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P1254 Association of complement receptor 5a polymorphisms with PVL-positive Staphylococcus aureus

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Background: Some *Staphylococcus aureus* isolates produce the Panton-Valentine leukocidin (PVL) which is a pore forming toxin that can be associated with severe necrotizing infections. The prevalence of PVL is low in isolates from Europe (3%), but high in Africa (e.g. 56% in Gabonese Pygmies). PVL exerts its cytolytic action via binding to the complement 5a receptor (C5aRI/II) of neutrophils. The objective of this study was to assess if colonization with PVL-positive *S. aureus* is associated with singe nucleotide polymorphisms (SNPs) of the C5aRI/II in African Babongo Pygmies.

Materials/methods: We screened Gabonese Babongo for nasal and pharyngeal colonization with S aureus. All isolates were screened for the presence of PVL-encoding genes (*lukF*-PV/*lukS*-PV). Buccal mucosal epithelial cells were used for DNA extraction (Forensic Swab, Sarstedt). The C5aRI/II loci were genotyped (Sanger sequencing) and sequences were screened for SNPs using the UCSC Genome Browser and the Human Genome 38 assembly. Binary logistic regression adjusted for age and gender was applied to screen for potential association of C5aRI/II SNPs with colonization of PVL-positive *S. aureus.*

Results: 107 Pygmies were included; 69% (n=74) were colonized with *S. aureus*; 45% (n=33) were colonized with PVL-positive *S. aureus*. SNPs were detected in *C5aRI* (n=12) and *C5aRII* (n=7). No significant association was observed between any of these SNPs and the colonization with *S. aureus*. However, the allele frequencies of *C5aR I* SNPs rs11880097, *C5aR II* rs150649665 and *C5aR II* rs187635721 differed significantly between individuals being colonized with PVL-positive and PVL-negative *S. aureus* ($p<0.01$). These SNPs carry a missense mutation at position 279 of the 3rd extracellular domain (rs11880097), synonymous mutation (rs150649665) or an intron variant (rs187635721).

Conclusions: African Babongo Pygmies have three *C5aR* SNPs associated with the colonization of PVL-positive *S. aureus*. Since PVL most likely binds to the three extracellular domains of C5aRI and II, the SNP *C5aRI* rs11880097 is a promising candidate to further study why PVL is widespread Africa but less common in Europe. Further functional assays are warranted to analyze the impact of this SNP on the cytotoxicity of PVL.