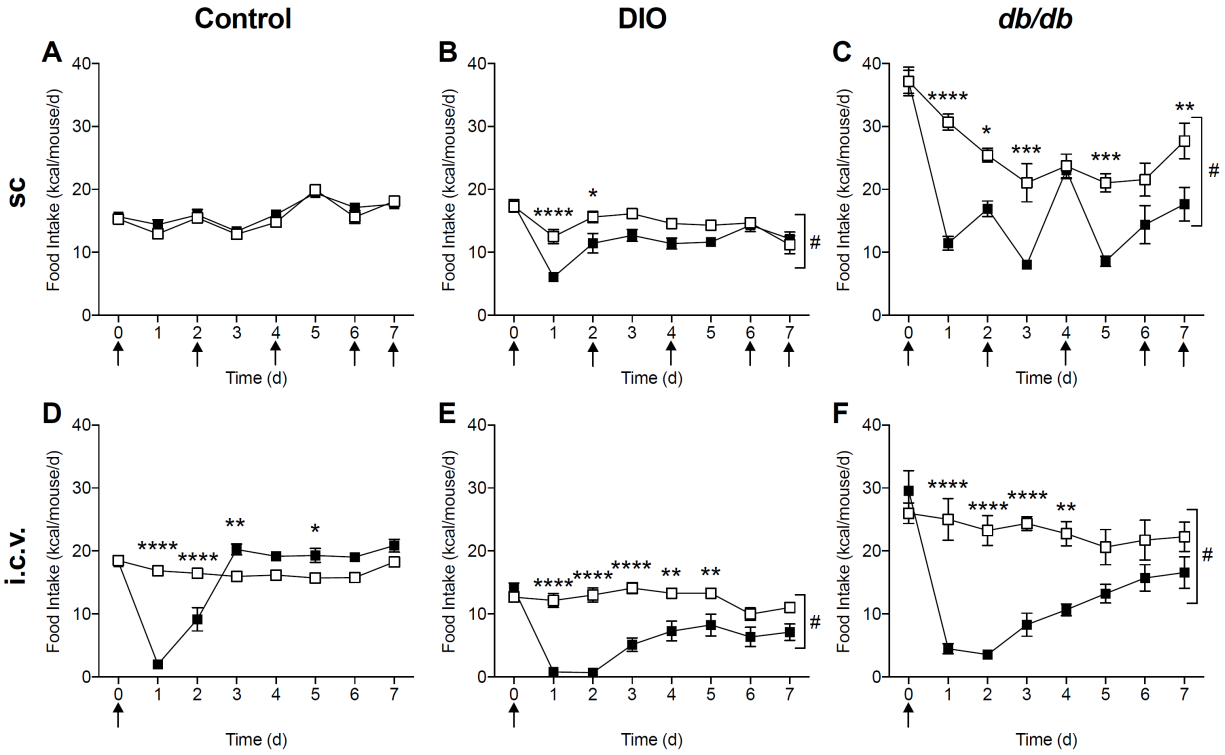
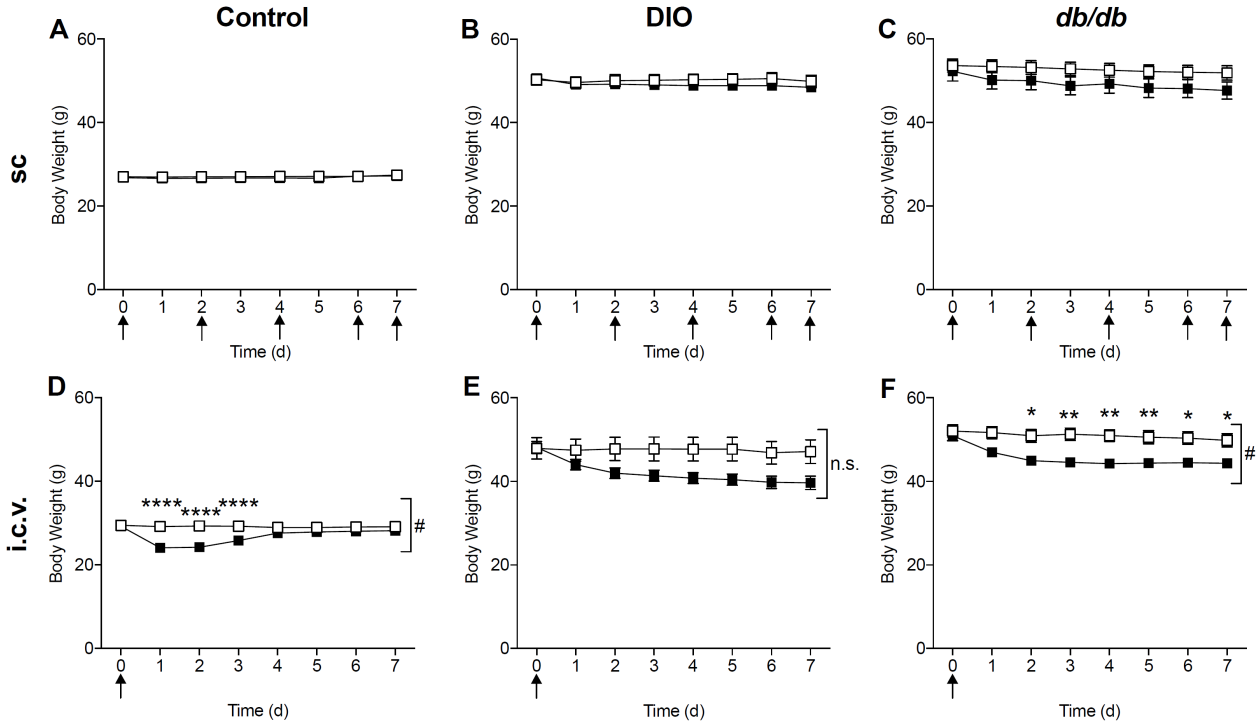
SUPPLEMENTARY DATA

Supplementary Figure S1. Central and peripheral FGF1 transiently reduced food intake. **A-C**, Daily food intake after q.o.d-subcutaneous injections of FGF1 (filled squares) or vehicle (open squares) in **(A)** control (n = 6), **(b)** DIO (n = 6), and **(c)** *db/db* mice (n = 6). **D-F**, Daily food intake after a single i.c.v. injection of FGF1 or vehicle in **(D)** control (n = 5 for vehicle; n = 6 for FGF1), **(E)** DIO (n = 6), and **(F)** *db/db* mice (n = 8 for vehicle; n = 9 for FGF1). Arrows represent injection time course. Data are expressed as mean ± SEM; p-values determined by two-way ANOVA; *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, #p<0.05 for overall treatment effect.



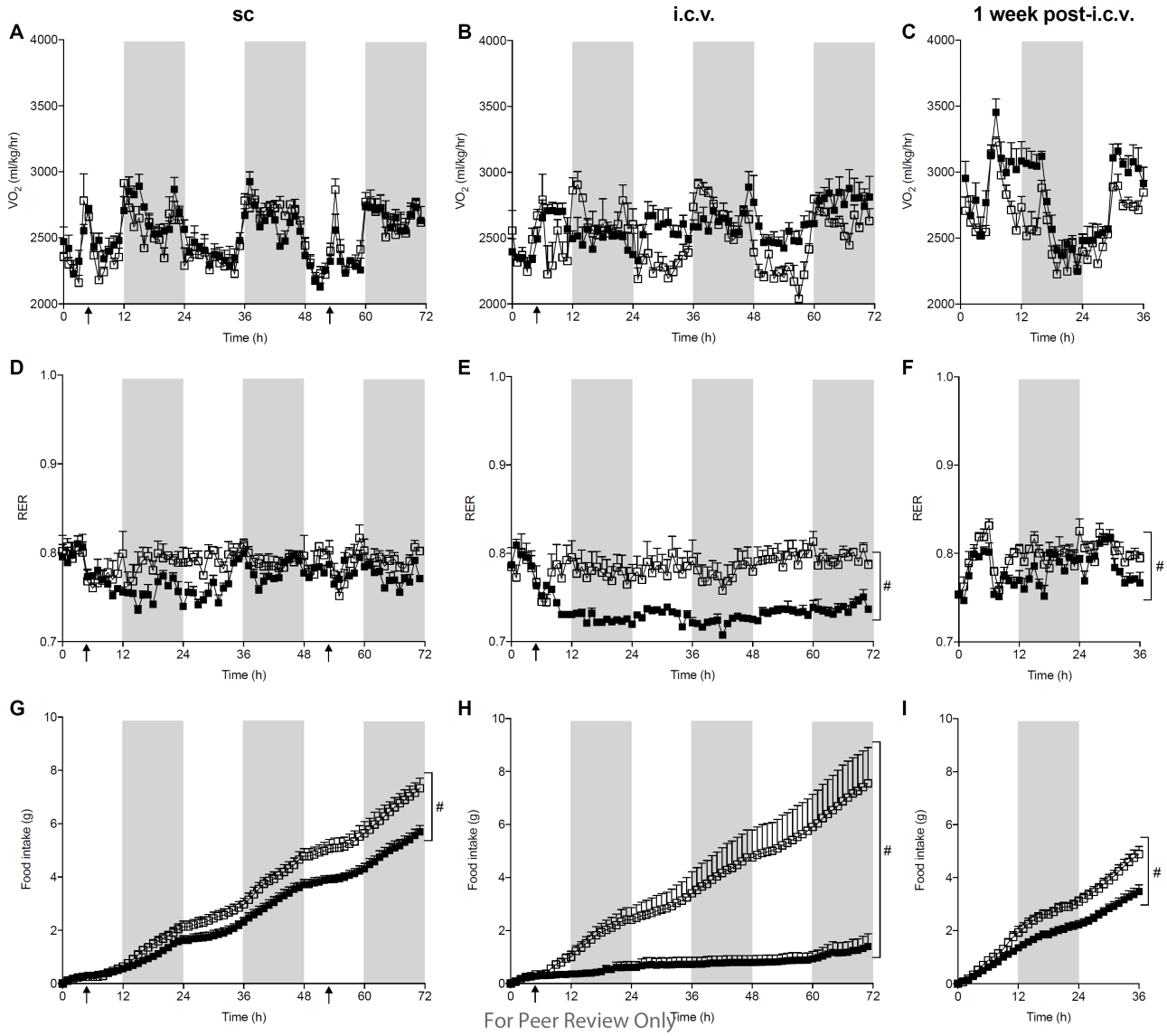
SUPPLEMENTARY DATA

Supplementary Figure S2. Effects of central and peripheral FGF1 on body weight. **A-C,** Daily body weight after q.o.d-subcutaneous injections of FGF1 (filled squares) or vehicle (open squares) in **(A)** control (n = 6), **(B)** DIO (n = 6), and **(C)** *db/db* mice (n = 6). **D-F**, Daily body weight after a single i.c.v. injection of FGF1 or vehicle in **(D)** control (n = 5 for vehicle; n = 6 for FGF1), **(E)** DIO (n = 6), and **(F)** *db/db* mice (n = 8 for vehicle; n = 9 for FGF1). Arrows represent injection time course. Data are expressed as mean ± SEM; p-values determined by two-way ANOVA; ****p<0.0001, #p<0.05 for overall treatment effect, n.s. not significant.



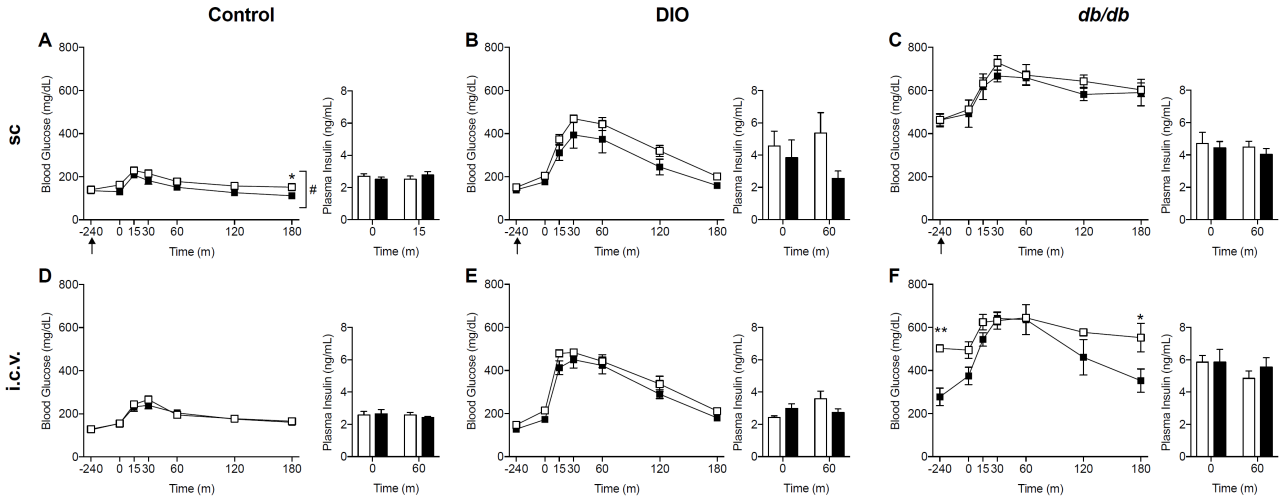
SUPPLEMENTARY DATA

Supplementary Figure S3. Central, but not peripheral FGF1 altered metabolic rate in DIO mice. **A-C,** Volume of oxygen consumed (VO_2) following **(A)** multiple subcutaneous injections or **(B-C)** a single i.c.v. injection of FGF1 (filled squares) or vehicle (open squares). **D-F**, Respiratory exchange ratio (RER) following **(D)** multiple subcutaneous injections or **(E-F)** a single i.c.v. injection of FGF1 or vehicle. **G-I**, Cumulative food intake following **(G)** multiple subcutaneous injections or **(H-I)** a single i.c.v. injection of FGF1 or vehicle. n = 4 per group. Arrows represent injection time course. Data are expressed as mean ± SEM; p-values determined by two-way ANOVA; #p<0.05 for overall treatment effect.



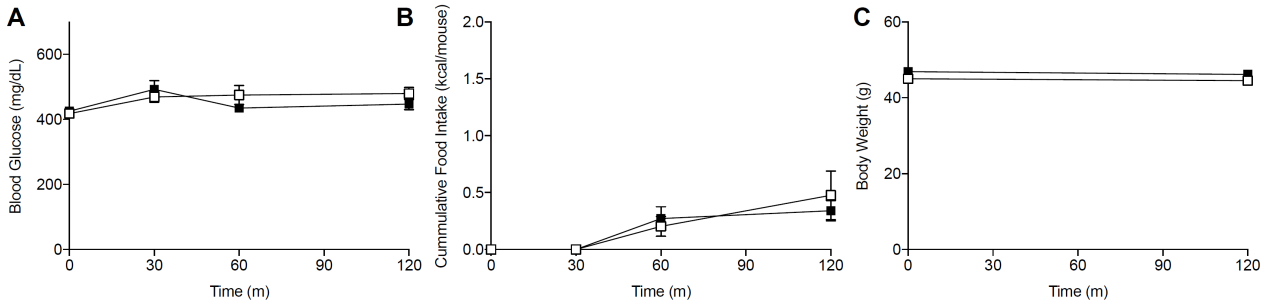
SUPPLEMENTARY DATA

Supplementary Figure S4. Response to an ipGTT after central and peripheral administration of FGF1 in diabetic and control mouse models. A-C, Blood glucose levels and plasma insulin during an ipGTT after 6 days of q.o.d.-subcutaneous injections of FGF1 (filled squares) or vehicle (open squares) in fasted **(A)** control (n = 6), **(B)** DIO (n = 6), and **(C)** *db/db* mice (n = 5 for vehicle; n = 6 for FGF1). **D-F**, Blood glucose levels and plasma insulin during an ipGTT 6 days after a single i.c.v. injection of FGF1 or vehicle in in fasted **(D)** control (n = 5 for vehicle; n = 6 for FGF1), **(E)** DIO (n = 6), and **(F)** *db/db* mice (n = 4). Arrows represent FGF1/vehicle injection, glucose bolus given at time 0. Data are expressed as mean ± SEM; p-values determined by two-way ANOVA; *p<0.05, #p<0.05 for overall treatment effect.



SUPPLEMENTARY DATA

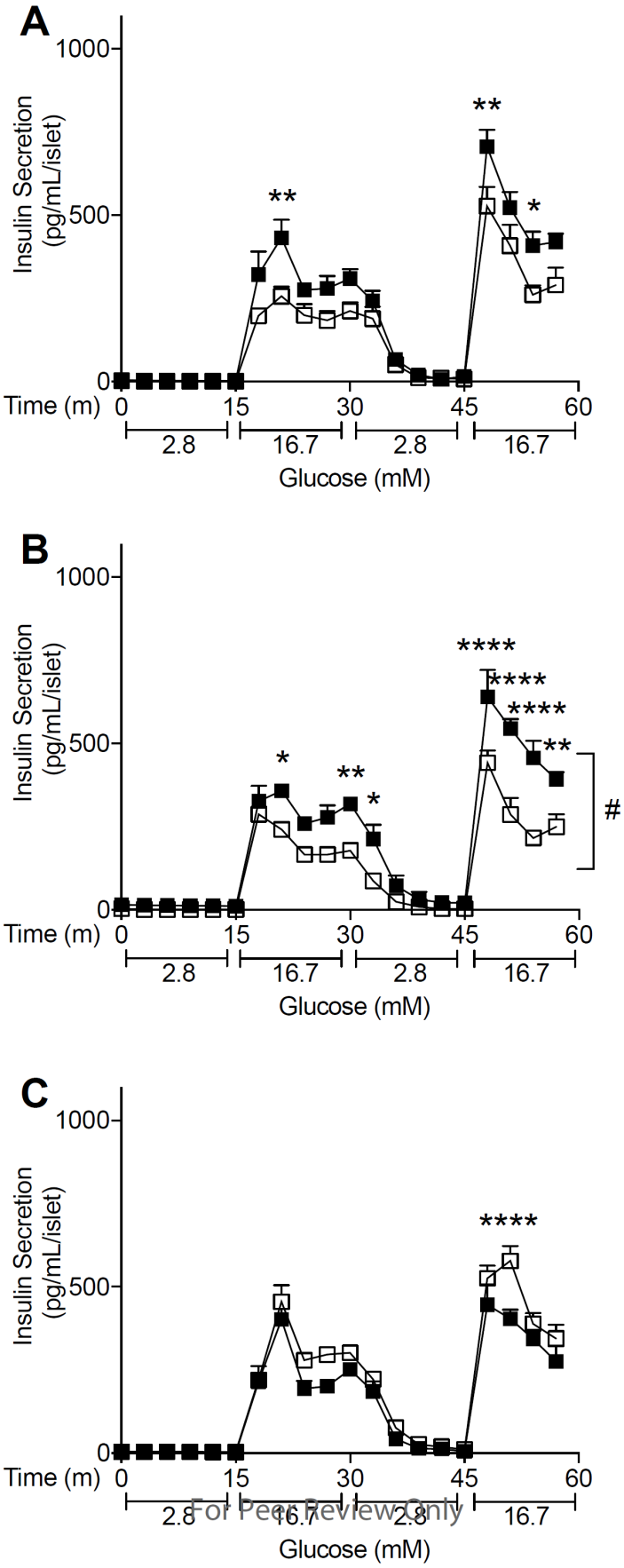
Supplementary Figure S5. Effects of acute peripheral FGF1 *in vivo* in *db/db* mice. (A) blood glucose, **(B)** food intake, and **(C)** body weight were monitored for 2 hours following a subcutaneous injection of FGF1 (filled squares) or vehicle (open squares) in *db/db* mice. n = 6 per group. Data are expressed as mean ± SEM.



SUPPLEMENTARY DATA

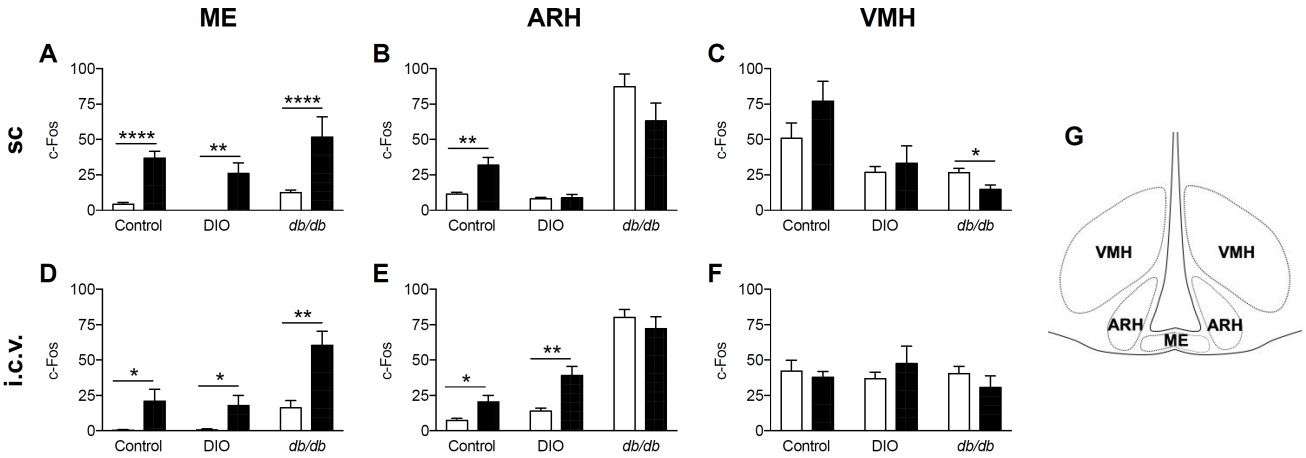
Supplementary Figure S6. Acute peripheral and central FGF1 increased *ex vivo* insulin secretion from DIO mouse islets. **A**, GSIS from DIO islets isolated 2 hours after subcutaneous administration of FGF1 (filled squares) or vehicle (open squares). **B-C**, GSIS from DIO islets isolated **(B)** 2 hours or **(C)** 48 hours after i.c.v. administration of FGF1 or vehicle. Isolated islets were cultured overnight prior to GSIS assay. n = 3 per group for *in vivo* treatment. Data are expressed as mean ± SEM; p-values determined by two-way ANOVA; *p<0.05, **p<0.01, ****p<0.0001, #p<0.05 for overall treatment effect.

SUPPLEMENTARY DATA



SUPPLEMENTARY DATA

Supplementary Figure S7. Effect of central and peripheral FGF1 on c-Fos activation in multiple hypothalamic areas. C-Fos activation 90 minutes after a single subcutaneous or i.c.v. injection of FGF1 (filled bars) or vehicle (open bars) in the **(A, D)** median eminence (ME), **(B, E)** arcuate nucleus (ARH), and **(C, F)** ventromedial nucleus of the hypothalamus (VMH). **G**, Illustration of criteria for selecting cell populations within the ME, ARH, and VMH. n = 3 per group. Data are expressed as mean ± SEM; p-values determined by unpaired Student's t-test; *p<0.05, **p<0.01, ****p<0.0001.



SUPPLEMENTARY DATA

Supplementary Figure S8. Colocalization of c-Fos (green) and the α-tanycyte-specific marker, S100B (red), 90 minutes after a single **(A)** subcutaneous or **(B)** i.c.v. injection of FGF1. DAPI (blue) was used for detection of nuclei.