UNIVERSITI TEKNOLOGI MARA

A GLYCOPROTEOMICS STUDY OF *Staphylococcus epidermidis* BIOFILM

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ABSTRACT

Staphylococcus epidermidis is the leading opportunistic bacteria among the coagulase-negative staphylococci (CoNS) which caused many biofilm-associated infections. Biofilm exhibits an extraordinary resistance towards antimicrobial agents. To date, biofilm-associated infections have increased worldwide with no promising treatment. Yet, the impact of protein glycosylation on biofilm and antibiotic resistance is still not understood. A preliminary study of protein glycosylation in *S. epidermidis* was conducted to investigate the relationship of membrane glycoproteins towards biofilm formation and antimicrobial resistance. This study focused on *S. epidermidis* ATCC 12228 and ATCC 35984, alongside seven clinical *S. epidermidis* isolates that were characterized based on their biofilm forming ability as well as the predominant component of their biofilm matrices. The microtitre plate biofilm quantification method classified the isolates into three groups which are weak- (B2, B3 and B55), strong- (B81, B103 and B171) and very strong- (B44) biofilm producers. Proteins were found to be the major component of the weak-biofilm producers whilst polysaccharides were the main component in both strong- and very strong-biofilm producers. Biofilm formation of ATCC 35984 pre-treated with tunicamycin (*N*-linked glycosylation inhibitor) was reduced as opposed to ATCC 12228. In contrast, tri-*O*-benzyl-D-galactal (*O*-linked glycosylation inhibitor) slightly reduced biofilm formation of ATCC 35984 and may affect ATCC 12228 biofilm. The pre-treatment of *S. epidermidis* with glycosylation inhibitors slightly increased susceptibility in MICs by one-fold against clindamycin, gentamicin, rifampicin, tetracycline and vancomycin. However, the deglycosylation showed no effect on the resistance of biofilm cells against antimicrobial agents as the MBICs were similar to the untreated cells. The induction of ATCC 12228 biofilm by tunicamycin displayed increased resistance against all tested antimicrobial agents compared to the untreated. Proteomics analysis highlighted the membrane glycoproteins of ATCC 12228 compared to ATCC 35984 from which ten differentially expressed membrane glycoproteins were identified *via* MALDI-TOF-MS. An online glycosylation site predicting tool, GlycoPP, revealed the presence of potential glycosylation sites either *N*- or *O*-linked glycosite in nine proteins except for alkyl hydroperoxide reductase subunit C. Most of the glycoproteins were expressed at higher levels in ATCC 35984 suggesting that these glycoproteins may be involved in biofilm formation. These data could be further explored to identify potential new targets for effective treatment and clinical management against biofilm-producing bacteria.

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