

**Supplementary Table 1. Statistical tests**

Figures	Statistical test	Comparisons	p-value
1d_food intake	Two-way ANOVA with Fisher's LSD test	Light:WT vs. Dark:WT	0.0002
		Light:KO vs. Dark:KO	0.0007
		Dark:WT vs. Dark:KO	0.6011
		Light:WT vs. Light:KO	> 0.9999
1f_GTT_ZT0	Two-way ANOVA with Holm-Sidak's multiple comparisons test	WT vs. KO 0 min	0.2889
		WT vs. KO 15 min	0.6357
		WT vs. KO 30 min	0.8518
		WT vs. KO 60 min	0.0929
		WT vs. KO 90 min	0.0317
		WT vs. KO 120 min	0.0362
1h_GTT_ZT12	Two-way ANOVA with Holm-Sidak's multiple comparisons test	WT vs. KO 0 min	0.6719
		WT vs. KO 15 min	0.0002
		WT vs. KO 30 min	< 0.0001
		WT vs. KO 60 min	0.0006
		WT vs. KO 90 min	0.2643
		WT vs. KO 120 min	0.5829
1j_GIR	Two-way ANOVA with Fisher's LSD test	ZT0-2:WT vs. ZT0-2:KO	0.0009
		ZT6-8:WT vs. ZT6-8:KO	0.0018
		ZT12-14:WT vs. ZT12-14:KO	< 0.0001
		ZT0-2:WT vs. ZT6-8:WT	0.0253
		ZT0-2:WT vs. ZT12-14:WT	0.6632
		ZT6-8:WT vs. ZT12-14:WT	0.0099
1k_HGP	Two-way ANOVA with Fisher's LSD test	ZT0-2:WT vs. ZT0-2:KO	0.0215
		ZT6-8:WT vs. ZT6-8:KO	0.0017
		ZT12-14:WT vs. ZT12-14:KO	0.0001
		ZT0-2:WT vs. ZT6-8:WT	0.0012
		ZT0-2:WT vs. ZT12-14:WT	0.2819
		ZT6-8:WT vs. ZT12-14:WT	< 0.0001
1l_GDR	Two-way ANOVA with Fisher's LSD test	ZT0-2:WT vs. ZT0-2:KO	0.0898
		ZT6-8:WT vs. ZT6-8:KO	0.8612
		ZT12-14:WT vs. ZT12-14:KO	0.1216
		ZT0-2:WT vs. ZT6-8:WT	0.1896
		ZT0-2:WT vs. ZT12-14:WT	0.4984
		ZT6-8:WT vs. ZT12-14:WT	0.0548
1m_Basal HGP	Two-way ANOVA with Fisher's LSD test	ZT0-2:WT vs. ZT0-2:KO	0.7985
		ZT6-8:WT vs. ZT6-8:KO	0.6466
		ZT12-14:WT vs. ZT12-14:KO	0.6645
		ZT0-2:WT vs. ZT6-8:WT	0.2222
		ZT0-2:WT vs. ZT12-14:WT	0.0178
		ZT6-8:WT vs. ZT12-14:WT	0.1957
2a_firing	Two-way ANOVA with Fisher's LSD test, n = 15 neurons from 3 WT mice and 16 neurons from 3 KO mice for ZT0-2, n = 17 neurons from 3 WT mice and 16 neurons from 3 KO mice at ZT6-8, n =	ZT0-2:WT vs. ZT0-2:KO	0.0002
		ZT6-8:WT vs. ZT6-8:KO	0.2038
		ZT12-14:WT vs. ZT12-14:KO	<0.0001
		ZT0-2:WT vs. ZT6-8:WT	0.0659
		ZT0-2:WT vs. ZT12-14:WT	0.0324

	12 neurons from 3 WT mice and 16 neurons from 3 KO mice for ZT12-14	ZT6-8:WT vs. ZT12-14:WT	0.0001
2b_RM	Two-way ANOVA with Fisher's LSD test, n = 15 neurons from 3 WT mice and 18 neurons from 4 KO mice for ZT0-2, n = 18 neurons from 4 WT mice and 17 neurons from 3 KO mice for ZT6-8, n = 15 neurons from 3 WT mice and 17 neurons from 3 KO mice for ZT12-14	ZT0-2:WT vs. ZT0-2:KO	<0.0001
		ZT6-8:WT vs. ZT6-8:KO	0.297
		ZT12-14:WT vs. ZT12-14:KO	<0.0001
		ZT0-2:WT vs. ZT6-8:WT	0.0002
		ZT0-2:WT vs. ZT12-14:WT	0.6676
		ZT6-8:WT vs. ZT12-14:WT	<0.0001
2c_amp EPSC	Two-way ANOVA with Fisher's LSD test, n = 15 neurons from 3 WT mice and 12 neurons from 3 KO mice for ZT0-2, n = 12 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT6-8, n = 12 neurons from 3 WT mice and 10 neurons from 3 KO mice for ZT12-14	ZT0-2:WT vs. ZT0-2:KO	<0.0001
		ZT6-8:WT vs. ZT6-8:KO	<0.0001
		ZT12-14:WT vs. ZT12-14:KO	<0.0001
		ZT0-2:WT vs. ZT6-8:WT	0.0161
		ZT0-2:WT vs. ZT12-14:WT	0.5455
		ZT6-8:WT vs. ZT12-14:WT	0.082
2d_freq EPSC	Two-way ANOVA with Fisher's LSD test, n = 15 neurons from 3 WT mice and 12 neurons from 3 KO mice for ZT0-2, n = 12 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT6-8, n = 12 neurons from 3 WT mice and 10 neurons from 3 KO mice for ZT12-14	ZT0-2:WT vs. ZT0-2:KO	0.0013
		ZT6-8:WT vs. ZT6-8:KO	0.0751
		ZT12-14:WT vs. ZT12-14:KO	0.0285
		ZT0-2:WT vs. ZT6-8:WT	0.2538
		ZT0-2:WT vs. ZT12-14:WT	0.4059
		ZT6-8:WT vs. ZT12-14:WT	0.7663
2e_amp IPSC	Two-way ANOVA with Fisher's LSD test, n = 11 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT0-2, n = 12 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT6-8, n = 12 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT12-14	ZT0-2:WT vs. ZT0-2:KO	0.9566
		ZT6-8:WT vs. ZT6-8:KO	0.9831
		ZT12-14:WT vs. ZT12-14:KO	0.0247
		ZT0-2:WT vs. ZT6-8:WT	0.629
		ZT0-2:WT vs. ZT12-14:WT	0.002
		ZT6-8:WT vs. ZT12-14:WT	0.0068
2f_freq IPSC	Two-way ANOVA with Fisher's LSD test, n = 11 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT0-2, n = 12 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT6-8, n = 12 neurons from 3 WT mice and 11 neurons from 3 KO mice for ZT12-14	ZT0-2:WT vs. ZT0-2:KO	0.0124
		ZT6-8:WT vs. ZT6-8:KO	0.9079
		ZT12-14:WT vs. ZT12-14:KO	0.062
		ZT0-2:WT vs. ZT6-8:WT	0.0015
		ZT0-2:WT vs. ZT12-14:WT	0.3055
		ZT6-8:WT vs. ZT12-14:WT	0.0224
2h_Nr1d1	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.3608
		ZT6:WT vs. ZT6:KO	<0.0001
		ZT12:WT vs. ZT12:KO	0.4618
		ZT0:WT vs. ZT6:WT	<0.0001
		ZT0:WT vs. ZT12:WT	0.2847
		ZT6:WT vs. ZT12:WT	<0.0001
2i_Nr1d2	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.2351
		ZT6:WT vs. ZT6:KO	<0.0001
		ZT12:WT vs. ZT12:KO	0.3303
		ZT0:WT vs. ZT6:WT	<0.0001
		ZT0:WT vs. ZT12:WT	0.3593
		ZT6:WT vs. ZT12:WT	<0.0001
2j_Rgs16	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	< 0.0001
		ZT6:WT vs. ZT6:KO	0.3071
		ZT12:WT vs. ZT12:KO	0.0407
		ZT0:WT vs. ZT6:WT	0.0004

		ZT0:WT vs. ZT12:WT	0.4171
		ZT6:WT vs. ZT12:WT	< 0.0001
2k_Takusan	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	< 0.0001
		ZT6:WT vs. ZT6:KO	0.0033
		ZT12:WT vs. ZT12:KO	< 0.0001
		ZT0:WT vs. ZT6:WT	0.0097
		ZT0:WT vs. ZT12:WT	0.7734
		ZT6:WT vs. ZT12:WT	0.0193
		3b_M3 ZT14 CNO	Two-way ANOVA with Holm-Sidak's test
mCherry vs hM3Dq 15 min	0.959		
mCherry vs hM3Dq 30 min	< 0.0001		
mCherry vs hM3Dq 60 min	< 0.0001		
mCherry vs hM3Dq 90 min	0.0595		
mCherry vs hM3Dq 120 min	0.8553		
3e_M4_GTT ZT14 wo CNO	Two-way ANOVA with Holm-Sidak's test	WT vs KO 0 min	0.5598
		WT vs KO 15 min	0.0265
		WT vs KO 30 min	< 0.0001
		WT vs KO 60 min	< 0.0001
		WT vs KO 90 min	0.0265
		WT vs KO 120 min	0.2664
3g_M4 PTT ZT14 wo CNO	Two-way ANOVA with Holm-Sidak's multiple comparisons test	WT vs KO 0 min	0.5367
		WT vs KO 15 min	0.0959
		WT vs KO 30 min	0.0017
		WT vs KO 60 min	0.0157
		WT vs KO 90 min	0.3134
		WT vs KO 120 min	0.3134
3k_DoxZT0_GTT ZT14	Two-way ANOVA with Holm-Sidak's multiple comparisons test	Control vs iRev-erb 0 min	0.5838
		Control vs iRev-erb 15 min	0.0002
		Control vs iRev-erb 30 min	< 0.0001
		Control vs iRev-erb 60 min	< 0.0001
		Control vs iRev-erb 90 min	0.5838
		Control vs iRev-erb120 min	0.9124
4b_CGM	Two-way ANOVA with Holm-Sidak's multiple comparisons test (DP- vs. DP+ at the indicated time points)	-2	0.9941
		-1.91667	0.9941
		-1.83333	0.9941
		-1.75	0.9941
		-1.66667	0.9941
		-1.58333	0.9941
		-1.5	0.9941
		-1.41667	0.9941
		-1.33333	0.9935
		-1.25	0.9883
		-1.16667	0.9855
		-1.08333	0.9636
		-1	0.9855
		-0.91667	0.9855
-0.83333	0.988		

-0.75	0.9941
-0.66667	0.9941
-0.58333	0.9941
-0.5	0.9941
-0.41667	0.9941
-0.33333	0.9941
-0.25	0.9941
-0.16667	0.9941
-0.08333	0.9935
0	0.9721
0.083333	0.9721
0.166667	0.9138
0.25	0.7865
0.333333	0.6772
0.416667	0.4055
0.5	0.2299
0.583333	0.1183
0.666667	0.0977
0.75	0.0571
0.833333	0.0484
0.916667	0.019
1	0.0145
1.083333	0.008
1.166667	0.0048
1.25	0.0025
1.333333	0.0015
1.416667	0.0005
1.5	0.0005
1.583333	0.0004
1.666667	0.0002
1.75	< 0.0001
1.833333	< 0.0001
1.916667	< 0.0001
2	< 0.0001
2.083333	< 0.0001
2.166667	< 0.0001
2.25	< 0.0001
2.333333	< 0.0001
2.416667	< 0.0001
2.5	< 0.0001
2.583333	< 0.0001
2.666667	0.0002
2.75	0.0007
2.833333	0.0037
2.916667	0.0092
3	0.0118
3.083333	0.0283

		3.166667	0.0845
		3.25	0.1462
		3.333333	0.2976
		3.416667	0.4319
		3.5	0.6953
		3.583333	0.8956
		3.666667	0.9865
		3.75	0.9941
		3.833333	0.9941
		3.916667	0.9941
		4	0.9941
4g_Rev-erba	Two-way ANOVA with Holm-Sidak's multiple comparisons test	7am DP- vs. DP+	0.8585
		1pm DP- vs. DP+	0.8585
		7pm DP- vs. DP+	0.0454
		1am DP- vs. DP+	0.8257
4h_Rev-erbb	Two-way ANOVA with Holm-Sidak's multiple comparisons test	7am DP- vs. DP+	0.9326
		1pm DP- vs. DP+	0.7803
		7pm DP- vs. DP+	0.0408
		1am DP- vs. DP+	0.1355
Extended Data 1c	Two-sided student's t-test	KO vs. WT	<0.0001
Extended Data 1g	Two-sided student's t-test	KO vs. WT	<0.0001
Extended Data 2b_food for 6hr fasting	Two-way ANOVA with Fisher's LSD test	ZT18-0:WT vs. ZT18-0:KO	0.6608
		ZT0-6:WT vs. ZT0-6:KO	0.8107
		ZT6-12:WT vs. ZT6-12:KO	0.8107
		ZT18-0:WT vs. ZT0-6:WT	< 0.0001
		ZT18-0:WT vs. ZT6-12:WT	0.0012
		ZT0-6:WT vs. ZT6-12:WT	0.1456
Extended Data 2c_food for 12hr fasting	Two-way ANOVA with Fisher's LSD test	ZT12-0:WT vs. ZT12-0:KO	0.5897
		ZT18-6:WT vs. ZT18-6:KO	0.9174
		ZT0-12:WT vs. ZT0-12:KO	0.8037
		ZT12-0:WT vs. ZT18-6:WT	0.0024
		ZT12-0:WT vs. ZT0-12:WT	< 0.0001
		ZT18-6:WT vs. ZT0-12:WT	0.069
Extended Data 2d_glucose	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.0375
		ZT6:WT vs. ZT6:KO	0.414
		ZT12:WT vs. ZT12:KO	0.7979
		ZT18:WT vs. ZT18:KO	0.4257
Extended Data 2g_Corticosterone	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.4436
		ZT6:WT vs. ZT6:KO	0.6346
		ZT12:WT vs. ZT12:KO	< 0.0001
		ZT18:WT vs. ZT18:KO	0.0643
Extended Data 2h_GLP-1	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.0001
		ZT6:WT vs. ZT6:KO	0.0883
		ZT12:WT vs. ZT12:KO	0.1006
		ZT18:WT vs. ZT18:KO	0.0003
Extended Data 2i_GH	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.8875
		ZT6:WT vs. ZT6:KO	0.5553

		ZT12:WT vs. ZT12:KO	0.0063
		ZT18:WT vs. ZT18:KO	0.3708
Extended Data 2k_GTT	Two-way ANOVA with Holm-Sidak's test	WT vs KO 0 min	0.7532
		WT vs KO 15 min	0.0003
		WT vs KO 30 min	0.0154
		WT vs KO 60 min	0.1755
		WT vs KO 90 min	0.7532
		WT vs KO 120 min	0.7532
		Extended Data 2o_HGP suppression	Two-way ANOVA with Fisher's LSD test
ZT6-8:WT vs. ZT6-8:KO	0.0015		
ZT12-14:WT vs. ZT12-14:KO	0.0002		
ZT0-2:WT vs. ZT6-8:WT	0.0026		
ZT0-2:WT vs. ZT12-14:WT	0.1059		
ZT6-8:WT vs. ZT12-14:WT	< 0.0001		
Extended Data 3c_GTT	Two-way ANOVA with Holm-Sidak's test	WT vs KO 0 min	0.8045
		WT vs KO 15 min	0.005
		WT vs KO 30 min	0.0038
		WT vs KO 60 min	0.0009
		WT vs KO 90 min	0.0374
		WT vs KO 120 min	0.6857
Extended Data 3e_ITT	Two-way ANOVA with Holm-Sidak's test	WT vs KO 0 min	0.0003
		WT vs KO 15 min	< 0.0001
		WT vs KO 30 min	< 0.0001
		WT vs KO 60 min	0.015
		WT vs KO 90 min	0.0005
		WT vs KO 120 min	< 0.0001
Extended Data 3h_glucose	Two-way ANOVA with Fisher's LSD test	0:WT vs. 0:KO	0.7175
		5:WT vs. 5:KO	0.2068
		10:WT vs. 10:KO	0.0013
		15:WT vs. 15:KO	< 0.0001
Extended Data 3i_glucose	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.0325
		ZT6:WT vs. ZT6:KO	0.0467
		ZT12:WT vs. ZT12:KO	0.0082
		ZT18:WT vs. ZT18:KO	0.0081
Extended Data 4a_VIP	One-way ANOVA with Tukey post-test	SCN vs. LH	<0.0001
		SCN vs. PVN	<0.0001
		SCN vs. VMH	<0.0001
		SCN vs. ARC	<0.0001
Extended Data 4b_Pmch	One-way ANOVA with Tukey post-test	SCN vs. LH	<0.0001
		LH vs. PVN	<0.0001
		LH vs. VMH	<0.0001
		LH vs. ARC	<0.0001
Extended Data 4c_CRF	One-way ANOVA with Tukey post-test	SCN vs. PVN	<0.0001
		LH vs. PVN	<0.0001
		PVN vs. VMH	<0.0001
		PVN vs. ARC	<0.0001
	One-way ANOVA with Tukey post-test	SCN vs. VMH	<0.0001

Extended Data 4d_Rfrp		LH vs. VMH	<0.0001
		PVN vs. VMH	<0.0001
		VMH vs. ARC	<0.0001
Extended Data 4e_Pomc1	One-way ANOVA with Tukey post-test	SCN vs. ARC	<0.0001
		LH vs. ARC	<0.0001
		PVN vs. ARC	<0.0001
		VMH vs. ARC	<0.0001
Extended Data 4f_Nr1d1	Two-sided student's t-test	SCN: KO vs. WT	0.0004
		LH: KO vs. WT	0.0048
		PVN: KO vs. WT	0.3442
		VMH: KO vs. WT	0.1244
		ARC: KO vs. WT	0.4985
		Liver: KO vs. WT	0.6002
Extended Data 4g_Nr1d2	Two-sided student's t-test	SCN: KO vs. WT	<0.0001
		LH: KO vs. WT	0.0007
		PVN: KO vs. WT	0.1053
		VMH: KO vs. WT	0.0826
		ARC: KO vs. WT	0.2370
		Liver: KO vs. WT	0.2201
Extended Data 4h_BMAL1	Two-sided student's t-test	SCN: KO vs. WT	0.0092
		LH: KO vs. WT	0.0070
		PVN: KO vs. WT	0.6281
		VMH: KO vs. WT	0.5381
		ARC: KO vs. WT	0.3627
		Liver: KO vs. WT	0.1097
Extended Data 4i_Npas2	Two-sided student's t-test	SCN: KO vs. WT	0.0304
		LH: KO vs. WT	0.2737
		PVN: KO vs. WT	0.5182
		VMH: KO vs. WT	0.6693
		ARC: KO vs. WT	0.2593
		Liver: KO vs. WT	0.2153
Extended Data 5h_Nr1d1	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	<0.0001
		ZT6:WT vs. ZT6:KO	0.0035
		ZT12:WT vs. ZT12:KO	0.1251
		ZT0:WT vs. ZT6:WT	0.0042
		ZT0:WT vs. ZT12:WT	0.0661
		ZT6:WT vs. ZT12:WT	<0.0001
Extended Data 5i_Nr1d2	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.0003
		ZT6:WT vs. ZT6:KO	0.0921
		ZT12:WT vs. ZT12:KO	0.1814
		ZT0:WT vs. ZT6:WT	0.0013
		ZT0:WT vs. ZT12:WT	0.0364
		ZT6:WT vs. ZT12:WT	<0.0001
Extended Data 5j_BMAL1	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	0.5385
		ZT6:WT vs. ZT6:KO	0.8035
		ZT12:WT vs. ZT12:KO	<0.0001
		ZT0:WT vs. ZT6:WT	0.9873

		ZT0:WT vs. ZT12:WT	0.0163
		ZT6:WT vs. ZT12:WT	0.0157
Extended Data 5k_Npas2	Two-way ANOVA with Fisher's LSD test	ZT0:WT vs. ZT0:KO	<0.0001
		ZT6:WT vs. ZT6:KO	0.0035
		ZT12:WT vs. ZT12:KO	0.1822
		ZT0:WT vs. ZT6:WT	0.0549
		ZT0:WT vs. ZT12:WT	0.0768
		ZT6:WT vs. ZT12:WT	0.0006
Extended Data 5m_RNAscope	Two-way ANOVA with Fisher's LSD test	WT:ZT4 vs. WT:ZT16	0.0028
		WT:ZT4 vs. KO:ZT4	0.5841
		WT:ZT16 vs. KO:ZT16	0.012
Extended Data 5o_ISH	Two-way ANOVA with Fisher's LSD test	WT:ZT4 vs. WT:ZT16	0.0075
		WT:ZT4 vs. KO:ZT4	0.0053
		WT:ZT16 vs. KO:ZT16	0.0008
Extended Data 5q_ChIP-qPCR	Two-way ANOVA with Fisher's LSD test	Control: ZT21 vs. ZT9	0.9796
		Rgs16: ZT21 vs. ZT9	0.0047
		Gm10406: ZT21 vs. ZT9	0.0058
		Gm2897: ZT21 vs. ZT9	0.0372
		Gm3411: ZT21 vs. ZT9	0.0004
		Npas2: ZT21 vs. ZT9	0.0016
		Bmal1: ZT21 vs. ZT9	<0.0001
Extended Data 6b_GTT_ZT6	Two-way ANOVA with Holm-Sidak's test	GFP vs. Rgs16 0 min	0.9592
		GFP vs. Takusan 0 min	0.9736
		GFP vs. Rgs16 15 min	0.0089
		GFP vs. Takusan 15 min	0.0052
		GFP vs. Rgs16 30 min	< 0.0001
		GFP vs. Takusan 30 min	< 0.0001
		GFP vs. Rgs16 60 min	0.4989
		GFP vs. Takusan 60 min	0.2
		GFP vs. Rgs16 90 min	0.5859
		GFP vs. Takusan 90 min	0.2271
		GFP vs. Rgs16 120 min	0.6244
		GFP vs. Takusan 120 min	0.6244
Extended Data 6c_GTT_ZT12	Two-way ANOVA with Holm-Sidak's test	GFP vs. Rgs16 0 min	0.9697
		GFP vs. Takusan 0 min	0.9697
		GFP vs. Rgs16 15 min	< 0.0001
		GFP vs. Takusan 15 min	< 0.0001
		GFP vs. Rgs16 30 min	< 0.0001
		GFP vs. Takusan 30 min	< 0.0001
		GFP vs. Rgs16 60 min	< 0.0001
		GFP vs. Takusan 60 min	0.0006
		GFP vs. Rgs16 90 min	0.6603
		GFP vs. Takusan 90 min	0.3222
		GFP vs. Rgs16 120 min	0.9916
		GFP vs. Takusan 120 min	0.894
Extended Data 6e_ITT_ZT14	Two-way ANOVA with Holm-Sidak's test	GFP vs. Rgs16 0 min	> 0.9999
		GFP vs. Takusan 0 min	> 0.9999



		GFP vs. Rgs16 15 min	0.2091
		GFP vs. Takusan 15 min	0.0102
		GFP vs. Rgs16 30 min	0.0142
		GFP vs. Takusan 30 min	< 0.0001
		GFP vs. Rgs16 60 min	0.0005
		GFP vs. Takusan 60 min	< 0.0001
		GFP vs. Rgs16 90 min	0.3282
		GFP vs. Takusan 90 min	0.113
		GFP vs. Rgs16 120 min	0.822
		GFP vs. Takusan 120 min	0.1683
Extended Data 8e_RT-qPCR	Two-sided student's t-test	Bmal1: Control vs. iRev-erb	0.0739978
		Clock: Control vs. iRev-erb	0.364558
		Npas2: Control vs. iRev-erb	0.0089462
		Rgs16: Control vs. iRev-erb	0.0024738
		Takusan: Control vs. iRev-erb	0.002927

**Supplementary Table 2.** Primer sequences for RT-qPCR and ChIP-qPCR.**RT-qPCR (mouse)**

Rev-erba (span loxP)	TACAAGTGGCCATGGAAGAC	CCCACACACCTTACACAGTAG
Rev-erbβ (span loxP)	TCGATGGTGTCTGAAGAGTG	CCCACAGACTTTACACAGTAGAA
Rev-erba (not span loxP)	TACATTGGCTCTAGTGGCTCC	CAGTAGGTGATGGTGGGAAGTA
Rev-erbβ (not span loxP)	TGAACGCAGGAGGTGTGATTG	GAGGACTGGAAGCTATTCTCAGA
Rgs16	GGTACTTGCTACTCGCTTTTCC	CAGCCGCGTCTTGA ACTCT
α7-Takusan (GM10406)	AGAGAAGTGCTGGAGGAAGA	GCATTTCTCTGAGTCCCTTT
Bmal1	CGCCGCTCTCTGTTCTGTAG	GTGTCGAGAAACGTA CTCCATAG
Npas2	ATGTTTCGAGTGGAAAGGAGAC	CAAGTGCATTAAAGGGCTGTG
Vip	GA ACTTCAGCACCCCTAGACAG	GAAGAGTATCAGGAATGCCAGG
Pmch	GTCTGGCTGTAAAACCTTACCTC	CCTGAGCATGTCAAATCTCTCC
Crf	CCTCAGCCGGTTCTGATCC	GCGGAAAAAGTTAGCCGCAG
Rfrp	CTGATTTGCCACAGAAACCC	CATCTGTTTCCACAAACGCTC
Pomc1	GAGGTTAAGAGCAGTGA CTAAAGAG	AGAATCTCGGCATCTTCCAC
18S	AGTCCCTGCCCTTTGTACACA	CGATCCGAGGGCCTCACTA

**RT-qPCR (human)**

Rev-erba	CCTTGGAGACTTCCCGCTTC	ATTTACAAGAAGGCTCAGGGGG
Rev-erbβ	TCATGCTTGCGAAGGCTGTAA	CGCTTAGGAATACGACCAAACC
PER2	GCGTGTTCCACAGTTTCACC	GCGGATTTCA TTCTCGTGCC
PER3	TTTGTGAATCCCTGGAGCCG	TCATTTAGTGGGCTCGTTCCG
CLOCK	TGCGAGGAACAATAGACCCAA	ATGGCCTATGTGTGCGTTGTA
BMAL1	CATTAAGAGGTGCCACCAATCC	TCATTCTGGCTGTAGTTGAGGA
18S	ATCACCATTATGCAGAATCCACG	GACCTGGCTGTATTTTCCATCC

**ChIP-qPCR (mouse)**

Bmal1	AGCGGATTGGTCGGAAAGT	ACCTCCGTCCCTGACCTACT
Npas2	CTTGCCGATCCTTGACCCAT	CTCAGGTTACTGGGGACGTG
Rgs16	CACTCTCTTATTGGTCGGCG	GTAGCAAGTACCAGGCTGCG
Takusan (GM10406)	CAGCCTGGGAGGAAATGGTG	CTTCCGGAACGGAACCTGG
Takusan (LOC100861615, or NM_001270812)	TTCCATTCCGGAAGCGGTC	GCACGGAAATGGTCCTCTCT
Takusan (Gm2897)	GGCTCACCTCTTGACCTCG	GTCCTTGACCCTCGGAACAG

**ISH probe for Takusan  
(Gm3500) (mouse)**

AAATTGGATATGAGGAAGATCAGCAATGACATGGAGGAAATGTGTGGAATCCTGAACCTTTACATGTAT  
GAGGATTTGAACTACAGGATGAACACTGAATTCAACATCATTAAATCACAACATGAGAAGACAATGTTGG  
ATATGAATAAAATGATCCAGTCCATAATTGGTTCCATGCAGTATTCCAAGGAACTGATAGAAGATAACTA  
TTCCTACAGCATTAAAGGAGGACCACCTCCTCCGTGAGTGC ACTCAACTCAACGAAAACGTAAGGATATT  
ACTGAATGAGAACAGAAGGCTGCTGGTGGAGCAGGCTGGCCATAAGTGTCTGTGGGGGAAGAAAAGA  
GGTTCTCTGAGGAGGCCAGGAAGTACATCTGTGTCCCAAGTGCCAAGGAACAGCAGT

### Supplementary Table 3. Inclusion and exclusion criteria for patient recruitment

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#### Inclusion criteria

- 25 -70 years old
- Regular diet and sleep in the past two weeks before hospitalization. Patients wake up at 5:30 AM - 8:00 AM, have breakfast at 6:00 AM - 8:30 AM, have lunch at 11:00 AM - 13:30 PM, have dinner at 17:00 PM - 19:30 PM, and fall asleep at 21:00 PM - 23:30 PM.
- Type 2 diabetes according to the WHO criteria (1999) at the time of admission into the hospital
- Fingertip blood glucometer measurement with fasting glucose 90-180 mg/dL and postprandial glucose < 288 mg/dL with a fixed medication regimen when the study was started

#### Exclusion criteria

- Type 1 diabetes, gestational diabetes, monogenic diabetes, or cystic fibrosis-related diabetes
  - Nighttime hypoglycemia (glucose < 70 mg/dL) (Somogyi effect)
  - Acute complications of diabetes such as ketoacidosis or hyperosmolar hyperglycemic state
  - Acute infection
  - Pregnancy or lactation
  - Currently on glucocorticoids
  - Currently on continuous subcutaneous insulin infusion (insulin pump)
  - Poor control of hypertension (SBP  $\geq$  160 mmHg and/or DBP  $\geq$  100 mmHg with treatment)
  - Abnormal liver function with ALT or AST over twofold of the upper limit of the reference value
  - Abnormal renal function with eGFR < 60 mL/min/1.73 m<sup>2</sup>
  - Myocardial infarction, unstable angina pectoris, heart arrhythmia, heart failure, cerebrovascular accident, or severe cardiovascular diseases with sequelae in the past 6 months
  - Night shift, time-zones crossing, or other irregular sleep behaviors in the past 2 weeks
  - Less than 3 matched measurements from the fingertip glucometer readings and CGMs readings in a day (correlation coefficient < 0.79 between fingertip glucometer and CGM values) during the study
-

**Supplementary Table 4.** Characteristics of human subjects

	DP- n = 16	DP+ n = 11	p
Age (years)	48.56 (3.00)	51.55 (3.03)	0.505 <sup>#</sup>
Sex ratio (males/females)	12/4	6/5	0.268 <sup>*</sup>
Duration of disease (years)	8.35 (1.69)	8.70 (2.23)	0.900 <sup>#</sup>
Body mass index (kg/m <sup>2</sup> )	27.73 (1.51)	25.93 (1.02)	0.381 <sup>#</sup>
Waist-to-hip ratio	1.02 (0.06)	0.93 (0.02)	0.307 <sup>#</sup>
<b>Blood parameters</b>			
Hemoglobin (g/L)	141.93 (1.92)	134.91 (3.56)	0.072 <sup>#</sup>
Hematocrit (%)	39.46 (3.25)	39.89 (1.11)	0.915 <sup>#</sup>
Fasting blood glucose (mg/dl)	133.11 (4.96)	135.93 (7.84)	0.752 <sup>#</sup>
Basal Insulin (μIU/ml)	12.95 (1.65)	9.73 (2.02)	0.226 <sup>#</sup>
C-Peptide (ng/ml)	1.33 (0.19)	1.16 (0.14)	0.513 <sup>#</sup>
HbA1C (%)	8.41 (0.39)	8.80 (0.54)	0.552 <sup>#</sup>
Total cholesterol (mmol/L)	4.59 (0.27)	4.66 (0.35)	0.860 <sup>#</sup>
Triglycerides (mmol/L)	1.87 (0.17)	1.92 (0.34)	0.890 <sup>#</sup>
HDL-C (mmol/L)	1.06 (0.07)	1.09 (0.06)	0.772 <sup>#</sup>
LDL-C (mmol/L)	2.94 (0.23)	3.00 (0.23)	0.860 <sup>#</sup>
Homocysteine (umol/l)	13.06 (1.23)	12.89 (1.07)	0.925 <sup>#</sup>
Uric acid (umol/l)	336.75 (18.92)	310.63 (14.51)	0.322 <sup>#</sup>
<b>Fingertip blood glucose</b>			
7am (pre-breakfast) (mg/dl)	136.80 (5.36)	150.38 (9.06)	0.182 <sup>#</sup>
11am (pre-lunch) (mg/dl)	135.79 (10.08)	147.60 (9.96)	0.430 <sup>#</sup>
5pm (pre-dinner) (mg/dl)	123.64 (7.12)	140.24(5.54)	0.102 <sup>#</sup>
9pm (before bed) (mg/dl)	127.93 (4.98)	131.45 (7.72)	0.690 <sup>#</sup>
<b>Sleep</b>			
The time to fall asleep	23:09 (0:23)	22:46 (0:31)	0.556 <sup>#</sup>
The time to wake up	6:08 (0:09)	6:04 (0:10)	0.806 <sup>#</sup>
Total sleep duration (min)	411.57 (22.48)	429.17 (26.80)	0.620 <sup>#</sup>
Light sleep duration (min)	298.56 (19.65)	284.03 (18.95)	0.614 <sup>#</sup>
Deep sleep duration (min)	105.72 (8.88)	134.25 (14.46)	0.087 <sup>#</sup>
<b>Sleep (pre-hospital)</b>			
The time to fall asleep	22:15 (0:10)	22:21 (0:12)	0.673 <sup>#</sup>
The time to wake up	6:28 (0:08)	6:16 (0:10)	0.410 <sup>#</sup>
<b>Mealtime</b>			
Breakfast time	7:27 (0:09)	7:11 (0:06)	0.218 <sup>#</sup>
Lunch time	11:53 (0:05)	12:04 (0:13)	0.413 <sup>#</sup>
Dinner time	17:50 (0:11)	17:56 (0:14)	0.765 <sup>#</sup>
<b>Mealtime (pre-hospital)</b>			
Breakfast time	7:31 (0:07)	7:27 (0:10)	0.714 <sup>#</sup>
Lunch time	11:56 (0:02)	12:10 (0:08)	0.082 <sup>#</sup>
Dinner time	18:21 (0:08)	18:30 (0:08)	0.487 <sup>#</sup>
<b>Activity</b>			
Step count	6786 (640)	5912 (1457)	0.546 <sup>#</sup>

Walking distance (km)	4.43 (0.41)	3.87 (0.99)	0.562 <sup>#</sup>
<b>Medication usage</b>			
Insulin (%)	31.25 (5/16)	45.45 (5/11)	0.453 <sup>*</sup>
Metformin (%)	93.75 (15/16)	81.82 (9/11)	0.332 <sup>*</sup>
Sulfonylurea (%)	37.50 (6/16)	54.55 (6/11)	0.381 <sup>*</sup>
Meglitinides (%)	6.25 (1/16)	0 (0/11)	0.398 <sup>*</sup>
α-glucosidase inhibitor (%)	68.75 (11/16)	45.45 (5/11)	0.226 <sup>*</sup>
DPP-4 inhibitor (%)	31.25 (5/16)	36.36 (4/11)	0.782 <sup>*</sup>
SGLT2 inhibitor (%)	18.75 (3/16)	9.09 (1/11)	0.487 <sup>*</sup>
GLP-1 analogue (%)	6.25 (1/16)	9.09 (1/11)	0.782 <sup>*</sup>
Single drug (%)	12.5 (2/16)	9.09 (1/11)	0.782 <sup>*</sup>
Combination of two drugs (%)	18.75 (3/16)	27.27 (3/11)	0.601 <sup>*</sup>
Combination of three drugs (%)	37.50 (6/16)	36.36 (4/11)	0.952 <sup>*</sup>
Combination of four drugs (%)	25 (4/16)	27.27 (3/11)	0.895 <sup>*</sup>
Combination of five drugs (%)	6.25 (1/16)	0 (0/11)	0.398 <sup>*</sup>

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DP-, patients without dawn phenomenon.

DP+, patients with dawn phenomenon.

Data are expressed as mean (SEM).

<sup>#</sup>, two-sided student t-test; <sup>\*</sup>, chi-square test.

**Supplementary Table 5.** Cardiopulmonary Coupling-Polysomnography (CPC-PSG) of human subjects

	DP- n = 10	DP+ n = 8	p
<b>Sleep</b>			
Testing time (min)	448.73 (13.96)	392.98 (48.96)	0.245
Sleep onset latency (min)	52.40 (7.81)	33.25 (10.45)	0.153
Total sleep interval time (min)	396.55 (14.15)	351.00 (43.94)	0.296
Total sleep time (min)	311.00 (19.73)	306.00 (39.01)	0.905
Stable sleep duration (min)	50.60 (6.36)	44.06 (10.98)	0.596
Unstable sleep duration (min)	186.95 (14.06)	194.19 (27.44)	0.806
REM duration (min)	84.45 (7.56)	67.75 (8.55)	0.162
Stable sleep duration (%)	16.39 (1.61)	14.41 (2.78)	0.527
Unstable sleep duration (%)	60.56 (3.39)	63.44 (2.70)	0.532
REM duration (%)	27.60 (2.76)	22.14 (0.91)	0.108
Total number of awakenings (n)	26.40 (2.07)	16.14 (2.32)	0.005
<b>Breathe</b>			
Apnea hypopnea index (times/hour)	6.56 (1.89)	4.74 (1.86)	0.509
Total number of obstructive apnea (n)	8.75 (3.09)	2.50 (1.71)	0.119
The maximum duration of obstructive apnea (s)	25.98 (7.22)	8.78 (4.75)	0.078
Obstructive apnea index (times/hour)	1.65 (0.79)	0.59 (0.30)	0.269
Total number of central apnea (n)	0.60 (0.27)	0 (0)	0.063
The maximum duration of central apnea (s)	6.45 (2.78)	0 (0)	0.056
Central apnea index (times/hour)	0.11 (0.05)	0 (0)	0.059
Total number of mixed apnea (n)	1.00 (0.89)	0 (0)	0.369
The maximum duration of mixed apnea (s)	6.78 (4.53)	0 (0)	0.202
Mixed apnea index (times/hour)	0.24 (0.22)	0 (0)	0.344
Total number of all types of apnea (n)	10.35 (3.91)	2.50 (1.71)	0.111
The maximum duration of all types of apnea (s)	39.21 (11.87)	8.78 (4.75)	0.045
Total number of hypopnea (n)	37.60 (13.50)	28.14 (12.91)	0.634
The maximum duration of hypopnea (s)	52.39 (10.47)	49.60 (12.36)	0.865
Hypopnea index (times/hour)	6.51 (2.05)	4.15 (1.85)	0.416
<b>Snore</b>			
Number of snoring incidents (n)	60.60 (28.51)	10.88 (3.62)	0.142
Average snoring time (s)	23.68 (5.68)	25.31 (8.47)	0.871
Total snoring time (min)	30.86 (15.17)	4.88 (1.83)	0.149
The ratio of sleeping time (%)	8.36 (3.99)	2.66 (1.42)	0.240
<b>Blood oxygen</b>			
Mean vein oxygen of REM (%)	96.30 (0.21)	96.38 (0.26)	0.826
Mean vein oxygen of stable sleep (%)	96.10 (0.31)	96.38 (0.38)	0.579
Mean vein oxygen of unstable sleep (%)	96.00 (0.26)	96.38 (0.26)	0.329
Mean vein oxygen of total sleep time	95.90 (0.31)	96.38 (0.26)	0.279
ODI of REM (times/hour)	9.32 (2.44)	6.80 (2.00)	0.452
ODI of stable sleep (times/hour)	2.45 (1.65)	0.91 (0.60)	0.437
ODI of unstable sleep (times/hour)	12.12 (4.50)	6.39 (2.33)	0.310
ODI of total sleep time (times/hour)	10.49 (3.42)	5.61 (2.06)	0.269

MORT of REM (s)	57.40 (30.59)	35.00 (17.39)	0.561
MORT of stable sleep (times/hour)	3.30 (1.87)	1.50 (1.00)	0.443
MORT of unstable sleep (times/hour)	31.80 (8.28)	38.75 (15.21)	0.677
MORT of total sleep time (s)	65.80 (29.79)	47.63 (16.62)	0.626
MOS of REM (%)	89.00 (1.23)	90.50 (1.51)	0.448
MOS of stable sleep (%)	94.00 (0.56)	94.50 (0.50)	0.525
MOS of unstable sleep (%)	85.30 (1.69)	88.13 (1.79)	0.270
MOS of total sleep time (%)	84.60 (1.62)	85.63 (1.61)	0.664
<b>Heart rate</b>			
Average heart rate of REM (bpm)	70.57 (2.56)	70.83 (6.77)	0.970
Average heart rate of stable sleep (bpm)	67.89 (2.62)	70.61 (7.19)	0.704
Average heart rate of unstable sleep (bpm)	69.91 (2.30)	71.08 (6.90)	0.863
Average heart rate of total sleep time (bpm)	70.83 (2.38)	71.98 (6.83)	0.865
Minimum heart rate of REM (bpm)	60.20 (2.24)	64.38 (7.08)	0.546
Minimum heart rate of stable sleep (bpm)	59.50 (2.10)	63.63 (7.13)	0.550
Minimum heart rate of unstable sleep (bpm)	62.60 (2.39)	67.75 (7.53)	0.485
Minimum heart rate of total sleep time (bpm)	58.60 (2.08)	63.13 (7.00)	0.505
Maximum heart rate of REM (bpm)	90.10 (3.09)	85.75 (5.21)	0.463
Maximum heart rate of stable sleep (bpm)	91.10 (4.17)	87.38 (5.49)	0.590
Maximum heart rate of unstable sleep (bpm)	76.80 (2.92)	75.63 (6.63)	0.864
Maximum heart rate of total sleep time (bpm)	108.00 (3.43)	102.38 (3.55)	0.275
<b>Indicator of heart rate variability</b>			
The mean of the RR interval (ms)	856.12 (28.77)	891.93 (84.33)	0.666
SDNN (ms)	94.12 (17.39)	69.15 (14.94)	0.306
SDANN (ms)	53.13 (8.17)	43.01 (8.91)	0.416
RMSSD (ms)	67.36 (20.18)	36.79 (8.12)	0.218
PNN50 (%)	6.11 (2.29)	4.40 (2.56)	0.625

REM, Rapid eye movement.

ODI, oxygen desaturation index.

MORT, maximum oxygen reduction time.

MOS, Minimum oxygen saturation.

SDNN, the standard deviation of the RR interval for all cardiac sinus beats.

SDANN, the standard deviation of the interval mean.

RMSSD, the root mean square of the difference between adjacent RR intervals.

PNN50, the number of >50ms between adjacent periods accounted for the percentage of the total sinus cardiac beats.

P values were from two-sided student t-test.

**Supplementary Table 6.** Medications in patients

Subject	INS	DMBG	SU		M G	α-GCase inhibitor	DPP-4 inhibitor		SGLT2 inhibitor		GLP -1a
			Glic	Glim			Sita	Sax a	Empa	Dap a	
<b>DP-</b>	1	-	500mg tid	-	-	-	50mg tid	-	-	-	-
	2	-	1000mg bid	60m g qd	-	-	50mg tid	100mg qd	-	-	-
	3	-	1000mg bid	-	-	-	100mg tid	100mg qd	-	-	-
	4	18IU qn	500mg tid	-	-	-	100mg tid	100mg qd	-	-	-
	5	24IU qn	500mg qid	-	-	2m g tid	100mg tid	-	-	-	-
	6	-	500mg tid	60m g qd	-	-	50mg tid	-	-	-	-
	7	20IU 8am	500mg 8am; 1000mg 4pm	30m g qd	-	-	50mg tid	-	5m g qd	-	-
	8	8IU 8am; 8IU 11am; 26IU 10pm	1000mg bid	-	-	-	-	100mg qd	-	100m g qd	-
	9	22IU 8am; 6IU 11am; 14IU 4pm	-	-	-	-	-	-	-	-	-
	10	-	500mg tid	-	2mg bid	-	50mg id	-	-	-	-
	11	-	500mg bid	-	2mg 8am; 1mg 4pm	-	-	-	-	-	-
	12	-	1000mg bid	-	-	-	50mg tid	-	-	-	10m g qd
	13	-	500mg bid	-	-	-	50mg tid	-	-	-	0.6m g 8am
	<b>DP+</b>	14	-	500mg qid	-	-	-	-	-	-	-
15		-	500mg tid	60m g qd	-	-	-	-	-	-	-
16		-	500mg qid	-	-	-	100mg tid	-	-	100m g qd	-
17		18IU qn	500mg tid	60m g qd	-	-	-	-	-	-	-
18		-	500mg tid	-	-	-	-	100mg qd	-	-	-
19		-	500mg tid	-	-	-	-	100mg qd	-	-	-
20		8IU 8am;	1000mg bid	-	2mg qd	-	50mg tid	-	-	-	-



5	8IU 11am; 8IU 4pm; 20IU qn	-	500mg tid	60m g 8am; 30m g 4pm	-	-	-	-	-	-	-	-
6	8IU 8am; 6IU 11am; 6IU 4pm; 16IU qn	-	-	-	-	-	-	-	-	-	-	-
7	-	500mg bid	-	2mg bid	-	100mg tid	-	-	-	-	-	-
8	-	500mg bid	-	-	-	-	100mg qd	-	-	10m g qd	-	-
9	16IU 8am	500mg tid	30m g qd	-	-	50mg tid	-	-	-	-	-	-
10	-	-	-	-	-	100mg tid	100mg qd	-	-	-	-	1.2m g 8am
11	18IU 8am	500mg tid	60m g bid	-	-	50mg 8am; 100mg 11am; 100mg 4pm	-	-	-	-	-	-

INS, insulin. DMBG, dimethylbiguanide (Metformin). SU, sulfonylurea. Glic, Gliclazide. Glim, Glimperide. MG, Meglitinides.  $\alpha$ -GCCase inhibitor,  $\alpha$ -glucosidase inhibitor. DPP-4 inhibitor, dipeptidyl peptidase-4 inhibitor. Sita, Sitagliptin. Saxa, Saxagliptin. SGLT2 inhibitor, sodium-dependent glucose transporters 2 inhibitor. Empa, Empagliflozin. Dapa, Dapagliflozin. GLP-1a, glucagon-like peptide-1 analogue. qn, quaque nocte. qd, quaque die. bid, bis in die. tid, ter in die. qid, quater in die