

Supplementary Figure Legends

Supplementary Figure 1 - Quantitative PCR. A scatterplot of human *ND4* relative to endogenous mouse *ND4* in the heart, liver, brain, skeletal muscle, spinal cord and lung.

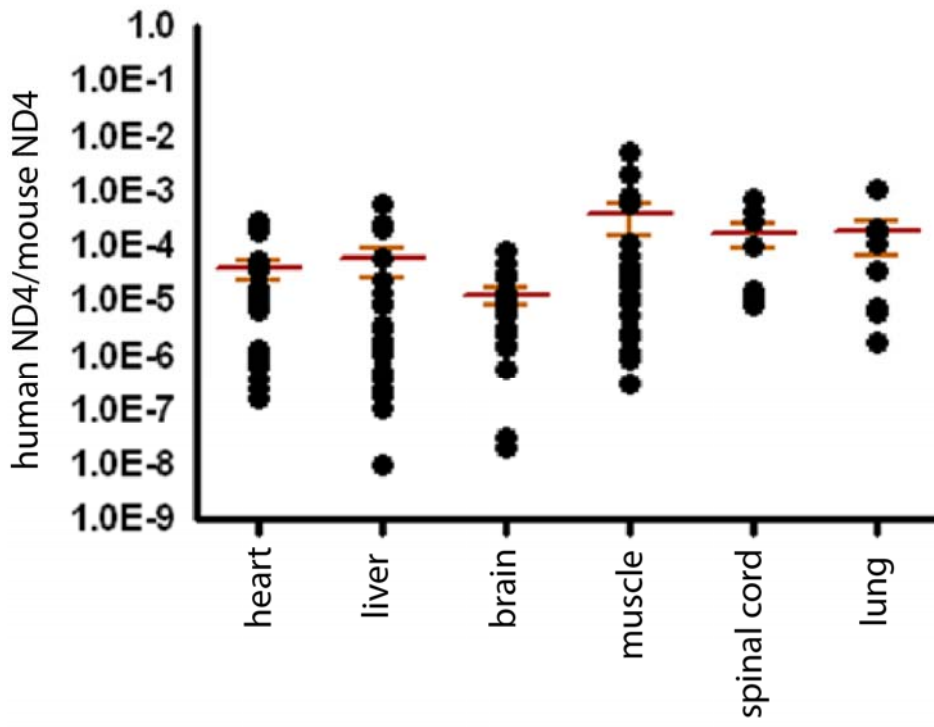
Supplementary Figure 2- Immunofluorescence of ocular transgene expression. Confocal micrographs of longitudinal sections of transgenic mice retinas with perinuclear mCherry (A) and mutND4FLAG (B), VDAC/porin (C-D), mCherry and porin (E) mutND4FLAG and porin (F), Thy1.2 labeled RGCs (G-H). Scale bar = 50 μ m, RGC = retinal ganglion cell layer, INL = inner nuclear layer

Supplementary Figure 3 - Immunofluorescence of extraocular transgene expression. Confocal micrographs of mCherry, Thy1.2 and porin immunolabeling of transgenic mouse optic nerve (A), brain (B), heart (C), liver (D) and skeletal muscle (E). Scale bar = 80 μ m

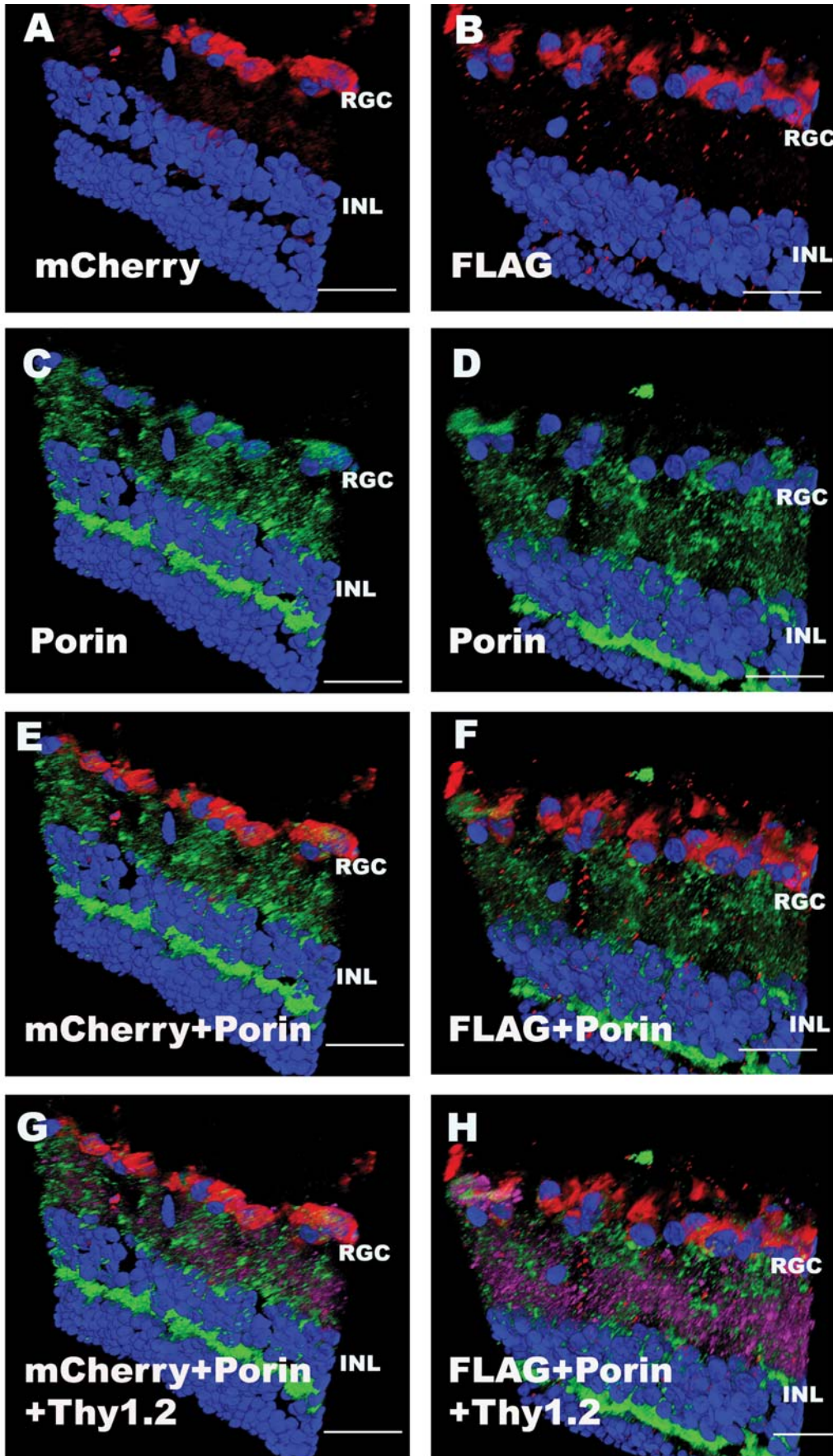
Supplementary Figure 4 - Ultrastructure of extraocular tissues. Transmission electron micrograph of the brain (A), heart (B), and skeletal muscle (C) of transgenic mutND4 mice.

Supplementary Figure 5 - Oxidative phosphorylation and stress. Confocal micrographs of mutant ND4 transgenic mice vitreally injected with 2',7'-dichlorofluorescein diacetate (DCFDA) shows green fluorescence in the presence of endogenous reactive oxygen species (A-B) and a normal control (C). Endogenous mCherry autofluorescence in transgenic mice (D-E) and absence in a control (F). Merged panels of DCFDA and mCherry (G-H). A bar plot of cells in the RGC layer positive for DCFDA (I). Bar plots of complex I activity (J) and the rate of ATP synthesis in transgenic mice relative to control optic nerves (K). Scale bar = 20 μ m, RGC = retinal ganglion cell layer, IPL = inner plexiform layer, INL = inner nuclear layer

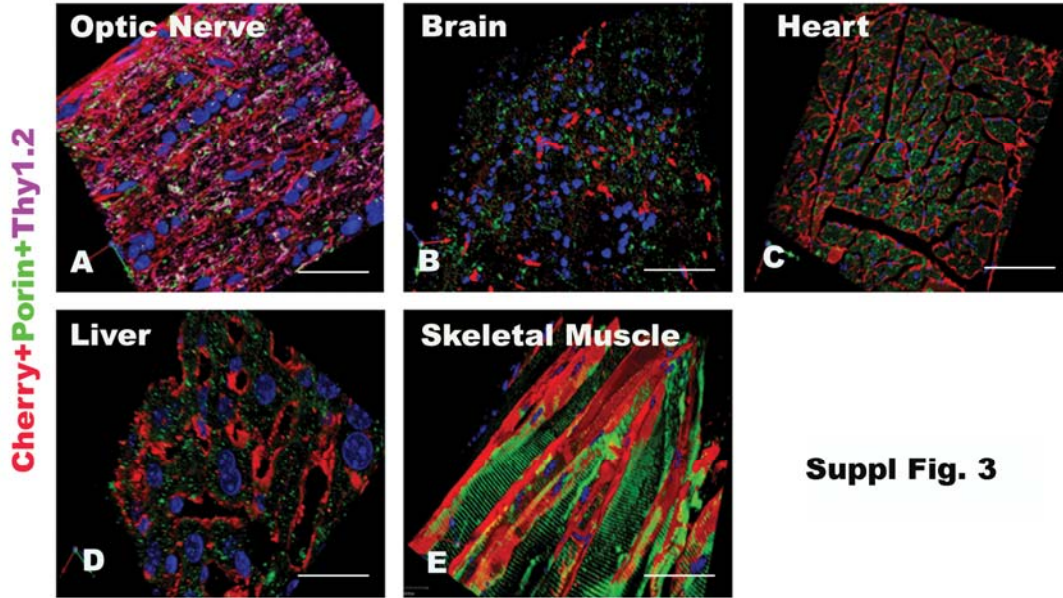
Supplementary Figure 6 – MRI. MRI of the brains of transgenic mutant ND4 mice (A, B, C) and normal mice (D, E, F).

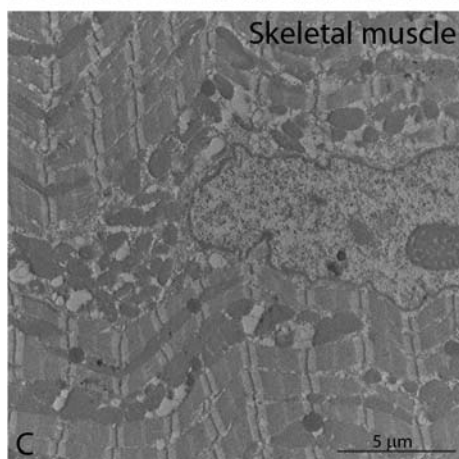
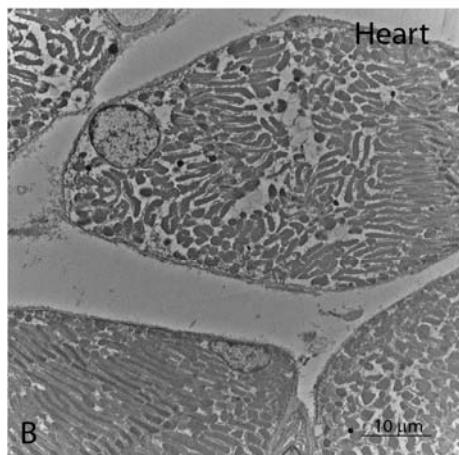
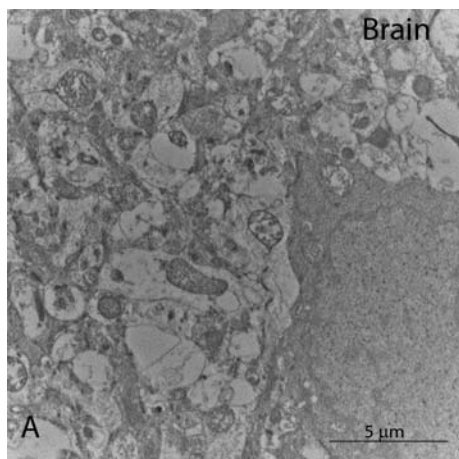


Supplementary Fig. 1

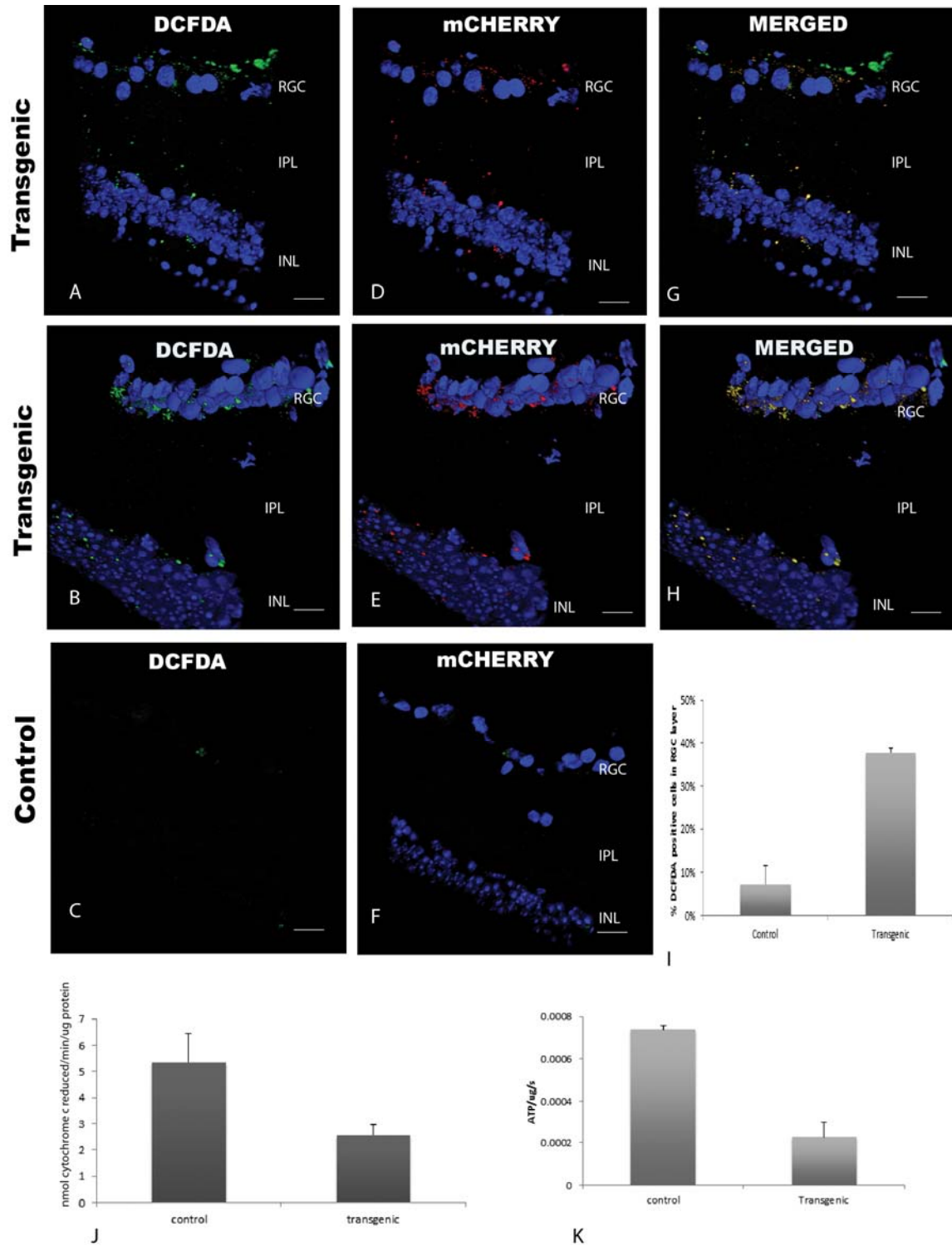


Suppl Fig.2

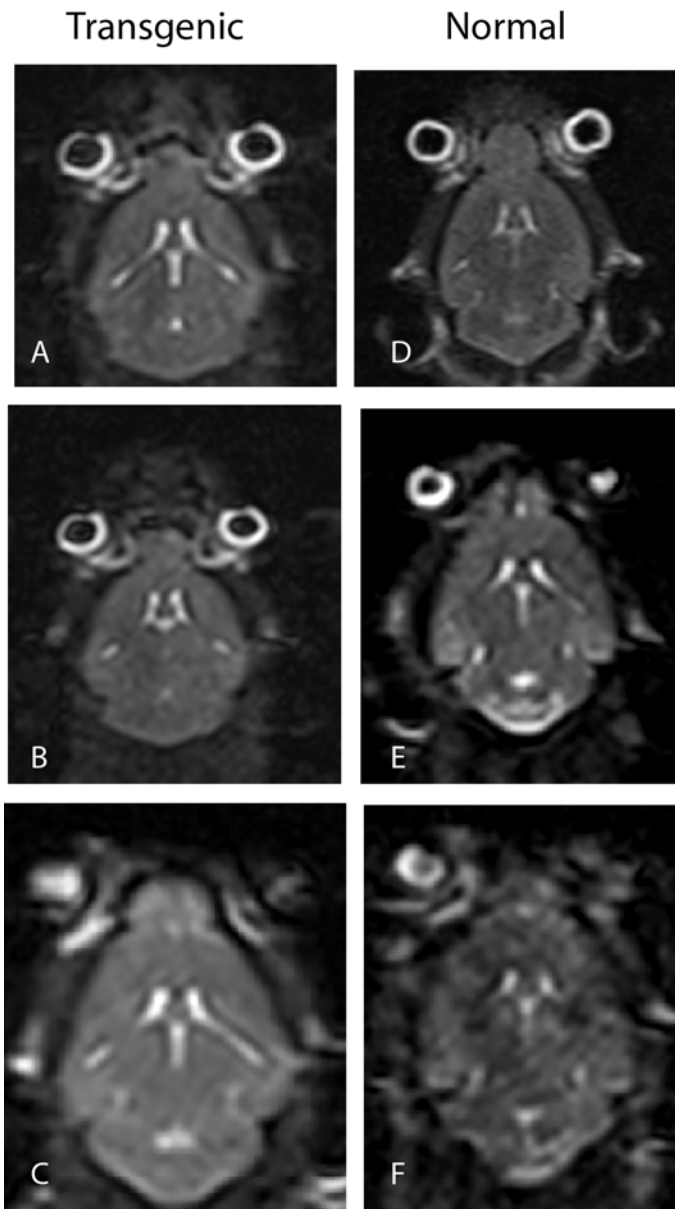




Suppl Fig. 4



Supple Fig. 5



Supplementary Figure 6