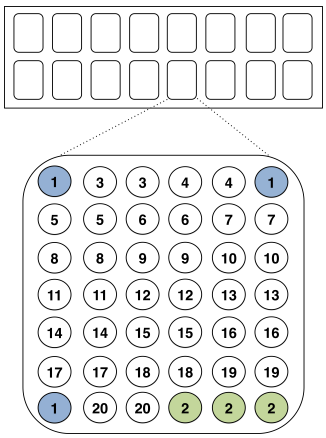
Supplementary Material

Incretin mimetics restore the ER-mitochondria axis and switch neuronal fate towards survival

Target	Blocking Buffer	Dilution Ratio	Isotype	Manufacturer	Catalog No.	RRID
β-Actin	5% w/v skimmed milk	$1:10^4$	Mouse IgG	Cell Signaling Technology	#3700	RRID:AB_2242334
ATF6[1-7]	5% w/v skimmed milk	1 : 500	Mouse IgG	Abcam	ab122897	RRID:AB_10899171
Atg3	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3415	RRID:AB_2059244
Atg7	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#8558	RRID:AB_10831194
Bcl-2	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3498	RRID:AB_1903907
BID	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#2002	RRID:AB_10692485
BiP	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3177	RRID:AB_2119845
Beclin-1	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3495	RRID:AB_1903911
Calnexin	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#2679	RRID:AB_2228381
CASP12	5% w/v skimmed milk	1 : 2000	Rabbit IgG	Abcam	ab62484	RRID:AB_955729
Chop	5% w/v skimmed milk	1 : 1000	Mouse IgG	Cell Signaling Technology	#2895	RRID:AB_2089254
Ero1-Lα	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3264	RRID:AB_823684
IRE1α	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3294	RRID:AB_823545
LC3B	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#2775	RRID:AB_915950
PDI	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3501	RRID:AB_215643
Phospho-Bcl-2 (Ser70)	5% w/v BSA	1 : 1000	Rabbit IgG	Cell Signaling Technology	#2827	RRID:AB_659950
Phospho-IRE1 (Ser724)	5% w/v BSA	1 : 1000	Rabbit IgG	Abcam	ab48187	RRID:AB_873899
PSD95	5% w/v/ skimmed milk	1 : 1000	Rabbit IgG	Cell Signaling Technology	#3450	RRID:AB_2292883
Synaptophysin	5% w/v skimmed milk	1 : 1000	Rabbit IgG	Abcam	ab7837	RRID:AB_306124

Supplementary Table 1. **List of the primary antibodies used in the Western blotting experiments**. For the list of the abbreviations used, please refer to the main text.



#	Target	Modification Site	Modification Type
1	Positive Control	N/A	N/A
2	Negative Control	N/A	N/A
3	ERK1/2	Thr 202/Tyr 204	Phosphorylation
4	Stat1	Tyr 701	Phosphorylation
5	Stat3	Tyr 705	Phosphorylation
6	Akt	The 308	Phosphorylation
7	Akt	Ser 4731	Phosphorylation
8	AMPKα	Thr 172	Phosphorylation
9	rpS6	Ser 235/236	Phosphorylation
10	mTOR	Ser 2448	Phosphorylation
11	HSP27	Ser 78	Phosphorylation
12	BAD	Ser 112	Phosphorylation
13	p70S6K	Thr 389	Phosphorylation
14	PRAS40	Thr 246	Phosphorylation
15	p53	Ser 15	Phosphorylation
16	p38	Thr 180/Tyr 182	Phosphorylation
17	SAPK/JNK	Thr 183/Tyr 185	Phosphorylation
18	PARP	Asp 214	Cleavage
19	CASP3	Asp 175	Cleavage
20	GSK3β	Ser 9	Phosphorylation

Supplementary Figure 1. **Array of the intercellular signalling targets included in the slide-based Pathscan® ELISA immunoassay.** Abbreviations used for modification sites: Asp, Aspartic Acid; Ser, Serine; Thr, Threonine; Tyr, Tyrosine.

Target	Modification Site	Mean ± SEM						One-way ANOVA	
		CNTRL	LIRA	DA	TG	TG + LIRA	TG + DA	$F_{(5,42)}$	p
ERK1/2	Thr 202/Tyr 204	1.00 ± 0.129	1.00 ± 0.105	1.00 ± 0.108	0.638 ± 0.158	0.830 ± 0.131	1.10 ± 0.197	1.385	0.2493
Stat1	Tyr 701	1.00 ± 0.205	0.891 ± 0.192	0.865 ± 0.212	0.855 ± 0.272	0.694 ± 0.160	1.05 ± 0.243	0.3311	0.8913
AMPKα	Thr 172	1.00 ± 0.062	0.881 ± 0.162	0.997 ± 0.109	0.678 ± 0.059	0.704 ± 0.079	0.733 ± 0.065	2.312	0.0607
p70S6K	Thr 389	1.00 ± 0.081	0.869 ± 0.255	0.893 ± 0.142	0.508 ± 0.084	0.887 ± 0.171	0.670 ± 0.066	1.478	0.2176
p38	Thr 180/Tyr 182	1.00 ± 0.116	1.12 ± 0.107	0.882 ± 0.106	0.787 ± 0.045	0.851 ± 0.156	0.864 ± 0.108	1.187	0.3317
SAPK/JNK	Thr 183/Tyr 185	1.00 ± 0.056	1.07 ± 0.102	0.911 ± 0.100	0.848 ± 0.088	0.836 ± 0.04	0.763 ± 0.084	1.937	0.1085

Supplementary Table 2. Signalling targets with non-significant differences in the expression levels. On d 6 of the differentiation period, post-mitotic neurones from the LUHMES cell line were treated with 0 and 100 nM of thapsigargin (TG) in the presence or absence of 100 nM Liraglutide (LIRA) or of 100 nM novel GLP-1/GIP Dual Agonist (DA) for 16 h. Neurones were then harvested, and 0.3 mg mL^{-1} protein of whole-cell lysate was processed with the PathScan® Intracellular Signalling Array Kit (#7323; Cell Signaling Technology, Greater London, UK). All samples per experiment were processed in duplicate. Data is expressed as fold change to the control (CNTRL; unstressed/untreated conditions). Differences among the groups was assessed with one-way ANOVA.