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Digital dermatitis of cattle and sheep - laboratory pointers to treatment and prevention

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Introduction

Bovine digital dermatitis (DD) was first reported in the UK in 1987 where it is now considered to be endemic, occurring in nearly all dairy herds. Worldwide, the infectious nature of DD makes it a major problem in all countries with dairy cattle. The ensuing lameness is an important animal health concern and is an important worldwide food security issue as it results in reduction in milk yield and reproductive performance and has significant treatment costs. An effective prevention/treatment that completely eliminates bovine DD has yet to be identified. Threateningly, this infection has now also emerged in sheep causing contagious ovine digital dermatitis and the bacteria considered causal have also been associated with newly described, very destructive, non healing hoof lesions in cattle suggesting an even greater economic and animal welfare cost of this infection.

Spirochetes and more specifically treponemes have been implicated as important in the aetiology of DD. This report describes work carried out at the University of Liverpool to further characterise the digital dermatitis treponemes of cattle and sheep and how this work may point to future treatments.

Materials and Methods

Isolation and genotypic and phenotypic characterisations of spirochetes were carried out as described (Evans, et al. 2008, Evans, et al. 2011b). Molecular detection of treponemes in lesions and various host tissues and environment samples used specific PCR assays as described (Evans, et al. 2009c). Antimicrobial susceptibility testing was carried out as described (Evans, et al. 2009a). Quantitative reverse transcriptase PCR (qRT-PCR) analyses of bovine keratinocytes and fibroblasts were carried out according to standard methods.

Results

Optimised isolation methods initially allowed for genotyping and phenotyping of 23 bovine DD treponemes and division into three groups/phylotypes (Evans, et al. 2008) and subsequently, the number of strains isolated has increased (~80). Following additional characterisations we were able to designate one BDD treponeme phylotype as a new species, Treponema pedis (Evans, et al. 2009b). We have developed an in vitro antimicrobial susceptibility testing method for bovine DD treponemes and identified the most effective antibiotics for use against these bacteria as penicillin, penicillin derivatives and specific macrolides (Evans, et al. 2009a, Evans, et al. 2012a). To investigate the molecular epidemiology of the DD spirochetes we developed PCR assays specific for the different bovine DD treponeme phylotypes and identified the presence of all three phylotypes as together in 74.5% of BDD lesions surveyed (Evans, et al. 2009c). Immunohistochemistry studies identified hair follicles in foot skin as likely entry routes for the treponemes, contributing to understanding treponeme host invasion. The specific PCR assays were used to identify the presence of DD treponemes in sheep DD lesions (Sayers, et al. 2009) and new ‘non-healing’ manifestations of other bovine foot diseases (Evans, et al. 2011a). Inflammatory host response studies using qRT-PCR assays for relevant bovine genes demonstrated that skin fibroblasts and not keratinocytes are most responsive to BDD treponemes, producing macrophage elastase and RANTES, potentially important inflammatory mediators (paper submitted). Successful experiments to isolate, analyse and compare commensal bovine Gl tract treponemes with BDD treponemes identified these micro-organisms as belonging to two large separate phylogenetic clusters, differing in serum dependence and in the presence of a gene encoding tissue attachment machinery (Evans, et al. 2011b). We have also surveyed large numbers of oral and rectal tissues for BDD treponemes which identified occasional colonisation by BDD treponemes (Evans, et al. 2012b).

Discussion

All the aforementioned studies need to be considered to try and understand how to best prevent or treat cattle and sheep DD. Immunohistochemistry and the identification of multiple treponeme phylootypes together in bovine DD lesions identified the disease as polytreponemal rather than more broadly polymicrobial. This is in agreement with other molecular studies carried out in other countries. This suggests treponeme targeted antibiotics, vaccines or transmission blocking may allow for eradication of this disease. We have identified...
similarities between cattle and sheep DD suggesting similar prevention/treatment methods should work. Potentially best antibiotic choices from the in vitro methods described here can be made for in vivo use although considerations with regards to antibiotic usage for specific animal types and environmental damage need to be considered. The upregulation of RANTES and macrophage elastase expression is a similar inflammatory signature to human psoriasis suggesting that treatments for the human skin condition might be worth considering for DD.

Whilst the flora of ruminant GI tracts appears to contain different treponemes to those associated with DD we have found occasional presence of DD treponemes in oral and rectal tissues and further pinpointing may allow for better understanding transmission routes. Future and ongoing studies at Liverpool include more comprehensive infection reservoir investigations and transmission studies. Genomics and proteomics studies are needed to further clarify vaccine studies and are currently underway. In the future hopefully we may be able to finally prevent this disease in cattle and sheep by using a mixture of vaccines, good farm practice and effective treatment.

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References