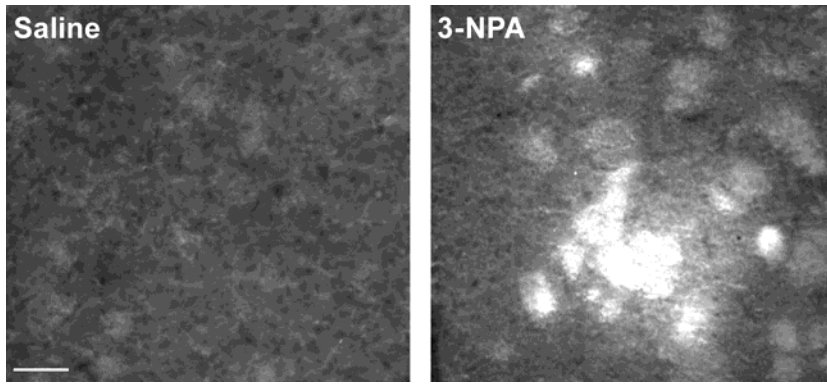
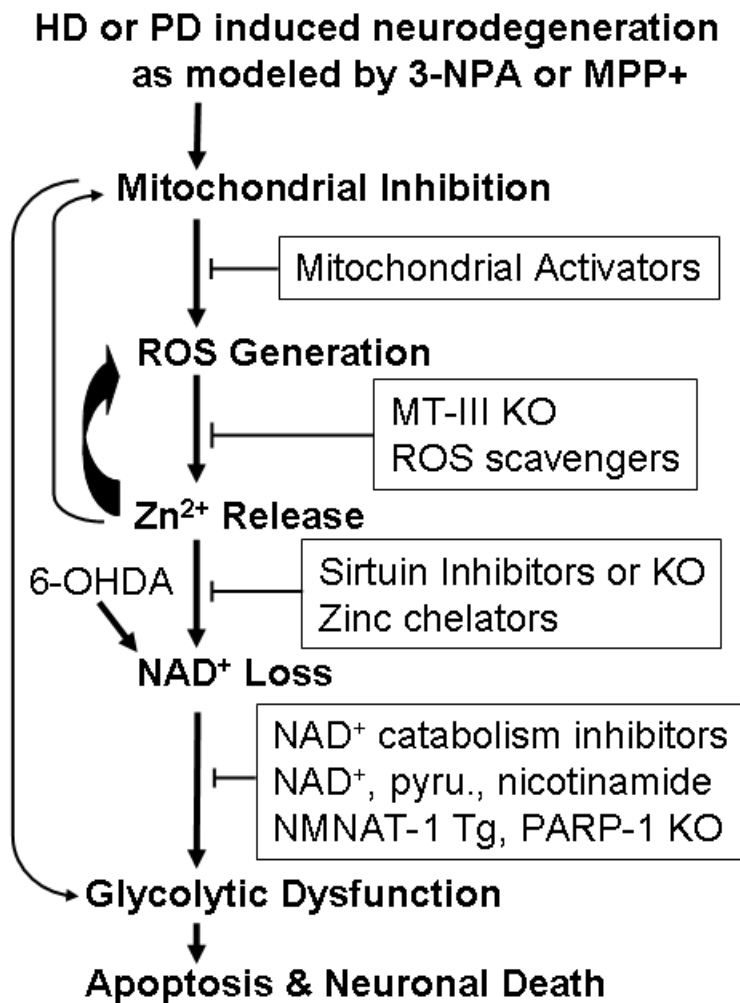


Supplemental Figure 1. Neuronal loss in PNC cultures from *Wld^S* mice induced by 3-NPA, 6-OHDA, and MPP⁺ was attenuated; Zn²⁺ therapeutics further attenuated toxicity.

A) Near-pure cortical neuronal cultures (PNC) were made from ZnT3 or MT3 knockout mice, *Wld^S* mice, and C57/Bl6J controls and exposed as indicated. The percentage of neuronal death after 24-48 hours is plotted. B) PNC cultures from *Wld^S* mice were exposed as indicated to Zn²⁺ therapeutics. The percentage of neuronal death after 24-48 hours is plotted (mean ± SEM, n = 6-9 cultures per condition). *, #, or & indicates difference from neurotoxin exposure alone at *P* < 0.05 by one-way ANOVA followed by a Bonferroni test.



Supplemental Figure 2. *In vivo* intraperitoneal injection of 3-NPA induces zinc staining in the striatum. Mice were given 7 injections of 50 mg/kg of 3-NPA (two injections/day), and the brains were immediately removed, frozen, sectioned, dried, and stained with 5 μ M Zinpyr-1 to determine if there was an increase in zinc accumulation. Epifluorescence photomicrographs were taken at equivalent exposures for control and 3-NPA-exposed mice at 485/530.



Supplemental Figure 3. Model of neurotoxicity induced by different mitochondrial inhibitors. Neurons exposed to Huntington's (HD) or Parkinson's disease (PD) conditions as modeled by 3-NPA or MPP⁺, cause mitochondrial inhibition and ROS generation, causing Zn²⁺ release, NAD⁺ loss, and glycolytic inhibition resulting in neuronal death. Treatments or genetics shown in the boxes are potentially therapeutic by inhibiting progressive steps as shown in this model.