

SUPPLEMENTARY DATA

Supplementary Table 1. Selected genes *higher* in the subcutaneous fat of from 4 week high fat fed (see Table 1) 11 -HSD1^{-/-} mice (>1.5-fold compared to C57BL/6J).

Selection criteria were based on the analysis of most significant pathways by the WebGestalt and Ingenuity Programs as described in Materials and Methods. Fold change represents the ratio of mean mRNA expression level

| Gene symbol | Gene name | Accession | Mean fold difference | Family |
|----------------------------------|--|-----------|----------------------|-------------|
| <i>Insulin signaling</i> | | | | |
| Pkkb | Phosphorylase kinase β | 102093 | 1.6 | Kinase |
| Phka1 | Phosphorylase kinase alpha 1 | 18697 | 2.42 | Kinase |
| Phkg1 | Phosphorylase kinase gamma 1 | 18682 | 2.79 | kinase |
| Pkm2 | Pyruvate kinase | 18746 | 1.57 | kinase |
| Socs3 | Suppressor of cytokine signaling 3 | 12702 | 1.54 | other |
| <i>-adrenergic signaling</i> | | | | |
| Akap6 | A kinase (PRKA) anchor protein 6 | 238161 | 2.57 | other |
| Pkia | Protein kinase (cAMP-dependent, catalytic) inhibitor alpha | 18767 | 2.67 | transporter |
| Ppm1l | Protein phosphatase 1 | 242083 | 1.97 | other |
| Ppp1r14c | Protein phosphatase 1, regulatory (inhibitor) | 76142 | 2.65 | other |
| Ppp2r3a | Protein phosphatase 2 regulatory subunit B, alpha | 19054 | 2.11 | phosphatase |
| Slc8a3 | Solute carrier family 8 (sodium-calcium exchanger), member 3 | 110893 | 2.05 | transporter |
| <i>Glucose metabolism</i> | | | | |
| Prkaa2 | Protein kinase, AMP-activated, alpha 2 catalytic subunit | 108079 | 2.11 | kinase |
| Prkab2 | Protein kinase, AMP-activated, β 2 non-catalytic subunit | 108097 | 1.78 | kinase |
| Eno3 | Enolase 3 | 13808 | 2.65 | enzyme |
| Fbp2 | Fructose-1,6-biphosphatase 2 | 14120 | 2.13 | phosphatase |
| Pfkm | Phosphofructokinase | 18642 | 2.52 | kinase |
| Pgam2 | Phosphoglycerate mutase 2 | 56012 | 3.2 | Phosphatise |
| <i>Lipid metabolism</i> | | | | |
| Cpt1b | Carnitine palmitoyltransferase 1 | 12895 | 2.02 | kinase |
| Acsf6 | Acyl-CoA synthetase long-chain family member 6 | 216739 | 2.06 | ligase |
| Fabp3 | Fatty acid binding protein 3 | 14077 | 2.79 | transporter |
| <i>Oxidative phosphorylation</i> | | | | |
| Cox6a2 | Cytochrome c oxidase, subunit VI a, polypeptide 2 | 12682 | 2.89 | transporter |
| Cox7a1 | Cytochrome c oxidase, subunit VIIa | 12865 | 1.94 | transporter |
| Cox8b | Cytochrome c oxidase, subunit VIIIb | 12869 | 1.57 | transporter |
| <i>MAPK/ERK signaling</i> | | | | |
| Cacna2d1 | Calcium channel voltage dependent, alpha2/delta subunit 1 | 12293 | 2.17 | ion channel |
| Cacnb1 | Calcium channel, voltage dependent, β | 12295 | 2.39 | ion channel |

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|--------------------------|--|-------|------|----------------------|
| | subunit 1 | | | |
| Cacng1 | Calcium channel, voltage dependent, gamma subunit 1 | 12299 | 2.44 | ion channel |
| Egf | Epidermal growth factor | 13645 | 2.11 | growth factor |
| Mef2c | Myocyte enhancer factor 2C | 17260 | 1.67 | transcription factor |
| Mapk12 | Mitogen-activated protein kinase 12 | 29857 | 1.54 | kinase |
| Finc | Flamin C | 68794 | 1.79 | other |
| Casq1 | Calsequestin 1 | 12372 | 2.47 | other |
| <i>Calcium signaling</i> | | | | |
| Asph | Aspartate β -hydroxylase | 65973 | 2.73 | enzyme |
| Atp2a1 | ATPase calcium transportin | 11937 | 2.25 | transporter |
| Cacna1s | Calcium channel, voltage dependent, L type, alpha 1S subunit | 12292 | 2.97 | ion channel |
| Cacna2d1 | Calcium channel voltage dependent, alpha2/delta subunit 1 | 12293 | 2.17 | ion channel |
| Cacnb1 | Calcium channel, voltage dependent, β subunit 1 | 12295 | 2.39 | ion channel |
| Cacng1 | Calcium channel, voltage dependent, gamma subunit 1 | 12299 | 2.44 | ion channel |
| Camk2a | Calcium/calmodulin-dependent protein kinase (CaM kinase)II alpha | 12322 | 2.49 | kinase |
| Casq1 | Calsequestin 1 | 12372 | 2.47 | other |
| Plcd4 | Phospholipase C, delta 4 | 18802 | 2.44 | |

Supplementary Table 2. Selected genes lower in the mesenteric fat from 4 week high fat fed (see Table 1) 11 -HSD1^{-/-} mice (>1.5-fold compared to C57BL/6J).

Selection criteria were based on the analysis of most significant pathways by the WebGestalt and Ingenuity programs as described in Materials and Methods. Fold change represents the ratio of mean mRNA level between HF fed 11 β -HSD1^{-/-} and C57BL/6J, a negative number indicates the transcript is lower in adipose from 11 -HSD1^{-/-} mice.

| Gene symbol | Gene title | Accession | Mean fold difference | Family |
|------------------------------|--|-----------|----------------------|-------------------------|
| <i>Immune cell signaling</i> | | | | |
| Cd28 | CD28 antigen | 12487 | 3.04 | Other |
| Cd3d | CD3-TCR complex | 12500 | 3.47 | Transmembrane receptor |
| Cd3G | CD3-TCR complex | 12502 | 3.55 | Transmembrane receptor |
| Cd8A | CD8A | 12525 | 3.34 | other |
| Cd8B | CD8B | 12526 | 3.4 | Other |
| Itk | IL-2-inducible T-cell kinase | 16428 | 3.52 | Kinase |
| Lat | Linker for activation of T cells | 16797 | 2.6 | Other |
| Lcp2 | Lymphocyte cytosolic protein 2 | 16822 | 2.29 | other |
| Pik3cd | Phosphoinositide-3-kinase, catalytic, delta polypeptide | 18707 | 2.32 | Kinase |
| Ptpcr | Protein tyrosine phosphatase, receptor type C | 19264 | 2.77 | Phosphatase |
| Rasgrp1 | RAS guanyl releasing protein 1 (calcium and DAG regulated) | 19419 | 2.42 | other |
| Vav1 | Vav 1 oncogene | 22324 | 2.19 | Transcription regulator |
| Klrd1 | Killer cell lectin-like receptor subfamily D, | 16643 | 2.73 | Transmembrane |

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|--|---|--------|------|----------------------------|
| | member 1 | | | receptor |
| Bcl2a1 | BCL2-related protein A1 | 12044 | 2.27 | Other |
| Camk2b | Calcium/calmodulin-dependent protein kinase II β | 12323 | 2.57 | Kinase |
| Cd19 | CD19 | 12478 | 3.18 | Other |
| Cd22 | CD22 | 12483 | 4.46 | Other |
| Cd79A | CD79A immunoglobulin associated alpha | 12518 | 3.59 | Transmembrane receptor |
| Cd79B | CD79A immunoglobulin associated β | 15985 | 3.46 | Transmembrane receptor |
| Csf2rb2 | Colony stimulating factor receptor, β 2 | 12984 | 2.51 | Transmembrane receptor |
| Card11 | caspase recruitment domain family, member 11 | 108723 | 2.08 | other |
| <i>NF-kappaB signaling</i> | | | | |
| Cd40 | CD40, TNF receptor superfamily member 5 | 21939 | 2.25 | Transmembrane receptor |
| Prkcb1 | Protein kinase C, β 1 | 18751 | 2.29 | kinase |
| Tlr1 | Toll-like receptor 1 | 21897 | 2.26 | Transmembrane receptor |
| Tcr Alpha | T cell receptor alpha locus | 21473 | 3.51 | other |
| Zap70 | Zeta-chain (TCR) associated protein kinase | 22637 | 2.36 | kinase |
| Lck | Lymphocyte-specific protein tyrosine kinase | 16818 | 3.37 | kinase |
| <i>Antigen processing and presentation</i> | | | | |
| Hla-dmb | Major histocompatibility complex, class II, DM β | 14999 | 2.96 | Transmembrane receptor |
| Hla-doa | Major histocompatibility complex, class II, DO alpha | 15001 | 3.33 | Transmembrane receptor |
| Hla-e | Major histocompatibility complex, class I, E | 15006 | 2.5 | Transmembrane receptor |
| Tap1 | Transporter 1, ATP-binding cassette, subfamily (MDR/TAP) | 21354 | 2.2 | Transporter |
| <i>SAPK/JNK signaling</i> | | | | |
| Lck | Lymphocyte-specific protein tyrosine kinase | 16818 | 3.37 | Kinase |
| Mapk4k1 | Mitogen-activated protein kinase1 | 26411 | 2.5 | kinase |
| Rac2 | Ras-related C3 botulinum toxin substrate 2 (rho family, small GTP binding protein Rac2) | 19354 | 2.47 | enzyme |
| Tcr Alpha | T cell receptor alpha | 21473 | 3.51 | other |
| <i>Chemokine signaling</i> | | | | |
| Ccr6 | Chemokine (C-C motif)receptor6 | 12458 | 3.21 | other |
| Ccr7 | Chemokine (C-C motif)receptor7 | 12775 | 3.93 | other |
| Cxcr4 | Chemokine (C-X-C motif) receptor 4 | 12767 | 2.56 | G-protein coupled receptor |
| Prkcb1 | Protein kinase C, β 1 | 18751 | 2.81 | Kinase |
| Ltb | lymphotoxin B | 16994 | 3.91 | Other |
| Tnfrsf13c | tumor necrosis factor receptor superfamily, | 72049 | 3.5 | Other |

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| | | | | |
|--------------------------------------|---|--------|------|-------------------------|
| | member 13c | | | |
| <i>IL-2 /IL-4 signaling</i> | | | | |
| Il2rg | Interleukin 2 receptor, gamma | 16186 | 2.53 | Transmembrane receptor |
| Pik3cd | Phosphoinositide-3-kinase, catalytic, delta polypeptide | 18707 | 2.32 | Kinase |
| Ptpn6 | Protein tyrosine phosphatase, non-receptor type 6 | 15170 | 2.42 | Phosphatase |
| Lck | Lymphocyte-specific protein tyrosine kinase | 16818 | 3.37 | Kinase |
| <i>JAK/STAT signalling</i> | | | | |
| Stat 1 | Signal transducer and activator of transcription 1 | 20846 | 2.02 | Transcription regulator |
| Stat4 | Signal transducer and activator of transcription Protein tyrosine | 20849 | 2.51 | Transcription regulator |
| Ptpn6 | phosphatase, non-receptor type 6 | 15170 | 2.42 | Phosphatase |
| Pik3cd | Phosphoinositide-3-kinase, catalytic, delta polypeptide | 18707 | 2.32 | Kinase |
| Cblb | Casitas B-lineage lymphoma b | 208650 | 1.78 | Other |
| Il7r | interleukin 7 receptor | 16197 | 2.29 | Transmembrane receptor |
| <i>Toll-like receptor signalling</i> | | | | |
| Cxcl10 | chemokine (C-X-C motif) ligand 10 | 15945 | 2.82 | Other |
| Ccl5 | Chemokine (C-C motif) ligand 5 | 20304 | 2.81 | Other |
| Stat 1 | Signal transducer and activator of transcription 1 | 20846 | 2.02 | Transcription regulator |
| <i>Wnt signaling</i> | | | | |
| Camk2b | Calcium/calmodulin-dependent protein kinase II, β | 12323 | 2.57 | Kinase |
| Lef1 | lymphoid enhancer binding factor 1 | 16842 | 3.03 | other |
| Tcf7 | transcription factor 7, T-cell specific | 21414 | 2.91 | Transcription regulator |

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Supplementary Table 3. Comparison of key gene expression levels in control diet fed C57BL/6J and 11 -HSD1^{-/-} mice. Key genes that were found to be differentially regulated with HF feeding (Fig 1) in adipose tissue of 4 week control diet-fed C57BL/6J and 11 -HSD1^{-/-} mice were compared in mice fed normal diet. Data are mean±SEM of the ratio between the gene and the TBP internal control as described in Materials and Methods. There were no significant differences in relative gene expression between the genotypes on control diet.

| gene | C57BL/6J | 11 -HSD1^{-/-} |
|---------------------|-----------------|-------------------------------|
| <i>Subcutaneous</i> | | |
| Ppar | 1.01±0.1 | 1.11±0.12 |
| Glut4 | 0.87±0.09 | 1.33±0.19 |
| Prkaa2 | 0.94±0.07 | 1.14±0.09 |
| Cpt1b | 1.25±0.19 | 0.82±0.07 |
| Hsbp6 | 0.91±0.15 | 1.29±0.1 |
| Cd8 | 0.73±0.25 | 0.72±0.33 |
| Stat4 | 0.64±0.13 | 0.79±0.11 |
| L-Sel | 0.85±0.23 | 0.93±0.22 |
| Marco | 0.93±0.24 | 0.84±0.19 |
| <i>mesenteric</i> | | |
| Ppar | 1.08±0.23 | 0.96±0.15 |
| Glut4 | 1.07±0.23 | 1.12±0.15 |
| Prkaa2 | 1.11±0.18 | 0.98±0.1 |
| Cpt1b | 1.22±0.18 | 0.7±0.16 |
| Hsbp6 | 1.02±0.11 | 1.1±0.1 |
| Cd8 | 0.92±0.14 | 1.18±0.31 |
| Stat4 | 0.86±0.06 | 1.01±0.12 |
| L-Sel | 0.99±0.19 | 1.17±0.19 |
| Marco | 0.86±0.25 | 1.25±0.38 |

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Supplementary Table 4. Levels of mRNA for cytokine and macrophage polarisation markers in purified mouse stromovascular macrophages after chronic HF feeding. Data are mean±SEM of the ratio between the gene and the TBP internal control as described in Materials and Methods. There was no significant effect of genotype.

| | <i>depot</i> | <i>C57BL/6J</i> | <i>11 -HSD^{-/-}</i> |
|--------------|--------------|-----------------|------------------------------|
| <i>TNF-</i> | SC | 0.41±0.17 | 0.36±0.11 |
| | mes | 0.38±0.15 | 0.36±0.13 |
| <i>MCP-1</i> | SC | 0.42±0.5 | 0.28±0.11 |
| | mes | 0.26±0.5 | 0.24±0.07 |
| <i>IL-6</i> | SC | 0.28±0.11 | 0.18±0.06 |
| | mes | 0.25±0.03 | 0.26±0.04 |
| <i>MIF</i> | SC | 1.05±0.14 | 0.69±0.32 |
| | mes | 0.78±0.21 | 0.98±0.08 |
| <i>IL-10</i> | SC | 1.22±0.45 | 3.35±1.66 |
| | mes | 3.99±1.33 | 2.96±0.77 |
| <i>Arg1</i> | SC | 0.74±0.44 | 0.67±0.27 |
| | mes | 2.02±0.33 | 3.84±1.87 |

Supplementary Table S5. Adipocytokine Release from isolated primary mouse adipocytes. b.d.=below detection. There was no significant effect of genotype.

| | <i>depot</i> | <i>C57BL/6J</i> | | <i>11 -HSD^{-/-}</i> | |
|-----------------------------------|--------------|-----------------|---------|------------------------------|---------|
| | | C | HF | C | HF |
| <i>TNF-</i> <i>pg/ g/24hr</i> | SC | 1.9±0.2 | 1.9±0.3 | 1.9±0.2 | 2.4±0.3 |
| | mes | 1.3±0.3 | 1.2±0.2 | 1.5±0.1 | 1.1±0.1 |
| <i>IL-10</i> <i>pg/ g/24hr</i> | SC | 0.8±0.1 | 0.9±0.2 | 0.9±0.2 | 0.7±0.4 |
| | mes | b.d. | b.d. | b.d. | b.d. |