Antiviral effect and BMAP28 induction by toll-like receptor 7 after bovine alpha-herpesviruses infection

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The cross-talk mechanisms between Toll-like receptors (TLRs) and cathelicidins that participate in airway epithelial host defences remain undefined. TLR7 expression is differentially modulated by bovine alpha-herpesvirus (BoHV) 1 and 5 infection. This work investigated cathelicidin expression in the respiratory tract of BoHV-1- and 5-infected calves and whether TLR7 activation modulates cathelicidin expression and viral replication in bovine respiratory cells *in vitro*. BMAP28 expression was determined by RT-qPCR from nasal mucosa, tracheal epithelium and lung of infected calves [6 days post-infection (pi), n=4] relative to mock-infected animals (n=2). Primary cultures of fetal bovine lung were stimulated with TLR7 agonist (Imiquimod, 5 µg/mL) and infected 1h later with BoHV-1 or BoHV-5 (MOI: 0.1). Viral titres in supernatants and BMAP28 and TLR7 expression were determined at 6 and 24 hpi and analysed by t-test, Mixed Procedure of SAS, and REST software, respectively ($P < 0.05$). BoHV-5 infection decreased BMAP28 mRNA in nasal mucosa and lungs (0.27-fold and 0.07-fold, respectively). In tracheal epithelium of mock-infected calves, BMAP28 expression was undetectable. However, BoHV infection induced the expression of this cathelicidin. In vitro TLR7 induction after BoHV-1 or BoHV-5 infection was higher in cells stimulated with Imiquimod (238-fold and 712-fold, respectively). At 24 hpi, the antiviral effect of Imiquimod was demonstrated by the significant decrease ($P < 0.05$) observed in viral replication ($10^{5.4}$ $TCID_{50}$/mL) with respect to the untreated control ($10^{6.6}$ $TCID_{50}$/mL). Concomitantly, up-regulation of BMAP28 in BoHV-5 infected-cells was observed (27-fold). Previously, we had found that in nasal mucosa and lung TLR7 expression is only induced by BoHV-1. Interestingly, we observed that this cathelicidin decreases only

during BoHV-5 infection. Overall, it is demonstrated that TLR7 activation has a protective effect and induces BMAP28 expression in bovine respiratory cells, suggesting a relevant interaction for controlling infection. Understanding the modulation of the innate immune response by TLRs, cathelicidins and their signalling pathways would be useful for preventive and therapeutic strategies against bovine alpha-herpesviruses infections.