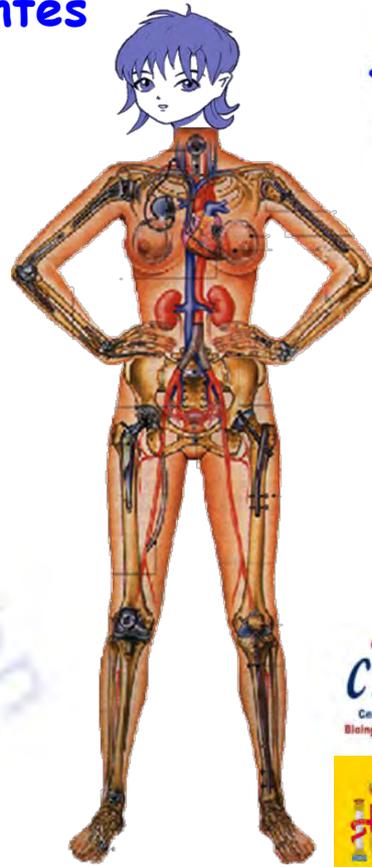


Biomateriales: avances recientes

María Vallet-Regí

<http://www.valletregigroup.esy.es>



V Curso de divulgación



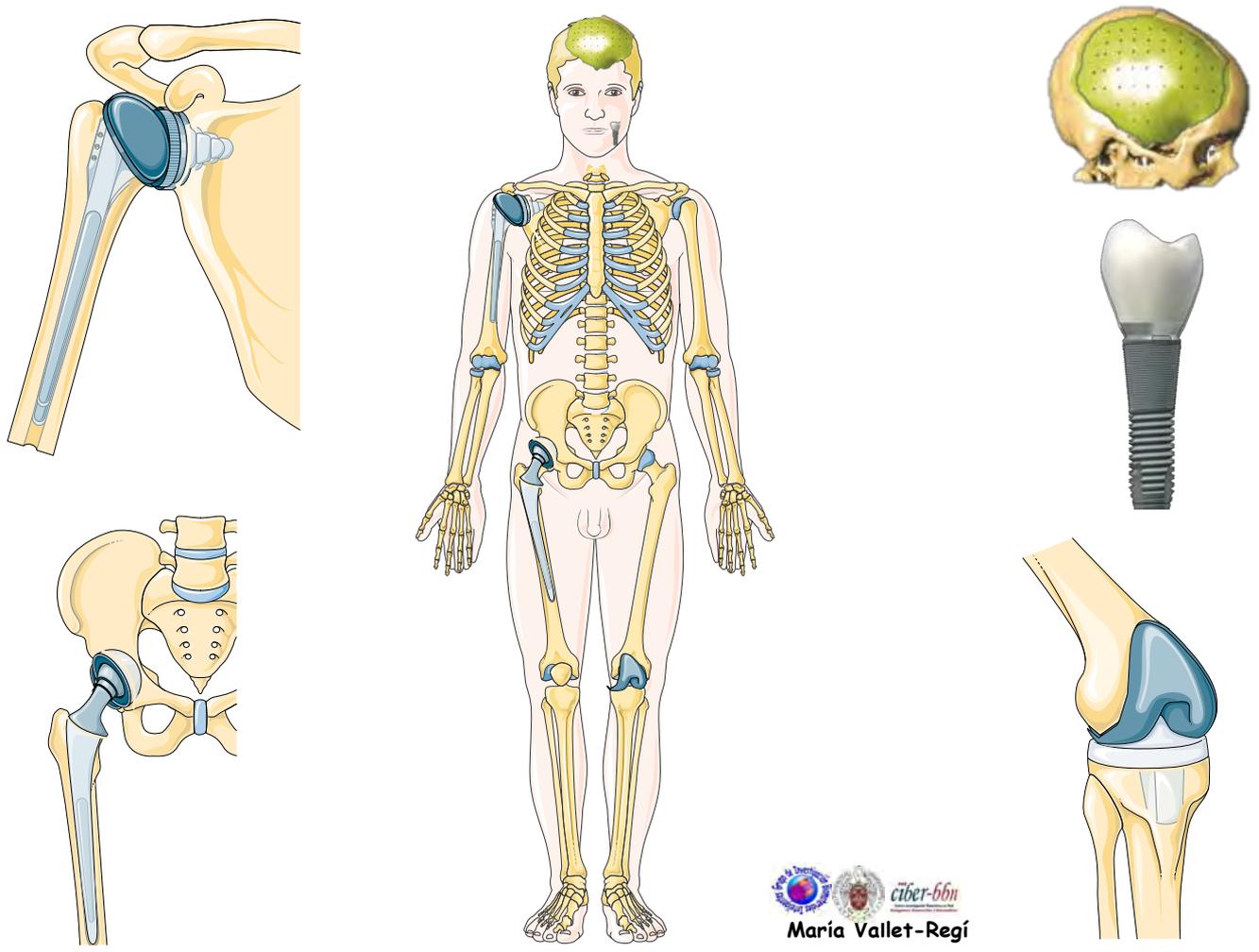
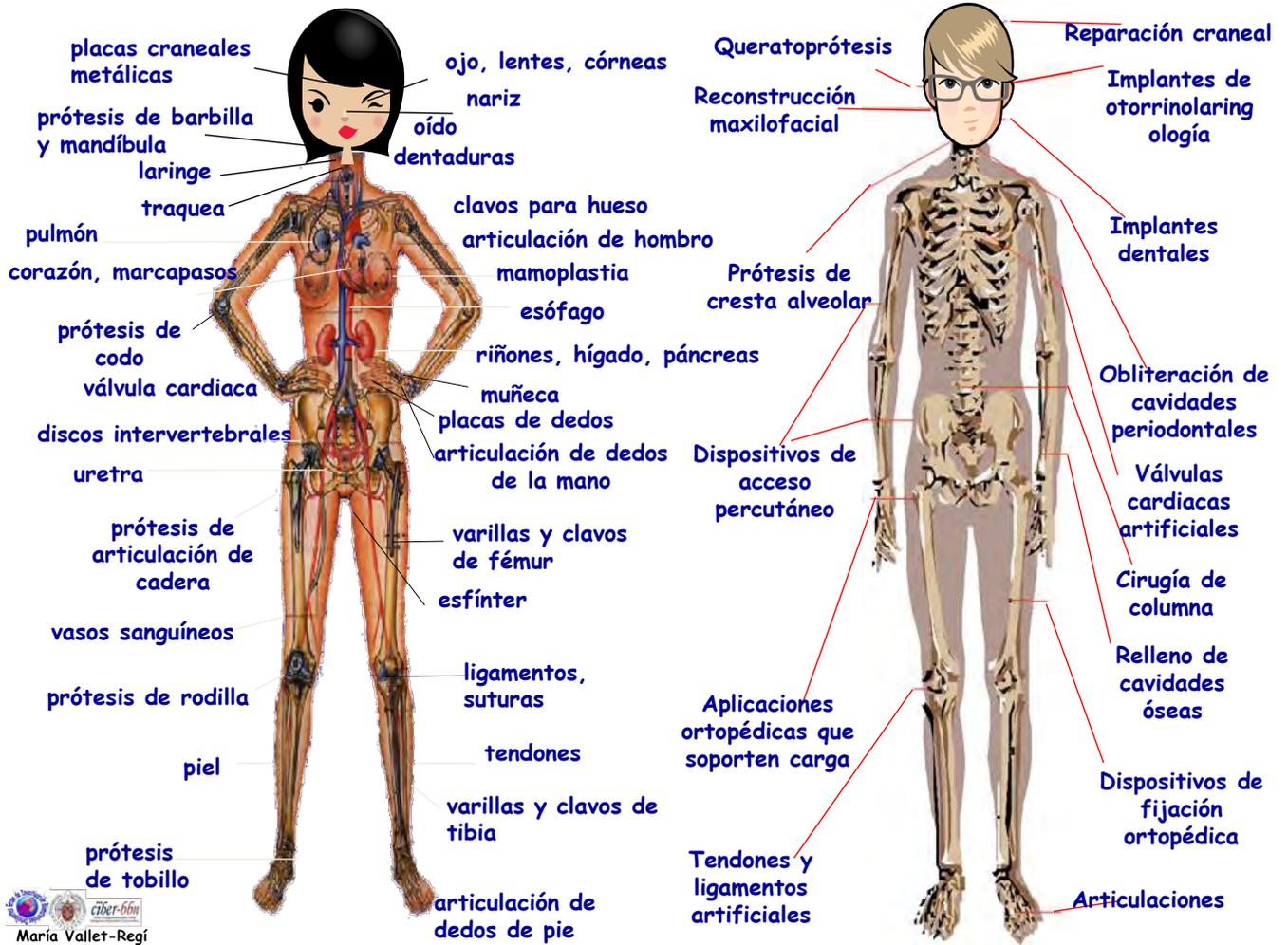
Los Avances de la Química y su Impacto en la Sociedad

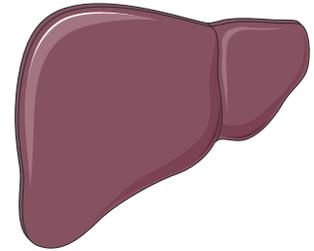
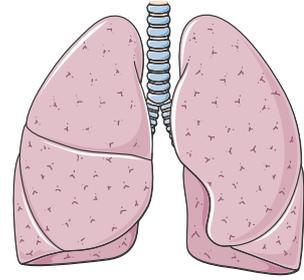
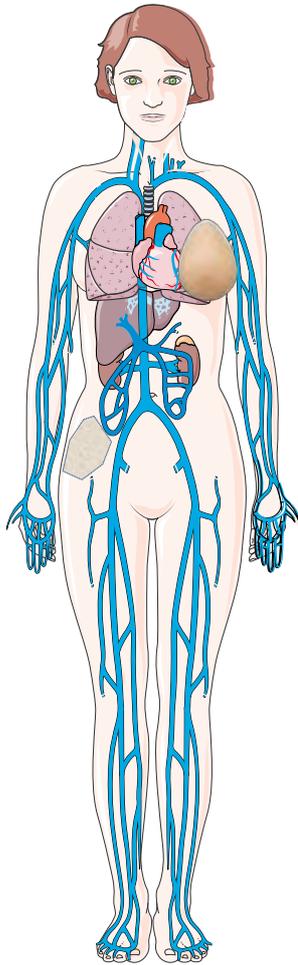
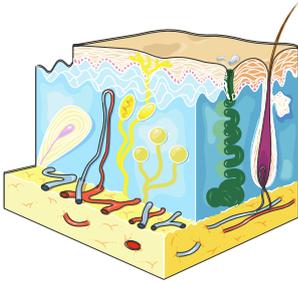
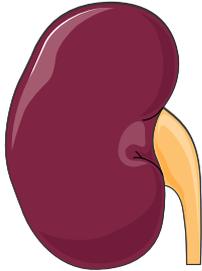
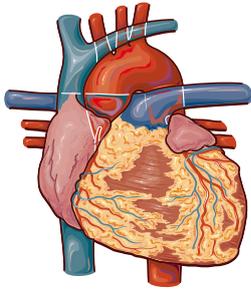
V Edición del Curso de Divulgación

Los Avances de la Química y su Impacto en la Sociedad

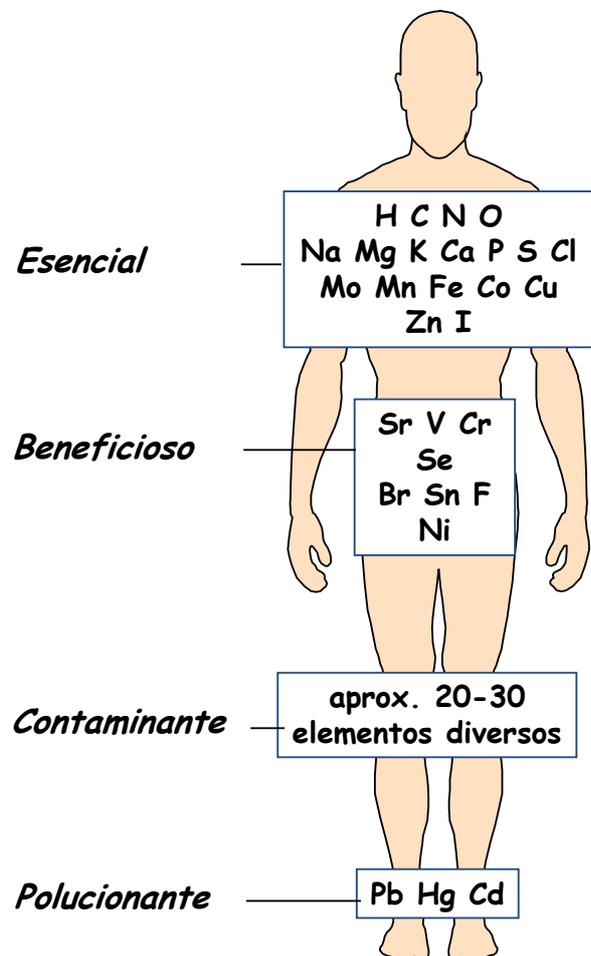
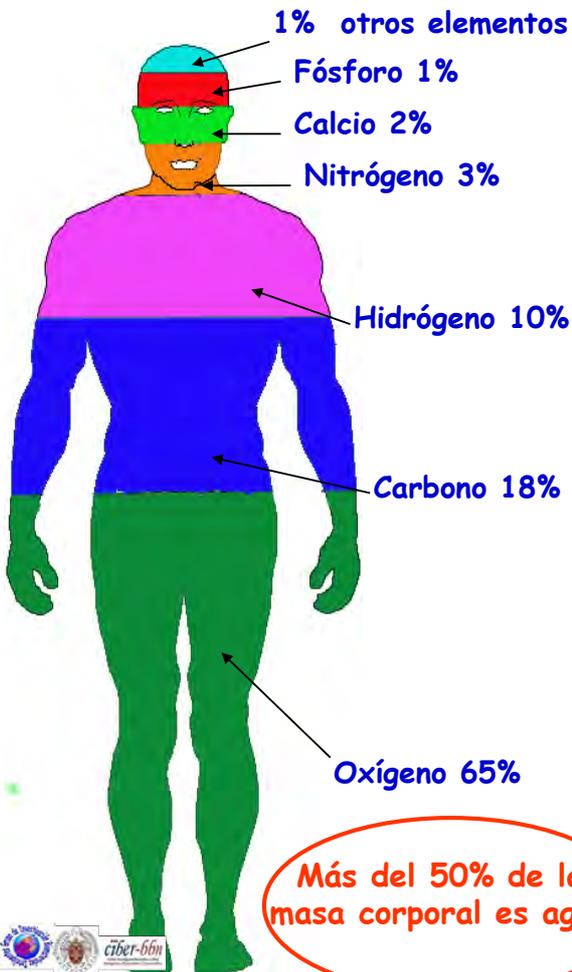
Madrid, 18 de febrero 2016







María Vallet-Regí



Esperanza de vida

Roma Imperial:
22 años

Principios de siglo XX
40 años

Final siglo XX
80 años

España 2015
83,2



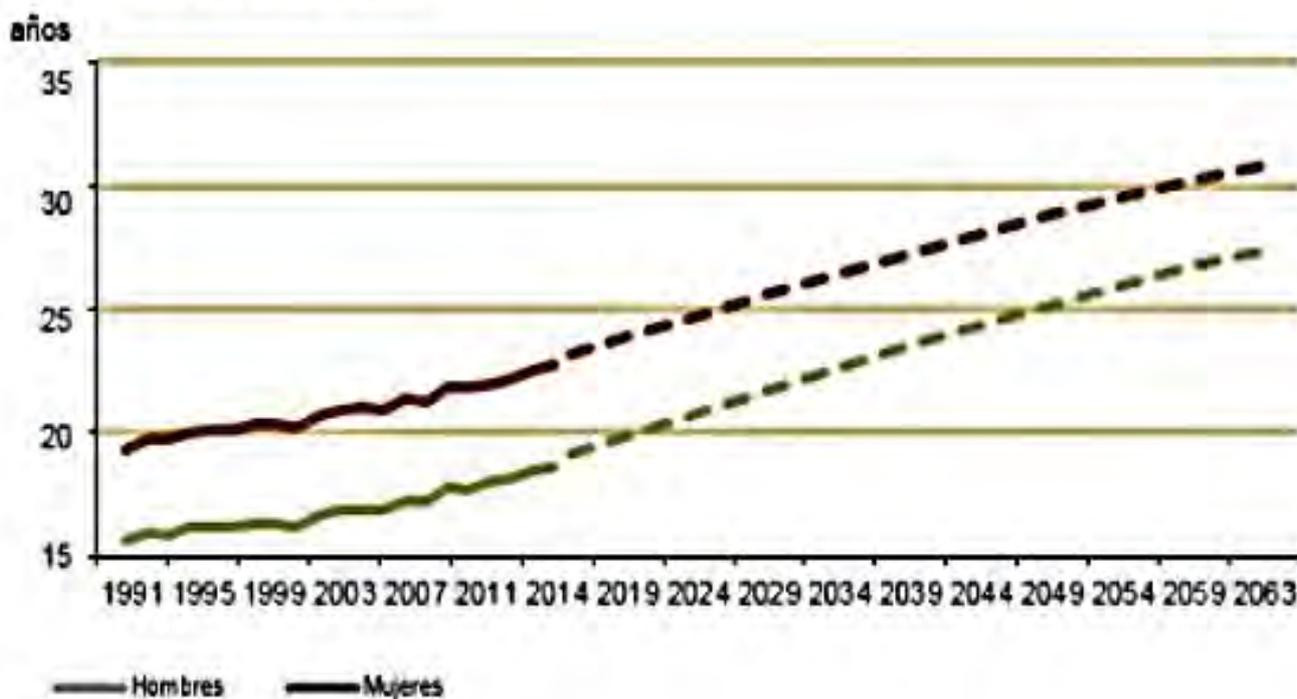
CUÁNTO VIVEN

Mosca	17 días
Abeja	10 semanas
Musaraña	1 año
Araña	4 años
Rata	6 años
Perro	16 años
Jirafa	20 años
Oca	30 años
Oso	40 años
Cocodrilo	55 años
Elefante asiático	60 años
Humano	78 años
Tortuga	150 años
Palmera	200 años
Olivo	1.000 años
Castaño pedunculado	2.000 años
Ciprés de lawson	3.000 años
Secuoya gigante	6.000 años

*J. Hitzig:
El organismo humano
está programado para
durar de 100 a 120
años*

Proyección de la esperanza de vida a los 65 años. Brecha de género. España

Esperanza de vida a los 65 años



Fuente: Proyecciones de población. INE

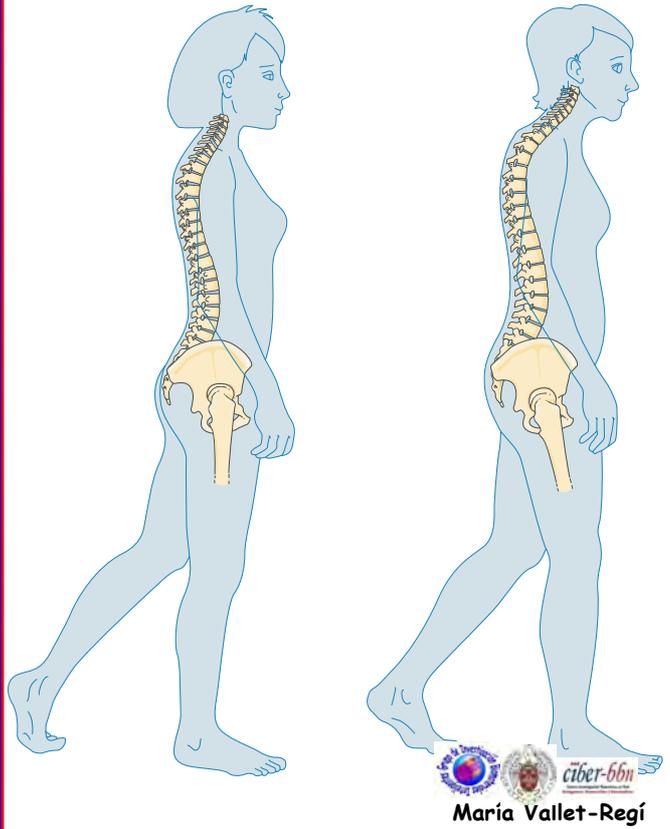
ESPERANZA DE VIDA AL NACER EN ESPAÑA



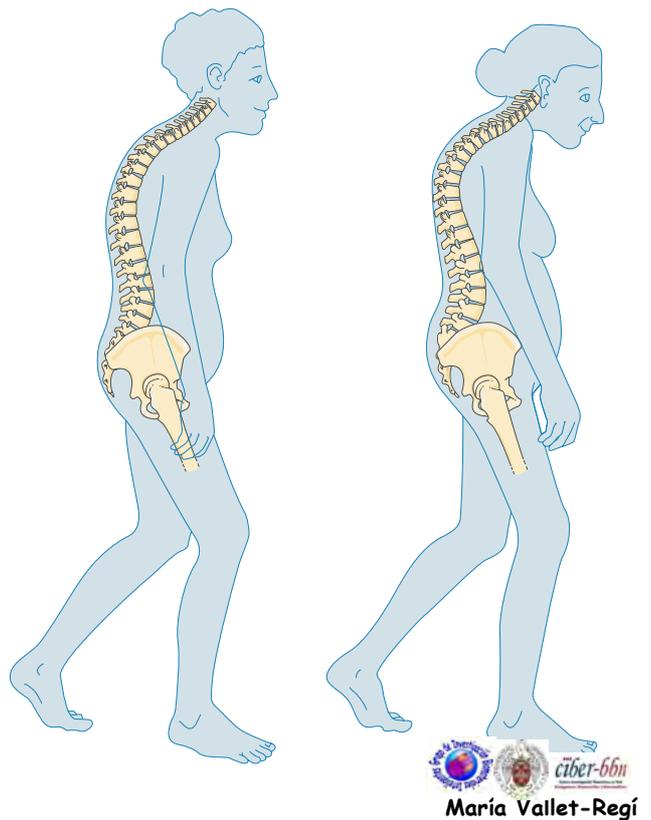
Fuente: Revista Española de Investigaciones Sociológicas.



Adult-Premenopause



Menopause-Osteoporosis





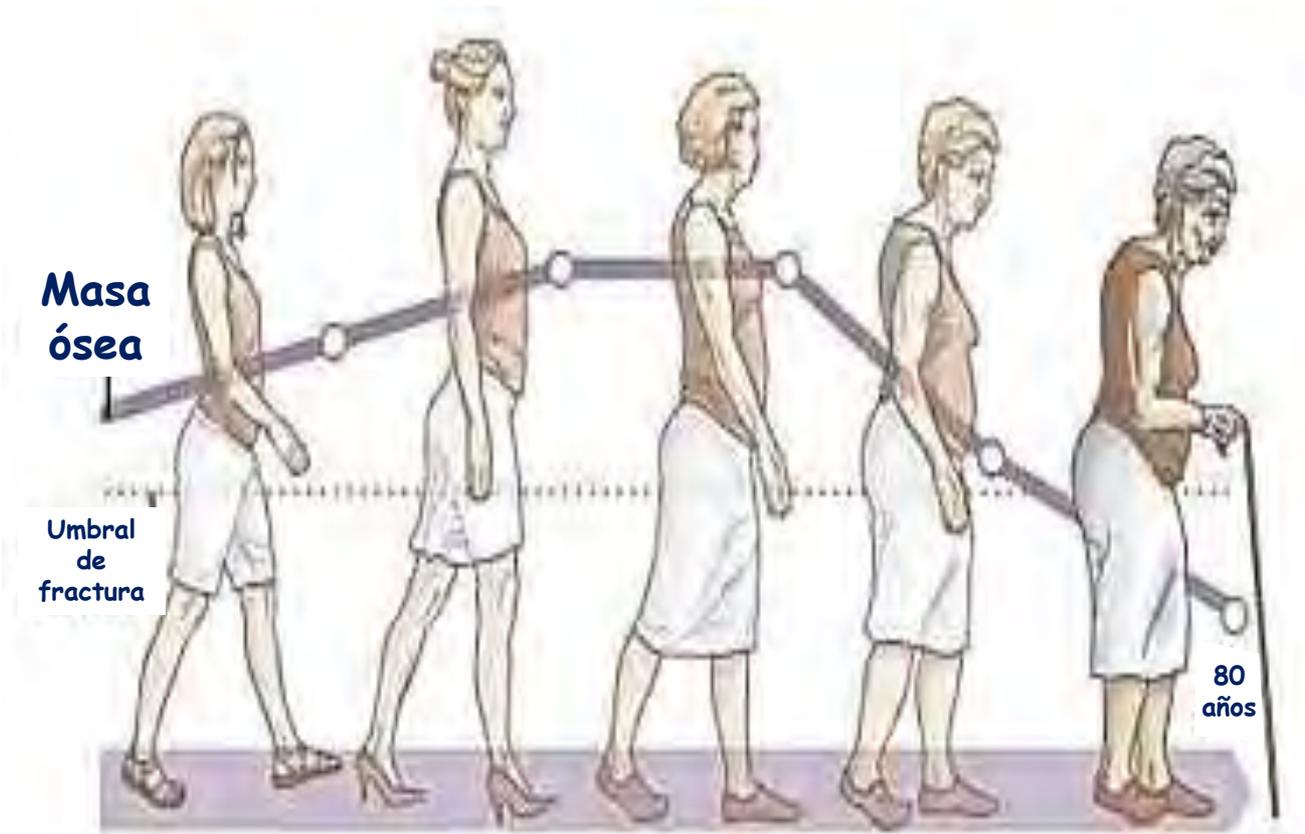
Normal



Osteoporosis

Deterioro del soporte vertebral



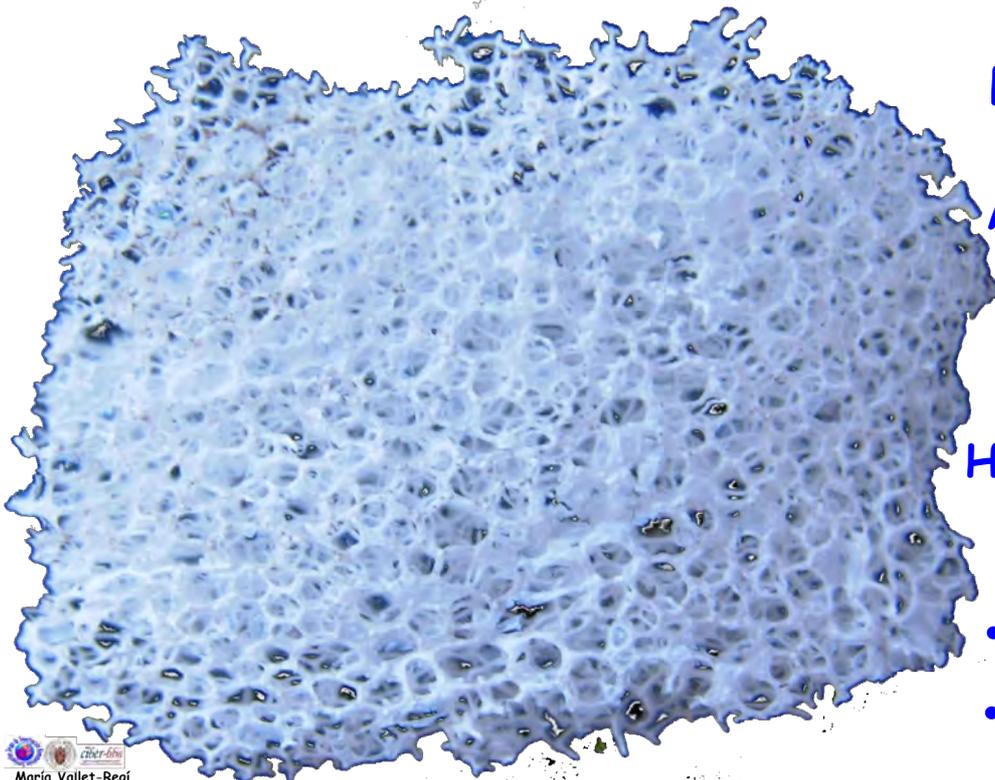




 María Vallet-Regí

Síntesis de HA macroporosa:

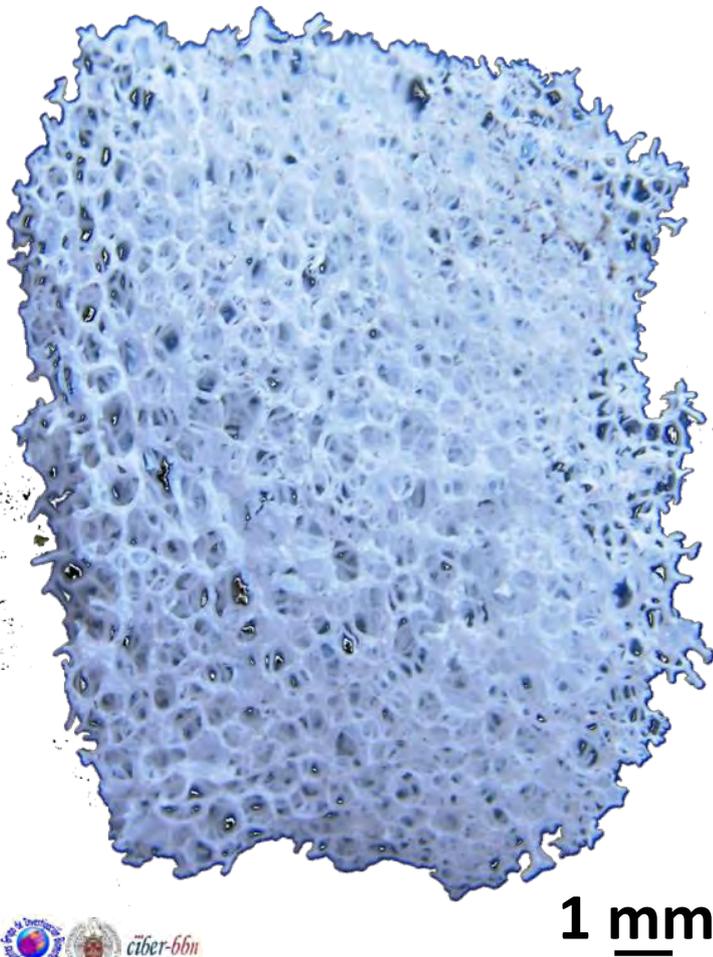
Método sol gel
 +
 Pluronic F127
 agente
 inductor de la
 porosidad



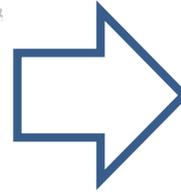
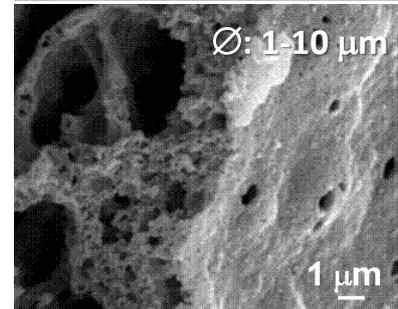
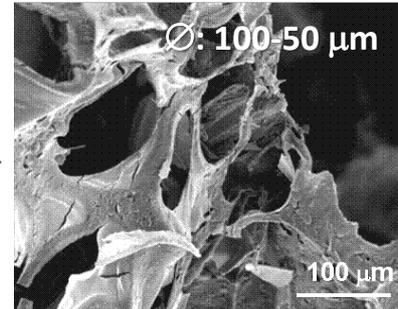
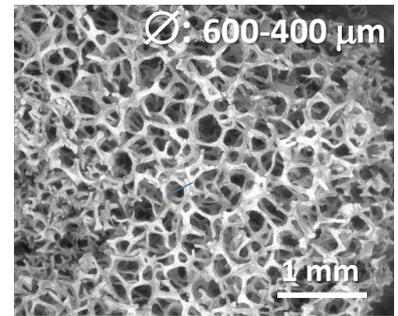
HA nanocristalina
 Rango de
 porosidad:
 • 10-15 nm
 • 1- 400 μm



 María Vallet-Regí



María Vallet-Regí

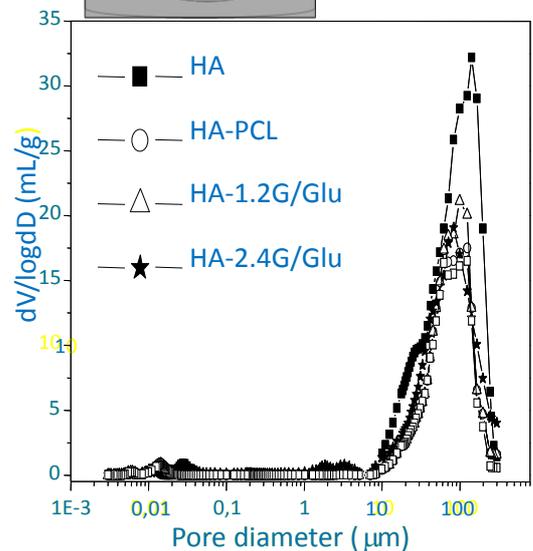
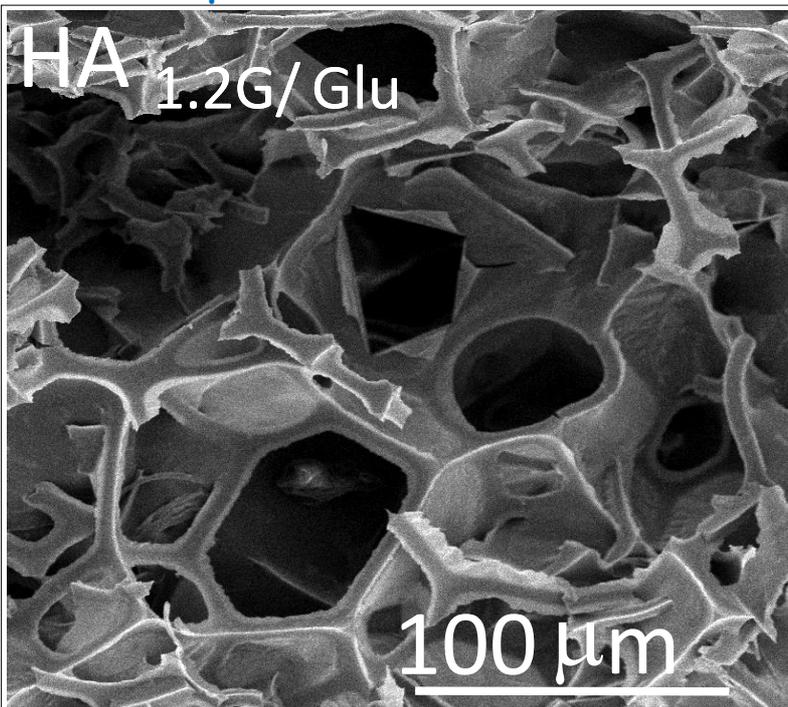
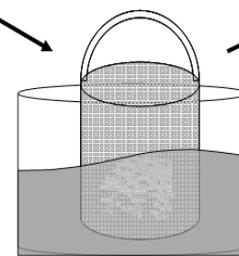


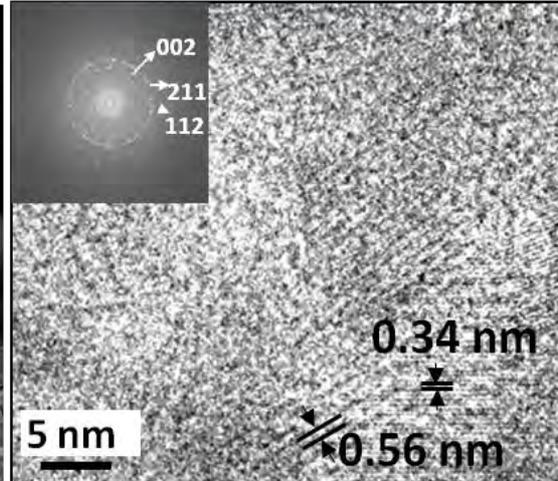
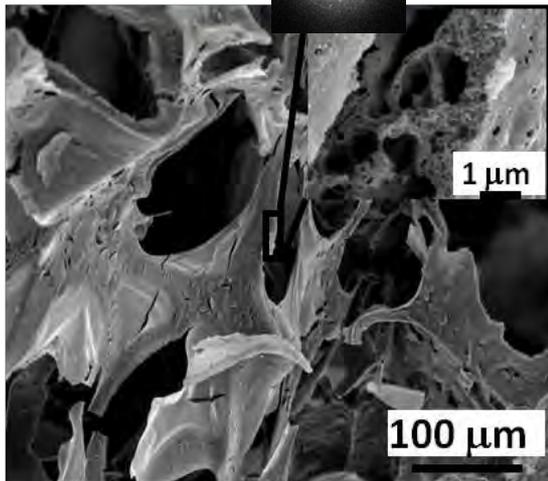
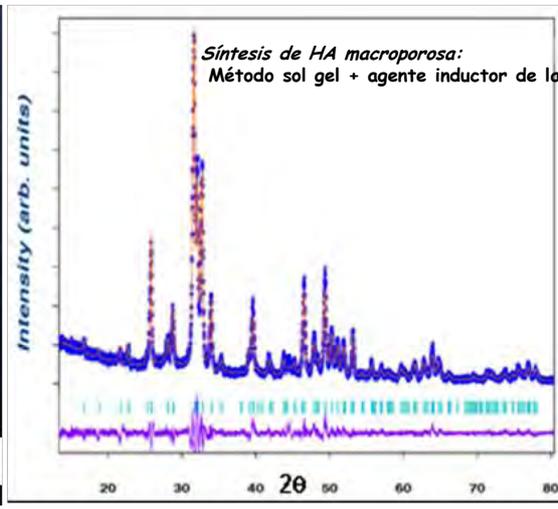
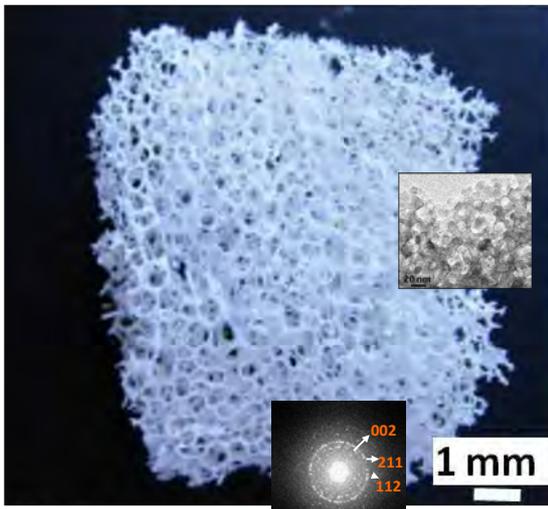
Recubrimiento polimérico:

→ Gelatina entrecruzada con Glutaraldeído (solución acuosa):

1.2; 2.4

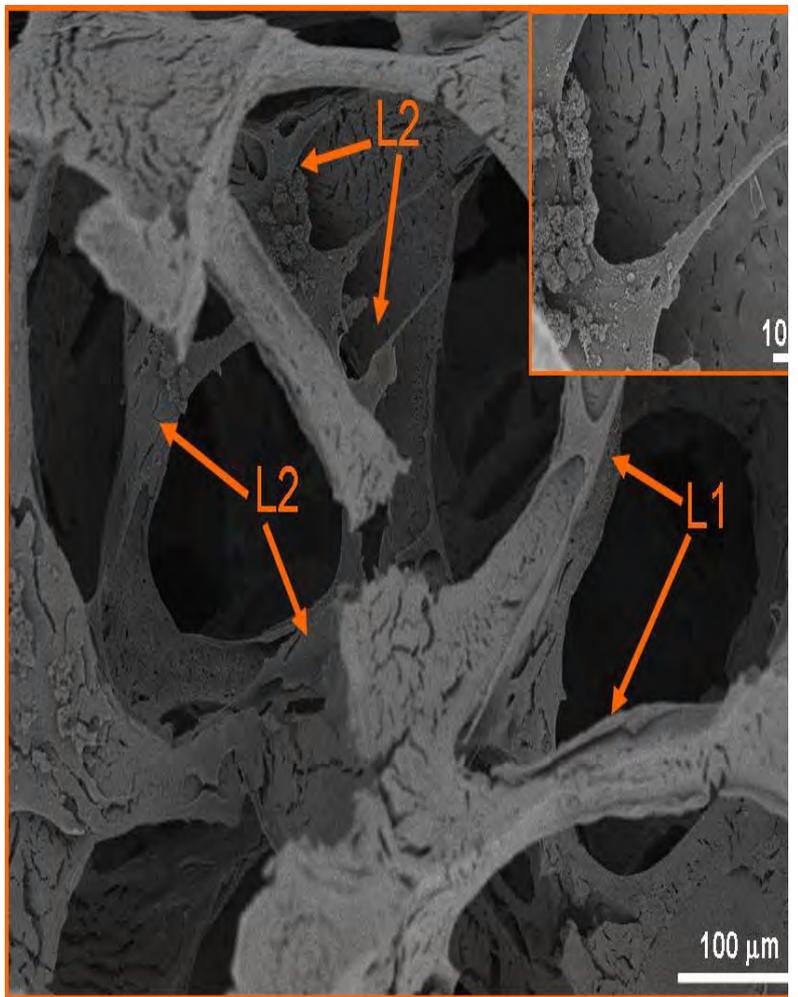
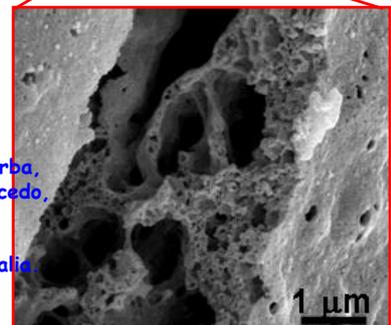
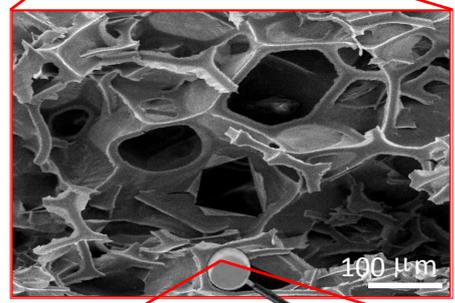
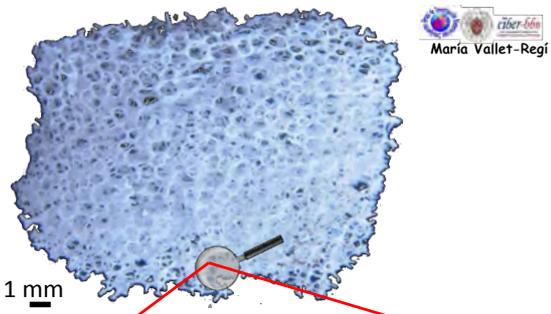
→ ε-Policaprolactona





HA nanocristalina
Rango de porosidad

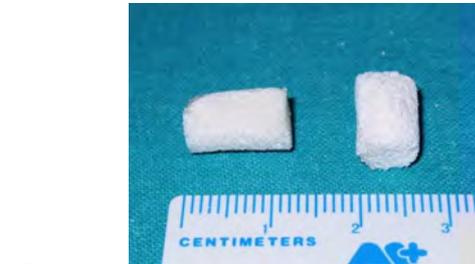
- 10-15 nm
- 1- 400μm



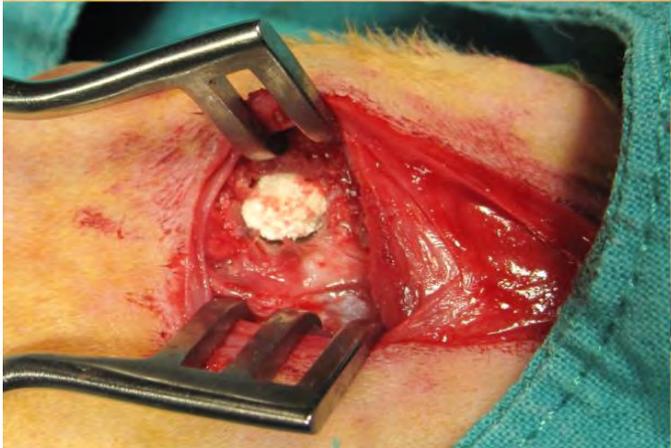
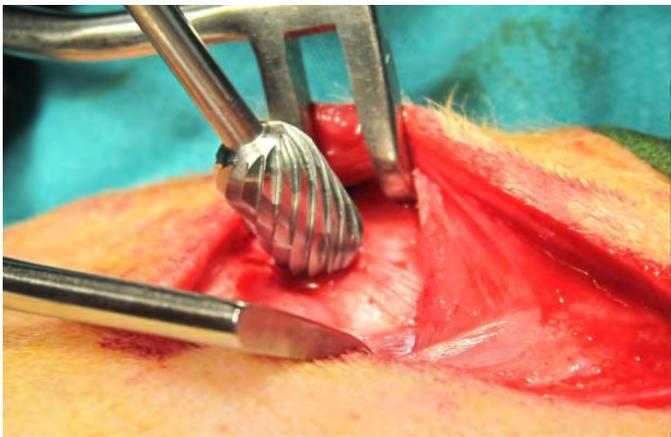
M. Cicuéndez,
I. Izquierdo-Barba,
S. Sánchez-Salcedo,
M. Vila,
M. Vallet-Regí.
Acta Biomaterialia
8, 802-810
(2012).

· Left femur:

- Bone defect 6 mm \varnothing x 10 mm in depth
- HA foam cylinder filling the bone defect

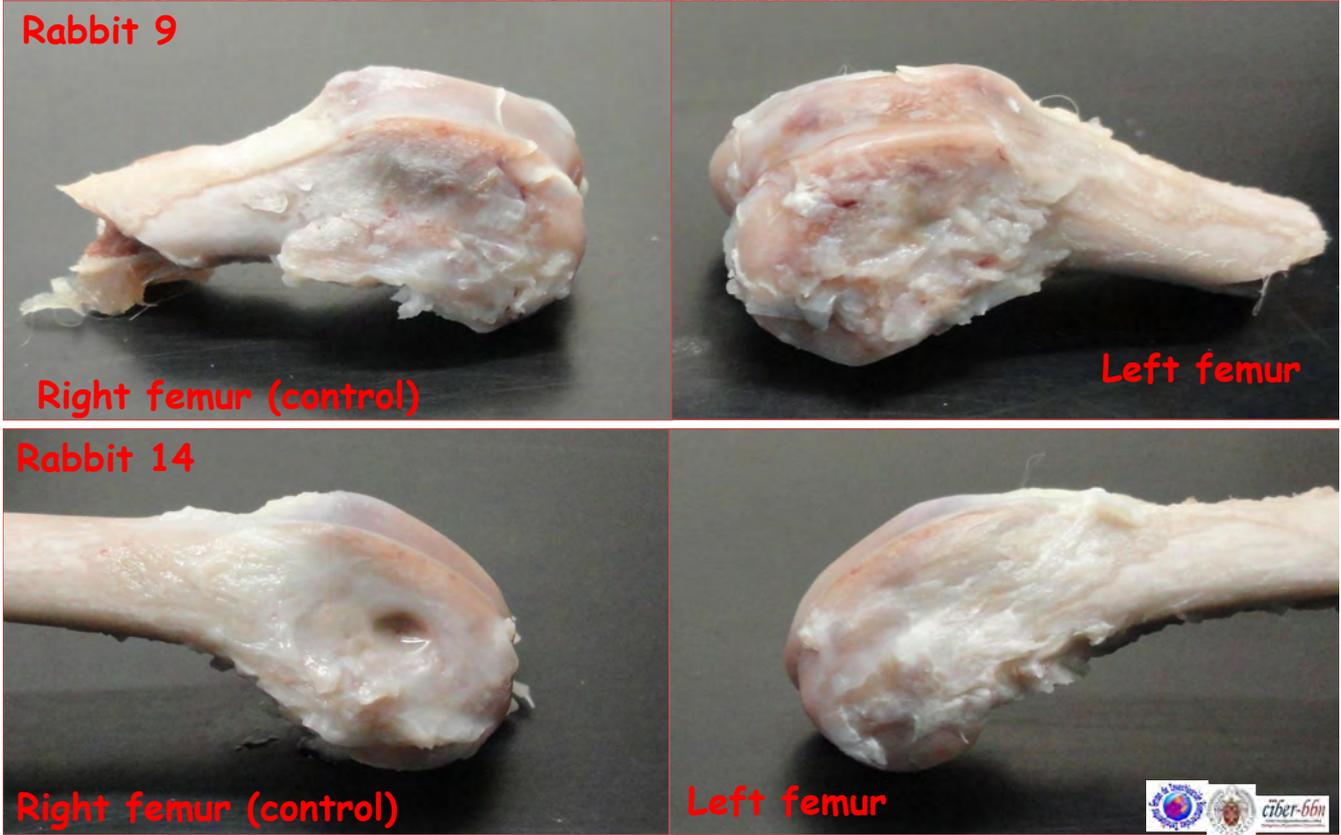


J. Gil-Albarova, M. Vila, J. Badiola, S. Sánchez-Salcedo, A. Herrera, M. Vallet-Regí.
Acta Biomaterialia. 8, 3777-3783 (2012).



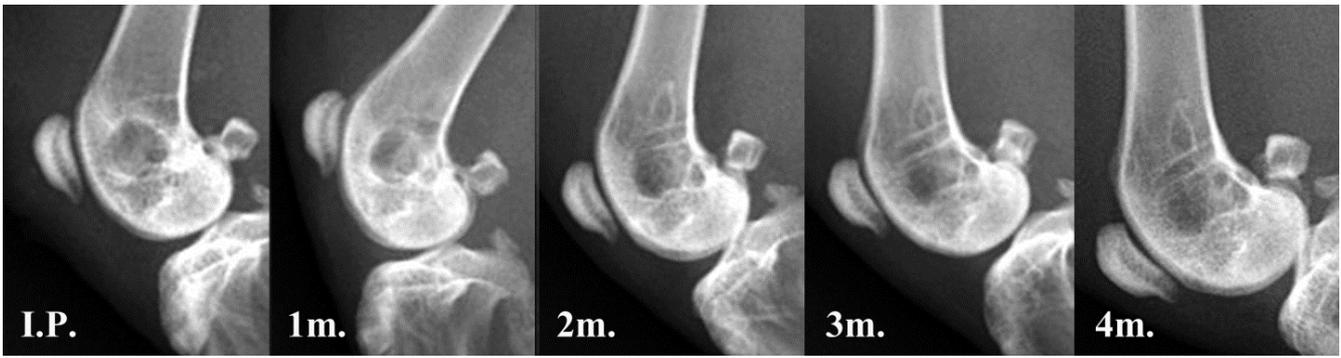
Proceso de implantación de las espumas en la epífisis femoral de conejos de Nueva Zelanda.

- **Macroscopic appearance after scheduled euthanasia :4 months**

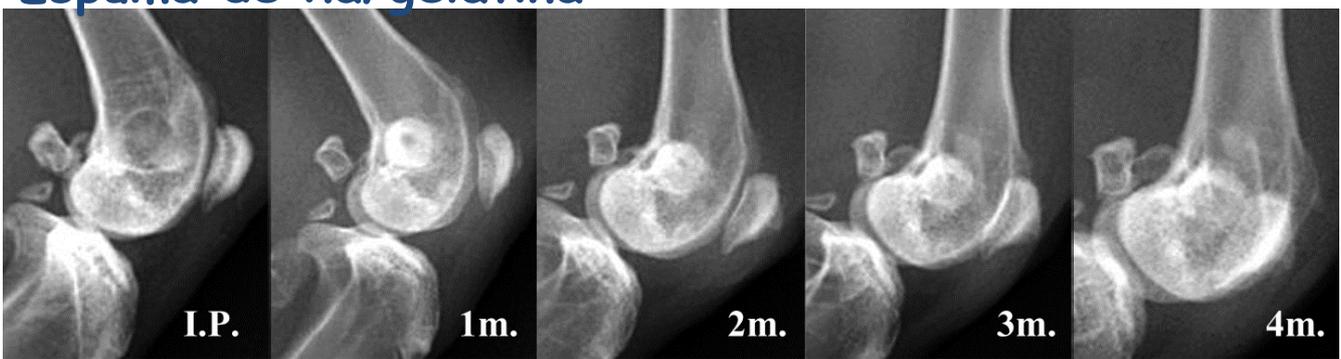


J. Gil-Albarova, M.Vila, J.Badiola-Vargas, S.Sánchez, A.Herrera, M.Vallet-Regí, Acta Biomaterialia. 8, 377-3783(2012). María Vallet-Regí

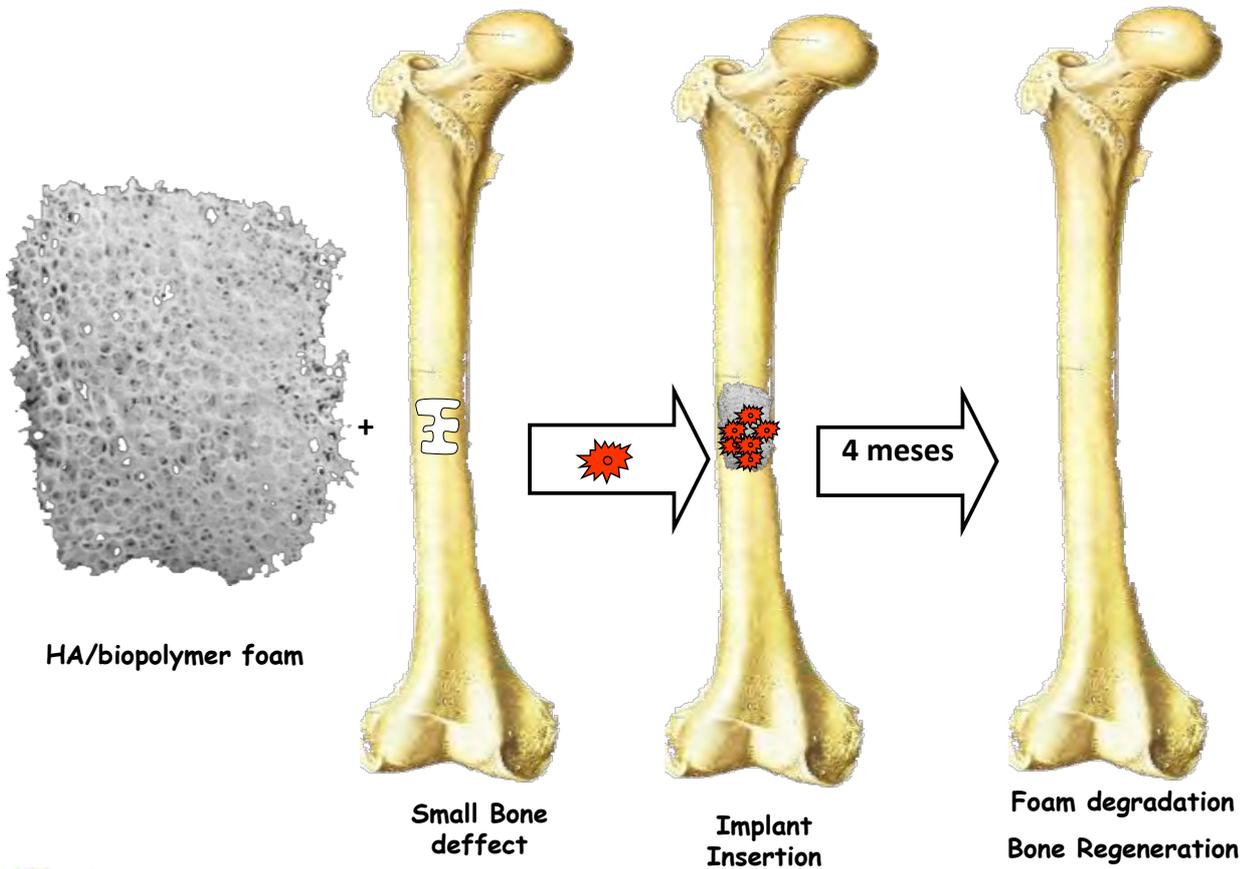
Control



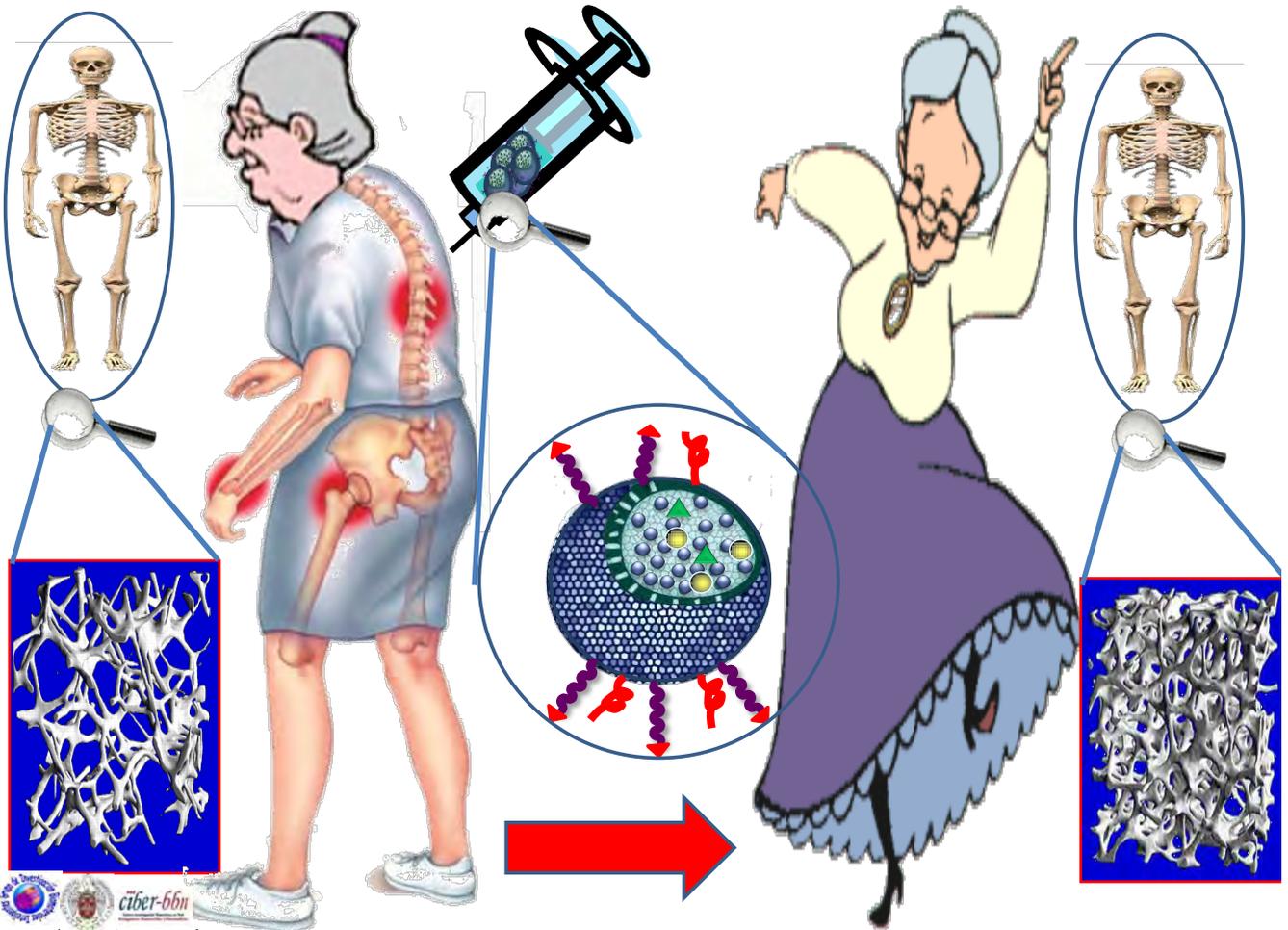
Espuma de ha/gelatina

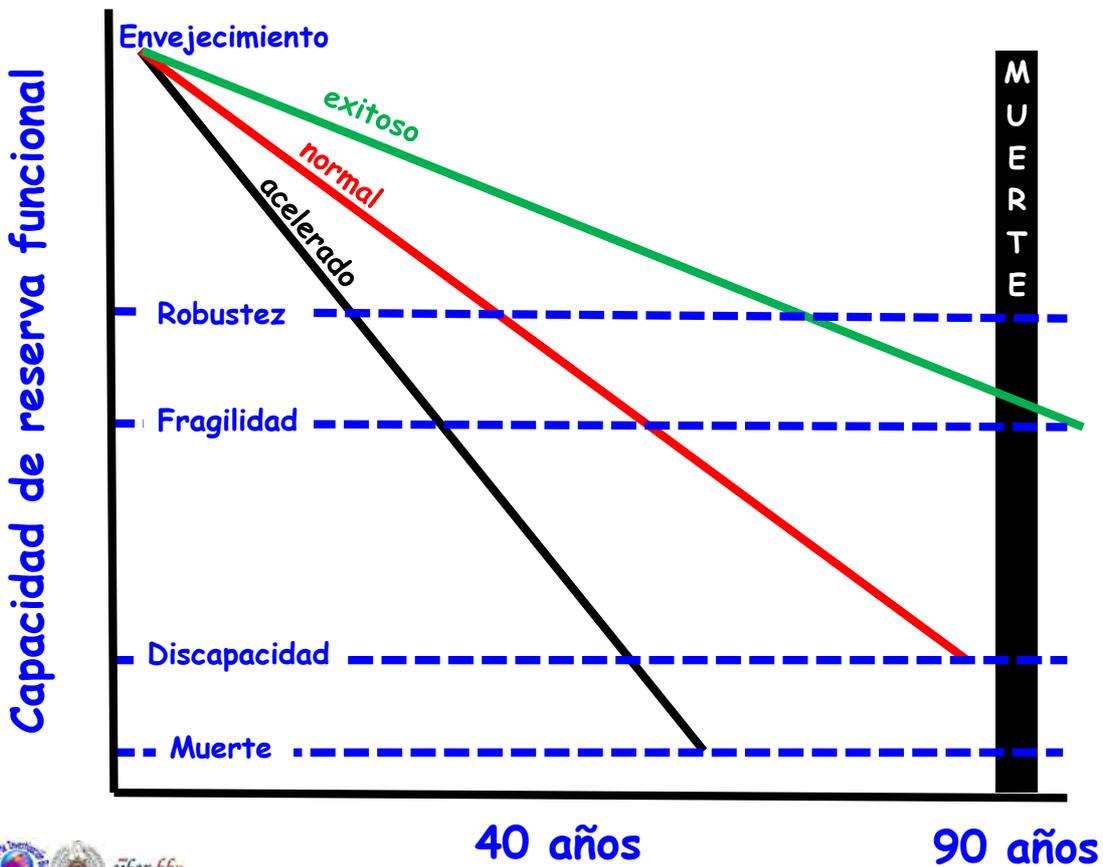
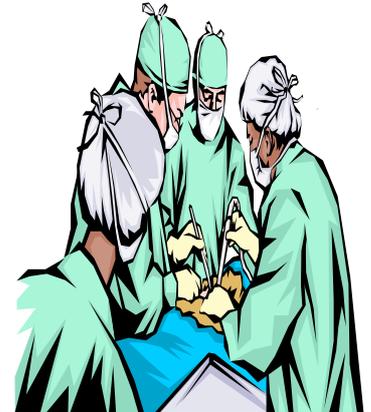


Los estudios radiológicos sugieren una reabsorción de la espuma y regeneración de nuevo hueso tras 4 meses.




 María Vallet-Regí





Reparación del cuerpo humano

Aproximación
biónica

Aproximación
medicina regenerativa

Prótesis e implantes
*Ortopedia, Oftalmología,
Cardiología, Vascular,
Cirugía Estética,
Odontología, Urología, etc.*

1ª y 2ª generación



Reparación del cuerpo humano

Aproximación
biónica

Aproximación
medicina regenerativa

Terapia
celular

Ingeniería
de
tejidos

3ª generación

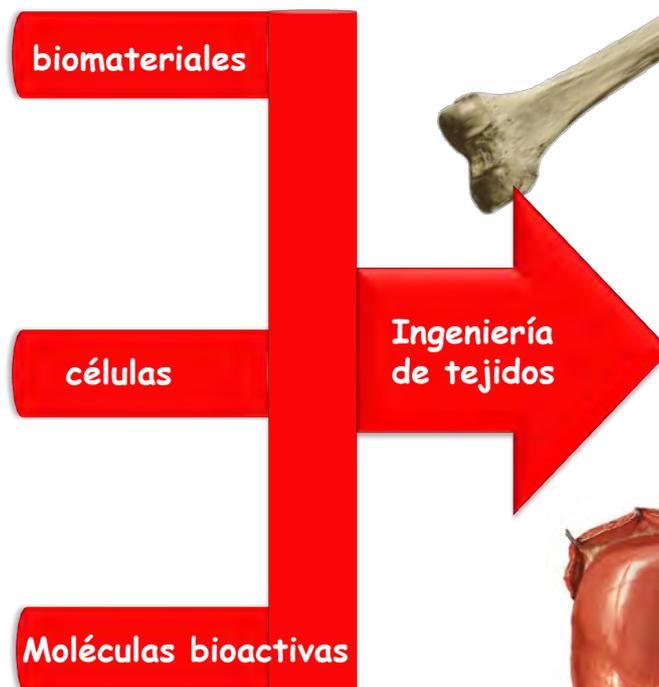
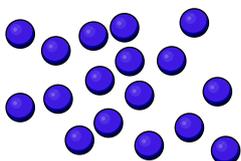
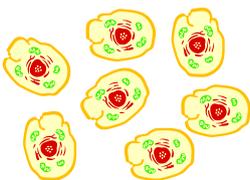
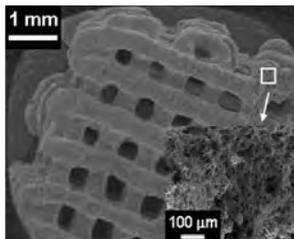


-He oído que los científicos están creciendo órganos humanos en placas de laboratorio

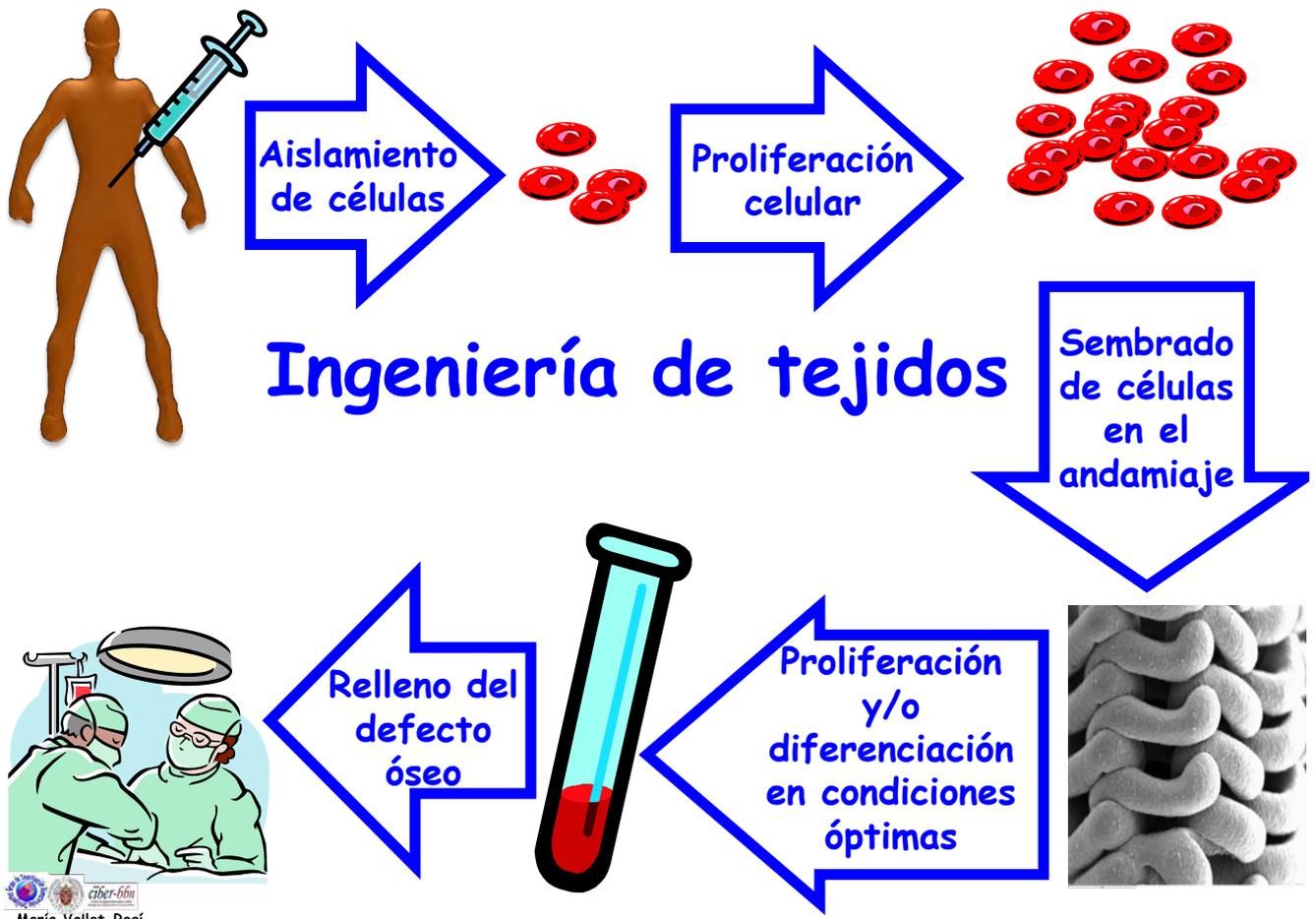
-¿es verdad?



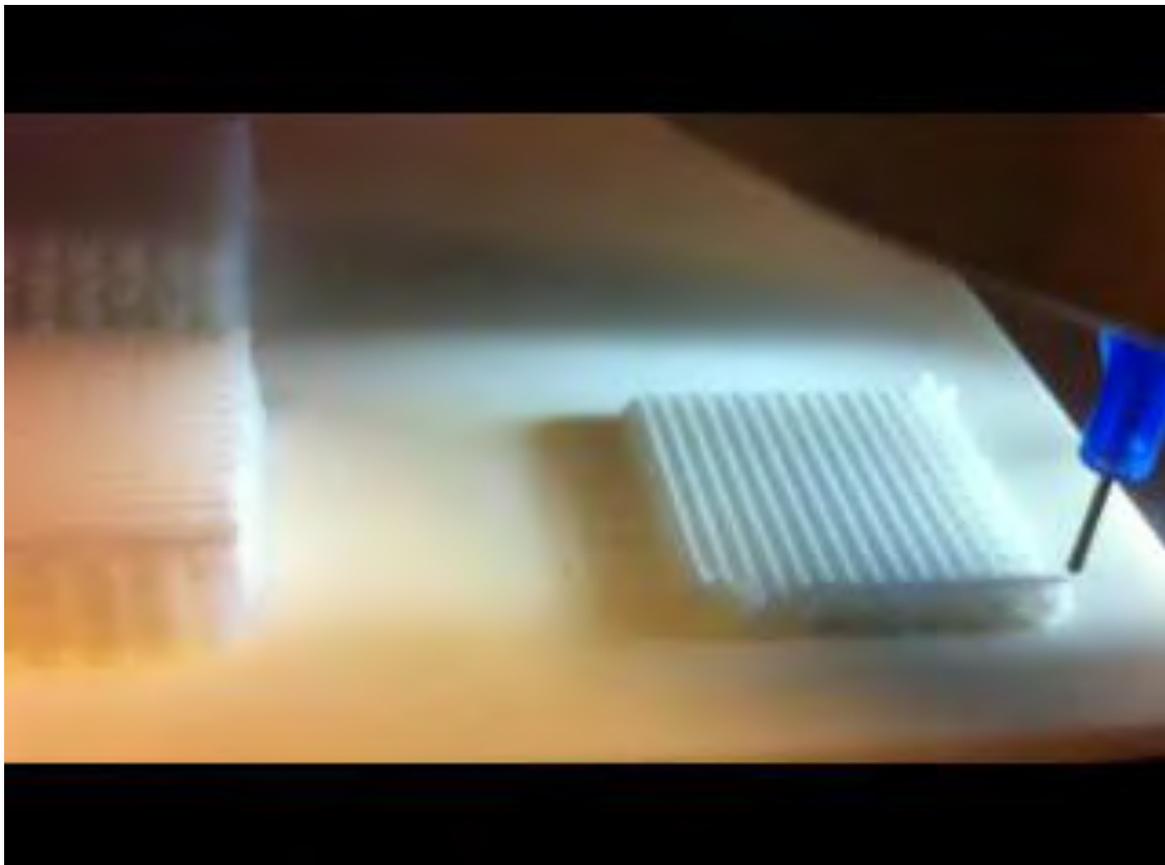
Ensamblando tejidos y órganos a partir de células

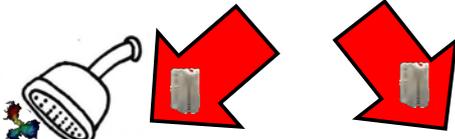
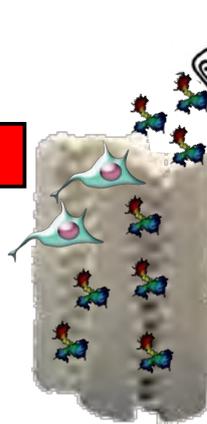
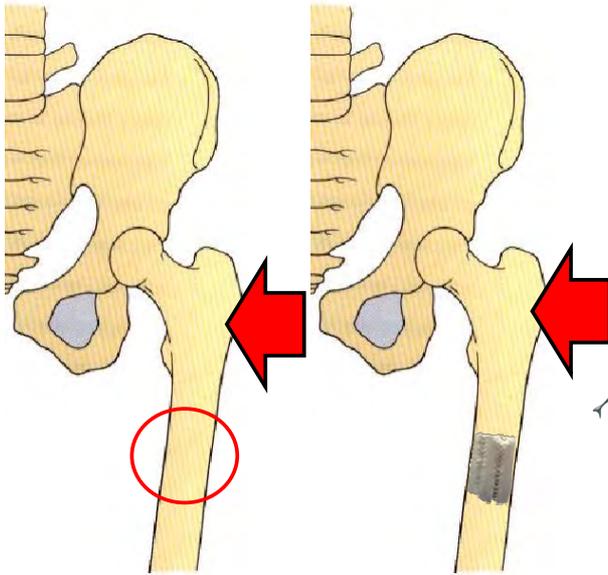
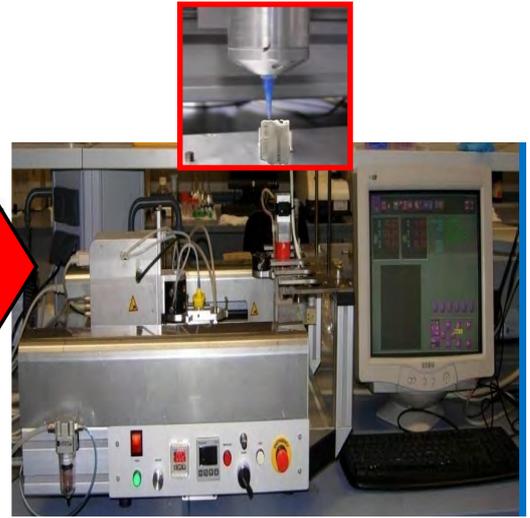


Recolección de células




María Vallet-Regí

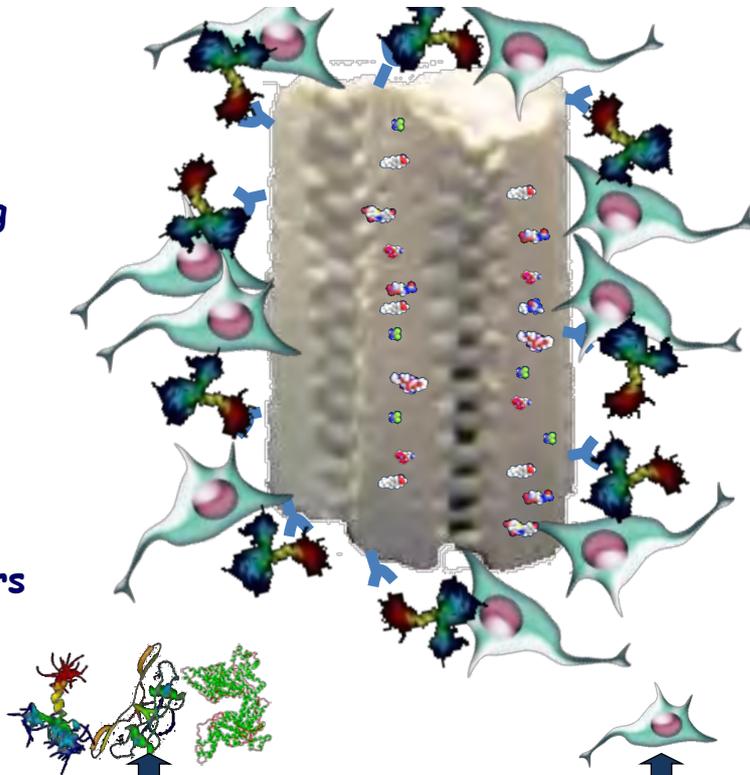




María Vallet-Regí

Functionalizing

**Growth Factors
Peptides
Proteins**

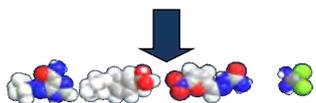


Osteoblasts

Drugs

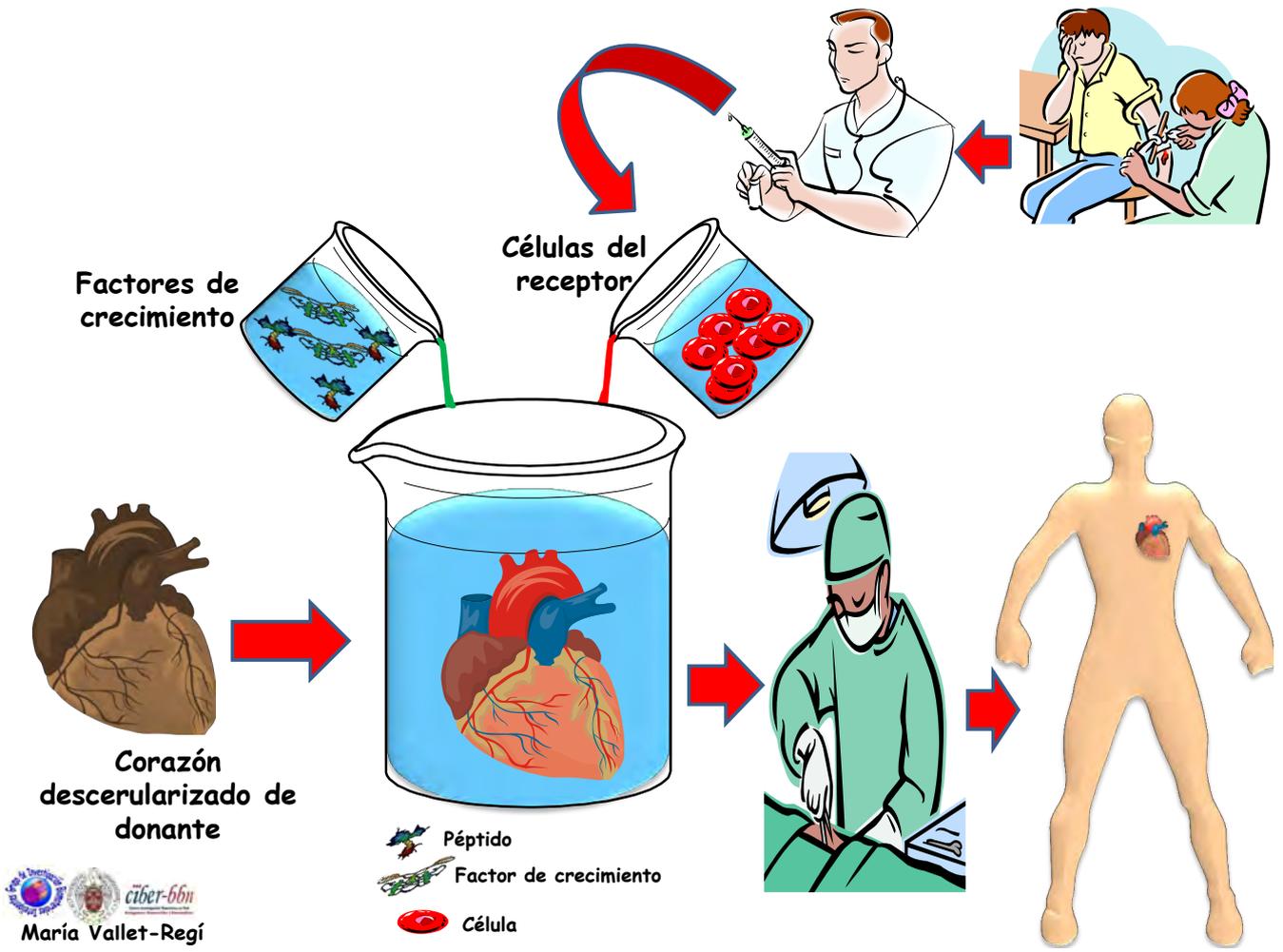
A. Salinas, P. Esbrit,
M. Vallet-Regí,
Biomater. Sci. 1,
40-51 (2013).

0,1nm 1nm 10nm 100nm 1µm 10µm 100µm mm



Pores of bone

María Vallet-Regí



Implant placement

Alto índice de infecciones asociadas a los implantes



ingresos hospitalarios



- Biofilms
- Resistencia bacteriana
- Efectos secundarios para el paciente

tratamientos sistémicos de antibióticos, prologados durante meses



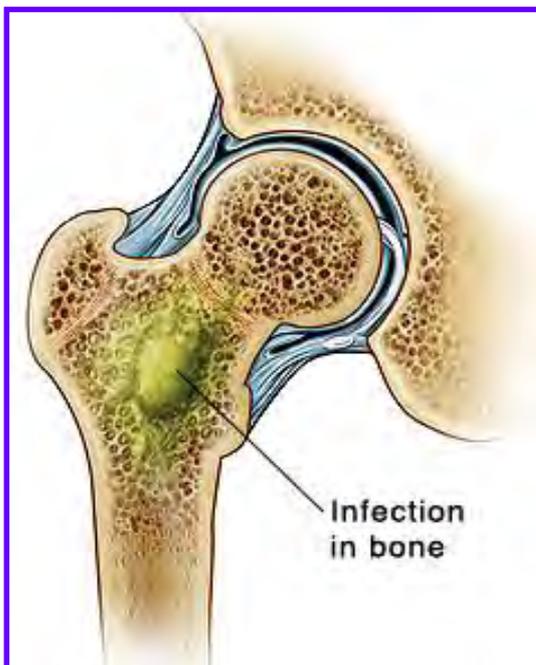
María Vallet-Regí

-Clin Infect. Dis 2009;59:337
 -N Engl J Med 2004;350:1422
 -National Healthcare Safety Network (NHSN) data base

Tipos de Implantes	Implantes /año	Índice de Infección (%)	Coste Hospitalario /paciente
Cardiovasculares:			
Válvulas cardiacas	85.000	4	50.000 \$
Vascular	450.000	4	40.000 \$
Marcapasos	300.000	4	35.000 \$
Dispositivos de circulación asistida	700	40	50.000 \$
Ortopédicos:			
Protesis articulares	600.000	2	30.000 \$
Dispositivos de fijación de fracturas	2.000.000	5	15.000 \$
Neurocirugía	40.000	6	50.000 \$
Mamoplastia aumentativa	130.000	2	20.000 \$

Infección ósea: osteomielitis

- Proceso inflamatorio acompañado de destrucción de hueso
- Provocado por infección de microorganismos, generalmente bacterias
- La formación de un biofilm dificulta el tratamiento



Tratamiento convencional

Enfoque combinado

Quirúrgico

Resección del hueso dañado e infectado

- × Posible recaída
- × Complicaciones propias de la cirugía
- × Inestabilidad del hueso

Antimicrobiano

Antibióticos por vía intravenosa durante 4-6 semanas

- × Distribución del antibiótico por el organismo

La evolución de las técnicas modernas de asepsia

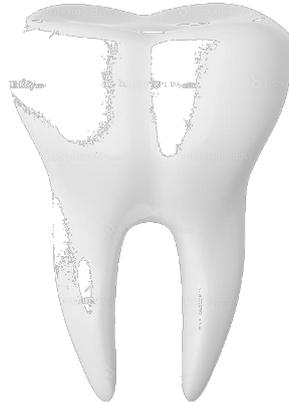


La curación de Justiniano, Fra Angelico, Museo San Marco, Florencia.






María Vallet-Regí



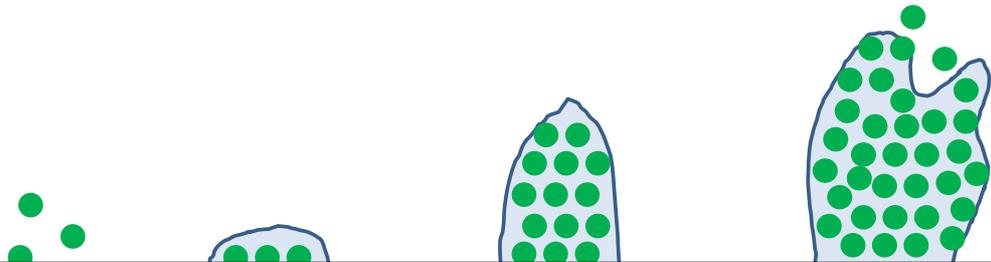
Utilizar el saber
hacer de la naturaleza:
mimetismo

Biomimética:
*transferencia de tecnología
desde la naturaleza al mundo
mineral donde vive el hombre.*



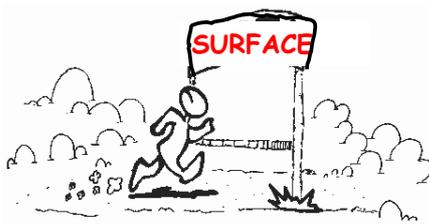
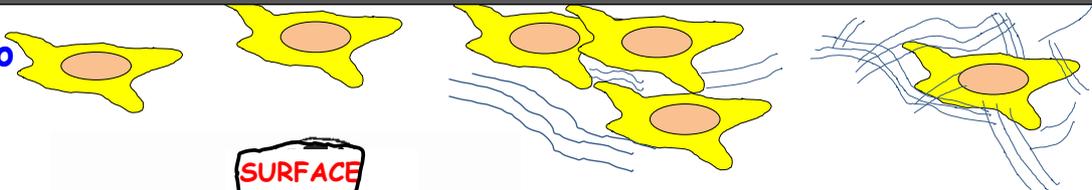
La carrera por la superficie

Bacteria



Superficie del implante

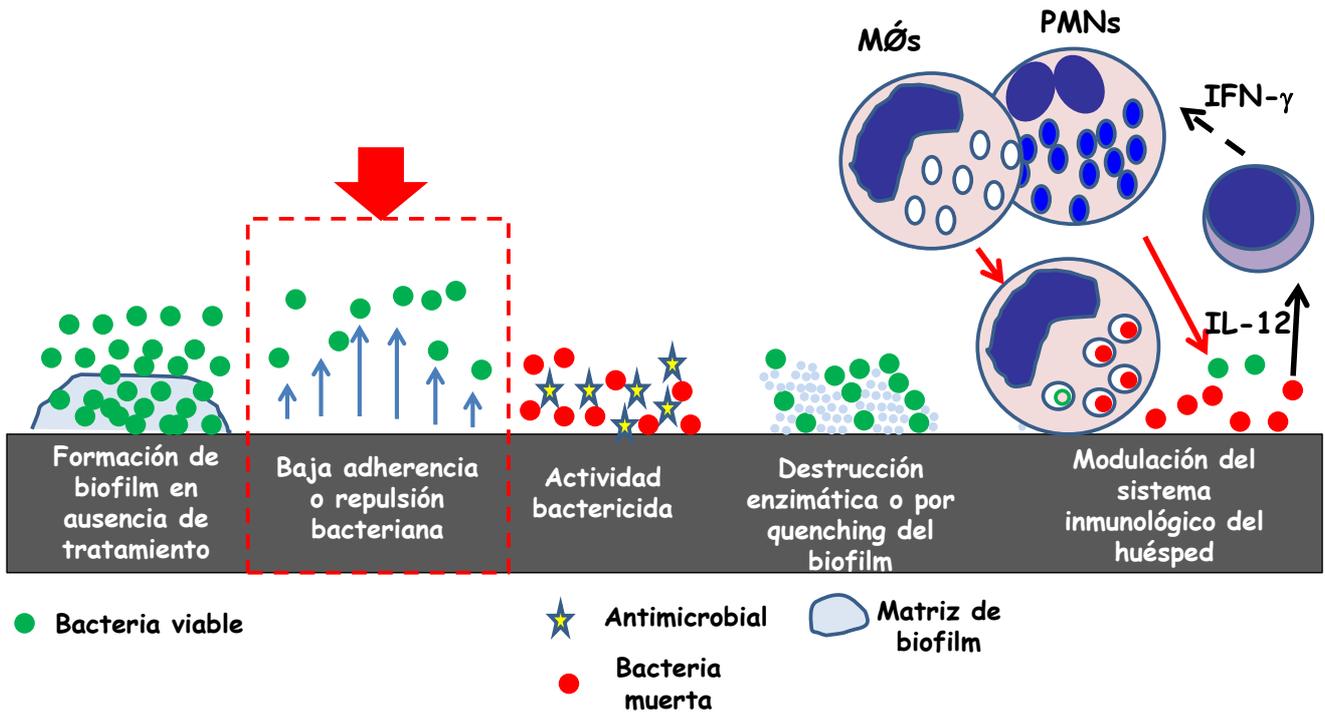
Osteoblasto




María Vallet-Regí

Gristina AG. Science 1987;237:1588-95.
Vallet-Regí M, Izquierdo-Barba I, Colilla M. Philos Trans A Math Phys Eng Sci; 2012;370:1400-21

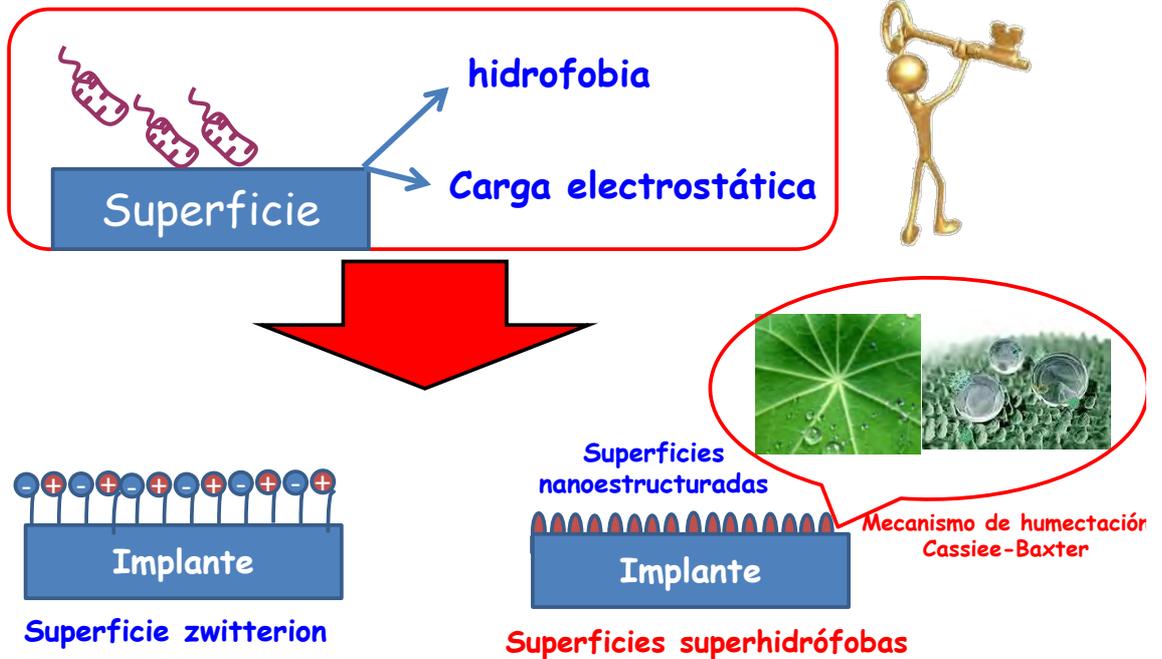
Estrategias actuales para evitar la infección en implantes



María Vallet-Regí

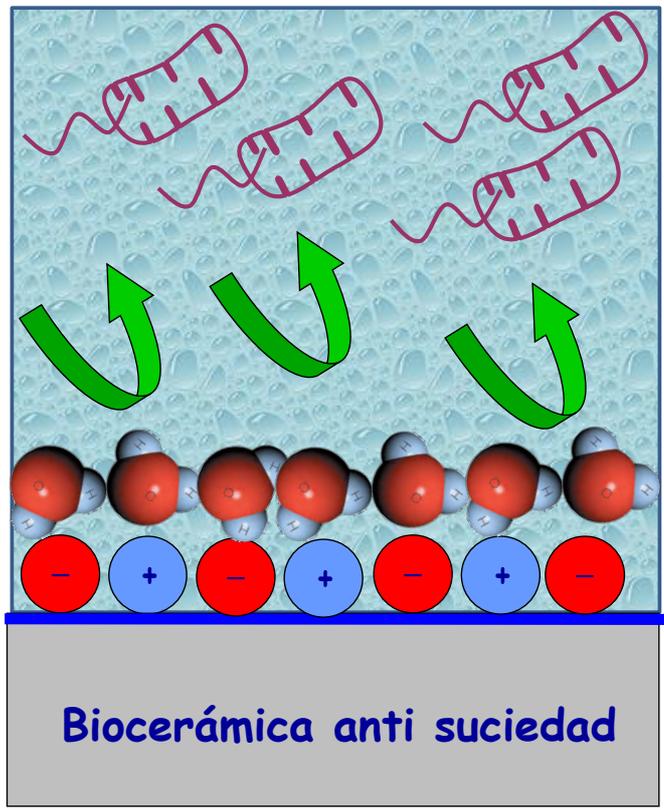
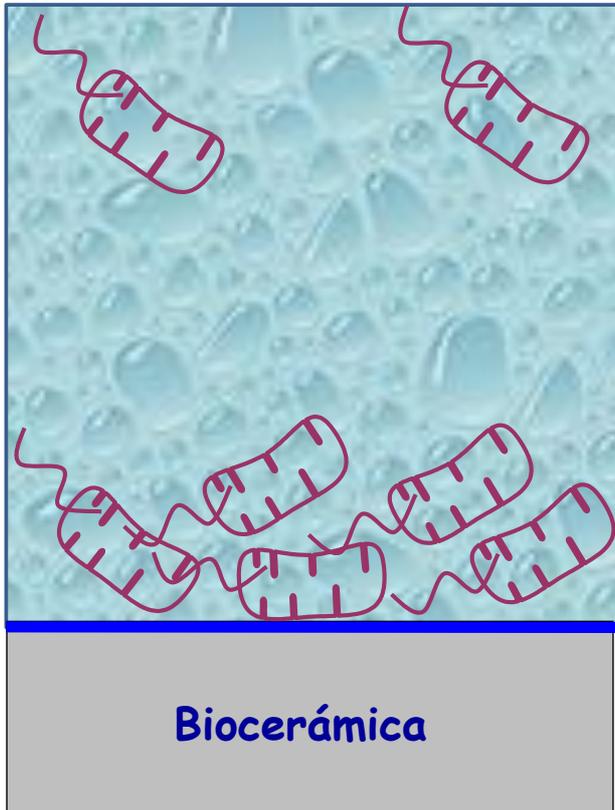
D. Campoccia, L. Montanaro, C.R. Arciola. *Biomaterials* 34 (2013) 8533-8554
 Bio-Ceramics with Clinical Applications. Editor M. Vallet-Regí. Wiley 2013 ISBN: 978-1-118-40675-5

Inhibición de la adhesión de bacterias



I. Izquierdo, M. Colilla, M. Vallet-Regí. *Acta Biomaterialia*. In Press.
 D. Campoccia, L. Montanaro, C.R. Arciola. *Biomaterials* 34 (2013) 8533-8554
 I. Izquierdo-Barba, S. Sánchez-Salcedo, M. Colilla, M.J. Feito, C. Ramírez-Santillán, M.T. Portolés, M. Vallet-Regí. *Acta Biomaterialia* 7 (2011) 2977.
 K. Anselme, P. Davidson, A.M. Popa, M. Giazzon, M. Liley, L. Ploux. *Acta Biomater.* 2010, 6, 3824.

María Vallet-Regí



I. Izquierdo, M. Colilla, M. Vallet-Regí. Acta Biomaterialia. In Press. Smart Drug Delivery from Silica Nanoparticles.

Autores: Montserrat Colilla and María Vallet-Regí

Editorial: Royal Society of Chemistry UK (2013). ISBN 9781849735520



La adherencia sobre superficies:

Bacterias

Proteínas (al azar)

son serios problemas para muchas aplicaciones

**Polímeros
Zwitterion**



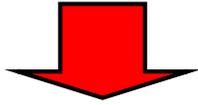
In chemistry, a **zwitterion** (from German zwitter "hybrid") is a neutral molecule with positive and negative charges onto different atoms.

**Formación de una capa de hidratación vía:
interacción electrostática y enlace de hidrógeno
→ Fuerzas repulsivas**

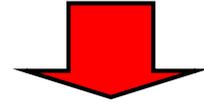


I. Izquierdo, M. Colilla, M. Vallet-Regí. Acta Biomaterialia. In Press.

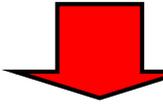
Inhibición de la adhesión bacteriana



Uso de materiales que impiden la adhesión bacteriana



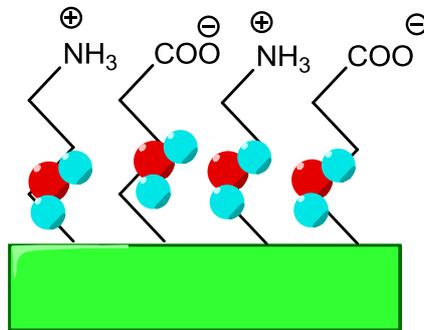
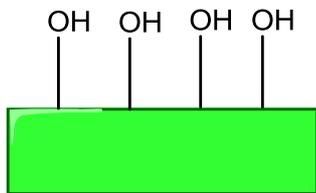
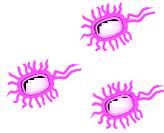
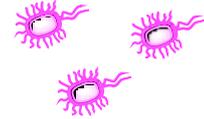
Uso de agentes antimicrobianos



In chemistry, a *zwitterion* (from German *zwitter* "hybrid") is a neutral molecule with positive and negative charges onto different atoms.

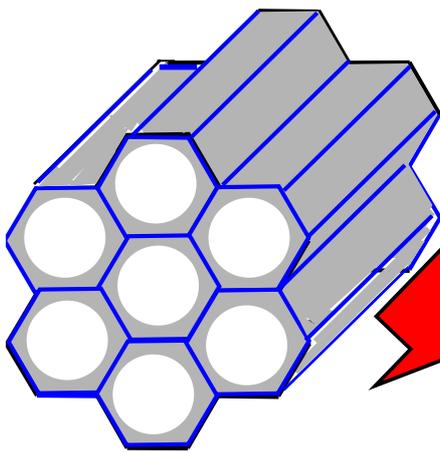


Materiales Zwitterionicos

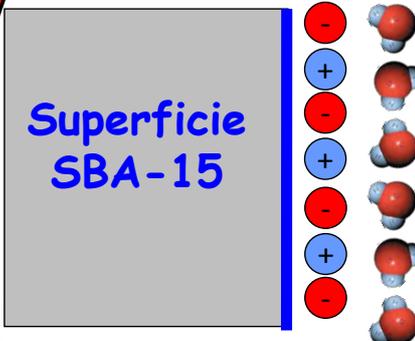
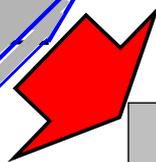


Materiales mesoporosos *Zwitterion* con superficies antiadherentes

In chemistry, a *zwitterion* (from German *zwitter* "hybrid") is a neutral molecule with positive and negative charges onto different atoms.



SBA-15



Hidroxiapatita Zwitterion

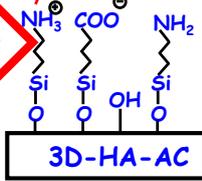
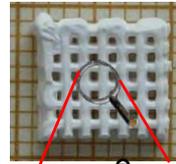


Preparación de andamios por robocasting



3D-HA

Zwitterionización

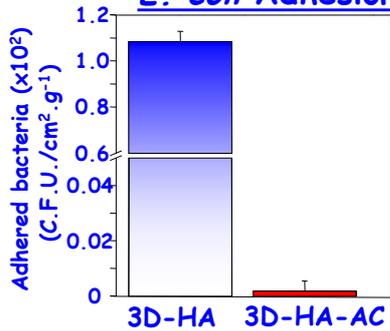


3D-HA-AC

Zwitterionica HA

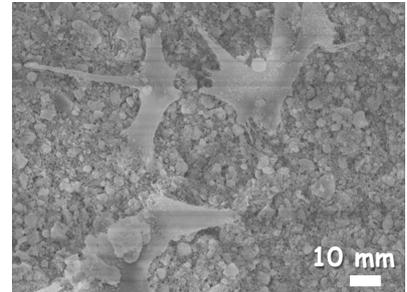
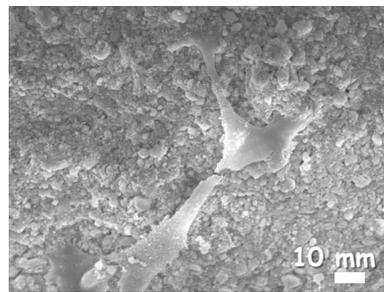
S. Sánchez, M. Colilla, I. Izquierdo, M. Vallet-Regí. J. Mater. Chem, B 115, 2013

E. coli Adhesión

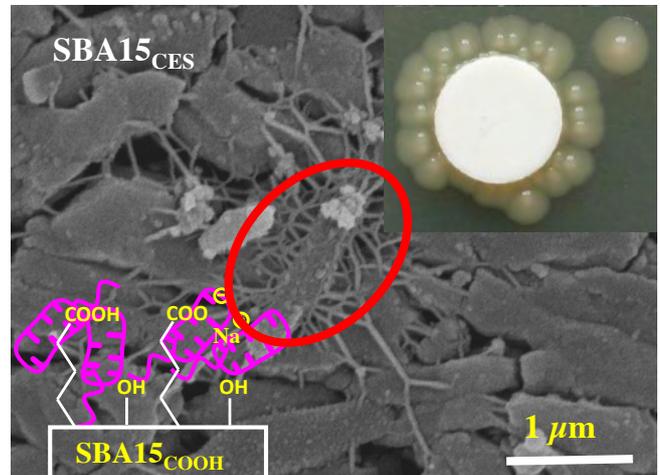
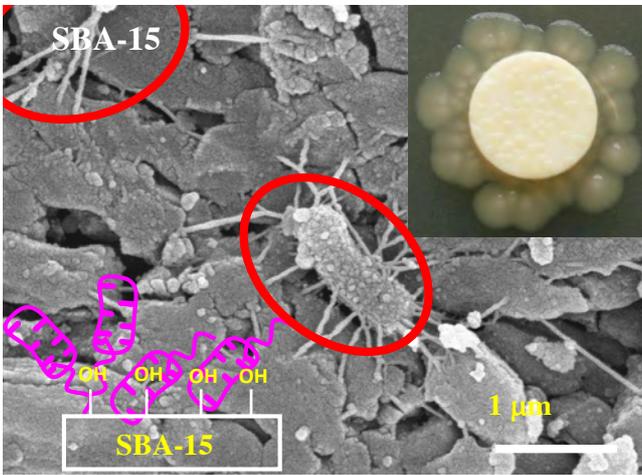


María Vallet-Regí

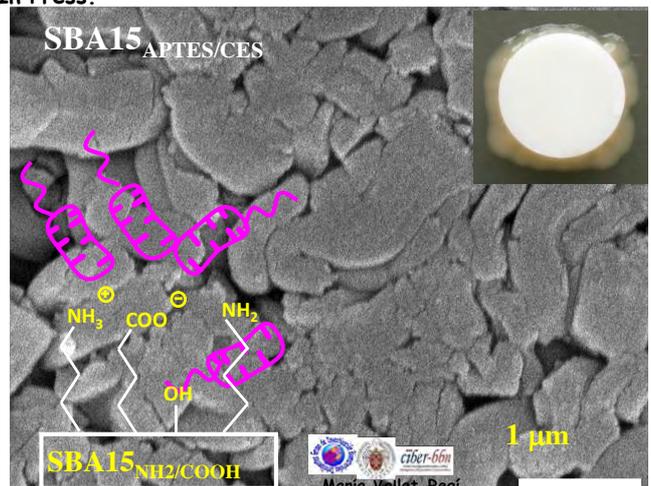
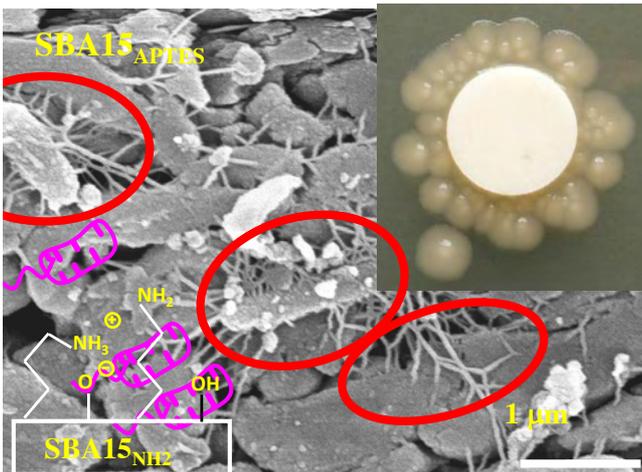
Adhesión y extensión Osteoblastica



I. Izquierdo, M. Colilla, M. Vallet-Regí. Acta Biomaterialia. In Press.



I. Izquierdo, M. Colilla, M. Vallet-Regí. Acta Biomaterialia. In Press.

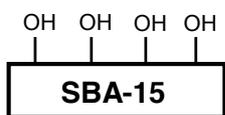
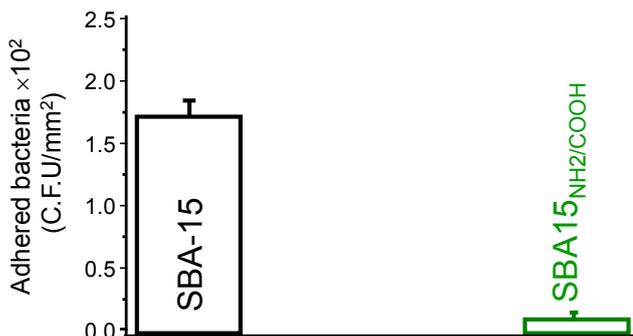


Antiadherencia bacteriana

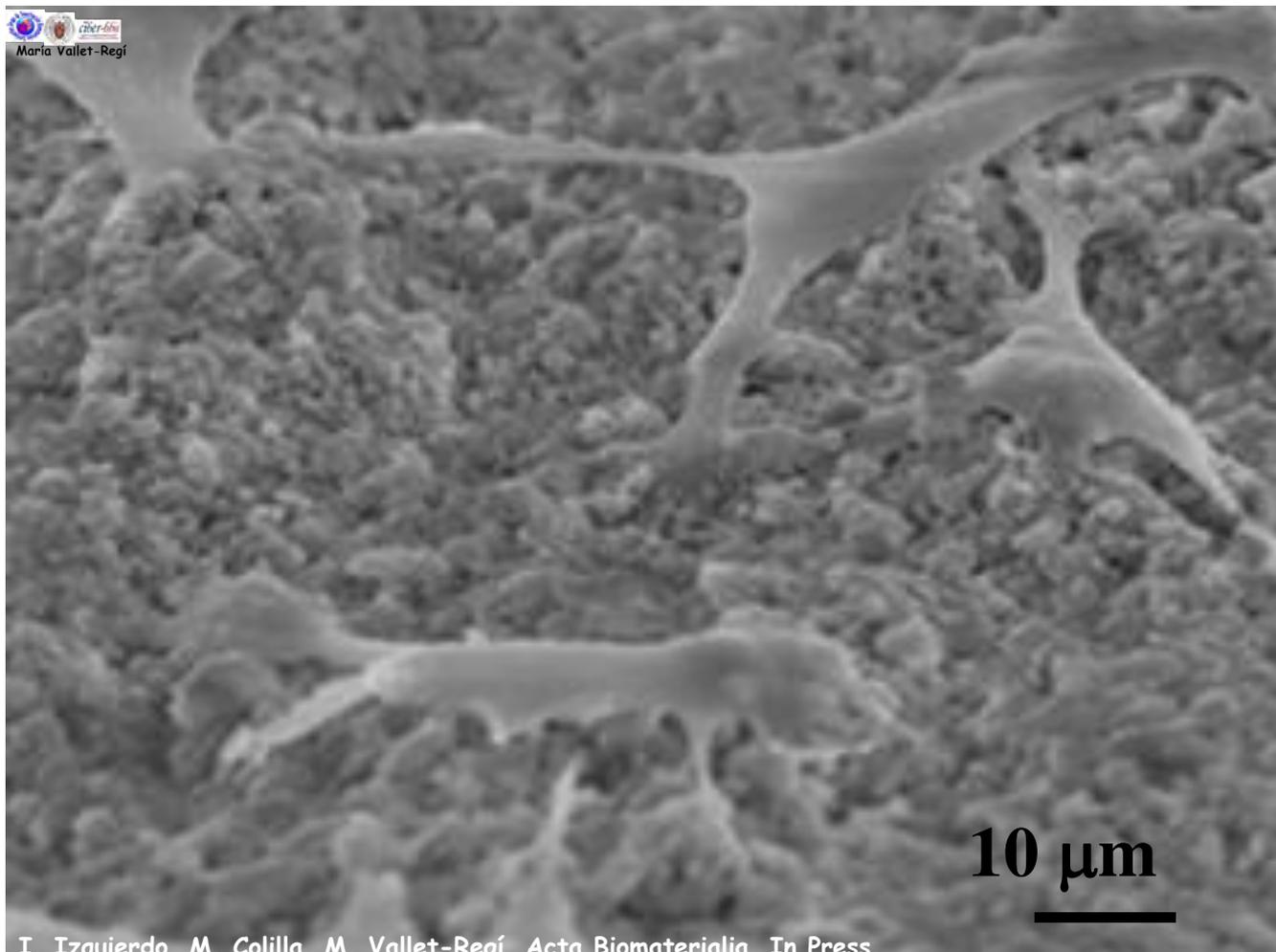
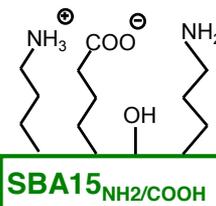
M.Colilla, I. Izquierdo, S. Sánchez, J.L.G. Fierro, J.L. Hueso, M. Vallet-Regí. *Chem. Mater.* 22, 6459-6466 (2010)

I. Izquierdo, S. Sánchez,, M.Colilla, M. Feito, C. Ramirez, M.T. Portolés, M. Vallet-Regí. *Acta Biomat.* 7, 2977-2985, 2011

Bacteria:
Escherichia Coli



I. Izquierdo, M. Colilla, M. Vallet-Regí. *Acta Biomaterialia*. In Press.

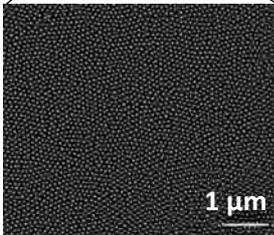
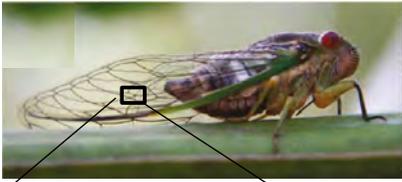


I. Izquierdo, M. Colilla, M. Vallet-Regí. *Acta Biomaterialia*. In Press.

Bioinspirado en la Naturaleza...: La nanoestructura es la clave

Alas antibacterianas

Cicada, *Psaltoda claripennis*



Nanopilares
($h = 200 \text{ nm}$ and
 $\varnothing = 100 \text{ nm}$)

WCA = 158°



"Efecto Loto"
altamente
hidrófobo



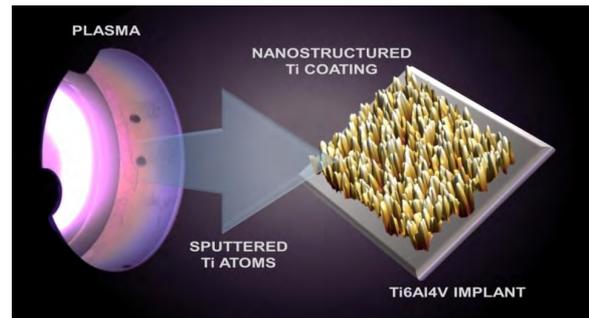
Elena P. Ivanova et al *Small* 2012, 8, 2489.

Para evitar infecciones en un implante ortopédico....

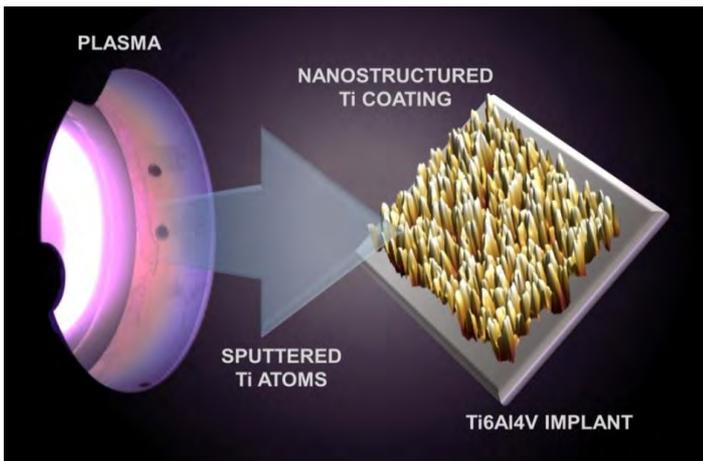


Aleación
TiAl4V

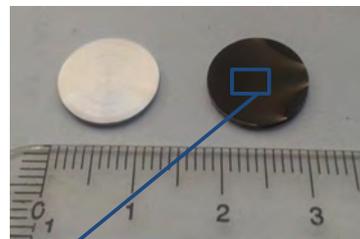
Recubrir con nanocolumnas,
Similares a las de las alas de la Cicada...???



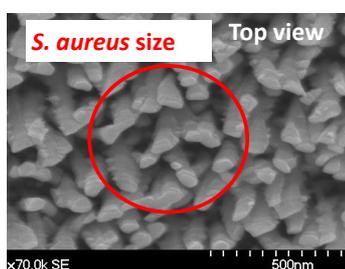
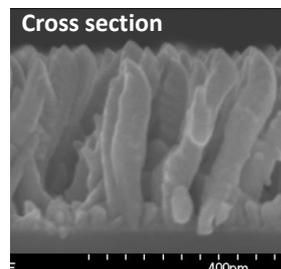
Fabricación sostenible por magnetron sputtering



Sin sustancias químicas Baja energía
En incidencia oblicua



Ti Nanocolumns



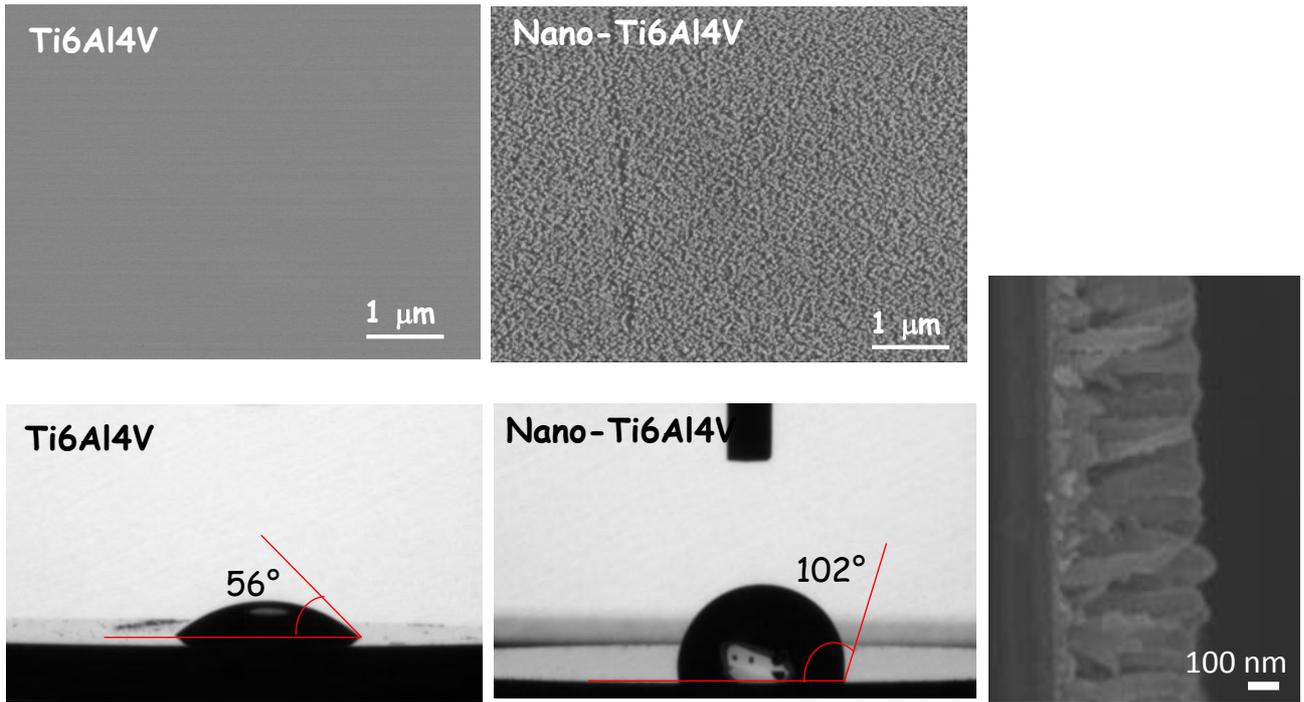
Hidrófobo

Sustrato

Con recubrimiento



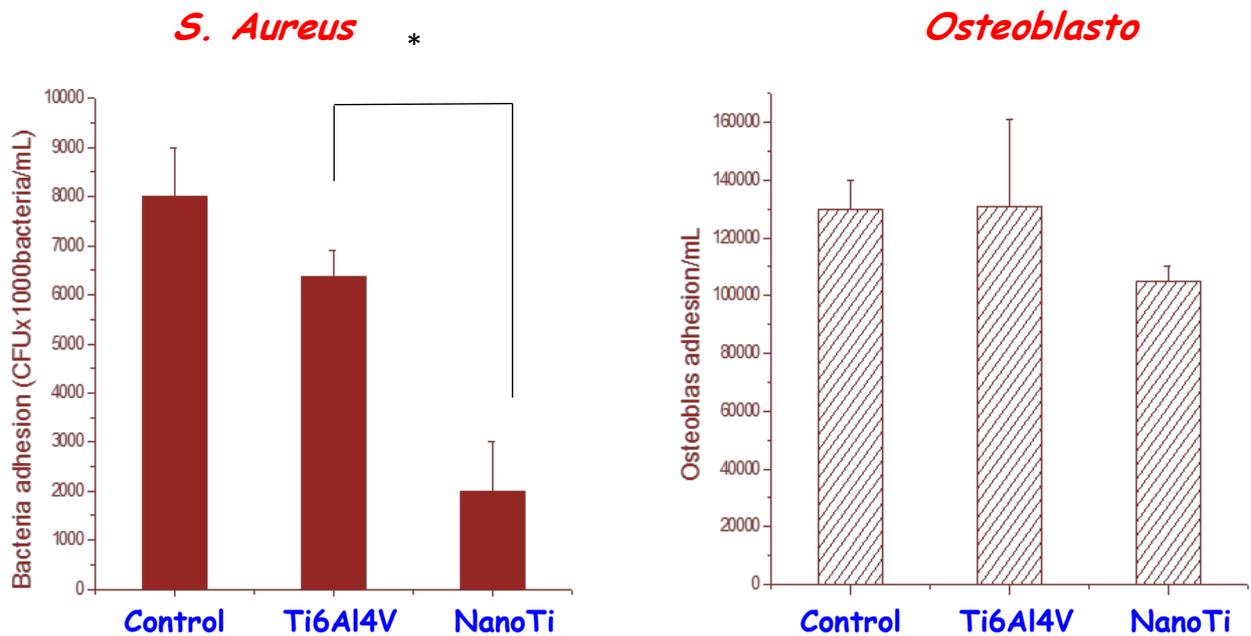
Caracterización estructural



Nanocolumnas
(h = 300 nm y \varnothing = 50 nm,
separadas 150 nm)

Comportamiento selectivo de bacterias frente a osteoblastos

Adhesión a los 90 min de incubación



Ensayos in vitro con *Staphylococcus aureus*

Cepas recolectadas



S. aureus cepa #5981

Cepa clínica

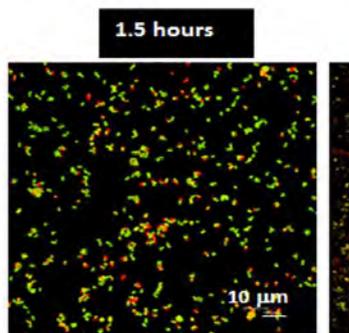


Cepas P1, P2, P4, P18, P95, P61T3

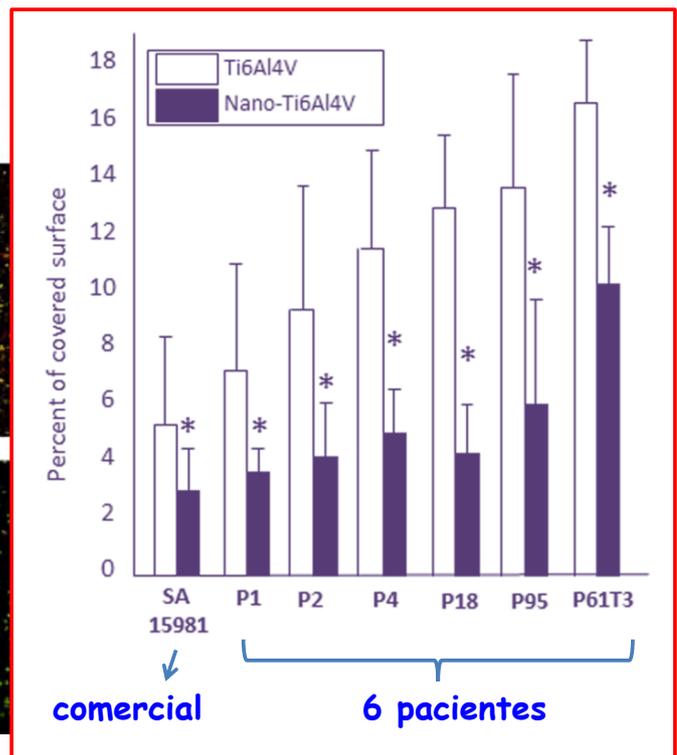
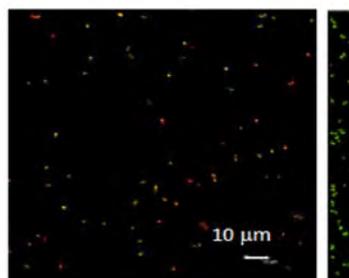
Propiedades antibacterianas

Staphylococcus aureus attachment

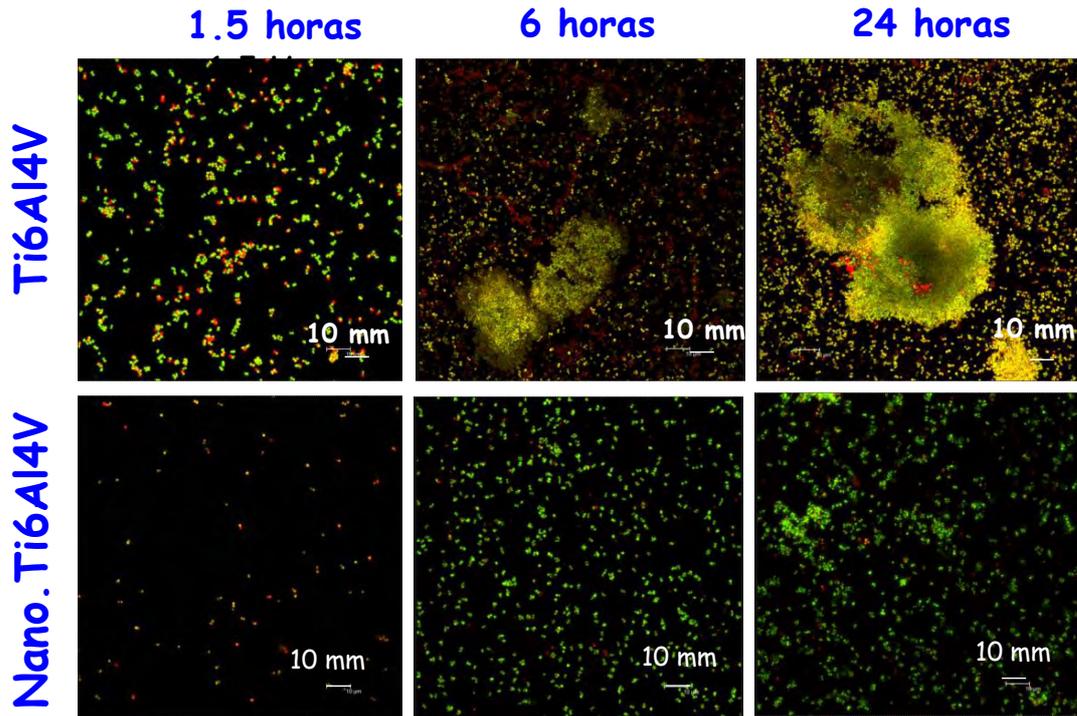
Sustrato



Con recubrimiento



Formación de biofilm de *S. aureus*



Tintes syto-9/ yoduro propidio

Por qué???

- Tamaño 1 μm
- Rigidez
- Pocos puntos de anclaje
- Tamaño 10-50 μm
- Flexibilidad
- Muchos puntos de anclaje

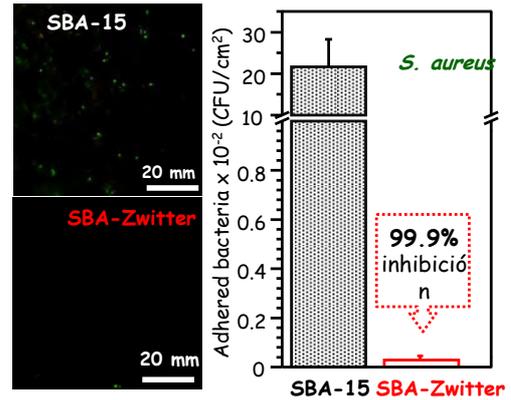
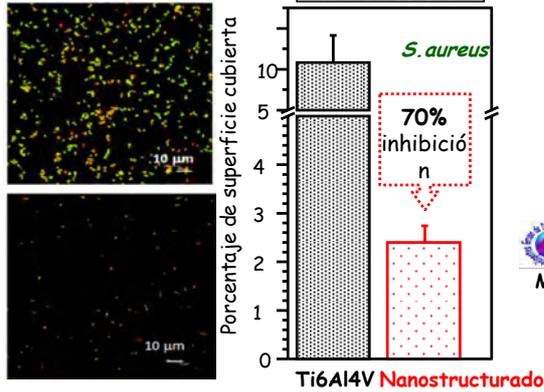
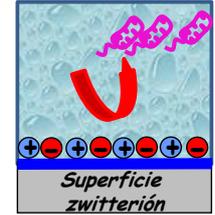
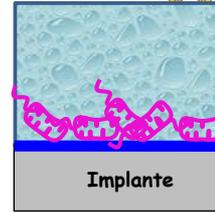
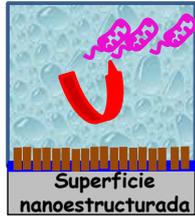
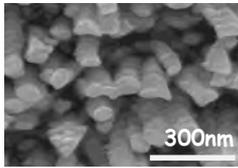


Matar ← **Lucha contra la infección** → Impedir la adhesión bacteriana

Superficies nanoestructuradas

Superficies zwitterion

In chemistry, a **zwitterion** (from German *zwitter* "hybrid") is a neutral molecule with positive and negative charges onto different atoms.

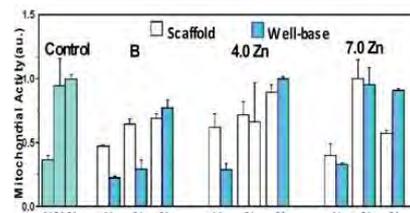
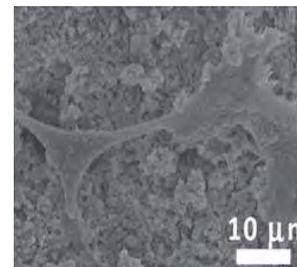
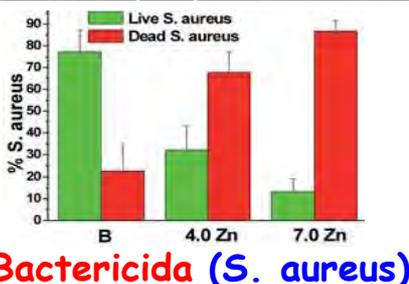
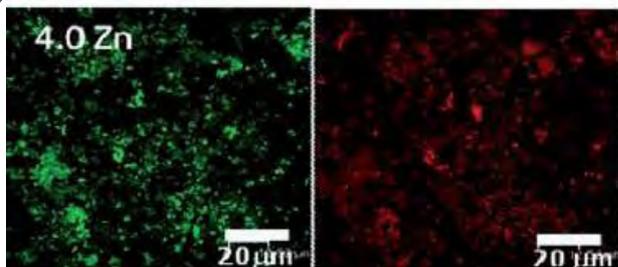


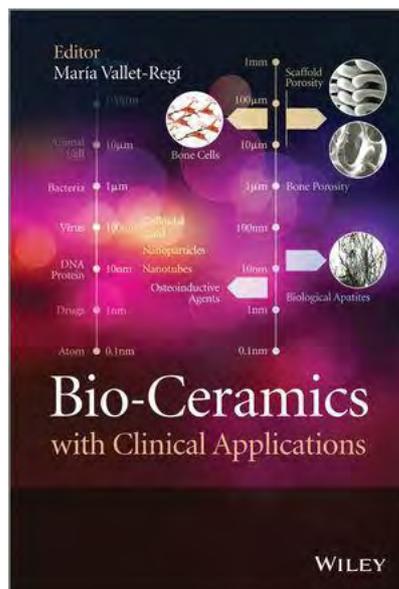
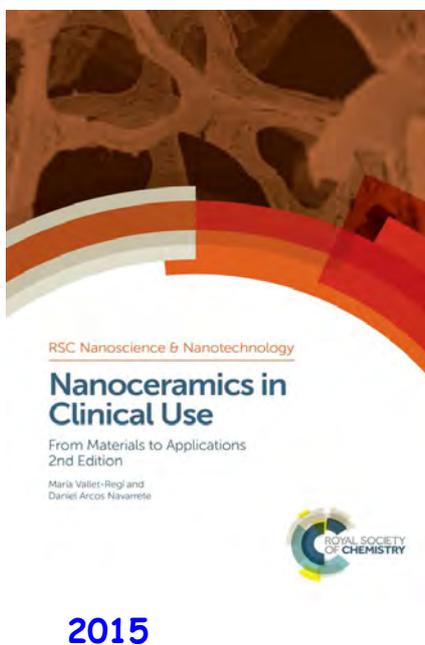
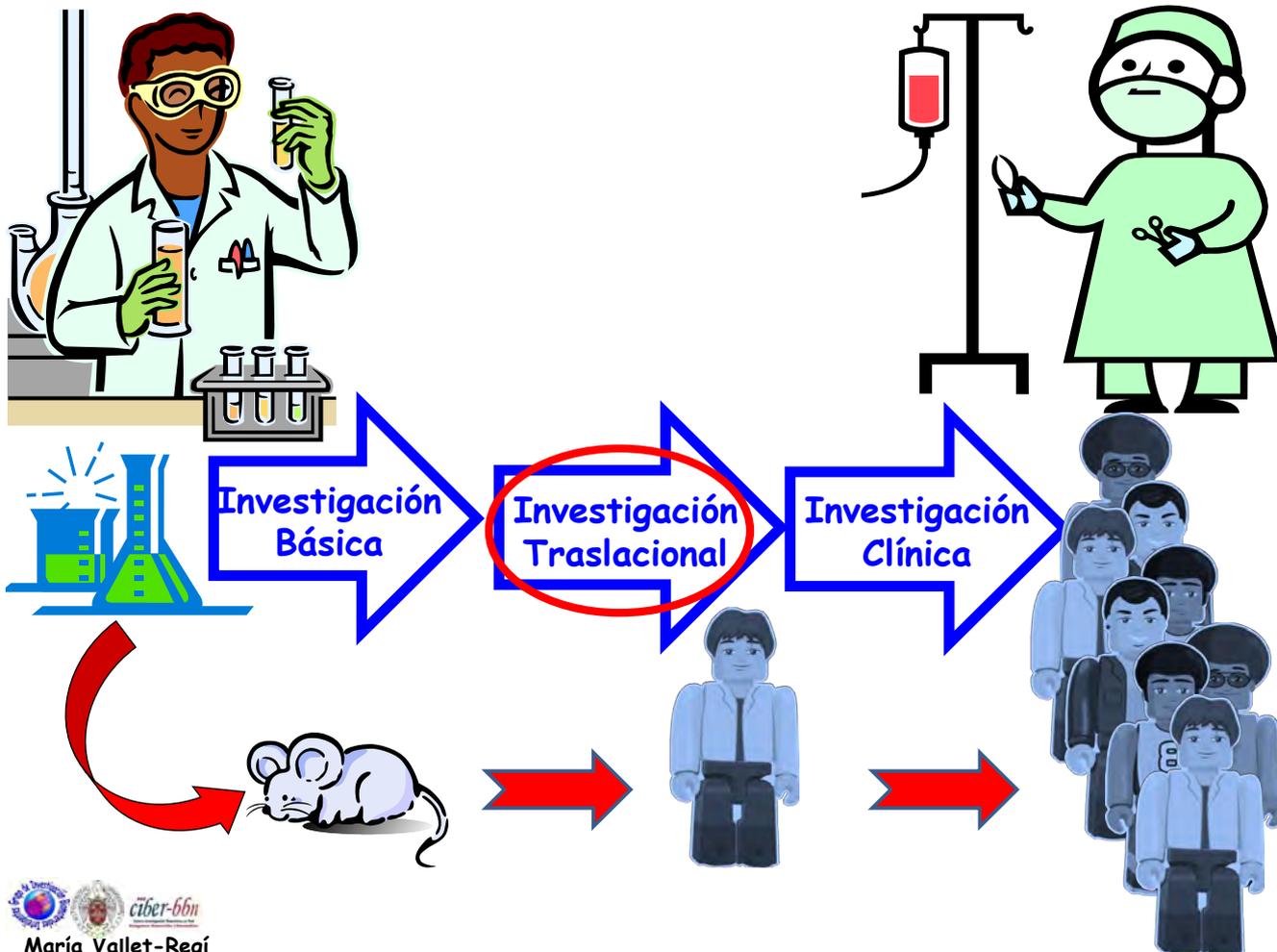
María Vallet-Regí

I. Izquierdo, M. Colilla, M. Vallet-Regí. *Acta Biomaterialia*. In Press.
 I. Izquierdo-Barba, J.M. García-Martín, R. Álvarez, A. Palmero, J. Esteban, C. Pérez-Jorge, D. Arcos, M. Vallet-Regí et al. *Acta Biomaterialia* 2015, 15, 20 PCT/ES2015/070345

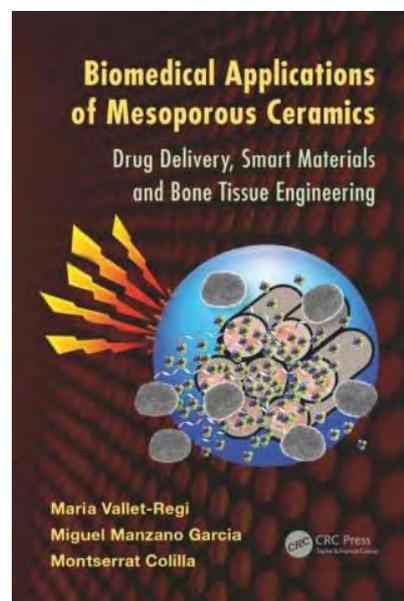
Colilla, Izquierdo, Sánchez, Fierro, Hueso, Vallet-Regí. *Chem. Mater.* 2010.
 Izquierdo, Sánchez, Colilla, Feito, Ramírez, Portolés, Vallet-Regí. *Acta Biomaterialia*, 2011
 Sánchez, Colilla, Izquierdo, Vallet-Regí. *J. Mater. Chem. B*, 2013, 1, 1595
 Colilla, Martínez, Sánchez, Ruiz, G-Calbet, Vallet-Regí. *J. Mater. Chem. B*, 2014,

Matar ← **Lucha contra la infección** → Impedir la adhesión bacteriana





2014



2013

<http://www.valletregigroup.esy.es>

