Novel anti-infective implant substrates: Controlled release of antibiofilm compounds from mesoporous silica-containing macroporous titanium

A Braem\textsuperscript{2}, K De Cremer\textsuperscript{1,3}, K De Brucker\textsuperscript{4}, N Delattin\textsuperscript{1}, E Gerits\textsuperscript{1}, B Neirinck\textsuperscript{2}, K Vandamme\textsuperscript{4}, JA Martens\textsuperscript{5}, J Michiels\textsuperscript{1}, J Vleugels\textsuperscript{2}, BPA Cammue\textsuperscript{1,3}, K Thevissen\textsuperscript{1}

\textsuperscript{1}Centre of Microbial and Plant Genetics (CMPG), KU Leuven, Kasteelpark Arenberg 20 Box 2460, 3001 Leuven, Belgium. \textsuperscript{2}Department of Materials Engineering (MTM), KU Leuven, Kasteelpark Arenberg 44 Box 2450, 3001 Leuven, Belgium. \textsuperscript{3}Department of Plant Systems Biology, VIB, Technologiepark 927, 9052 Ghent, Belgium. \textsuperscript{4}Biomaterials - BIOMAT, Department of Oral Health Sciences and Prosthetic Dentistry, KU Leuven and University Hospitals Leuven, Kapucijnenvoer 7 Box 7001, 3000 Leuven, Belgium. \textsuperscript{5}Centre of Surface Chemistry and Catalysis (COK), KU Leuven, Kasteelpark Arenberg 23 Box 2461, 3001 Leuven, Belgium

INTRODUCTION: Bone implants with open porosity enable fast osseointegration, but also present an increased risk of biofilm-associated infections. Since an implant, as a biocompatible surface, presents a favorable support for microbial adherence and because the local immune system is temporarily repressed at the implant/tissue interface due to the occurrence of a foreign body response, the implantation site is inherently at risk for microbial contamination [1,2]. To reduce microbial biofilm formation on titanium substrates, we designed a novel implant material enabling controlled release of antibiofilm molecules.

METHODS: The novel implant material consisted of a mesoporous SiO\textsubscript{2} diffusion barrier with controlled drug release functionality integrated in a macroporous Ti load-bearing structure. Using an in house made \textit{in vitro} tool consisting of Ti/SiO\textsubscript{2} disks in an insert set-up (Fig 1), through which molecules can diffuse from feed side to release side, a continuous release without initial burst effect of various broad-spectrum antibiofilm compounds was sustained for at least 9 days. We used the fungal pathogen \textit{Candida albicans} and the bacterial pathogen \textit{Streptococcus mutans} as a model to assess anti-infective properties of the new titanium substrates.

RESULTS: We found that the \textit{C. albicans} and \textit{S. mutans} biofilm growth on the compound-release side was significantly inhibited, establishing a proof-of-concept for the drug delivery functionality of mesoporous SiO\textsubscript{2} incorporated into a high-strength macroporous Ti-carrier.

DISCUSSION & CONCLUSIONS: Next-generation implants made of this composite material and equipped with an internal reservoir (feed side) can yield long-term controlled release of antibiofilm compounds, effectively treating infections on the implant surface (release side) over a prolonged time.


ACKNOWLEDGEMENTS: The research leading to these results has received funding from the Industrial Research Fund (IOF) of KU Leuven (IOF/KP/11/007), the Flemish government via the Methusalem grant to J.A.M. and the Hercules Foundation (projectZWO9-09). B.N., K.T. and N.D. acknowledge the receipt of a postdoctoral grant from FWO-Vlaanderen (1.2.B62.12N), from IOF (IOFm/05/022) and from IWT-Vlaanderen (IWT101095), respectively.

http://www.ecmjournal.org