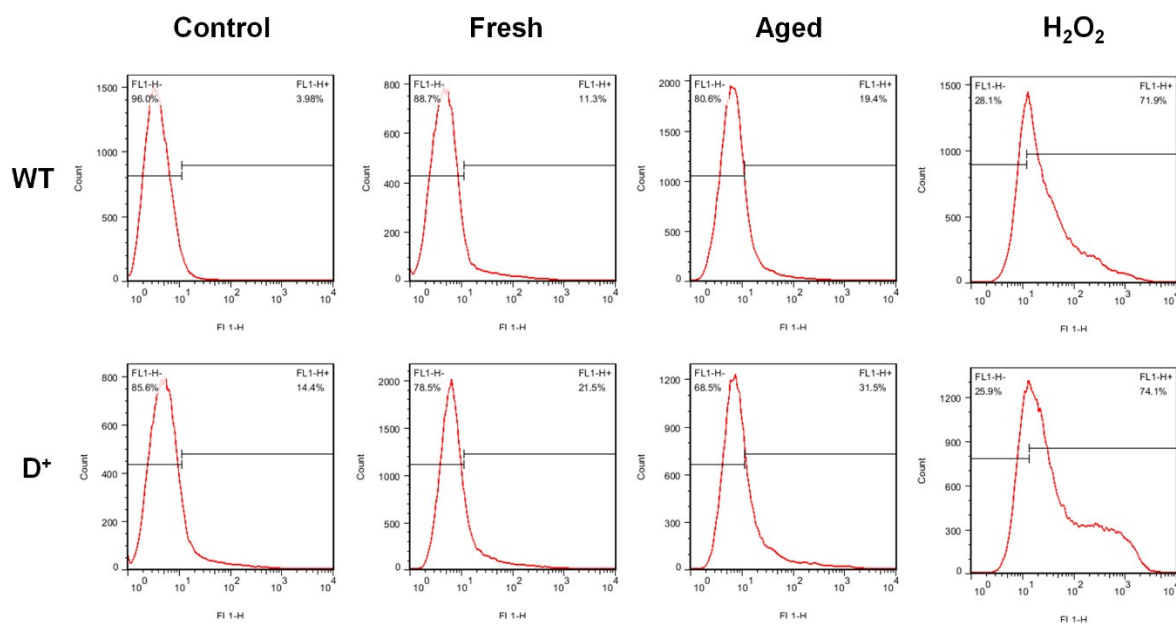
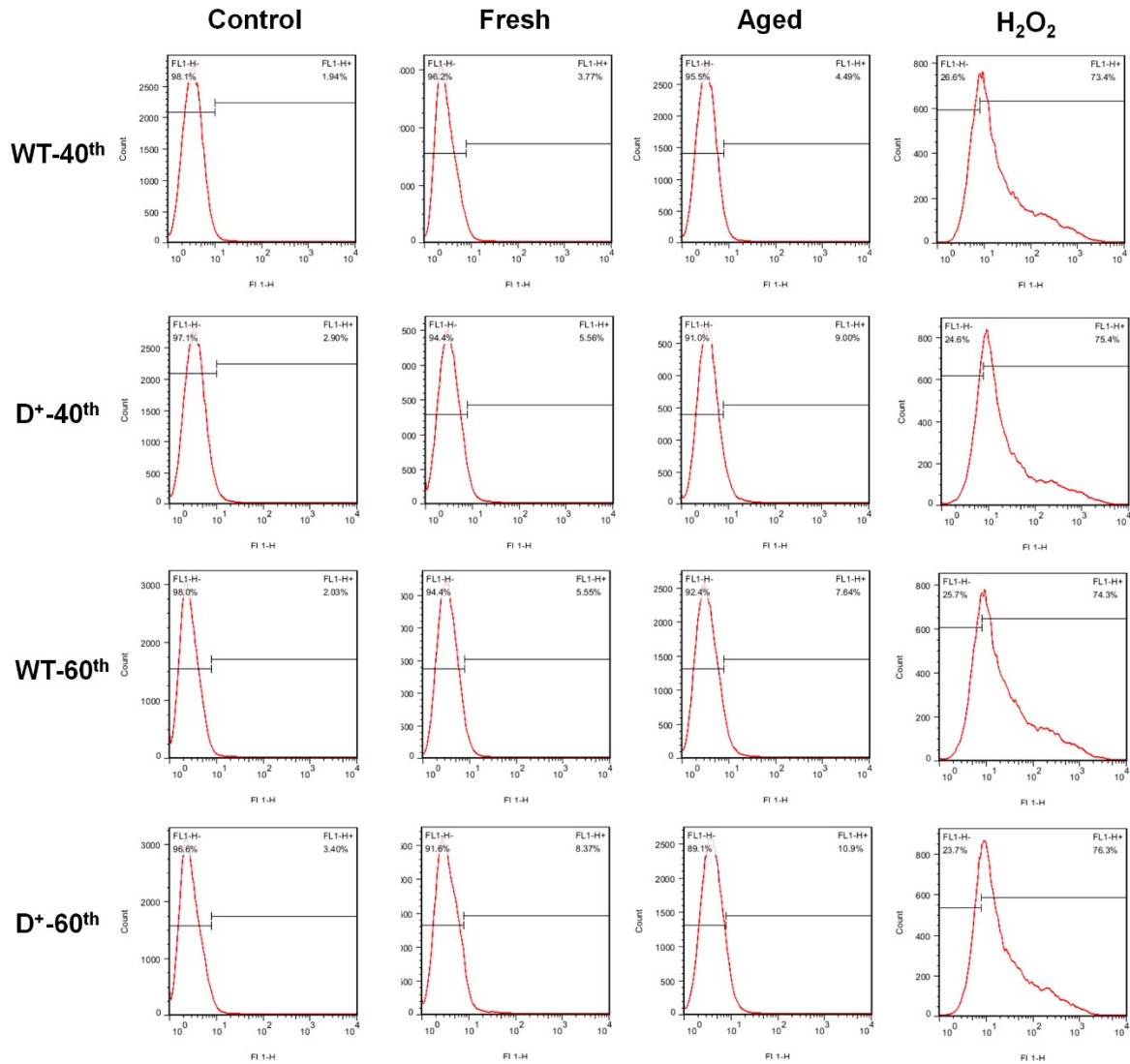


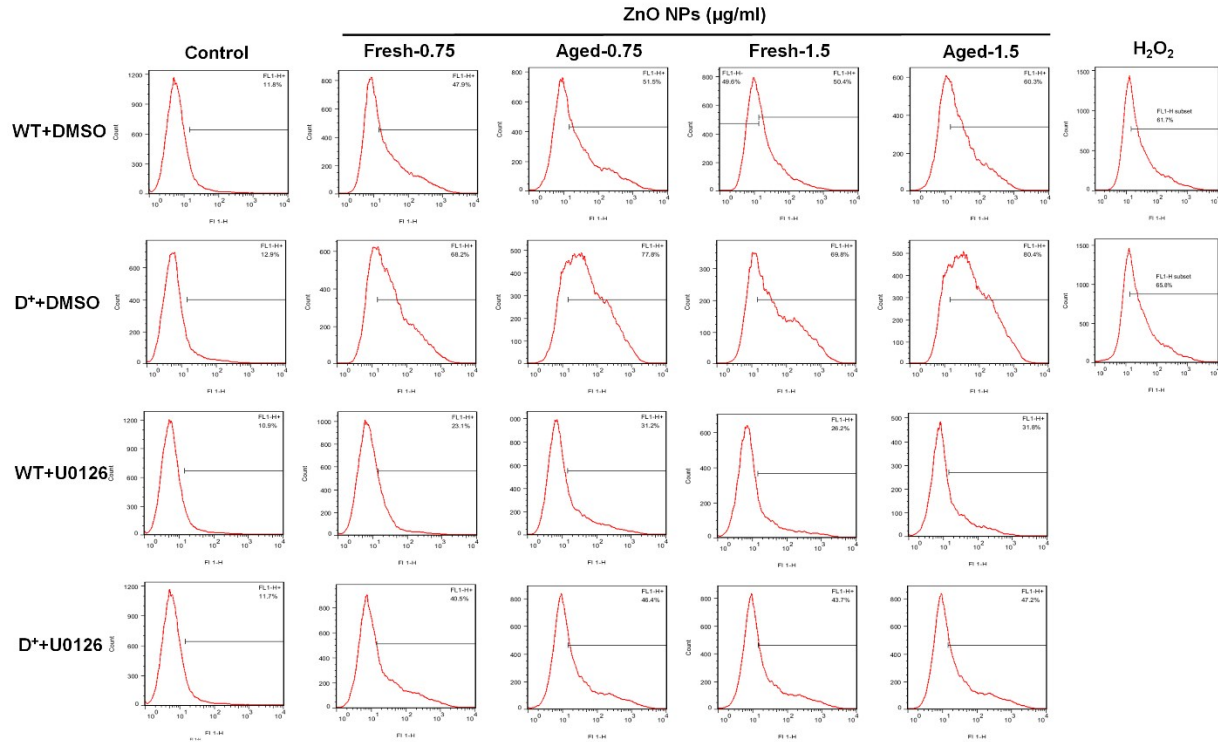
Supplemental data



S.1 Acute exposure to ZnO NPs induced ROS generation in MEF cells. WT and D⁺ MEF cells were treated with 10 µg/ml fresh or aged ZnO NPs for 12 h. Intracellular ROS was detected by flow cytometry as described in Methods. Note: Positive control: 0.1mM H₂O₂ for 15 mins.



S.2 Long-term exposure to low doses of ZnO NPs induced ROS generation in MEF cells. The percentage of intracellular ROS of WT and D⁺ MEF cells that were treated with 1.5 µg/ml fresh or aged ZnO NPs for 16 and 24 weeks. Intracellular ROS was detected by flow cytometry as described in Methods. Note: Positive control: 0.1mM H₂O₂ for 15 mins.



S.3 Inhibition of p-Erk activation decreased the percentage of ROS in ZnO NP-induced MEF cells. MEF cells were pretreated with 20 µM U0126 or DMSO for 6 hours and then treated with ZnO NPs for 12 hours. The percentage of ROS was measured by flow cytometry assay as described in Methods. Note: Positive control: 0.1mM H₂O₂ for 15 mins.