

Xerogel Coatings to bone implants prevent development of biofilm formation and severe osteomyelitis

Marilina Douloudi¹, Eleni Nikoli¹, Michaela Papageorgiou^{1,3}, Michael Arkas¹, Paraskevi Gomoza^{2,3}, Michalis Vardavoulas², Ioanna Kitsou³, Athina Tsetsekou³, Yuly López⁴, Sara Soto⁴, Amalie Blirup-Plum⁵, Bent Aalbæk⁵, Henrik Elvang Jensen⁵, Louise Kruse Jensen⁵

¹*Institute of Nanoscience Nanotechnology NCSR “Demokritos” Patriarchou Gregoriou Str., 15310 Aghia Paraskevi, Athens, Greece*

²*PyroGenesis SA, Technological Park of Lavrion, 1 Athens-Lavrion Ave., 195 00 Lavrion, Greece*

³*Laboratory of Metallurgy, School of Mining & Metallurgical Engineering, National Technical University of Athens, 9 Heroon Polytechniou Ave., Zografos, 157 80 Athens, Greece*

⁴*ISGlobal, Hospital Clínic—Universitat de Barcelona, 08036 Barcelona, Spain*

⁵*Ridebanevej 3, 1870 Frederiksberg C, Department of Veterinary and Animal Sciences, University of Copenhagen, Denmark*

Chirurgical insertion risks and biofilm formation constitute major drawbacks to orthopaedical implants applications, since they may induce severe infections such as prosthetic joint infection (PJI) and implant associated osteomyelitis (IAO). The immobilization of antibacterial, antibiotic and/or antibiofilm compounds to metals is problematic.

A pretreatment of model bone implants with metallic titanium microspheres via cold High Velocity Oxygen Fuel (Cold HVOF) thermal spray induces microporosity. Hydrogel formation reaction from orthosilicic acid and hyperbranched polyethylene imine takes place into these artificial pores. The active ingredient may be introduced to the initial solution or for best results at the last stage to the dried xerogel. Multiple gel coatings and xerogel wettings by aqueous and/or organic solutions can be performed.

Chemical reactions and supramolecular interactions of gentamicin (antibiotic) and lauroyl lactylate derivatives with the dendritic polymer were monitored spectroscopically and by DLC whereas their content was estimated by thermogravimetric analysis. Antibacterial and Antibiofilm tests were conducted for *E. coli* (HC1501), *S. aureus* (S207) and a *C. parapsilosis* (SMI416). Toxicity assessment was carried out using *Caenorhabditis elegans* model.

The implants were tested in vivo in a clinical representative large animal model (pigs inoculated with *S. aureus* S54F9) by Macroscopic pathology, Serum analysis, Computed Tomography, Microbiology, Histology, Immunohistochemistry and Pharmacokinetics. They exhibited excellent results in preventing development of IAO and eradicating surgical contamination induced by a high virulent bacterium. This already established potential for prophylactic and therapeutic clinical applications may be extended to all pharmaceutical and osteo-synthetic compounds.