Supplemental Figure 1. Increased reactive aldehydes and reactive oxygen species in doxycycline treated $Sod2^{flox/flox} VMD2cre$ mice. (A and B) $Rosa26$-lacZ mice and $Rosa26$-$VMD2$-cre mice were treated with doxycycline as neonates, and at one month of age eyes were prepared for cryosectioning. Frozen sections were reacted with goat antibody to β-galactosidase (Santa Cruz) which was detected using fluorescently-labeled anti-goat antiserum. (C) Western blot of RPE protein extracts separated on a 12% SDS polyacrylamide gel and probed with antibody to tubulin and to MnSOD. This was the antibody used to decorate RPE flat mounts shown in Fig. 2. (D and E) $Sod2^{flox/flox}$ and $Sod2^{flox/flox} VMD2cre$ mice were treated with doxycycline as neonates and one month later (6 weeks of age) they were sacrificed and flat mounts of the RPE were prepared. They were stained for actin filaments using fluorescently tagged phalloidin (red) and for 4-hydroxy-2-nonenal (green). Mice were given intraperitoneal injections of dyhydroethidium (DHE) and euthanized after 18 hours. Superoxide oxidizes DHE to ethidium, which generates a red fluorescent signal. Tissues were prepared for cryosectioning and fluorescence microscopy (blue: DAPI, red: DHE). (F) $Sod2^{flox/flox}$ mouse without doxycycline treatment. (G) $Sod2^{flox/flox} VMD2cre$ mouse with doxycycline treatment.
Supplemental Figure 2. Increased deposition of CD46 and C5 following deletion of Sod2 in the RPE. RPE/choroid dissected from doxycycline treated Sod2\textsuperscript{flo/flo} VMD2\textsuperscript{cre} mice and from Sod2\textsuperscript{flo/flo} mice without doxycycline treatment were prepared for cyrosectioning from mice sacrificed at 4 months (CD46) or at 9 months of age (C5). CD46 and C5 were detected by immunohistochemistry and were elevated in RPE of mice in which Sod2 had been deleted.
Supplemental Fig. 3 Degeneration of photoreceptors in doxycycline treated Sod2flox/flox VMD2cre mice. (A) Average ONL thickness at 9 months measured at 4 locations relative to the optic nerve head in 8 Sod2flox/flox VMD2cre mice treated with doxycycline (+Dox) or not exposed to doxycycline as neonates (-Dox). (B) Representative SD-OCT b-scans from doxycycline treated and naïve Sod2flox/flox VMD2cre mice. (C) ERG a-wave and b-wave amplitudes in doxycycline induced and uninduced Sod2flox/flox VMD2cre mice at 9 months (n=8; **=p<0.01). (D) Average a-wave and b-wave amplitudes at 0 dB (2.68 cd/s/m²) in eight 9-month old mice (**=p<0.01 relative to C57Bl/6J mice; ##=p<0.01 relative to uninduced Sod2flox/flox VMD2cre mice.)
Supplemental Figure 4. Longer outer segments in doxycycline induced Sod2^floxflo^VM2Cre mice. The contour lengths of rod outer segments was analyzed from the center optic nerve head to the ora serata in both inferior and superior hemispheres. Five
locations in the inferior retina and five locations of superior area separated by 400\(\mu\)m were measured in 40X light micrographs of longitudinal plastic sections from mice sacrificed at 1, 4 and 9 months of age. (A) Average outer segment lengths for inferior hemisphere, superior hemisphere and overall retina; (B) “Spidergram” indicating the thickness at each location measured. \((n=4\) at each time point; \(* p<0.05\), \(** p<0.01\), 1 month time point compared with the 9 month time point. \#, \#\# p<0.05\), 4 month time point compared with the 9 month time point. \(+ p<0.05\), \;++p<0.01\), 4 month time point compared with 9 month time point).
Supplemental Fig. 5. Vascular leakage or telangiectasia apparent at nine months but not at three months after deletion of Sod2. A fundus micrograph was made and fluorescein angiography was performed in a doxycycline induced Sod2\textsuperscript{lox/lox} VMD2\textsuperscript{cre} mouse at (A) three months and at (B) nine months of age in doxycycline induced Sod2\textsuperscript{lox/lox} VMD2\textsuperscript{cre} mice. We noted...
a vascular leak (upper right at 10 minutes and around the optic nerve head after 5 minutes) and increased bifurcation of deeper vessels in the older animal. These features were never seen in younger mice.

Supp. Fig. 6

Supplemental Fig. 6. Signs of geographic atrophy in \( Sod2^{\text{flo}x/\text{flo}x} VMD2\text{cre} \) six and nine months after doxycycline induction. These are light micrographs of plastic sections taken at original magnification of 40X (top and middle) or 20X (bottom). Arrows demarcate the border between atrophic RPE and intact RPE (to the tight of the arrows as shown). In some eyes amorphous deposits were seen beneath the photoreceptor layer (top). In other eyes, inflammatory cells had invaded the outer retina (middle). By nine, months all layers of the retina had deteriorated in areas of atrophic RPE in some eyes (bottom).
Supplemental Figure 7. Basal laminar deposits and subretinal hemorrhage following Sod2 deletion. (A) Electron micrographs from a doxycycline treated Sod2$^{floxflox}$VMD2Cre mice at 7 months of age. BlamD, basal laminar deposits; asterisk, lipofuscin filled vesicles; arrowheads, immature melanosomes. (B) Red blood cells accumulating between the photoreceptors and RPE in a 9-month old doxycycline-induced Sod2$^{floxflox}$VMD2cre mouse.