Copper-electrodeposition onto Ti6Al4V-ELI produces a bactericidal and immunomodulatory biomaterial for orthopaedic implant applications.

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INTRODUCTION:

Implanted biomaterials are used to restore or prevent the loss of function associated with ageing and physical trauma. However, infection and ineffective immune responses to these devices result in a significant proportion of implant failure. Currently, no prosthetic or fixation device is completely resistant to bacterial colonisation and as such, it is vital that new biomaterials are investigated. In this project, we aimed to characterise the microbiological and host cell responses to a novel biomaterial, in which metallic copper was electroplated onto an orthopaedic Ti6Al4V-ELI surface, to endow it with functional bactericidal and immunomodulatory properties.

METHODS:

In this investigation, bacterial viability counting and scanning electron microscopy were performed to quantify and visualise the direct and indirect bactericidal effects of the Cu-electroplated titanium (Cu-Ep Ti) against a lab strain (*Staphylococcus aureus* ATCC 25923), and a clinical *S. aureus* periprosthetic joint infection (PJI) isolate in tryptic soy broth (TSB) and Roswell Park Memorial Institute (RPMI) at early (4 h) and extended (24, 48 h) time points. The effect of the copper electroplating on human THP-1 macrophage adhesion and viability was analysed by nucleocounting. Further, characterisation on how interactions with the copper surface modulated macrophage phagocytosis of pHrodo *S. aureus* bioparticles was evaluated.

RESULTS:

Results showed potent antimicrobial activity against *S. aureus* ATCC 25923 and clinical PJI isolate, alongside promising host-immunomodulatory properties. Direct and indirect exposure to Cu-Ep-Ti surfaces produced potent bactericidal effects resulting in significant reductions in bacterial viability at 24 h in TSB (94-98 %) and RPMI (99-100 %), with complete eradication of *S. aureus* in some cases. As expected, cytotoxicity was observed in THP-1 macrophages without media exchange, though when media was exchanged at 8, 24 and 48 h THP-1 cell viability was equivalent to that of the Ti control. Interestingly macrophages adhered to the copper material or grown in the presence of copper ions from the material showed a significant increase in phagocytosis of *S. aureus* bioparticles compared to Control-Ti (7-fold increase), suggesting a dual bactericidal and host immunomodulatory mechanism.

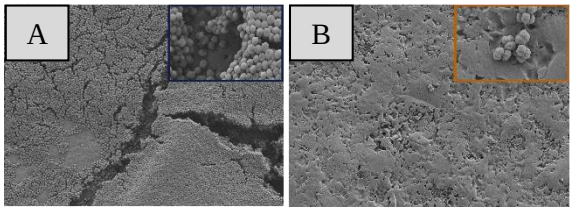

***Fig. 1**: S. aureus biofilm morphology on (A) Control-Ti or (B) Cu-Ep-Ti after 24 h growth*

DISCUSSION & CONCLUSIONS:

We have shown that this novel Cu-electroplated Ti biomaterial can limit bacterial contamination on the implant surface, whilst simultaneously promoting a beneficial antimicrobial immune response.