

Faecal CWD prion excretion and inflammation

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SUMMARY

Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) - or prion disease (PD) - that has become of increasing concern throughout years among different captive and free-living deer species and populations in North America.

Starting from the recent pre-clinical evidence of prion infectivity in faecal material from CWD-infected mule deer (*Odocoileus hemionus*), this contribution takes into special consideration the potential role of certain gut inflammatory conditions as a factor modulating the infectivity titres and, consequently, also the CWD prion faecal excretion rate.

KEY WORDS: Chronic wasting disease, Prion diseases, Transmissible spongiform encephalopathies, Prion infectivity, Inflammation

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Chronic wasting disease (CWD) is a transmissible spongiform encephalopathy (TSE) - or prion disease (PD) - that has become of increasing concern over the years among different captive and free-living deer species and populations in North America. In this respect, clear-cut evidence has recently been shown for the first time on faecal prion excretion in chronic wasting disease (CWD)-infected mule deer (*Odocoileus hemionus*) long before the onset of neurological symptoms, thus providing another relevant basis for the horizontal spread of CWD infection among cervids (Tamgüney *et al.*, 2009).

Since variable prion titres were detected in faeces from the orally infected deer under study, this raises the question of gastrointestinal tract (GIT) inflammation as a factor potentially contributing, among others, to the above differences.

Chronic lymphocytic inflammation has been shown to enable prion accumulation in otherwise prion-free organs and tissues, such as the kidney, pancreas and liver from experimentally scrapie-

infected mice (Heikenwalder *et al.*, 2005), as well as the mammary gland from scrapie - and Maedi-Visna virus (MVV) - naturally coinfecting sheep (Ligios *et al.*, 2005).

A similar behaviour has also been reported in granulomas from intraperitoneally scrapie-infected *Prnp* (+/+) mice, with lymphotoxin-dependent prion replication occurring in the inflammatory stromal cell component (Heikenwalder *et al.*, 2008).

As in many other species, granulomatous inflammation of the intestine may also be frequently found in free-ranging deer under disease conditions such as paratuberculosis - or Johne's disease -, a naturally occurring mycobacterial infection of wild and domestic ruminants (Balseiro *et al.*, 2008).

Although a number of "intrinsic" host factors (such as age, PrP genotype and other unknown individual components) may account, alone or in combination, for the above differences, we believe that more research is needed to better characterize the pathogenetic role of both granulomatous and other concurrent GIT inflammatory disorders, along with the role of such lesions, if any, in enhancing prion replication and faecal excretion in CWD-infected deer.

Lastly, this could also be of relevance in relation to a better understanding of both the pathogen-

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esis and the mechanisms involved in the epidemiology and transmission dynamics of other spontaneously occurring animal and human prion diseases.

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REFERENCES

- BALSEIRO A., GARCÍA MARÍN J.F., SOLANO P., GARRIDO J.M., PRIETO J.M. (2008). Histopathological classification of lesions observed in natural cases of paratuberculosis in free-ranging fallow deer (*Dama dama*). *J. Comp. Pathol.* **138**, 180-188.
- HEIKENWALDER M., ZELLER N., SEEGER H., PRINZ M., KLÖHN P.C., SCHWARZ P., RUDDLE N.H., WEISSMANN C. AND AGUZZI A. (2005). Chronic lymphocytic inflammation specifies the organ tropism of prions. *Science*. **307**, 1107-1110.
- HEIKENWALDER M., KURRER M.O., MARGALITH I., KRANICH J., ZELLER N., HAYBAECK J., POLYMERIDOU M., MATTER M., BREMER J., JACKSON W.S., LINDQUIST S., SIGURDSON C.J. AND AGUZZI A. (2008). Lymphotoxin-dependent prion replication in inflammatory stromal cells of granulomas. *Immunity*. **29**, 998-1008.
- LIGIOS C., SIGURDSON C.J., SANTUCCIU C., CARCASSOLA G., MANCO G., BASAGNI M., MAESTRALE C., CANCEDDA M.G., MADAU L., AGUZZI A. (2005). PrPSc in mammary glands of sheep affected by scrapie and mastitis. *Nature Med.* **11**, 1137-1138.
- TAMGÜNEY G., MILLER M.W., WOLFE L.L., SIROCHMAN T.M., GLIDDEN D.V., PALMER C., LEMUS A., DEARMOND S.J., PRUSINER S.B. (2009). Asymptomatic deer excrete infectious prions in faeces. *Nature*. **461**, 529-532.