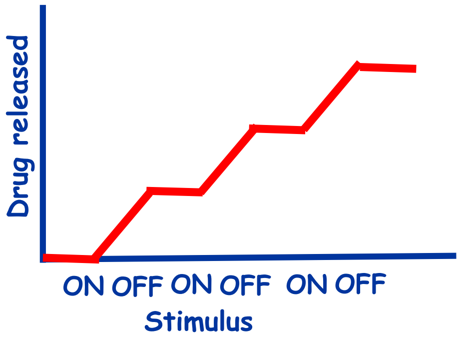
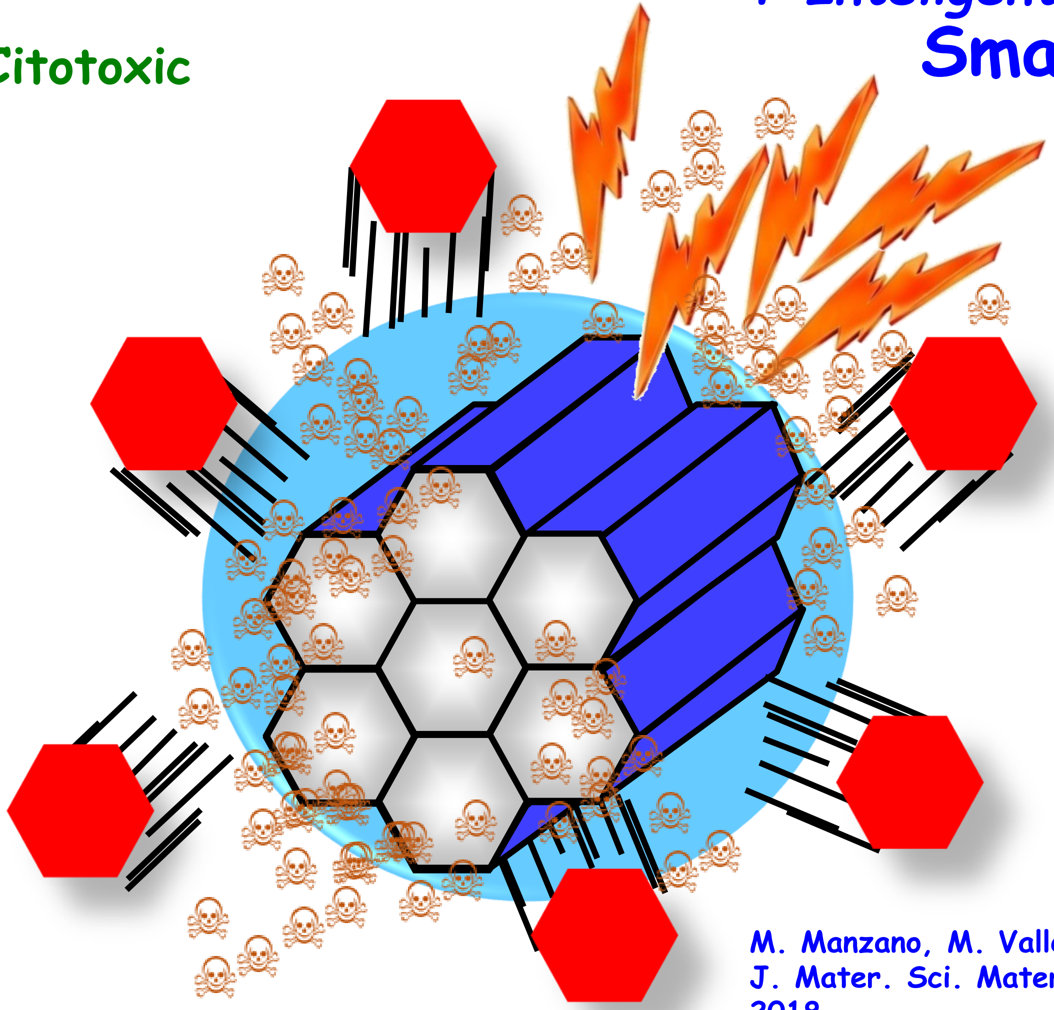
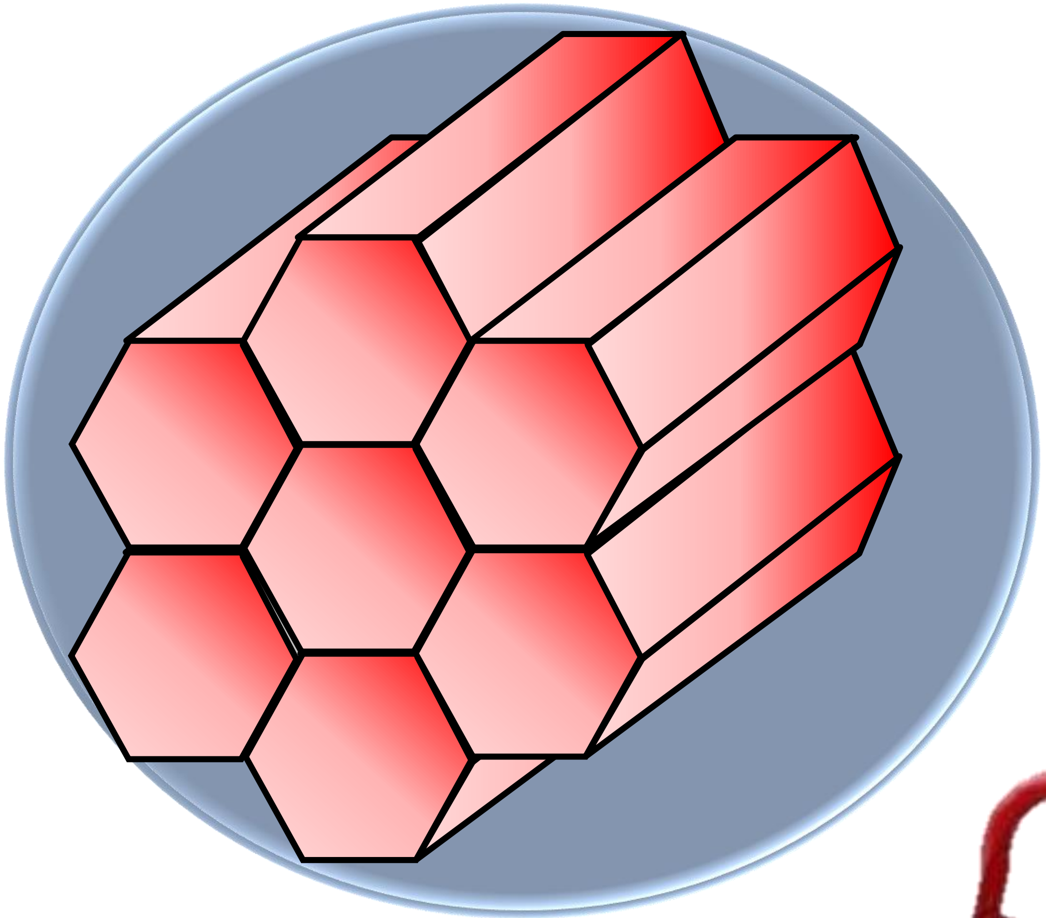
4-Inteligentes
Smarts







M. Manzano, M. Vallet-Regí. J. Mater. Sci. Mater. Med. 2018.



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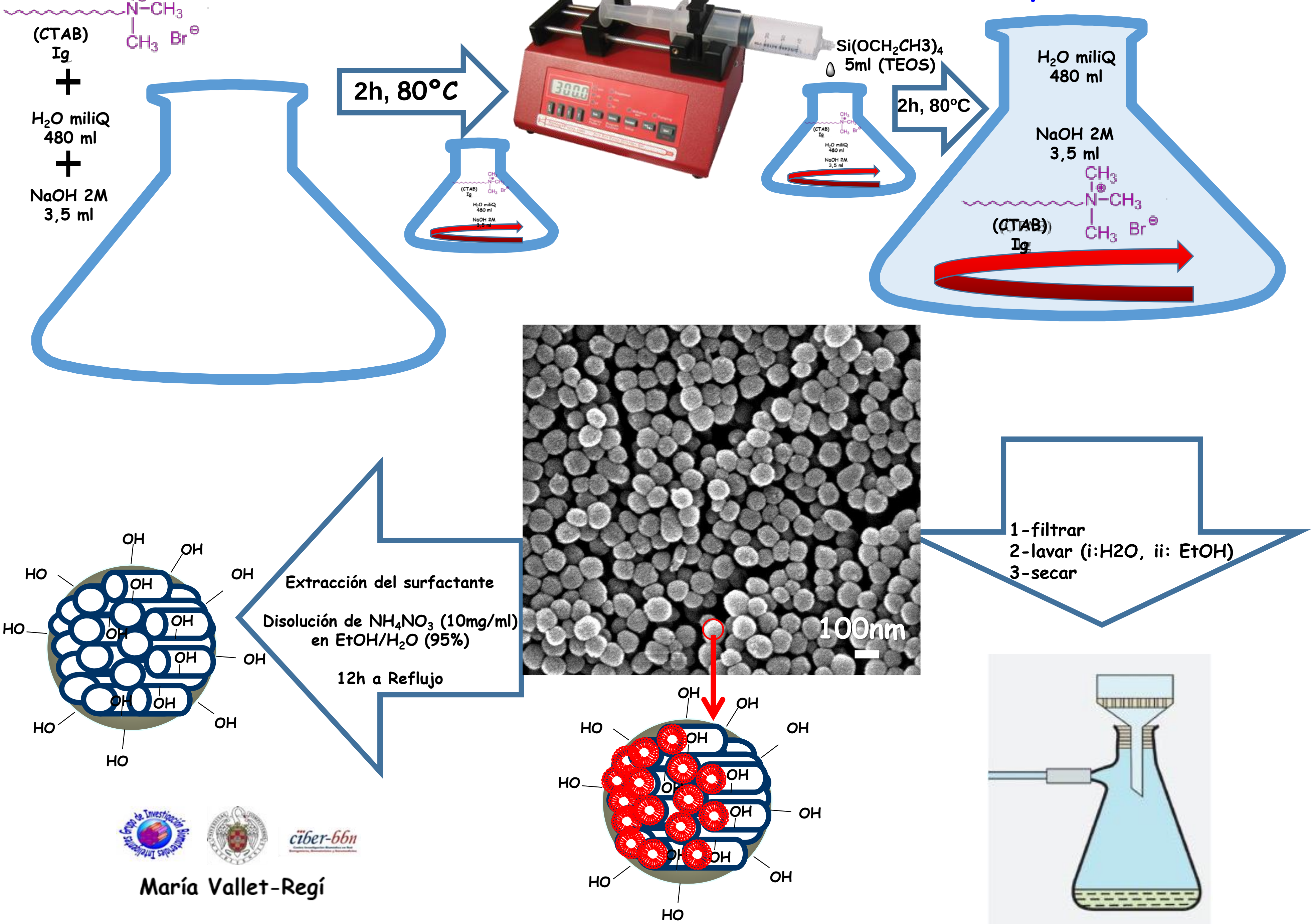
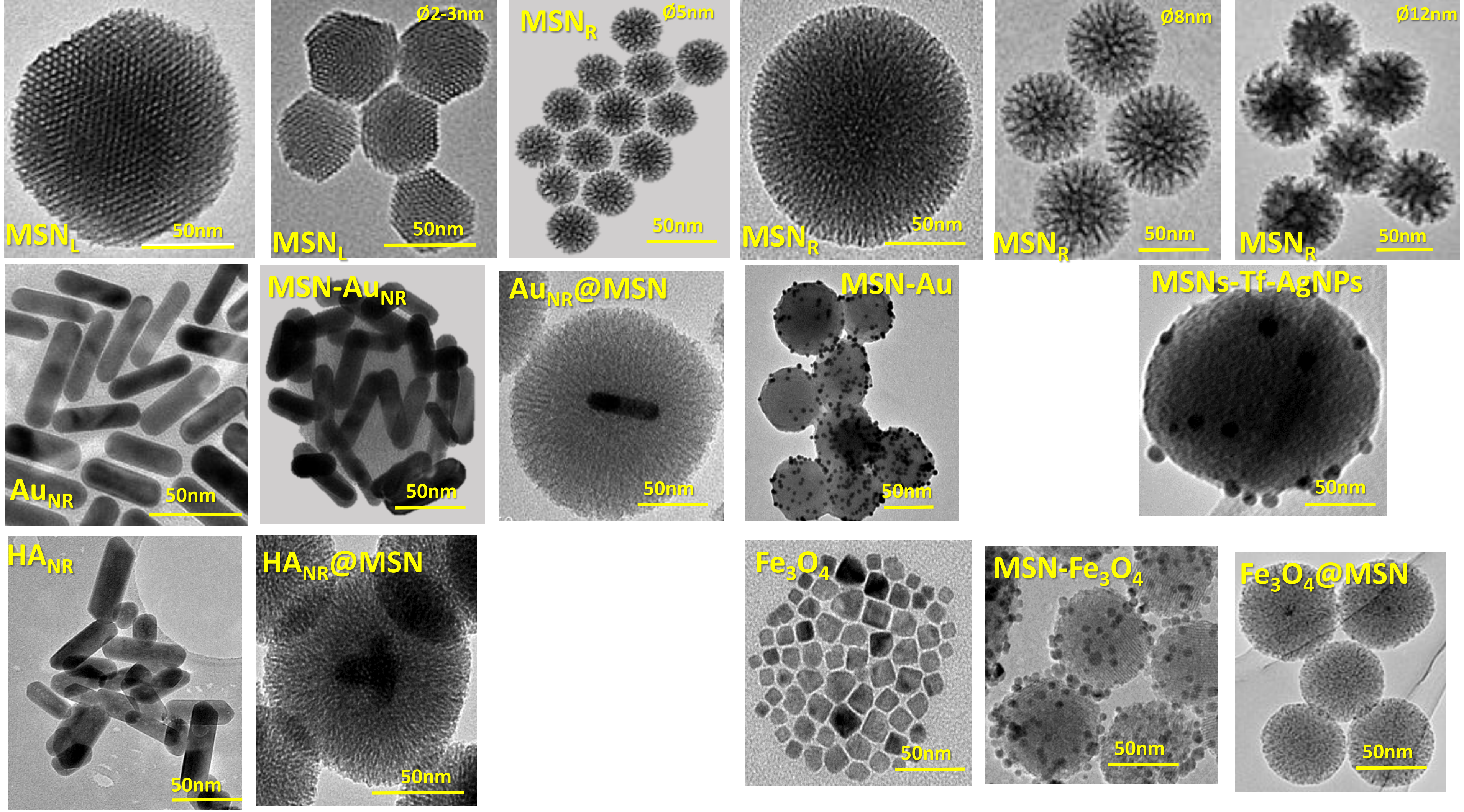
1-Fabricación y caracterización



María Vallet-Regí



1-Fabricación y caracterización

High load charge ($S \approx 1000\ m^2/g$)
Homogeneous preparation
Particle diameter:70- 130 nm
1400 pores/particle
Pore diameter 2…..12 nm
Large scale preparation
Well established chemistry can be used to modify surface or to attach nanomachines

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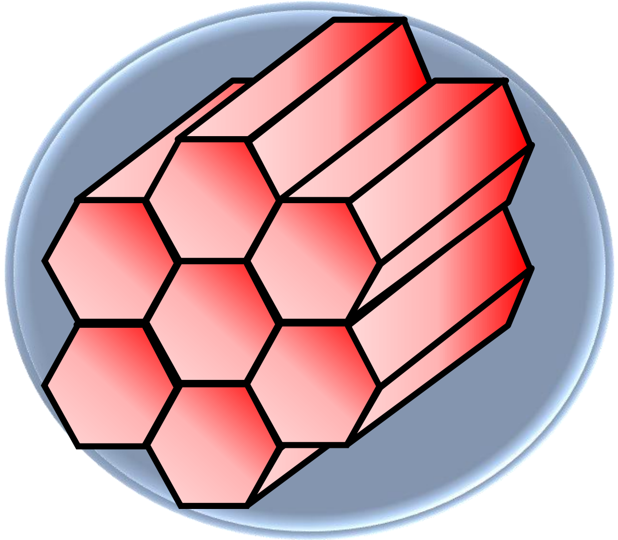

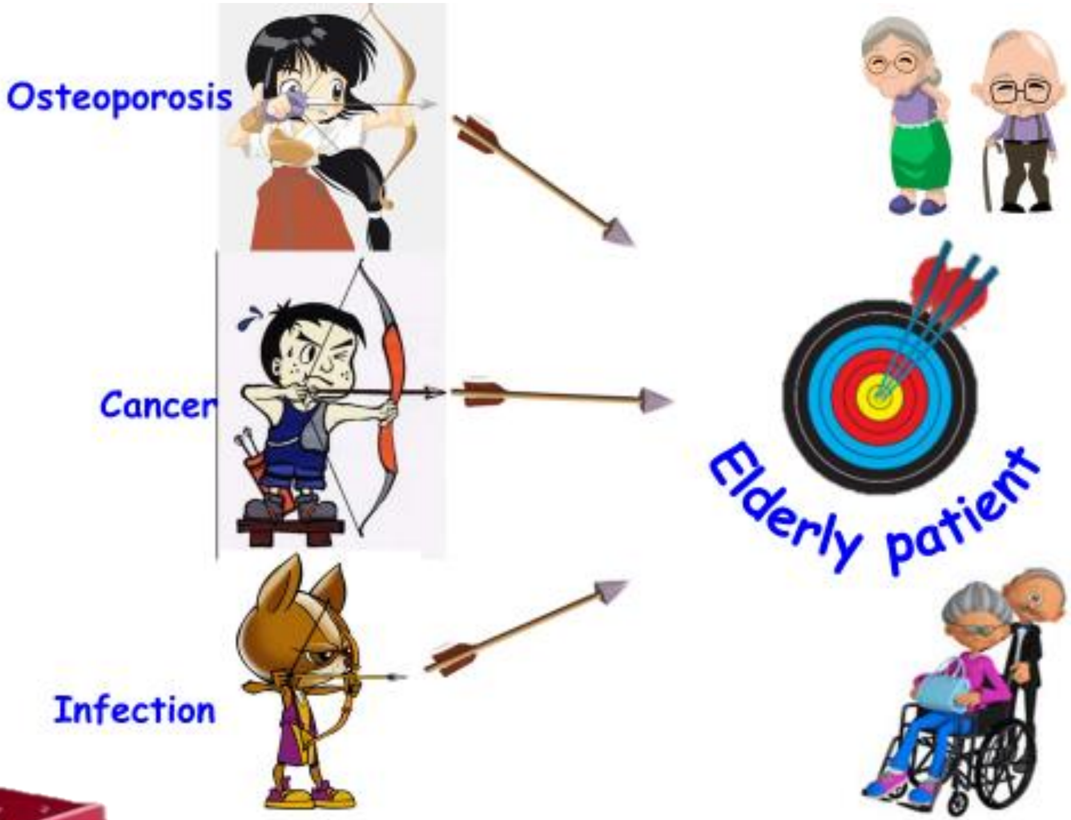

VERDI
polyValent
mEsopoRous
nanosystem for
bone DIseases

erc

María Vallet-Regí

Targeting elements

- Bisphosphonates
- E-selectine
- Tetracyclines
- Antibodies

Therapeutic agents

- Antibiofilm proteolitic enzymes
- Antimicrobial peptides
- Antimicrobial agents
- Antitumor drugs
- Oligonucleotides
- Therapeutic oligopeptides
- Proteins

Stimuli-responsive components

- Nanocapsules Polymer/enzyme/protein
- Oligopeptides
- Metallic nanoparticles
- Stimuli-sensitive bonds

Stealth agents

- Zwitterionization agents
- PEG

VERDI polyValent mEsopoRous nanosystem for bone DIseases

erc

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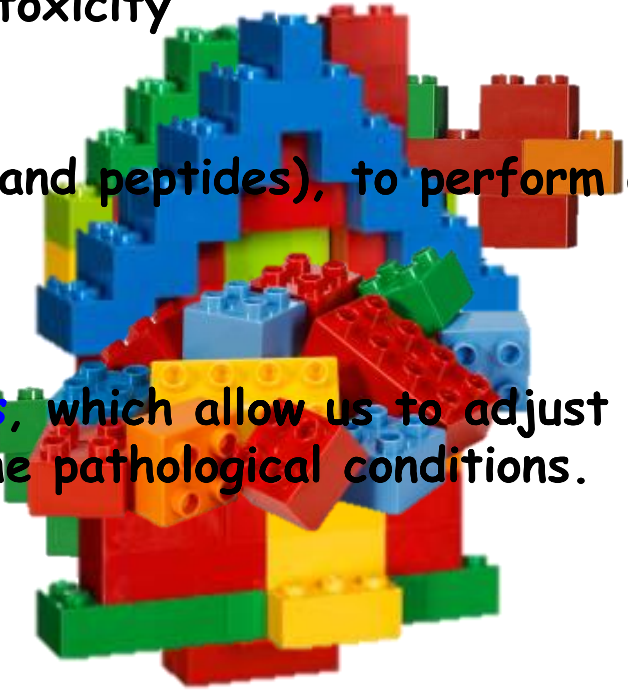
María Vallet-Regí

VERDI
polyValent mEsopoRous nanosystem for bone DIseases



Vectorisation ligans, to guide the nanosystems towards the diseased bone, increasing bioavailability and reducing toxicity

Therapeutic agents (drugs and peptides), to perform a combined therapy and increase its efficacy

Stimuli sensitive components, which allow us to adjust the pharmacokinetic profiles against certain stimuli related to the pathological conditions.

6-Que se internalicen

Internalisation oriented to tumour cells:targeting

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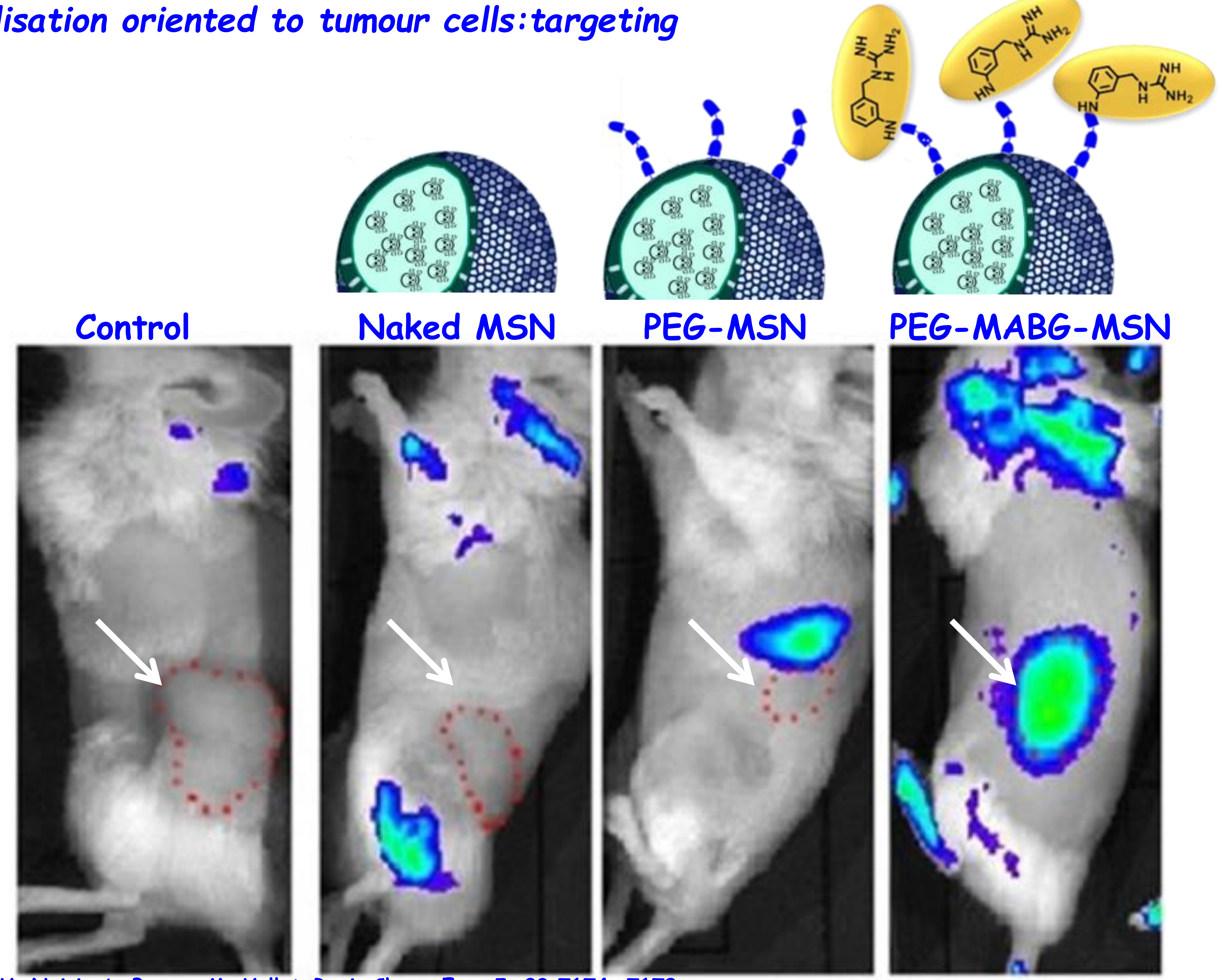

G. Villaverde, V. Nairi, A. Baeza, M. Vallet-Regi. Chem. Eur. J. 23,7174 -7179 (2017).

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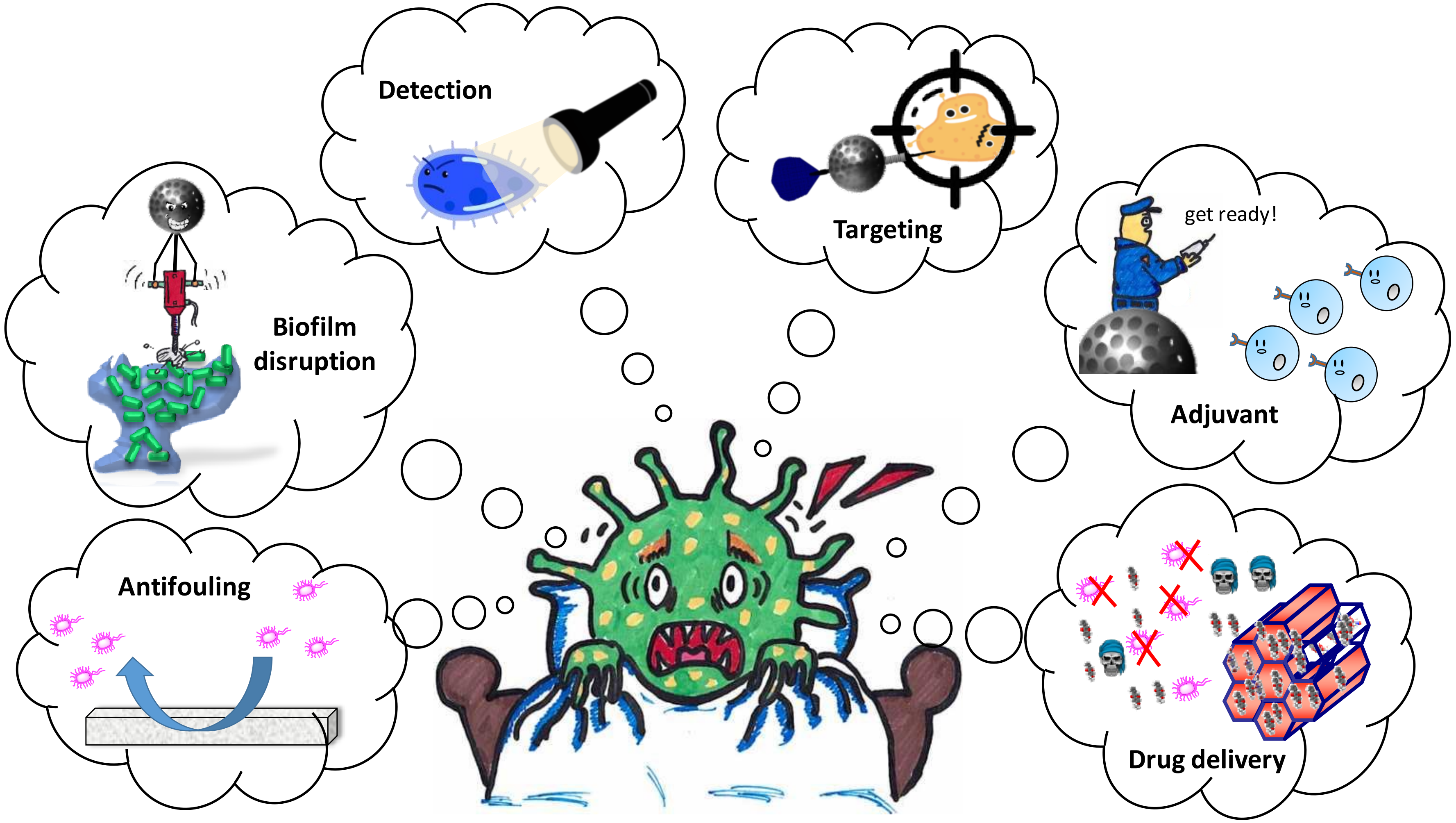
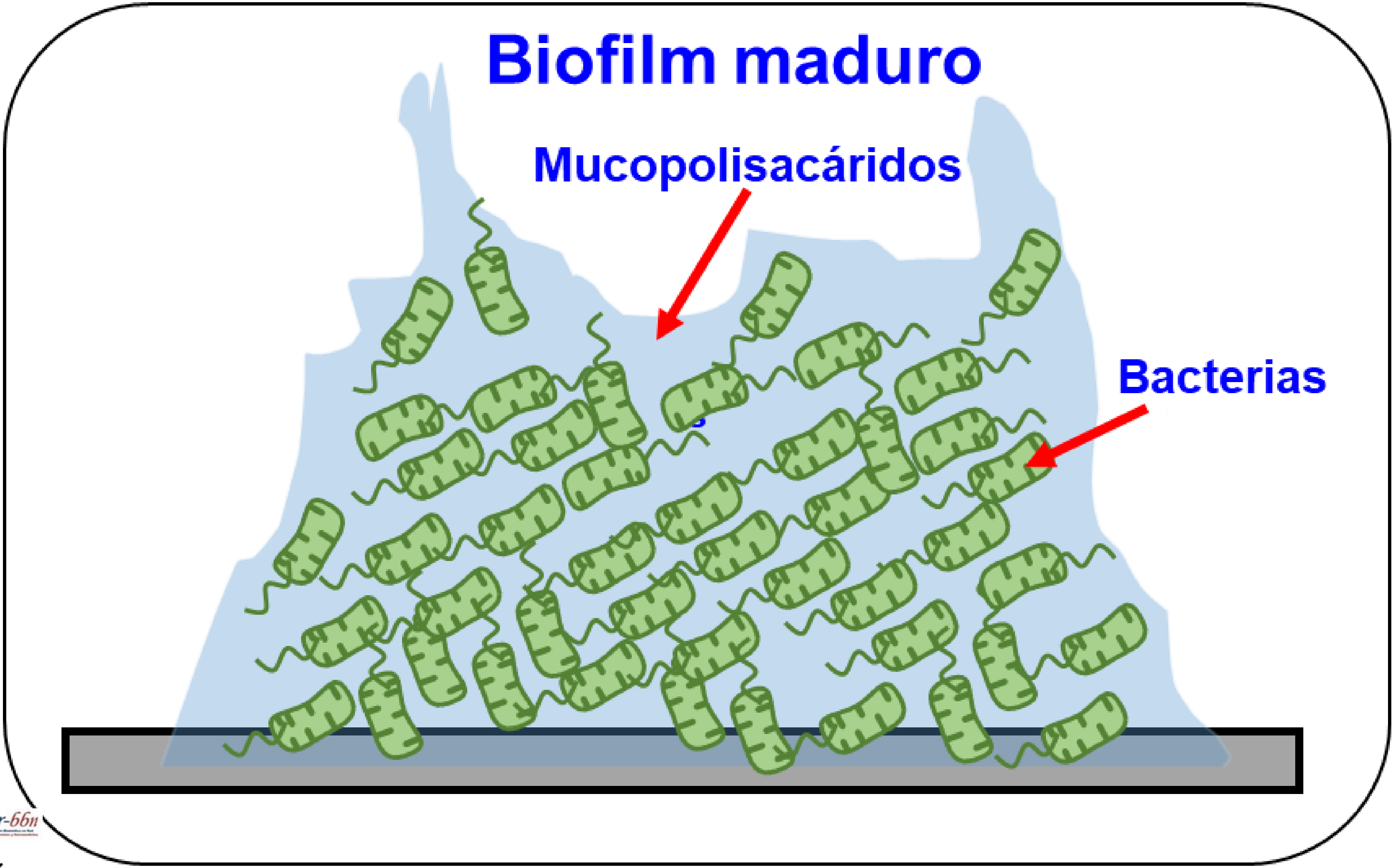


M Martínez-Carmona, Y Gun'ko, M Vallet-Regí. Pharmaceutics 10 (4), 279, 2018

La resistencia a los antibioticos es un grave problema de salud pública que causa 670 000 infecciones y 33 000 muertes al año sólo en Europa.



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Mesoporous Silica Nanoparticles: New Weapon againts Osteoporosis

Osteoporosis Disease and Treatment

Healthy

Treatment

Osteoblast

~~Osteoclast~~

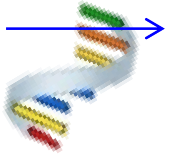
→

↓Osteoporosis

↑Osteoblast

Osteoclast

Gene therapy



siRNA

Osteoblast

Problem

DELIVERY

-short half-life

-poor penetration capacity

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ACS NANO

Cite This: ACS Nano XXXX, XXX, XXX−XXX

www.acsnano.org

ARTICLE

Nanoparticles to Knockdown Osteoporosis-Related Gene and Promote Osteogenic Marker Expression for Osteoporosis Treatment

Patricia Mora-Raimundo,[†] Daniel Lozano,[†,‡] Miguel Manzano,[*,†,‡] and María Vallet-Regí[*,†,‡]

[†]Chemistry in Pharmaceutical Sciences, School of Pharmacy, Universidad Complutense de Madrid, Spain, Instituto de Investigación Sanitaria Hospital 12 de Octubre i + 12, Plaza de Ramón y Cajal s/n, E-28040 Madrid, Spain

[‡]Networking Research Center on Bioengineering, Biomaterials and Nanomedicine (CIBER-BBN), E-28034 Madrid, Spain

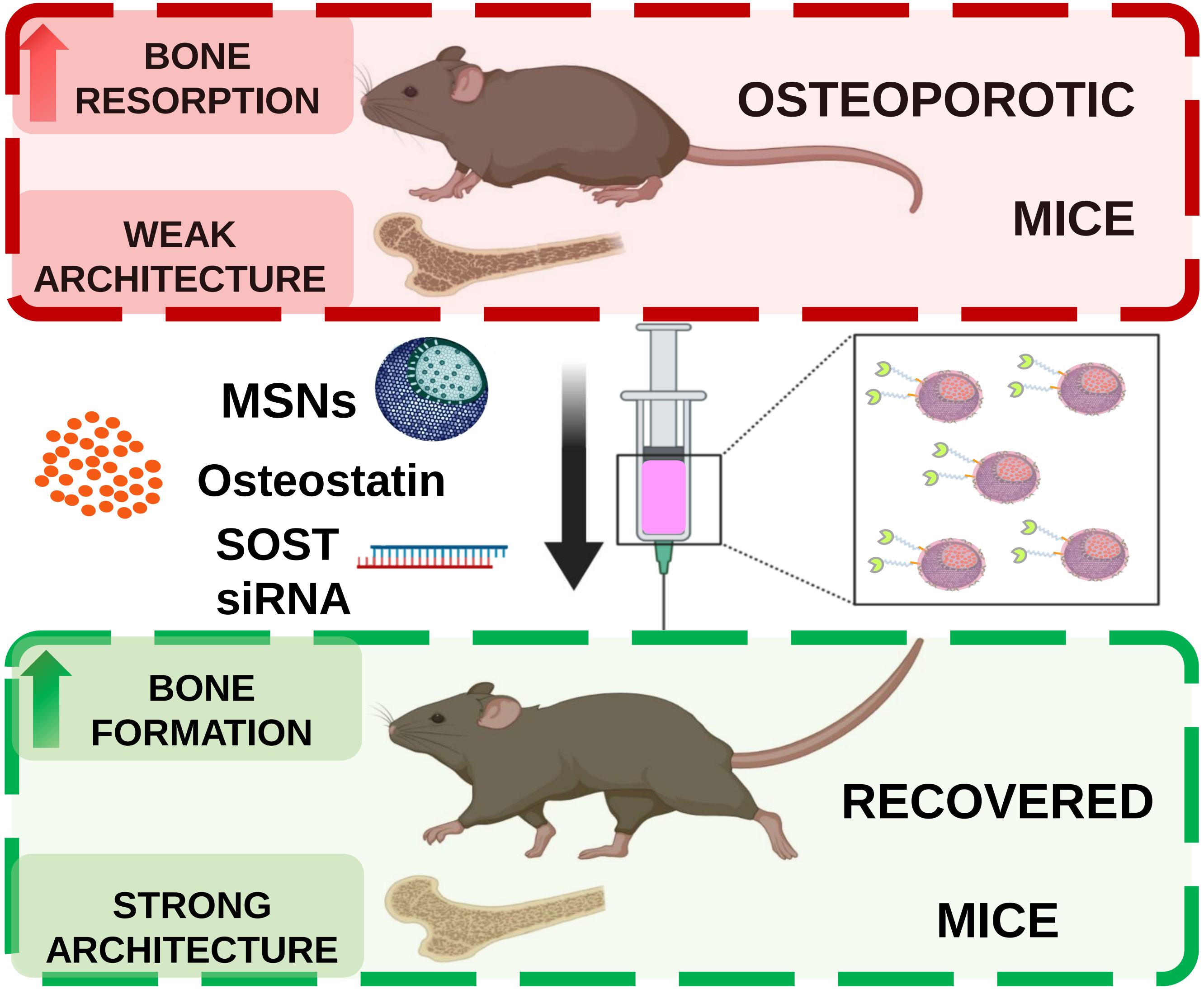
Supporting Information

ABSTRACT: Osteoporosis is the most common disease involving bone degeneration. Current clinical treatments are not able to offer a satisfying curative effect, so the development of effective treatments is desired. Gene silencing through siRNA delivery has gained great attention as a potential treatment in bone diseases. SOST gene inhibits the Wnt signaling pathway reducing osteoblast differentiation. Consequently, silencing SOST genes with a specific siRNA could be a potential option to treat osteoporosis. Generally, siRNAs have a very short half-life and poor transfection capacity, so an effective carrier is needed. In particular, mesoporous silica nanoparticles (MSNs) have attracted great attention for intracellular delivery of nucleic acids. We took advantage of their high loading capacity to further load the pores with osteostatin, an osteogenic peptide. In this study, we developed a system based on MSNs coated with poly(ethylenimine), which can effectively deliver SOST siRNA and osteostatin inside cells, with the consequent augmentation of osteogenic markers with a synergistic effect. This established the potential utility of MSNs to co-deliver both biomolecules to promote bone formation, this being a potential alternative to treat osteoporosis.

KEYWORDS: mesoporous nanoparticles, gene silencing, osteoporosis, therapeutic co-delivery, osteogenic stimulation

María Vallet-Regí

María Vallet-Regí



P Mora D Lozano, M Benito, F Mulero, M Manzano, M Vallet-Regí

Advanced Science 2101107. 2021

Volume 51
Number 13
7 July 2022
Pages 5241–5732

Chem Soc Rev

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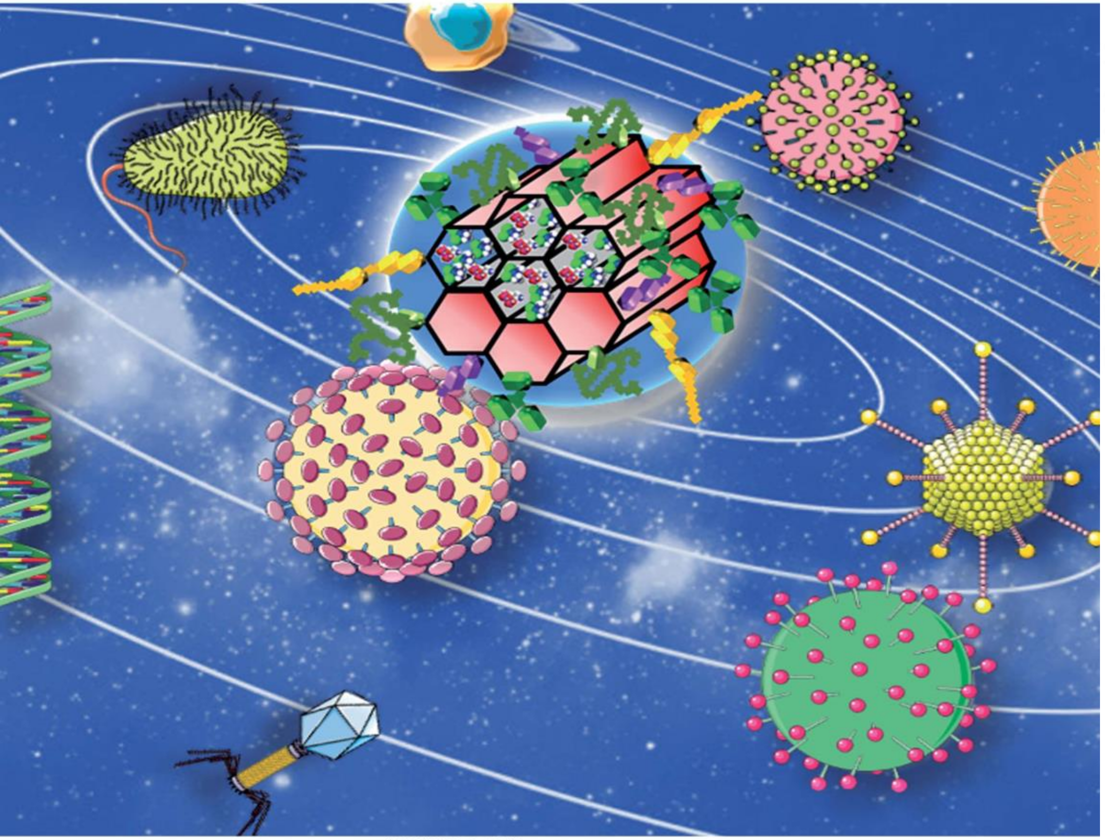

ISSN 0306-0012

ROYAL SOCIETY OF CHEMISTRY

REVIEW ARTICLE
María Vallet-Regí *et al.*
Engineering mesoporous silica nanoparticles for drug delivery: where are we after two decades?

Chem Soc Rev

ROYAL SOCIETY OF CHEMISTRY

REVIEW ARTICLE

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Cite this: *Chem. Soc. Rev.*, 2022, 51, 5365

Engineering mesoporous silica nanoparticles for drug delivery: where are we after two decades?

María Vallet-Regí, *[ab] Ferdi Schüth,[c] Daniel Lozano,[ab] Montserrat Colilla[ab] and Miguel Manzano[ab]

Received 27th January 2022

DOI: 10.1039/d1cs00659b

rsc.li/chem-soc-rev

The present review details a chronological description of the events that took place during the development of mesoporous materials, their different synthetic routes and their use as drug delivery systems. The outstanding textural properties of these materials quickly inspired their translation to the nanoscale dimension leading to mesoporous silica nanoparticles (MSNs). The different aspects of introducing pharmaceutical agents into the pores of these nanocarriers, together with their possible biodistribution and clearance routes, would be described here. The development of smart nanocarriers that are able to release a high local concentration of the therapeutic cargo on-demand after the application of certain stimuli would be reviewed here, together with their ability to deliver the therapeutic cargo to precise locations in the body. The huge progress in the design and development of MSNs for biomedical applications, including the potential treatment of different diseases, during the last 20 years will be collated here, together with the required work that still needs to be done to achieve the clinical translation of these materials. This review was conceived to stand out from past reports since it aims to tell the story of the development of mesoporous materials and their use as drug delivery systems by some of the story makers, who could be considered to be among the pioneers in this area.

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1. Introduction

1.1. Historical background of the synthesis of ordered mesoporous materials

Carriers for controlled drug delivery had traditionally been based on biopolymers or synthetic polymers,[1] but in the 1990s, silicas, especially in the form of nanoparticles, moved

María Vallet-Regí

María Vallet-Regí, pioneer in the field of mesoporous silica materials with application in controlled drug release. She is the manager of the Intelligent Biomaterials Research Group (GIBI), CIBER-BBN, at Complutense University of Madrid, where currently she is developing different strategies to cure bone-related diseases such as cancer, osteoporosis or infections in implants. She was the first woman to receive the gold medal from the European Federation of Materials Science Societies (FEMS) and the George Winter Award from the European Biomaterials Society (ESB).

CHEMICAL SOCIETY REVIEWS

Journal Impact Factor ™

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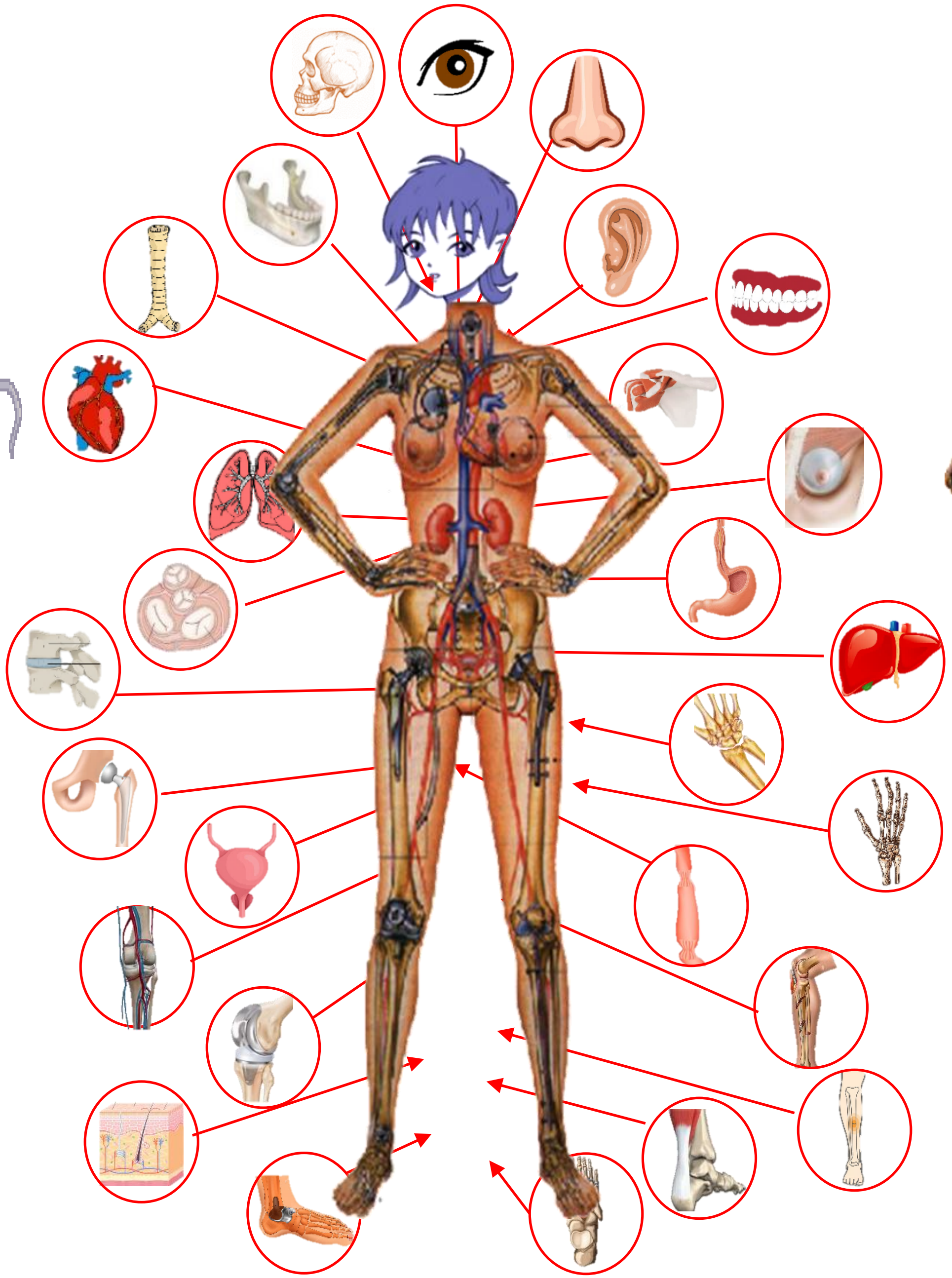
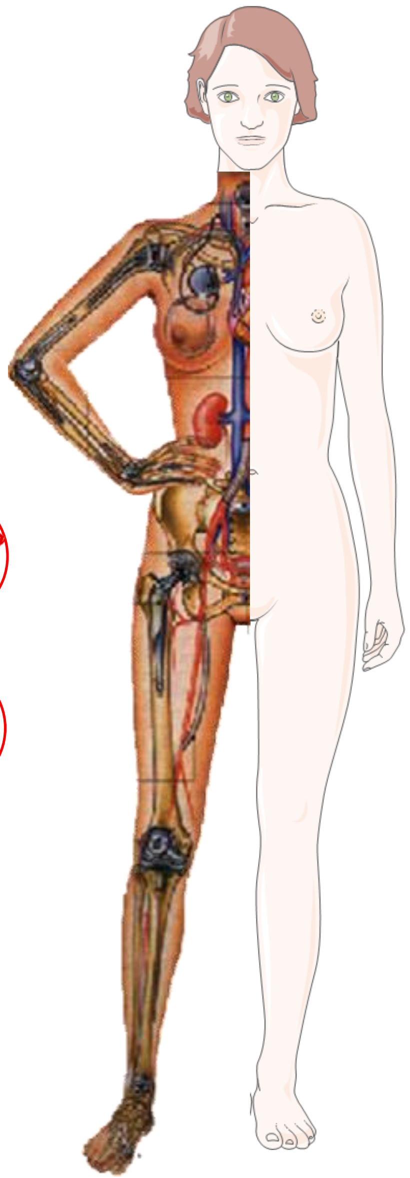
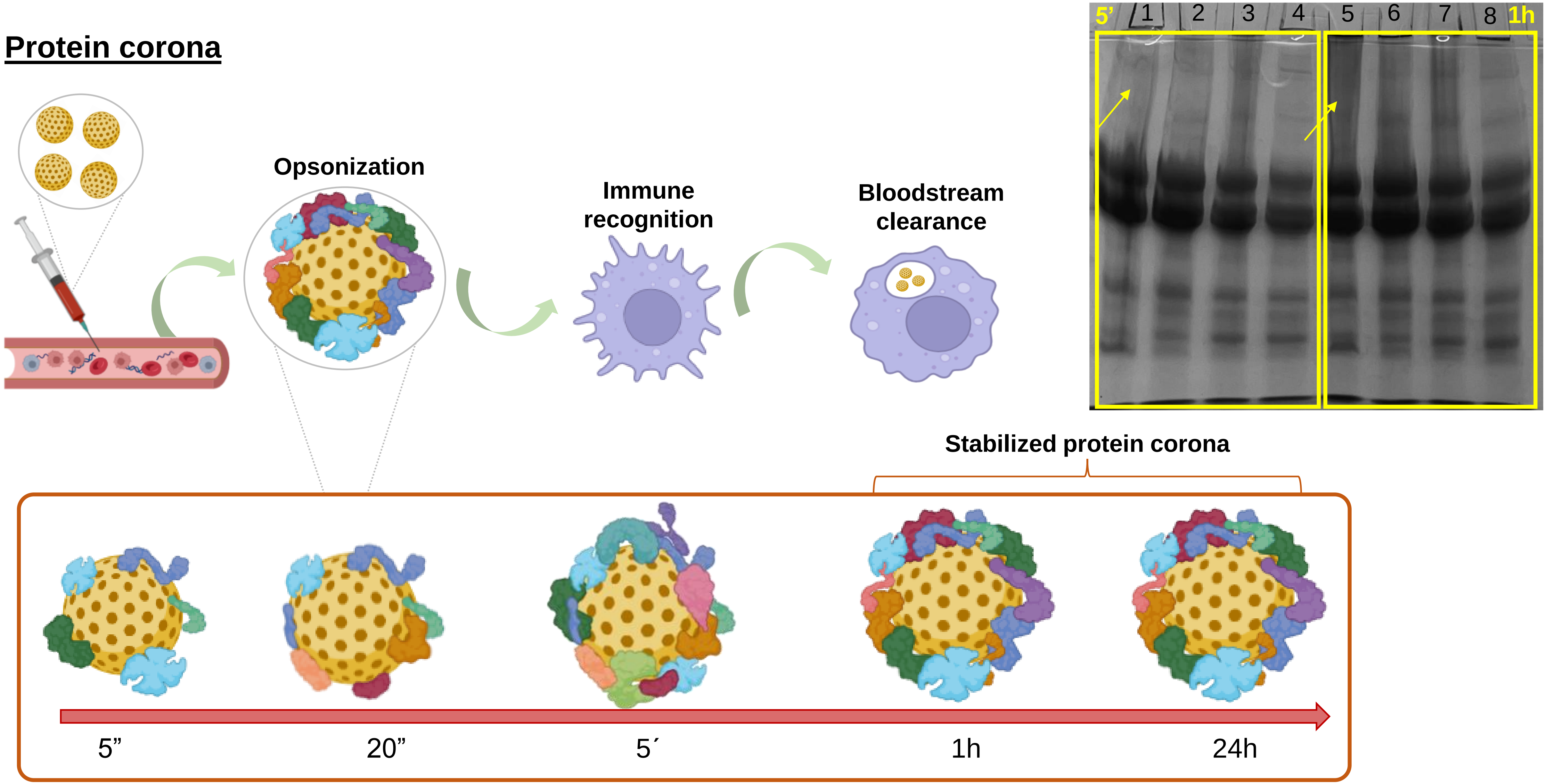
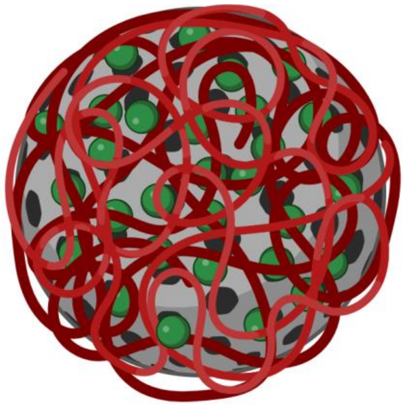




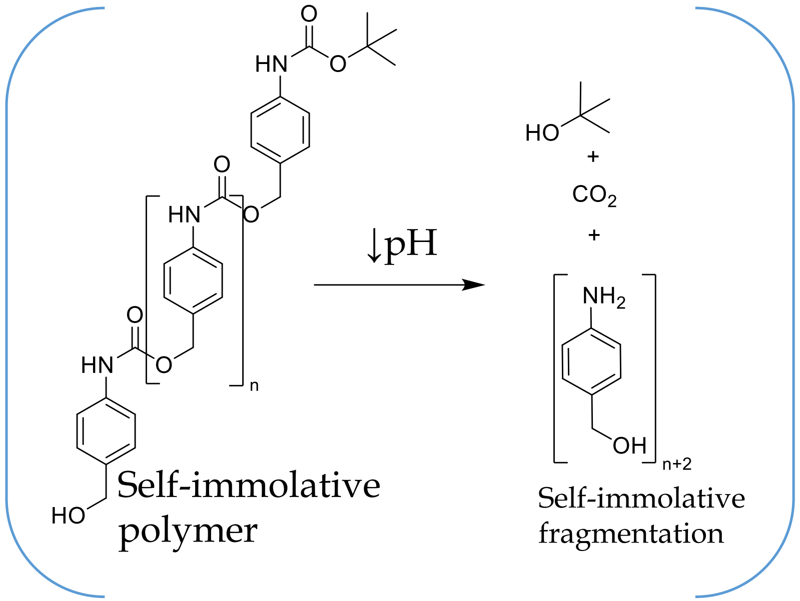


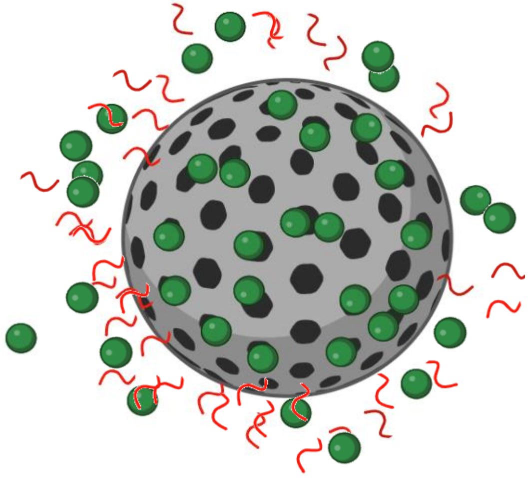
Protein corona
Opsonization
Immune recognition
Bloodstream clearance
5’
1
2
3
4
5
6
7
8
1h
Stabilized protein corona
5”
20”
5´
1h
24h

pH-responsive nanoparticles



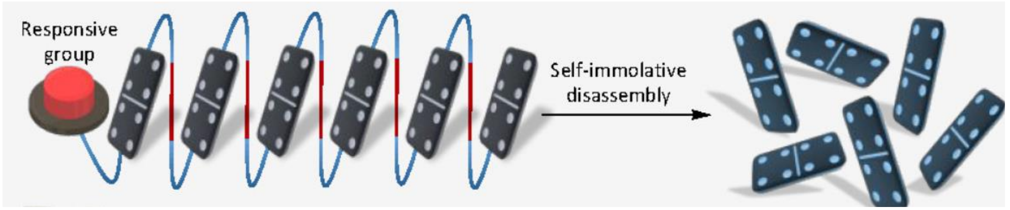
pH-Responsive Mesoporous Carbon Nanoparticle



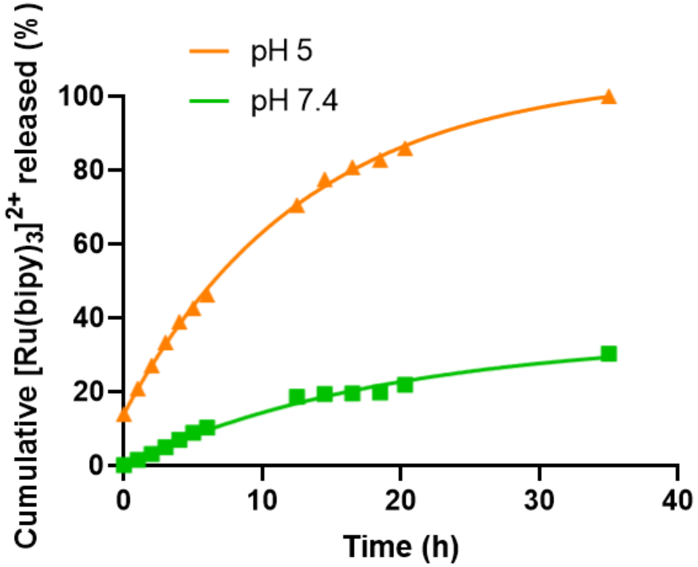


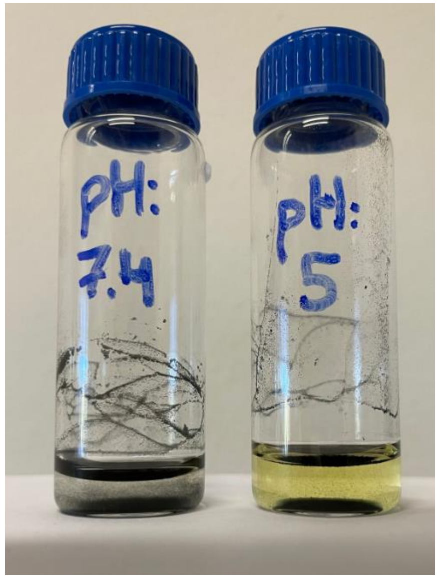
Cargo release in acidic environments

Self-immolative polymers are programmed to disassemble spontaneously from head to tail, through a **domino-like fragmentation**, upon response to extremal stimuli.

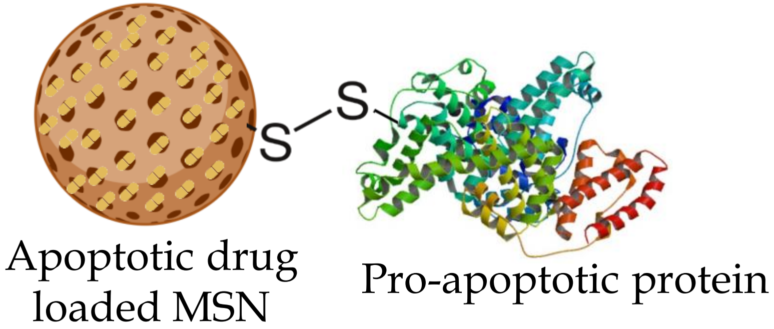


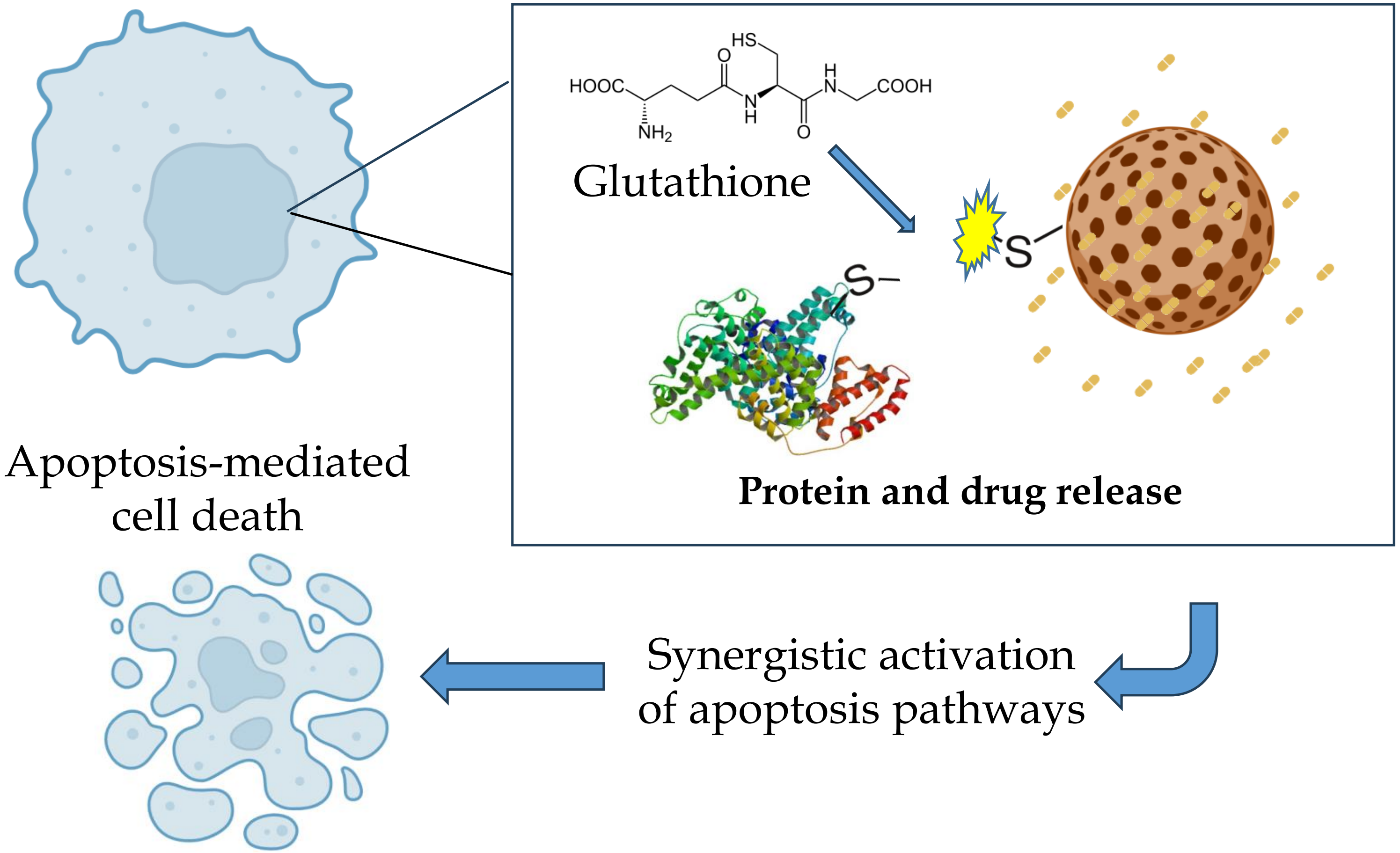
Self-Immolative Polymers: An Emerging Class of Degradable Materials with Distinct Disassembly Profiles. *J. Am. Chem. Soc.* 2021, 143, 50, 21177–21188





Redox-responsive nanoparticles for synergistic effect in cancer cells



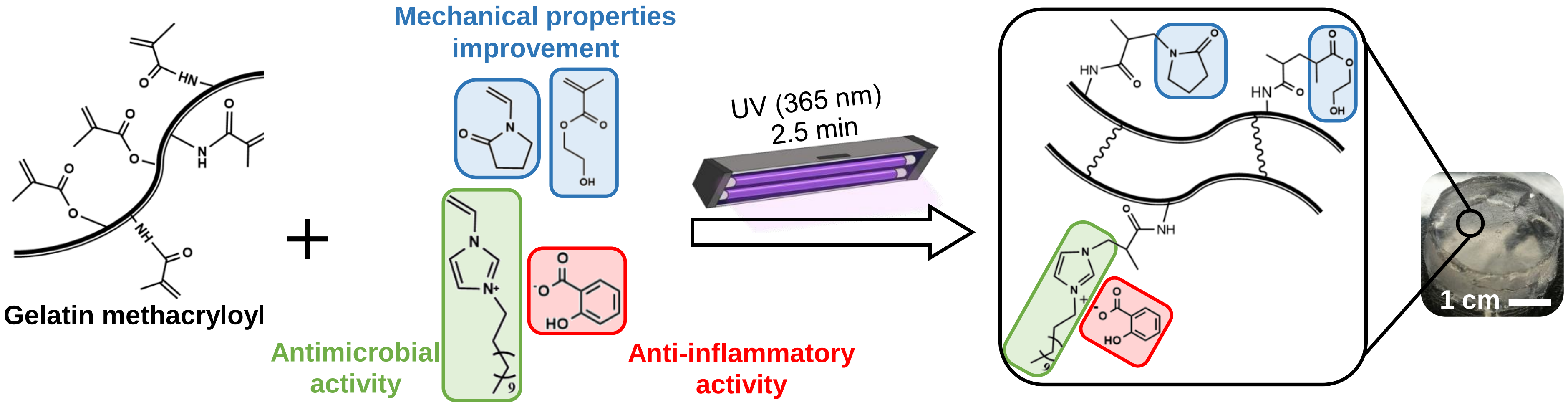


- Elevated intracellular levels of glutathione are a characteristic feature of the tumor microenvironment.
- We designed a system triggered by Glutathione to release pro-apoptotic drug and protein.

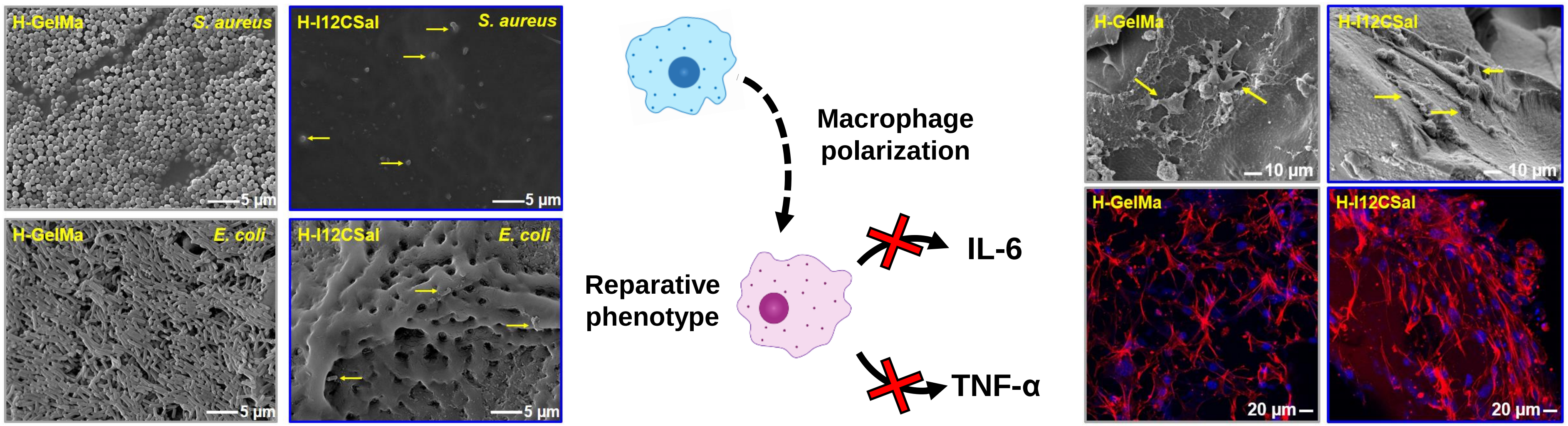
Recent work: Dual-action hydrogel for wound dressing

Objective: To develop a hydrogel that targets not only the **pathogen**, but also the associated **inflammation**

Synthesis: **Gelatin methacryloyl** matrix copolimerized with an **anion-exchanged polymerizable ionic liquid**



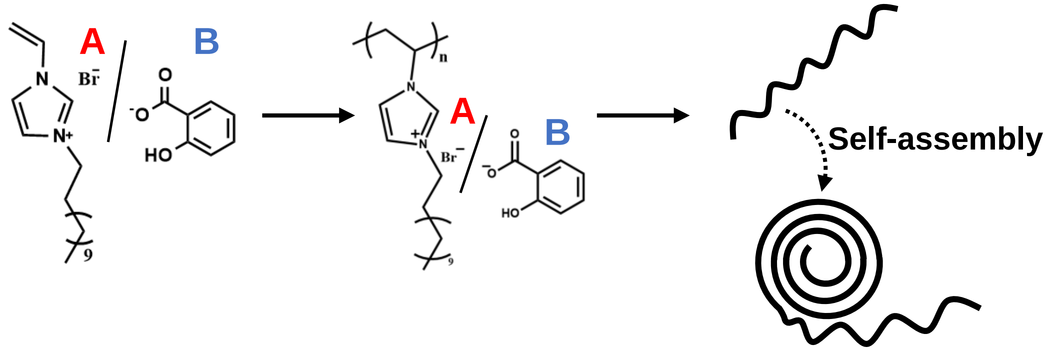
Results confirmed antibacterial and anti-inflammatory effects, and reparative macrophage differentiation

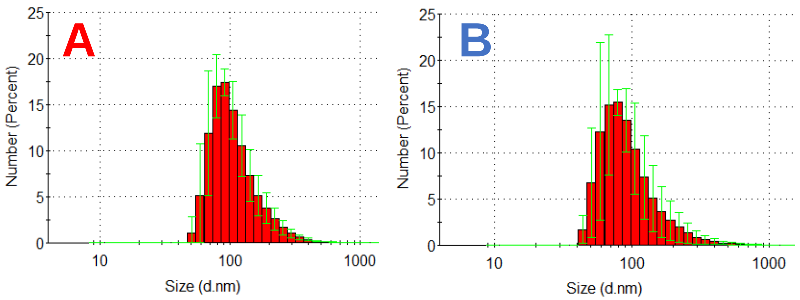


Current work: Polymeric Ionic Liquids Nanoparticles

Objective: Synthesis and biological evaluation of Polymeric Ionic Liquids Nanoparticles (PILs NPs)

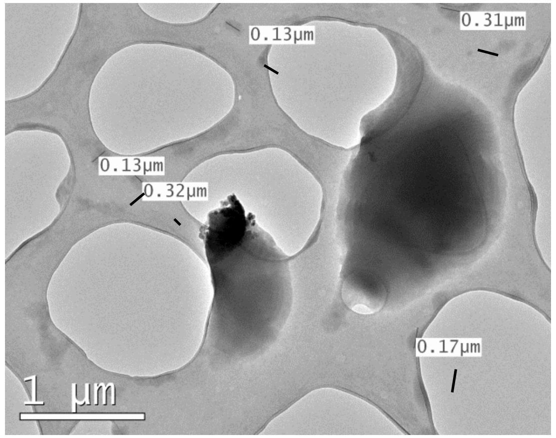
Currently optimising the synthesis and characterization of the PILs NPs.

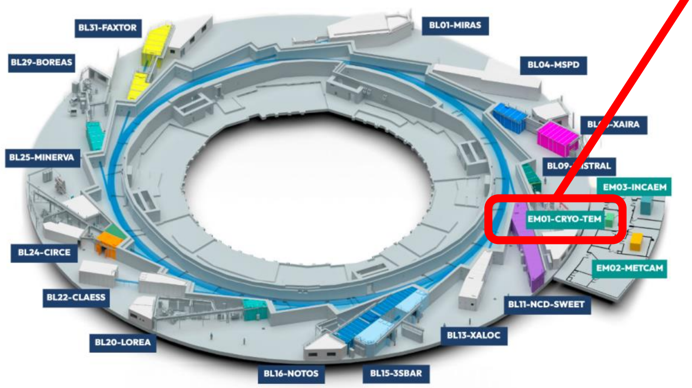




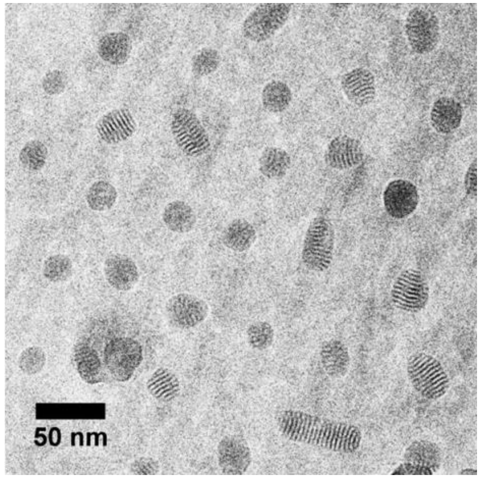
≈ 100 nm in both cases

Conventional TEM = Bad imaging



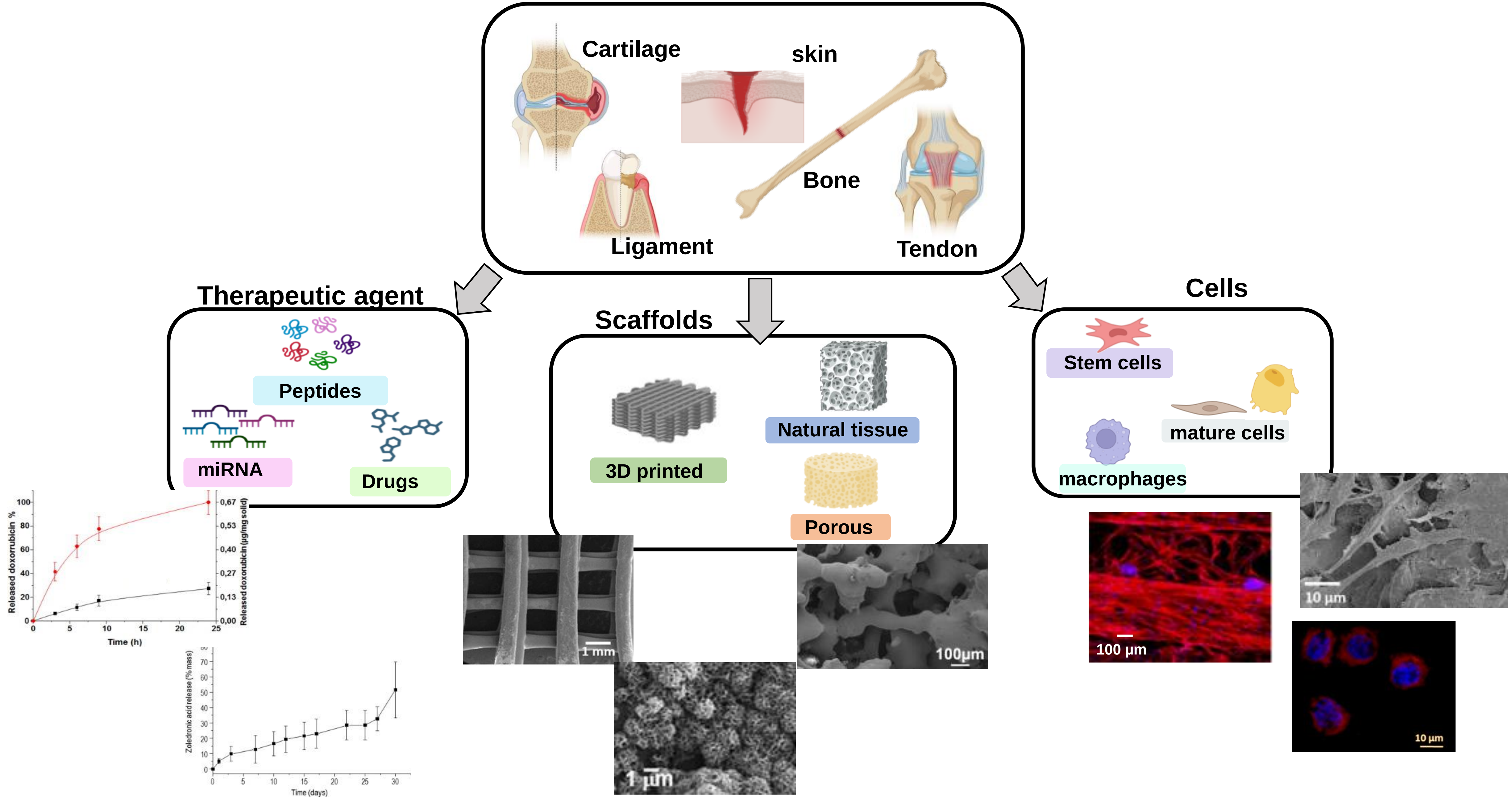


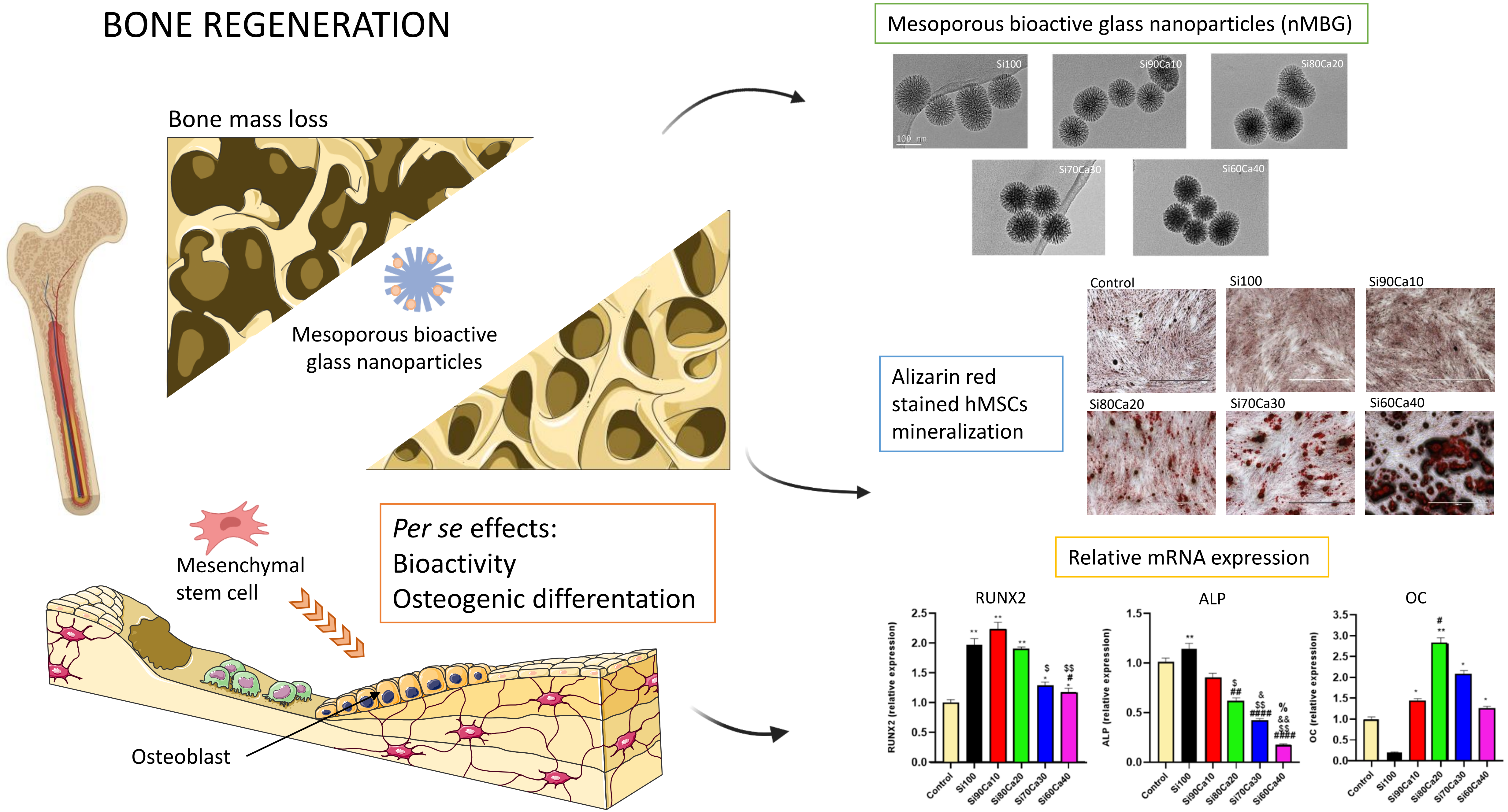
Cryo-TEM



ACS Nano (**2016**), 10, 8, 7731–7737

Macroporous scaffolds for tissue regeneration





BONE REGENERATION
Bone mass loss
Mesoporous bioactive glass nanoparticles
Mesenchymal stem cell
Osteoblast
Per se effects:
Bioactivity
Osteogenic differentation
Mesoporous bioactive glass nanoparticles (nMBG)
Si100
Si90Ca10
Si80Ca20
Si70Ca30
Si60Ca40
100 nm
Alizarin red stained hMSCs mineralization
Control
Si100
Si90Ca10
Si80Ca20
Si70Ca30
Si60Ca40
Relative mRNA expression
RUNX2
ALP
OC
RUNX2 (relative expression)
ALP (relative expression)
OC (relative expression)
Control
Si100
Si90Ca10
Si80Ca20
Si70Ca30
Si60Ca40

Pleiotrophin-Loaded Mesoporous Silica Nanoparticles as a Potential Treatment for Senescence-related Osteoporosis

Osteoporosis - Senescence

Bone density

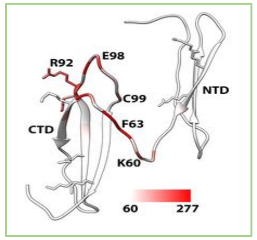
Risk of fracture

Reactive Oxygen Species
Oxidative stress
Senescence

Limitations and problems with conventional treatments

ALTERNATIVES

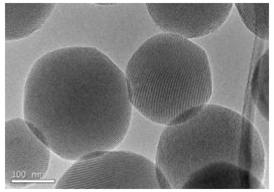
Pleitrophin (PTN)



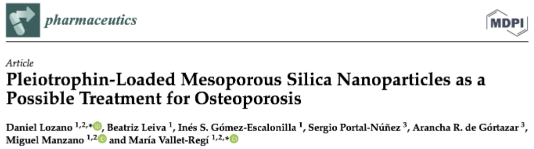
Mitogenic, angiogenic and chemogenetic activity

Nanomedicine: MSNs

To deliver PTN to specific bone tissues to obtain optimal concentrations



Background

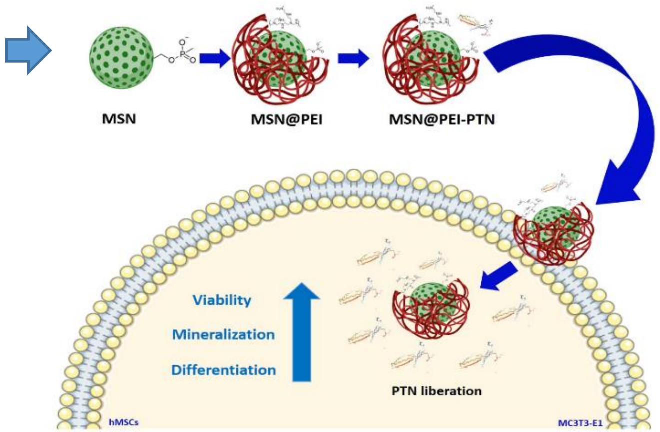

pharmaceutics

MDPI

Article

Pleiotrophin-Loaded Mesoporous Silica Nanoparticles as a Possible Treatment for Osteoporosis

Daniel Lozano [1,2,*], Beatriz Leiva [1], Inés S. Gómez-Escalonilla [1], Sergio Portal-Núñez [3], Arancha R. de Górtazar [3], Miguel Manzano [1,2] and María Vallet-Regí [1,2,*]

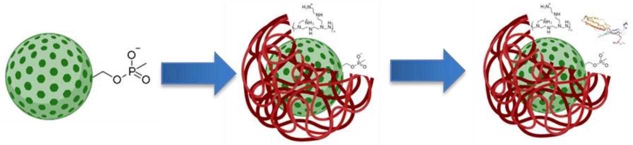


Objective

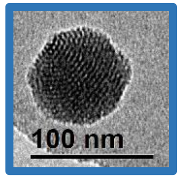
To develop a nanocarrier based on MSNs that exert a protective action of the deleterious effect of senescence-related osteoporosis

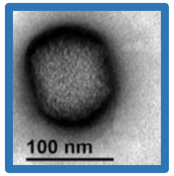
Synthesis and Physico-chemical characterization

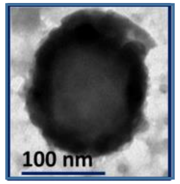
Polimeric coating whith Polyethylenimine (PEI)



MSNs MSN@PEI MSN@PEI-PTN







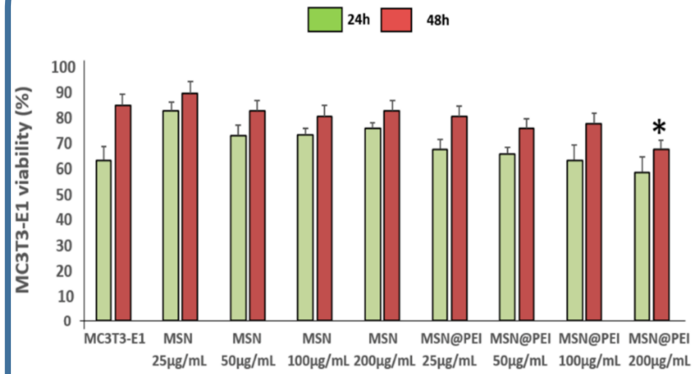
PTN LOADED by ADSORPTION (24h)

UNIVERSIDAD COMPLUTENSE MADRID

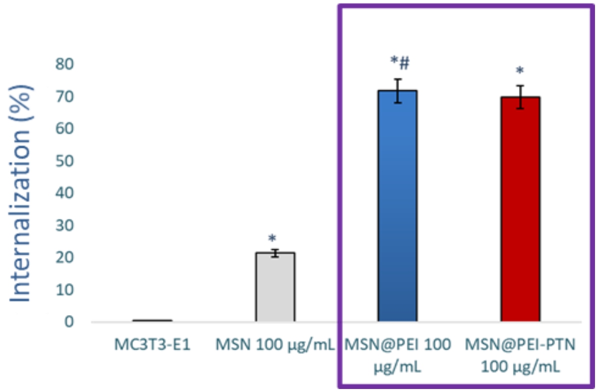
Pleiotrophin-Loaded Mesoporous Silica Nanoparticles as a Potential Treatment for Senescence-related Osteoporosis

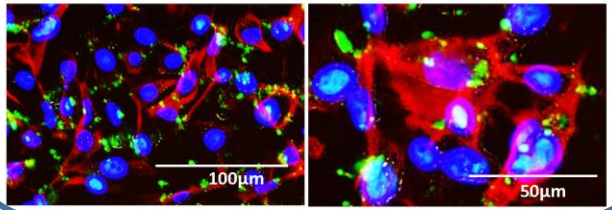
ALBA

Cell Viability: no toxicity



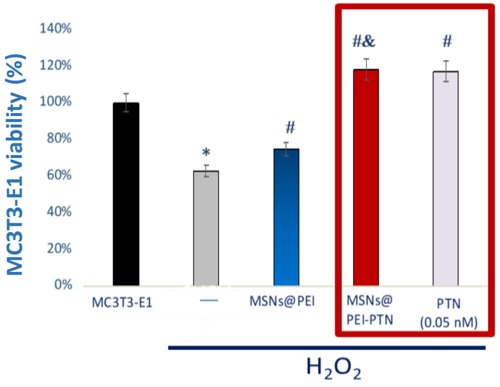
Improved cell Internalization

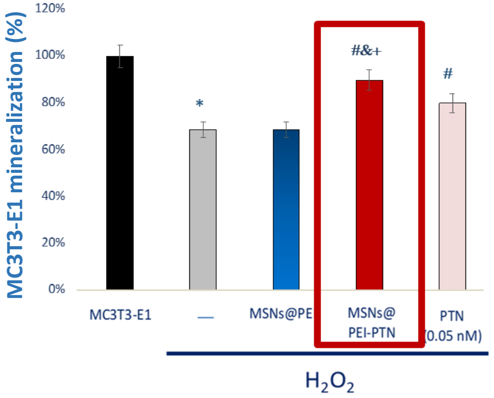




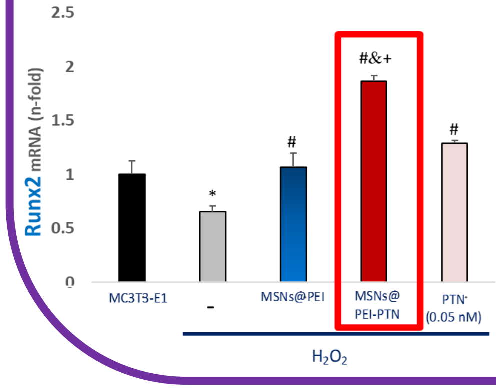
Senescence model induced by H_2O_2

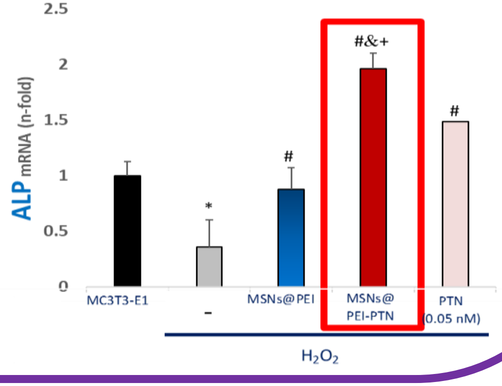
MSN@PEI-PTN protect against the deleterious effect of senescence in viability and mineralization





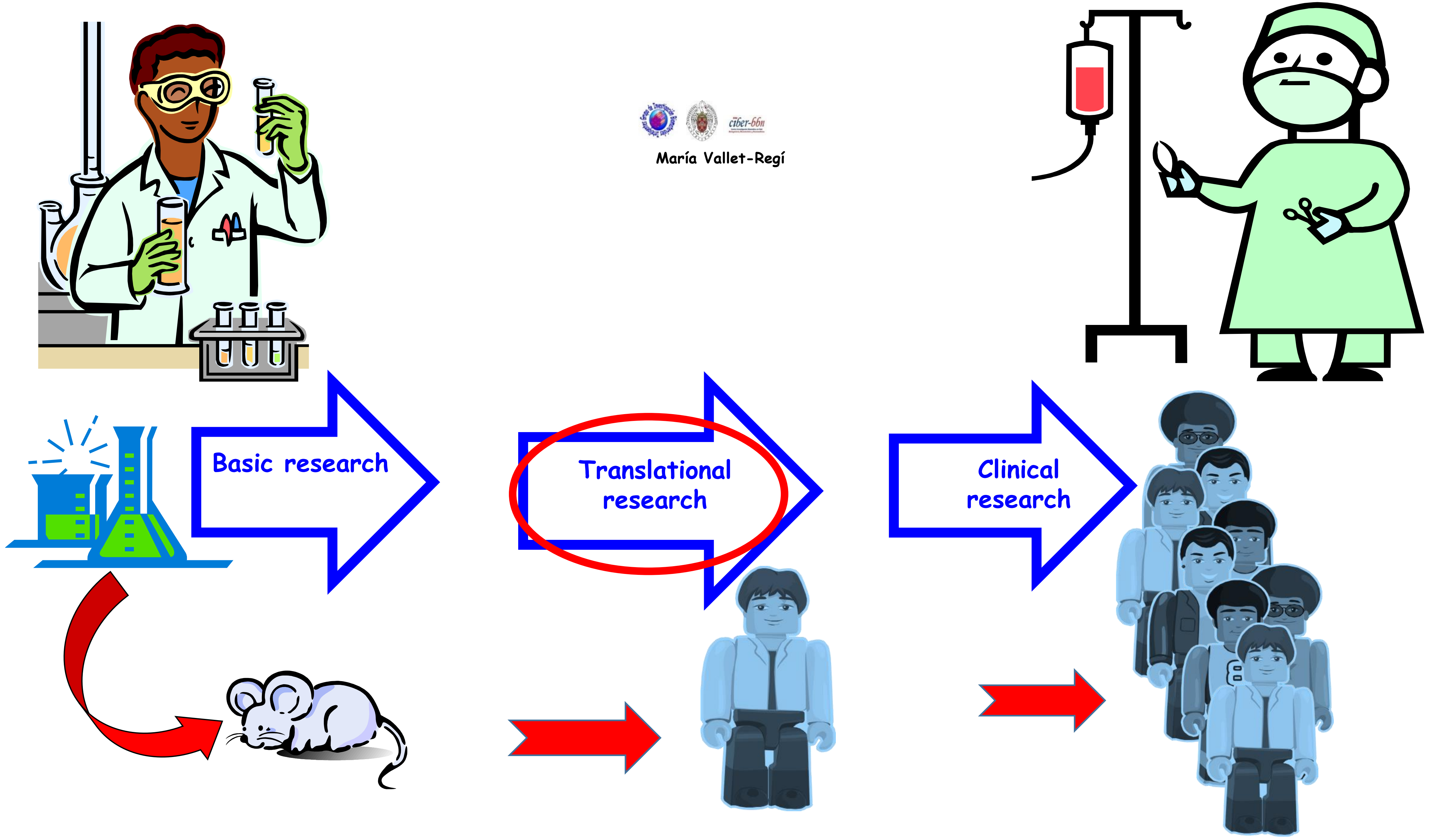
MSN@PEI-PTN protect against the deleterious effect of senescence in cell differentiation (gene expression)





p*<0.05 vs MC3T3-E1; #<0.05 vs MSNs

P*<0.05 vs control MC3T3-E1; #p<0.05 vs H2O2; &p<0.05 vs MSNs@PEI; +p<0.05 vs PTN


María Vallet-Regí
Basic research
Translational research
Clinical research


SOLO NO….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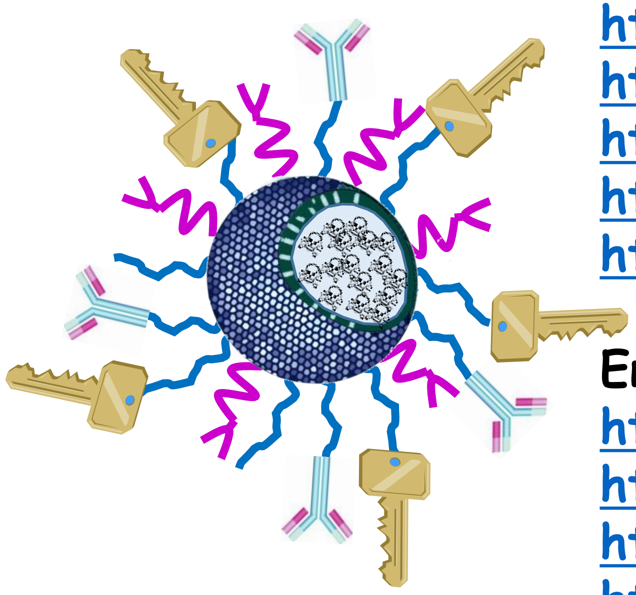
Champion

María Vallet-Regí



En Inglés

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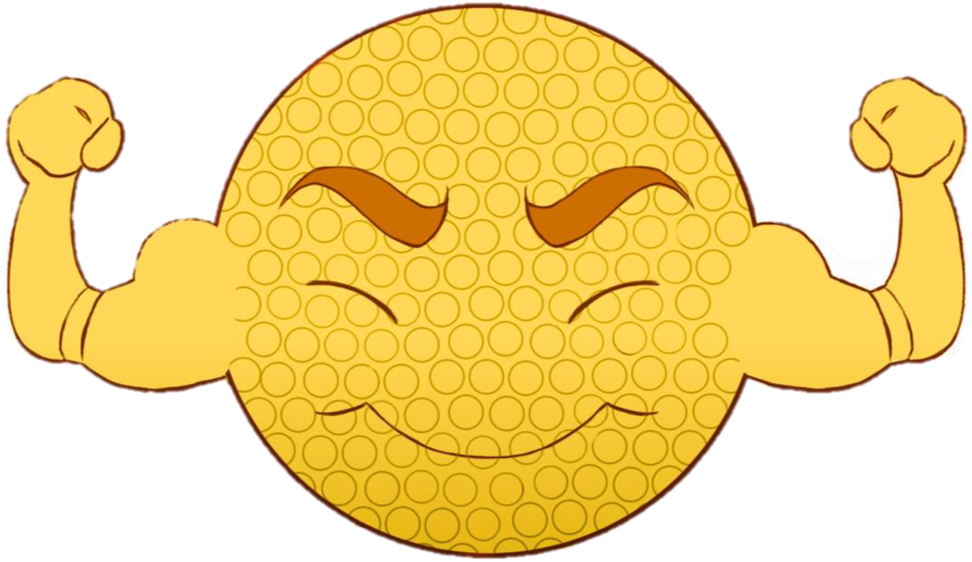

En Español

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