A novel approach to probe host-pathogen interactions of bovine digital dermatitis, a model of a complex polymicrobial infection

Polymicrobial infections represent a great challenge for the clarification of disease etiology and the development of comprehensive diagnostic or therapeutic tools, particularly for fastidious and difficult-to-cultivate bacteria. Using bovine digital dermatitis (DD) as a disease model, we introduce a novel strategy to study the pathogenesis of complex infections. The strategy combines meta-transcriptomics with high-density peptide-microarray technology to screen for in vivo-expressed microbial genes and the host antibody response at the site of infection. Bacterial expression patterns supported the assumption that treponemes were the major DD pathogens but also indicated the active involvement of other phyla (primarily Bacteroidetes). Bacterial genes involved in chemotaxis, flagellar synthesis and protection against oxidative and acidic stress were among the major factors defining the disease. The extraordinary diversity observed in bacterial expression, antigens and host antibody responses between individual cows pointed toward microbial variability as a hallmark of DD. Persistence of infection and DD reinfection in the same individual is common; thus, high microbial diversity may undermine the host's capacity to mount an efficient immune response and maintain immunological memory towards DD. The common antigenic markers identified here using a high-density peptide microarray address this issue and may be useful for future preventive measures against DD.