Using MGN-3 to mediate innate immunity in a diabetic (hyperglycaemic) model of an infected chronic wound.

Sana Shah, Mohamed El Mohtadi and Jason Ashworth*

* Centre for Bioscience, Manchester Metropolitan University, Manchester, United Kingdom.
Jason Ashworth (J.Ashworth@mmu.ac.uk)

Presented at the Microbiology Society EARLY CAREER MICROBIOLOGISTS' (ECM) FORUM SUMMER CONFERENCE, 12 - 13 July 2022, Faculty of Engineering, University of Sheffield, UK

Background

The diabetic foot ulcer (DFU) is a type of chronic wound presenting in type 2 diabetics that frequently becomes infected by polymicrobial communities, leading to significant morbidity and mortality. Antibiotics are used as the first line of defence against DFU infections but over-usage has led to widespread antibiotic resistance. To reduce the reliance on antibiotics, novel therapies are desired that can promote infection clearance by stimulating innate host immune responses, thereby either replacing or working alongside antibiotic intervention. This study investigated the use of Biobran (MGN-3) to mediate innate host clearance of typical wound pathogens in a diabetic (hyperglycaemic) model of an infected DFU.

Methods

Host-pathogen interaction assays (n = 12) were used to assess the effect of MGN-3 treatments on M1 (classically activated macrophage)-mediated phagocytosis of Gram-positive Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Gram-negative *Pseudomonas aeruginosa* (PA01) under euglycemic (11mM) and hyperglycaemic (15mM, 20mM and 30mM) culture conditions. The phagocytic ability of M1 macrophage exposed to MGN-3 (0.5, 1.0, 2.0 mg/ml) was compared against bacterial clearance observed in the absence of MGN-3 (untreated control), following treatment with rice starch (0.5, 1.0, 2.0 mg/ml; negative control) and following treatment with bacterial lipopolysaccharide (LPS 5μg/ml; positive control).

Results

Increasing levels of hyperglycaemia significantly ($p<0.05$) increased the bacterial recovery by impairing M1-mediated phagocytosis. However, MGN-3 and LPS supplementation reversed the detrimental effect of glucose by significantly increasing ($p<0.05$) M1-mediated phagocytosis of both MRSA and PAO1 in a dose dependent manner compared to the untreated and rice starch-treated controls.

Conclusion

MGN-3 significantly reversed the detrimental impact of increasing hyperglycaemia on M1-mediated phagocytosis, highlighting the beneficial effect of MGN-3 on promoting bacterial clearance in a dose-dependent manner under hyperglycaemic conditions. These findings suggest the use of MGN-3 in local wound dressings as a potential cost-effective therapeutic strategy to resolve clinical DFU infections warrants further investigation.