

SUPPLEMENTARY DATA

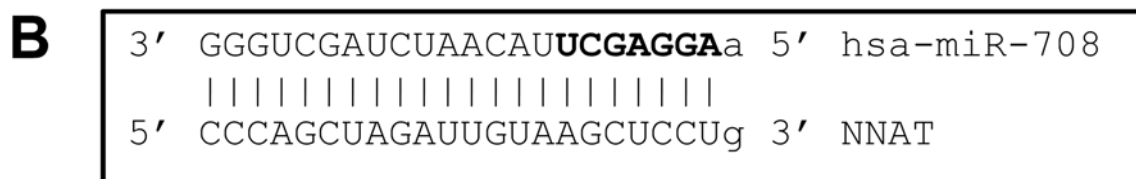
Supplementary Table S1. Primer sequences used for gene expression analysis for qPCR.

Gene	Species	Fw	Rv
<b>Ddit3/Chop</b>	Mouse	TCATCCCCAGGAAACGAAGAG	GCTTTGGGATGTGCGTGTG
<b>Odz4</b>	Mouse	CGGGCCAACTCCAACCTC	GCAGGCTGCTGGGATGATC
<b>Nnat</b>	Mouse	CACCCACTTTTCGGAACCATG	GCACGCGGAAGATGTACCAG
<b>Hprt1</b>	Mouse	GGTTAAGCAGTACAGCCCCA	TCCAACACTTCGAGAGGTCC
<b>Tbp1</b>	Mouse	ACCCTTACCAATGACTCCTATG	ATGATGACTGCAGCAAATCGC
<b>Pdx1</b>	Mouse	CCCCAGTTTACAAGCTCGCT	CTCGGTTCCATTCCGGGAAAGG
<b>Xbp1s</b>	Mouse	GAACCAGGAGTTAAGAACACG	AGGCAACAGTGTGAGAGTCC
<b>Atf6</b>	Mouse	CATTCGAAGGGATCATCTG	GTCTTGTGGTCTTGTTGTG
<b>Atf3</b>	Mouse	TCGGATGTCCTCTGCGCTGGA	CTGACTCTTCTGCAGGCACTCTGT
<b>Ddit/Chop</b>	Rat	CCAGCAGAGGTCACAAGCAC	CGCACTGACCACTCTGTTTT
<b>Tbp1</b>	Rat	GAGATCACCTGCAGCATCA	GCAGTGCCGCCCAAGTAG
<b>Nnat</b>	Rat	CAGCAGCCTCGGCAGAACT	CCCAGTAAATGCAGCATTCCAG
<b>Nnat*</b>	Mouse / Human	CTCGGCTGAACTGCTCATCA	GCAGCATTCCAGGAACACCT

\*These primers amplify both mouse and human *neuronatin*.

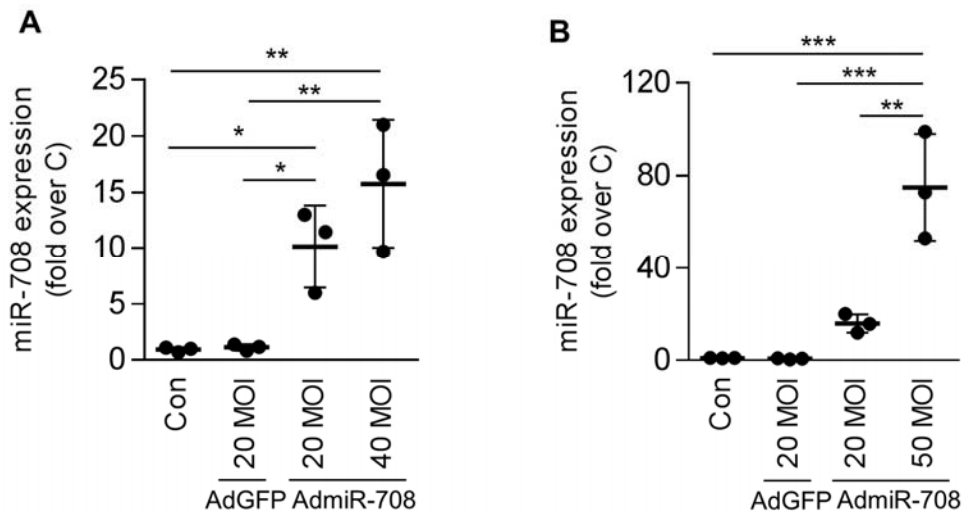
**Supplementary Figure S1. miR-708 sequence perfectly matches a 3'UTR region of *Nnat* mRNA.** (A-B) miR-708 sequence alignment of miR-708 from (A) mouse and from (B) human and the potential miR-708 binding site at *Nnat* 3'UTR from mouse (A) and human NNAT (B). Bold letters represent the seed sequence matching to the putative complementary site.

miR-708 / Nnat alignment



SUPPLEMENTARY DATA

**Supplementary Figure S2. miR-708 overexpression in islets and in DICs.** (A) miR-708 expression levels in non-transduced islets (Control) or islets transduced with AdGFP or AdmiR-708 (20 MOI and 40 MOI) 48h after transduction. (B) Dose-induced miR-708 overexpression in DICs transduced with AdmiR-708 20 MOI and 50 MOI 72h post-transduction. Further experiments were performed at 20 MOI given that miR-708 levels were similar to those induced by low glucose conditions. Results are expressed as mean  $\pm$  standard deviation from three independent experiments. \* $p$ <0.05, \*\* $p$ <0.01, \*\*\* $p$ <0.001.



SUPPLEMENTARY DATA

**Supplementary Figure S3. miR-708 inhibition and human neuronatin (*hNNAT*) and miR-708 overexpression in islets.** (A) *Nnat* expression in non-treated islets (Con) or islets treated with a control microRNA (Neg. Ctrl.; 500nM) or with an inhibitor of miR-708 ( $\alpha$ miR-708; 500nM) during a 2-day culture at 5mM glucose (G5) or at 11mM glucose (G11). (B) Effects of different doses of *hNNAT*-encoding adenoviruses on the expression of endogenous (*mNnat*) and transgene (*hNNAT*) neuronatin in pancreatic islets cultured at 11mM glucose for 2.5 days. Further experiments were performed at 5 MOI AdNnat. The primers used for this analysis recognized both the murine and human forms of *neuronatin*. (C) Endogenous (*mNnat*) and transgene (*hNNAT*) neuronatin expression in islets non-transduced (Con) or transduced with AdNnat (5 MOI), AdmiR-708 (20 MOI) or with both adenoviruses. (D) miR-708 expression in the same experiment as in B. Note in Figure B that, as expected, endogenous *Nnat* levels are decreased when miR-708 is overexpressed, whereas co-transduction of miR-708 and *hNNAT* results in total *neuronatin* levels similar to those observed in control islets. Results are expressed as mean  $\pm$  SEM from three independent experiments. \* $p$ <0.05, \*\* $p$ <0.01, \*\*\* $p$ <0.001. ### $p$ <0.001 to its respective control (G11).

