Resistance to diet-induced adiposity in cannabinoid receptor-1 deficient mice is not due to impaired adipocyte function

Oosterveer, Maaike H.; Koolman, Anniek H.; de Boer, Pieter T.; Bos, Trijnie; Bleeker, Aycha; Bloks, Vincent W.; Kuipers, Folkert; Sauer, Pieter J. J.; van Dijk, Gertjan

Published in:
Nutrition & Metabolism

DOI:
10.1186/1743-7075-8-93

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2011

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):
Oosterveer, M. H., Koolman, A. H., de Boer, P. T., Bos, T., Bleeker, A., Bloks, V. W., Kuipers, F., Sauer, P. J. J., & van Dijk, G. (2011). Resistance to diet-induced adiposity in cannabinoid receptor-1 deficient mice is not due to impaired adipocyte function. Nutrition & Metabolism, 8(1), 93-1-93-12. [93].
https://doi.org/10.1186/1743-7075-8-93

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
Additional File 1, Table S1. Composition experimental diets.

|                | CHOW | HF  | HF/FO |
|----------------|------|-----|-------|
| Starch         | 363  | 147 | 147   |
| Protein        | 211  | 201 | 201   |
| Glucose        | 47   | 158 | 158   |
| Fatty acids    |      |     |       |
| C14:0          | 0.5  | 12.2| 16.1  |
| C16:0          | 8.4  | 92.5| 79.5  |
| C16:1          | 0.7  | 11.5| 18.0  |
| C18:0          | 3.7  | 76.3| 50.5  |
| C18:1          | 13.7 | 133.2| 101.0|
| C18:2          | 16.9 | 11.5| 9.7   |
| C18:3          | 1.9  | 2.9 | 15.2  |
| C20-22         | 0.4  | 4.0 | 53.3  |

Values are given in g/kg.
### Additional File 1, Table S2. Primer and probe sequences used for qPCR.

| Gene               | Sense          | Antisense         | Probe          | Accession number |
|--------------------|----------------|-------------------|----------------|------------------|
| Adiponectin (Adipoq) | AGG ACA TCC TGG CCA CAA TG | CTT AGG ACC AAG AAG ACC TGC AT | CTC TCC AGG AGT GCC AT TCT GCC A | NM_009605 |
| Acc1 (Acaca)       | CCA TCC AAA CAG AGG GAA CAT C | CTA CAT GAG TCA TGC CAT AGT GGT T | ACG CTA AAC AGA ATG TCC TTT GCC TCC AAC | NM_133360 |
| Angptl3            | CCC AGA GCA CAC AGA CCT | CAC CAC CAG CCA CCT GAG | AGC TGT CCC TTT GCT CTG TGA TTC CAT | NM_013913 |
| Angptl4            | AGA TCC AGC AAT TGT TCC AGA AG | AAG AGG TCT ATC TGG CTC TGA AGA TT | CCC AGC AGC AGA GAT ACC TAT CAA AGC AG | NM_020581 |
| Ap2 (Fabp4)        | CAC CAT CCG GTC AGA GAG TAC TT | TCT AGG GTT ATG ATG CTC TTC ACC T | CAT CGA ATT CCA CGC CCA GTT TGA | NM_024406 |
| Apoc1              | GGG CAGCCA TTG AAC ATA TCA | TTG CCA AAT GCC TCT GAG AAC | CCC GGG TCT TGG TCA AAA TTT CCT TC | NM_007469 |
| Apoc3              | CCA AGA CGG TCC AGG ATG C | ACT TGC TCC AGT AGC CTT TCA GG | CCA TCC AGC CCC TGG CCA CC | NM_023114 |
| Atgl (Pnpla2)      | AGC ATC TGC CAG TAT CTG GTAT | CAC CTG CTC AGA CAG TCT GGA A | ATG GTC ACC CAA TTT CCT CTT GGC CC | NM_025802 |
| Cb1 (Cnr1)         | ACA AGC TTA TCA AGA CGG TGT TTG | TGC TCC TCA GAG CAT AGA TGA TG | CTC TGC CTG CTG AAC TCC ACC GTG | NM_007726 |
| Cd36 (Fat)         | GAT CGG AAC TGT GGG CTC AT | GGT TCC TTC TCT AAG GAC AAC TTC | AGA ATG CCT CCA AAC ACA GCC AGG AC | BC010262 |
| Cd68               | CAC TTC GGG CCA TGT TTC TC | AGG ACC AGG CCA ATG ATG AG | CAA CCG TGA CCA GTC CCT CTT GCT G | NM_009853 |
| Gene     | 5' UTR | CDS      | 3' UTR | Accession |
|----------|--------|----------|--------|-----------|
| C/ebp (Cebpa) | CCA AGA AGT CCG TGG ACA AGA A AGG CGG TCA TTG TCA CTG GT CGC AAC AAC ATC GCG GTG CG | | | NM_007678 |
| Cpt1a    | CTC AGT GGG AGC GAC TCT TCA GGC TCT TGT GGT ACA CGA CAA CCT GGG GAG GAG ACA GAC ACC ATC CAA C | | | NM_013495 |
| Faah     | CAG AAG CTG TGC TCT TTA CCT ACC CAG ATA GGA GGT CAC ACA GAA TTA TCC ACC | | | NM_010173 |
| Fas (Fasn) | GGC ATC ATT GGG CAC TCC TT GCT GCA AGC TGG CTA GCA CAG | | | NM_007988 |
| Fatp4 (Slc27a4) | CCA GAC AAG GGT TTT ACA GAT AAG CT ACC ACC TGC TGT GCA CCA CAA TG CCG GCA CCA CGG GGC TAC CC | | | NM_011989 |
| Gpihbp1  | GCG GAA CCG ACA AAG GCTT A TTT ACC TGC TCT CCA | | | NM_026730 |
| Hsl (Lipe) | GAG GCC TTT GAG ATG CCA CT TGG TCA ACA GCA TGG CTA GCA CAG | | | NM_010719 |
| Lpl      | AAG GTC AGA GCC AAG AGA AGC A CCA GAA AAG TGA ATC TTG AC ACT TGG T | | | NM_008509 |
| Napepld  | GGC CTT GGA GTC GAT TCT TCT GTA TTT CAT AAA CCA CCT TGG TTC AT AGG TCA AAA GGA CCA AAC CTT TTT CCA ATC TC | | | NM_178728 |
| Pepck (Pck1) | GTG TCA TCC GCA AGC TGA AG GTC TGA TCT CTG TCC ATC CAA CTG TTG CCA AAC GCT GTC AATG AATG CAC TAA | | | NM_011044 |
| Ppary2 (Pparg) | CTA TGA GCA CTT CAC AAG AAA TTA CCA CAC AGA GCT GAT TCC GAA GGG CCA C | | | U09138 |
| Scd1     | ATG CTC CAA GAG ATC TCC AGT TCT CTT CAC CTT CTC TCG TTC ATT TCC CCA CCA CCA CCA TCA CTC CTC | | | NM_009127 |
|                   | GGA GCC ATG     | CCT GTC TCA     | CAG CTC ATC     | AF286470 |
|-------------------|----------------|----------------|----------------|----------|
| Srebp-1c (Srebf1) | GAT TGC ACA TT | CCC CCA GCA TA | AAC AAC CAA GAC AGT GAC TTC C |          |
Additional File 1, Figure S1. (A) VO₂, (B) VCO₂ and (C) RER values during light and dark phases. Open symbols, CB₁⁺/⁺ mice; closed symbols, CB₁⁻/⁻ mice. Values are given as means ± SEM for n=5-7. (D) Gene expression levels in epididymal fat tissue of 3-week old CB₁⁺/⁺ and CB₁⁻/⁻ mice receiving regular chow. Open bars, CB₁⁺/⁺ mice; closed bars, CB₁⁻/⁻ mice. Values are given as means ± SEM for n=4-8.
**Additional File 1, Table S3.** Detailed indirect calorimetry data of $CB_1^{+/+}$ and $CB_1^{-/-}$ mice fed chow, a HF or a HF/FO diet during 6 weeks.

|                  | chow   | HF     | HF/FO   |
|------------------|--------|--------|---------|
|                  | $CB_1^{+/+}$ | $CB_1^{-/-}$ | $CB_1^{+/+}$ | $CB_1^{-/-}$ | $CB_1^{+/+}$ | $CB_1^{-/-}$ |
| **Values expressed per mouse** |        |        |         |
| Dark phase       |        |        |         |
| Carbohydrate oxidation (mg/hr) | 128±7  | 128±6  | 76±2#   | 79±5#   | 68±3#   | 73±3#   |
| Fat oxidation (mg/hr)   | -11±2  | -10±2  | 15±1#   | 19±2#   | 17±2#   | 19±2#   |
| Energy expenditure (cal/hr) | 455±16 | 465±20 | 481±9   | 554±23#* | 470±13  | 506±9#  |
| Light phase       |        |        |         |
| Carbohydrate oxidation (mg/hr) | 93±6   | 79±3*  | 60±3#   | 57±5#   | 53±3#   | 56±4#   |
| Fat oxidation (mg/hr)   | -1±6   | 6±1*   | 17±1#   | 24±2#*  | 19±1#   | 22±2#   |
| Energy expenditure (cal/hr) | 397±13 | 401±16 | 436±12  | 509±18#* | 419±16  | 464±10#$*|
| **Values expressed per gram lean body mass** |        |        |         |
| Dark phase       |        |        |         |
| Carbohydrate oxidation (mg/hr) | 25±1   | 28±1   | 15±1#   | 17±1#   | 14±1#   | 15±0#   |
| Fat oxidation (mg/hr)   | -2.1±0.4| -2.1±0.4| 3.0±0.3#| 4.2±0.4#| 3.5±0.3#| 3.7±0.4#|
| Energy expenditure (cal/hr) | 89±2   | 101±3* | 97±5    | 121±7#* | 96±3    | 106±3*  |
| Light phase       |        |        |         |
| Carbohydrate oxidation (mg/hr) | 18±1   | 17±1   | 12±1#   | 12±1#   | 11±1#   | 12±1#   |
| Fat oxidation (mg/hr)   | -0.2±0.4| 1.2±0.3*| 3.5±0.3#| 5.3±0.4#*| 3.9±0.4#| 4.6±0.5#|
| Energy expenditure (cal/hr) | 78±1   | 87±3*  | 88±5    | 111±5#* | 86±3    | 97±2#$*|
Values are given as means ± SEM for \( n=5-7 \); \# \( p<0.05 \) compared to chow group of the same genotype, $ p<0.05 \) compared to HF group of the same genotype, * \( p<0.05 \) \( CB_{1}^{-/-} \) vs. \( CB_{1}^{+/+} \) (Student t-test).

General linear model analysis revealed overall effects for the following parameters (\( p<0.05 \)):

- Genotype: dark phase energy expenditure per mouse, light phase energy expenditure per mouse, normalized dark phase energy expenditure, normalized light phase energy expenditure, normalized light phase fat oxidation.
- Chow versus HF: dark/light phase carbohydrate/fat oxidation per mouse, light phase carbohydrate/fat oxidation per mouse, dark/light phase energy expenditure per mouse, dark/light phase normalized carbohydrate/fat oxidation, dark/light phase normalized energy expenditure.
- Chow versus HF/FO: dark/light phase carbohydrate/fat oxidation per mouse, light phase carbohydrate/fat oxidation per mouse, light phase energy expenditure per mouse, dark/light phase normalized carbohydrate/fat oxidation.