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Lysostaphin-Coated Titan-Implants Preventing Localized Osteitis by *Staphylococcus aureus* in a Mouse Model

CEYLAN D. WINDOLF¹*, TIM LÖGTERS¹, MARTIN SCHOLZ^{1,2}, JOACHIM WINDOLF¹, SASCHA FLOHÉ¹

¹Department of Trauma- and Hand Surgery, Heinrich-Heine University Duesseldorf, Moorenstr. 5, 40225 Duesseldorf, Germany,

²LEUKOCARE AG, Am Klopferspitz 19, 82152 Munich/Martinsried, Germany

*ceylan.windolf@uni-duesseldorf.de

The increasing incidence of implant-associated infections induced by Staphylococcus aureus (SA) in combination with growing resistance to conventional antibiotics requires novel therapeutic strategies. In the current study we present the first application of the biofilmpenetrating antimicrobial peptide lysostaphin in the context of bone infections. In a standardized implant-associated bone infection model in mice beta-irradiated lysostaphincoated titanium plates were compared with uncoated plates. Coating of the implant was established with a poly(D,L)-lactide matrix (PDLLA) comprising lysostaphin formulated in a stabilizing and protecting solution (SPS). All mice were osteotomized and infected with a defined count of SA. Fractures were fixed with lysostaphin-coated locking plates. Plates uncoated or PDLLA-coated served as controls. All mice underwent debridement and lavage on Days 7, 14, 28 to determine the bacterial load and local immune reaction. Fracture healing was quantified by conventional radiography. On Day 7 bacterial growth in the lavages of mice with lysostaphin-coated plates showed a significantly lower count to the control groups. Moreover, in the lysostaphin-coated plate groups complete fracture healing were observed on Day 28. The fracture consolidation was accompanied by a diminished local immune reaction. However, control groups developed an osteitis with lysis or destruction of the bone and an evident local immune response. The presented approach of terminally sterilized lysostaphincoated implants appears to be a promising therapeutic approach for low grade infection or as prophylactic strategy in high risk fracture care e.g. after severe open fractures.