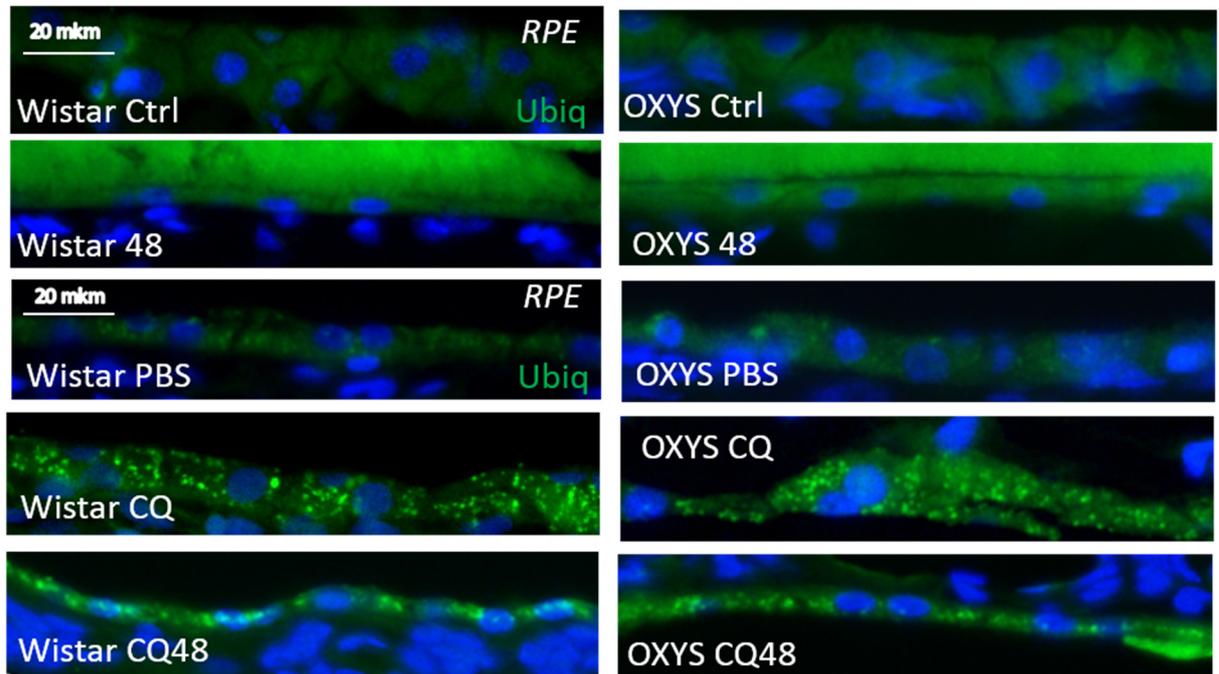


**Table S1.** Autophagy-related differentially expressed genes (DEGs)

Age	Autophagy-related DEGs
20 days	<p>Upregulated: <i>Akt3, Ap1b1, Ap3b2, Arhgap26, Atf4, Atg16l1, Atg16l2, Camk1g, Camkk1, Cbr1, Ddit4, Dnm1, Ehmt2, Elnf2, Flnb, Fos, Gabarapl1, Gapdhs, Grtp1, Hap1, Harbi1, Hdac4, Hif1a, Klhl6, Mapk12, Mapk13, Mapk14, Mapt, Nlrc3, Optn, Plcd3, Prr5l, Qsox1, Ralgapa2, Rnf5, Sh3bgrl2, Shroom3, Slc1a3, Stab2, Stk11, Stx17, Tbc1d5, Trim65, Tsga10ip, Ugt2b17, Ulk3</i></p> <p>Downregulated: <i>Actr2, Actr3, Alk, Alpl2, Bcl2, Cdk2, Cdkl5, Cdkn1b, Csnk1g3, Deptor, Dram2, Eif4e, Exoc2, Exoc5, Fam134b, Fgfr2, Gopc, Hdac9, Hunk, Ikbke, Iptr1, Klhl4, Lamp2, Lamp3, Mitf, Mtmr2, Ngf, Pik3cg, Pkn2, Plcb4, Ppp2r2b, Ppp2r3c, Ppp6c, Prkaa2, Prr5, Pten, Rab10, Rblcc1, RGD1566251, Rps6ka3, Rps6ka6, Scfd1, Sesn3, Sirt1, Slc7a11, Snx2, Sos2, Tm9sf2, Tm9sf3, Tns1, Ube2d2, Ube2d3, Vamp7, Vps13a, Yes1</i></p>
3 months	<p>Upregulated: <i>Ap2a2, Ap3b2, Atg7, Camk1g, Cdk17, Dnm1, Ehmt2, Fos, Gabarapl1, Hdac5, Hdac9, Hspa8, Kdr, Klhl18, LOC503238, Mapk12, Mlst8, Mtdh, Nlrc3, Npc1, Phf23, Pik3r2, Pip5k1c, Plcd3, S100a9, Sgk1, Sik1, Smpd1, Supt5h, Tbc1d5, Trappe9, Ugt2b17, Vps18, Vps39</i></p> <p>Downregulated: <i>Actr2, Alk, Ap1s3, Arhgef4, Capn13, Capns2, Cdk1, Cdkn1b, Eif2ak2, Foxo3, Gfap, Iars, Irgm, Krt76, Lamp3, LOC102554129, Lyn, Mx1, Mx2, Myd88, Nfkb1, Nfkbia, Nfkbiz, Pdk1, Rps6ka2, Sesn2, Sesn3, Sh3gl3, Shc3, Slc1a1, Slc1a4, Zc3h12a</i></p>
18 months	<p>Upregulated: <i>Camk1g, Cdkl1, Hdac5, Hdac9, Mx2, Npas1, Ntrk2, Slc1a3, Stxbp1, Tbc1d5, Ugt2b17, Vps4b</i></p> <p>Downregulated: <i>Anxa7, Ap1s3, Arhgef4, Capn1, Capn2, Capn3, Capn5, Capns2, Cdk1, Dnm2, Ehmt2, Fgfr3, Lamp3, Lpin2, Mink1, Mtmr2, Pld2, Plk2, Ppp2r5a, Rab10, Ryr1, Smpd13a, Ube2j2</i></p>
From 3 to 18 months	<p>Upregulated with age in OXYS: <i>Alk, Arhgef4, Bcl2l1, Ephb2, Exoc3l4, Gfap, Hap1, Hspa2, Iptr3, Map2k1, Mapt, Npas1, Ntrk2, Prkcb, Prkcg, Prkcz, Ralgapa2, Rps6ka2, Sesn3, Shc3, Slc1a3, Tcirg1, Tnik, Tns3, Trim8</i></p> <p>Downregulated with age in OXYS: <i>Arhgap10, Atf4, Cdk16, Epha3, Fos, Hdac2, Ikbkb, Klhl18, Man2b1, Npas2, Plcd3, Scfd1, Sh3gl3, Sh3glb1, Sirt1, Tecpr1, TP53INP2, Vps39, Wac, Wdr45</i></p> <p>Upregulated with age in Wistar: <i>Actg1, Ap3b2, Atp6v0a1, Ehmt2, Hap1, Lpin2, Map3k6, Mapk13, Mapk14, Mapt, Mertk, Mink1, Mlst8, Pak1, Phf23, Prkcg, Ralgapa2, Ripk4, Tns3,</i></p> <p>Downregulated with age in Wistar: <i>Atf4, Dram2, Eif2ak2, Foxo3, Hdac9, Iars, Kdm4a, Mx1, Mx2, S100a9, Sesn2, Sh3gl3, Slc1a4, Wdr3</i></p>

**Figure S2.** Immunostaining for ubiquitin (green) uncovered an increase of ubiquitin-positive granules in RPE cells of rats treated with CQ. Cell nuclei were stained with DAPI. The scale bar is 20  $\mu$ m.



**Figure S2.** Representative TEM images assembly of ultrastructure of RPE cells in 16-month-old OXYS rat.

