Supplementary Materials and Methods

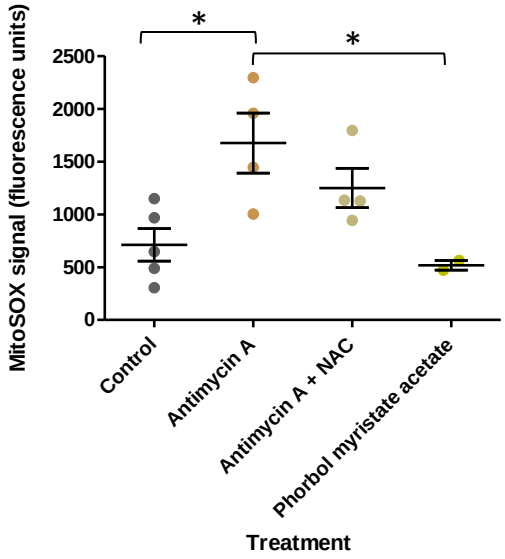
S1 Table: antibody specifications

ANTIGEN	PROVIDER	REFERENCE	DILUTION	INCUBATION
ENDOG	Abcam	ab76122	1:1.000	O.N. 4ºC
pSer473-AKT	Cell Signaling	4060	1:1.000	O.N. 4ºC
AKT	Santa Cruz Techn	Sc-1618	1:1.000	O.N. 4ºC
pSer21/9-GSK3ß	Cell Signaling	9331	1:1.000	O.N. 4ºC
GSK3ß	Abcam	ab18893	1:1.000	O.N. 4ºC
HDAC4	Santa Cruz Techn	SC-11418	1:500	O.N. 4ºC
GAPDH	Abcam	ab8245	1:10.000	1h RT
LAMIN A/C	Abcam	ab8984	1:1.000	O.N. 4ºC
MEF2A	Cell Signaling	9736	1:2.000	O.N. 4ºC
α-actinin	Sigma	A7811	1:500 1:20000	1h RT (IF) Overnight 4ºC (WB)

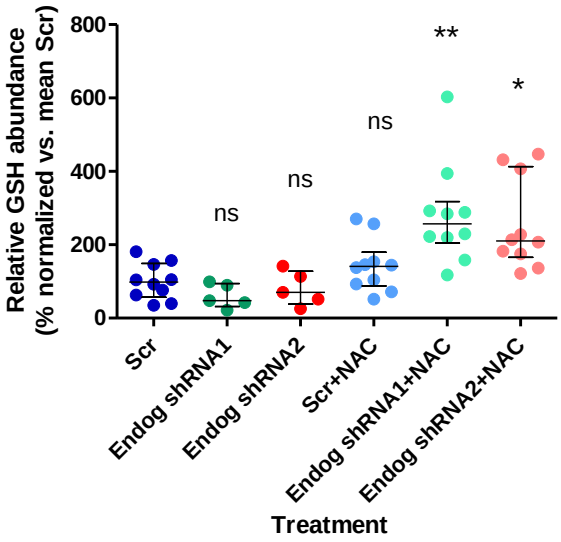
S2 Table: primers and probes used for assessing mtDNA copy number

PRIMERS	Sequence 5′- 3′
16S Fw	5′ AATGGTTCG TTT GTT CAA CGA TT 3′
16S Rv	5′ AGA AAC CGA CCT GGA TTG CTC 3′
ND4 Fw	5' TGCATCAATCATAATCCAAACTCCATGA 3'
ND4 Rv	5' GGCAGAATAGGAGTGATGATGTGA 3'

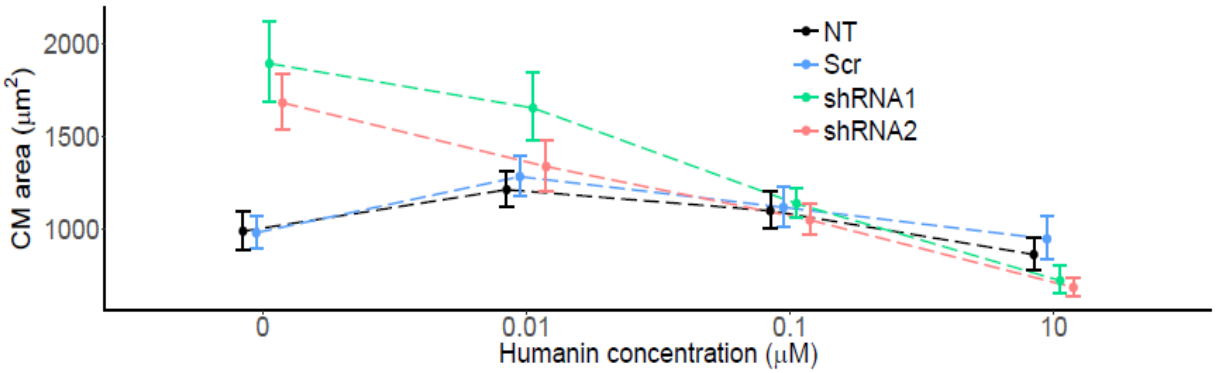
PROBES	
16S	FAM-5′ AAG TCC TAC GTG ATC TGA GTT 3′-MGB
ND4	FAM-5' CCGACATCATTACCGGGTTTTCCTCTTG 3'- MGB
ANG1	Life Technologies: Mm00833184_s1



Suppl. Fig .S1**. MitoSOX signal in cardiomyocytes after induction of superoxide ($O_2^{\cdot -}$) production.** Rat neonatal cardiomyocytes were cultured as described in the article and treated during 30 minutes with 50 µM Antimycin A (antibiotic interrupting the electron flux through the electron transport chain and inducing $O_2^{\cdot -}$ within the mitochondria), in the presence or absence of 200µM N-Acetyl-L-Cysteine (NAC, precursor of GSH, which is involved in the transformation of H_2O_2 in water), or with 0.1 µM Phorbol myristate acetate (an agonist of PKC, which in turn activates NADPH oxydase generating $O_2^{\cdot -}$ in the cytosol. Then, cells were processed as described in the article to detect ROS production with the MitoSOX fluorescent indicator. Values represent fluorescence signal. Lines indicate means ± standard errors. N=5. One way analysis of variance (ANOVA) indicated that mean differences were statistically significant ($P<0.05$). *Post hoc* Bonferroni's test was used to perform multiple comparisons. * , $P<0.05$.



Suppl. Fig .S2. **Effects of *Endog* silencing and NAC addition on reduced thiol abundance (mostly GSH) in the Rat-1 rat fibroblast cell line.** Rat-1 fibroblast cells were transduced with a scrambled (Scr) or two different Endog shRNA constructs used in the article to silence the expression of *Endog*. N-Acetyl-L-Cysteine (NAC) was added (200µM) to some of the plates. Forty-eight hours later, the plates were processed following the manufacturer instructions to detect intracellular reduced thiol (mostly GSH) using the ThiolTracker™ violet fluorescent indicator (Molecular Probes) (Ex/Em= 404/526nm). The ThiolTracker™ signal was divided by the total protein concentration in the plate (mg). The graphic shows individual values normalized to the Scr mean in %. Non-parametric Kruscall-Wallis test was used to identify differences between groups and were found to be statistically significant ($P<0.001$). *Post hoc* Dunnett's test was carried to compare each group to Scr. Ns: not significant, *, $P<0.05$; **, $P<0.001$. Lines are medians± interquartile ranges.



Suppl. Fig .S3. **Interaction assessment of *Endog* expression and humanin concentration in the hypertrophy of rat neonatal cardiomyocytes.** Cross sectional areas of CM from the experiment shown in Fig.5B were analyzed using linear regression models. Fitted cross sectional areas of CM and 95% confidence interval. P<0.001 for the interaction.