New publications in the PARATUBERCULOSIS database (873-876)

Herd-level prevalence of Johne’s disease in Utah and adjacent areas of the Intermountain West as detected by a bulk-tank milk surveillance project
Journal of Dairy Science, 93, 5792-5797

The objectives of this study were to estimate the dairy herd-level prevalence of Johne’s disease (JD) in Utah and nearby areas of the Intermountain West and to estimate the sensitivity of a single bulk-tank milk test for JD detection. Two milk samples from all bulk tanks on the study farms were collected 1 mo apart. Samples were frozen and shipped to a laboratory for JD testing. An ELISA to measure total IgG antibody specific against Mycobacterium avium ssp. paratuberculosis, the etiological agent that causes JD, and a quantitative real-time PCR to detect M. avium ssp. paratuberculosis DNA were used; both tests were designed for bulk milk. Of the dairy farms in the study area, 170/246 (69%) participated. Positive JD results were found in bulk milk from 67/170 (39%) of dairy farms in Utah and adjacent areas. There were 138 JD-positive bulk-tank results from 241 bulk-tank samples from the 67 positive herds. The sensitivity of the bulk milk testing for detection of JD was 138/241 (57%). From the 103 JD-negative farms, 235 bulk-tank samples tested negative for JD. The probability of false-negative results on a single bulk-milk sample was (1 - 0.57) = 0.43. For farms with 1 bulk tank, 2 samples collected 1 mo apart, with both samples testing negative (by both ELISA and quantitative real-time PCR) for JD, the true-negative probability was (1 - (0.43)(2)) = (1 - 0.18) = 82%. For farms with at least 2 bulk tanks, at least 4 samples tested, with all results negative for JD, the true-negative probability was at least 97%. Results support other estimates that prevalence of JD has increased over the last 15 to 20 yr. However, the prevalence detected was 3 times that from a recent report where 13% of dairy herds in the western US were positive. The increase in JD suggests that current control programs, at least as applied, are not effective. Bulk milk testing is a practical way to screen dairy herds for presence of JD. Studies are needed regarding the use of individual cow milk tests for accuracy, practicality, and effectiveness in reducing the prevalence of JD in dairy herds.

SP110 as a novel susceptibility gene for Mycobacterium avium subspecies paratuberculosis infection in cattle
Journal of Dairy Science, 93, 5950-5958

The intracellular pathogen resistance 1 (lpr1) gene has been reported to play a role in mediating innate immunity in a mouse model of Mycobacterium tuberculosis infection, and polymorphisms of its human ortholog, SP110 nuclear body protein, have been suggested to be associated with tuberculosis. Thus, the bovine SP110 gene was considered to be a promising candidate for a genetic association study of bovine paratuberculosis, or Johne’s disease, a chronic granulomatous enteritis caused by Mycobacterium avium ssp. paratuberculosis (MAP). Initially, single nucleotide polymorphisms (SNP) within the bovine SP110 gene were identified, and subsequently a population-based genetic association study was carried out. Seventeen new SNP along the SP110 gene were identified in Holstein-Friesian cattle, and 6 more were compiled from public databases. A total of 14 SNP were included in the association study of 2 independent populations. The SNP c. 587A>G was found to be significantly associated with MAP infection, with the major allele A appearing to
confers greater disease susceptibility in one of the analyzed populations. In addition, 2 haplotypes containing this SNP were also found to be associated with infection in the same population. The SNP c. 587A>G is a nonsynonymous mutation that causes an amino acid change in codon 196 from asparagine to serine. In silico analyses point to SNP c. 587A>G as a putative causal variant for susceptibility to MAP infection. The elucidation of the precise mechanism by which this SNP can exert its effect in the protein and, as a result, in the risk of infection, requires future functional analyses. Likewise, the absence of genetic association in one of the analyzed populations renders it necessary to carry out this study in other independent populations, with the aim of substantiating the repeatability of the present results. Nevertheless, the present results deepen our understanding of the genetic basis of susceptibility and resistance mechanisms related to MAP infection in cattle and, in turn, constitute a step forward toward the implementation of marker-assisted selection in breeding programs aimed at controlling paratuberculosis.


Microbes that reside in the human intestinal tract and interact with immune and epithelial cells are strongly implicated as causative or predisposing agents of inflammatory bowel disease (IBD). Recent studies using metagenomic approaches have revealed differences in the fecal and mucosa-associated microbiota of patients with IBD, but it remains unclear whether this is a cause or consequence of chronic intestinal inflammation. A few microbes have been singled out as candidate pathogens in IBD and remain the subject of ongoing study. Complex imbalances in gut bacterial community structure and/or deficiencies in their functional capabilities may be a greater issue in IBD development. A more complete understanding of host-microbiota interactions in IBD is hampered by several remaining but surmountable methodological and technical challenges.


Nucleotide-Binding Oligomerization Domain 2 (NOD2) has been reported to be a candidate gene for Mycobacterium avium subsp. paratuberculosis (MAP) infection in a Bos taurus x Bos indicus mixed breed based on a genetic association with the c.2197T>C single nucleotide polymorphism (SNP). Nevertheless, this SNP has also been reported to be monomorphic in the B. taurus species. In the present work, 18 SNPs spanning the bovine NOD2 gene have been analysed in a genetic association study of two independent populations of Holstein-Friesian cattle. We found that the C allele of SNP c.*1908C>T, located in the 3'-UTR region of the gene, is significantly more frequent in infected animals than in healthy ones, which supports the idea that the bovine NOD2 gene plays a role in susceptibility to MAP infection. However, in silico analyses of the NOD2 nucleotide sequence did not yield definitive data about a possible direct effect of SNP c.*1908C>T on susceptibility to infection and led us to consider its linkage disequilibrium with the causative variant. A more exhaustive genetic association study including all putative, functional SNPs from this gene and subsequent functional analyses needs to be conducted to achieve a more complete understanding of how different variants of NOD2 may affect susceptibility to MAP infection in cattle.

New publications in the CROHN'S DISEASE AND PARATUBERCULOSIS database (486-489)

Vaitaitis, G.M., Wagner, D.H. (2010) CD40 glycoforms and TNF-receptors 1 and 2 in the formation of CD40 receptor(s) in autoimmunity. Molecular Immunology, 47, 2303-2313
The CD40-CD154 dyad is an intensely studied field as is glycosylation status and both impact immunological functions and autoimmune conditions. CD40 has several isoforms modified by glycosylation and trimerizes to form the functional receptor. We described a CD4(+)CD40(+) T cell (Th40) subset which is expanded in autoimmunity and is necessary and sufficient in transferring type 1 diabetes. Glycosylation impacts immunological events and T cells from autoimmune mouse strains express 30-40% less GlcNAc-branched N-glycans than T cells from non-autoimmune strains. A decrease known to activate T cells. Here we demonstrate that several CD40 receptor constellations exist on CD4 T cells. However, rather than containing different isoforms of CD40, they contain different glycoforms of isoform I. The glycoform profile is dependent on availability of CD154 and autoimmune NOD mice express a high level of a less glycosylated form. Interestingly, CD40 stimulation induces some CD40 receptor constellations that contain TNF-receptors 1 and 2 and targeting of those alters CD40 signaling outcomes in NOD Th40 cells. CD40-stimulation in vivo of non-autoimmune BALB/c mice expands the Th40 population and alters the CD40 glycoform profile of those cells to appear more like that of autoimmune prone NOD mice. Further understanding the dynamics and composition of the different CD40 receptor constellations will provide important insights into treatment options in autoimmunity. (C) 2010 Elsevier Ltd. All rights reserved.

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The pathologic spectrum of the inflamed appendix encompasses a wide range of infectious entities, some with specific histologic findings, and others with nonspecific findings that may require an extensive diagnostic evaluation. The appendix is exclusively involved in some of these disorders, and in others may be involved through extension from other areas of the gastrointestinal tract. This review discusses the pathologic features of bacterial, viral, fungal, and parasitic infections affecting the appendix, including adenovirus; cytomegalovirus; Yersinia, Actinomycetes, Mycobacterium, or Histoplasma species; Enterobius vermicularis; schistosomiasis; and Strongyloides stercoralis. Pertinent ancillary diagnostic techniques and the clinical context and significance of the various infections are also discussed.

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