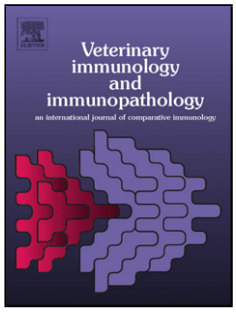

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Interleukin 8 haplotypes drive divergent responses in uterine endometrial cells and are associated with somatic cell score in Holstein-Friesian cattle

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ABSTRACT

Interleukin 8 is a proinflammatory chemokine involved in neutrophil recruitment and activation in response to infection and also in the resolution of inflammation. Our previous studies identified a number of genetic polymorphisms in the bovine IL8 promoter region which segregate into two haplotypes, with balanced frequencies in the Holstein-Friesian (HF). We subsequently showed that these haplotypes confer divergent IL8 activity both *in vitro* in mammary epithelial cells and *in vivo* in response to LPS. In this study, we hypothesised that the balanced frequency of IL8 haplotype in HF could be explained by divergent selection pressures acting on this locus. To address this hypothesis, an association study was carried out aiming to identify a putative link between the IL8 haplotype and somatic cell score (SCS) in 5746 Holstein-Friesian dairy cows. In addition, the basal and inducible promoter activity of the two IL8 haplotypes was characterised in bovine endometrial epithelial (BEND) cells and in monocyte-derived macrophages. Results showed a significant association between IL8 haplotype 2 (IL8-h2) with increased SCS ($P<0.05$). Functional analysis showed that the same haplotype was a more potent inducer of IL8 expression in BEND cells in response to LPS and TNFα stimulation. In contrast, co-transfection of the BEND cells with a DNA construct encoding a bovine Herpes virus 4 antigen, induced significantly higher IL8 expression from IL8-h1. The present study sheds light on the molecular mechanisms underlying selection for SCS and provides evidence that