**Supplemental Figure 1**

Immunohistochemistry of HIV-TAT protein *in vivo* and *in vitro*. Although no staining for HIV-TAT protein was observed in control retina, the intraperitoneal injection of cell permeable HIV-TAT BH4 protein (8$\mu$g/g) showed diffuse localization of this protein into retinal cells *in vivo* (A to C). The high-magnification image shows cytosolic localization of the cell permeable protein in photoreceptors (C). The primary retinal cell culture was incubated with HIV-TAT BH4 protein or control vehicle. Control culture showed no staining for HIV-TAT protein, however, HIV-TAT BH4 coculture showed incorporation of the protein into most cells *in vitro* (D, E).

**Supplemental Figure 2**

HIV-TAT BH4 protein preserves mitochondrial potential in retinal cells. To examine the protective effect of HIV-TAT BH4 protein, the primary retinal cell cultures were incubated with HIV-TAT BH4 protein and MitoTracker CMTMRos. CMTMRos is a sensitive dye for mitochondrial outer membrane permeabilization (MOMP). After starvation or coculture with macrophages, CMTMRos positive cells decreased (B, D)

compared to control (A). HIV-TAT BH4 protein preserved mitochondrial potential in starvation or coculture with macrophages (C, E) The results were shown in F (n=10 per group, ***$p$*<0.01).

**Supplemental Figure 3**

HIV-TAT BH4 protein has an additive neuroprotective effect on hypomorphic mutant mice. Intraperitoneal injection of HIV-TAT protein (8$\mu$g/g) decreased activation of caspase-9 as well as TUNEL in Hq/Y mice after 3 days of RD. The results were shown in E. (n=5, **<0.01).

**Supplemental Figure 4**

Immunoblot analysis of mitochondrial and cytosolic fractions for inner membrane components. The cytosolic and mitochondrial fraction were collected from primary retinal cell culture and were stained for inner membrane protein, translocase of the inner membrane (Tim 23). The mitochondria fraction shows positive staining for Tim23, in contrast the cytosolic fraction showed no staining, showing the cellular fractionation

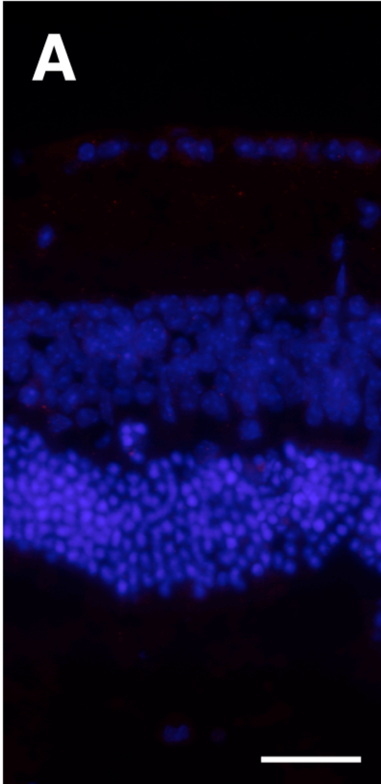
properly worked in the experiments.

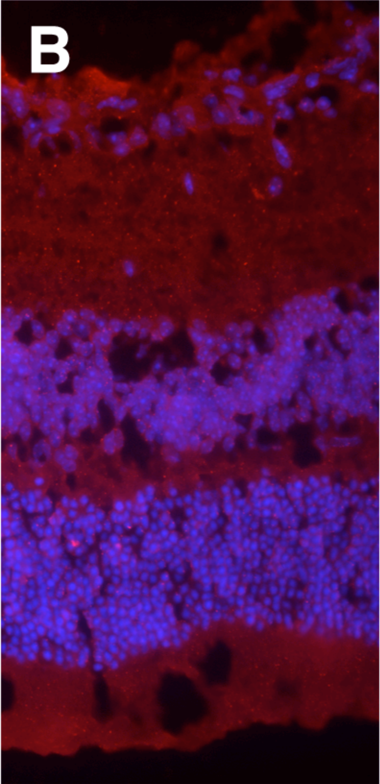
**Supplemental Figure 5**

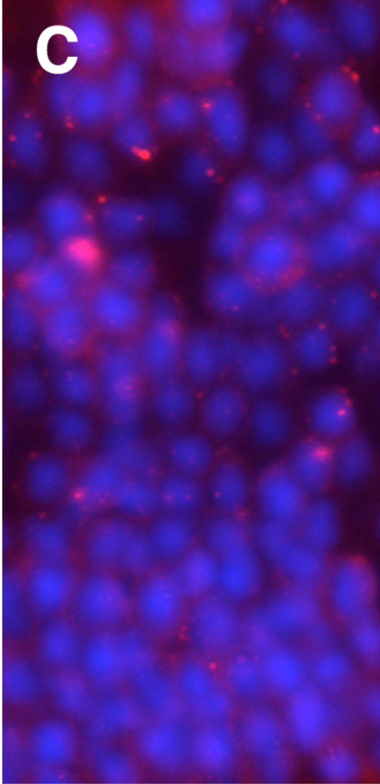
CD4+ / CD8+T cells in circulating blood with / without HIV protease inhibitors. To quantify the number of CD4+ / CD8+ T cells in the blood, we performed flow cytometry (A). The ratio of circulating CD4+ / CD8+ cells in the blood did not change significantly during 3 days of the experimental period with/without RD or PIs treatment (A to C).

# Supplemental Figure 1

*in vivo*



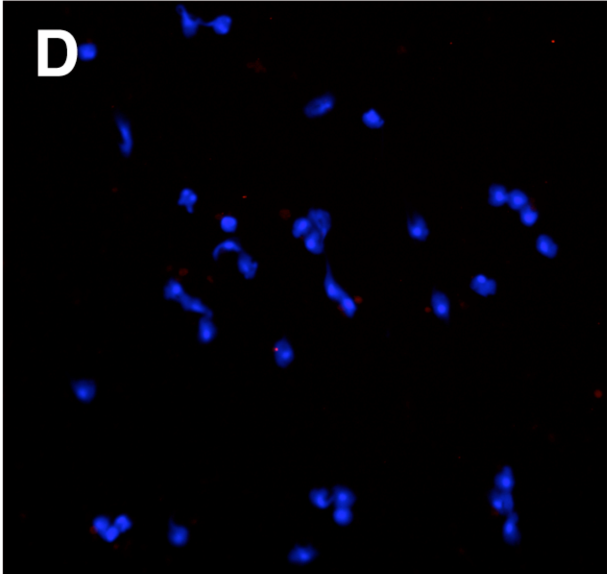



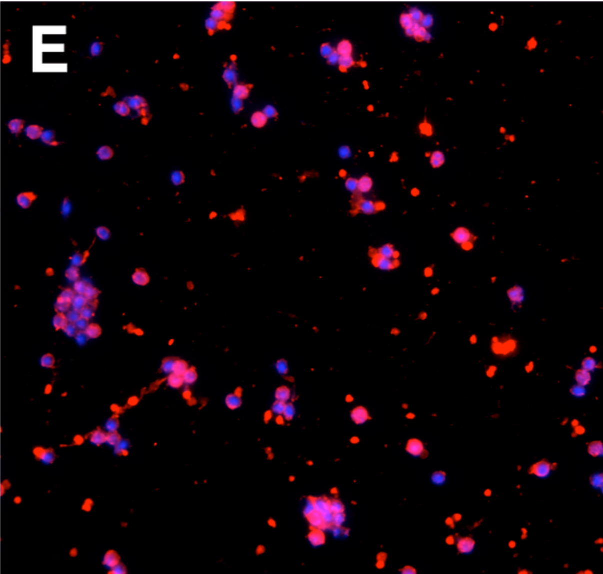




control

HIV-TAT BH4

*in vitro*

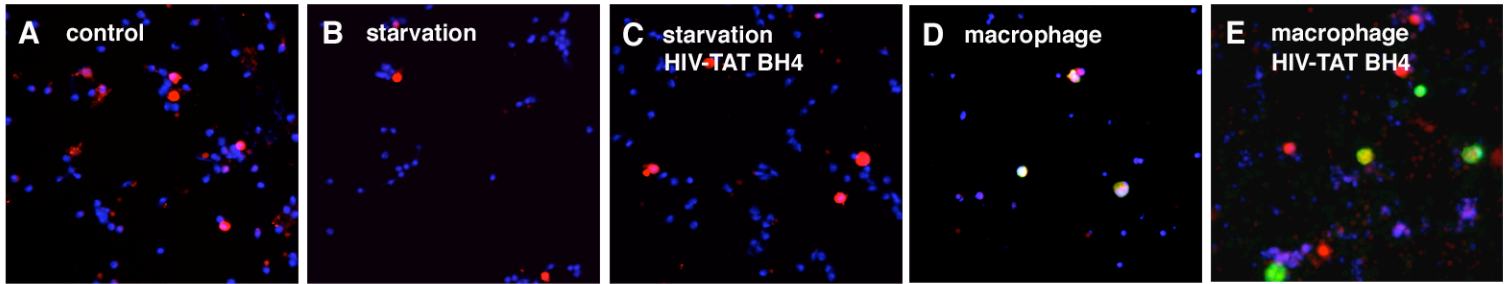


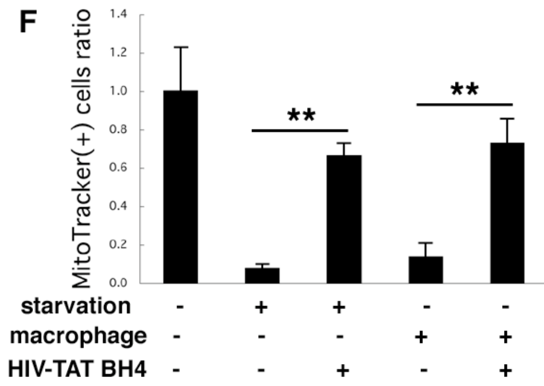




control

HIV-TAT BH4

## Supplemental Figure 2



## Supplemental Figure 3

A B

AIF

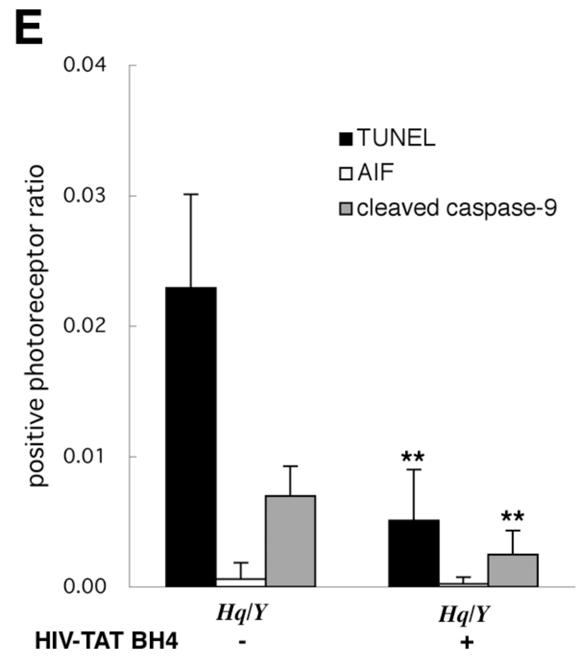
C D

cleaved caspase-9

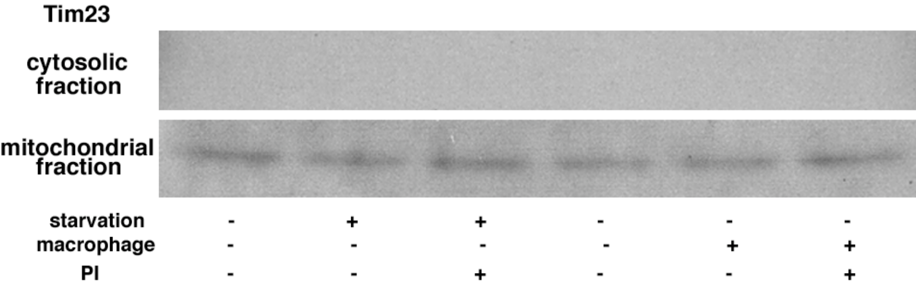
Hq/Y
vehicle control

Hq/Y
HIV-TAT BH4

E



**Supplemental Figure 4**



## Supplemental Figure 5