

Implications of TSE infection and disease for maintaining the safety of biologics source materials

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Rationale

Human TSEs / Prion diseases may be underreported due to their **similarity to more common diseases** (Alzheimer's disease, Parkinson's disease etc.).

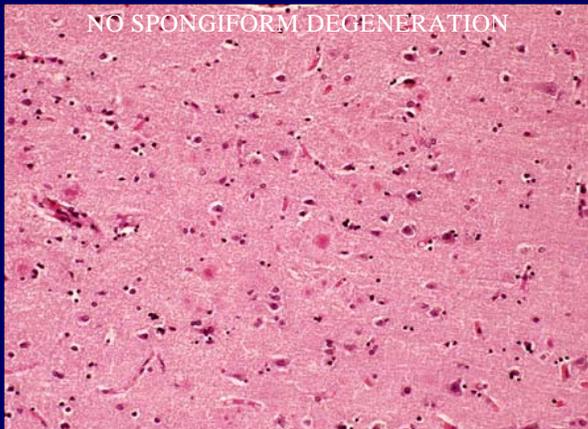
Aim 1. Characterize atypical TSE variants

Prion hypothesis: pathologic PrP (PrP^{Sc}) is the infectious agent

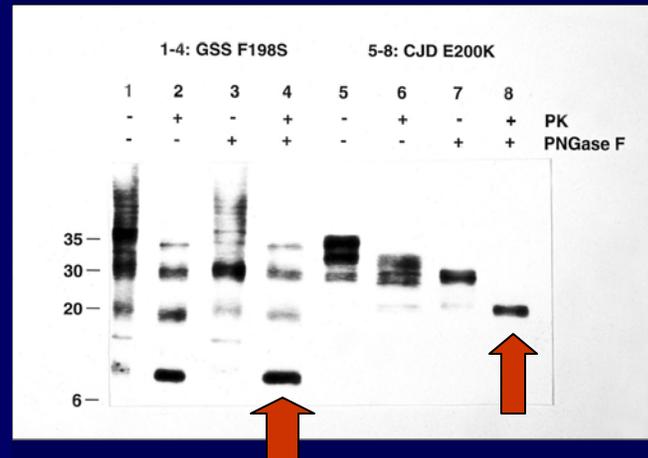
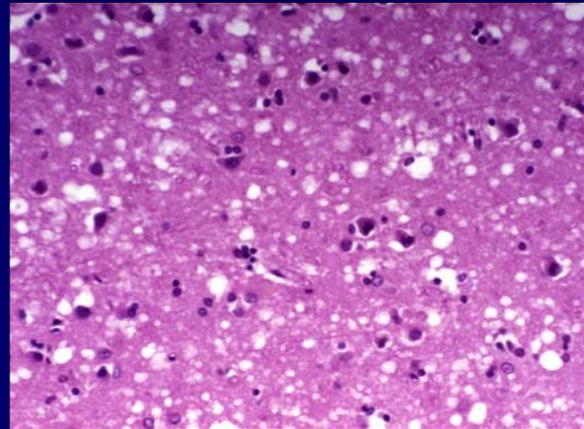
If PrP molecules **not associated with infectivity** can accumulate during disease, it is important to define them, since **PrP accumulation is commonly assumed to indicate the presence of infectivity in animals and humans.**

Aim 2. Is PrP^{Sc} always associated with infectivity?

Patient with **atypical** TSE



Patient with **typical** TSE



PrP^{Sc} 8 kDa

PK: proteinase-K
PNGase F: deglycosidase
Mab 3F4: PrP-mid-region

PrP^{Sc} 21 kDa

Low *mw* PrP^{Sc} peptides in TSEs with amyloid / no spongiosis.
Is infectivity associated with PrP^{Sc} 8 kDa ?

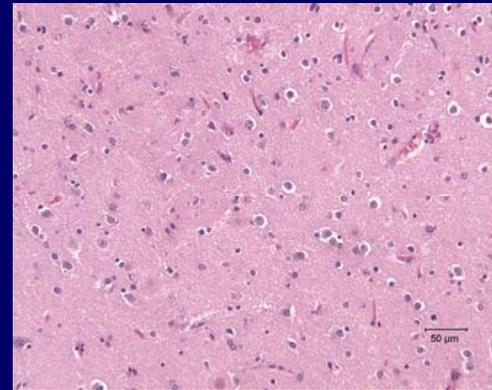
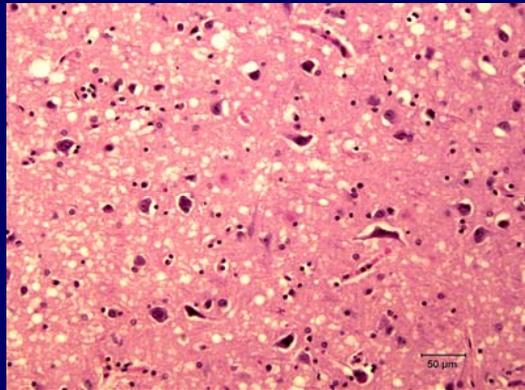
Bioassays to determine the infectivity associated with PrP-21 and PrP-8

Patient - typical TSE

Patient - atypical TSE

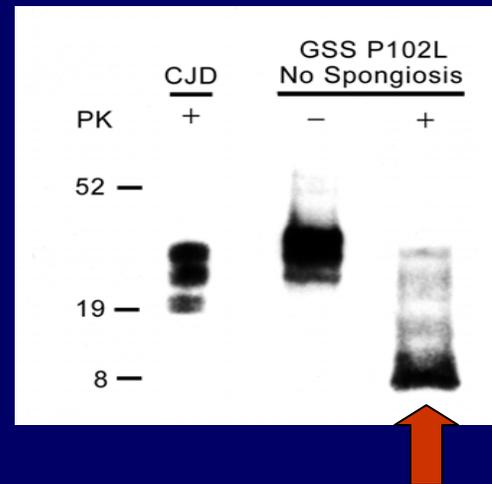
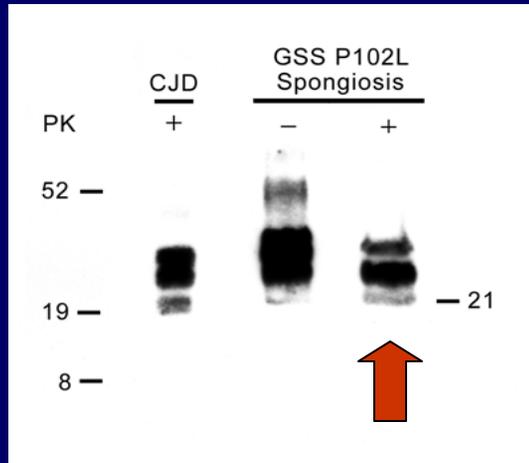
Spongiosis

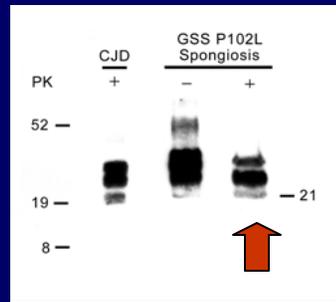
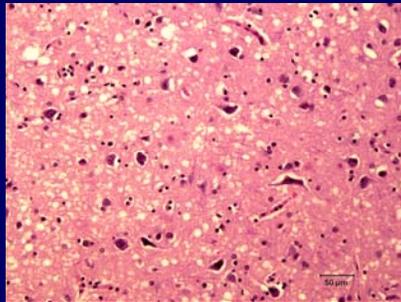
No spongiosis



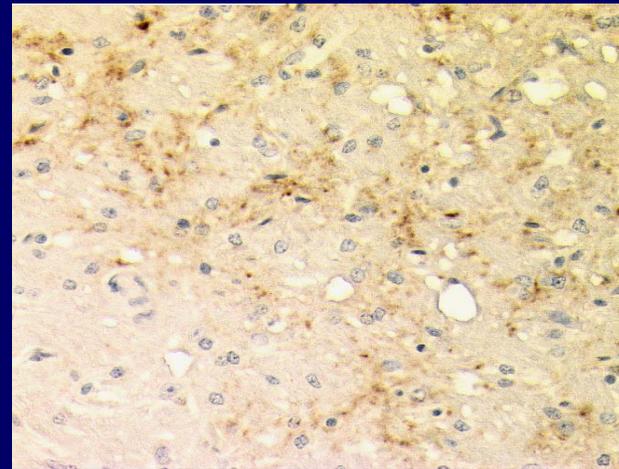
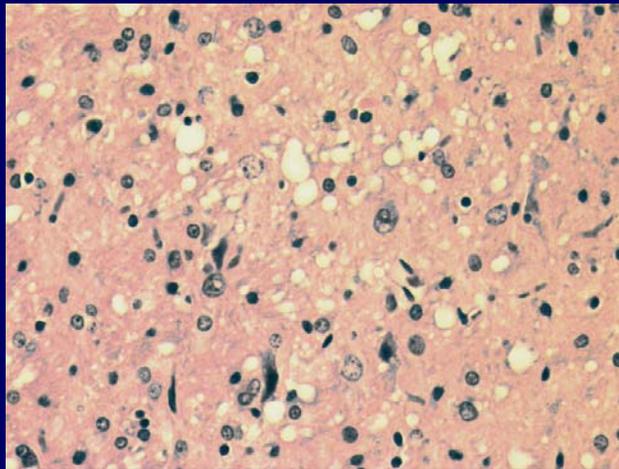
PrP^{Sc} 21

PrP^{Sc} 8





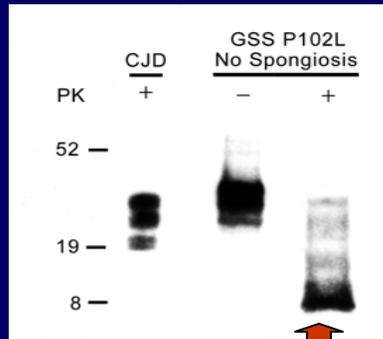
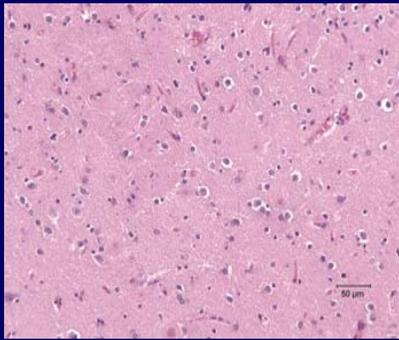
Patient - typical TSE
PrP^{sc} 21kDa



**Tg mouse model
highly susceptible
to TSE**

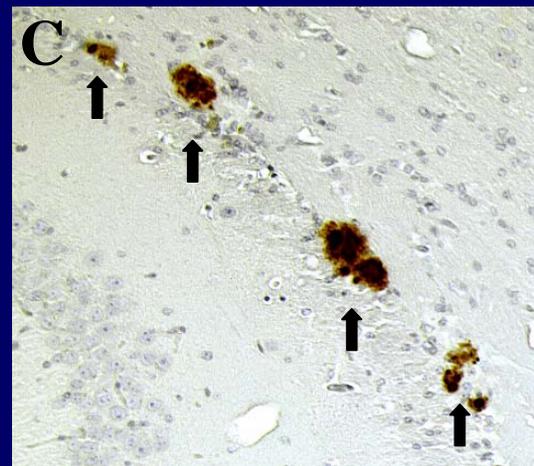
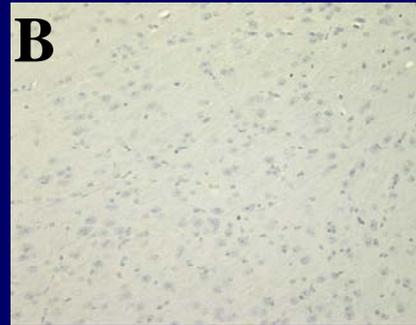
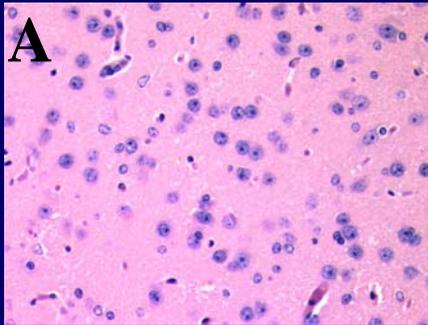
Symptomatic - spongiosis- widespread PrP accumulation (*in some Tgs*)

Efficient transmission of disease



Patient - atypical TSE

PrP^{Sc} 8 kDa



Tg mouse model
highly susceptible
to TSE

Asymptomatic, no spongiosis, PrP amyloid

- **Inefficient** transmission of disease
- Detection of PrP^{Sc} in the apparent absence of infectivity
- Is amyloid formation a protective mechanism?

Collaborators: Washington Univ - Indiana Univ - NPU Scotland