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N-glycan signature of activated neutrophil region of *S. aureus* skin infection mouse models

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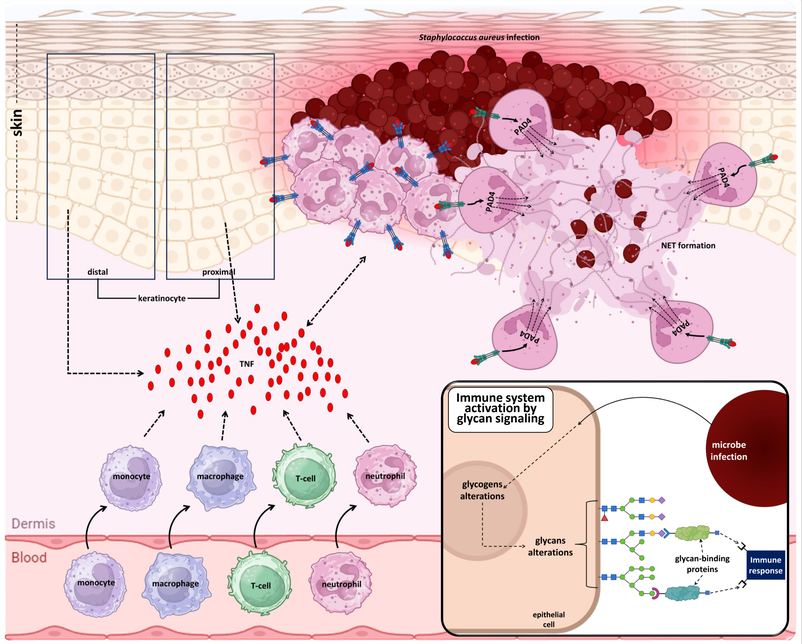
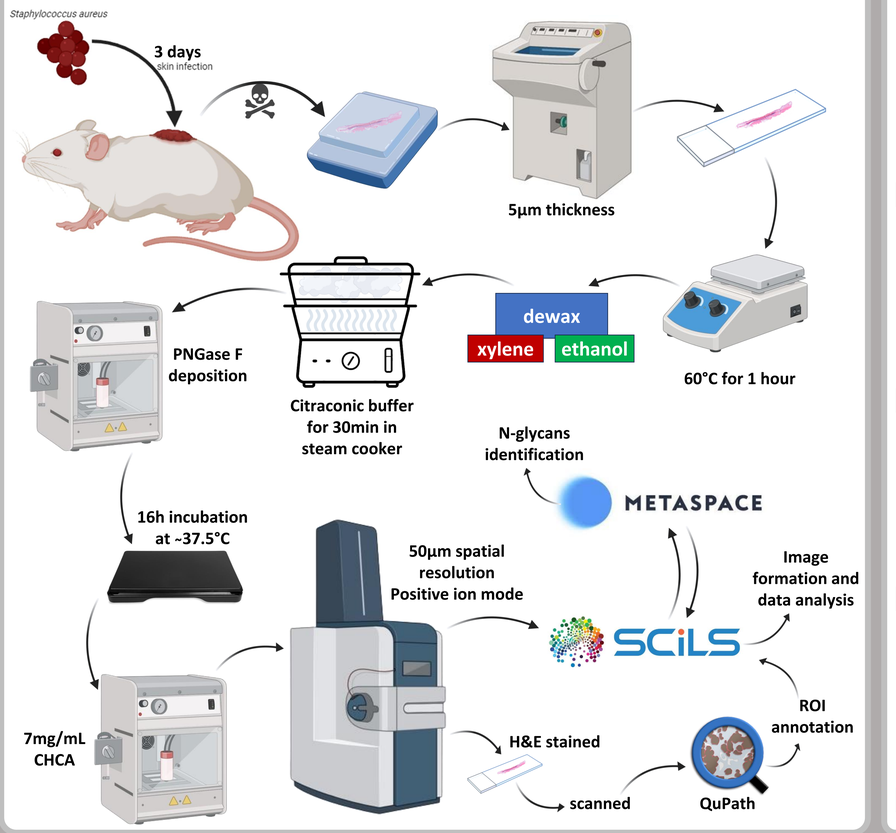
INTRODUCTION

Staphylococcus aureus, a primary cause of skin infections, has emerged as a significant public health concern due to the rise of antibiotic-resistant strains. In humans, the inhibition of tumor necrosis factor (TNF) has been associated with an elevated risk of *S. aureus* infections. Neutrophils (PMNs) are the primary cells expressing the TNF receptors TNFR1 and TNFR2 and have the ability to activate the immune system. TNFR2, including *PAD4*+/+ (peptidylarginine-deiminase-4) induces the synthesis of NETs (neutrophil extracellular traps) which is related to an effective host defense. Several studies have investigated alterations of the *N*-glycan structures during innate and adaptive immune responses. Biologic and structural alterations in the cell membrane, like *N*-glycans and *PAD4-/-*, have been correlated to increased skin infections.

The aim of this study is to compare the *N*-glycan signature between wild type (WT), TNFR1 knockout, TNFR2 knockout and *PAD4-/-* groups in PMN, keratinocyte proximal and distal regions using MALDI-MSI.

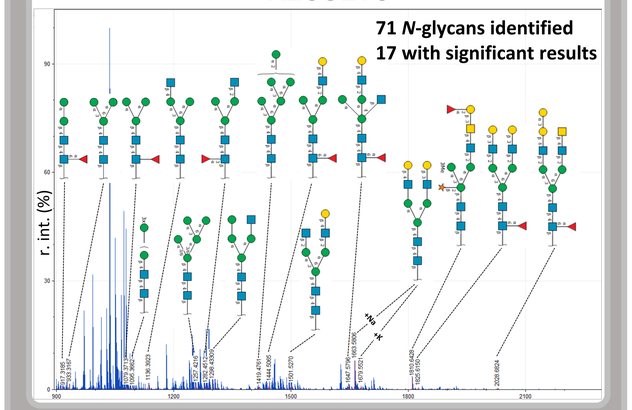


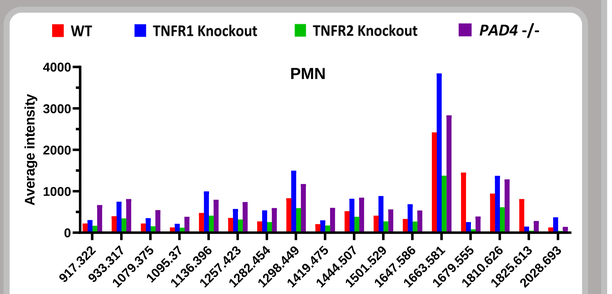
METHODS

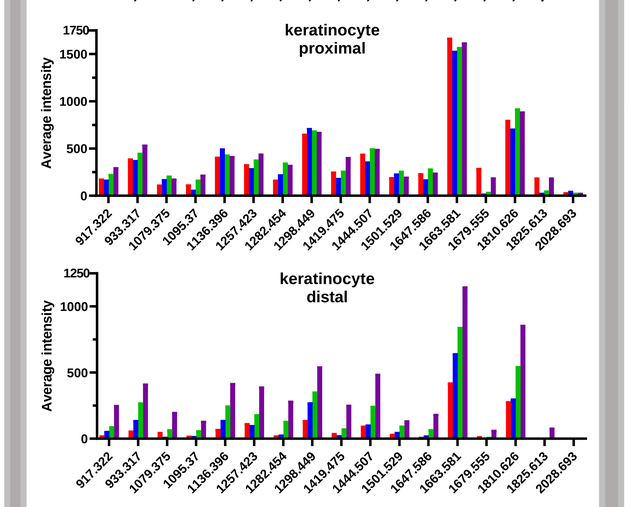


METHODS – sample groups in triplicate

RESULTS

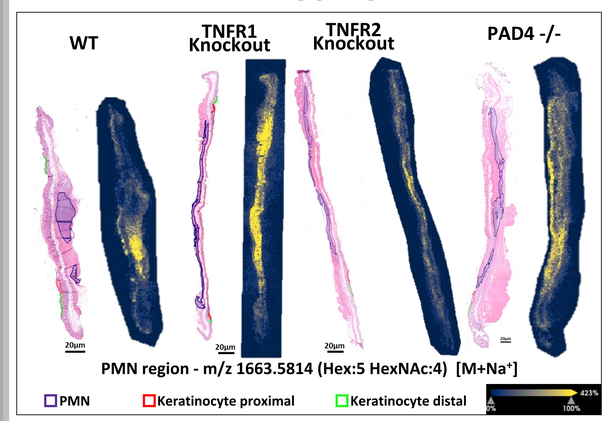


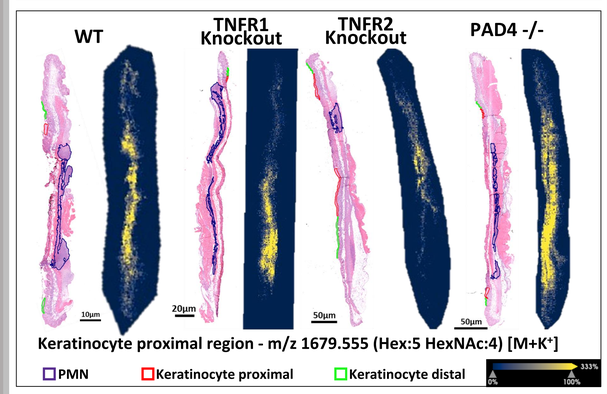


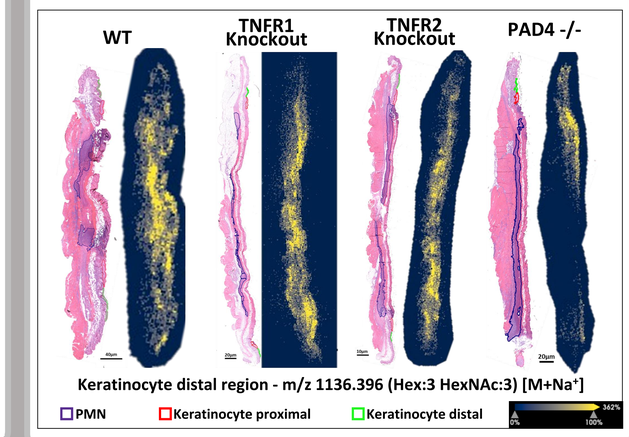


N-glycans with significant difference in the average intensity between the groups PMN (neutrophil region) and proximal and distal keratinocyte region adjacent to PMN.

RESULTS







In the PMN region, TNFR1 knockout and PAD4-/- groups showed higher intensity of several *N*-glycans compared to WT group. Only 1679.555 was higher in the WT group. In the TNFR2 group, all *N*-glycans were decreased.

The analysis of the Keratinocyte regions showed no significant differences between the groups in the proximal region, besides the 1679.555 and 1825.613 with higher intensity in WT and *PAD4-/-* groups. In the distal region, all *N*-glycans were higher in the *PAD4-/-* and TNFR2 groups. The 2028.693 was absent in all groups and the 1825.613 was present only in the *PAD4-/-* mice.

CONCLUSIONS

Our study found specific alterations in the *N*-glycan intensity between the different regions analyzed around the *S. aureus* infected area in the mouse skin. These alterations can be related to specific adaptive immune response in the neutrophil region and induction of NET formation in the keratinocyte distal region.