

ÁREA: ENFERMEDADES INFECCIOSAS, INFLAMATORIAS Y CRÓNICAS

Grupos:

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Javier Cuesta Herranz
Victoria del Pozo Abejón
Vanesa Esteban Vázquez
Joaquín Sastre Domínguez

Investigación: Básica y Clínica

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José Miguel Benito Huete

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Investigación: Básica y Clínica

Grupo Asociado

Grupo de Traumatología

Responsable: Emilio Calvo Crespo

Investigación: Clínica y Básica

ÁREA: ENFERMEDADES INFECCIOSAS, INFLAMATORIAS Y CRÓNICAS

MICROBIOLOGÍA

Jaime Esteban Moreno

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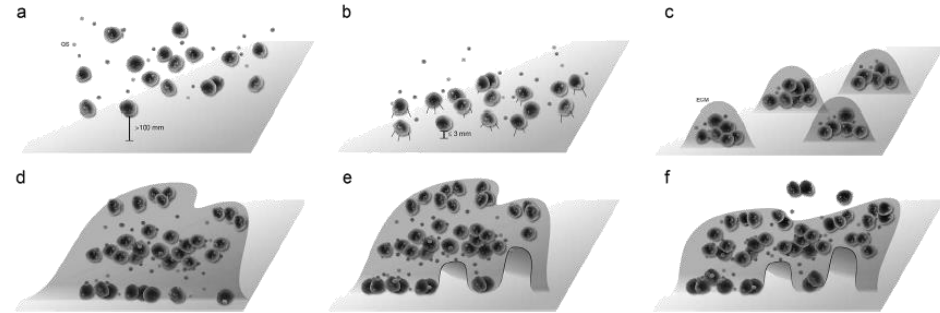
REUNIÓN ANUAL DEL ÁREA DE ENFERMEDADES INFECCIOSAS, INFLAMATORIAS Y CRÓNICAS DEL IIS-FJD
21 de abril del 2022

 Universidad Autónoma
de Madrid

 Hospital Universitario
Fundación Jiménez Díaz
Grupo Quirónsalud

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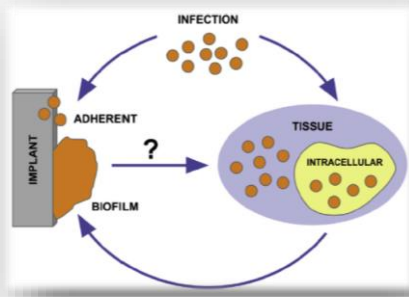
- La infección es un problema asociado a la cirugía de implantes que, aunque puede ser minimizado, posiblemente no puede ser completamente eliminado.
- La importancia de dichas infecciones es grande en términos de morbilidad, realización de nuevas cirugías, incremento del gasto, estancias prolongadas, etc.



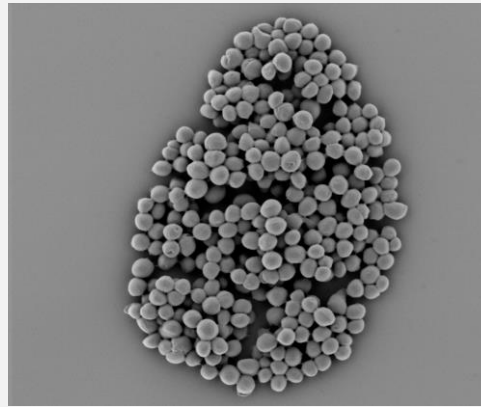
La investigación en infecciones asociadas a biomateriales incluye varios campos esenciales

- ✦ Patogenia
- ✦ Diagnóstico
- ✦ Tratamiento
- ✦ Prevención

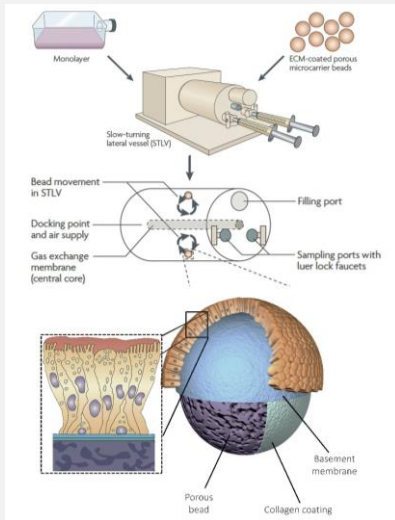




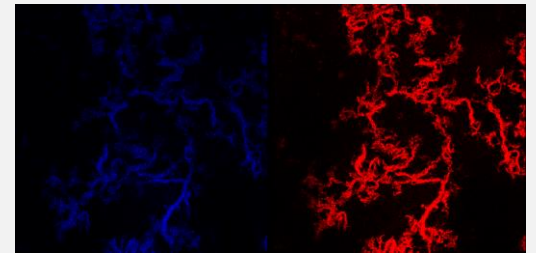
La formación de un biofilm y la capacidad de supervivencia intracelular en los tejidos vecinos son los factores patogénicos principales de la IP e influyen en el manejo de los pacientes.

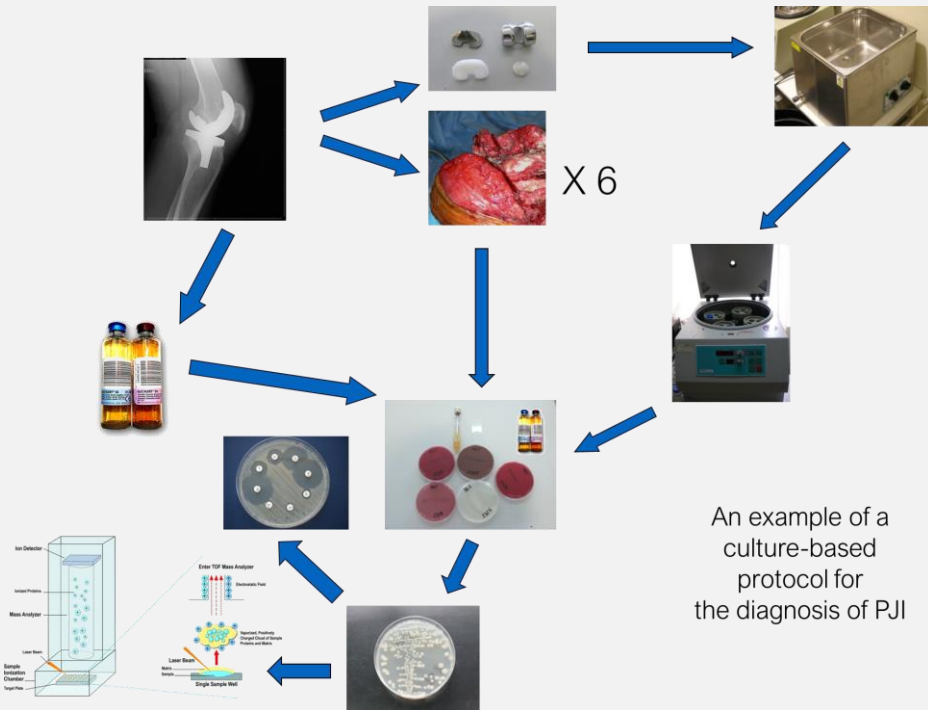


Se han estudiado los biofilms producidos por múltiples microorganismos (e incluso biofilms mixtos) de cara a establecer sus características de desarrollo, sensibilidad antimicrobiana, clonalidad, etc.



Se han evaluado diversas estrategias de tratamiento antibiofilm basadas en sustancias conocidas y en otras alternativas.





An example of a culture-based protocol for the diagnosis of PJI

Esteban J, Gómez-Barrena E, Cordero J, Martín-de-Hijas NZ, Kinnari TJ, Fernández-Roblas. Evaluation Of Quantitative Cultures From Sonicated Retrieved Orthopaedic Implants In The Diagnosis Of Orthopaedic Infection. Journal of Clinical Microbiology. 2008. 46 (2): 488-492. Journal Impact Factor: 3.945. QI (Microbiology 18/91).

Table 2. Molecular techniques used in prosthetic joint infections.

Category	Diagnostic test
Homemade PCR	16S rDNA + sequencing Specific PCR Multiplex PCR RT-PCR
Commercial PCR	Multiplex PCR 16S rDNA + hybridization
Other techniques	FISH Pyrosequencing Ibis Microcalorimetry
Future techniques	MALDI-TOF Microarrays DGGE

DGGE: Denaturing gradient gel electrophoresis; MALDI: Matrix-assisted laser desorption/ionization; RT: Reverse transcription.



Esteban J, Gomez-Barrena E. An update about molecular biology techniques to detect orthopaedic implant-related infections. EFORT Open Reviews. 2021. Feb 1;6(2):93-100. Journal Impact Factor (2019): 4.618. Q1 (Orthopaedics I2/82).

Esteban, Sorli, Alertorn-Geli et al. Expert Rev Mol Diagn 2014.14:83-96

Article

Genomic Analysis of *Cutibacterium acnes* Strains Isolated from Prosthetic Joint Infections

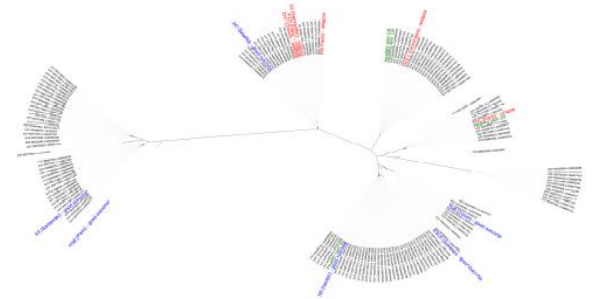
Llanos Salar-Vidal ^{1,*}, Yvonne Achermann ^{2,3}, John-Jairo Aguilera-Correa ¹, Anja Poehlein ⁴, Jaime Esteban ¹, Holger Brüggemann ⁵ and on behalf of the ESCMID Study Group for Implant-Associated Infections (ESGIAI) [†]



CLINICAL ARTICLE

Usefulness of a Multiplex PCR Assay for the Diagnosis of Prosthetic Joint Infections in the Routine Setting

Álvaro Auñón, MD, PhD^{1,2}, Ismael Coifman, MD¹, Antonio Blanco, MD^{2,3}, Joaquín García Cañete, MD³, Raúl Parrón-Cambero, MD^{1,2}, Jaime Esteban, MD, PhD^{1,4}



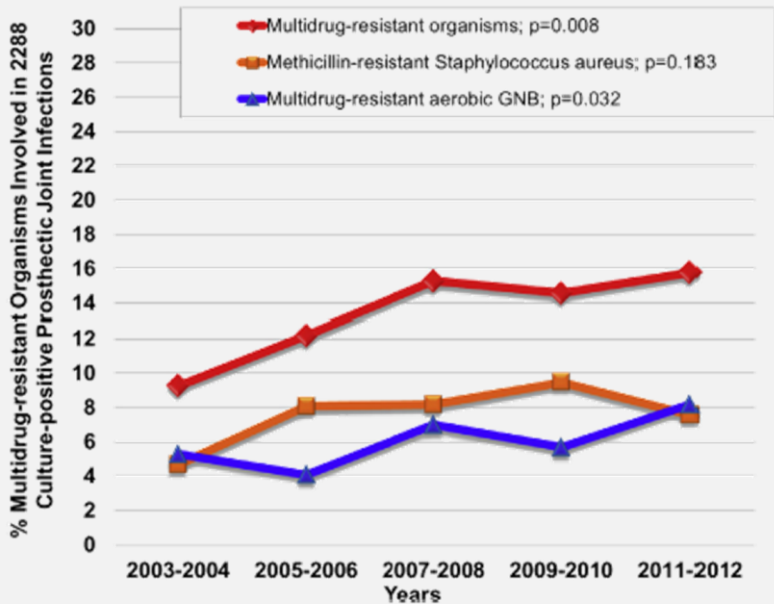
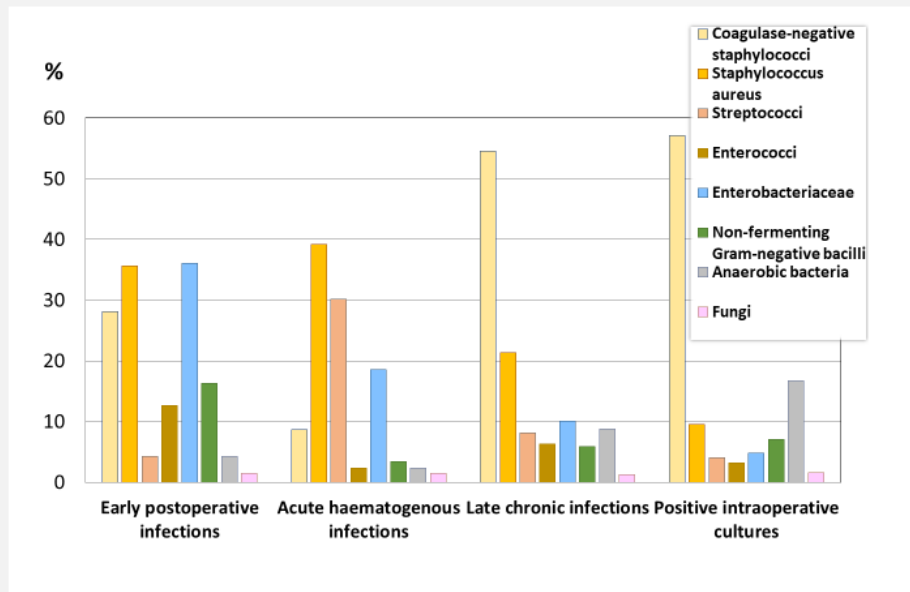


Fig. 2. Trends in the multidrug-resistant organisms involved in prosthetic joint infections. GNB indicates Gram-negative bacilli. p values indicate p for trend from 2003–2004 to 2011–2012.



Estudios multicéntricos sobre etiología de la infección protésica



Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



Consensus statement

Executive summary of management of prosthetic joint infections. Clinical practice guidelines by the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)



Javier Ariza (Coordinator)^a, Javier Cobo (Coordinator)^{b,*}, Josu Baraia-Etxaburu^c, Natividad Benito^d, Guillermo Bori^e, Javier Cabo^f, Pablo Corona^g, Jaime Esteban^h, Juan Pablo Horcajadaⁱ, Jaime Lora-Tamayo^j, Oscar Murillo^k, Julián Palomino^l, Jorge Parra^m, Carlos Pigrauⁿ, José Luis del Pozo^o, Melchor Riera^p, Dolores Rodríguez^q, Mar Sánchez-Somolinos^q, Alex Soriano^r, M. Dolores del Toro^s, Basilio de la Torre^t, on behalf of the Spanish Network for the Study of Infectious Diseases and the Sociedad Española de Enfermedades Infecciosas Microbiología Clínica (SEIMC)

Short- versus long-duration levofloxacin plus rifampicin for acute staphylococcal prosthetic joint infection managed with implant retention: a randomised clinical trial ^{*}

Jaime Lora-Tamayo^{1,*}, Gorane Euba², Javier Cobo³, Juan Pablo Horcajada⁴, Alex Soriano⁵, Enrique Sandoval⁶, Carles Pigrau⁷, Natividad Benito⁸, Luis Falgueras⁹, Julián Palomino¹⁰, María Dolores del Toro¹¹, Alfredo Jover-Sáenz¹², José Antonio Iribarren¹³, Mar Sánchez-Somolinos¹⁴, Antonio Ramos¹⁵, Marta Fernández-Sampedro¹⁶, Melchor Riera¹⁷, Josu Mirena Baraia-Etxaburu¹⁸, Javier Ariza², Prosthetic Joint Infection Group of the Spanish Network for Research in Infectious Diseases—REIPI

TRATAMIENTO

Oral Antibiotics are Effective for Highly Resistant Hip Arthroplasty Infections

José Cordero-Ampuero MD, PhD, Jaime Esteban MD, PhD, Eduardo García-Cimbrello MD, PhD

Clinical Infectious Diseases

MAJOR ARTICLE



The Not-So-Good Prognosis of Streptococcal Periprosthetic Joint Infection Managed by Implant Retention: The Results of a Large Multicenter Study

Jaime Lora-Tamayo,^{1,2} Eric Senneville,^{3,4,5} Alba Ribera,^{6,7,8,9} Louis Bernard,¹⁰ Michel Dupon,¹¹ Valérie Zeller,¹² Ho Kwong Li,¹³ Cédric Arvieux,^{14,15} Martin Claus,¹⁶ Ilker Uckay,¹⁷ Dace Vignate,¹⁸ Iratxe Ferry,¹⁹ José Antonio Iribarren,²⁰ Trishia N. Peat,²¹ Parham Sendi,²² Nina Garišić Mikšić,²³ Dolores Rodríguez-Pardo,²⁴ María Dolores del Toro,²⁵ Marta Fernández-Sampedro,^{26,27} Ulrike Dupont,²⁸ Kaia Houtari,²⁹ Joshua S. Davis,³⁰ Julián Palomino,^{31,32} Danielle Ness,³³ Benjamin M. Clark,³⁴ Thomas Gottlieb,³⁵ Richard Trebbe,³⁶ Alex Soriano,^{37,38} Alberto Bahamonde,³⁹ Laura Guo,⁴⁰ Alicia Rico,⁴¹ Mauro J. C. Salles,⁴² M. Jose G. Patz,⁴³ Natividad Benito,⁴⁴ Melchor Riera,⁴⁵ Lucia Gómez,⁴⁶ Craig A. Abelson,⁴⁷ Jaime Esteban,⁴⁸ Juan Pablo Horcajada,⁴⁹ Karim O'Connell,⁵⁰ Matteo Ferraro,⁵¹ Gaber Skaricak,⁵² Indul San-Juan,⁵³ Javier Cobo,⁵⁴ Mar Sánchez-Somolinos,⁵⁵ Antonio Ramos,⁵⁶ Ethymia Giannitzi,⁵⁷ Alfredo Jover-Sáenz,⁵⁸ Josu Mirena Baraia-Etxaburu,⁵⁹ Jose Maria Barbero,⁶⁰ Peter F. M. Choong,⁶¹ Nathalie Assery,⁶² Severine Ansart,⁶³ Gwenael Le Moal,⁶⁴ Werner Zimmer,⁶⁵ and Javier Ariza⁶⁶ for the Group of Investigators for Streptococcal Prosthetic Joint Infection*

Clinical Infectious Diseases

MAJOR ARTICLE



The Impact of Surgical Strategy and Rifampin on Treatment Outcome in *Cutibacterium* Periprosthetic Joint Infections

Katharina Kusejko,¹ Álvaro Auiún,² Bernhard Jost,³ Benito Natividad,⁴ Carol Strahm,⁵ Christine Thummeel,⁶ Daniel Pablo-Marcos,⁷ Dorsaf Slama,⁸ Gisela Scanferla,⁹ Ilker Uckay,¹⁰ Isabelle Waldmann,¹¹ Jaime Esteban,¹² Jaime Lora-Tamayo,¹³ Martin Claus,¹⁴ Marta Fernández-Sampedro,¹⁵ Marjan Wouthuyzen-Bakker,¹⁶ Matteo Carlo Ferrari,¹⁷ Natalie Gassmann,¹⁸ Parham Sendi,¹⁹ Philippe Jent,²⁰ Philippe C. Morand,²¹ Prkhar Vijayvargiya,²² Richard Trebbe,²³ Robin Patel,²⁴ Roger D. Kouryos,²⁵ Stéphane Corvec,²⁶ Tobias Siegfried Kramer,²⁷ Vincent A. Stadelmann,²⁸ and Yvonne Achermann,²⁹ on behalf of the ESCMID Study Group for Implant-Associated Infections (ESGII)

REUNIÓN ANUAL DEL ÁREA DE ENFERMEDADES INFECCIOSAS, INFLAMATORIAS Y CRÓNICAS DEL IIS-FJD
21 de abril del 2022

UAM Universidad Autónoma de Madrid

Hospital Universitario Fundación Jiménez Díaz
Grupo Quironsalud

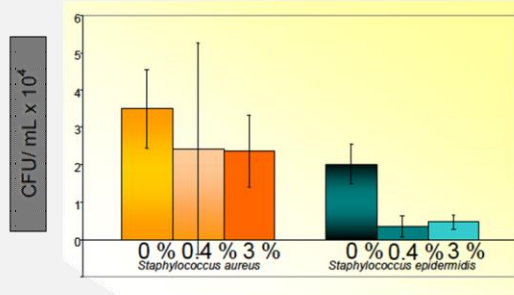
IIS FJD INSTITUTO DE INVESTIGACIÓN SANITARIA FUNDACIÓN JIMÉNEZ DÍAZ

• UHMWPE-Vitamin E

- Hace varios años se propuso la adición de Vitamina E al UHMWPE para disminuir la oxidación y el desgaste.



- Pero esta adición tiene efecto en la adherencia bacteriana, dependiendo de la especie e incluso de la cepa.

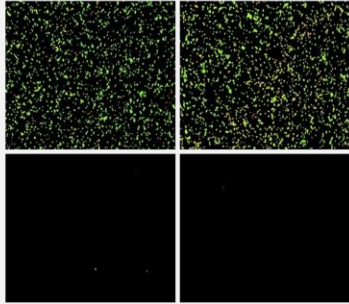


Los buenos estudios deben analizar cepas clínicas, y no solo cepas de colección

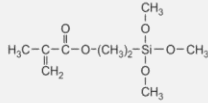
J Mater Sci: Mater Med (2011) 22:1701–1706

Estudios de adherencia y formación de biofilms sobre superficies y materiales modificados.

- Los recubrimientos de sol-gel híbrido organo-inorgánico MAPTMS-TMOS disminuyen la actividad antimicrobiana.
- Son capaces de ser cargados con antibióticos.



3-methacryloxypropyltrimethoxysilane
AMPTMS



Tetramethyl orthosilicate
TMOS

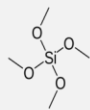
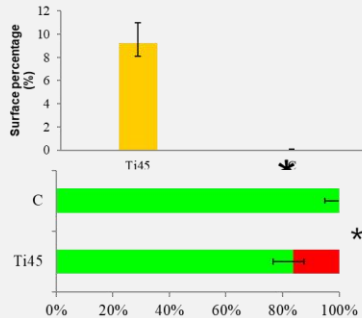
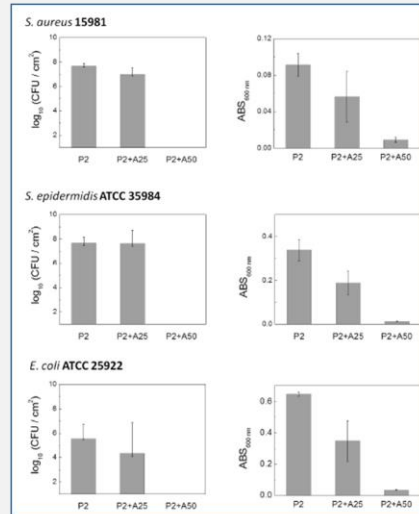


Figure 2. Micrographs of live (green) and dead (red) bacteria adhered of *S. aureus* 15981 on Ti45 (a-b) and on MAPTMS-TMOS sol-gel coating (c-d).



Aguilera-Correa JJ et al. 24th annual meeting EORS 2016



Patent P201730628

Recubrimiento sol-gel capaz de ser usado sobre distintos materiales

A New Antibiotic-Loaded Sol-Gel Can Prevent Bacterial Prosthetic Joint Infection: From *in vitro* Studies to an *in vivo* Model

John Jairo Aguilera-Correa^{1*}, Amaya García-Casas¹, Aranzazu Mediero¹, David Romero¹, Francisca Mulero⁴, Irene Cuevas-López², Antonia Jiménez-Morales^{2,4} and Jaime Esteban^{1*}

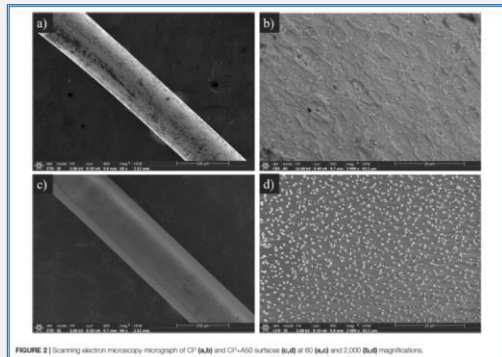


FIGURE 2 | Scanning electron microscopy micrograph of CP (A) and CP-ASO surfaces (B) at 40 (a,b) and 2,000 (c,d) magnifications.

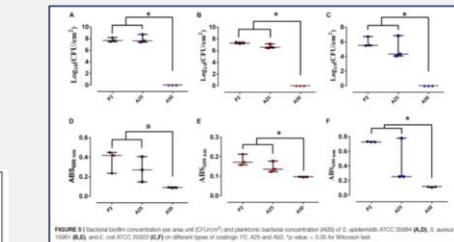


FIGURE 3 | Bacterial bioburden per area and antibiotic resistance (AR) of *S. epidermidis* ATCC 35984 (A), *S. aureus* 15981 (B), and *E. coli* ATCC 25922 (C-F) on different types of coatings (P2, A25 and ASO). *p-value < 0.05 for Wilcoxon test.

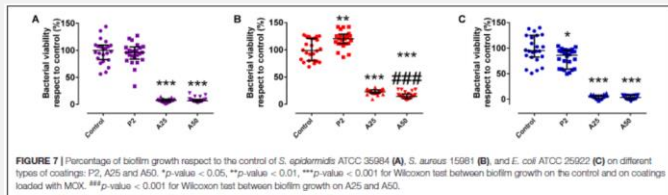
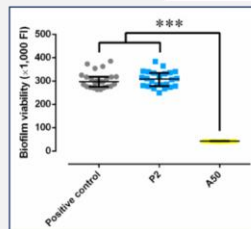
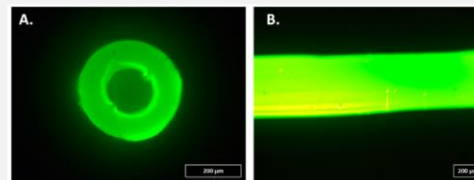


FIGURE 7 | Percentage of biofilm growth respect to the control of *S. epidermidis* ATCC 35984 (A), *S. aureus* 15981 (B), and *E. coli* ATCC 25922 (C) on different types of coatings: P2, A25 and ASO. *p-value < 0.05, **p-value < 0.01, ***p-value < 0.001 for Wilcoxon test between biofilm growth on the control and on coatings loaded with MDK. ###p-value < 0.001 for Wilcoxon test between biofilm growth on A25 and ASO.



A New Antibiotic-Loaded Sol-Gel can Prevent Bacterial Intravenous Catheter-Related Infections

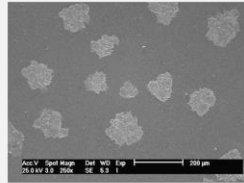
John Jairo Aguilera-Correa^{1,*}, Rosa Vidal-Laso², Rafael Alfredo Carias-Cáliz³, Beatriz Toirac⁴, Amaya García-Casas⁴, Diego Velasco-Rodríguez², Pilar Llamas-Sillero², Antonia Jiménez-Morales^{4,5} and Jaime Esteban¹

Modelos experimentales de infección de cateter IV y de infección protésica

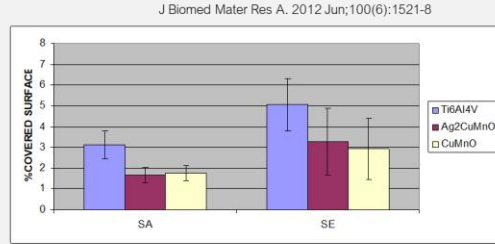
Incorporación de Plata

PREVENCIÓN

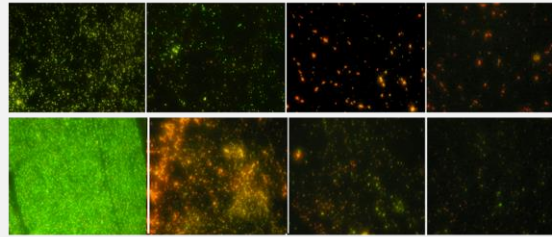
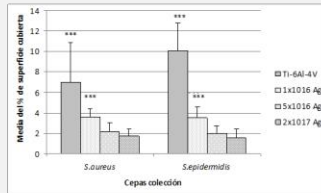
Islas de Plata



Silver islands dispersion at the surface of Ag_2CuMnO_4 amorphous thin films annealed in air



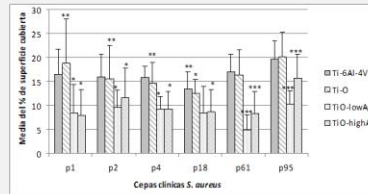
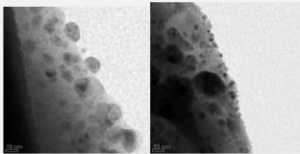
Implantación iónica



20th Annual Meeting of EORS

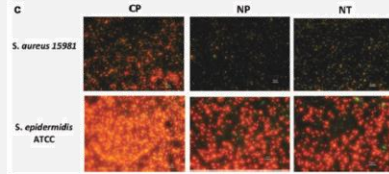
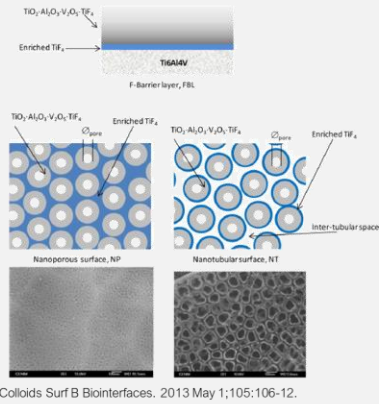
Modificación superficial incorporando plata

TiO₂-Ag

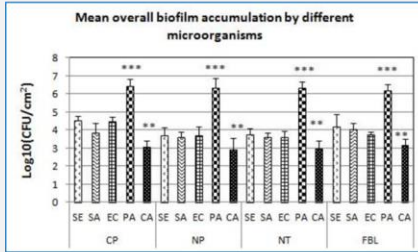
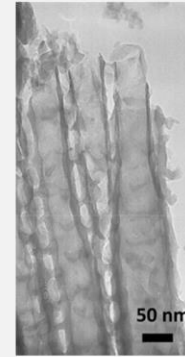
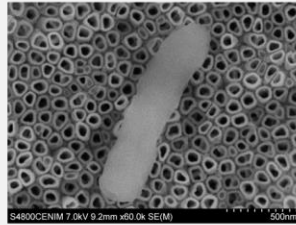


20th Annual Meeting of EORS

- Incorporación de fluor + modificaciones nanoestructurales mediante anodización.

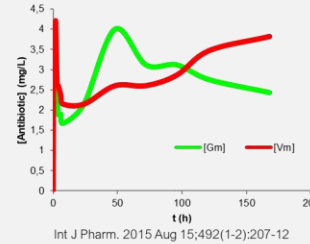


J Biomed Mater Res A. 2012 Jul;100(7):1696-705
 J Biomed Mater Res A. 2015 Jun;103(6):1985-90

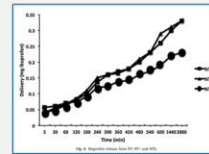


J Mater Sci Mater Med. 2017 Jan;28(1):8

Uso potencial como transporte de fármacos con capacidad osteointegradora, antiadherente y antibiofilm



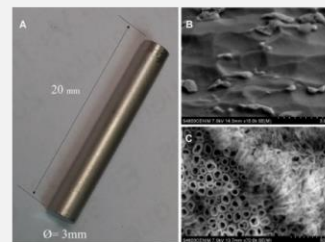
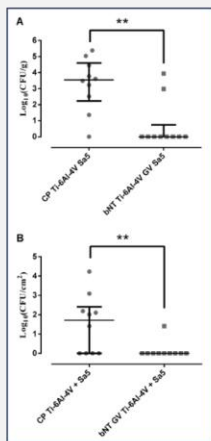
Int J Pharm. 2015 Aug 15;492(1-2):207-12



Modificación superficial incorporando flúor u modificando la nanoestructura superficial

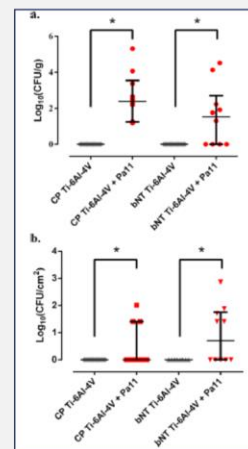
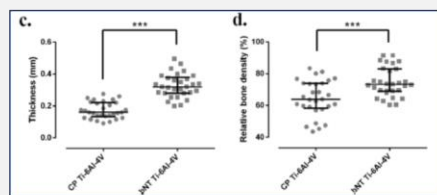
Staphylococcus aureus Prosthetic Joint Infection Is Prevented by a Fluorine- and Phosphorus-Doped Nanostructured Ti-6Al-4V Alloy Loaded With Gentamicin and Vancomycin

Álvaro Auñón,¹ Jaime Esteban,² Antonio L. Doadrio,³ Macarena Boiza-Sánchez,⁴ Aranzazu Mediero,⁵ Diego Eguiar-Blázquez,⁶ José Cordero-Ampuero,⁷ Ana Conde,⁸ María-Ángeles Arenas,⁹ Juan-José de-Damborenea,⁹ John J. Aguilera-Correa¹⁰



Urine Aluminum Concentration as a Possible Implant Biomarker of Pseudomonas aeruginosa Infection Using a Fluorine- and Phosphorus-Doped Ti-6Al-4V Alloy with Osseointegration Capacity

John-Jairo Aguilera-Correa,^{*,1} Álvaro Auñón,² Macarena Boiza-Sánchez,³ Ignacio Mahillo-Fernández,¹¹ Aranzazu Mediero,¹ Diego Eguiar-Blázquez,² Ana Conde,³ María-Ángeles Arenas,⁴ Juan-José de-Damborenea,¹ José Cordero-Ampuero,⁵ and Jaime Esteban⁶



Modelos experimentales de infección protésica

• Cerámicas

- Compuestos de óxidos metálicos. Presentan propiedades diferentes en cuanto a la adherencia bacteriana.

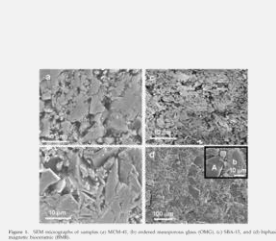


Figure 3. SEM micrographs of samples for MCM, SEA, and CMG.

J Biomed Mater Res A. 2009 Apr;89(1):215-23

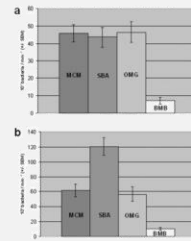
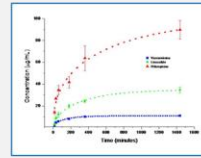
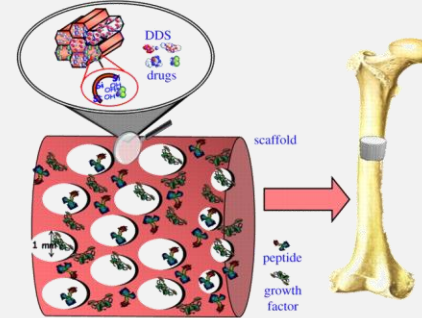


Figure 3. Adherence of *S. aureus* (a) and *S. epidermidis* (b) colony forming units (CFU/cm²) on the external surface of multifunctional bio ceramics.

Int J Antimicrob Agents. 2012 Sep;40(3):252-6



Philos Trans A Math Phys Eng Sci. 2012 Mar 28;370(1963):1400-21



Las cerámicas mesoporosas pueden usarse como reemplazo de hueso, moldes (*scaffolds*) y vehículo de fármacos.

- Nanocomposite Ag-YSZ (Yttria Stabilized Zirconia)

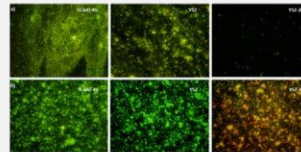
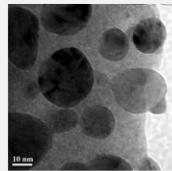
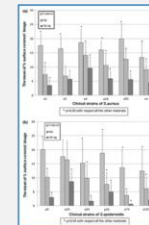
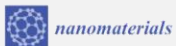


Fig. 4. Example of the fluorescence microscopy images for Ti-6Al-4V surface, Ti-6Al-4V coated with YSZ surface and Ti-6Al-4V coated with YSZ-Ag surface covered by the collection matrix of a *S. aureus* and *S. epidermidis*.

J Mater Sci Mater Med. 2016 Jan;27(1):6



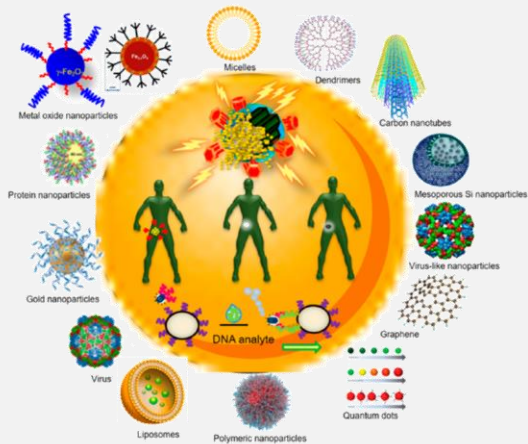
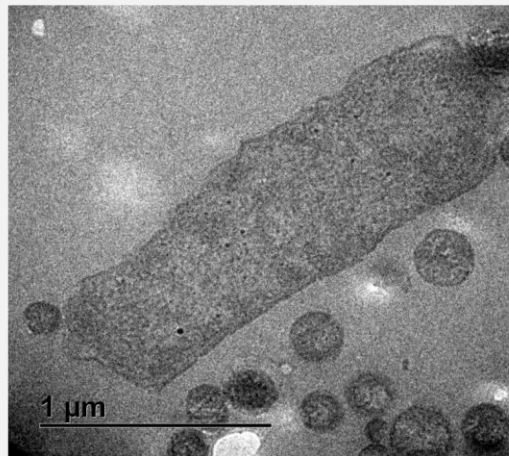
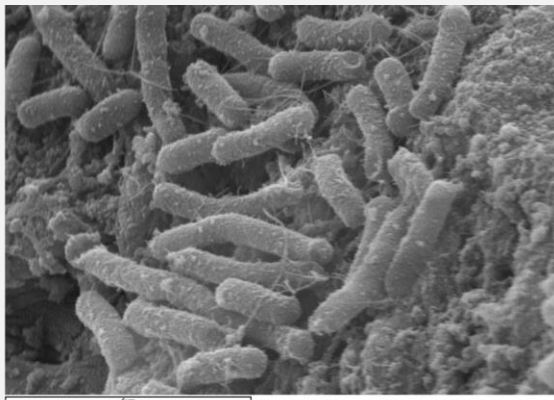
Nanopartículas



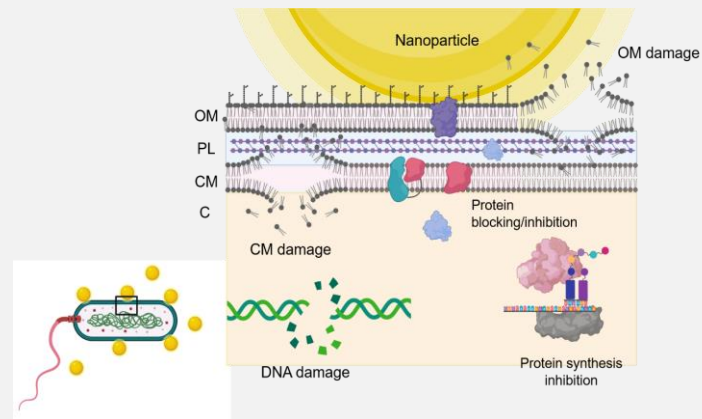
Review

Inorganic and Polymeric Nanoparticles for Human Viral and Bacterial Infections Prevention and Treatment

John Jairo Aguilera-Correa ^{1,*}, Jaime Esteban ² and María Vallet-Regí ^{1,3,*}



NUEVAS ALTERNATIVAS



Impact of the antibiotic-cargo from MSNs on gram-positive and gram-negative bacterial biofilms

Anna Aguilar-Colomer^{a,b}, Montserrat Colilla^{a,b}, Isabel Izquierdo-Barba^{a,b},
Carla Jiménez-Jiménez^{a,b}, Ignacio Mahillo^c, Jaime Esteban^{d,e*}, María Vallet-Regí^{a,b,*}

Microporous and Mesoporous Materials 311 (2021) 110681

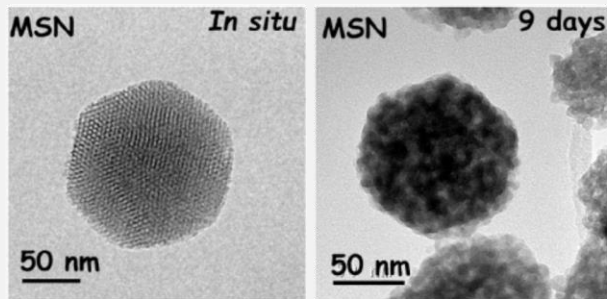
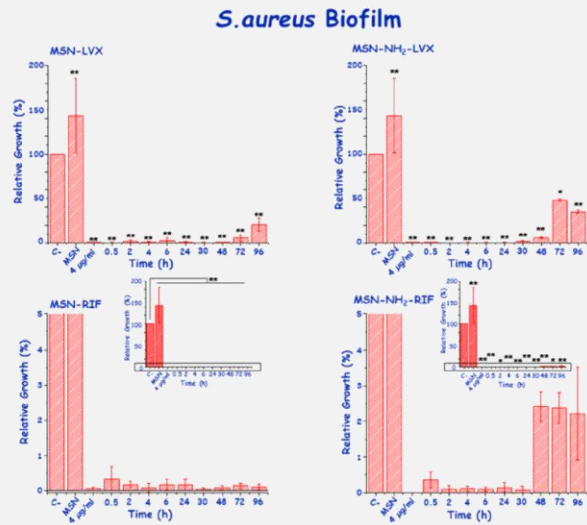
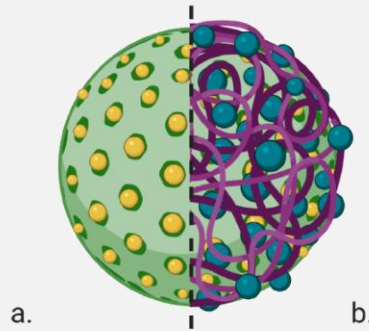


Fig. 2. TEM images of pristine MSNs before and after 9 days being soaked in PBS under physiological conditions.

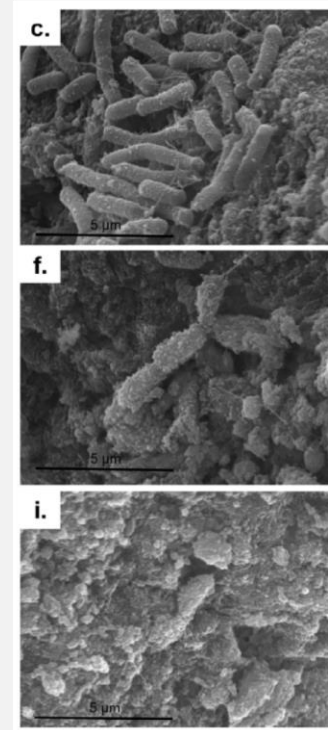
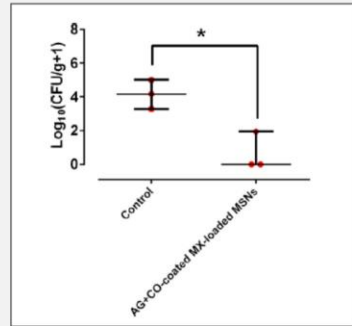
The results demonstrate that MSNs are biocompatible and versatile nanocarriers able to load and release diverse antibiotic-cargoes with positive and prolonged antibiofilm effect, which opens up promising expectations to locally treat chronic bone infection. The preliminary *in vitro* studies to assess the colloidal stability of MSNs in physiological conditions support the formation of a protein corona on the nanoparticles surface. Such protein coverage could compromise the efficiency and biological outcome of the nanoparticles *in vivo* and therefore much research effort is still needed in the path from bench to bedside.



- El empleo de distintos tipos de nanopartículas permitiría realizar un tratamiento individualizado de cada caso.



Scheme 1. Mesoporous silica nanoparticles (green) loaded with moxifloxacin (yellow) (a) and coated with Arabic gum (purple) plus colistin (blue).



Estudios con nanopartículas funcionalizadas

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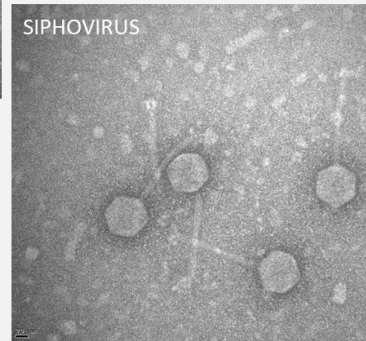
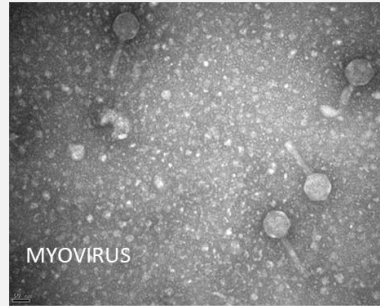
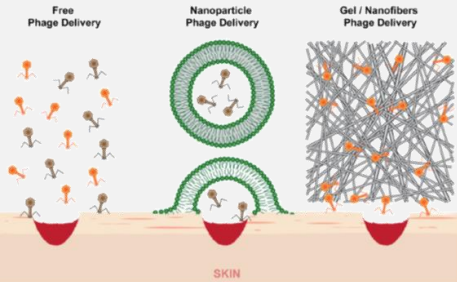
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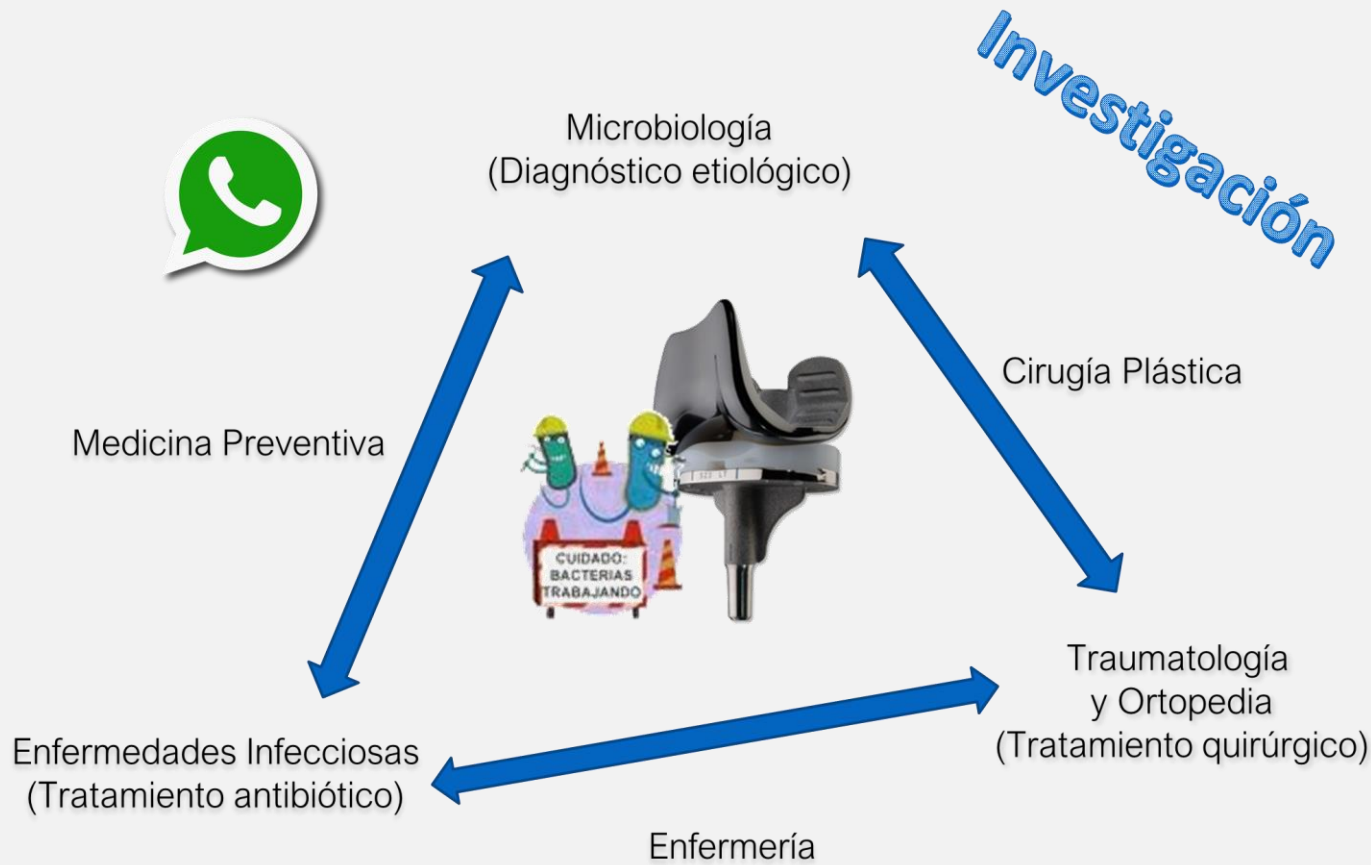
Arabic gum plus colistin coated moxifloxacin-loaded nanoparticles for the treatment of bone infection caused by *Escherichia coli*

J.J. Aguilera-Correa^{a,b,1}, M. Gisbert-Garzarán^{a,c,1}, A. Mediero^d, R.A. Carías-Cálix^e, C. Jiménez-Jiménez^{a,c}, J. Esteban^{b,f,*}, M. Vallet-Regí^{a,c,*}

Bacteriófagos

El uso de virus bacteriófagos para destruir las bacterias sería una herramienta potencialmente muy útil para tratar infecciones por microorganismos multirresistentes.





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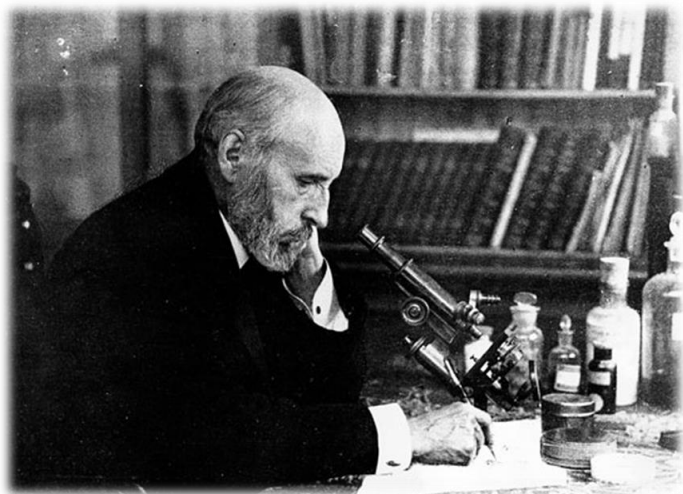
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REUNIÓN ANUAL DEL ÁREA DE ENFERMEDADES INFECCIOSAS, INFLAMATORIAS Y CRÓNICAS DEL IIS-FJD
21 de abril del 2022



“El secreto para llegar es muy sencillo; se reduce a dos palabras: trabajo y perseverancia.”



G. Ramon Cayal