Figure number	Statistical test	n Number of samples	*P* value
Figure 1C	Wilcoxon matched-pair test (two-tailed)	8 cells, 5 mice (Control) 8 cells, 5 mice (4-CIN)	*P*=0.0078
Figure 1E	Repeated measures one-way ANOVA followed by Tuckey's post hoc test	6 cells, 4 mice (Control) 6 cells, 4 mice (0 Glc) 6 cells, 4 mice (0 Glc + Lactate)	*P*=0.0015 (Control vs. 0 Glc) *P*=0.2007 (Control vs. 0 Glc + Lactate) *P*=0.0280 (O Glc vs. 0 Glc + Lactate)
Figure 1G	Repeated measures one-way ANOVA followed by Tuckey's post hoc test	5 cells, 4 mice (Control) 5 cells, 4 mice (Oxamate) 5 cells, 4 mice (Oxamate+ Lactate)	*P*=0.0008 (Control vs. Oxamate) *P*=0.0004 (Control vs. Oxamate + Lactate) *P*=0.7811 (Oxamate vs. Oxamate + Lactate)
Figure 1I	Repeated measures one-way ANOVA followed by Tuckey's post hoc test	7 cells, 5 mice (Control) 7 cells, 5 mice (Oxamate) 7 cells, 5 mice (Oxamate + Pyruvate)	*P* =0.0277 (Control vs. Oxamate) *P*=0.9561 (Control vs. Oxamate + Pyruvate) *P* =0.0460 (Oxamate vs. Oxamate + Pyruvate)
Figure 1K	Repeated measures one-way ANOVA followed by Tuckey's post hoc test	7 cells, 5 mice (Control) 7 cells, 5 mice (Oxamate POMC neuron) 7 cells, 5 mice (Oxamate POMC neuron + Pyruvate)	*P* =0.0236 (Control vs. Oxamate POMC neuron) *P* =0.9603 (Control vs. Oxamate POMC neruon + Pyruvate) *P* =0.0145 (Oxamate POMC neuron vs. Oxamate POMC neuron + Pyruvate)
Figure 2C	Odinary one-way ANOVA followed by Tuckey's post hoc test	n=6 (Ctrl) n=5 (2-DG) n=6 (4-CIN) n=6 (CBX)	*P*=0.0016 (Ctrl vs 2-DG) *P*=0.0120 (Ctrl vs. 4-CIN) *P*=0.0355 (Ctrl vs. CBX) *P*=0.7092 (2-DG vs. 4-CIN) *P*=0.4239 (2-DG vs. CBX) *P*=0.9558 (4-CIN vs. CBX)
Figure 2D	Odinary one-way ANOVA followed by Tuckey's post hoc test	n=5 (Ctrl) n=5 (2-DG) n=6 (4-CIN) n=6 (CBX)	*P*<0.0001 (Ctrl vs 2-DG) *P*<0.0001 (Ctrl vs. 4-CIN) *P*=0.0009 (Ctrl vs. CBX) *P*<0.0001 (2-DG vs. 4-CIN) *P*<0.0001 (2-DG vs. CBX) *P*=0.6091 (4-CIN vs. CBX)
Figure 2I	Repeated measures one-way ANOVA followed by Tuckey's post hoc test	6 cells, 5 mice (Control + Tanycytic lactate) 6 cells, 5 mice (0 glc + Tanycytic lactate) 6 cells, 5 mice (4-CIN + Tanycytic lactate)	*P*=0.9974 (Control + Tanycytic lactate vs. 0 Glc + Tanycytic lactate) *P*=0.0288 (Control + Tanycytic lactate vs. 4-CIN + Tanycytic lactate) *P*=0.0258 (0 Glc + Tanycytic lactate vs. 4-CIN + Tanycytic lactate)
Figure 2M	Repeated measures one-way ANOVA followed by Tuckey's post hoc test	6 cells, 5 mice (Control) 6 cells, 5 mice (Oxamate Tanycytic) 6 cells, 5 mice (Oxamate tanycytic + lactate)	*P*=0.0143 (Control vs. Oxamate tanycytic) *P*=0.9099 (Control vs. 4-CIN Oxamate tanycytic + Lactate) *P*=0.0474 (Oxamate tanycytic vs. Oxamate tanycytic + Lactate)
Figure 3B	Unpaired Student's t-tests (two-tailed)	5 mice (Tanycyte) 4 mice (POMC neuron)	*Mct1*: *P* =0.0009 (Tanycyte vs. POMC neurons) *Mct2*: *P* =0.0028 (Tanycyte vs. POMC neurons) *Mct4*: *P* =0.0272 (Tanycyte vs. POMC neurons)
Figure 3C	Odinary one-way ANOVA followed by uncorrected Fisher's LSD	4 mice (*Mct1/4*^{TanScramble}) 4 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0231 (*Mct1/4*^{TanScramble} positive cells vs. *Mct1/4*^{TanycyteKD} positive cells) *P*=0.8494 (*Mct1/4*^{TanScramble} negative cells vs. *Mct1/4*^{TanycyteKD} negative cells) *P*=0.0037 (*Mct1/4*^{TanScramble} positive cells vs. *Mct1/4*^{TanScramble} negative cells) *P*=0.0053 (*Mct1/4*^{TanScramble} positive cells vs. *Mct1/4*^{TanycyteKD} negative cells)
Figure 3D	Odinary one-way ANOVA followed by uncorrected Fisher's LSD	4 mice (*Mct1/4*^{TanScramble}) 4 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0320 (*Mct1/4*^{TanScrambld} positive cells vs. *Mct1/4*^{TanycyteKD} positive cells) *P*=0.8944 (*Mct1/4*^{TanScramble} negative cells vs. *Mct1/4*^{TanycyteKD} negative cells) *P*=0.0415 (*Mct1/4*^{TanScramble} positive cells vs. *Mct*1/4^{TanScramble} negative cells) *P*=0.0324 (*Mct1/4*^{TanScramble} positive cells vs. *Mct1/4*^{TanycyteKD} negative cells)

Figure 3G	Mann-Whitney test (two-tailed)	26 cells, 5 mice (*Mct1/4*^{TanScramble}) 26 cells, 5 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0026
Figure 3H	Unpaired Student's t-test (two-tailed)	7 mice (*Mct1/4*^{TanScramble}) 7 mice (*Mct1/4*^{TanycyteKD})	*P*=0.03374
Figure 3I	Two-way ANOVA followed by uncorrected Fisher's LSD test	6 mice (*Mct1/4*^{TanScramble}) 8 mice (*Mct1/4*^{TanycyteKD})	Dark pharse: *P*=0.2454 ; Light phase: *P*=0.8866 ; Mean: *P*=0.360
Figure 3J	Perason correlation	7 mice (*Mct1/4*^{TanScramble}) 7 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0378 (*Mct1/4*^{TanScramble}) *P*=0.5351 (*Mct1/4*^{TanycyteKD})
Figure 3K	Perason correlation	7 mice (*Mct1/4*^{TanScramble}) 7 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0084 (*Mct1/4*^{Scramble}) *P*=0.2553 (*Mct1/4*^{TanycyteKD})
Figure 3L	Two-way ANOVA followed by uncorrected Fisher's LSD test	7 mice (*Mct1/4*^{TanScramble}) 8 mice (*Mct1/4*^{TanycyteKD})	Dark pharse: *P*=0.0012 ; Light phase: *P*=0.3476 ; Mean: *P*=0.0324
Figure 3M	Two-way ANOVA followed by uncorrected Fisher's LSD test	5 mice (*Mct1/4*^{TanScramble}) 7 mice (*Mct1/4*^{TanycyteKD})	Dark pharse: *P*=0.0459 ; Light phase: *P*=0.3042 ;Mean: *P*=0.0037
Figure 3N	Two-way ANOVA followed by uncorrected Fisher's LSD test	5 mice (*Mct1/4*^{TanScramble}) 7 mice (*Mct1/4*^{TanycyteKD})	Dark pharse: *P*=0.0307 ; Light phase: *P*=0.5919 ;Mean: *P*=0.1018
Figure 4C	Wilcoxon matched-pair test (two-tailed)	6 cells, 4 mice (Control) 6 cells, 4 mice (CBX)	*P*=0.0312
Figure 4E	Wilcoxon matched-pair test (two-tailed)	5 cells, 4 mice (Control) 5 cells, 4 mice (CBX + Lactate)	*P*=0.6250
Figure 4G	Unpaired Student's t-tests (two-tailed)	6 mice (*Cx43*$^{+/+}$;*tdTomato*) 6 mice (*Cx43*^{TanycyteKO};*tdTomato)*	*P*=0.0449 (*Cx43*$^{+/+}$;*tdTomato* / Tomato positive vs. *Cx43*^{TanycyteKO};*tdTomato* / Tomato positive) *P*=0.8611 (*Cx43*$^{+/+}$;*tdTomato* /Tomato negative vs. *Cx43*^{TanycyteKO};*tdTomato* /Tomato negative)
Figure 4I	Unpaired Student's t-test (two-tailed)	5 cells, 2 mice (*Cx43*$^{loxP/loxP}$) 10 cells, 4 mice (*Cx43*^{TanycyteKO})	*P*=0.0011
Figure 4L	Mann-Whitney test (two-tailed)	6 cells, 5 mice (*Cx43*$^{loxP/loxP}$; *tdTomato* ^{POMC}) 5 cells, 4 mice (*Cx43*^{TanycyteKO}; *tdTomato* ^{POMC})	*P*=0.0043
Figure 4N	Wilcoxon matched-pair test (two-tailed)	6 cells, 5 mice (*Cx43*^{TanycyteKO}; *tdTomato* ^{POMC} - Control) 6 cells, 5 mice (*Cx43*^{TanycyteKO}; *tdTomato* ^{POMC} - Lactate)	*P*=0.0312
Figure 5C	Two-way ANOVA followed by uncorrected Fisher's LSD test	Basal: 6 mice (*Cx43*$^{loxP/loxP}$) and 10 mice (*Cx43*^{TanycyteKO}) 1 - 4 (Saline): 6 mice (*Cx43*$^{loxP/loxP}$) and 10 mice (*Cx43*^{TanycyteKO}) 1-7 (Glucose 20%): 6 mice (*Cx43*$^{loxP/loxP}$) and 10 mice (*Cx43*^{TanycyteKO})	*P*<0.0001 (Time factor) *P*<0.0001 (Column factor) *P*=0.1326 (Time factor x Column factor)
	Unpaired Student's t-test (two-tailed)	6 mice (*Cx43*$^{loxP/loxP}$) and 10 mice (*Cx43*^{TanycyteKO})	*P*=0.0130
Figure 5D	Unpaired Student's t-tests (two-tailed)	6 mice (*Cx43*$^{+/+}$;*tdTomato*) 6 mice (*Cx43*^{TanycyteKO};*tdTomato*)	*Mct1*: *P*=0.2001 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Mct4*: *P*=0.3336 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Ldha*: *P*= 0.9195 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato)* *Ldhb*: *P*=0.0119 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Glut1*: *P*=0.9195 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Glut2*: *P*=0.0071 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*)
Figure 5E	Unpaired Student's t-test (two-tailed)	7 mice (*Cx43*$^{loxP/loxP}$) 9 mice (*Cx43*^{TanycyteKO})	*P*=0.0428

Figure 5F	Paired Student's t-test (two-tailed)	$Cx43^{loxP/loxP}$: 9 mice (day 0) and 9 mice (day 10) $Cx43^{TanycyteKO}$: 9 mice (day 0) and 9 mice (day 10)	P=0.2103 ($Cx43^{loxP/loxP}$/d0 vs. $Cx43^{loxP/loxP}$/d10) P=0.0075 ($Cx43^{TanycyteKO}$/d0 vs. $Cx43^{TanycyteKO}$/d10)
	Unpaired Student's t-test (two-tailed)		P=0.7400 ($Cx43^{loxP/loxP}$/d0 vs. $Cx43^{TanycyteKO}$/d0) P=0.0121 ($Cx43^{loxP/loxP}$/d10 vs. $Cx43^{TanycyteKO}$/d10)
Figure 5G	Unpaired Student's t-test (two-tailed)	8 mice ($Cx43^{loxP/loxP}$) 9 mice ($Cx43^{TanycyteKO}$)	P=0.0287
Figure 5H	Mann-Whitney test (two-tailed)	8 mice ($Cx43^{loxP/loxP}$) 9 mice ($Cx43^{TanycyteKO}$)	P=0.1139
Figure 5I	Two-way ANOVA followed by uncorrected Fisher's LSD test	18h - 17h: 7 mice (before TAT-Cre) and 7 mice (6 days after TAT-Cre)	P<0.0001 (Time factor) P=0.0206 (Column factor) P=0.0001 (Time factor x column factor)
Figure 5J	Two-way ANOVA followed by uncorrected Fisher's LSD test	14h - 13h: 7 mice (before TAT-Cre) and 7 mice (6 days after TAT-Cre)	P<0.0001 (Time factor) P=0.0037 (Column factor) P<0.0001 (Time factor x column factor)
Figure 5K	Two-way ANOVA followed by uncorrected Fisher's LSD test	14h - 13h: 7 mice (before TAT-Cre) and 7 mice (6 days after TAT-Cre)	P<0.0001 (Time factor) P=0.1704 (Column factor) P<0.0001 (Time factor x column factor)
Figure 5L	Two-way ANOVA followed by uncorrected Fisher's LSD test	14h - 13h: 7 mice (before TAT-Cre) and 7 mice (6 days after TAT-Cre)	P<0.0001 (Time factor) P=0.0002 (Column factor) P=0.0147 (Time factor x column factor)
Figure 5M	Unpaired Student's t-tests (two-tailed)	Dark phase: 7 mice (before TAT-Cre) and 7 mice (6 days after TAT-Cre) Light phase: 7 mice (before TAT-Cre) and 7 mice (6 days after TAT-Cre)	Dark phase: P=0.0261 (Before TAT-Cre vs. 6 days after TAT-Cre) Light phase: P=0.0394 (Before TAT-Cre vs. after TAT-Cre)
Figure 5N	Unpaired Student's t-tests (two-tailed)	6 mice ($Cx43^{+/+}$;*tdTomato*) 6 mice ($Cx43^{TanycyteKO}$;*tdTomato*)	*Mct2*: P=0.7581 ($Cx43^{+/+}$;*tdTomato* vs. $Cx43^{TanycyteKO}$;*tdTomato*) *Cartpt*: P=0.4184 ($Cx43^{+/+}$;*tdTomato* vs. $Cx43^{TanycyteKO}$;*tdTomato*) *Pomc*: P= 0.6335 ($Cx43^{+/+}$;*tdTomato* vs. $Cx43^{TanycyteKO}$;*tdTomato*) *Agrp*: P=0.4722 ($Cx43^{+/+}$;*tdTomato* vs. $Cx43^{TanycyteKO}$;*tdTomato*) *Npy*: P=0.0492 ($Cx43^{+/+}$;*tdTomato* vs. $Cx43^{TanycyteKO}$;*tdTomato*)
Figure S2C	Unpaired Student's t-tests (two-tailed)	4 mice (Tomato Positive) 4 mice (Tomato Negative)	*Pomc*: P=0.071 (Tomato Positive vs. Tomato Negative) *Darpp32:* P=0.158 *(Tomato Positive vs. Tomato Negative)* *Gpr50:* P=0.319 *(Tomato Positive vs. Tomato Negative)* *HuC:* P=0.027 *(Tomato Positive vs. Tomato Negative)*
Figure S2F	Unpaired Student's t-tests (two-tailed)	5 mice (GFP Positive) 5 mice (GFP Negative)	*Darpp32*: *P<0.001* (GFP Positive vs. GFP Negative) *Gpr50:* P=0.001 *(GFP Positive vs. GFP Negative)* *Pomc:* P=0.06 *(GFP Positive vs. GFP Negative)* *HuC:* P=0.07 *(GFP Positive vs. GFP Negative)*
Figure S3B	Unpaired Student's t-tests (two-tailed)	7 mice ($Mct2^{POMCScrambled}$) 6 mice ($Mct2^{PomcKD}$)	P=0.0003 (Week 1) P=0.0018 (Week 2) P=0.0045 (Week 3) P=0.0008 (Week 4)

Figure S3C	Unpaired Student's t-tests (two-tailed)	7 mice (*Mct2*^{POMCScrambled}) 6 mice (*Mct2*^{POMCKD})	*P*=0.1135 (Week 1) *P*=0.0534 (Week 2) *P*=0.5188 (Week 3) *P*=0.7470 (Week 4) *P*=0.8773 (Week 5)
Figure S4A	Unpaired Student's t-tests (two-tailed)	4 mice (*Mct1/4*^{TanScramble}) 4 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0200 (*Mct1/4*^{TanScramble} positive cells vs. *Mct1/4*^{TanScramble} negative cells) *P*=0.0134 (*Mct1/4*^{TanycyteKD} positive cells vs. *Mct1/4*^{TanycyteKD} negative cells)
Figure S4B	Unpaired Student's t-tests (two-tailed)	4 mice (*Mct1/4*^{TanScramble}) 4 mice (*Mct1/4*^{TanycyteKD})	*P*=0.0037 (*Mct1/4*^{TanScramble} positive cells vs. *Mct1/4*^{TanScramble} negative cells) *P*=0.0324 (*Mct1/4*^{TanycyteKD} positive cells vs. *Mct1/4*^{TanycyteKD} negative cells)
Figure S4C	Unpaired Student's t-tests (two-tailed)	4 mice (*Mct1/4*^{TanScramble}) 4 mice (*Mct1/4*^{TanycyteKD})	*Mct2*: *P*=0.8204 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD}) *Ldha*: *P*=0.5561 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD}) *Ldhb*: *P*= 0.5457 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD}) *Gck*: *P*=0.1381 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD}) *Glut1*: *P*=0.2479 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD}) *Glut4*: *P*= 0.9174 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD}) *Cx30*: *P*=0.7825 (*Mct1/4*^{TanScramble} vs. *Mct1/4*^{TanycyteKD})
Figure S4D	Two-way ANOVA followed by uncorrected Fisher's LSD test	20h - 19h: 6 *Mct1/4*^{TanScramble} mice and 8 *Mct1/4*^{TanycyteKD} mice	*P*<0.0001 (Time factor) *P*=0.2310 (Column factor) *P*=0.9890 (Time factor x column factor)
Figure S4E	Two-way ANOVA followed by uncorrected Fisher's LSD test	20h - 19h: 7 *Mct1/4*^{TanScramble} mice and 8 *Mct1/4*^{TanycyteKD} mice	*P*<0.0001 (Time factor) *P*=0.2308 (Column factor) *P*=0.3695 (Time factor x column factor)
Figure S4F	Two-way ANOVA followed by uncorrected Fisher's LSD test	20h - 19h: 7 *Mct1/4*^{TanScramble} mice and 8 *Mct1/4*^{TanycyteKD} mice	*P*<0.0001 (Time factor) *P*=0.5215 (Column factor) *P*=0.6883 (Time factor x column factor)
Figure S4G	Two-way ANOVA followed by uncorrected Fisher's LSD test	20h - 19h: 7 *Mct1/4*^{TanScramble} mice and 8 *Mct1/4*^{TanycyteKD} mice	*P*<0.0001 (Time factor) *P*=0.0305 (Column factor) *P*=0.0034 (Time factor x column factor)
Figure S5D	Mann-Whitney test	5 cells, 4 mice (WT) 7 cells, 5 mice (WT+CBX)	P=0.0025
Figure S5K	Mann-Whitney test	7 cells, 6 mice (*Cx43*$^{loxP/loxP}$) 7 cells, 6 mice (*Cx43*^{TanycyteKO})	*P*=0.0006
Figure S5M	Paired Student's t test (two-tailed)	6 cells, 6 mice (*Cx43*$^{loxP/loxP}$; *tdTomato*^{POMC} - Control) 6 cells, 6 mice (*Cx43*$^{loxP/loxP}$; *tdTomato*^{POMC} - Lactate)	*P*=0.6042
Figure S6D	Unpaired Student's t-tests (two-tailed)	6 mice (*Cx43*$^{+/+}$;*tdTomato*) 6 mice (*Cx43*^{TanycyteKO};*tdTomato*)	*P*=0.0070 (*Cx43*$^{+/+}$;*tdTomato* / Tomato Positive vs. *Cx43*$^{+/+}$;*tdTomato* /Tomato Negative) *P*=0.0056 (*Cx43*^{TanycyteKO};*tdTomato* / Tomato Positive vs. *Cx43*^{TanycyteKO};*tdTomato* / Tomato Negative)
Figure S6E	Unpaired Student's t-tests (two-tailed)	6 mice (*Cx43*$^{+/+}$;*tdTomato*) 6 mice (*Cx43*^{TanycyteKO};*tdTomato*)	*Mct1*: *P*=0.5679 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Mct4*: *P*=0.6651 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Ldha*: *P*= 0.8780 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Ldhb*: *P*=0.5127 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Glut1*: P>0.9999 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*) *Glut2*: *P*=0.5127 (*Cx43*$^{+/+}$;*tdTomato* vs. *Cx43*^{TanycyteKO};*tdTomato*)