

## SUPPLEMENTARY INFORMATION FOR EDITORIAL PURPOSES

### **REF: SREP-15-02633-B**

**Title:** Involvement of PrP<sup>C</sup> in kainate-induced excitotoxicity in several mouse strains

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### **Supplementary Figures/Movies legends:**

**Supplementary Tables 1-6:** Description of the seizure level reached by each mouse plotted in the Figure 1a.

**Supplementary Figure 1:** Full size Western blot corresponding to Figure 1b for Tubulin and PrP<sup>C</sup> levels in brain extracts from B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>+/+</sup>, B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>0/0</sup>, 129/Ola *Prnp*<sup>Edbg/Edbg</sup> *Prnp*<sup>+/+</sup>, 129/Ola *Prnp*<sup>Edbg/Edbg</sup> *Prnp*<sup>0/0</sup>, FVB/N *Prnp*<sup>+/+</sup> and FVB/N *Prnp*<sup>0/0</sup> mice. (a) 1 minute exposure. (b) 5 minutes exposure. L points to the ladder lines. Notice that the L lines were omitted in Fig. 1b. Red arrows points the portions of the Western blot showed in the Figure 1b.

**Supplementary Figure 2:** Full size blot corresponding to Figure 3a for Tubulin and PrP<sup>C</sup> levels in protein extracts of pcDNA, pcDNA-PrP<sup>C</sup>, pcDNA-PrP<sup>C</sup> + PLC and pcDNA-PrP<sup>C</sup> + Gli treated N2a cells. Arrows point proteins of interest (Tubulin and PrP<sup>C</sup>). sd

**Supplementary Figure 3:** Full size Western blot corresponding to Figure 4b for Tubulin and PrP<sup>C</sup> levels in brain extracts obtained from untreated B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>+/+</sup>, B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>+/0</sup> and B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>0/0</sup>, B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>0/0</sup> ΔC4 and B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>0/0</sup> ΔF35 mice. (a) 2 minutes exposure. (b) 5 minutes exposure. L points to the ladder lines. Notice that the L lines and the lines showing B6129 *Prnp*<sup>Zrchl/Zrchl</sup> *Prnp*<sup>+/0</sup> were omitted in Fig. 4b. Red arrows points the portions of the Western blot showed in the Figure 4b.

**Supplementary Figure 4:** Neuronal death in  $\Delta F35$  and  $\Delta C4$  mice. Low power photomicrographs of Nissl-stained sagittal sections of the hippocampus (**a,b**) and cerebellum (**c-f**) of  $\Delta F35$  (**a,c,e**) and  $\Delta C4$  (**b,d,f**) mice at 90 days. Note that the hippocampus (**a,b**) of both mutants remains healthy with a well defined pyramidal layer. In contrast,  $\Delta F35$  mice showed relevant cerebellar degeneration starting in the granule cell layer in medial cerebellar folia (box in **c**). A higher magnification of the box in (**c**) is showed in (**e**). Arrows in (**e**) point to Purkinje cells and cerebellar folia numbering is included in (**c** and **d**). Abbreviations as in Figure 2 and ml = molecular layer; pcl = pukinge cell layer and gl = granule cell layer in (**e** and **f**). Scale bars: **a** = 200  $\mu\text{m}$  pertains to **b-d**; **e** = 100  $\mu\text{m}$  pertains to **f**.

**Supplementary Figure 5:** Full size Western blot corresponding to Figure 5b for Tubulin and PrP<sup>C</sup> levels in protein extracts of pcDNA, pcDNA-PrP<sup>C</sup>, pcDNA-PrP <sup>$\Delta$ CD</sup> and pcDNA-PrP <sup>$\Delta$ F35</sup> treated N2a cells. (**a**) 2 minutes exposure. (**b**) 5 minutes exposure. Red arrows points the parts of the Western blot showed in the Figure 5b.

**Supplementary Movie 1.** Representative examples of KA-induced seizures in B6129 and B6.129 *Prnp*<sup>0/0</sup> mice. Results from the microsatellite analysis are included in the first frames of the video in the bottom right corner. The genotype of each mouse is also showed.

**Supplementary Movie 2.** Three examples of KA-induced seizures in 129/Ola<sup>*Edbg/Edbg*</sup> *Prnp*<sup>0/0</sup> mice. Results from the microsatellite analysis are included in the first frames of the video as in Supplementary Movie 1. The genotype of each mouse is also included in the video.

**Supplementary Movie 3.** Examples of KA-induced seizures in FVB/N *Prnp*<sup>0/0</sup> and *Prnp*<sup>+/+</sup> mice. The genotype of each mouse is also is showed in the video.

**Supplementary Movie 4.** Examples of KA-induced seizures in  $\Delta F35$  and  $\Delta C4$  mice (B6129 *Prnp*<sup>0/0</sup> background). The genotype of each mouse is showed in the video.

Animal Code	Seizure Intensity Reached			
	Grade I-IV	Grade V	Grade VI	Death
B6129.Ko.1				
B6129.Ko.2				
B6129.Ko.3				
B6129.Ko.4				
B6129.Ko.5				
B6129.Ko.6				
B6129.Ko.7				
B6129.Ko.8				
B6129.Ko.9				
B6129.Ko.10				
B6129.Ko.11				
B6129.Ko.12				
B6129.Ko.13				
B6129.Ko.14				
B6129.Ko.15				
B6129.Ko.16				
B6129.Ko.17				
B6129.Ko.18				
B6129.Ko.19				
B6129.Ko.20				

Animal Code	Seizure Intensity Reached			
	Grade I-IV	Grade V	Grade VI	Death
B6129.Wt.1				
B6129.Wt.2				
B6129.Wt.3				
B6129.Wt.4				
B6129.Wt.5				
B6129.Wt.6				
B6129.Wt.7				
B6129.Wt.8				
B6129.Wt.9				
B6129.Wt.10				
B6129.Wt.11				
B6129.Wt.12				
B6129.Wt.13				
B6129.Wt.14				
B6129.Wt.15				
B6129.Wt.16				

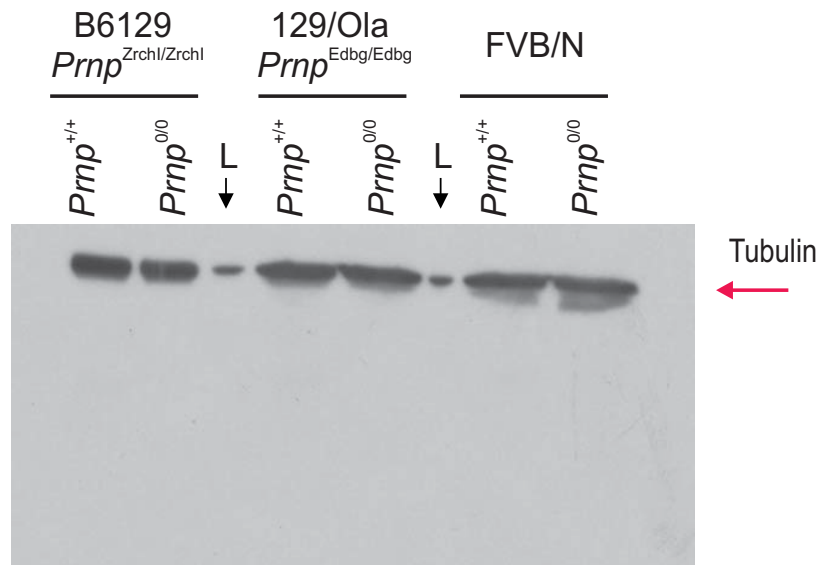
Animal Code	Seizure Intensity Reached			
	Grade I-IV	Grade V	Grade VI	Death
129/Ola.Ko.1	■	■		
129/Ola.Ko.2	■			
129/Ola.Ko.3	■	■		
129/Ola.Ko.4	■	■	■	
129/Ola.Ko.5	■	■		
129/Ola.Ko.6	■	■	■	
129/Ola.Ko.7	■	■		
129/Ola.Ko.8	■			
129/Ola.Ko.9	■	■		

Animal Code	Seizure Intensity Reached			
	Grade I-IV	Grade V	Grade VI	Death
129/Ola.Wt.1				
129/Ola.Wt.2				
129/Ola.Wt.3				
129/Ola.Wt.4				
129/Ola.Wt.5				
129/Ola.Wt.6				
129/Ola.Wt.7				
129/Ola.Wt.8				
129/Ola.Wt.9				
129/Ola.Wt.10				
129/Ola.Wt.11				

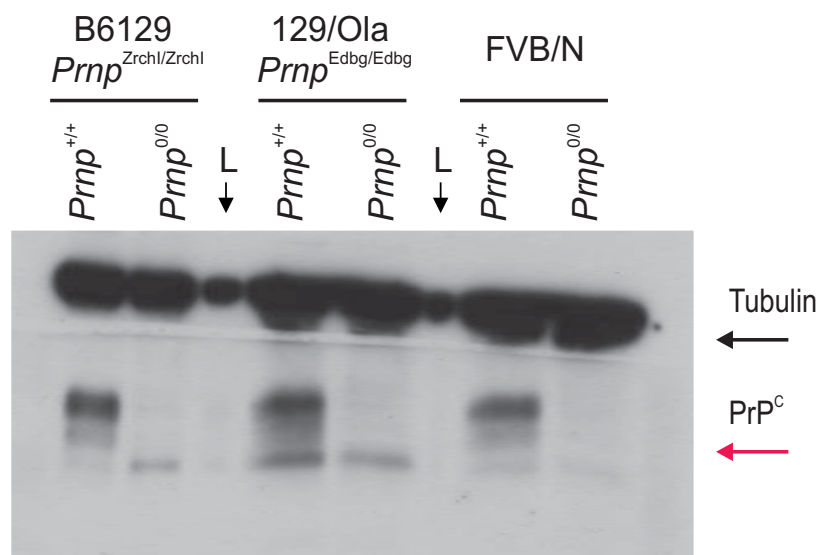
Animal Code	Seizure Intensity Reached			
	Grade I-IV	Grade V	Grade VI	Death
FvB/N.Ko.1				
FvB/N.Ko.2				
FvB/N.Ko.3				
FvB/N.Ko.4				
FvB/N.Ko.5				
FvB/N.Ko.6				
FvB/N.Ko.7				

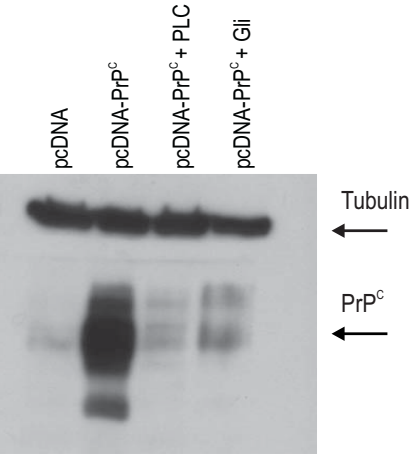
Animal Code	Seizure Intensity Reached			
	Grade I-IV	Grade V	Grade VI	Death
FvB/N.Wt.1				
FvB/N.Wt.2				
FvB/N.Wt.3				
FvB/N.Wt.4				
FvB/N.Wt.5				
FvB/N.Wt.6				
FvB/N.Wt.7				
FvB/N.Wt.8				



**a**

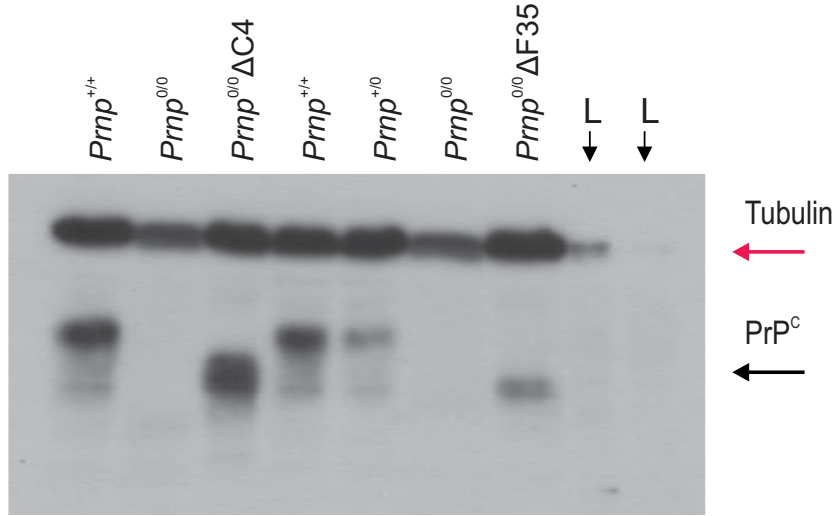
Tubulin Figure 1b

**b**PrP<sup>C</sup> Figure 1b

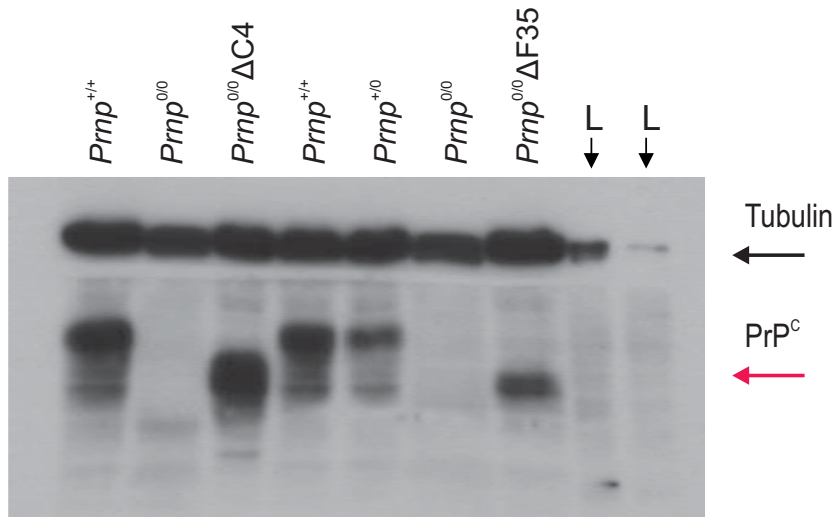


Tubulin and PrP<sup>C</sup> Figure 3a

**a**

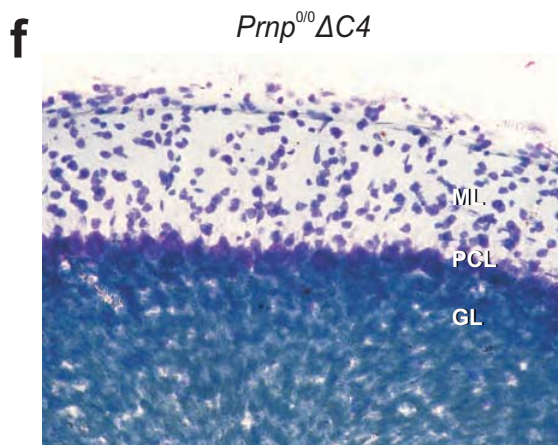
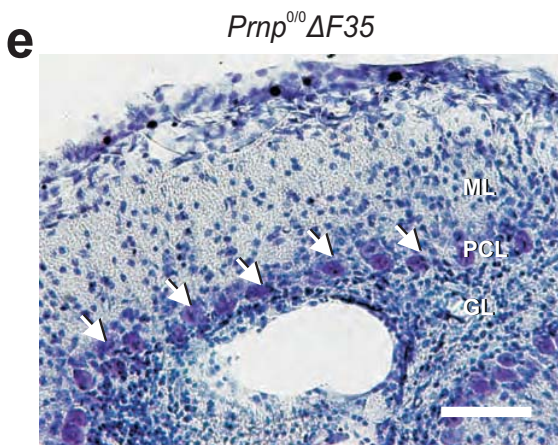
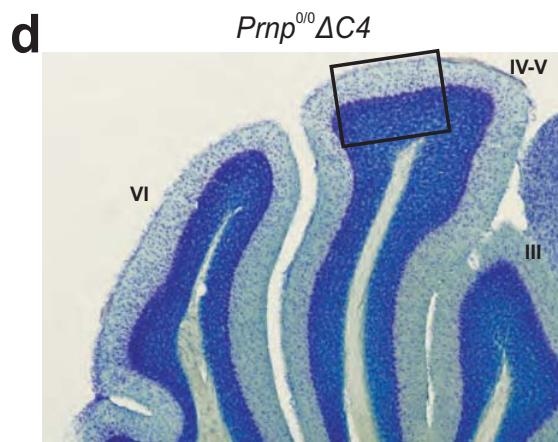
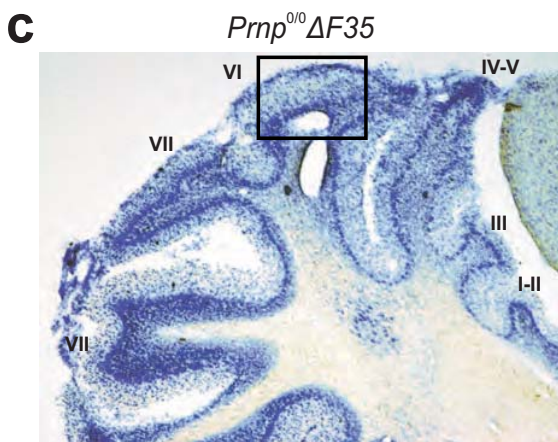
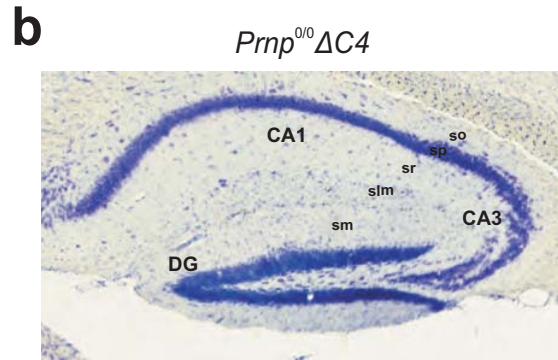
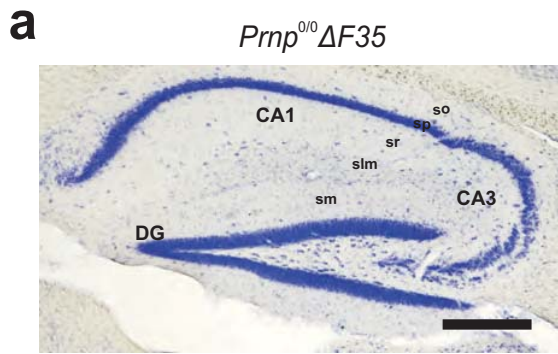


**b**

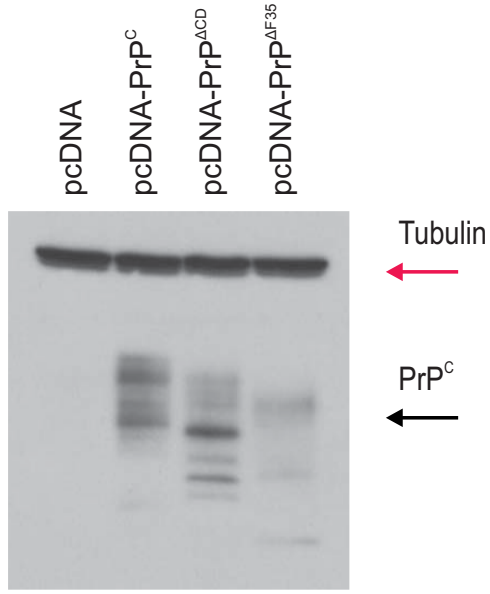


Tubulin Figure 4b

PrP<sup>C</sup> Figure 4b

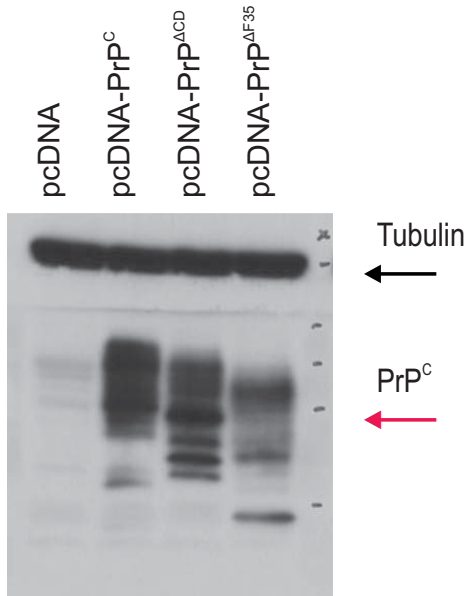


**a**



Tubulin Figure 5b

**b**



PrP<sup>C</sup> Figure 5b