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Perspective

Impacts of Osseo Integration by Engineered Probiotics Biofilm

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1. Description

Infections associated with implants and insufficient osteogenic activity may result in implant failure or postpone a patient's recovery. It is impossible to prevent the ensuing financial load and physical suffering. In particular, elderly people with osteoporosis have a very high fracture incidence. After undergoing fracture surgery, the elderly patients typically suffer from cardiovascular disorders such as thrombus formation and subsequent myocardial infarction due to delayed healing and long periods of bed rest, which increase the mortality of senior patients. Additionally, following orthopaedic surgery, patients typically require systemic antibiotic therapy to prevent bacterial infection. However, due to the overuse or improper use of antibiotics, the prevalence of multidrug-resistant bacterial diseases has significantly jeopardised human health. The incapacity of current antibiotics to treat all infections linked to superbacteria is already developing into a very significant issue. As a result, the ideal implant would both speed up bone tissue repair and avoid drug-resistant bacterial infections. Different approaches have been tried to address this problem, integrating both antibacterial and osteogenic properties into the implant, using components like Ag/Zn, Ag/Sr, Cu/Mg, or ZnO/osteogenic peptides.

The use of intricate production processes or heavy metals that could cause tissue harm may limit the clinical potential of present techniques.

To minimise bacterial infection and enhance tissue regeneration, it is therefore extremely desired to establish a straightforward and secure method, especially when employing U.S. Food and Drug Administration-approved products. Widespread interest has been shown in microbial-mediated therapies for a number of disorders. Some bacteria, including *Salmonella, Escherichia*, and *Listeria*, have the capacity to target the hypoxic microenvironment of tumour tissues in cancer therapy. To inhibit the growth of tumours, non-pathogenic microorganisms can be genetically modified or mixed with nanomaterials. Probiotics are crucial for the gut microbiome, which helps to keep the bowels in good health. Probiotics, which are nonpathogenic organisms, are frequently used to treat a variety of digestive disorders such inflammatory bowel disease, irritable bowel syndrome, and infectious diarrhoea due to their capacity to eradicate pathogenic bacteria and control the immune response of the host. Probiotics can also be engineered to generate useful proteins or chemicals that can reduce inflammation or aid in tissue repair. Although such genetically modified bacteria offer untold promise, their therapeutic uses have been constrained by the possible biosafety issue brought on by off-target toxicity. Additionally, since introducing live bacteria into the bloodstream increases the risk of bacteremia or sepsis, the majority of probiotics must be taken orally.

Dairy products like yoghurt and cheese include probiotics that are naturally present in the human mouth and intestine. The synthesis of bacteriocin, lactic acid, and hydrogen peroxide by *L. casei* results in outstanding antibacterial efficacy against pathogenic bacteria, including methicillin-resistant *Staphylococcus Aureus* (MRSA). Its application in the prevention of implant-related infections by MRSA is still understudied, nonetheless, given the risk of sepsis. Additionally, probiotic bacteria's cell walls contain substances like peptidoglycan, lipoteichoic acid, and some particular proteins that are important in the modulation of the human immune system. As is well known, the early inflammatory response caused by biomaterial implantation. On the surface of implants, host macrophages proliferate during the foreign body reaction. In order to balance inflammation and regeneration, the activity of macrophages is essential. Osteogenic factors can be induced in macrophages to hasten bone fusion with the implant. By attaching sugar units to carbohydrate receptors on the macrophage surface, polysaccharides like lipopolysaccharide can activate macrophages.

According to a recent study, zymosan, a fungus polysaccharide, can be used to change the surface of titanium implants and enhance implant-bone integration by encouraging macrophages to release osteogenic cytokines. It is well known that *L. casei*'s cell walls and EPS (polysaccharides, proteins, and nucleic acids) both contain polysaccharides and that bacteria and the Extracellular Polymeric Substance (EPS) matrix make up the majority of bacterial biofilms. The exposed polysaccharides of *L. casei* biofilms can so easily excite macrophages that come into contact with the organism. We hypothesised that *L. casei* biofilms can encourage macrophages to release osteogenic factors and increase osteogenic differentiation of Mesenchymal Stem Cells (MSCs) based on the aforementioned polysaccharide component of bacterial biofilms. *L. casei* was selected in this instance as a secure probiotics-based agent to alter the surface of Ti implants. To stop colonisation by live bacteria, *L. casei* biofilms were cultivated on the surface of Ti substrates that had undergone alkali heat treatment before being inactivated by Ultraviolet (UV) irradiation. We anticipated that an inactivated *L. casei* biofilm may both inhibit MRSA infection and enhance bone tissue regeneration because the active component of *L. casei* biofilms survives after brief UV exposure.

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