Table S1. Primer sequences

Gene symbol	Gene name	Forward	Reverse
CAT	Catalase	gctcattttgaccgagagaga	tgacctcaaagtagccaaagg
CD36	Cluster of differentiation 36	tggaacagaggctgacaactt	ttgattttgatagatatgggatgc
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase	gagccaaaagggtcatcatctc	aggaggcattgctgatgatct
GCLM	Glutamate-cysteine ligase modifier subunit	gacaaaacacagttggaacagc	cagtcaaatctggtggcatc
GPX1	Glutathione peroxidase 1	cgccaagaacgaagagattc	gttcacctcgcacttctcg
HMOX1	Heme oxygenase 1	ggcagagggtgatagaagagg	agctcctgcaactcctcaaa
NFE2L2	Nuclear factor, erythroid 2 like 2	acacggtccacagctcatc	tgcctccaaagtatgtcaatca
NQO1	NAD(P)H quinone dehydrogenase 1	cagctcaccgagagcctagt	gagtgagccagtacgatcagtg
PPIA	Peptidylprolyl isomerase A	cctaaagcatacgggtcctg	tttcactttgccaaacacca
PRDX1	Peroxiredoxin 1	aggccttccagttcactgac	tttgctcttttggacatcagg
PRDX3	Peroxiredoxin 3	agcaaaattattcagcaccagtt	ccttaaaatagggtgcatgctg
PRDX5	Peroxiredoxin 5	tcctggctgatcccactg	atgccatcctgtaccaccat
SOD1	Superoxide dismutase 1	tccatgttcatgagtttggagat	cccaccgtgttttctggata
SOD2	Superoxide dismutase 2	aatcaggatccactgcaagg	taagcgtgctcccacacat
TXN2	Thioredoxin 2	gagacaccagtggttgtgga	ttggccaccatcttctctaac
TXNRD1	Thioredoxin reductase 1	caattggaatccaccctgtc	ccacactggggcttaacct
YWHAZ	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein zeta	gcaattactgagagacaacttgaca	tggaaggccggttaatttt

Table S2. Statistical comparisons and p-values

	Pair compared		Adjusted p-value
Figure 1A			
	$NaIO_3$ 0 mM	$NaIO_3$ 6.25 mM	0.0161
	$NaIO_3$ 0 mM	$NaIO_3$ 12.5 mM	0.0004
	$NaIO_3$ 0 mM	$NaIO_3$ 25 mM	<0.0001
Figure 1B			
	$NaIO_3$ 0 mM	$NaIO_3$ 6.25 mM	<0.0012
	$NaIO_3$ 0 mM	$NaIO_3$ 12.5 mM	<0.0001
	$NaIO_3$ 0 mM	$NaIO_3$ 25 mM	<0.0001
Figure 1C			
	$NaIO_3$ 0 mM	$NaIO_3$ 6.25 mM	0.8518
	$NaIO_3$ 0 mM	$NaIO_3$ 12.5 mM	0.2394
	$NaIO_3$ 0 mM	$NaIO_3$ 25 mM	<0.0001
Figure 2A			
	$NaIO_3$ 0 mM	$NaIO_3$ 6.25 mM	0.0029
	$NaIO_3$ 0 mM	$NaIO_3$ 12.5 mM	<0.0001
	$NaIO_3$ 0 mM	$NaIO_3$ 25 mM	<0.0001
	$NaIO_3$ 0 mM	MPE-001 + $NaIO_3$ 0 mM	>0.9999
	$NaIO_3$ 6.25 mM	MPE-001 + $NaIO_3$ 6.25 mM	0.0477
	$NaIO_3$ 12.5 mM	MPE-001 + $NaIO_3$ 12.5 mM	0.0042
	$NaIO_3$ 25 mM	MPE-001 + $NaIO_3$ 25 mM	0.9723
Figure 2B			
	Vehicle	$NaIO_3$	0.0011
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0188
Figure 2C			
	Vehicle	$NaIO_3$	0.0037
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0261
Figure 2F			
	Vehicle	$NaIO_3$	0.0002
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0075
Figure 2H			
siCON	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0304
siCD36	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.9951
Figure 3A			
HMOX1	Vehicle	MPE-001	>0.9999
	Vehicle	$NaIO_3$	0.0003

	$NaIO_3$	MPE-001+ $NaIO_3$	0.9999
Figure 3A			
NQO1	Vehicle	MPE-001	0.9596
	Vehicle	$NaIO_3$	0.0005
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9266
Figure 3A			
GCLM	Vehicle	MPE-001	0.9442
	Vehicle	$NaIO_3$	0.0009
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9442
Figure 3A			
PRDX 1	Vehicle	MPE-001	0.8235
	Vehicle	$NaIO_3$	0.0002
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9607
Figure 3A			
TXNR D1	Vehicle	MPE-001	0.9987
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9293
Figure 3A			
CAT	Vehicle	MPE-001	0.2255
	Vehicle	$NaIO_3$	0.2255
	$NaIO_3$	MPE-001+ $NaIO_3$	0.2255
Figure 3A			
GPX1	Vehicle	MPE-001	0.9100
	Vehicle	$NaIO_3$	0.9100
	$NaIO_3$	MPE-001+ $NaIO_3$	0.6008
Figure 3A			
SOD1	Vehicle	MPE-001	0.6876
	Vehicle	$NaIO_3$	0.8048
	$NaIO_3$	MPE-001+ $NaIO_3$	0.6601
Figure 3A			
SOD2	Vehicle	MPE-001	0.6639
	Vehicle	$NaIO_3$	0.7285
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9463
Figure 3A			
PRDX 3	Vehicle	MPE-001	0.5645
	Vehicle	$NaIO_3$	0.1908
	$NaIO_3$	MPE-001+ $NaIO_3$	0.5645
Figure 3A			
PRDX 5	Vehicle	MPE-001	0.8548
	Vehicle	$NaIO_3$	0.8548
	$NaIO_3$	MPE-001+ $NaIO_3$	0.8548

Figure 3A			
TXN2	Vehicle	MPE-001	0.1318
	Vehicle	$NaIO_3$	0.5323
	$NaIO_3$	MPE-001+ $NaIO_3$	0.1148
Figure 3B			
	Vehicle	MPE-001	0.8258
	Vehicle	$NaIO_3$	0.0301
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9812
Figure 3C			
2h	Vehicle	$NaIO_3$	>0.9999
	$NaIO_3$	MPE-001+ $NaIO_3$	>0.9999
Figure 3C			
4h	Vehicle	$NaIO_3$	0.9985
	$NaIO_3$	MPE-001+ $NaIO_3$	>0.9999
Figure 3C			
16h	Vehicle	$NaIO_3$	0.0125
	$NaIO_3$	MPE-001+ $NaIO_3$	>0.9999
Figure 4A LC3-II/I			
	Vehicle	MPE-001	0.9962
	Vehicle	$NaIO_3$	0.0159
	Vehicle	MPE-001+ $NaIO_3$	0.0010
	$NaIO_3$	MPE-001+ $NaIO_3$	0.6748
Figure 4A LC3-II/I			
+Bafilomycin A1	Vehicle	MPE-001	0.9907
	Vehicle	$NaIO_3$	0.5643
	Vehicle	MPE-001+ $NaIO_3$	0.0005
	$NaIO_3$	MPE-001+ $NaIO_3$	0.0189
Figure 4A LC3-II/GAPDH			
	Vehicle	MPE-001	0.96
	Vehicle	$NaIO_3$	0.3555
	Vehicle	MPE-001+ $NaIO_3$	0.1759
	$NaIO_3$	MPE-001+ $NaIO_3$	0.9902
Figure 4A LC3-II/GAPDH			
+Bafilomycin A1	Vehicle	MPE-001	0.9996
	Vehicle	$NaIO_3$	0.9727
	Vehicle	MPE-001+ $NaIO_3$	0.0123
	$NaIO_3$	MPE-001+ $NaIO_3$	0.0414
Figure 4C			
	Vehicle	MPE-001	0.9726
	Vehicle	$NaIO_3$	0.0024
	Vehicle	MPE-001+ $NaIO_3$	0.0722

	$NaIO_3$	MPE-001+ $NaIO_3$	<0.0001
Figure 4D Left			
	Vehicle	Wortmannin	>0.9999
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0259
	Wortmannin	$NaIO_3$ + Wortmannin	<0.0001
	$NaIO_3$ + Wortmannin	MPE-001 + $NaIO_3$ + Wortmannin	>0.9999
Figure 4D Right			
	Vehicle	Bafilomycin A1	0.9997
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0004
	Bafilomycin A1	$NaIO_3$ + Bafilomycin A1	<0.0001
	$NaIO_3$ + Bafilomycin A1	MPE-001 + $NaIO_3$ + Bafilomycin A1	>0.9999
Figure 5B			
	Vehicle	MPE-001	0.8481
	Vehicle	$NaIO_3$	0.1137
	Vehicle	MPE-001+ $NaIO_3$	<0.0001
	$NaIO_3$	MPE-001+ $NaIO_3$	0.0006
Figure 5C			
	Vehicle	MPE-001	0.7872
	Vehicle	$NaIO_3$	0.0923
	Vehicle	MPE-001+ $NaIO_3$	0.0045
Figure 6A			
	$NaIO_3$ 0 mM	$NaIO_3$ 6.25 mM	0.1925
	$NaIO_3$ 0 mM	$NaIO_3$ 12.5 mM	0.0126
	$NaIO_3$ 0 mM	$NaIO_3$ 25 mM	0.0045
Figure 6B Left			
	Vehicle	Wortmannin	0.8714
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0458
	Wortmannin	$NaIO_3$ + Wortmannin	<0.0001
	$NaIO_3$ + Wortmannin	MPE-001 + $NaIO_3$ + Wortmannin	0.9996
Figure 6B Right			
	Vehicle	Bafilomycin A1	>0.9999
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0095
	Bafilomycin A1	$NaIO_3$ + Bafilomycin A1	0.0105
	$NaIO_3$ + Bafilomycin A1	MPE-001 + $NaIO_3$ + Bafilomycin A1	0.9931

Figure 6D			
	Vehicle	MPE-001	0.0050
	Vehicle	$NaIO_3$	0.4974
	Vehicle	MPE-001+ $NaIO_3$	0.0007
	$NaIO_3$	MPE-001+ $NaIO_3$	<0.0001
Figure S2B			
	Vehicle	MPE-001	0.9999
	Vehicle	$NaIO_3$	0.0010
	$NaIO_3$	MPE-001+ $NaIO_3$	0.0361
Figure S3A			
	Vehicle	NAC	0.9794
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	NAC+ $NaIO_3$	0.0374
Figure S3B			
	Vehicle	Bafilomycin A1	0.9207
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	NAC + $NaIO_3$	0.0369
	Bafilomycin A1	$NaIO_3$ + Bafilomycin A1	<0.0001
	$NaIO_3$ + Bafilomycin A1	NAC + $NaIO_3$ + Bafilomycin A1	0.0387
Figure S4			
	Vehicle	Bafilomycin A1	0.9989
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MPE-001 + $NaIO_3$	0.0423
	Bafilomycin A1	$NaIO_3$ + Bafilomycin A1	<0.0001
	$NaIO_3$ + Bafilomycin A1	MPE-001 + $NaIO_3$ + Bafilomycin A1	0.9999
Figure S5B			
	Vehicle	MPE-001	0.4804
	Vehicle	$NaIO_3$	0.0013
	Vehicle	MPE-001+ $NaIO_3$	0.0112
	$NaIO_3$	MPE-001+ $NaIO_3$	0.7070
Figure S6A			
	Vehicle	$NaIO_3$	0.0044
	$NaIO_3$	MitoTEMPO+ $NaIO_3$	0.8997
Figure S6B			
	Vehicle	MitoTEMPO	0.0926
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MitoTEMPO+ $NaIO_3$	0.6774
Figure S6C			
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MitoQ+ $NaIO_3$	0.0364

Figure S6D			
	Vehicle	MitoQ	0.6014
	Vehicle	$NaIO_3$	<0.0001
	$NaIO_3$	MitoQ+ $NaIO_3$	0.7568

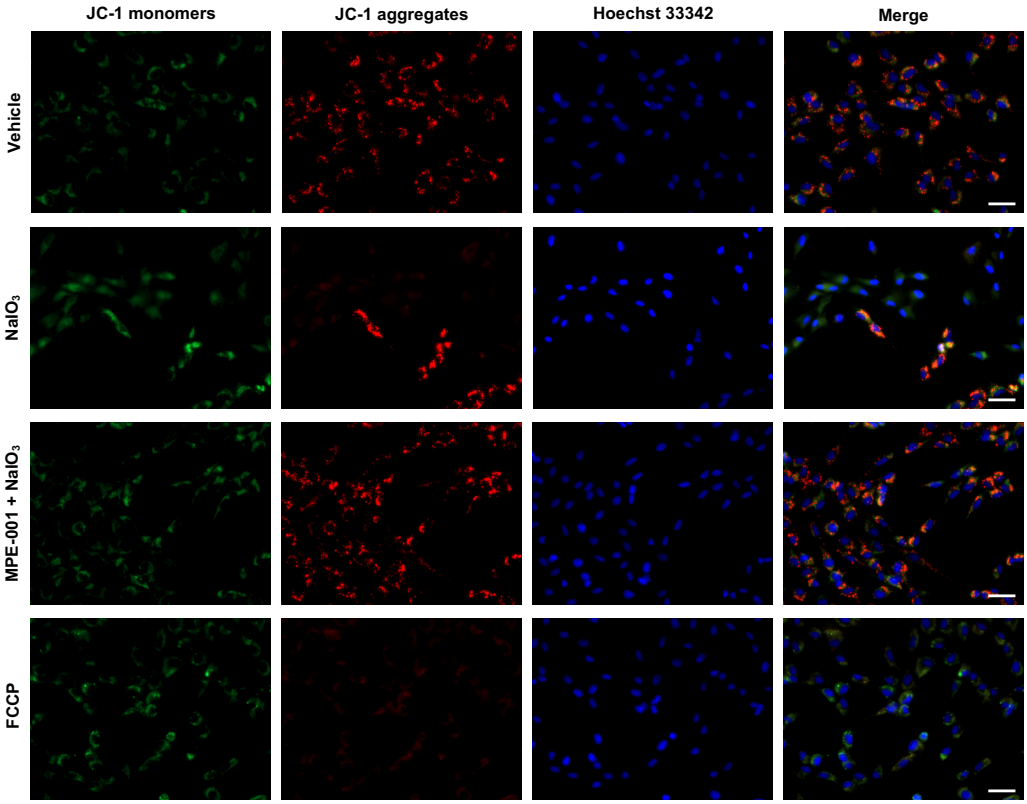

Figure S1. MPE-001 pretreatment prevents the $NaIO_3$-induced loss of mitochondrial membrane potential. hTERT RPE-1 cells were pretreated with 1 μM MPE-001 for 2 h and then exposed to 12.5 mM $NaIO_3$ for 4 h or were treated with 5 μM FCCP for 4 h. Representative images of JC-1 staining are shown (scale bar = 50 μm).

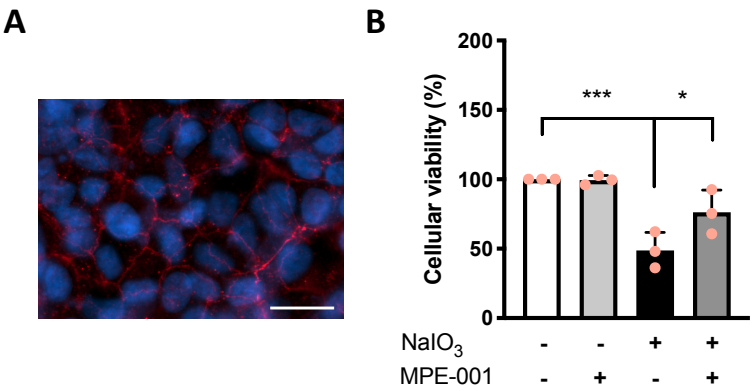

Figure S2. MPE-001 improved the viability of differentiated ARPE-19 cells exposed to $NaIO_3$. (A) Representative image of ZO-1 (red) and Hoechst 33342 (blue) staining of differentiated ARPE-19 cells grown on Transwell inserts (scale bar = 20 μm). (B) Differentiated ARPE-19 cells on Transwell inserts were pretreated with 10 nM MPE-001 through the lower compartment for 2 hours and then exposed to 12.5 mM $NaIO_3$ for 24 hours. Cellular viability was assessed by CCK-8 (n=3). Mean ± SD, * $p < 0.05$, *** $p < 0.001$.

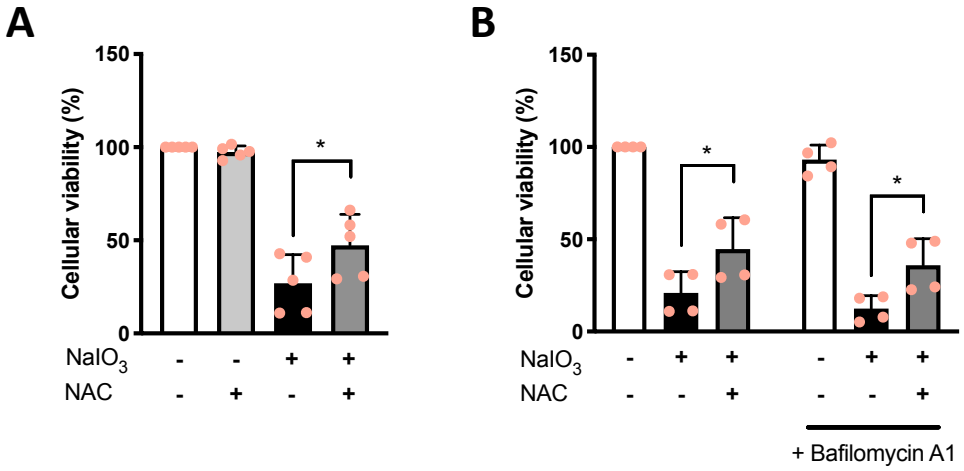

Figure S3. NAC protected hTERT RPE-1 cells against $NaIO_3$-induced cytotoxicity in an autophagy-independent manner. hTERT RPE-1 cells were co-treated with 1.25 mM NAC and $NaIO_3$ for 24 hours. (A) Cellular viability assessed by CCK-8 in the absence (n=5) and (B) in the absence/presence of 10 nM bafilomycin A1 (n=4). Mean ± SD, ns = non-significant, * $p < 0.05$.

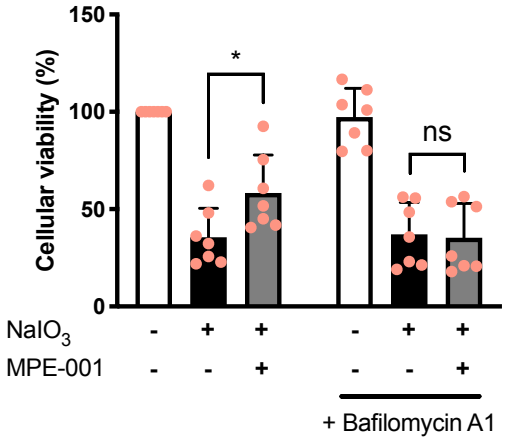

Figure S4. Bafilomycin A1 abolished the cytoprotective effect of MPE-001 on differentiated ARPE-19 cells. Differentiated ARPE-19 cells on Transwell inserts were pretreated with 10 nM MPE-001 through the lower compartment for 2 hours and then exposed to 12.5 mM $NaIO_3$ for 24 hours in the presence/absence of 10 nM bafilomycin A1. Cellular viability was assessed by CCK-8 (n=7), Mean ± SD, ns = non-significant, * $p < 0.05$.

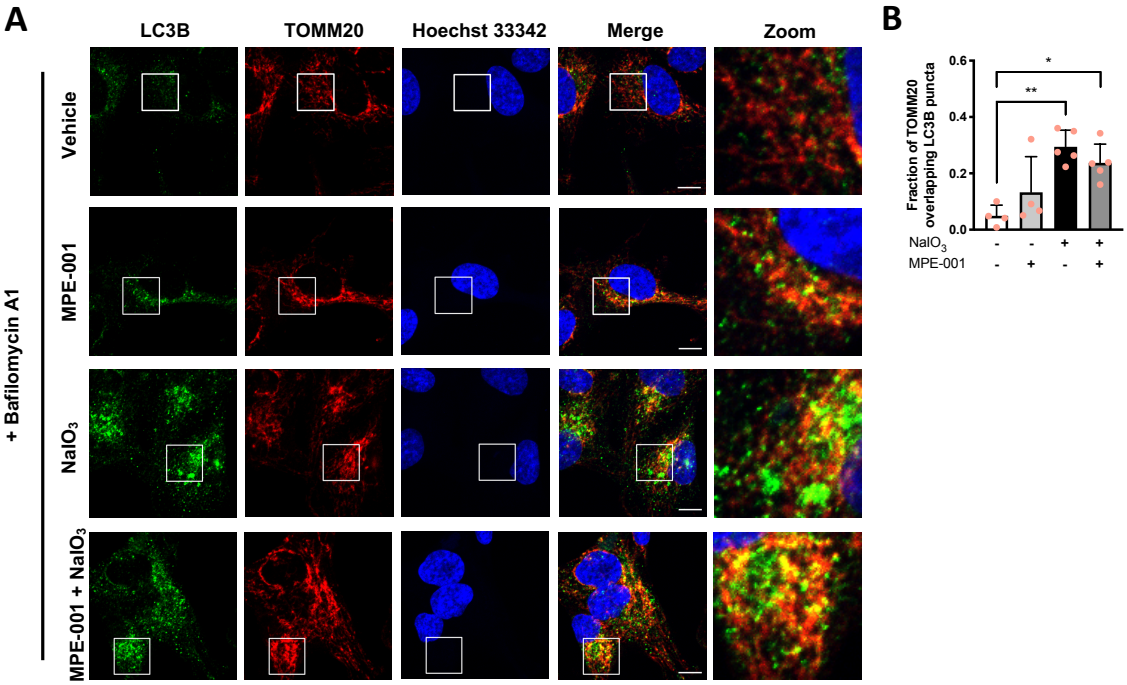

Figure S5. The effect of MPE-001 and/or $NaIO_3$ treatments on LC3B and TOMM20 co-localization. hTERT RPE-1 cells were pretreated with 1 μM MPE-001 for 2 h and then exposed to 12.5 mM $NaIO_3$ for 4 h in the presence of 10 nM bafilomycin A1. (A) Representative images of LC3B and TOMM20 immunostaining are shown (scale bar = 10 μm). The same gamma correction was applied to all images. (B) Manders' colocalization coefficient analysis was carried out across series of 4 to 5 images of 4 to 18 cells each. Mean ± SD, * $p < 0.05$. ** $p < 0.01$.

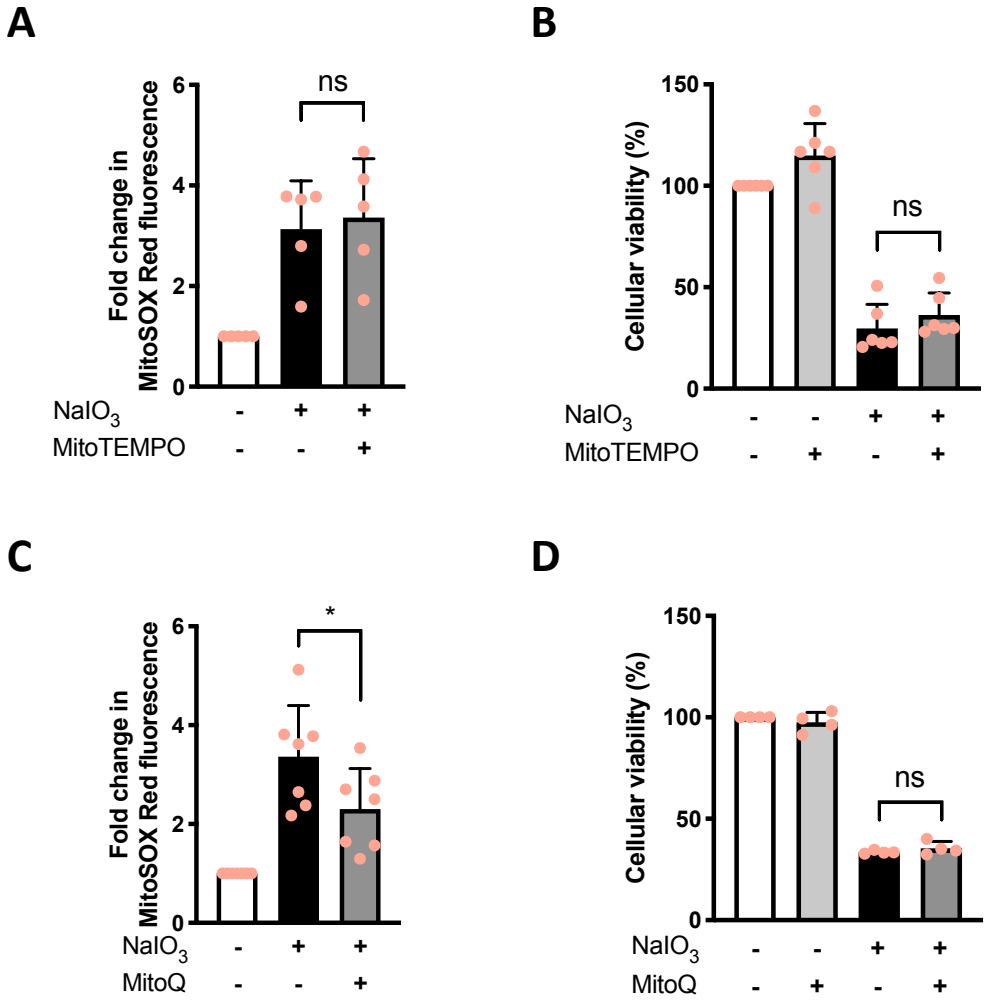

Figure S6. The effect of mitochondria-selective antioxidant compounds on $NaIO_3$-induced cytotoxicity. (A and B) Cells were pretreated with 20 μM MitoTEMPO for 1 hour and then exposed to 12.5 mM $NaIO_3$. (A) Mitochondrial superoxide formation after 2 hours of $NaIO_3$ treatment relative to vehicle-treated cells (n=5) and (B) cellular viability assessed by CCK-8 after 24 hours of $NaIO_3$ treatment (n=6). (C and D) Cells were pretreated with 5 nM MitoQ for 1 hour and then exposed to 12.5 mM $NaIO_3$. (C) Mitochondrial superoxide formation after 2 hours of $NaIO_3$ treatment relative to vehicle-treated cells (n=7) and (D) cellular viability assessed by CCK-8 after 24 hours of $NaIO_3$ treatment (n=4). Mean ± SD, ns = non-significant, * $p < 0.05$.