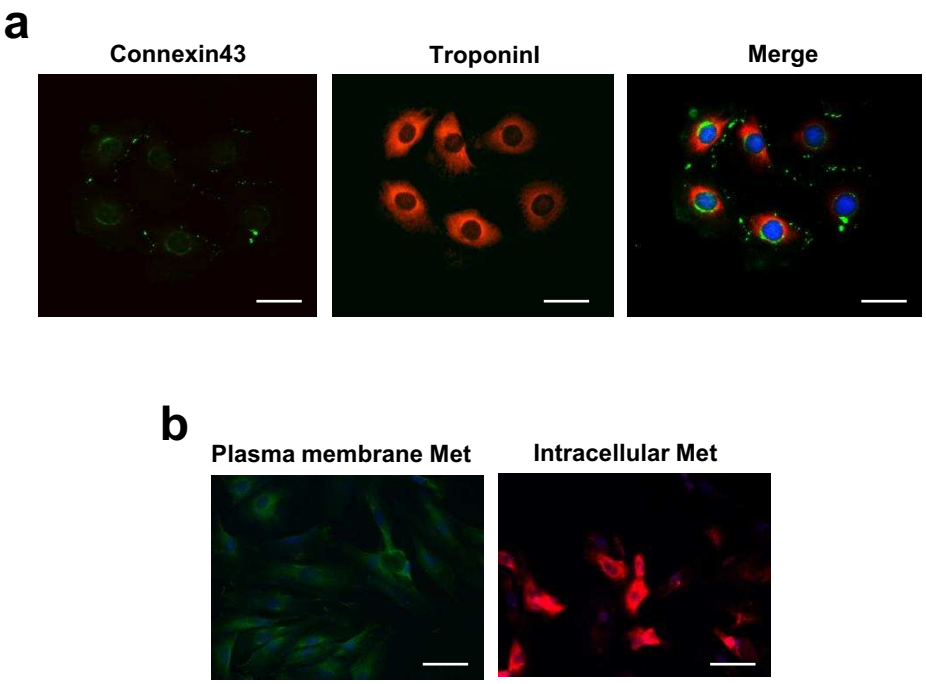
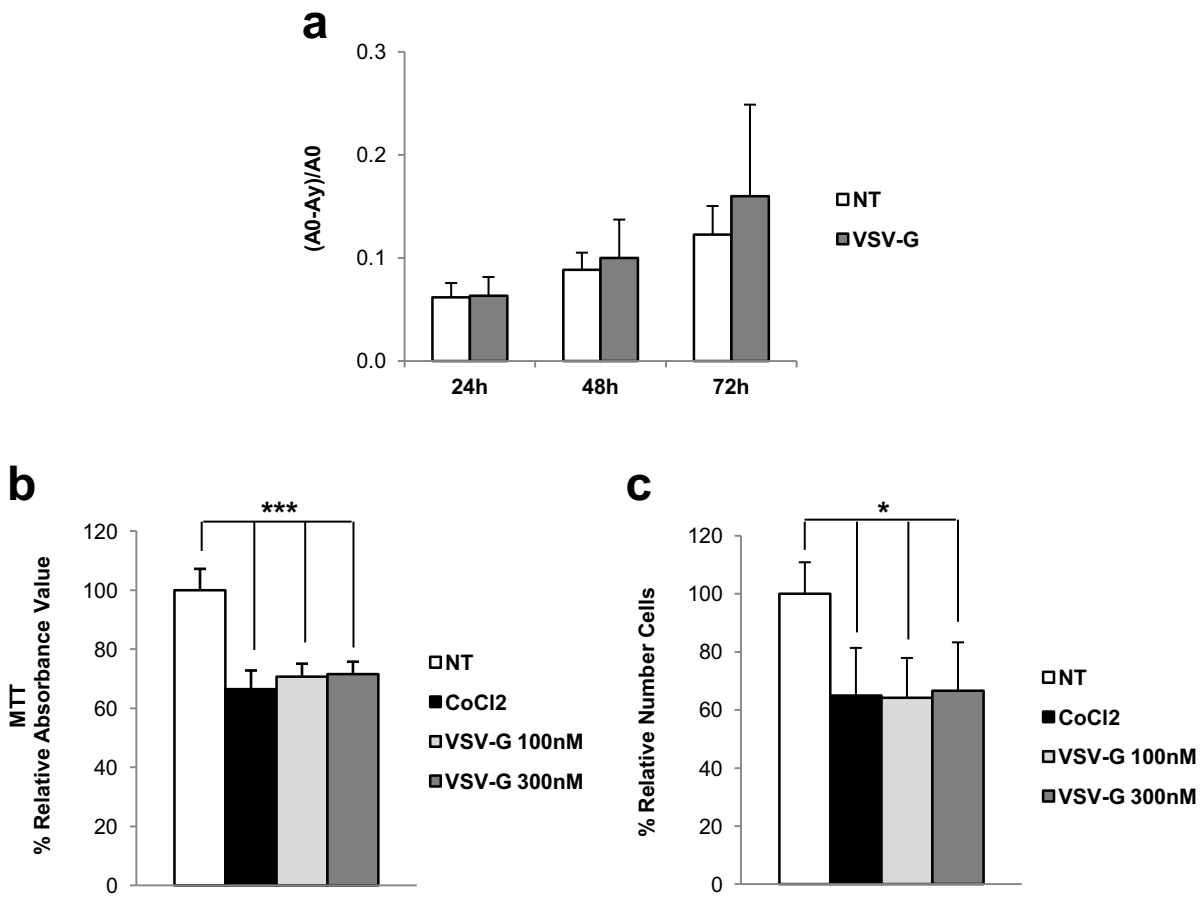
Supplementary Figure S1



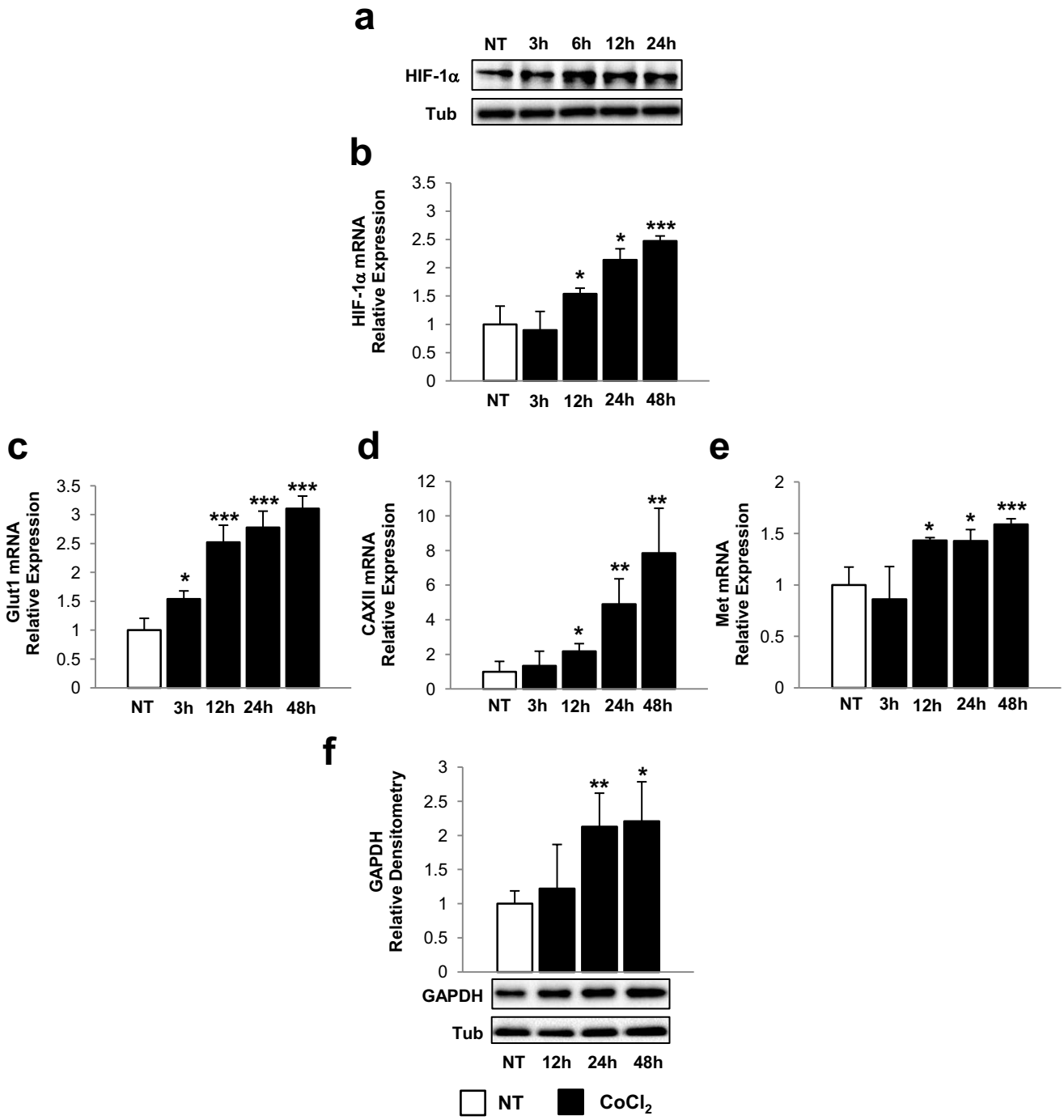
Supplementary Figure S1 H9c2 rat cardiomyoblasts cell line. (**a**) Immunofluorescence of cardiac markers: Connexin43 (green) and Troponin-I (red). DAPI-stained nuclei in blue. (**b**) Plasma membrane (green) and intracellular (red) immunofluorescence of Met (see Materials and methods section). Nuclei in blue. Bar: 35μm.

Supplementary Figure S2



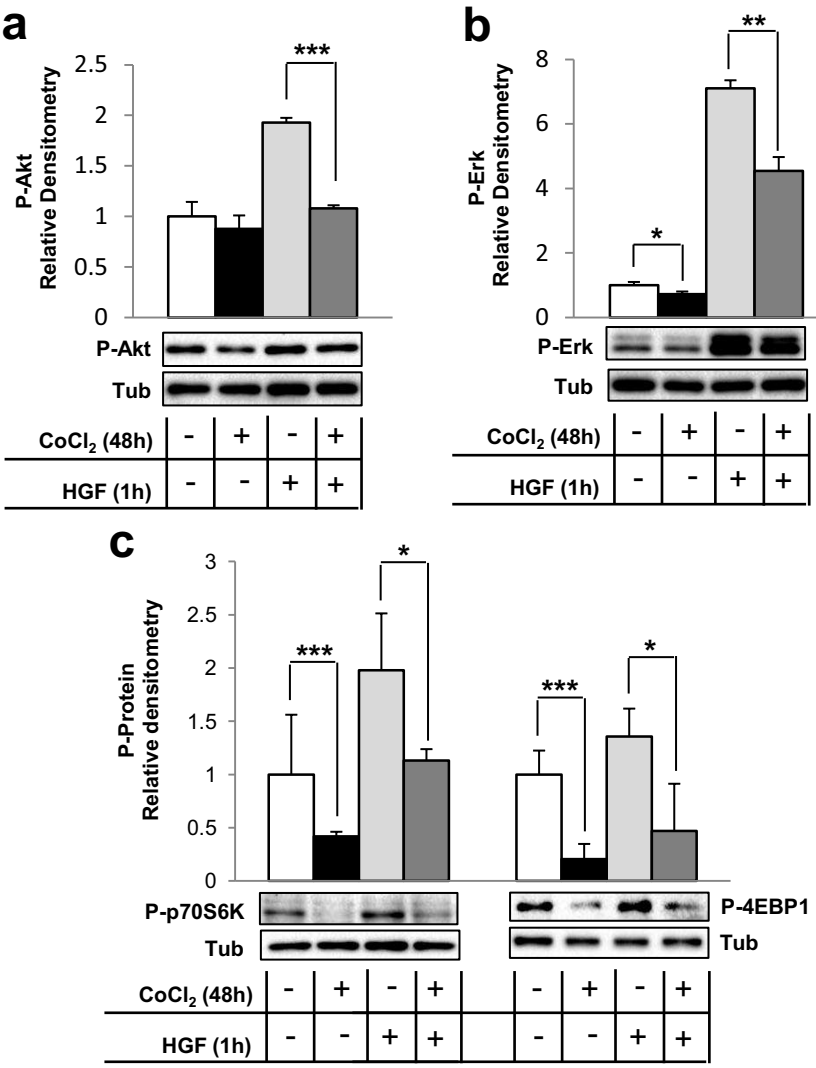
Supplementary Figure S2 The cardioprotective activity mediated by Met agonist DN30 and DO24 is specific. (**a**) Wound healing assay in cells not treated (NT, white) or treated with VSV-G mAb (100nM, grey) for 24, 48 or 72 hours. T-test was calculated between treated vs NT samples at each time point and was never statistically significant. (**b**-**c**) Cells were untreated (NT, white), treated with 300μM $CoCl_2$ (black) or $CoCl_2$+VSV-G (100nM: light grey, 300nM: dark grey). MAb was concomitantly added to $CoCl_2$ for 24h (**b**) and 48h (**c**). Cell viability was measured by MTT assay (**b**) and cells were counted (**c**). Results are expressed as the percentage of MTT or cell count reduction relative to NT. Values are the mean ± SD calculated in three independent experiments. For T-test each group of samples was compared to $CoCl_2$-treated cells, except for (**a**). *p<0.05 and ***p<0.005.

Supplementary Figure S3



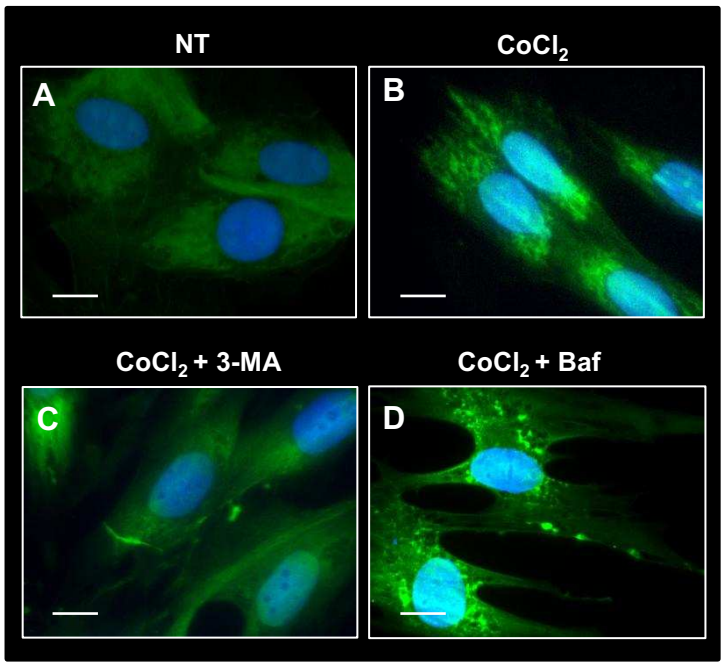
Supplementary Figure S3 $CoCl_2$ induces HIF-1α protein stabilization and mRNA up-regulation of its target genes in H9c2 cardiomyoblasts. Cells were treated with 300μM of $CoCl_2$ (black) for different lengths of time. (**a**) WB of HIF-1α protein. Tubulin is showed as loading control. HIF-1α (**b**), GLUT1 (**c**), CAXII (**d**) and Met (**e**) mRNA expression levels were analysed and normalized using the β-actin. (**f**) WB of GAPDH protein, normalized using tubulin. The values are expressed as fold relative to NT (white) and are the mean ± SD of three independent experiments. T-test was calculated between treated samples vs NT. In (**e**) one-tailed T-test was significant. *p<0.05, **p<0.01 and ***p<0.005.

Supplementary Figure S4



Supplementary Figure S4 $CoCl_2$ treatment decreases the prosurvival pathways Akt, Erk and mTOR and impairs the response to HGF. H9c2 cells were untreated (white) or treated with 300μM $CoCl_2$ (black), HGF (0.5nM, light grey) or HGF+$CoCl_2$ (dark grey). Cells were treated for 48h and HGF was added in the last 1h. P-Akt (**a**), P-Erk (**b**), P-p70S6K and P-4EBP1 (**c**) protein levels were analysed by WB densitometry. Tubulin was used as loading control. Representative images are shown below each graph. The values are expressed as fold relative to NT and are the mean ± SD of three independent experiments. T-test was calculated between NT vs $CoCl_2$ and HGF vs HGF+$CoCl_2$. *p<0.05, **p<0.01 and ***p<0.005.

Supplementary Figure S5



Supplementary Figure S5 $CoCl_2$ induces autophagosome formation and maturation. Immunofluorescence images of LC3 autophagic marker (green) in H9c2 cells untreated (A) or treated with 300μM $CoCl_2$ alone (B), $CoCl_2$+3-MA (C) or $CoCl_2$+Baf (D) for 48h. 3-MA and Baf were added in the last 12h and 6h, respectively. DAPI-stained nuclei in blue. Bar: 17μm.

Supplementary Table S1. Antibodies used throughout the study.

Primary Antibody	Company	Dilution	Product n.	Exp
Met	Santa Cruz	1:1000	SP-260	IP
Gab1	Millipore	1:1000/ 5ug	06-579	IP
P-Met (TyR 1234/1235)	Upstate	1:1000		IP
P-Tyrosines	Santa Cruz	1:1000	PY99	IP
Bax	Santa Cruz	1:1000	sc-7480	WB
Bcl-2	BD Biosciences	1:1000	pS70	WB
Total/Cleaved Caspase 3	Cell Signaling	1:1000	9662	WB
Parp-1/2	Santa Cruz	1:1000	sc-7150	WB
Redd1 (RTP801)	Sigma	1:1000	PRS4509	WB
Bnip3	abcam	1:1000	ANa40	WB
P-AMPK thr172	Sigma	1:1000	SAB4503754	WB
AMPK	Sigma	1:1000	SAB4502329	WB
P-P70s6K thr389	Cell Signaling	1:1000	92052	WB
p70s6k	New England BioLabs	1:1000		WB
P-4ebp1 ser65	Cell Signaling	1:1000	9451	WB
4ebp1	Santa Cruz	1:1000	sc-9977	WB
Beclin1	Sigma	1:1000	B6186	WB
LC3B	Sigma	1:1000/1:200	L7543	WB/IF
p62	Sigma	1:1000	P0067	WB
HIF-1α	Novus Biologicals	1:1000	NB-100-479	WB
GAPDH	Open biosystems	1:1000	TAB1001	WB
α-tubulin	Sigma	1:1000	B-5-1-2	WB
Met	Zymed	1:200	3D4	IF
Connexin 43	Sigma	1:200	C6219	IF
Troponin-I	Millipore	1:200	1691	IF
Secondary Antibody				
Goat anti-mouse IG	Amersham	1:1000	31430	WB
Goat anti-rabbit IG	Amersham	1:1000	31460	WB
Alexa Fluor 488 anti-mouse	Molecular Probes/Invitrogen	1:500		IF
Alexa Fluor 488 anti-rabbit	Molecular Probes/Invitrogen	1:500		IF
Alexa Fluor 546 anti-mouse	Molecular Probes/Invitrogen	1:500		IF

Supplementary Table S2. Primers used throughout the study.

Gene	Forward	Reverse	Tm (°C)	Size (bp)
Redd1 RT-PCR	5'-GCCGGAGGAAGACTCCTCATA	5'-CATCAGGTTGGCACACAGGT	63	97
Bnip3 RT-PCR	5'-GCCATTGGATTGGGGATCTAC	5'-ACTGTGTGAGCAGAAGGCAG	63	92
Redd1 SQ-PCR	5'-CTTGTCCGCAATCTTCGCTG	5'-TATGAGGAGTCTTCCTCCGGC	60	298
Bnip3 SQ-PCR	5'-TACCTCTCAGTGGTCACTTC	5'-GTGGGTGTCAATTTCAGCTC	60	297
Beclin1	5′-CGCCTCCTATTCCATCAAAA	5′-AACTGTGAGGACACCCAAGC	60	111
LC3	5'-CACTGCTCTGTCTTGTGTAGGTTG	5'-TCGTTGTGCCTTTATTAGTGCATC	65	170
p62	5'-CCCAGTGTCTTGGCATTCTT	5'-AGGGAAAGCAGAGGAAGCTC	60	154
HIF-1α	5'-GCTTGGTGCTGTTTGTGAACC	5'-GCATCCTGTACTGTCCTGTGGTG	64	267
GLUT1	5'-CAGAAGGTAATTGAGGAGTTCTACA	5'-ACAAAGGCCAACAGGTTCATCATC	60	206
CAXII	5'-CAGCCATCAAGAAGGAGG	5'-ACTCCTGCCCCCTAGTTC	58	256
Met	5'-ACACCGTGGCGTGCCAACAT	5'-TCGCCGCCGTTCAGCTTCAG	55	364
β-actin SQ-PCR	5'-CACGATGGAGGGGCCGGACTCAT	5'-TAAAGACCTCTATGCCAACACAG	63	241
β-actin RT-PCR	5'-CGCGAGTACAACCTTCTTGC	5'-CGTCATCCATGGCGAACTGG	63	70