Expression of selected genes isolated from whole blood, liver and obex in lambs with experimental classical scrapie and healthy controls, showing a systemic innate immune response at the clinical end-stage - DTU Orbit (01/10/2019)

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Background: Incubation period, disease progression, pathology and clinical presentation of classical scrapie in sheep are highly dependent on PRNP genotype, time and route of inoculation and prion strain. Our experimental model with precolostrum inoculation of homozygous VRQ lambs has shown to be an effective model with extensive PrPSc dissemination in lymphatic tissue and a short incubation period with severe clinical disease. Serum protein analysis has shown an elevation of acute phase proteins in the clinical stages of this experimental model, and here, we investigate changes in gene expression in whole blood, liver and brain. Results: The animals in the scrapie group showed severe signs of illness 22 weeks post inoculation necessitating euthanasia at 23 weeks post inoculation. This severe clinical presentation was accompanied by changes in expression of several genes. The following genes were differentially expressed in whole blood: TLR2, TLR4, C3, IL1B, LF and SAA, in liver tissue, the following genes differentially expressed: TNF-α, SAA, HP, CP, AAT, TTR and TF, and in the brain tissue, the following genes were differentially expressed: HP, CP, ALB and TTR. Conclusions: We report a strong and evident transcriptional innate immune response in the terminal stage of classical scrapie in these animals. The PRNP genotype and time of inoculation are believed to contribute to the clinical presentation, including the extensive dissemination of PrPSc throughout the lymphatic tissue.

General information
Publication status: Published
Organisations: Department of Biotechnology and Biomedicine, National Veterinary Institute, Translational Immunology, Innate Immunology, Innate Immunology, Norwegian University of Life Sciences
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Number of pages: 11
Publication date: 2018
Peer-reviewed: Yes

Publication information
Journal: B M C Veterinary Research
Volume: 14
Article number: 281
ISSN (Print): 1746-6148
Ratings:
BFI (2018): BFI-level 1
Scopus rating (2018): CiteScore 2.06 SJR 0.848 SNIP 1.026
Web of Science (2018): Impact factor 1.792
Web of Science (2018): Indexed yes
Original language: English
Keywords: Classical scrapie, Innate immune response, qPCR, Whole blood, Liver tissue, Brain tissue, Sheep
Electronic versions:
Meling et al. 2018
DOIs:
10.1186/s12917-018-1607-9

Bibliographical note
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Source: FindIt
Source ID: 2439225486
Research output: Contribution to journal › Journal article – Annual report year: 2018 › Research › peer-review