SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1. FKBP51 and SUMO2/3 are expressed in mouse hippocampus. (**a**) Brain cryosections were immunostained with anti-FKBP51 (green) and monoclonal anti-SUMO2/3 (red) antibodies. (**b**) Brain cryosections were immunostained with anti-FKBP51 or anti-NeuN (green) and anti-SUMO2/3 (red) antibodies. DAPI (blue) was used for nuclei staining.

Supplementary Figure 2. SUMO conjugation to FKBP51 does not alter protein half-life and is critical for its inhibitory effect on GR transcriptional activity. (a) HEK293T cells were transfected with TAT4-luc and GR plasmids, and with or without wt, K422R or 2KR FKBP51, and stimulated with Dex 1 nM or vehicle -B- for 8 h. Results are expressed as mean ±SEM (n=4). Protein levels were analyzed by western blotting. **(b)** HEK293T cells were transfected with wt or K422R FKBP51 plasmids, and treated with CHX (50 μg/ml) for the indicated time periods. Lysates were analyzed by western blotting using the indicated antibodies. FKBP51 protein levels were analyzed by densitometry using GAPDH as control. *** $p<0.001$.

Supplementary Figure 3. FKBP51 SUMOylation regulates Dex-induced expression of the endogenous target genes SGK1 and GILZ. HT22 cells transfected with GR plasmids with or without wt or K422R FKBP51 were stimulated with Dex 1 nM or vehicle -B- for 8 h, and SGK1 and GILZ mRNA levels were analyzed. Results are expressed as mean ±SEM (n=3).* $p<0.05$, ** $p<0.01$, *** $p<0.001$

Supplementary Figure 4. Mutation of K422 does not modify FKBP51 activity on NF-κB signaling. (**a**) HEK293T cells transfected with κB-luc, and with or without wt or K422R

FKBP51, were stimulated with PMA (50ng/ml) or vehicle for 8 h. Results, as folds of PMA stimulation, are expressed as mean ±SEM (n=3). (**b**) Lysates from HEK293T cells transfected with the indicated plasmids were immunoprecipitated with anti-FLAG antibody and analyzed by western blotting using the indicated antibodies. * $p<0.05$

Supplementary Figure 5. SUMO conjugation to FKBP51 regulates GR nuclear translocation. HT22 cells transfected with YFP-GR plasmid with or without wt or K422R FKBP51 were stimulated with Dex 1 μM. Results are expressed as mean ±SEM of one representative experiment (n=3).