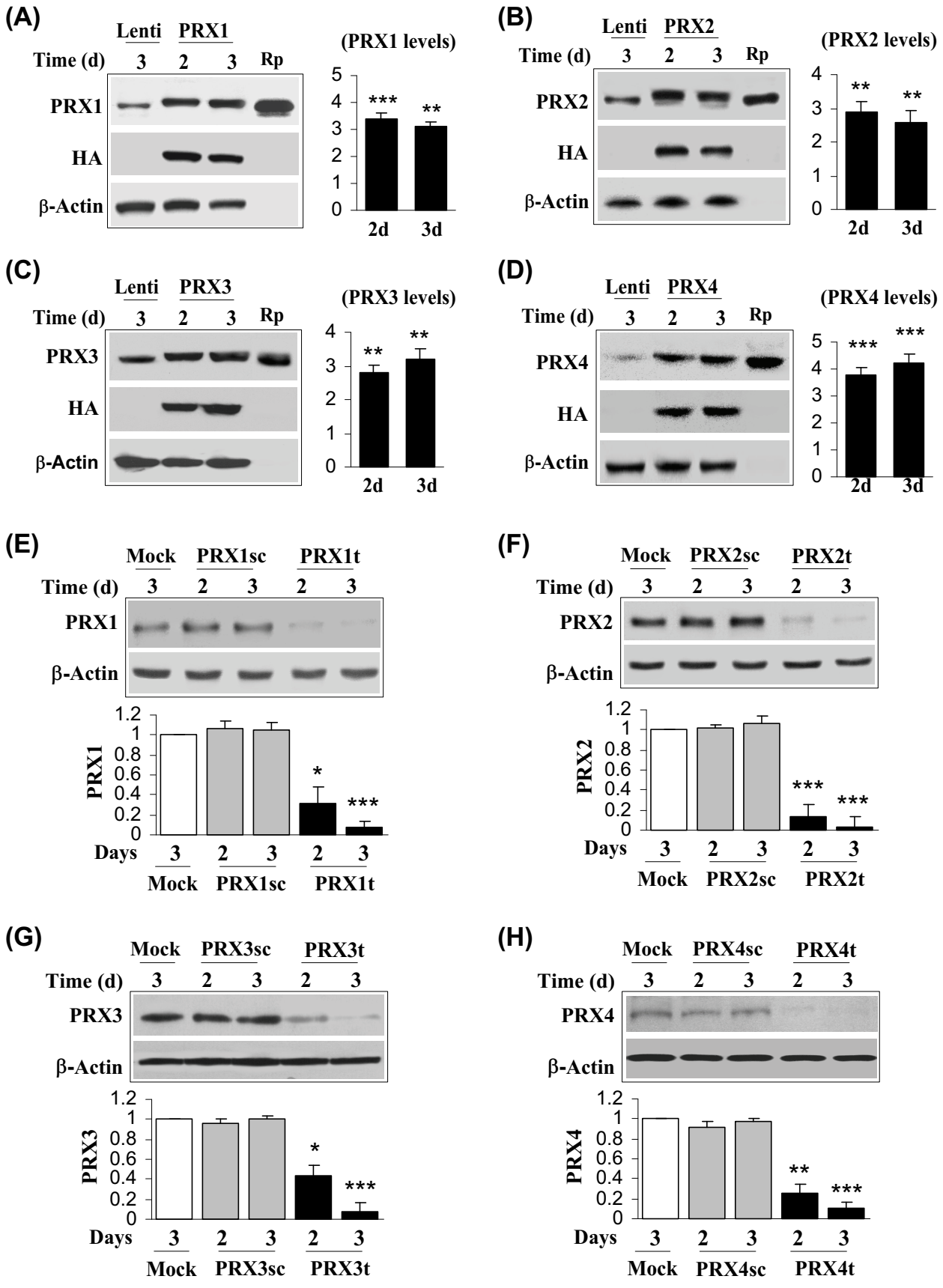
Supplemental Fig. 1. Verification of lentiviral vector-mediated manipulation of PRX expression in MN9D cells. (A-D) Lentivirus-mediated over-expression of PRXs. Neuronal differentiated MN9D cells were infected for 2 or 3 days with either the empty lentiviral vector or the vector containing cDNA of human PRX1, PRX2, PRX3, or PRX4, and then subjected to immunoblotting against the HA tag and the individual PRX. **p<0.01; ***p<0.001 *vs.* empty vector controls; data are from 3 independent experiments. In each PRX immunoblot, the purified recombinant PRX protein (Rp) was used as the positive control. (**E-H**) Lentivirus-mediated knockdown of PRX expression. Neuronal differentiated MN9D cells were infected for 2 or 3 days with lentiviral vectors containing shRNA targeting PRX1 (PRX1t), PRX2 (PRX2t), PRX3 (PRX3t), or PRX4 (PRX4t), or the scramble control sequence (PRXsc), and then subjected to immunoblotting against the individual PRX. *p<0.05; **p<0.01; ***p<0.001 *vs.* the mock control or PRXsc controls; data are from 3 independent experiments.

Supplemental Fig. 2. PRX2 inhibits the apoptotic profiles induced by 6-OHDA neurotoxicity in MN9D cells. (A-B) PRX2 over-expression attenuates 6-OHDA-induced apoptosis. Neuronal differentiated MN9D cells were infected for 3 days with Lenti-PRX2, the empty vector (Lenti), or Lenti-GFP, and then challenged with 6-OHDA (50 μM). Cells were fixed at 24 h after 6-OHDA exposure and subjected to nuclear staining with Hoechst 33258 and staining for *in situ* DNA fragmentation with TUNEL. The percentages of apoptotic nuclei (chromatin condensation/fragmentation) and TUNEL-positive cells are illustrated in (**A**) and (**B**), respectively. (**C-D**) PRX2 knockdown promotes 6-OHDA-induced apoptosis. MN9D cells were infected for 3 days with Lenti-PRX2t, Lenti-PRX2sc, or the empty vector (Lenti), and then challenged with 6-OHDA (50 μM). Cells were fixed at 24 h after 6-OHDA exposure and subjected to nuclear staining with Hoechst 33258 and staining for *in situ* DNA fragmentation with TUNEL. The percentages of apoptotic nuclei and TUNEL-positive cells are illustrated in (**C**) and (**D**), respectively. *p<0.05 *vs.* empty vector controls; data are from 3 independent experiments. (**E-G**) PRX2 over-expression does not inhibit staurosporine (STS)-induced apoptosis. Neuronal differentiated MN9D cells were infected for 3 days with Lenti-PRX2, the empty vector (Lenti), or Lenti-GFP, and then challenged with STS (3.0 μM). Cells were fixed at 24 h after STS exposure and subjected to cell viability assay or nuclear staining with Hoechst 33258 and staining for *in situ* DNA fragmentation with TUNEL. The percentages of cell viability (**E**), apoptotic nuclei (**F**) and TUNEL-positive cells (**G**) are quantified.

Supplemental Fig. 3. PRX2 over-expression confers long-term neuroprotection in the SNc of 6-OHDA-lesioned mice. Mouse SNc was infected for 21 days with empty lentiviral vector (Lenti), Lenti-GFP, or Lenti-PRX2, and then received striatal infusion of 6-OHDA (3.0 μg) or saline of the same volume. (**A**) Apomorphine-induced circling before 6-OHDA injection (Pre) or 8 weeks after the injections indicated is shown as the number of turns in the first 30 min after intraperitoneal injection of apomorphine. (**B**) Spontaneous turning using the corner test before 6-OHDA injection (Pre) or 8 weeks after the injections indicated. The mean numbers of right turns out of 10 trials/session are reported. (**C**) The numbers of TH-positive neurons in the left SNc (injected side) were counted using non-biased stereological methods 8 weeks after the injections indicated. *p<0.05; **p<0.01; ***p<0.001 *vs.* empty vector (Lenti) or Lenti-GFP controls; #p<0.05; ##p<0.01 between the indicated groups. n=10/group.

Supplemental Fig. 4. PRX2 expression levels determine the redox state of MN9D cells following 6-OHDA neurotoxicity. (**A**) Neuronal differentiated MN9D cells were infected for 3 days with Lenti-PRX2, Lenti-PRX2t, Lenti-PRX2sc, or the empty vector (Lenti), and then challenged with 6-OHDA (50 μM). At 2 h after 6-OHDA exposure, cells were incubated with CM-H_2DCFDA (10 μM), a relatively specific sensor for H_2O_2, at 37°C in the dark for 30 min**,** and subjected to flow cytometry measurement. A total of 10,000 cells were counted for each sample. The flow cytometry data presented are representative of 3 independent experiments with similar results and show the shift of DCF fluorescence intensity under various experimental conditions. The percentages of DCF fluorescence shift were calculated normalizing to the vehicle control (empty vector infection), and the mean values of shift are indicated in the upper-right corner. (**B-C**) PRX2 over-expression decreases DCF fluorescence after 6-OHDA exposure, whereas PRX2 knockdown increases DCF fluorescence. DCF fluorescence was measured at 2 and 6 h after 6-OHDA (50 μM) exposure on a fluorescence plate reader using 485 nm excitation and 530 nm emission. *p<0.05; **p<0.01 *vs.* non-transfected or empty vector control (**B**), or *vs.* empty vector control or Lenti-PRX2sc-infected cells (**C**); data are from 3 independent experiments.



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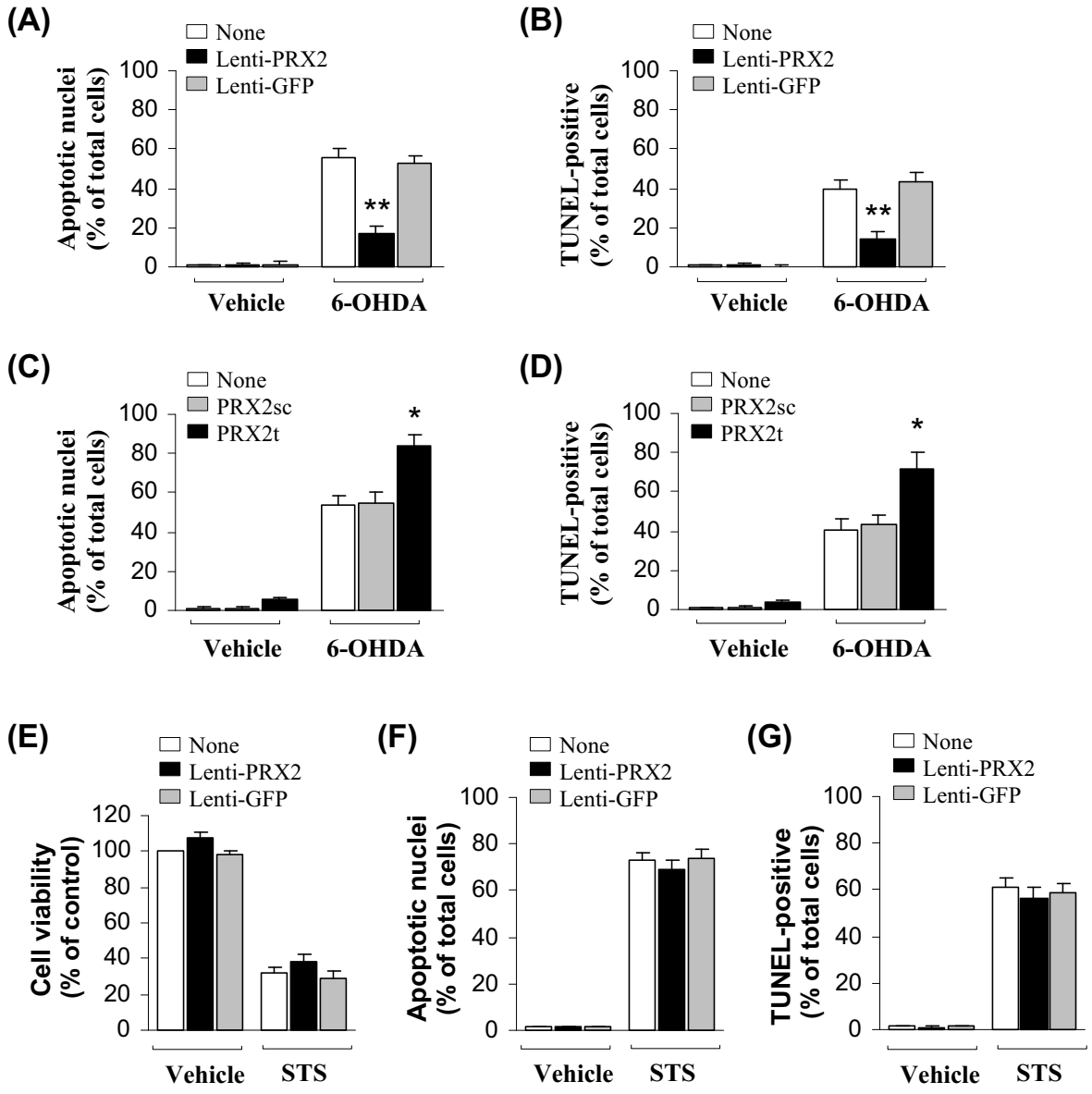

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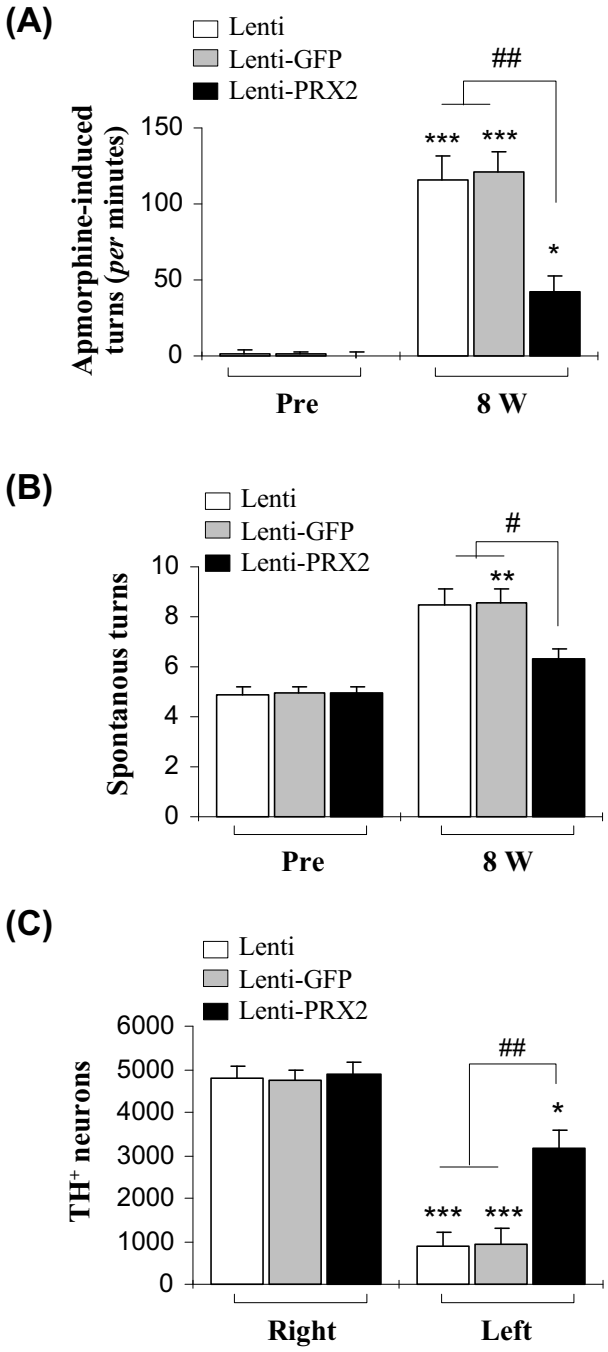

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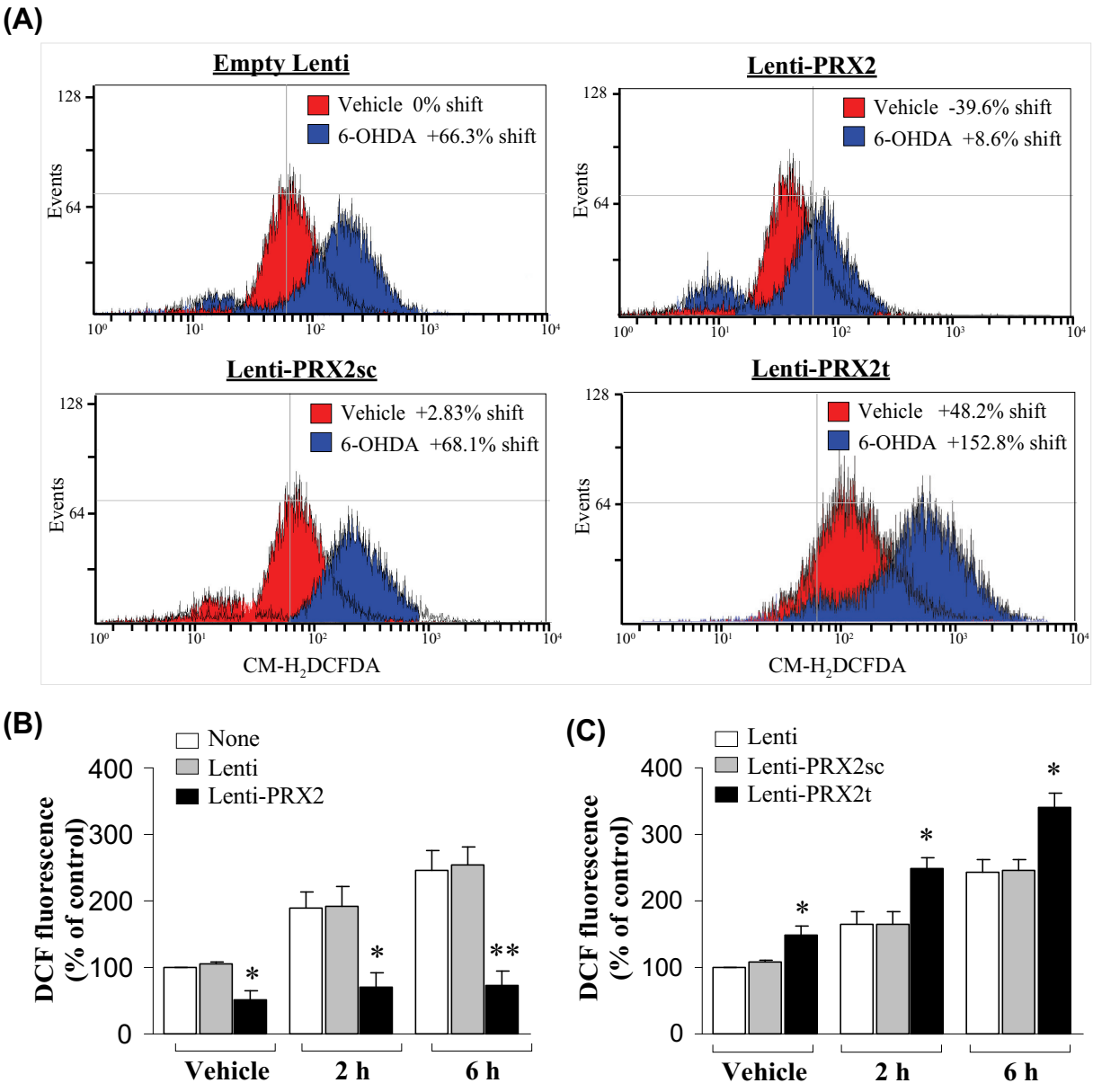

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