



Assays to discriminate CWD prions from scrapie prions in small ruminants

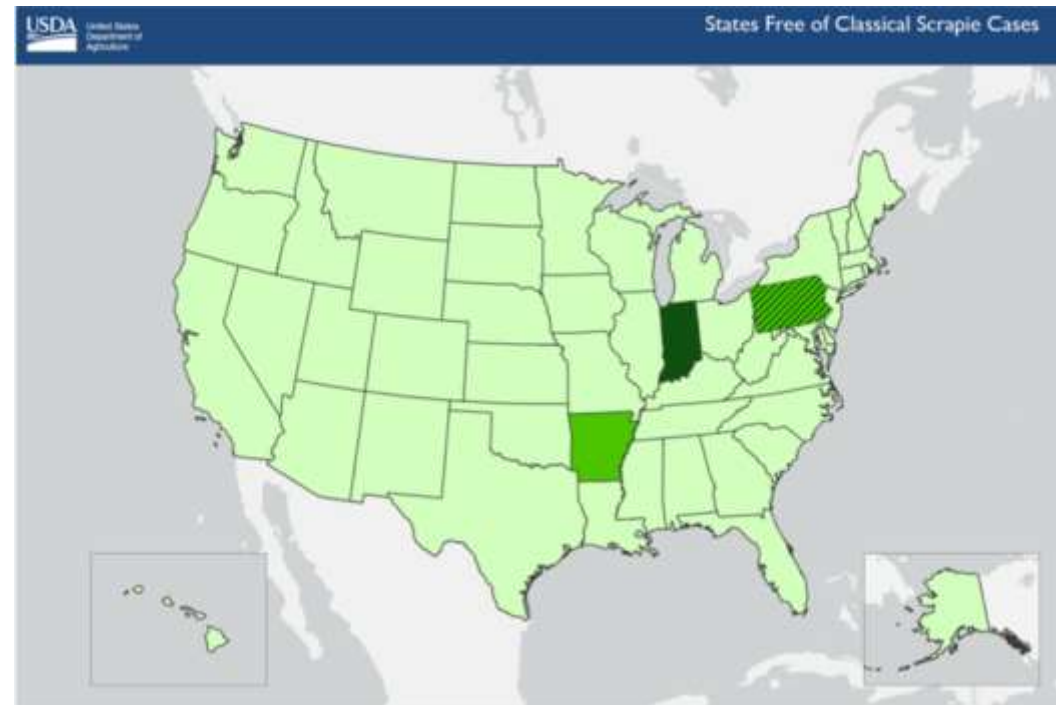
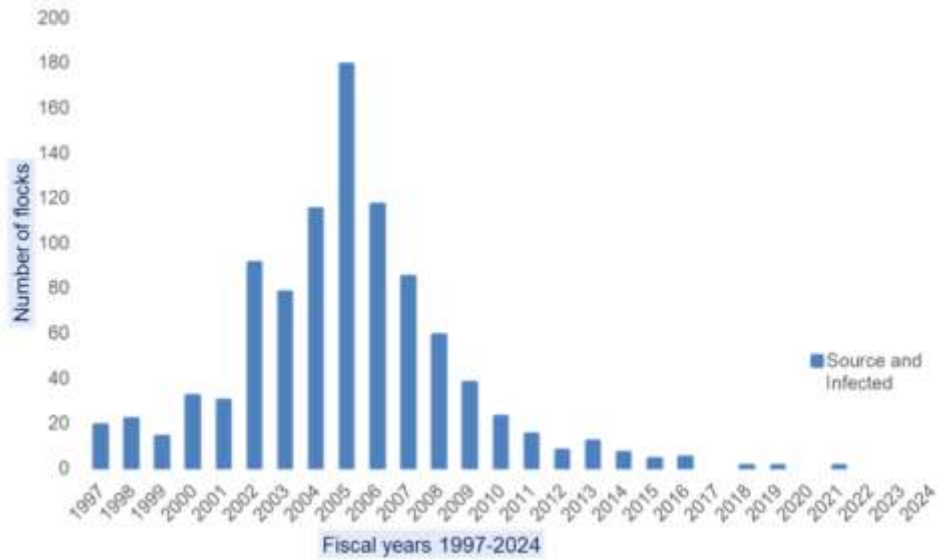
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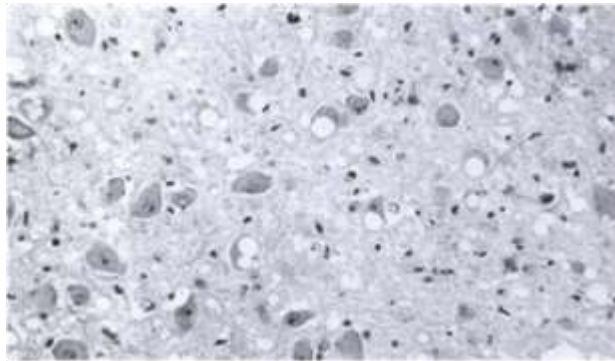
Great success of scrapie eradication efforts





Chronic Wasting Disease (CWD)

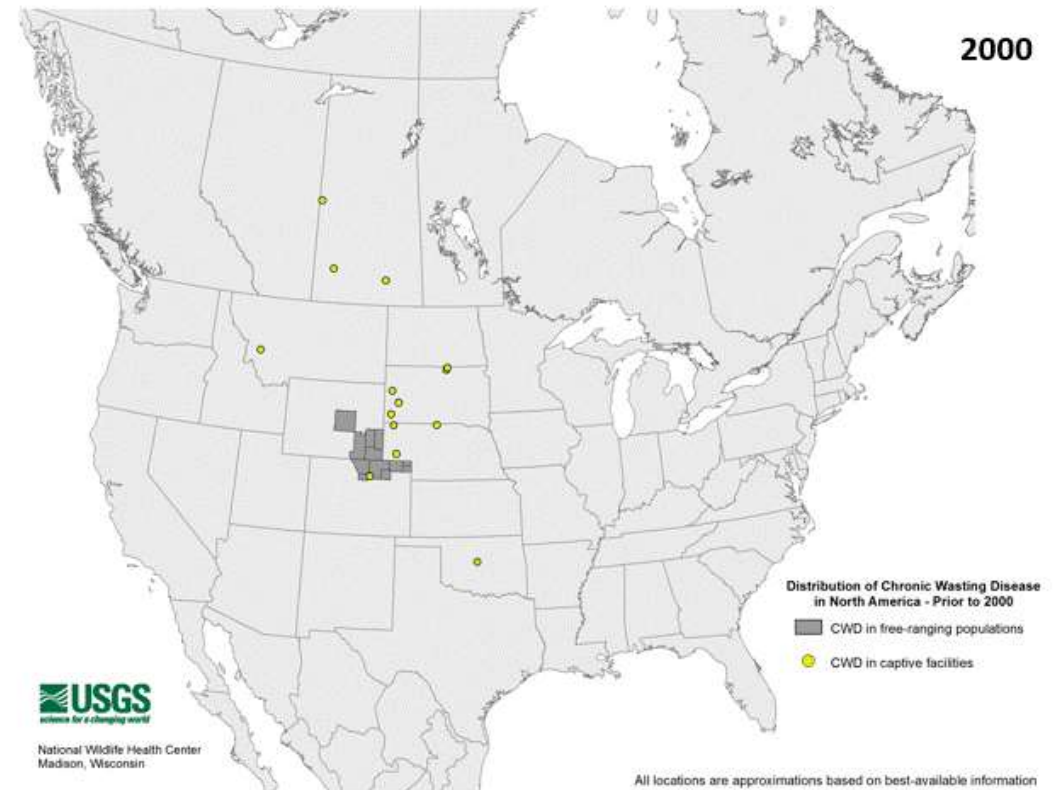
- Natural hosts: cervid species including mule deer, white-tailed deer, elk, and moose
- Slow pre-clinical phase
- Ultimately fatal





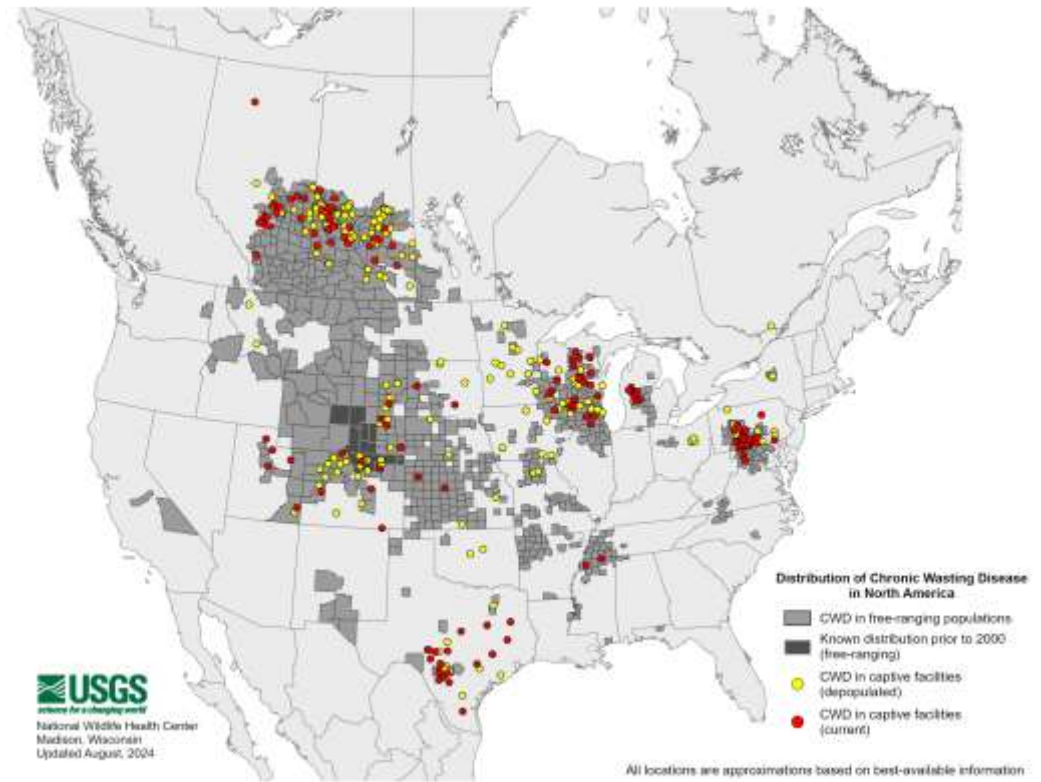
Brief history of CWD in the North America

- 1967 – first cases reported in captive mule deer
- 1981 – first cases reported in free-ranging cervids
- 2000 CWD distribution map
 - Dark grey counties: free-ranging cervids
 - Filled circles: farmed cervids



Brief history of CWD in North America

- 1967 – first cases reported in captive mule deer
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- 2000 CWD distribution map
 - Dark grey counties: free-ranging cervids
 - Filled circles: farmed cervids
- Today:
 - 35 states and 4 provinces
 - Majority cases in white-tailed and mule deer, and elk.



Experimental transmission to sheep

- Prion infection after intracranial inoculation of brain homogenate from CWD-infected
 - ✓ Mule deer
 - ✓ Elk
 - ✓ WTD



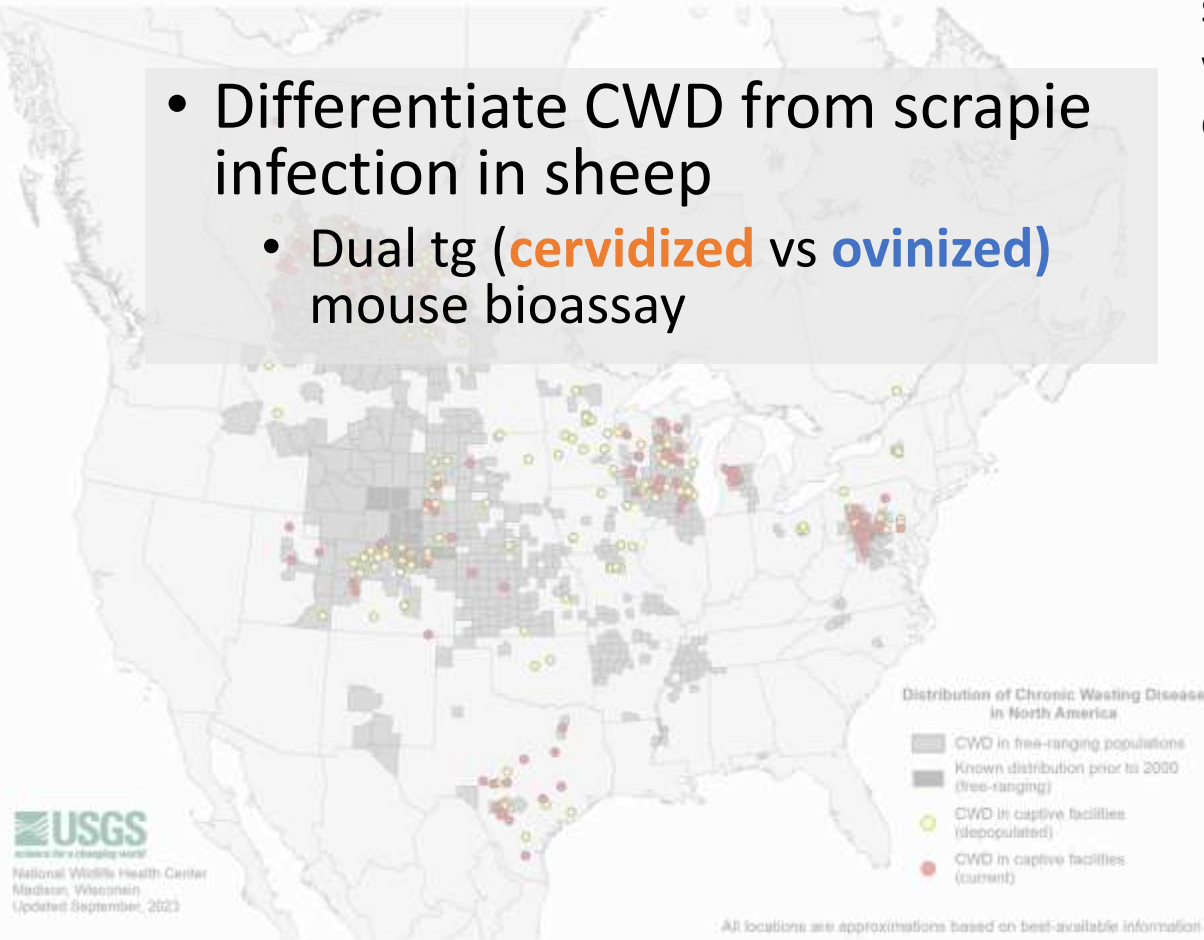


Sheep and Goats are *experimentally* susceptible to Chronic Wasting Disease (CWD) prions

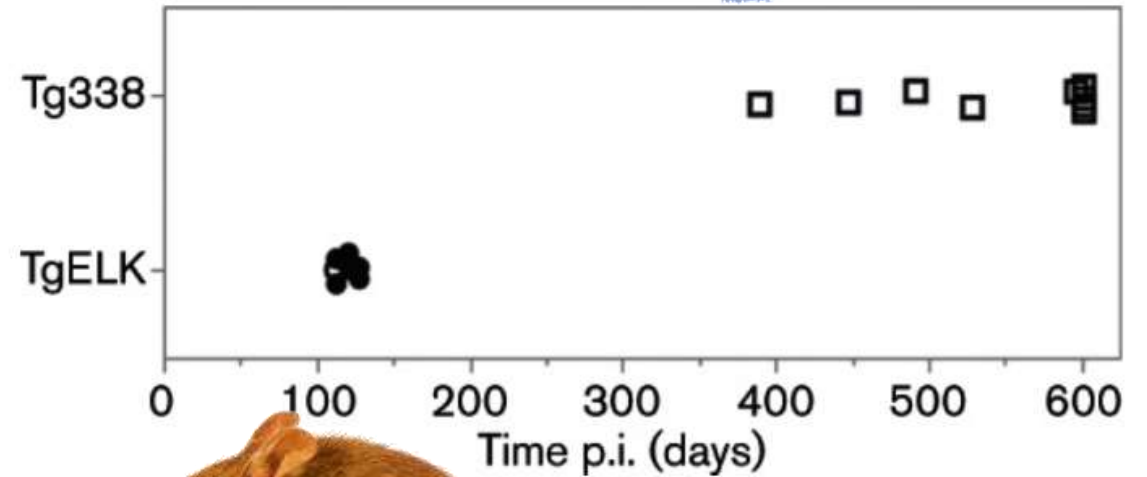
Can we distinguish CWD from scrapie in sheep and goats should natural transmission occur?



- Differentiate CWD from scrapie infection in sheep
 - Dual tg (**cervidized** vs **ovinized**) mouse bioassay

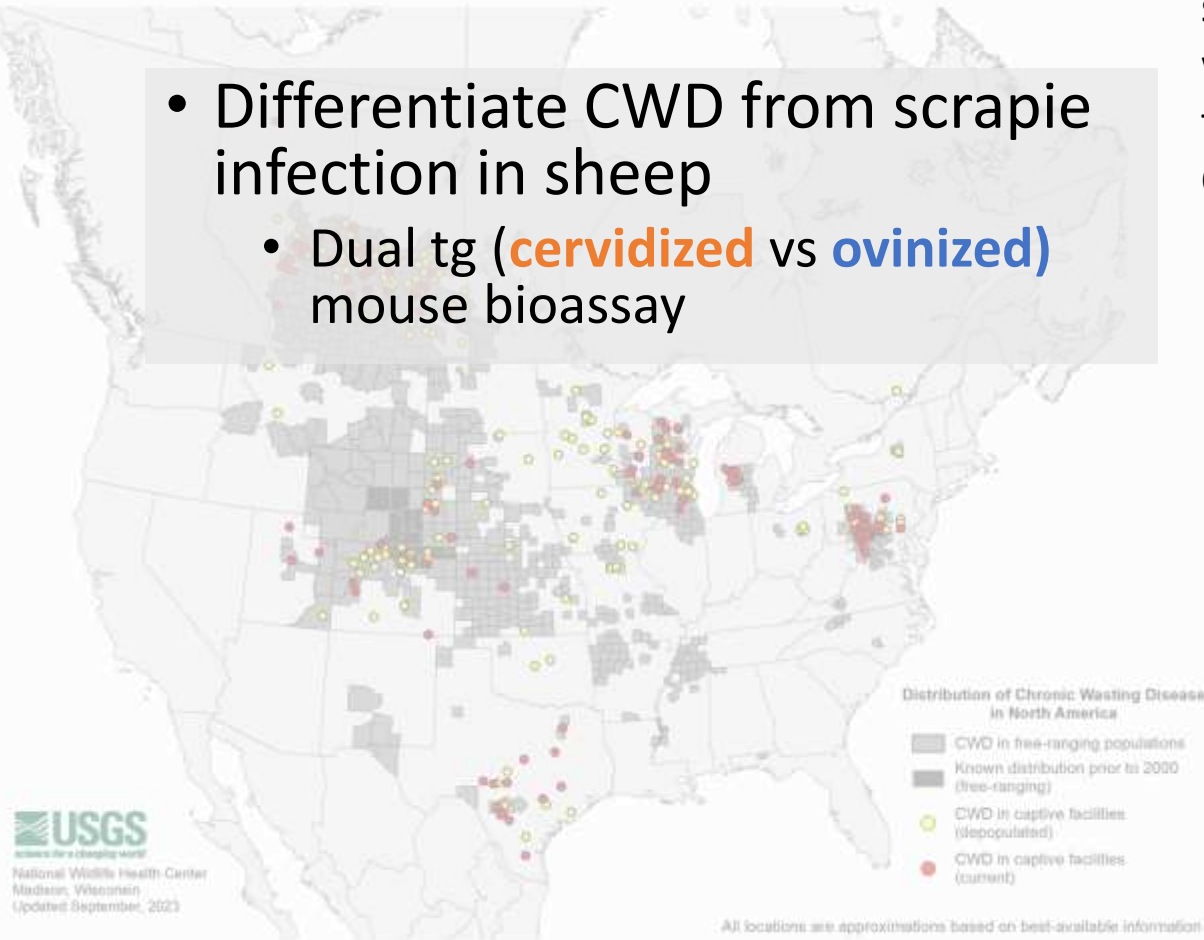


Source of inoculum: brain from sheep experimentally inoculated with brain homogenate pool from elk with naturally acquired CWD

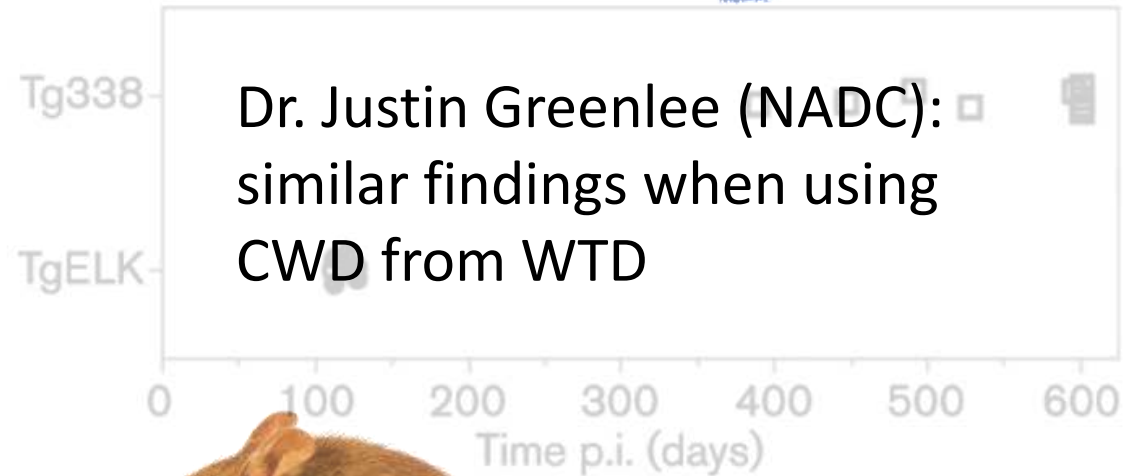




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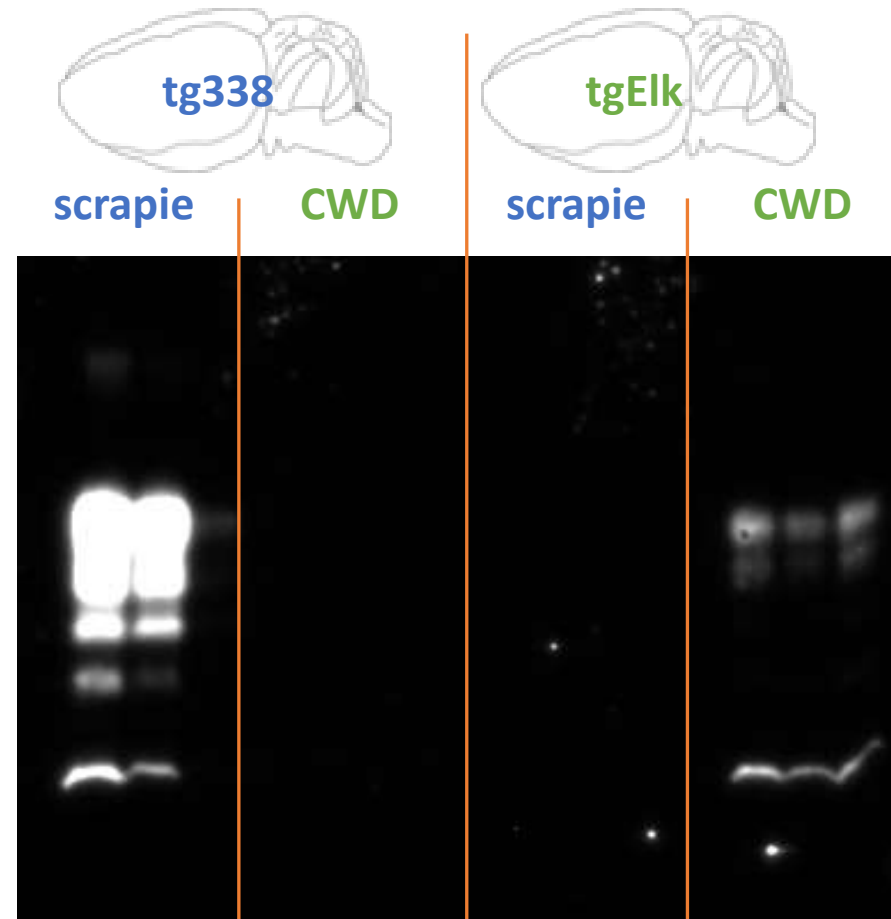


Source of inoculum: brain from sheep experimentally inoculated with brain homogenate from white-tailed deer with naturally acquired CWD



serial Protein Misfolding Cyclic Amplification (sPMCA)

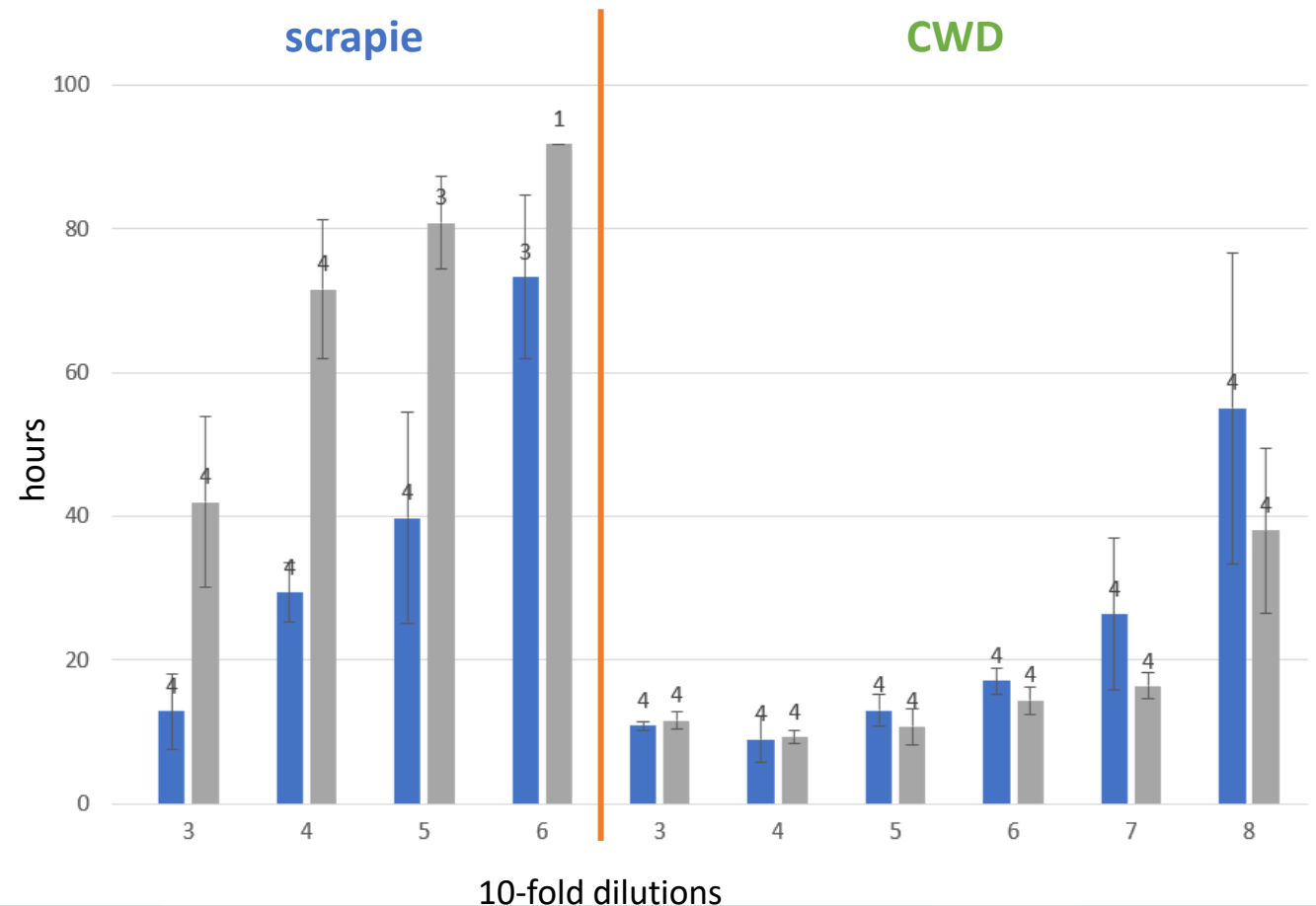
- Assay substrate:
brain homogenate of tg338
(ovine) or tgElk
- Prion-seeded misfolding and
aggregation of PrP detected by
western blot
- *Preliminary* data from P1 and P2
IC inoculated sheep





Real-Time Quaking-Induced Conversion (RT-QuIC) assay

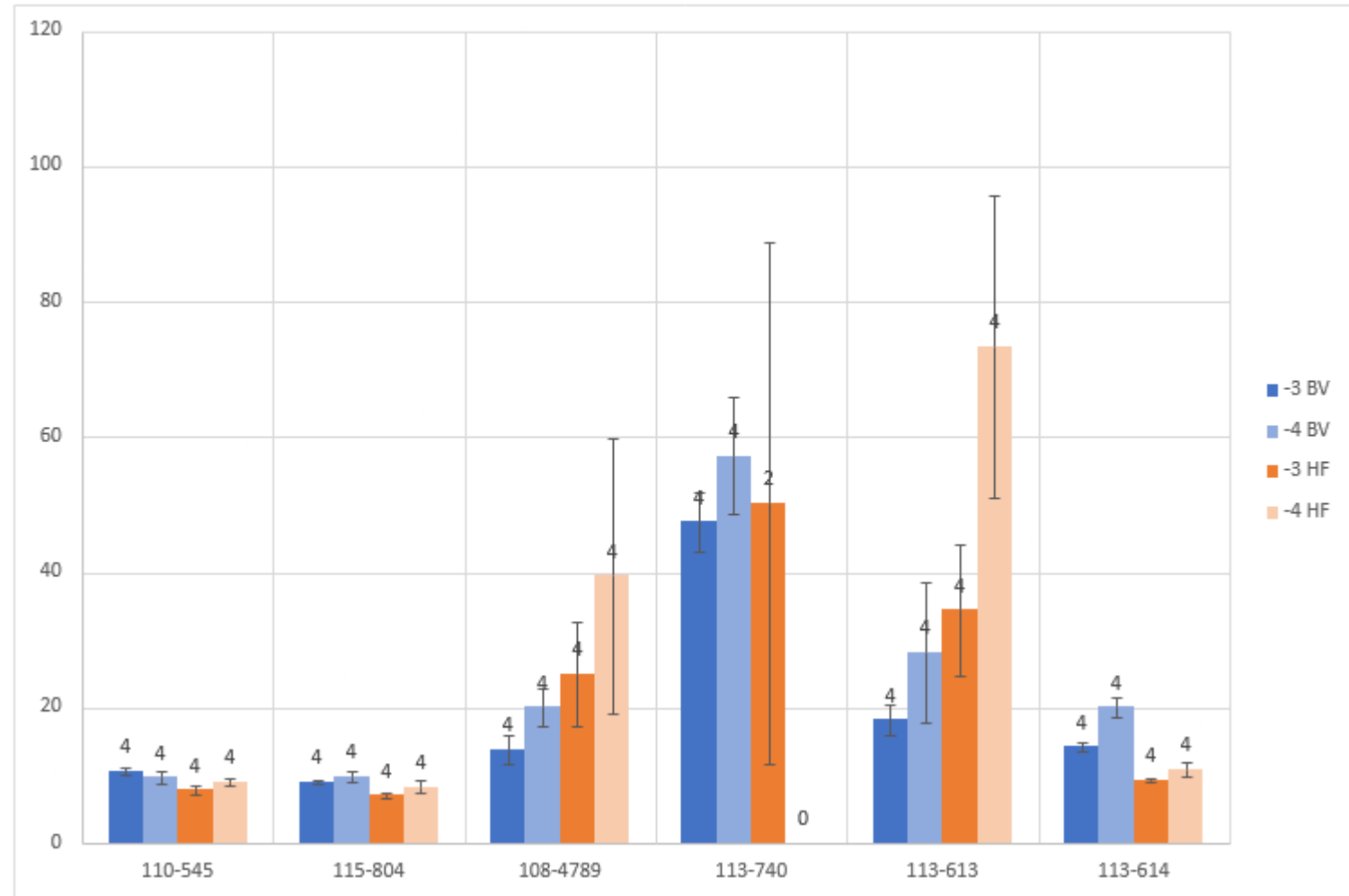
- Assay substrate:
bacterial recPrP
bank vole vs. **hamster**
- Prion-seeded misfolding and aggregation of PrP detected by fluorescence





Real-Time Quaking-Induced Conversion (RT-QuIC) assay

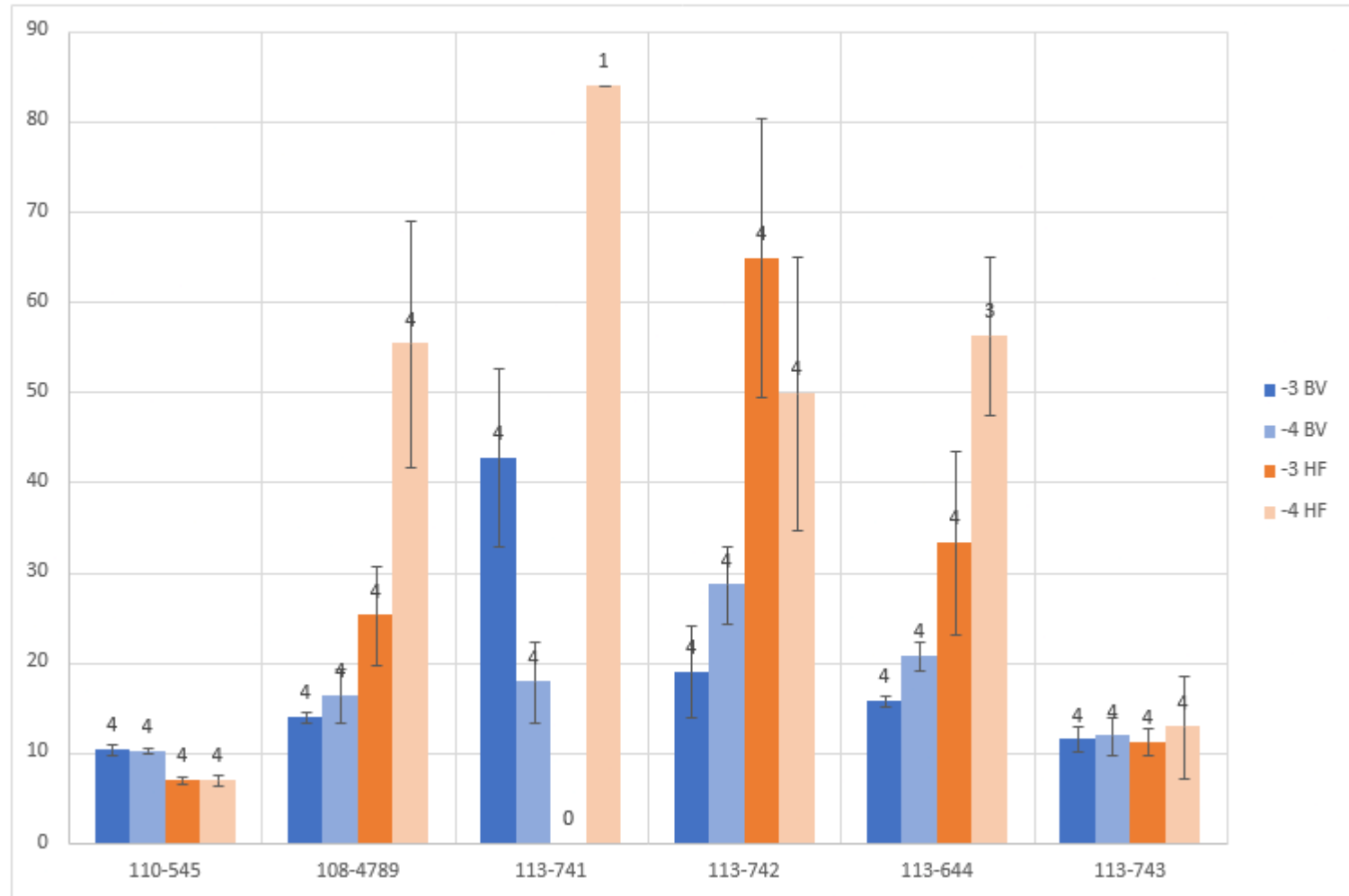
- P1 IC inoculated sheep
 - Two scrapie-like signature
 - One CWD-like





Real-Time Quaking-Induced Conversion (RT-QuIC) assay

- P2 IC inoculated sheep
 - Two scrapie-like signature
 - One CWD-like
- Stability of phenotypes





Summary

Prion differentiating assay progress

- Dual tg mouse bioassay differentiates CWD infection from elk and WTD in sheep from classical scrapie in sheep
- Prion protein misfolding/aggregation assays
 - Completed in under a week
 - Don't require making animals sick
 - Currently differentiates scrapie in sheep/goats from CWD in cervids
 - First experiments ...

CWD to small ruminants actual risk?

- These experiments do not tell us if transmission of CWD from cervids to small ruminants occurs naturally in the field.
- Limited data and all via experimental exposures
 - IC inoculation bypass barriers
 - infection not detected in four ARQ/AR^R sheep 6-years post-ic inoculation
 - Infection detected in ARQ and VRQ sheep
 - Infection detected in single goat, genotype unknown



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