

## **Innovative coating technologies and nanotechnological approaches to reduce bacterial biofilms**

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Bacterial resistance, one of the biggest threats to human health in the 21st century, is the ability of bacterial cells to resist one or more types of antibiotics. Few antibiotics have been developed in the last two decades. With limited antibiotic options and an escalating bacterial resistance there is an urgent need to explore alternative ways of meeting this global challenge. Antibiotic-resistance can be developed by bacteria using different mechanisms but one of this is related to the capacity to form biofilms. Biofilms are functional aggregates of sessile microorganisms encased within a self-generated extracellular polymeric matrix composed of polysaccharides, lipids, proteins, and DNA. Microorganisms living in biofilms are much more resistant to hostile environments than their planktonic counterparts and exhibit enhanced resistance against the microbicides. From the human perspective, biofilms can be classified into beneficial, neutral, and harmful: most of the actions are oriented to eradicate harmful biofilms. In particular biofilm infections in medical implants are a global problem presenting a significant socioeconomic impact. Infact, biofilm is considered a leading cause of medical devices failure and infection recurrence: at present, the only treatment strategy to eradicate the infection is implant removal. Despite the multifactorial causes that lead to biofilm-related medical device infections, bacterial adhesion to the implant surface is a common and essential step in all instances. The ideal implant surface would be one that minimises bacterial adhesion, inhibits biofilm formation, and confers an effective bactericidal action. Different type of coatings technologies have been developed and classified into i) passive surface modification that rely on repulsion of microbes, ii) active surface modification that attempt to kill the microorganism, and iii) approaches that affect biofilm architecture, which focus on reducing biofilm virulence factors. Whilst the strategies outlined above exist with the aim of preventing biofilm formation, there remains a need to treat biofilms that have already formed. Several studies indicate that various types of nanomaterials (both organic and inorganic) have demonstrated promising results regarding antibacterial and antibiofilm activity. It has also been claimed that the use of nanoparticles is one of the most promising strategies to overcome microbial drug resistance. The size of the nanomaterials provides a large surface-area to volume ratio, which allows the binding of a large number of high affinity ligands, equipping nanoparticles with a multivalency in eradicating bacterial cells. In particular, owing to the optical and electrical properties of gold nanoparticles (AuNPs), they have gained increasing attention. One particularly important feature is their localized surface plasmon resonance (LSPR), which plays an important role in many nanotechnological applications. Two main approaches that employ light activation in enhancing the antibacterial activity of gold nanoparticles are antibacterial photothermal therapy (APTT) and antibacterial photodynamic therapy (APDT). Although the safety and toxicity of the AuNPs is still a topic that needs to be further addressed, there are some promising studies that feature both an excellent safety profile along with potential therapeutic benefits.

In summary, utilizing multimodal prevention and therapeutic strategies that do not function through the same mechanism of action have the highest potential to terminate bacteria, without allowing for resistant strains to evolve.