Supporting Information

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Table S1. Residue 226 controls replication of sheep prions by deer and elk PrP

PrP expressed in Tg mice	Inoculum					
	SSBP/1	SSBP/1 in Tg(DeerPrP)	SSBP/1 in deer 6331	SSBP/1 in deer 6339	SSBP/1 in deer 6340	SSBP/1 in Tg(ElkPrP)
Deer	257 ± 13 (10/10)*	163 ± 1 (8/8)*	147 ± 3 (8/8)	164 ± 8 (10/10)	146 ± 2 (7/7)	ND
Elk	497 (0/6)†	241 ± 8 (7/7)	203 ± 9 (9/9)	232 ± 12 (8/8)	191 ± 1 (4/4)	ND
Deer-S96	245 ± 15 (6/6)	ND	ND	ND	ND	ND
Sheep	132 ± 2 (8/8)	151 ± 3 (10/10)	ND	ND	ND	558 (1/7)

The numbers in parentheses refer to data reported in ref. 1. ND, not determined.
*Previously reported (1).
†One mouse was found dead at 481 d.

1. Green KM, et al. (2008) The elk PRNP codon 132 polymorphism controls cervid and scrapie prion propagation. *J Gen Virol* 89(Pt 2):598–608.

Table S2. Transgenic mouse modeling of the effects of deer PrP polymorphisms on prion susceptibility

PrP expressed in Tg mice	Inoculum					
	None	D10 (WT)	135 (96G/S)	04–7951 (225F/S)	D10 in TgF225	SSBP/1 in Tg(DeerPrP)
DeerPrP	606 (0/5)	225 ± 1(8/8)	298 ± 36 (5/5)	207 ± 4 (6/6)	267 ± 8 (5/5)	163 ± 1 (8/8)
PrPS96	495 (0/6)	517 ± 48 (3/5)*	530 (0/5)			155 ± 3 (7/7)
PrPH95	345 (0/5)	518 (0/6)	509 (0/5)			203 ± 9 (7/7)
PrPF225	600 (0/5)	548 ± 36 (2/7)†		503 (1/5)‡	>500 (0/5)	498 ± 11 (7/7)
PrPORI§	541 (0/3)	253 ± 16 (7/7)				
	602 (0/2)					

*Two inoculated mice were found dead at 563 d without having manifested clinical signs.
†Three mice survived without a diagnosis of prion disease until 623–665 d after inoculation; two other mice died of intercurrent illnesses after 447 and 555 d.
‡One mouse was diagnosed 268 d after infection.
§Three uninoculated mice were humanely killed at 541 d without manifesting neurological deficits; two remaining mice survived to 602 d and were killed.

Table S3. Susceptibility of Tg(DeerPrP) mice to CWD prions from wild-type and G/S96 deer

Tissues	Deer identities and genotypes		
	139 (96G/G)	142 (96G/G)	135 (96G/S)
Obex	182 ± 8 (7/7)	209 ± 15 (6/6)	298 ± 36 (5/5)
RPLN	336 ± 11 (7/7)	321 ± 14 (7/7)	344 ± 1 (8/8)

Table S4. Characterization of transgenic mice

PrP	Line	Approximate expression*	Transmissions
Deer (Q226)	1536	Fivefold > wild-type mouse	Yes[†]
Elk (E226)	5037	Fivefold > wild-type mouse	Yes[‡]
Deer-F225	5107	Equal to wild-type mouse	Yes
Deer-S96	7507	Eightfold > wild-type mouse	No
	7511	Fivefold > wild-type mouse	Yes
	7509	Twofold > wild-type mouse	No
	7508	0.5-level wild-type mouse	No
Deer-H95	7503	Twofold > wild-type mouse	No
	7505	Twofold > wild-type mouse	Yes
	7504	0.5-level wild-type mouse	No
	7502	0.5-level wild-type mouse	No

Deer-S96 from the 7507 line developed disease spontaneously. Brain extracts from spontaneously sick mice failed to cause disease upon inoculation of Tg(DeerPrP-S96)7511$^{+/-}$ mice. The numbers in parentheses refer to data reported in refs. 1 and 2.

*Ascertained by comparing signals of normalized amounts of proteins in the brains of transgenic and wild-type mice by Western blotting.

[†]Previously reported (1).

[‡]Previously reported (2).

1. Angers RC, et al. (2010) Prion strain mutation determined by prion protein conformational compatibility and primary structure. *Science* 328(5982):1154–1158.
2. Angers RC, et al. (2009) Chronic wasting disease prions in elk antler velvet. *Emerg Infect Dis* 15(5):696–703.