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Role of the *PRNP* S127 allele in experimental infection of goats with classical caprine scrapie

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Background: Classical scrapie is a transmissible spongiform encephalopathy affecting domestic goats and sheep and is associated with accumulation of a misfolded isoform (PrP^{Sc}) of the *PRNP* gene product. Multiple *PRNP* polymorphisms have been reported in goats.[1,2] Experimental scrapie inoculation studies revealed that *PRNP* polymorphisms at codons 146, 154, 211, and 222 can provide resistance or a prolonged incubation period.[3–5] A recent study identified the association between a polymorphism at codon 127 (c.127G > S) and reduced probability of developing clinical signs of scrapie in goats with PrP^{Sc} detectable in the brain.[6] In that study, the length of the incubation period (time from infection to clinical signs) was not known. The aim of this study was to identify whether goats with the heterozygous (G/S_{127}) genotype have an extended incubation period compared with goats homozygous for G_{127} (G/G_{127}) following classical caprine scrapie inoculation.

Methods: Intracerebral inoculation was performed with brain homogenates from two natural field cases of scrapie, one G/G_{127} and one G/S_{127}, as described (Table S1). Data were combined from previous reports[4,5] to achieve efficient animal use. Because the previous report[6] suggested a prolonged incubation time for G/S_{127} goats, a one-tailed nonparametric exact test (see Appendix S1) was used to assess the recipient genotype hypothesis that G/S_{127} goats have longer incubation times than do G/G_{127} goats when intracerebrally inoculated with classical caprine scrapie from G/G_{127} genotype source material. In the absence of preliminary data, two-tailed nonparametric exact tests were used for all other analyses.

Results/Discussion: All inoculated goats developed clinical signs of scrapie (Table S1), with disease confirmed by the detection of PrP^{Sc} in brainstem at the obex and most lymphoid tissues by immunohistochemistry[8] (Fig. S1). A significant ($P = 0.019$) increase in incubation time was observed in G/S_{127} goats following inoculation with the G/G_{127} caprine brain homogenate (range: 647–1333 days). No significant difference in incubation time was observed for G/G_{127} versus G/S_{127} inoculum in G/G_{127} goats ($P = 0.30$). Incubation times in control G/G_{127} goats inoculated with the G/G_{127} brain homogenate (range: 261–332 days) were significantly shorter than observed in prior work (both $P < 0.05$[4,5]). Our findings include the first reported classical scrapie incubation times for G/S_{127} goats, confirming that S127 is not protective in goats.[6,7] These data suggest that eradication programs need to include extended traceback periods and longer post-exposure monitoring times for infected herds containing G/S_{127} goats.

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Supporting information

Additional supporting information may be found in the online version of this article.

Appendix S1 Supplementary Methods.

Figure S1 Detection of PrPSc immunolabeling in lymph nodes and brainstem at the obex of G/S127 goats intracerebrally inoculated with classical caprine scrapie.

Table S1 Intracerebral inoculation of goat kids with homozygous (G/G127) or heterozygous (G/S127) brain-derived inocula prepared from clinically affected goats with naturally acquired classical caprine scrapie.

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The *DMRT3* gene mutation in Chinese horse breeds

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