**Supplementary table T1: Body composition and metabolic characteristics of F0-male breeders:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | F0-CD | F0-HF | n | *p value* |
| Body weight (g) | 563.7 ±11.4 | 628.9 ± 14.8 | 20/19 | ***0.001*** |
| Length (cm) | 25.0 ± 0.2 | 25.3 ± 0.2 | 20/19 | ***0.01*** |
| Glucose (mM) | 6.5 ± 0.2 | 7.1 ± 0.2 | 20/19 | ***0.01*** |
| Insulin (ng/ml) | 4.3 ± 0.4 | 5.5 ± 0.4 | 20/17 | ***0.05*** |
| Leptin (ng/ml) | 3.4 ± 0.3 | 5.4 ± 0.7 | 20/19 | ***0.01*** |
| Triglycerides (ng/ml) | 7.8 ± 0.6 | 13.8 ±1.0 | 20/19 | ***0.0001*** |
| Free fatty acids (mM) | 0.2 ± 0.1 | 0.28 ±0.1 | 15/15 | > 0.05 |
| HOMA-IR | 32.8 ± 2.9 | 42.2 ± 3.6 | 20/17 | ***0.05*** |
| BAT (mg) | 267.8 ± 15.2 | 375.8 ± 33.6 | 15/15 | ***0.01*** |
| Mesenteric WAT (g) | 4.0 ± 0.2 | 6.0 ± 0.6 | 15/15 | ***0.01*** |
| Gonadal WAT (g) | 6.2 ± 0.4 | 11.7 ± 1.2 | 15/15 | ***0.01*** |
| Retroperitoneal WAT (g) | 5.1 ± 0.4 | 12.7 ± 1.9 | 15/15 | ***0.01*** |
| Testes (g) | 5.1 ± 0.4 | 12.7 ± 1.9 | 15/15 | > 0.05 |
| Epididymis (mg) | 619.5 ± 28.2 | 611.6 ± 14.6 | 15/15 | > 0.05 |
| Cauda epididymis (mg) | 306.5 ± 43.4 | 289.8 ± 43.1 | 15/15 | ***0.05*** |
| Values are mean ± SEM |  |  |  |  |

BAT: brown adipose tissue; WAT: white adipose tissue. Results are mean ± SEM. Statistical analysis performed by Student’s t-test.

**Supplementary table T2: Body composition and metabolic characteristics of F0-female breeders.**

|  |  |  |
| --- | --- | --- |
|  | Breeders to F0-CD | Breeder to F0-HF |
| Body weight before breeding (g) | 245.7 ±6.5 | 248.0 ±3.5 |
| Body weight after weaning (g) | 307.8 ±6.8 | 303.6 ±5.2 |
| Glucose (mM) | 6.5 ± 0.2 | 6.5 ± 0.2 |
| Mesenteric WAT (g) | 2.8 ± 0.2 | 2.5 ± 0.1 |
| Gonadal WAT (g) | 3.1 ± 0.4 | 2.6 ± 0.3 |
| Retroperitoneal WAT (g) | 2.6 ± 0.2 | 2.4 ± 0.2 |
| Values are mean ± SEM; n=17/15 | |  |

WAT: white adipose tissue. Results are mean ± SEM. Statistical analysis performed by Student’s t-test.

**Supplementary table T3: Body composition and metabolic characteristics of F1-female offspring.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | PatCD-CD | PatHF-CD | PatCD-HF | PatHF-HF | n |
| Body weight (g) | 321.4 ± 5.6 | 297.7 ± 6.8\* | 347.3 ± 7.9\* | 322.5 ± 6.9#+ | 14-22 |
| Length (cm) | 21.6 ± 0.2 | 21.5 ± 0.2 | 21.9 ± 0.1 | 21.5 ± 0.1 | 14-22 |
| Glucose (mM) | 6.8 ± 0.2 | 6.3 ± 0.1\* | 7.2 ± 0.2\* | 7.0 ± 0.2# | 14-16 |
| Insulin (ng/ml) | 4.2 ± 0.4 | 3.1 ± 0.3\* | 5.5 ± 0.5\* | 4.4 ± 0.4# | 14-16 |
| Leptin (ng/ml) | 6.3 ± 0.5 | 5.8 ± 0.5 | 10.9 ± 0.9\* | 10.4 ± 1.4# | 14-16 |
| Triglycerides (ng/ml) | 1.0 ± 0.2 | 1.0 ± 0.2 | 1.8 ± 0.2\* | 1.4 ± 0.2 | 14-16 |
| Free fatty acids (mM) | 0.13 ± 0.02 | 0.37 ± 0.08\* | 0.26 ± 0.05\* | 0.3 ± 0.1 | 14-16 |
| HOMA-IR | 30.7 ± 2.5 | 24.2 ± 3.0\* | 44.5 ± 3.9\* | 35.5 ± 3.4# | 14-16 |
| BAT (mg) | 349.7 ± 21.2 | 312.0± 20.1 | 409.5 ± 20.8\* | 401.2 ± 19.0# | 14-16 |
| Mesenteric WAT (g) | 3.5 ± 0.2 | 2.7 ± 0.2\* | 3.8 ± 0.3 | 3.1 ± 0.3+ | 14-16 |
| Gonadal WAT (g) | 4.6 ± 0.3 | 4.0 ± 0.3 | 7.5 ± 0.5\* | 6.6 ± 0.6# | 14-16 |
| Retroperitoneal WAT (g) | 4.7 ± 0.4 | 3.3 ± 0.3\* | 7.7 ± 0.1\* | 6.6 ± 0.8# | 14-16 |
| Values are mean ±SEM |  |  |  |  |  |
| \*p<0.05 *vs* PatCD-CD |  |  |  |  |  |
| #p<0.05 *vs* PatHF-CD |  |  |  |  |  |
| +p<0.05 *vs* PatCD-HF |  |  |  |  |  |

PatCD-CD: Paternal-Chow on Chow; PatHF-CD: Paternal-HFD on Chow; PatCD-HF: Paternal-Chow on HFD; PatHF-HF: Paternal-HFD on HFD; BAT: brown adipose tissue; WAT: white adipose tissue. Results are mean ± SEM. Statistical analysis performed by two-way ANOVA followed by Bonferroni post-hoc test.

**Supplementary table T4: Body composition and metabolic characteristics of F2-female offspring**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **GpatCD-CD** | **GpatHF-CD** | **GpatCD-HF** | **GpatHF-HF** | **n** |
| **BW (g)** | 348.5 ± 8.6 | 339.0 ± 9.4 | 393.5 ± 16.2\* | 374.1 ± 9.5# | 10-13 |
| **Length (cm)** | 22.3 ± 0.4 | 21.9 ± 0.2 | 22.0 ± 0.2 | 22.3 ± 0.1 | 10-13 |
| **Glucose (mM)** | 7.1 ± 0.3 | 7.0 ± 0.2 | 7.1 ± 0.3 | 7.4 ± 0.2 | 7-8 |
| **Insulin (ng/ml)** | 3.2 ± 0.4 | 3.0 ± 0.4 | 5.8 ± 0.6\* | 4.3 ± 0.3#+ | 7-8 |
| **Leptin (ng/ml)** | 10.4 ± 1.5 | 6.7 ± 1.0 | 17.9 ± 2.1\* | 13.1 ± 1.6# | 7-8 |
| **Triglycerides (ng/ml)** | 1.1 ± 0.2 | 0.5 ± 0.1\* | 2.3 ± 0.1\* | 2.3 ± 0.3# | 7-8 |
| **Free fatty acids (mM)** | 0.30 ± 0.07 | 0.21 ± 0.04 | 0.4 ± 0.07 | 0.3 ± 0.10 | 7-8 |
| **HOMA-IR** | 25.0 ± 3.9 | 22.0 ± 3.4\* | 40.4 ± 3.5\* | 35.8 ± 3.3# | 7-8 |
| **BAT (mg)** | 408.4 ± 51.8 | 371.1 ± 36.5 | 651.5 ± 76.8 | 520.7 ± 31.5# | 5 |
| **Mesenteric WAT (g)** | 4.5 ± 0.9 | 3.5 ± 0.4 | 7.7 ± 0.9 | 5.9 ± 0.9# | 5 |
| **Gonadal WAT (g)** | 4.6 ± 0.5 | 4.7 ± 0.7 | 10.6 ± 0.9\* | 9.2 ± 0.9# | 5 |
| **Retroperitoneal WAT (g)** | 4.1 ± 0.3 | 4.1 ± 0.6 | 11.9 ± 1.4\* | 11.6 ± 1.0# | 5 |
| **Values are mean±SEM** |  |  |  |  |  |
| \*p<0.05 *vs* GpatCD-CD |  |  |  |  |  |
| #p<0.05 *vs* GpatHF-CD |  |  |  |  |  |
| **+**p<0.05 *vs* GpatCD-HF |  |  |  |  |  |

GpatCD-CD: Grandpaternal-Chow on Chow; GpatHF-CD: Grandpaternal-HFD on Chow; GpatCD-HF: Grandpaternal-Chow on HFD; GpatHF-HF: Grandpaternal-HFD on HFD; BAT: brown adipose tissue; WAT: white adipose tissue. Results are mean ± SEM. Statistical analysis performed by two-way ANOVA followed by Bonferroni post-hoc test.

**Supplementary table T5: Body composition and metabolic characteristics of F1-male offspring.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | PatCD-CD | PatHF-CD | PatCD-HF | PatHF-HF | n |
| Body weight (g) | 612.8 ± 13.03 | 595.2 ± 14.17 | 700.0 ± 11.99\* | 700.10 ± 20.6# | 18-21 |
| Length (cm) | 25.4 ± 0.23 | 25.3 ± 0.34 | 26.4 ± 0.2\* | 26.2 ± 0.3# | 18-21 |
| Glucose (mM) | 6.7 ± 0.16 | 7.0 ± 0.14 | 7.4 ± 0.3\* | 7.5 ± 0.1 | 15-16 |
| Insulin (ng/ml) | 6.0 ± 0.33 | 6.2 ± 0.46\* | 7.4 ± 0.6 | 8.3 ± 0.7# | 15-16 |
| Leptin (ng/ml) | 8.4 ± 1.07 | 9.0 ± 1.41 | 14.5 ± 1.9\* | 14.1 ± 1.8# | 15-16 |
| Triglycerides (mM) | 2.0 ± 0.25 | 1.6 ± 0.19 | 2.4 ± 0.2 | 2.5 ± 0.2# | 15-16 |
| Free fatty acids (mM) | 0.36 ± 0.04 | 0.36 ± 0.03 | 0.41 ± 0.05 | 0.32 ± 0.04 | 15-16 |
| HOMA-IR | 44.8 ± 2.72 | 47.1 ± 4.55 | 56.9 ± 3.9\* | 69.8 ± 6.1#+ | 15-16 |
| BAT (mg) | 345.0 ± 20.83 | 382.3 ± 22.09 | 504.4 ± 28.9\* | 485.9 ± 35.0# | 15-17 |
| Mesenteric WAT (g) | 4.7 ± 0.36 | 4.6 ± 0.36 | 7.2 ± 0.4\* | 6.9 ± 0.6# | 15-17 |
| Gonadal WAT (g) | 8.7 ± 0.65 | 8.1 ± 0.57 | 16.8 ± 0.7\* | 15.2 ± 1.7# | 15-17 |
| Retroperitoneal WAT (g) | 8.7 ± 0.67 | 8.4 ± 0.80 | 20.4 ± 1.3\* | 20.9 ± 2.2# | 15-17 |
| Testes (g) | 1.68 ± 0.09 | 1.74 ± 0.05 | 1.77 ± 0.04 | 1.76 ± 0.03 | 15-17 |
| Epididymis (mg) | 0.61 ± 0.03 | 0.64 ± 0.02 | 0.60 ± 0.01 | 0.62 ± 0.01 | 15-17 |
| Cauda epididymis (mg) | 0.31 ± 0.02 | 0.31 ± 0.01 | 0.30 ± 0.01 | 0.30 ± 0.01 | 15-17 |
| Values are mean ± SEM |  |  |  |  |  |
| \*p<0.05 *vs* PatCD-CD |  |  |  |  |  |
| #p<0.05 *vs* PatHF-CD |  |  |  |  |  |
| +p<0.05 *vs* PatCD-HF |  |  |  |  |  |

PatCD-CD: Paternal-Chow on Chow; PatHF-CD: Paternal-HFD on Chow; PatCD-HF: Paternal-Chow on HFD; PatHF-HF: Paternal-HFD on HFD; BAT: brown adipose tissue; WAT: white adipose tissue. Results are mean ± SEM. Statistical analysis performed by two-way ANOVA followed by Bonferroni post-hoc test.

**Supplementary table T6: Body composition and metabolic characteristics of F2-male offspring**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **GpatCD-CD** | **GpatHF-CD** | **GpatCD-HF** | **GpatHF-HF** | **n** |
| **BW (g)** | 619.6 ± 13.4 | 619.0 ± 13.0 | 722.1 ± 24.1\* | 736.9 ± 14.1# | 18-24 |
| **Length (cm)** | 25.6 ± 0.2 | 25.7 ± 0.2 | 26.5 ± 0.2\* | 26.7 ± 0.1# | 18-24 |
| **Glucose (mM)** | 6.5 ± 0.2 | 7.3 ± 0.3\* | 7.5 ± 0.3\* | 7.5 ± 0.2 | 18-24 |
| **Insulin (ng/ml)** | 5.7 ± 0.4 | 6.8 ± 0.5 | 8.4 ± 0.6\* | 8.3 ± 0.6 | 16-19 |
| **Leptin (ng/ml)** | 8.8 ± 1.0 | 8.8 ± 1.2 | 17.3 ± 2.4\* | 16.3 ± 1.5# | 17-19 |
| **Triglycerides (mM)** | 1.6 ± 0.2 | 1.8 ± 0.2 | 2.6 ± 0.2 | 2.4 ± 0.2# | 17-19 |
| **Free fatty acids (mM)** | 0.25 ± 0.09 | 0.27 ± 0.04 | 0.19 ± 0.03 | 0.14 ± 0.01# | 17-19 |
| **HOMA-IR** | 39.7 ± 2.7 | 56.0 ± 5.0\* | 74.0 ± 7.3\* | 70.7 ± 7.3# | 16-19 |
| **BAT (mg)** | 411.1 ± 40.9 | 481.5 ± 36.1 | 557.1± 33.6\* | 588.4 ± 54.8 | 11-13 |
| **Mesenteric WAT (g)** | 5.6 ± 0.5 | 5.4 ± 0.6 | 10.1 ± 1.2\* | 10.2 ± 1.2# | 11-13 |
| **Gonadal WAT (g)** | 9.2 ± 0.9 | 8.9 ± 0.8 | 21.2 ± 1.9\* | 20.8 ± 1.8# | 11-13 |
| **Retroperitoneal WAT (g)** | 9.41± 0.86 | 9.66 ± 1.36 | 26.9 ± 2.8\* | 26.0 ± 2.1# | 11-13 |
| **Testes (g)** | 1.87 ± 0.04 | 1.74 ± 0.10 | 1.79 ± 0.04 | 1.8 ± 0.1 | 11-13 |
| **Epididymis (mg)** | 0.62 ± 0.01 | 0.61 ± 0.03 | 0.57 ± 0.01\* | 0.59 ± 0.03 | 11-13 |
| **Cauda epididymis (mg)** | 0.33 ± 0.02 | 0.31 ± 0.01 | 0.28 ± 0.01\* | 0.29 ± 0.01 | 11-13 |
| **Values are mean±SEM** |  |  |  |  |  |
| \*p<0.05 *vs* GpatCD-CD |  |  |  |  |  |
| #p<0.05 *vs* GpatHF-CD |  |  |  |  |  |
| +p<0.05 *vs* GPatCD-HF |  |  |  |  |  |

GpatCD-CD: Grandpaternal-Chow on Chow; GpatHF-CD: Grandpaternal-HFD on Chow; GpatCD-HF: Grandpaternal-Chow on HFD; GpatHF-HF: Grandpaternal-HFD on HFD; BAT: brown adipose tissue; WAT: white adipose tissue. Results are mean ± SEM. Statistical analysis performed by two-way ANOVA followed by Bonferroni post-hoc test.

**Supplementary table T7: TaqManprobe assays or primer sequences for miRNA or gene expression analysis.**

|  |  |
| --- | --- |
| Target miRNA/mRNA | TaqMan assay number or primer sequence |
| rno-miR-293-5p | 463311\_mat |
| rno-miR-880-3p | 002666 |
| hsa-let-7a-5p | 000377 |
| hsa-let-7b-5p | 002619 |
| hsa-let-7c-5p | 000379 |
| hsa-let-7d-5p | 002283 |
| hsa-let-7e-5p | 002406 |
| hsa-let-7f-5p | 000382 |
| hsa-let-7g-5p | 002282 |
| hsa-let-7i-5p | 002221 |
| control miRNA snRNA U6 | 001973 |
| control miRNA U87 | 001712 |
| control snoRNA | 001718 |
| *Ppap2a* | Rn00574768\_m1 |
| *Rplp0, Arbp* | Rn00821065\_g1 |
| *Slc3a2* | FW: AGCTGCGACCTAGACAACTG/ RV: GGCTTACCGTTTAAAGCACCC |
| *Tbrg4* | FW: GGTGCTCTGGGTAGGGAGTA/ RV: AGTTGGCCGACTGAGACTTG |
| *Usp11* | FW: AACAATCAGGGGGCTACTGC/ RV: TCCACAAGGCACTAACGTCT |