

Assessing prion infectivity in the skin of sporadic CJD patients

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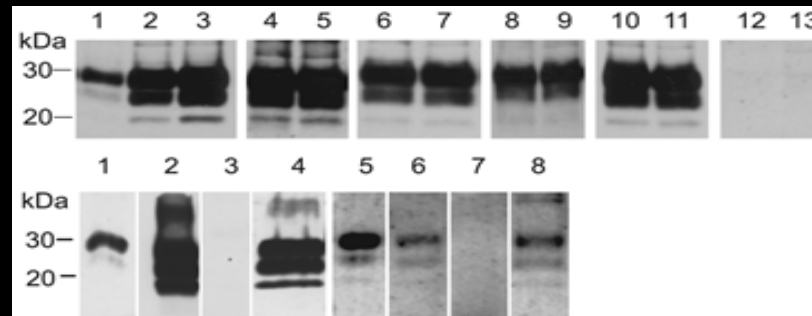
Background

Cunningham et al., 2004

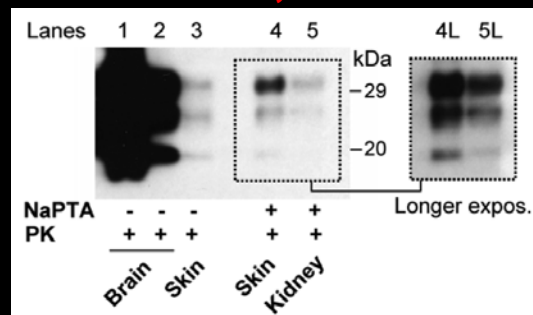
Table 2. Bioassay results for greater kudu tissues injected into C57Bl-J6 mice

Kudu identification no.	Tissue ^a injected	Positive mice/total ^b	Mean survival period post injection (days) ± SD ^c	Survival period range (d) ^d
A1212	Rostral cerebrum	13/20	595±84	428–745
	Cranial thoracic spinal cord	19/20 ^d	557±121	413–821
	Lumbar spinal cord	15/19	521±69	432–634
	Spleen	3/11 ^d	819±41	773–851
	Retropharyngeal lymph node	6/11 ^d	784±77	691–921
	(biceps brachii + vastus lateralis) Skin (flank)	2/18 ^d	713±22	697–728

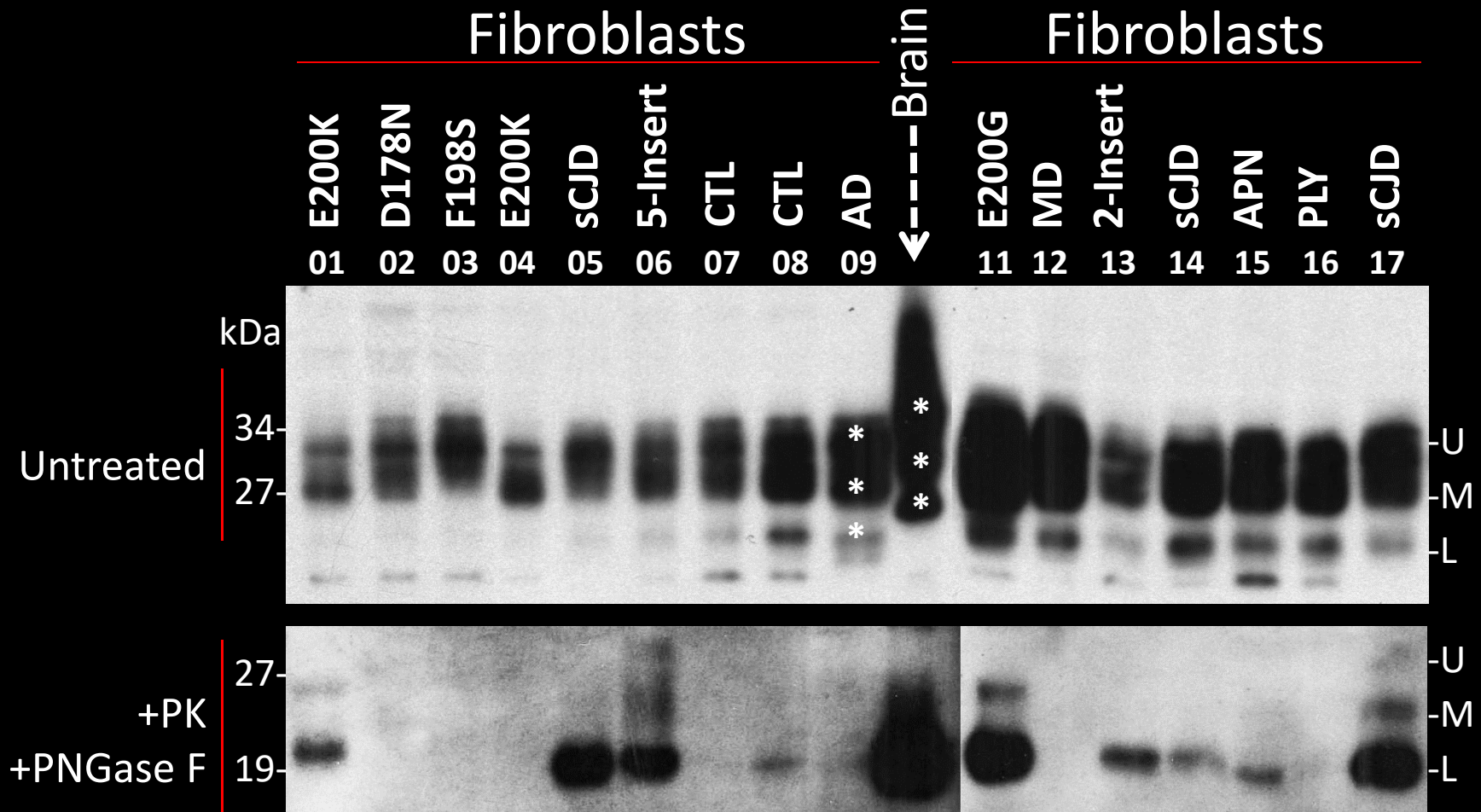
Thomzig et al., 2007



Notari et al., 2010



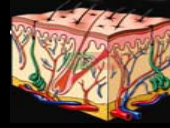
PrP^{res} in patient-specific skin-derived fibroblasts



Background/Aim

- Histories of non-CNS-surgeries could be a risk factor of sporadic CJD
- There are dermal prions in sCJD patients, which are infectious and can be a biomarker for diagnosis of human prion diseases

Subjects and Methods



Skin



Western blotting

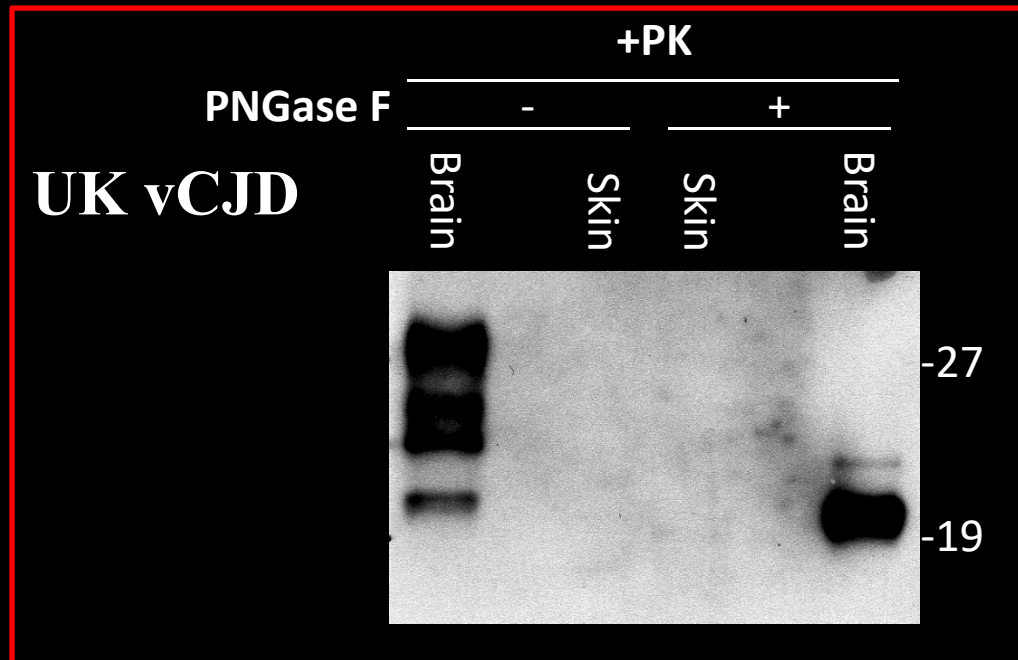
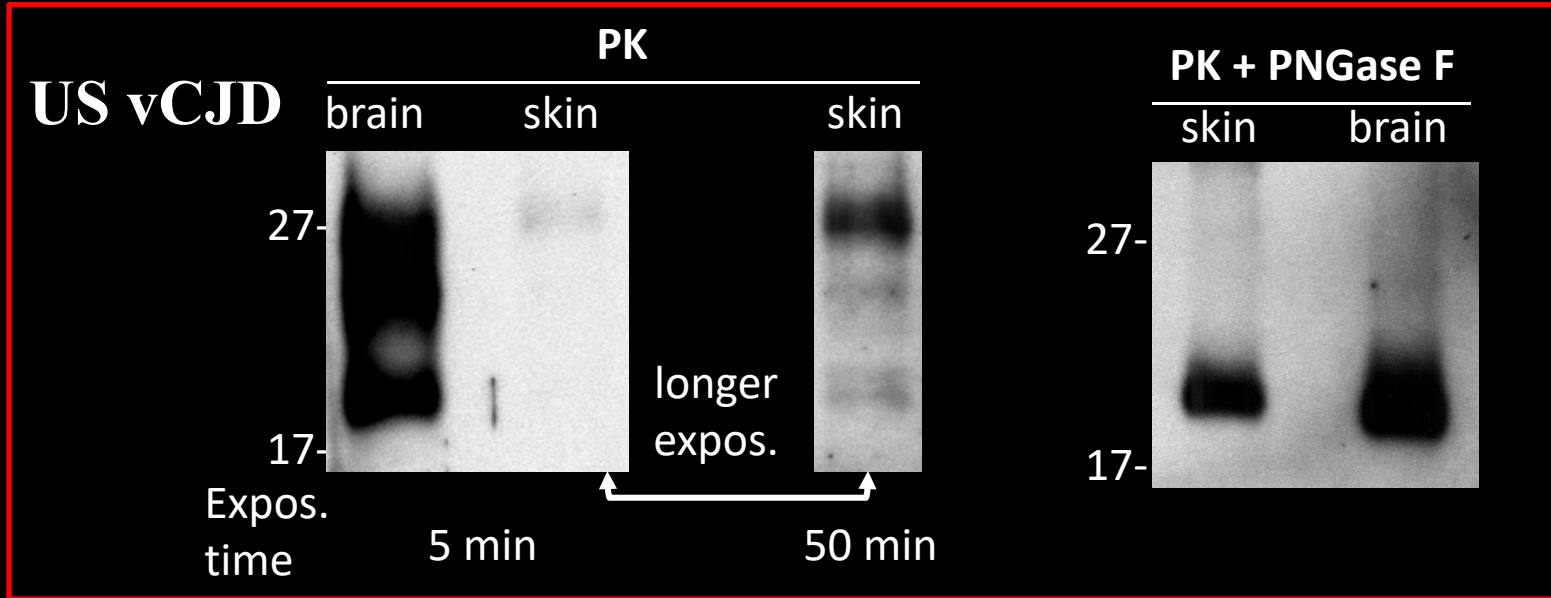


RT-QuIC



Bioassay

Western blotting of PrP^{Sc} in skin of vCJD patients



Detection of PrP^{Sc} in the skin of sCJD patients

+PK

sCJD Non-CJD Non-CJD Non-CJD Non-CJD sCJD Non-CJD sCJD Non-CJD Non-CJD Non-CJD sCJD sCJD Non-CJD Non-CJD vCJD

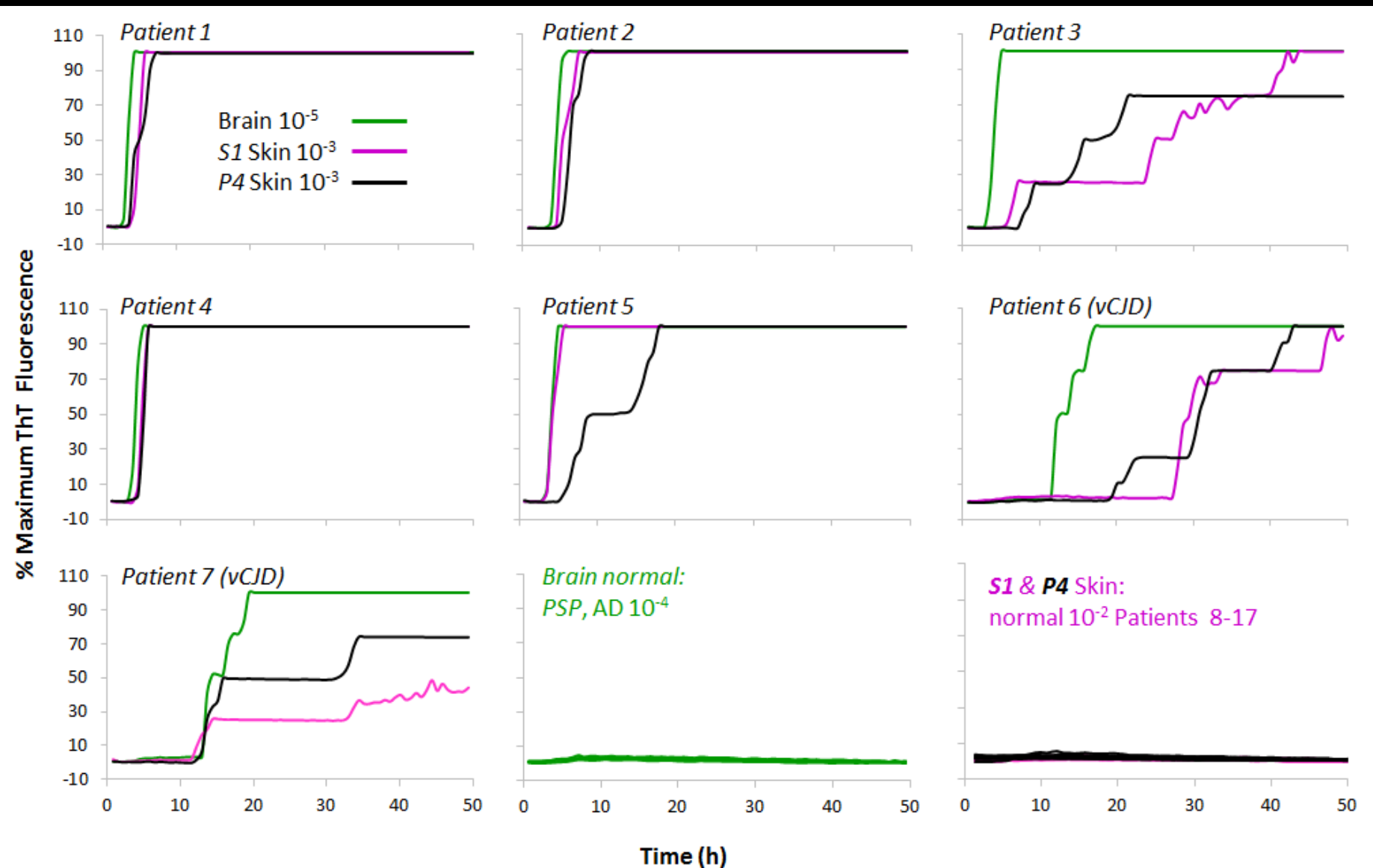


PK + PNGase F

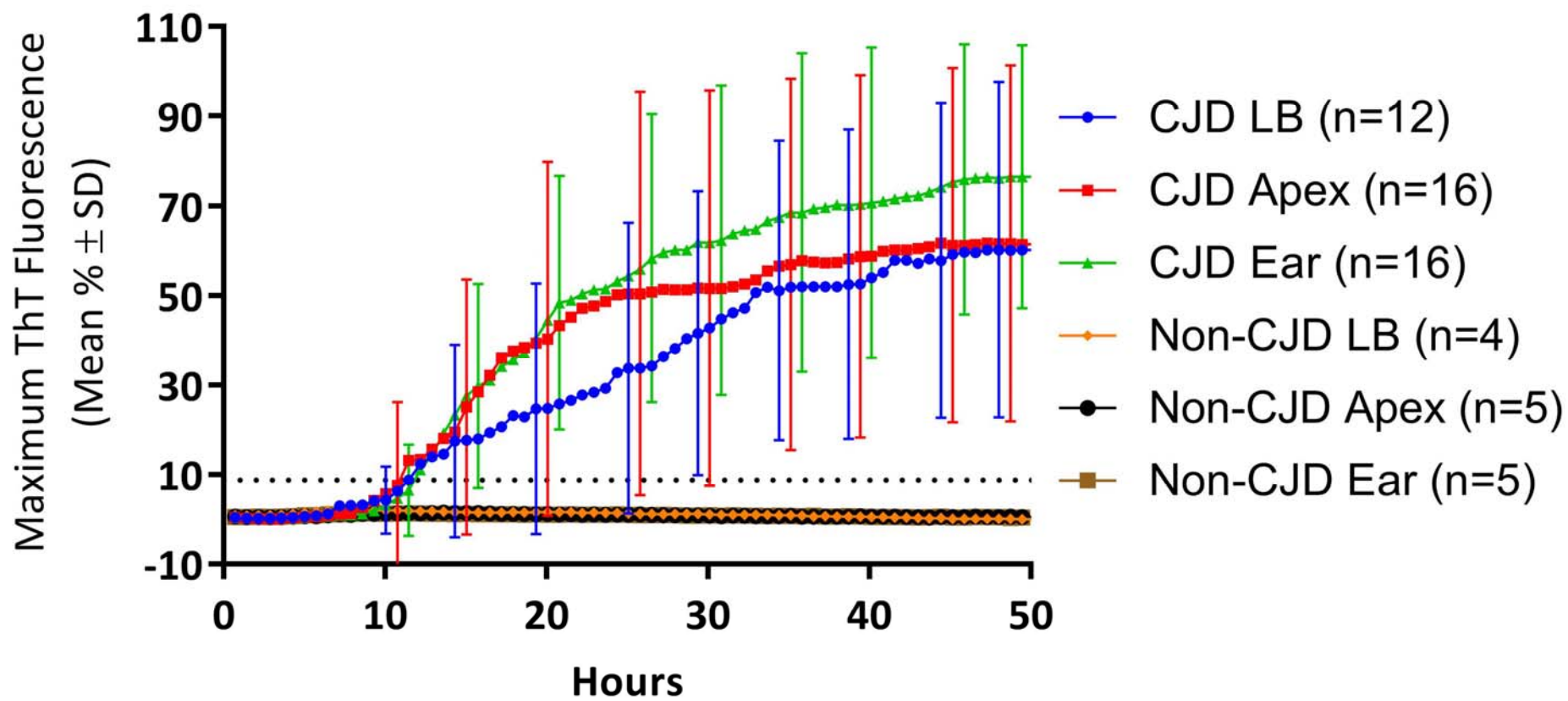
17-
Lane 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16



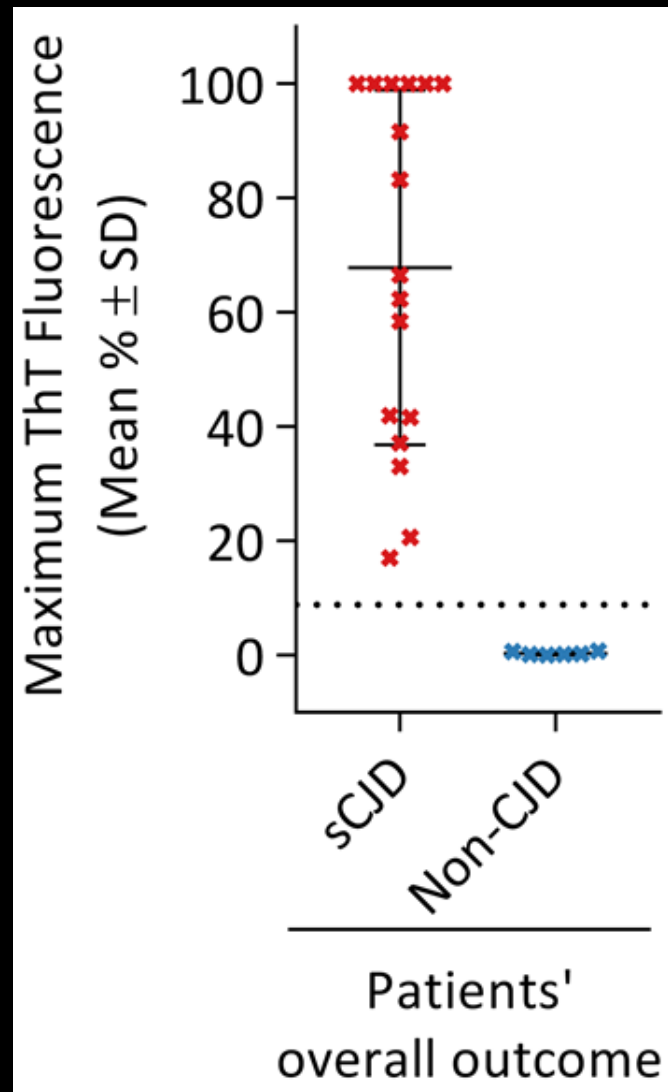
RT-QuIC assay of PrP seeding activity in the skin and brain of CJD patients



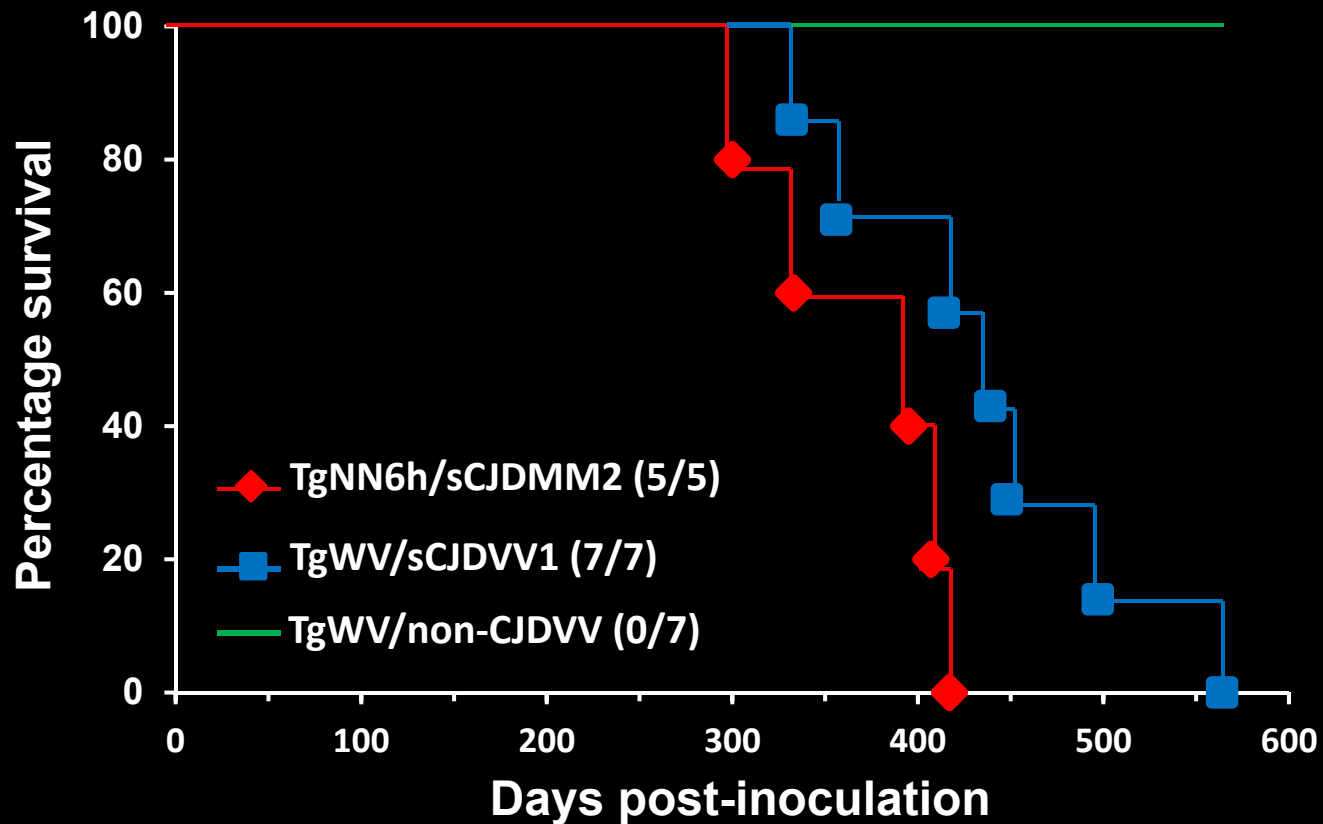
RT-QuIC analysis of PrP seeding activity in the skin and brain of CJD patients



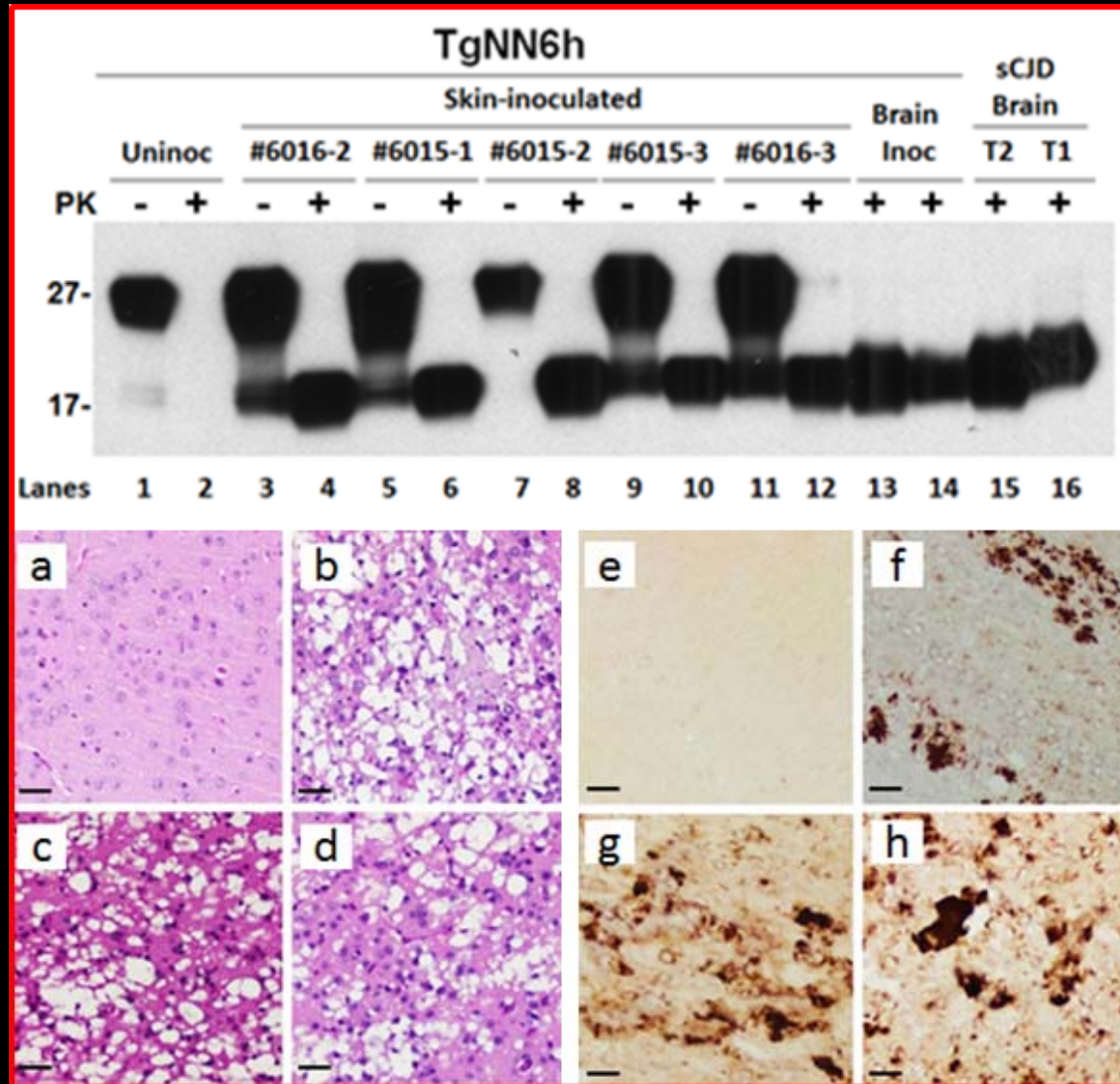
RT-QuIC analysis of PrP seeding activity in the skin and brain of CJD patients



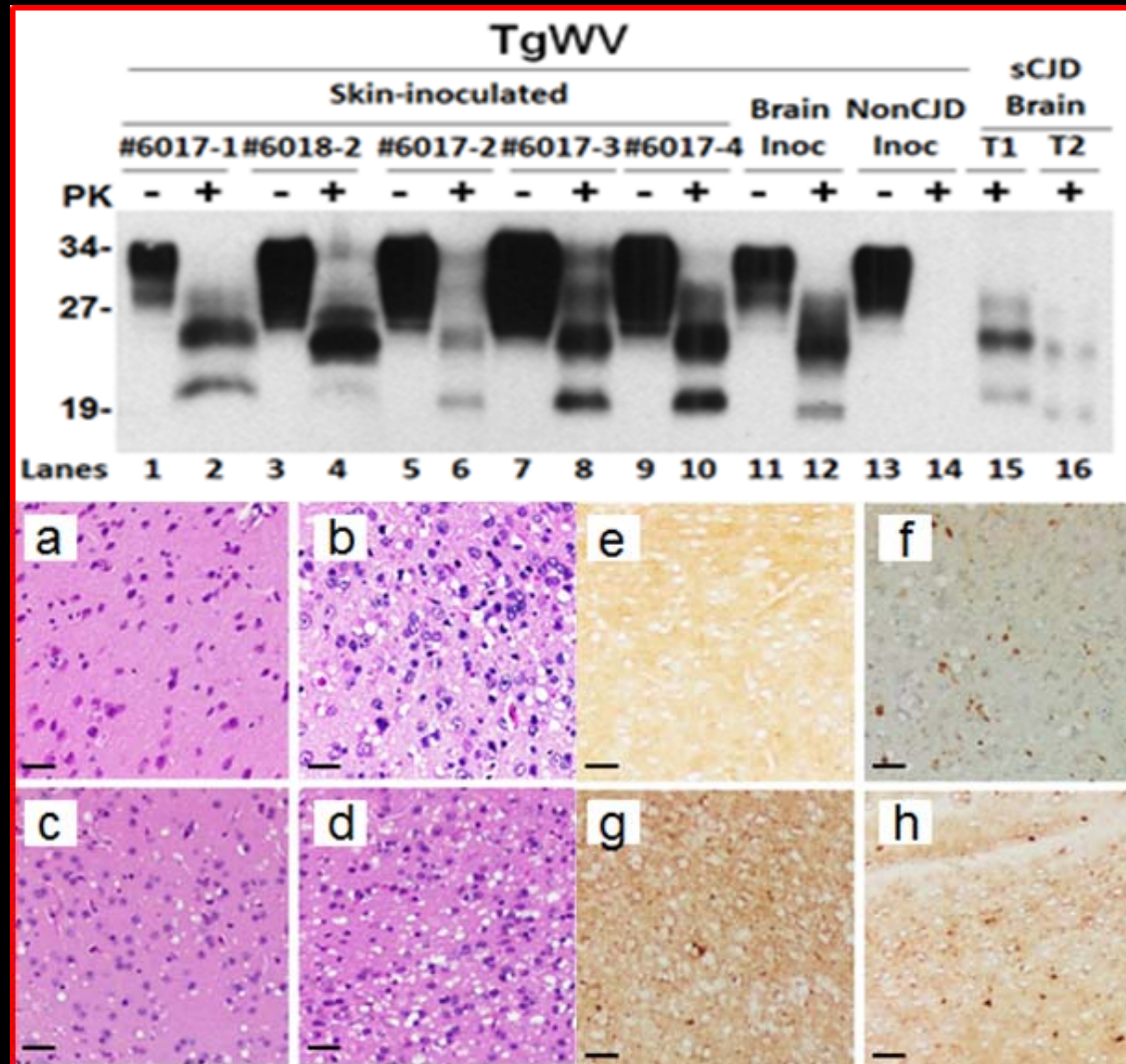
Bioassay of sCJD skin samples with humanized transgenic mice



Western blotting and histology of TgNN6h mouse brains inoculated with skin samples



Western blotting and histology of TgWV mouse brains inoculated with skin samples



Conclusions

- Prion seeding activity is detectable in the skin of sCJD patients, which may set up a basis for developing skin-based antemortem and postmortem RT-QuIC assay for CJD
- Dermal prions in sCJD are infectious, which may raise concerns about the potential for iatrogenic sCJD transmission through skin during non-CNS surgeries
- In no way does our study imply that prion transmission can occur via casual contact

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