

Supplemental Table S1. Comparison of percentages of mouse hypothalamic neurons expressing NPFF receptors in studies selected for the re-analysis (Data are shown as means \pm SEM) [37–40].

	Npffr1 *	Npffr2 *	Npffr1 + Npffr2 *	Adjust Factor **	Npffr2 Adjusted (Npffr2 x Adjusted Factor)
Campbell et al., 2017	5.8	1.17	0.19	1.0	1.17
Kim et al., 2019	11.68	1.4	0.26	0.71	0.99
Mickelsen et al., 2019	8.28	0.0	0.0	0.64	0.0
Romanov et al., 2017	5.68	0.58	0.22	0.72	0.40

* % of neurons expressing gene or co-expressing genes. ** based on genes detected per cell.

Supplemental Table S2. Percentages of neurons expressing different neuronal markers in Npffr2-positive neuron population in mouse ARC (Data are shown as means \pm SEM; data from re-analysis [37]).

Gene	Number of Positive Cells	%
<i>Npffr2</i>	152	100
<i>Npy</i>	98	64.47
<i>Gad2</i>	98	64.47
<i>Gad1</i>	97	63.81
<i>Agrp</i>	91	59.86
<i>Pomc</i>	61	40.13
<i>Sst</i>	43	28.28
<i>Ddc</i>	40	26.31
<i>Slc17a6</i>	33	21.71
<i>Npffr1</i>	25	16.45
<i>Pnoc</i>	24	15.79
<i>Th</i>	7	4.60

Supplemental Table S3. List of significantly enriched gene in *Npffr2*-positive compared to *Npffr2*-negative mouse arcuate neurons (Data are shown as means \pm SEM) [37].

Gene	<i>p</i> Value	Mean log Fold Change	% of Npffr2+ Neurons Expressing Gene	% of Npffr2- Neurons Expressing Gene	<i>p</i> Value Adjusted
<i>Npffr2</i>	0	1.21	1	0	0
<i>Acvr1c</i>	1.94×10^{-35}	0.73	0.48	0.13	4.42×10^{-31}
<i>Agrp</i>	2.97×10^{-27}	1.03	0.60	0.24	6.77×10^{-23}
<i>Serpina3n</i>	6.00×10^{-25}	0.72	0.62	0.26	1.37×10^{-20}
<i>Gm8773</i>	7.90×10^{-22}	0.38	0.22	0.05	1.80×10^{-17}
<i>Npy2r</i>	2.88×10^{-20}	0.41	0.57	0.23	6.56×10^{-16}
<i>Npy</i>	1.09×10^{-18}	1.06	0.65	0.36	2.48×10^{-14}
<i>Otp</i>	6.38×10^{-18}	0.44	0.51	0.21	1.45×10^{-13}
<i>Cited1</i>	2.99×10^{-17}	0.58	0.80	0.51	6.82×10^{-13}
<i>Csgalnact1</i>	2.05×10^{-16}	0.26	0.31	0.10	4.67×10^{-12}
<i>Hspb8</i>	1.02×10^{-14}	0.27	0.28	0.09	2.32×10^{-10}
<i>Irs4</i>	1.22×10^{-14}	0.50	0.68	0.40	2.79×10^{-10}
<i>Ghr</i>	5.98×10^{-14}	0.36	0.41	0.17	1.36×10^{-9}
<i>Vwa5a</i>	7.39×10^{-14}	0.28	0.30	0.11	1.68×10^{-9}
<i>Dgkk</i>	9.15×10^{-14}	0.36	0.55	0.26	2.09×10^{-9}
<i>Arhgef28</i>	1.22×10^{-13}	0.40	0.42	0.18	2.78×10^{-9}
<i>Hspa1a</i>	1.86×10^{-13}	0.46	0.38	0.16	4.24×10^{-9}
<i>Prune2</i>	3.35×10^{-13}	0.39	0.66	0.35	7.63×10^{-9}
<i>Gnal</i>	2.43×10^{-12}	0.30	0.59	0.30	5.54×10^{-8}
<i>Flrt3</i>	6.49×10^{-12}	0.25	0.42	0.18	1.48×10^{-7}
<i>Phf6</i>	1.47×10^{-11}	0.35	0.39	0.17	3.36×10^{-7}
<i>B2m</i>	2.10×10^{-10}	0.27	0.54	0.29	4.78×10^{-6}
<i>Rpl13</i>	4.65×10^{-10}	0.30	0.74	0.46	1.06×10^{-5}
<i>Angpt1</i>	1.42×10^{-9}	0.27	0.22	0.08	3.23×10^{-5}
<i>Ociad2</i>	2.20×10^{-9}	0.34	0.64	0.39	5.01×10^{-5}
<i>Arhgap6</i>	1.36×10^{-8}	0.31	0.62	0.38	3.10×10^{-4}
<i>Jun</i>	1.91×10^{-8}	0.36	0.61	0.39	4.36×10^{-4}
<i>Tmem255a</i>	3.05×10^{-8}	0.28	0.73	0.46	6.96×10^{-4}
<i>Dnm3</i>	6.50×10^{-8}	0.29	0.81	0.58	1.48×10^{-3}
<i>Arhgap36</i>	6.63×10^{-8}	0.32	0.59	0.37	1.51×10^{-3}
<i>1500012F01Rik</i>	7.43×10^{-8}	0.33	0.72	0.50	1.69×10^{-3}
<i>Gas5</i>	8.82×10^{-8}	0.27	0.90	0.77	2.01×10^{-3}
<i>Eef2</i>	9.33×10^{-8}	0.27	0.88	0.66	2.13×10^{-3}
<i>Rgs2</i>	1.26×10^{-7}	0.43	0.73	0.55	2.88×10^{-3}
<i>Ndn</i>	2.49×10^{-7}	0.26	0.92	0.74	5.67×10^{-3}
<i>Fos</i>	8.08×10^{-7}	0.27	0.49	0.29	1.84×10^{-2}

Supplemental Table S4. Results from the main gene expression analysis. The Delta (Δ CT) relative quantification method was used to evaluate mRNA levels of target genes relative to a housekeeping gene (ACTB) in hNSC, hDHN and hALN (Data are shown as means \pm SEM).

Gene ID	hNSC (n=3)		hDHN (n=3)		hALN (n=2)	
	Mean	SEM	Mean	SEM	Mean	SEM
<i>AGRP</i>	13.21	1.04	16.23	0.67	15.14	0.38
<i>ASCL1</i>	4.51	0.55	4.58	0.65	6.22	0.21
<i>CARTPT</i>	-	-	15.27~	~	11.30	0.30
<i>CRH</i>	7.66	0.19	12.96	1.03	12.80	0.20
<i>DBX1</i>	13.73	0.50	10.74*	0.09	13.98	0.15
<i>EMX1</i>	10.59	0.90	-	-	15.01~	~
<i>EN2</i>	15.42	0.78	15.89	0.72	14.01	0.23
<i>FOXP1</i>	4.13	0.52	4.75	0.10	6.83	0.01
<i>GAD1</i>	10.19	0.52	7.61	0.32	4.20	0.13
<i>GAD2</i>	10.70	0.23	7.26*	0.18	7.70	0.26
<i>KISS1</i>	-	-	-	-	15.65	0.63
<i>MAP2</i>	423	0.36	3.37	0.20	3.54	0.33
<i>MCH</i>	11.81	0.63	14.88	0.66	8.74	0.27
<i>NEUN</i>	10.21	0.57	10.83	0.27	9.13	0.24
<i>NEUROD1</i>	7.09	0.65	6.40	0.28	10.33	0.32
<i>NEUROG3</i>	9.83	1.61	12.65	1.57	15.08	1.12
<i>NHLH2</i>	9.86	1.69	12.32	0.92	12.11	0.10
<i>NKX2.1</i>	9.24*	0.52	7.17	0.05	8.46	0.88
<i>NPFFR1</i>	15.13	1.02	15.80	0.59	11.76	0.44
<i>NPFFR2</i>	12.88	0.91	13.67	0.24	9.99	0.67
<i>NPY</i>	11.58	0.28	14.38	0.31	9.65	0.39
<i>OTP</i>	15.71	1.25	13.90	0.32	7.75*	0.01
<i>PAX6</i>	3.45	0.45	7.25	0.20	7.23	0.01
<i>POMC</i>	12.24	1.66	-	-	13.29	0.50
<i>POU5F1</i>	10.01	2.38	12.33	1.77	11.47	0.11
<i>RAX</i>	13.94	1.16	15.56	0.35	15.43	0.06
<i>SIM1</i>	12.94	0.73	12.98	0.39	7.89	0.34
<i>SLC17A7</i>	13.14	0.77	13.50	0.24	12.39	0.04
<i>SOX1</i>	9.63	0.80	11.69	0.60	12.45	0.00
<i>SST</i>	9.46	0.29	8.38	0.27	8.55	0.21
<i>TH</i>	12.62	1.23	11.68 *	0.30	9.29*	0.11
<i>TRH</i>	11.08	1.10	11.39	0.26	6.94	1.12

- Undetermined Ct values after 40 cycles. ~ Only one Ct value available. * p value < 0.05.

Supplemental Table S5. List of primers used in this study.

Gene	TaqMan Reference
<i>18S</i>	Hs99999901_s1
<i>ACTB</i>	Hs01060665_g1
<i>AGRP</i>	Hs003614403_g1
<i>ASCL1</i>	Hs00269932_m1
<i>CARTPT</i>	Hs00182861_m1
<i>CRH</i>	Hs01921237_s1
<i>DDX1</i>	Hs01380082_m1
<i>EMX1</i>	Hs00417957_m1
<i>EN2</i>	Hs00171321_m1
<i>FOXG1</i>	Hs00702391_s1
<i>GAD1</i>	Hs01065893_m1
<i>GAD2</i>	Hs00609534_m1
<i>KISS1</i>	Hs00158486_m1
<i>MAP2</i>	Hs00258900_m1
<i>MCH</i>	Hs01041242_g1
<i>NEUN</i>	Hs02760627_g1
<i>NEUROD1</i>	Hs01922995_s1
<i>NEUROG3</i>	Hs01875204_s1
<i>NHLH2</i>	Hs00271585_s1
<i>NKX2.1</i>	Hs00968940_m1
<i>NPFFR1</i>	HS00223340_m1
<i>NPFFR2</i>	Hs01003259_m1
<i>NPY</i>	Hs00173470_m1
<i>OTP</i>	Hs00259528_m1
<i>PAX6</i>	Hs01088106_g1
<i>POMC</i>	Hs01596743_m1
<i>POU5F1</i>	Hs04995079_g1
<i>RAX</i>	Hs00429459_m1
<i>SIM1</i>	Hs00231914_m1
<i>SLC17A7</i>	Hs00220404_m1
<i>SOX1</i>	Hs01057642_s1
<i>SST</i>	Hs00356144_m1
<i>TH</i>	Hs00165941_m1
<i>TRH</i>	Hs00999489_m1