
Tissues of cattle intended for human consumption can be contaminated by Mycobacterium avium subsp. paratuberculosis (MAP). Although different studies attribute varying roles of MAP in Crohn's disease progression it is thought that the exposure of humans to this bacterium should in any case be minimised. In this study, we have collected samples of intestine, mesenteric lymph nodes, muscles of diaphragm (musculus diaphragma) and masseter muscles (musculus masseter) from twenty-five cows in a slaughterhouse. The infectious status of all animals was confirmed by culture of faeces. MAP was found in almost all the intestines and mesenteric lymph nodes examined, including three faecal culture-negative animals indicating intermittent shedding. As intestine is used for the traditional production of sausages, it is alarming that 84.2% of intestine samples were positive for MAP. F57 and 15900 real time PCR revealed MAP in 40 to 68% of diaphragms and 11.1 to 38.9% of masseters. A noticeable dependence of the probability of MAP positivity of faeces versus gastrointestinal tract (GIT) and of GIT and muscles was observed. Due to the changing behaviour of consumers, both of these muscles have started to be widely used in cuisine. Therefore, the results of this paper imply that the processing of cows with paratuberculosis in abattoirs without any precautions (restrictions) and the usage of meat for human consumption should be rethought. (C) 2011 Elsevier B.V. All rights reserved


Bovine liver catalase (BLC), catalase-related allene oxide synthase (cAOS) from Plexaura homomalla, and a recently isolated protein from the cattle pathogen Mycobacterium avium ssp. paratuberculosis (MAP-2744c (MAP)) are all tyrosinate-ligated heme enzymes whose crystal structures have been reported, cAOS and MAP have low (<20%) sequence similarity to, and significantly different catalytic functions from, BLC. cAOS transforms 8R-hydroperoxy-eicosatetraenoic acid to an allene epoxide, whereas the MAP protein is a putative organic peroxide-dependent peroxidase. To elucidate factors influencing the functions of these and related heme proteins, we have investigated the heme iron coordination properties of these tyrosinate-ligated heme enzymes in their ferric and ferrous states using magnetic circular dichroism and UV-visible absorption spectroscopy. The MAP protein shows remarkable spectral similarities to cAOS and BLC in its native Fe(III) state, but clear differences from ferric proximal heme ligand His93Tyr Mb (myoglobin) mutant, which may be attributed to the presence of an Arg(+)-N omega-H center dot center dot center dot(-)O-Tyr (proximal heme axial ligand) hydrogen bond in the first three heme proteins. Furthermore, the spectra of Fe(III)-CN(-), Fe(III)-NO, Fe(II)-NO (except for five-coordinate MAP), Fe(II)-CO, and Fe(II)-O(2) states of cAOS and MAP, but not H93Y Mb, are also similar to the corresponding six-coordinate complexes of BLC, suggesting that a tyrosinate (Tyr-O(-)) is the heme axial ligand trans to the bound ligands in these complexes. The Arg(+)-N(omega)-H to (-)O-Tyr hydrogen
bond would be expected to modulate the donor properties of the proximal tyrosinate oxyanion and, combined with the subtle differences in the catalytic site structures, affect the activities of cAOS, MAP and BLC (C) 2011 Elsevier Inc. All rights reserved


Pathology and molecular diagnosis of paratuberculosis of camels

Tropical Animal Health and Production, 44, 173-177

Camels are the prime source of meat and milk in many desert regions of the world including Saudi Arabia. Paratuberculosis of camels, locally called Silag, is a serious and invariably fatal disease in the Arabian camel. Six camels were used in this study. Five camels with clinical paratuberculosis were used to study the pathology of the disease and confirm its aetiology. The sixth camel was clinically healthy and used as a control. The camels were examined clinically and bled for haematological and blood chemistry analysis. They were then humanely killed with a high intravenous dose of thiopeptal sodium (10 mg/kg) for pathological studies as well as obtaining tissues for microbiological and molecular studies. The clinical signs of the disease were emaciation, diarrhoea, alopecia, wry neck and pale mucous membranes. Laboratory diagnosis showed reduced haemoglobin concentration, low haematocrit and high activity of the serum enzyme alanine aminotransferase. Serum creatinine concentration was normal. These results indicated the infected camels were anaemic and the function of their livers was affected. Postmortem examination showed thickened and corrugated intestinal mucosa, enlarged granulomatous mesenteric lymph nodes, miliary and diffuse granulomas in the liver (in four camels), generalized lymph node granulomas (in one camel), splenic granuloma (in one camel) and mediastinal lymph node granuloma (in two camels).

Histopathological examination showed diffuse infiltration of macrophages in all organs showing lesions. Ziehl-Neelsen staining of tissue scraping and tissue sections showed masses of acid fast bacilli, except for the spleen. Infection with Mycobacterium avium subsp. paratuberculosis was confirmed by PCR by targeting the IS900 gene


Detection of Mycobacterium avium ssp paratuberculosis in ileocaecal lymph nodes collected from elderly slaughter cows using a semi-nested IS900 polymerase chain reaction

Veterinary Microbiology, 154, 197-201

The aim of this study was to investigate the occurrence of subclinical Mycobacterium avium spp. paratuberculosis (MAP) infections at slaughter by testing ileocaecal lymph nodes with a semi-nested IS900 PCR. Tissue samples were available within the framework of a parallel study investigating BSE-susceptibility factors in members of BSE-cohorts in the German Federal State of Lower Saxony. Ileocaecal lymph nodes were collected over a 2-year sampling period from 99 slaughter cattle of a mean age of 6.5 years (5.5-7.5 years). A recently developed IS900 semi-nested polymerase chain reaction (snPCR) assay offering a sensitivity of 1 genome equivalent was used for the detection of MAP-DNA. Based on this snPCR, 17 out of the 99 samples gave positive results, indicating a MAP occurrence of 17.17% in the random sample. All PCR products were sequenced for screening of polymorphisms. Nucleotide homologies of 98.5-100% were found with respect to the MAP K10 reference sequence IS900 (GenBank: AE1 6958). PCR analysis of ileocaecal lymph nodes collected from slaughter cattle proved to be a suitable technique to determine MAP occurrence in the local cattle population. (C) 2011 Elsevier B.V. All rights reserved


Evaluation of 5 Indirect Elisa for the Detection of Antibodies to Paratuberculosis in Dromedaries

Journal of Camel Practice and Research, 18, 47-52
The four commercial indirect MAP ELISAs were only able to detect paratuberculosis positive camel sera when the kit conjugate was replaced with either Protein A or the goat anti-camel IgG conjugates from Bio-X or CVRL. The Triple J conjugate did not perform well in contrast to the findings of Kramsky and co-workers who used this in a similar protocol to detect anti-MAP antibodies in llama and alpaca sera. With the former combinations, the Checkit and ID Screen MAP antigen coated plates showed considerable non-specific cross-reactivity with paratuberculosis negative camel sera, viz. %S/P values >= 25% in 4 and 2 out of 4 negative sera, respectively. The Paratub MAP antigen coated plate/Protein A conjugate combination showed better non-specificity, although one camel sample E2A which had no history of paratuberculosis showed a % S/P of 27% and also a reduced response in camel 6BI after the second vaccination dose. Parachek, and in-house MAP antigen coated plates worked well in combination with Protein A conjugate showing acceptable non-specific cross reactivity (%S/P <= 12%), and a good colorimetric signal that provided an excellent anti-MAP immune response in the two vaccinated camels, with a response range of greater than 2 and 1.2 absorbance units in camels 47B and 6BI, respectively, after the second vaccine dose compared to the pre-treatment level. Similar profiles were obtained for the in-house ELISA protocol that employed OPD substrate, a format that was in common to other ELISAs in our laboratory. It was therefore concluded, that the in-house MAP ELISA was the method of choice for future studies on M. paratuberculosis infection in camels


The genus Mycobacterium represents more than 120 species including important pathogens of human and cause major public health problems and illnesses. Further, with more than 100 genome sequences from this genus, comparative genome analysis can provide new insights for better understanding the evolutionary events of these species and improving drugs, vaccines, and diagnostics tools for controlling Mycobacterial diseases. In this present study we aim to outline a comparative genome analysis of fourteen Mycobacterial genomes: M. avium subsp. paratuberculosis K-10, M. bovis AF2122/97, M. bovis BCG str. Pasteur 1173P2, M. leprae Br4923, M. marinum M, M. sp. KMS, M. sp. MCS, M. tuberculosis CDC1551, M. tuberculosis F11, M. tuberculosis H37Rv, M. tuberculosis KZN 1435, M. ulcerans Agy99, and M. vanbaalenii PYR-1, For this purpose a comparison has been done based on their length of genomes, GC content, number of genes in different data bases (Genbank, Refseq, and Prodigal). The BLAST matrix of these genomes has been figured to give a lot of information about the similarity between species in a simple scheme. As a result of multiple genome analysis, the pan and core genome have been defined for twelve Mycobacterial species. We have also introduced the genome atlas of the reference strain M. tuberculosis H37Rv which can give a good overview of this genome. And for examining the phylogenetic relationships among these bacteria, a phylogenic tree has been constructed from 16S rRNA gene for tuberculosis and non tuberculosis Mycobacteria to understand the evolutionary events of these species

New publications in the CROHN'S DISEASE AND PARATUBERCULOSIS database (628-635)


Environment and genetic are both relevant in determining development of Multiple Sclerosis. Many epidemiological observations converge on indicating EBV infection and Vitamin D levels as major players among the environmental factors. Bacteria and bacterial products are however potent triggers of immune responses, and recent work from several laboratories indicates that the microbiota plays a prominent role in "priming" or protecting individuals for development of experimental autoimmune diseases. Here we report our recent work dealing
with the role of non-pathogenic mycobacteria and their innate receptors in relapsing remitting experimental autoimmune encephalomyelitis in the SJL mouse and in mobilization of CNS-reactive T cells. We finally discuss how bacteria are likely involved in the pathogenesis of Multiple Sclerosis, especially with regard to their role in driving the recurring acute episodes of disease. (C) 2011 Elsevier B.V. All rights reserved


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Impaired innate inflammatory response has a key role in the Crohn's disease (CD) pathogenesis. The aim of this study was to investigate the possible role of the TLR10-TLR1-TLR6 gene cluster in CD susceptibility. A total of 508 CD patients (284, cohort 1 and 224, cohort 2) and 576 controls were included. TLR10-TLR1-TLR6 cluster single-nucleotide polymorphisms genotyping, NOD2 mutations and TLR10 mRNA quantification were performed using TaqMan assays. Nucleotide-binding oligomerization domain containing 2 (NOD2) and Toll-like receptor (TLR) loci interaction was analyzed by logistic regression and multifactor-dimensionality reduction (MDR). Entropy-based analysis was used to interpret combination effects. One TLR10 haplotype (TLR10(GGGG)) was found associated with CD susceptibility in both cohorts, individuals with two copies had approximately twofold more risk of CD susceptibility than individuals having no copies (odds ratio = 1.89, P-value = 0.0002). No differences in the mRNA levels were observed among the genotypes. The strongest model for predicting CD risk according to the MDR analysis was a two-locus model including NOD2 mutations and TLR10(GGGG) haplotype (P(c) < 0.0001). The interaction gain attributed to the combination of both genes was negative (IG= -2.36%), indicating redundancy or independent effects. Our results support association of the TLR10 gene with CD susceptibility. The effect of TLR10 would be independent of NOD2, suggesting different signaling pathways for both genes. Genes and Immunity (2011) 12, 635-642; doi:10.1038/gene.2011.41; published online 30 June 2011

Wallis, R.S. (2011) Biologics and Infections: Lessons from Tumor Necrosis Factor Blocking Agents
In the decade since tumor necrosis factor alpha (TNF-alpha) antagonists were first approved for clinical use, they have proven invaluable for the treatment of specific types of chronic inflammation. Currently licensed TNF blockers fall into two classes, monoclonal antibody (or antibody fragments) and soluble receptor. Although they are equally effective in rheumatoid arthritis and psoriasis, important differences have emerged with regard to efficacy in granulomatous inflammation and risks of granulomatous infections, particularly tuberculosis. This article focuses on recent studies that inform prevention and management of infections in this susceptible patient population.


Skin protects the body from the environment and is an important component of the innate and adaptive immune systems. Psoriasis is a frequent inflammatory skin disease of unknown cause determined by multigenic predisposition, environmental factors, and aberrant immune response. Peptidoglycan recognition proteins (Pglyrps) are expressed in the skin, and we report in this article that they modulate sensitivity in an experimentally induced mouse model of psoriasis. We demonstrate that Pglyrp2(-/-) mice (but not Pglyrp3(-/-) and Pglyrp4(-/-) mice) are more sensitive to the development of 12-O-tetradecanoylphorbol 13-acetate induced psoriasis-like inflammation, whereas Pglyrp1(-/-) mice are less sensitive. The mechanism underlying this increased sensitivity of Pglyrp2(-/-) mice to 12-O-tetradecanoylphorbol 13-acetate induced psoriasis-like inflammation is reduced recruitment of regulatory T cells to the skin and enhanced production and activation of Th17 cells in the skin in Pglyrp2(-/-) mice, which results in more severe inflammation and keratinocyte proliferation. Thus, in wild type mice, Pglyrp2 limits overactivation of Th17 cells by promoting accumulation of regulatory T cells at the site of inflammation, which protects the skin from the exaggerated inflammatory response. The Journal of Immunology, 2011, 187: 5813-5823


Dahiya, Y., Pandey, R.K., Sodhi, A. (2011). Nod2 Downregulates TLR2/1 Mediated IL1 beta Gene Expression in Mouse Peritoneal Macrophages. Plos One, 6, Nod2 is a cytosolic pattern recognition receptor. It has been implicated in many inflammatory conditions. Its signaling has been suggested to modulate TLR responses in a variety of ways, yet little is known about the mechanistic details of the process. We show in this study that Nod2 knockdown mouse peritoneal macrophages secrete more IL1 beta than normal macrophages when stimulated with peptidoglycan (PGN). Muramyl dipeptide (MDP, a Nod2 ligand) + PGN co-stimulated macrophages have lower expression of IL1b than PGN (TLR2/1 ligand) stimulated macrophages. MDP co-stimulation have similar effects on Pam3CSK4 (synthetic TLR2/1 ligand) mediated IL1b expression suggesting that MDP mediated down regulating effects are receptor dependent and ligand independent. MDP mediated down regulation was specific for TLR2/1 signaling as MDP does not affect LPS (TLR4 ligand) or zymosan A (TLR2/6 ligand) mediated IL1b expression. Mechanistically, MDP exerts its down regulating effects by lowering PGN/Pam3CSK4 mediated nuclear cRel levels. Lower nuclear cRel level were observed to be because of enhanced transporting back rather than reduced nuclear translocation of cRel in MDP + PGN stimulated macrophages. These
results demonstrate that Nod2 and TLR2/1 signaling pathways are independent and do not interact at the level of MAPK or NF-kappa B activation.

635 Breton, G. (2011)
**Immune reconstitution inflammatory syndrome**
Bulletin de l Academie Nationale de Medecine, 195, 561-575

The immune reconstitution inflammatory syndrome (IRIS), occurring in chronically HIV-infected patients, is a set of heterogeneous pathological manifestations attributed to an excessive and deregulated immune response to various pathogens and non infectious stimuli shortly after initiation of antiretroviral therapy. Mycobacteria and fungi are the main causes of IRIS, but many other pathogens and autoimmune-inflammatory disorders have also been incriminated. Diagnosis is difficult and the optimal therapeutic strategy remains to be determined. Steroids have been recommended for tuberculosis-associated IRIS. Outcome is generally favorable, with the exception of central nervous system involvement.