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Poster Session VI
Skin and soft tissue infections and diabetic food

POLYMORPHISMS IN CYTOKINE GENES IL6, TNF, IL10, IL17A AND IFNG INFLUENCE SUSCEPTIBILITY TO COMPLICATED SKIN AND SKIN STRUCTURE INFECTIONS

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Objectives: Complicated skin and skin structure infections (cSSSIs) involve deeper soft tissue, require surgical intervention or occur in individuals with a significant underlying disease. Depending on the clinical situation, location of the infection and medical history of the patient, the presence of Gram-positive or Gram-negative aerobic or anaerobic bacteria varies. Recognition of invading pathogens by the immune system results in the production of pro- and anti- inflammatory cytokines that exert their effect though binding to specific cytokine receptors and as such are extremely important for intercellular communication and control of infection. This study assessed whether genetic variation in genes coding for cytokines influences the susceptibility to cSSSIs.

Methods: 318 patients with cSSSIs from a multicentre clinical trial and 328 geographically matched healthy controls were genotyped for single nucleotide polymorphisms (SNPs) in cytokine genes encoding *IL1A*, *IL1B*, *IL1RN*, *TNF*, *IL10*, *IL17A*, *IL17F* and *IFNG.* The association between susceptibility to cSSSIs and a SNP was investigated by means of logistic regression analysis. Peripheral blood mononuclear cells obtained from 74 healthy individuals, genotyped for SNPs of interest, were stimulated with heat-killed cSSSI pathogens *Staphylococcus aureus* (*S. aureus*) or *Escherichia coli* (*E. coli*). Corresponding cytokine levels were determined in supernatants by enzyme-linked immunosorbent assays and correlated to genotypes of the SNPs of interest.

Results: Polymorphisms in cytokine genes *IL6* rs1800797, *TNF* rs1800629, *IL10* rs1800871, *IL17A* rs8193036 and *IFNG* rs2069705 influenced susceptibility to cSSSIs. No differences in cytokine responses, stratified for genotype of the cSSSI associated polymorphisms, were detected after *S. aureus* or *E. coli* PBMC stimulation. No association with cSSSIs was observed for polymorphisms *IL1A* rs17561 and rs1800587, *IL1B* rs16944 and rs1143627, *IL1RN* rs4251961, *TNF* rs361525, *IL10* rs1800896, *IL17A* rs2275913 and *IL17F* rs763780.
Conclusions: Polymorphisms in cytokine genes *IL6*, *TNF*, *IL10*, *IL17A* and *IFNG* are associated with susceptibility to cSSSIs. Further studies are warranted to determine the mechanisms through which these cytokine polymorphisms influence susceptibility to cSSSIs and whether they can play a beneficial role in the characterization of a predictive profile for individuals at risk of developing cSSSIs.