

Figure S1. Oxidative stress upregulates let-7f expression in RPE cells. **(A)** Human retinal pigment epithelial (ARPE-19) cells were treated with increasing doses of H₂O₂ (0, 125, 250 and 500 μM) for 24 h. Total miRNA was isolated from cells and expression of let-7f was evaluated by RT-qPCR. Expression levels are presented as a fold-change versus untreated cells (0 μM). ***p* < 0.01 vs Untr. **(B)** Six-eight-week-old female C57BL/6J mice received a 50 mg/kg SI tail-vein injection and were sacrificed on days 0, 3, 5, 7 and 10 to isolate total miRNA from the neural retina. Let-7f expression was evaluated by RT-qPCR and expressed as a fold-change versus control mice (day 0, PBS). ns: not significant.

50 mg/kg Sodium Iodate (SI) Tail-Vein Injection

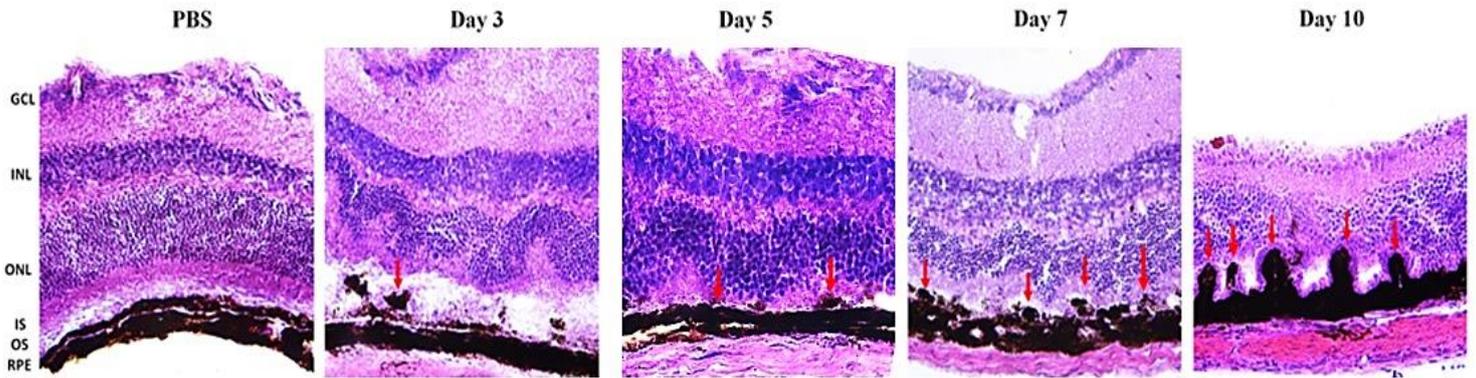


Figure S2. Hematoxylin & eosin (H&E) stained retinal sections demonstrate time-dependent retinal injury in the sodium iodate-induced mouse model of dry AMD. Six-eight-week-old female C57BL/6J mice were injected by tail-vein with 50 mg/kg SI or with vehicle (PBS) and sacrificed on days 0, 3, 5, 7 and 10. Eyes were collected and retinal cryosections (12 μ m) were prepared and stained with H&E. Areas with apparent lipofuscin accumulation and drusen formation are indicated by red arrows. Sections were imaged at 20X using a bright-field microscope. GCL: ganglion cell layer; ONL: outer nuclear layer; INL: inner nuclear layer; IS: inner segment; OS: outer segment; RPE: retinal pigment epithelium.

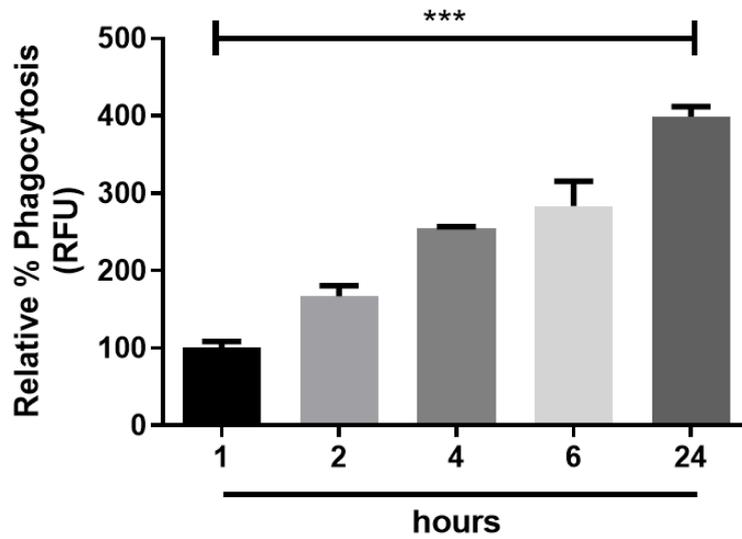


Figure S3. ARPE-19 time-dependent phagocytosis of photoreceptor outer segments (POS). Mature ARPE-19 cells were incubated with FITC-labelled POS for the indicated time points to determine optimal incubation period. Fluorescence intensity of engulfed POS was measured and expressed as a percentage compared to 1h-treated cells. *** $p < 0.001$ vs. $t=1h$.

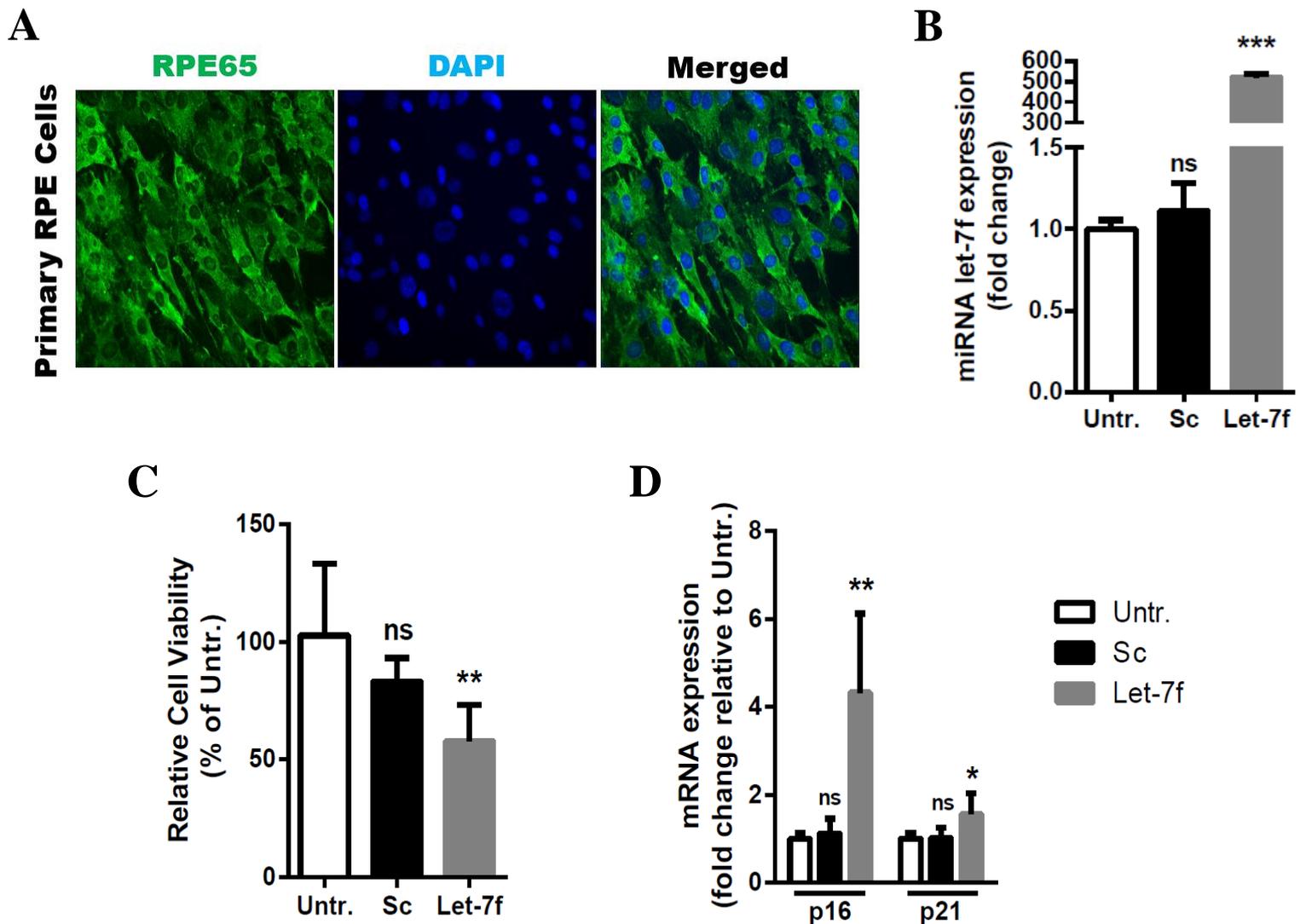


Figure S4. Overexpression of let-7f induces cellular dysfunction in primary RPE cells. **(A)** Primary RPE cell cultures were isolated from C57BL/6J mouse pups and their identity was validated by immunofluorescent staining of RPE-specific marker RPE65 (green) and DAPI (blue) (10X). **(B)** Upregulation of let-7f miRNA in primary RPE cells was confirmed by evaluating let-7f expression using RT-qPCR in untreated (Untr.) cells and in cells transfected with scramble miRNA (Sc) or 50 nM of a let-7f mimic. Results are expressed as a fold-change versus untreated cells. *** $p < 0.001$ vs. Untr. **(C)** Cellular viability was analyzed using PrestoBlue® assay. Fluorescence intensity was measured and presented as a percentage compared to untreated (Untr.) cells. **(D)** mRNA expression levels of cyclin-dependent kinase inhibitors p16^{INK4a} and p21^{Waf/Cip1} in primary RPE cells were detected by RT-qPCR. Expression levels are presented as a fold-change versus untreated (Untr.) cells. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. CTL. ns: not significant.

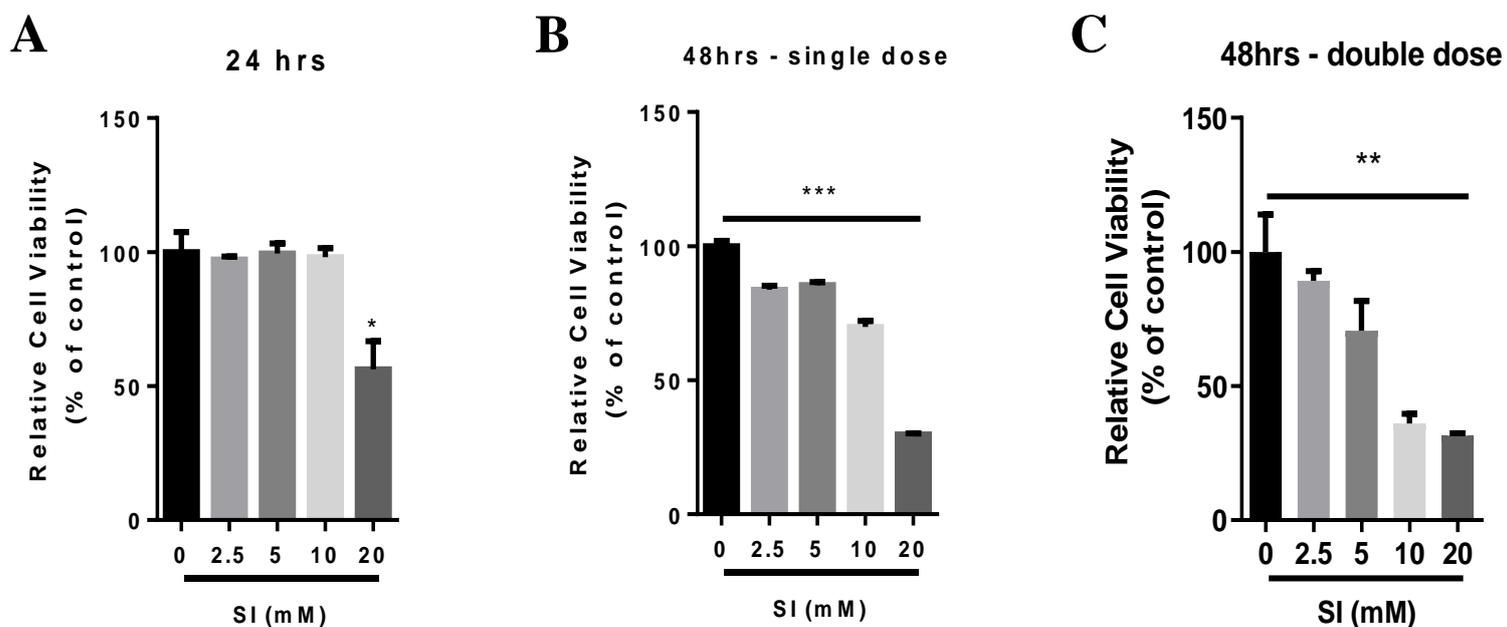


Figure S5. Sodium iodate (SI) decreases RPE cellular viability in a time and dose-dependent manner. ARPE-19 cells were treated with increasing doses of SI (0, 2.5, 5, 10 and 20 mM) for either (A) 24 h or 48 h with a (B) single or (C) double dose. Cellular viability was analyzed using PrestoBlue® assay and fluorescence intensity was measured and presented as a percentage compared to control cells (0 mM). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs. CTL.

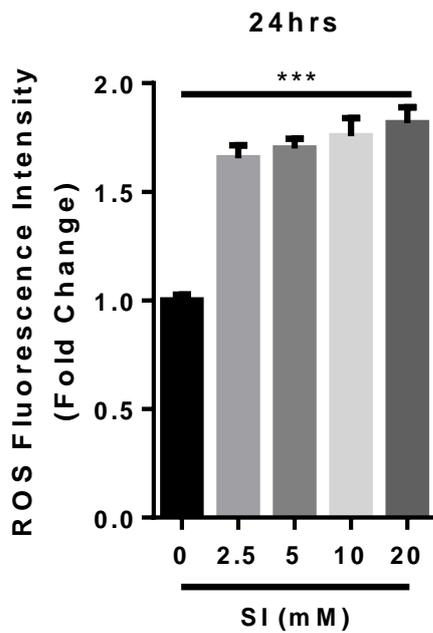
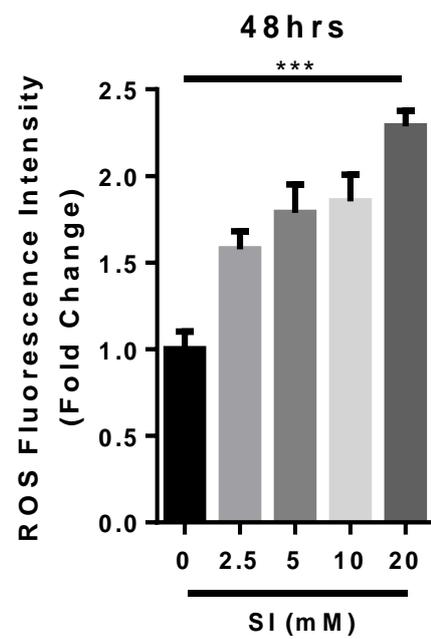
A**B**

Figure S6. Sodium iodate (SI) increases ROS production in RPE cells in a time and dose-dependent manner. ARPE-19 cells were treated with increasing doses of SI (0, 2.5, 5, 10 and 20 mM) for (A) 24h or (B) 48h (double dose). Intracellular production of ROS was evaluated using CM-H₂DCFDA assay. ROS fluorescence intensity was measured and presented as a fold-change versus to control cells (0 mM). *** $p < 0.001$ vs. CTL.