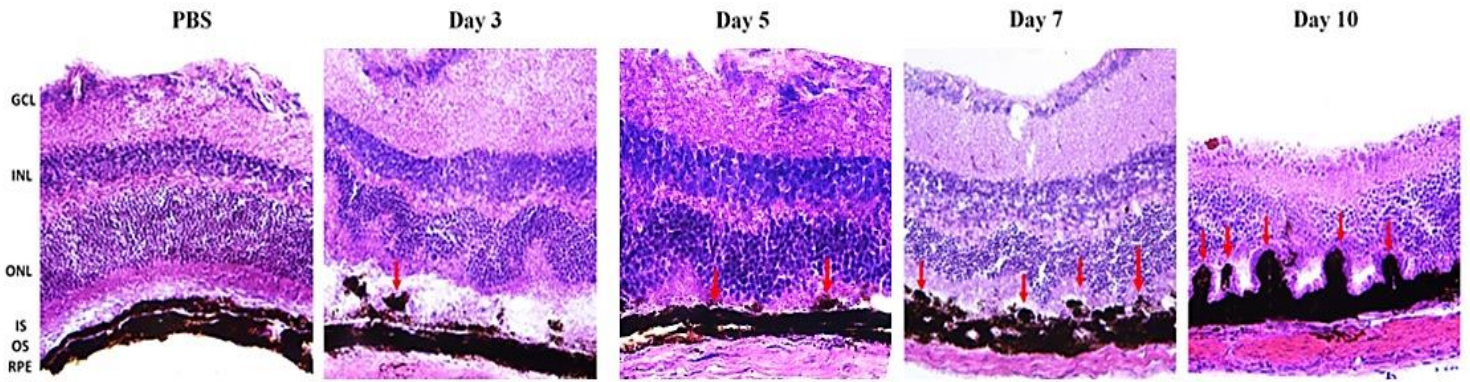
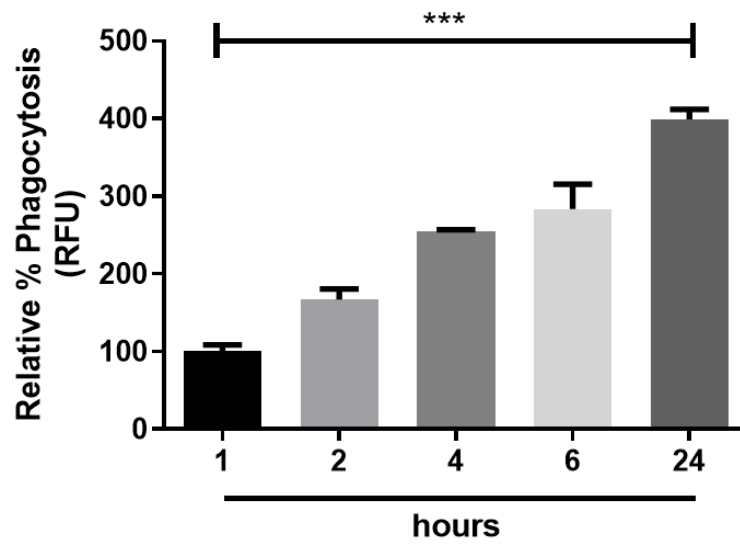


**Figure S1.** Oxidative stress upregulates let-7f expression in RPE cells. **(A)** Human retinal pigment epithelial (ARPE-19) cells were treated with increasing doses of H<sub>2</sub>O<sub>2</sub> (0, 125, 250 and 500  $\mu$ M) for 24 h. Total miRNA was isolated from cells and expression of let-7f was evaluated by RT-qPCR. Expression levels are presented as a fold-change versus untreated cells (0  $\mu$ M). \*\* $p < 0.01$  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.

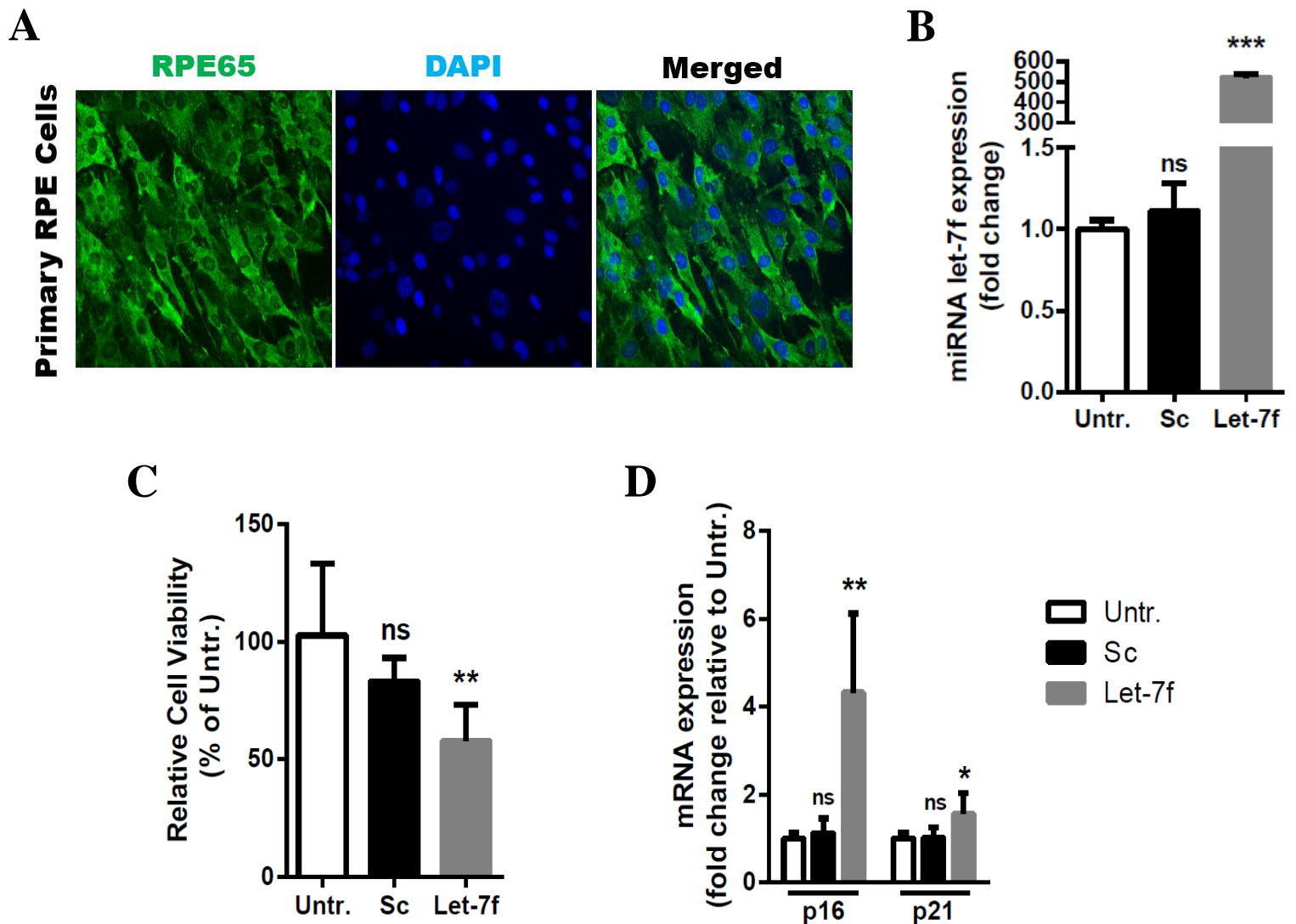
### 50 mg/kg Sodium Iodate (SI) Tail-Vein Injection



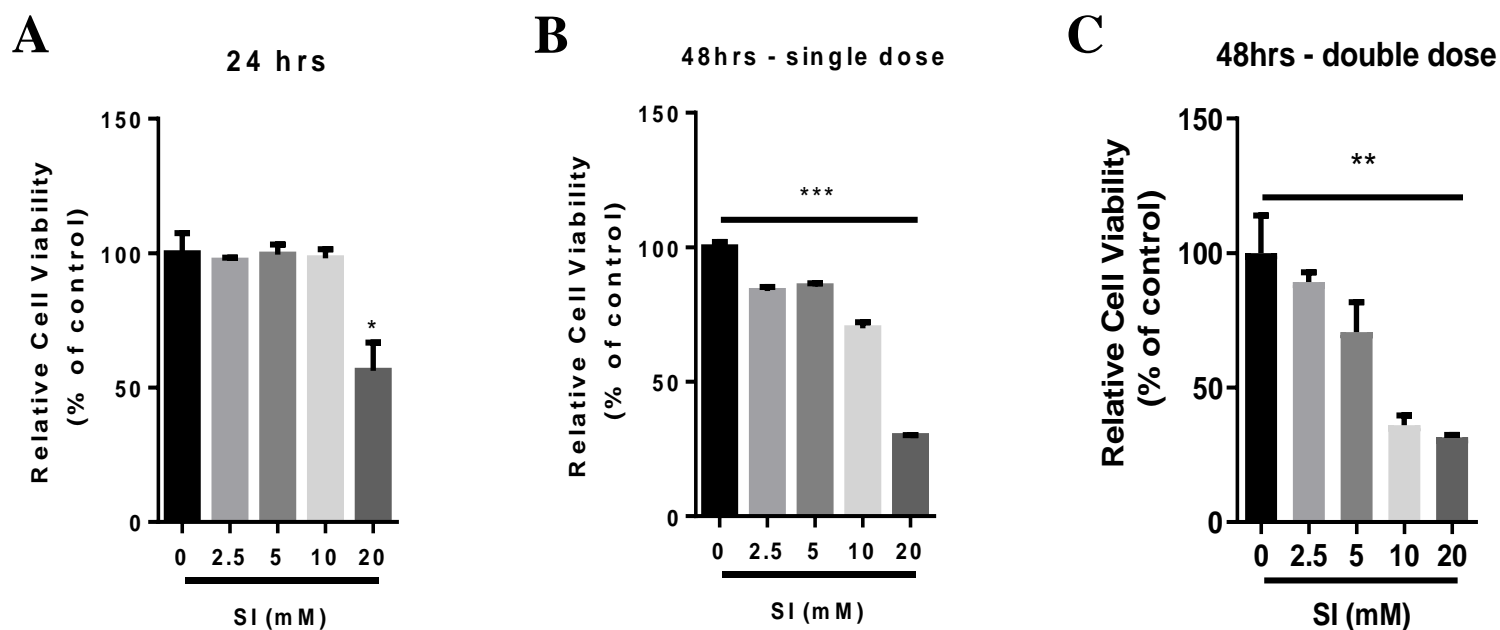
**Figure S2.** Hematoxylin & eosin (H&E) stained retinal sections demonstrate time-dependent retinal injury in the sodium iodate-induced mouse model of dry AMD. Six-eight-week-old female C57BL/6J mice were injected by tail-vein with 50 mg/kg SI or with vehicle (PBS) and sacrificed on days 0, 3, 5, 7 and 10. Eyes were collected and retinal cryosections (12  $\mu$ 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.



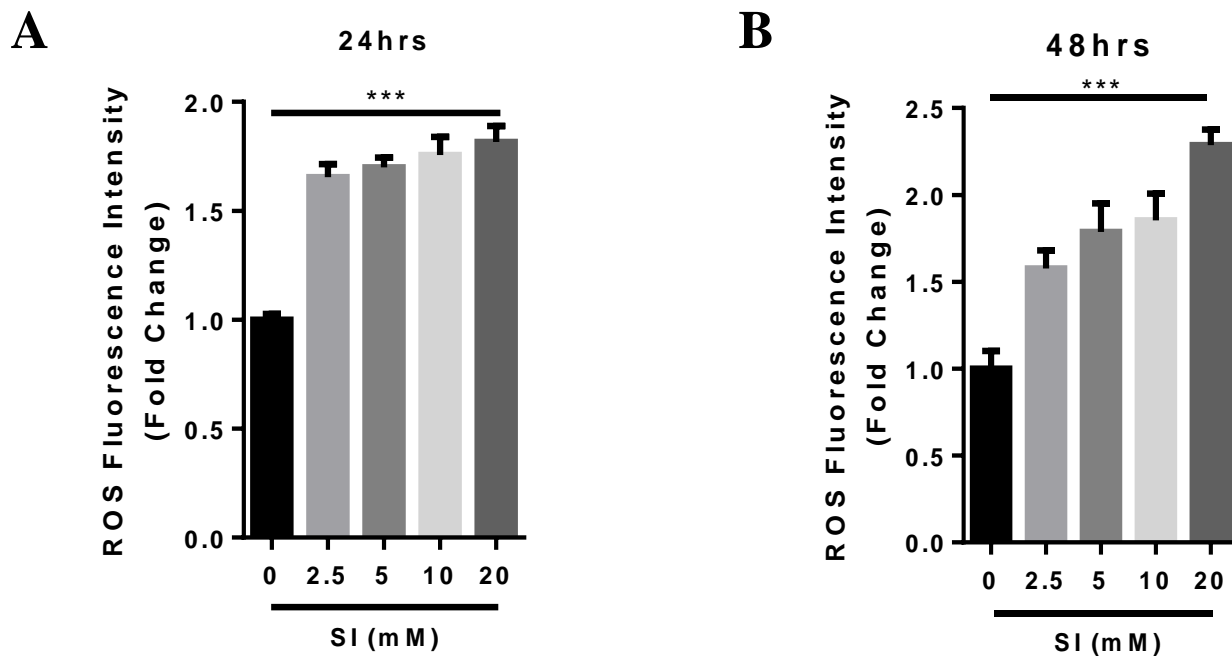
**Figure S3.** ARPE-19 time-dependent phagocytosis of photoreceptor outer segments (POS). Mature ARPE-19 cells were incubated with FITC-labelled POS for the indicated time points to determine optimal incubation period. Fluorescence intensity of engulfed POS was measured and expressed as a percentage 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<sup>INK4a</sup> and p21<sup>Waf/Cip1</sup> 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.



**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-H<sub>2</sub>DCFDA assay. ROS fluorescence intensity was measured and presented as a fold-change versus to control cells (0 mM). \*\*\* $p < 0.001$  vs. CTL.