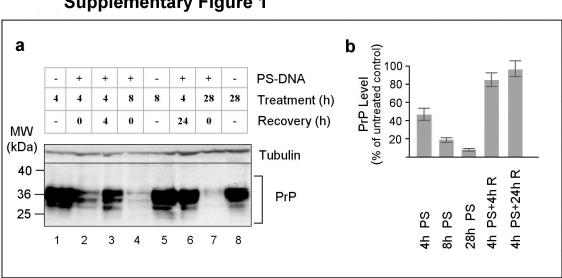
## SUPPLEMENTARY FIGURE LEGENDS

<u>Supplementary fig. 1.</u> PrP reduction by PS-DNA is transient. (a) Western blot analysis of N2a cells exposed to PS-DNA followed by recovery periods. Untreated N2a cells were harvested after 4, 8 and 28 hours (lanes 1, 5, and 8 respectively). (b) Densitometric quantification of Western blot analyses. (n=3 independent studies, p=0.04)

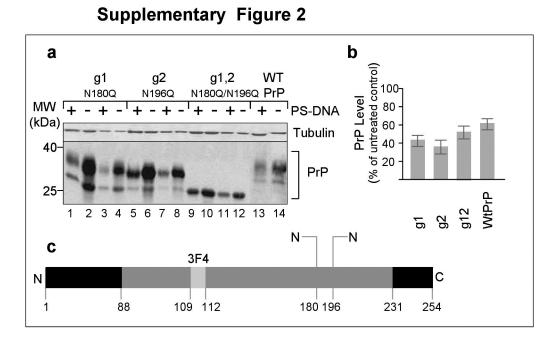
<u>Supplementary fig. 2.</u> PrP glycosylation has no effect on PS-DNA induced down-regulation. (a) Western blot analysis of N2a cells stably transfected with the three indicated PrP plasmid constructs differing in their glycosilation level. Transfected PrP was detected using the 3F4 monoclonal antibody, and the endogenous mouse PrP was detected using the D13 antibody. (b) Densitometric quantification of Western blot analyses. (c) Schematic representation of point mutations examined (n=3 independent studies, p=0.01).

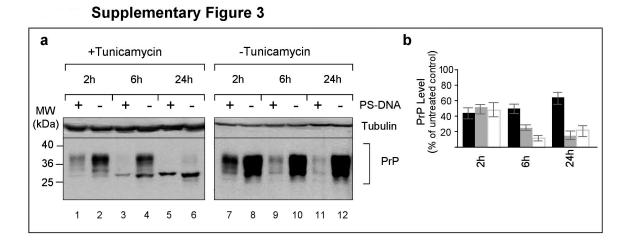
<u>Supplementary fig. 3.</u> PS-DNA treatment results in reduction of existing as well as newly synthesized PrP. (a) Western blot analysis of N2a cells treated with or without 1.5 mg/ml tunicamycin for the indicated times and PS-DNA. PrP was detected using the D13 antibody. (b) Densitometric quantification of Western blot analyses. Black bars represent the percentage of non-glycosilated PrP, containing mostly the newly synthesized PrP (3a, lower band in lane 1, 3, and 5; compared to lanes 2, 4, and 6 respectively). Gray bars represent the percentage of PrP in cells that were not treated with tunicamycin but were exposed to PS-DNA (3a, lanes 7, 9, and 11 as a percentage of lanes 8, 10, and 12 respectively). White bars represent the percentage of existing (fully glycosylated) PrP after exposure to PS-DNA (n=3 independent studies, p=0.04).

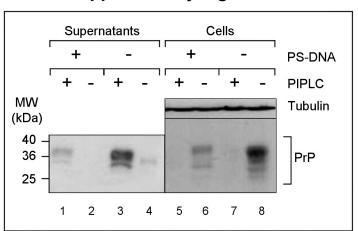
<u>Supplementary fig. 4.</u> Membrane-anchored PrP is down-regulateded in response to PS-DNA treatment. Western blot analysis of media or cellular fractions of N2a cultures exposed to PS-DNA for 72 hours (Lanes 1, 2, 5 and 6) and treated with 200mM PIPLC for 6 hours. The media of the cultures were TCA precipitated (Lanes 1-4). PrP was detected using the D13 antibody (n=3 independent studies, p=0.001).



Supplementary Figure 1







## Supplementary Figure 4