



Fig. S1 Neuropathology of case 3. The neuropathologic study on brain sample from case 3 showed findings overlapping those found in case 1 and 4. Severe neuronal loss and spongiform changes (**a**: frontal cortex, Haematoxylin-Eosin) associated with astrogliosis (**b**: frontal cortex, GFAP immunostaining) were observed in cerebral cortex. The pattern of PrP^{Sc} deposition was the same of cases 1 and 4, and consisted of diffuse, synaptic-like immunoreactivity (**c**: 3F4 immunostaining, frontal cortex). Similar changes were found in cerebellum: loss of Purkinje cells and spongiosis in the molecular layer (**d**: Haematoxylin-Eosin), diffuse astrogliosis in the granular layer (**e**: GFAP immunostaining) and finely granular PrP deposits in the molecular layer (**f**: 3F4 immunostaining). As in the other cases carrying the V189I mutation, coarse spots of PrP immunostaining were evident in the granular layer (**f**: 3F4 immunostaining).

Scale bars: in **(a)** = 100 μm (**a**, **b**, **d** and **f** are the same magnification); in **(c)** = 50 μm (**c** and **e** are the same magnification).