

Supplementary Material

Metformin prevents key mechanisms of obesity-related complications in visceral white adipose tissue of obese pregnant mice

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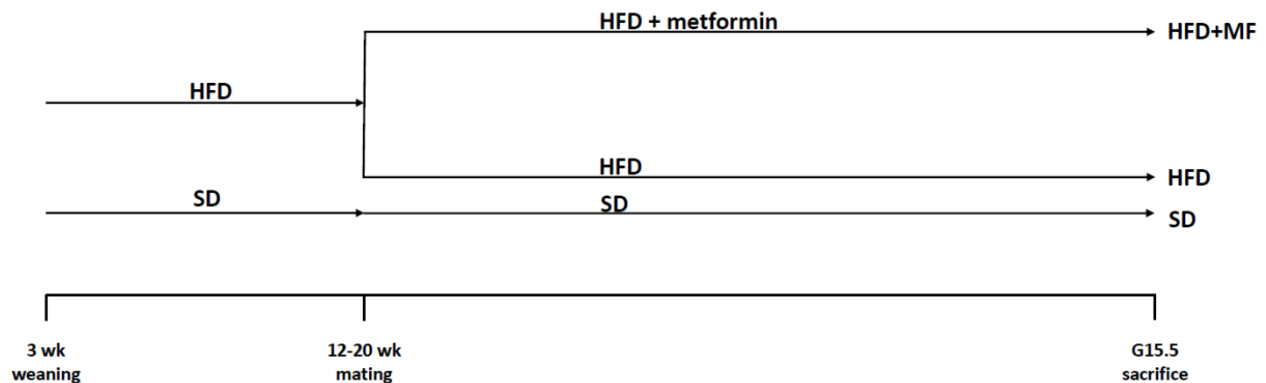


Figure S1. Schematic overview of the mouse groups used in this study. Female mice received either a SD or HFD after weaning until mating. After mating, the control group continued to receive the SD until the end of the experiment. The HFD group was randomly split in two subgroups after mating, while one subgroup continued to feed on HFD until sacrifice at G15.5 (HFD), and one subgroup received HFD plus metformin until G15.5 (HFD + MF). SD = standard diet; HFD = high fat diet; MF = metformin; G = gestational day; wk = week.

Table S1. Details on mouse diets used in this study. ME = metabolizable energy; SD = standard diet; HFD = high fat diet.

	SD	HFD
Company	Ssniff (Soest, Germany)	Altromin (Lage, Germany)
Catalog number	V1534 – R/M-Maintenance	C1057, modified
Metabolizable energy [kcal/kg]	3225	5237
Fat [% of ME]	9	60
Protein [% of ME]	33	16
Carbohydrates [% of ME]	58	24

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Summary tables from proteomic screen of pgWAT at the middle of last trimester

Proteins named in the discussion are highlighted in each table.

Table S2: Significantly and relevantly upregulated proteins in pgWAT at G15.5 in HFD vs SD. 53 proteins are significantly (qvalue < 0.05) and relevantly (fold change > 1.5) upregulated in obese (HFD) compared to lean dams (SD). Protein ID, protein name, gene, q-value (p-value corrected for multiple testing), fold change and valid values of both groups (= number of samples in which a protein was detected) are shown. The table is sorted according to fold change. 5 samples were analyzed per group.

Protein ID	Protein name	Gene	q-Value	Fold change	Valid values HFD	Valid values SD
P27601	Guanine nucleotide-binding protein subunit alpha-13	Gna13	< 0,01	6,92	5	0
Q6PGH2	Hematological and neurological expressed 1-like protein	Hn1l	< 0,05	5,72	5	0
Q0PD20	Ras-related protein Rab-34	Rab34	< 0,01	5,04	5	0
A0A0R4J0F6	Cyclin-G-associated kinase	Gak	< 0,0005	4,27	5	0
Q9WTQ5	A-kinase anchor protein 12	Akap12	< 0,01	4,23	5	5
Q9Z0F7	Gamma-synuclein	Sncg	< 0,05	4,03	5	5
P26645	Myristoylated alanine-rich C-kinase substrate	Marcks	< 0,05	4,03	5	5
Q3THG9	Alanyl-tRNA editing protein Aarsd1	Aarsd1	< 0,0005	3,88	5	0
Q8CG16	Complement C1r-A subcomponent	C1ra	< 0,05	3,83	5	0
Q6PE70	Integrin beta	Itgb5	< 0,001	3,35	5	0
Q8K0C9	GDP-mannose 4,6 dehydratase	Gmds	< 0,05	3,27	5	0
E9PUM4	Talin-2	Tln2	< 0,01	3,20	5	5
E9QA16	Caldesmon 1	Cald1	< 0,05	2,98	5	5
Q8BH58	TIP41-like protein	Tiprl	< 0,05	2,90	5	0
P06728	Apolipoprotein A-IV	Apoa4	< 0,0005	2,73	5	5
Q3UH59	Myosin-10	Myh10	< 0,05	2,69	5	5
O88492	Perilipin-4	Plin4	< 0,05	2,61	5	5
P17439	Glucosylceramidase	Gba	< 0,01	2,49	5	0
Q9DCC5	Chromobox protein homolog 3	Cbx3	< 0,05	2,32	5	5
Q63918	Serum deprivation-response protein	Sdpr	< 0,05	2,31	5	5
P10107	Annexin A1	Anxa1	< 0,001	2,16	5	5
P63024	Vesicle-associated membrane protein 3	Vamp3	< 0,05	2,15	5	5
B1AQF4	Dual specificity protein phosphatase 3	Dusp3	< 0,05	2,13	5	5
Q9Z0P4	Paralemmin-1	Palm	< 0,05	2,10	5	5
Q91VJ2	Protein kinase C delta-binding protein	Prkcdbp	< 0,05	2,09	5	5
Q9DBX6	Cytochrome P450 2S1	Cyp2s1	< 0,05	2,09	5	5
Q00898	Alpha-1-antitrypsin 1-5	Serpina1e	< 0,05	2,05	5	5
P07356	Annexin A2	Anxa2	< 0,01	2,04	5	5
Q61792	LIM and SH3 domain protein 1	Lasp1	< 0,05	2,04	5	5
Q8BGD9	Eukaryotic translation initiation factor 4B	Eif4b	< 0,05	2,01	5	5
Q8BJW6	Eukaryotic translation initiation factor 2A	Eif2a	< 0,05	1,98	5	5
P27546	Microtubule-associated protein 4	Map4	< 0,05	1,92	5	5
O54724	Polymerase I and transcript release factor	Ptrf	< 0,05	1,90	5	5
A0A0R4J034	Pyridoxal-dependent decarboxylase domaincontaining protein 1	Pdxdc1	< 0,05	1,89	5	5
P31324	cAMP-dependent protein kinase type II-beta regulatory subunit	Prkar2b	< 0,05	1,83	5	5
Q61739	Integrin alpha-6	Itga6	< 0,05	1,81	5	5
P48036	Annexin A5	Anxa5	< 0,05	1,79	5	5

Q78IS1	Transmembrane emp24 domain-containing protein 3	Tmed3	< 0,05	1,75	5	5
E9Q8I9	Protein furry homolog	Fry	< 0,05	1,74	5	0
J3QNU6	Beta-arrestin-1	Arrb1	< 0,05	1,73	5	5
Q8R2Y2	Cell surface glycoprotein MUC18	Mcam	< 0,05	1,70	5	5
F8VQJ3	Laminin subunit gamma-1	Lamc1	< 0,05	1,70	5	5
Q6IRU2	Tropomyosin alpha-4 chain	Tpm4	< 0,05	1,66	5	5
Q9JIW9	Ras-related protein Ral-B	Ralb	< 0,05	1,64	5	5
A2AVJ7	Ribosome-binding protein 1	Rrbp1	< 0,05	1,63	5	5
P20152	Vimentin	Vim	< 0,05	1,60	5	5
F7AAP4	Calcium-transporting ATPase	Atp2b4	< 0,05	1,59	5	5
A3KGU7	Spectrin alpha chain, non-erythrocytic 1	Sptan1	< 0,05	1,58	5	5
E9Q616	AHNAK nucleoprotein (desmoyokin)	Ahnak	< 0,05	1,54	5	5
Q62261	Spectrin beta chain, non-erythrocytic 1	Sptbn1	< 0,05	1,54	5	5
P47955	60S acidic ribosomal protein P1	Rplp1	< 0,05	1,54	5	5
Q9CWF2	Tubulin beta-2B chain	Tubb2b	< 0,05	1,53	5	5
F8WIT2	Annexin	Anxa6	< 0,05	1,53	5	5

Table S3: Significantly and relevantly downregulated proteins in pgWAT at G15.5 in HFD vs SD. 143 proteins are significantly (q-value < 0.05) and relevantly (fold change > 1.5) downregulated in obese (HFD) compared to lean dams (SD). Protein ID, protein name, gene, q-value (p-value corrected for multiple testing), fold change and valid values of both groups (= number of samples in which a protein was detected) are shown. The table is sorted according to fold change. 5 samples were analyzed per group.

Protein ID	Protein name	Gene	q-Value	Fold change	Valid values HFD	Valid values SD
Q62264	Thyroid hormone-inducible hepatic protein	Thrsp	< 0,01	-12,47	5	5
Q9JK42	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial	Pdk2	< 0,0005	-8,76	0	5
Q3V117	ATP-citrate synthase	Acly	< 0,0005	-8,52	5	5
F8VPN4	4-alpha-glucanotransferase	Agl	< 0,05	-8,32	5	5
Q5SWU9	Acetyl-CoA carboxylase 1	Acaca	< 0,001	-7,32	5	5
Q80Y98	Phospholipase DDHD2	Ddhd2	< 0,01	-6,98	5	5
Q99J39	Malonyl-CoA decarboxylase, mitochondrial	Mlycd	< 0,01	-6,34	0	5
Q8R2U6	Diphosphoinositol polyphosphate phosphohydrolase 2	Nudt4	< 0,05	-5,36	0	5
Q3TJZ6	Protein FAM98A	Fam98a	< 0,05	-5,17	0	5
A2AQN4	Acetyl-coenzyme A synthetase, cytoplasmic	Acss2	< 0,01	-5,15	5	5
A0A1B0GT63	Transmembrane protein 143	Tmem143	< 0,01	-5,09	0	5
Q9CQ20	Mid1-interacting protein 1	Mid1ip1	< 0,05	-4,85	0	5
Q8BGS7	Choline/ethanolaminephosphotransferase 1	Cept1	< 0,05	-4,81	0	5
P19096	Fatty acid synthase	Fasn	< 0,0005	-4,64	5	5
Q64521	Glycerol-3-phosphate dehydrogenase, mitochondrial	Gpd2	< 0,0005	-4,58	5	5
Q9CXI0	2-methoxy-6-polyprenyl-1,4-benzoquinol methylase, mitochondrial	Coq5	< 0,05	-4,29	0	5
A2AQZ2	Phytanoyl-CoA dioxygenase domain-containing protein 1	Phyhd1	< 0,05	-4,15	0	5
Q9CR26	Vacuolar protein sorting-associated protein VTA1 homolog	Vta1	< 0,05	-4,05	0	5
B7ZMP1	Probable Xaa-Pro aminopeptidase 3	Xpnpep3	< 0,05	-3,93	0	5
G3UZY2	Thioredoxin, mitochondrial	Txn2	< 0,01	-3,88	0	5
Q8K0Z7	Translational activator of cytochrome c oxidase 1	Taco1	< 0,0005	-3,83	0	5
P06801	NADP-dependent malic enzyme	Me1	< 0,01	-3,78	5	5

D3Z4P2	VIP36-like protein	Lman2l	< 0,01	-3,47	0	5
Q8BHE8	Uncharacterized protein C2orf47 homolog, mitochondrial	Maip1	< 0,01	-3,41	0	5
P70444	BH3-interacting domain death agonist	Bid	< 0,01	-3,25	0	5
Q9D2R0	Acetoacetyl-CoA synthetase	Aacs	< 0,05	-3,17	5	5
Q99LB7	Sarcosine dehydrogenase, mitochondrial	Sardh	< 0,05	-3,17	5	5
O08528	Hexokinase-2	Hk2	< 0,05	-3,07	5	5
P13516	Acyl-CoA desaturase 1	Scd1	< 0,01	-3,07	5	5
A2AKN9	Major urinary protein 6	Mup4	< 0,01	-3,04	5	5
P52196	Thiosulfate sulfurtransferase	Tst	< 0,0005	-2,99	5	5
Q9CZB0	Succinate dehydrogenase cytochrome b560 subunit, mitochondrial	Sdhc	< 0,05	-2,97	5	5
A0A1L1SRX2	AMP deaminase 3	Ampd3	< 0,05	-2,93	5	5
Q8JZU2	Tricarboxylate transport protein, mitochondrial	Slc25a1	< 0,01	-2,92	5	5
Q8VHY0	Chondroitin sulfate proteoglycan 4	Cspg4	< 0,05	-2,90	5	5
A0A0R4J0L6	28S ribosomal protein S35, mitochondrial	Mrps35	< 0,05	-2,88	0	5
A2A848	Peroxisomal acyl-coenzyme A oxidase 1	Acox1	< 0,05	-2,87	5	5
E9PXY1	Cullin-4B	Cul4b	< 0,05	-2,80	0	5
A0A140T8R8	DCN1-like protein	Dcun1d1	< 0,05	-2,76	0	5
Q8R086	Sulfite oxidase, mitochondrial	Suox	< 0,0005	-2,72	5	5
Q9D024	Coiled-coil domain-containing protein 47	Ccdc47	< 0,05	-2,71	5	5
Q9D6M3	Mitochondrial glutamate carrier 1	Slc25a22	< 0,001	-2,69	5	5
Q922B1	O-acetyl-ADP-ribose deacetylase MACROD1	MacroD1	< 0,05	-2,68	5	5
P30115	Glutathione S-transferase A3	Gsta3	< 0,05	-2,67	5	5
P40142	Transketolase	Tkt	< 0,05	-2,66	5	5
Q9DCW5	Cytochrome c oxidase subunit 6A, mitochondrial	Cox6a1	< 0,05	-2,65	5	5
S4R225	WD repeat-containing protein 13	Wdr13	< 0,05	-2,64	0	5
Q8K3J1	NADH dehydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial	Ndufs8	< 0,05	-2,64	5	5
Q8K411	Presequence protease, mitochondrial	Pitrm1	< 0,05	-2,63	5	5
Q9D6Y9	1,4-alpha-glucan-branching enzyme	Gbe1	< 0,0005	-2,60	5	5
Q9D023	Mitochondrial pyruvate carrier 2	Mpc2	< 0,05	-2,60	5	5
Q8CFR5	Dystrobrevin	Dtna	< 0,05	-2,59	0	5
Q99LY9	NADH dehydrogenase [ubiquinone] iron-sulfur protein 5	Ndufs5	< 0,05	-2,59	5	5
A0A0R3P9C8	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9, mitochondrial	Ndufa9	< 0,05	-2,59	5	5
Q9CYV5	Transmembrane protein 135	Tmem135	< 0,01	-2,58	0	5
A0A0B4J1G1	Low affinity immunoglobulin gamma Fc region receptor II	Fcgr2b	< 0,05	-2,56	0	5
Q3URE1	Acyl-CoA synthetase family member 3, mitochondrial	Acsf3	< 0,05	-2,56	5	5
J3QMN4	Thioredoxin reductase 2, mitochondrial	Txnrd2	< 0,01	-2,55	5	5
A0A0R4J023	Methylglutaconyl-CoA hydratase, mitochondrial	Auh	< 0,05	-2,52	5	5
Q9QZA0	Carbonic anhydrase 5B, mitochondrial	Ca5b	< 0,01	-2,48	5	5
Q8CAY6	Acetyl-CoA acetyltransferase, cytosolic	Acat2	< 0,05	-2,47	5	5
Q8R164	Valacyclovir hydrolase	Bphl	< 0,05	-2,46	5	5
Q9D0I4	Syntaxin-17	Stx17	< 0,05	-2,44	0	5
O70589	Peripheral plasma membrane protein CASK	Cask	< 0,05	-2,43	0	5
Q9CPR5	39S ribosomal protein L15, mitochondrial	Mrpl15	< 0,05	-2,42	0	5
Q9CQZ5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6	Ndufa6	< 0,01	-2,39	5	5

E9QLB2	Lysophospholipase-like protein 1	Lyplal1	< 0,05	-2,34	5	5
Q9DBL1	Short/branched chain specific acyl-CoA dehydrogenase, mitochondrial	Acadsb	< 0,01	-2,33	5	5
Q9CPQ1	Cytochrome c oxidase subunit 6C	Cox6c	< 0,05	-2,30	5	5
E9QNL5	Sulfotransferase	Sult1a1	< 0,05	-2,29	5	5
Q91VM9	Inorganic pyrophosphatase 2, mitochondrial	Ppa2	< 0,05	-2,28	5	5
Q9CR62	Mitochondrial 2-oxoglutarate/malate carrier protein	Slc25a11	< 0,0005	-2,27	5	5
Q8BWM0	Prostaglandin E synthase 2	Ptges2	< 0,01	-2,27	5	5
G5E8R3	Pyruvate carboxylase	Pcx	< 0,05	-2,25	5	5
F8WIU1	UPF0687 protein C20orf27 homolog	1700037 H04Rik	< 0,05	-2,25	5	5
Q9CQC7	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 4	Ndufb4	< 0,01	-2,25	5	5
Q8K0C4	Lanosterol 14-alpha demethylase	Cyp51a1	< 0,05	-2,23	0	5
Q505D7	Optic atrophy 3 protein homolog	Opa3	< 0,05	-2,20	0	5
Q9ET01	Glycogen phosphorylase, liver form	Pygl	< 0,01	-2,17	5	5
A0A0R4J1R7	Pterin-4-alpha-carbinolamine dehydratase 2	Pcbd2	< 0,05	-2,17	5	5
P0DN34	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 1	Ndufb1	< 0,01	-2,14	5	5
D3YUM1	NADH dehydrogenase [ubiquinone] flavoprotein 1, mitochondrial	Ndufv1	< 0,05	-2,10	5	5
O88696	ATP-dependent Clp protease proteolytic subunit, mitochondrial	Clpp	< 0,01	-2,10	5	5
Q9ERS2	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13	Ndufa13	< 0,05	-2,10	5	5
Q99JR6	Nicotinamide/nicotinic acid mononucleotide adenylyltransferase 3	Nmnat3	< 0,05	-2,09	0	5
Q9D7J9	Enoyl-CoA hydratase domain-containing protein 3, mitochondrial	Echdc3	< 0,01	-2,08	5	5
Q99LS3	Phosphoserine phosphatase	Psph	< 0,05	-2,07	5	5
Q91WD5	NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial	Ndufs2	< 0,05	-2,07	5	5
Q9CQQ7	ATP synthase F(0) complex subunit B1, mitochondrial	Atp5f1	< 0,01	-2,06	5	5
A0A1B0GT92	Glycogen [starch] synthase, muscle	Gys1	< 0,05	-2,03	5	5
Q99LC3	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 10, mitochondrial	Ndufa10	< 0,0005	-2,02	5	5
Q14DH7	Acyl-CoA synthetase short-chain family member 3, mitochondrial	Acss3	< 0,05	-2,01	5	5
P56135	ATP synthase subunit f, mitochondrial	Atp5j2	< 0,05	-2,00	5	5
Q9CQJ8	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9	Ndufb9	< 0,05	-2,00	5	5
Q7TMG8	Protein NipSnap homolog 2	Gbas	< 0,01	-1,99	5	5
P00405	Cytochrome c oxidase subunit 2	mt-Co2	< 0,05	-1,99	5	5
Q99P31	Hsp70-binding protein 1	Hspbp1	< 0,05	-1,93	0	5
Q91ZJ5	UTP--glucose-1-phosphate uridylyltransferase	Ugp2	< 0,05	-1,91	5	5
Q8CHT0	Delta-1-pyrroline-5-carboxylate dehydrogenase, mitochondrial	Aldh4a1	< 0,05	-1,91	5	5
A0A0A0MQ68	Glutaryl-CoA dehydrogenase, mitochondrial	Gcdh	< 0,05	-1,91	5	5
Q9DBL7	Bifunctional coenzyme A synthase	Coasy	< 0,05	-1,90	5	5
P35486	Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial	Pdha1	< 0,05	-1,88	5	5
Q9DCT2	NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial	Ndufs3	< 0,05	-1,87	5	5

P03911	NADH-ubiquinone oxidoreductase chain 4	mt-Nd4	< 0,05	-1,87	5	5
P52480	Pyruvate kinase PKM	Pkm	< 0,05	-1,86	5	5
Q9QZD8	Mitochondrial dicarboxylate carrier	Slc25a10	< 0,05	-1,85	5	5
Q8BGC4	Zinc-binding alcohol dehydrogenase domaincontaining protein 2	Zadh2	< 0,05	-1,82	5	5
Q91VT4	Carbonyl reductase family member 4	Cbr4	< 0,05	-1,82	5	5
Q8CG76	Aflatoxin B1 aldehyde reductase member 2	Akr7a2	< 0,05	-1,81	5	5
P97372	Proteasome activator complex subunit 2	Psme2	< 0,05	-1,80	5	5
P03888	NADH-ubiquinone oxidoreductase chain 1	mt-Nd1	< 0,05	-1,80	5	5
Q9QYR9	Acyl-coenzyme A thioesterase 2, mitochondrial	Acot2	< 0,05	-1,80	5	5
Q9D0M3	Cytochrome c1, heme protein, mitochondrial	Cyc1	< 0,01	-1,79	5	5
Q9DC61	Mitochondrial-processing peptidase subunit alpha	Pmpca	< 0,05	-1,79	5	5
P14142	Solute carrier family 2, facilitated glucose transporter member 4	Slc2a4	< 0,05	-1,79	5	5
P05202	Aspartate aminotransferase, mitochondrial	Got2	< 0,05	-1,78	5	5
Q9DCJ5	NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 8	Ndufa8	< 0,05	-1,77	5	5
Q9DB77	Cytochrome b-c1 complex subunit 2, mitochondrial	Uqcrc2	< 0,01	-1,77	5	5
Q92511	ATPase family AAA domain-containing protein 3	Atad3	< 0,05	-1,76	5	5
Q8CGK3	Lon protease homolog, mitochondrial	Lonp1	< 0,05	-1,74	5	5
Q8K2B3	Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial	Sdha	< 0,01	-1,72	5	5
P06745	Glucose-6-phosphate isomerase	Gpi	< 0,01	-1,72	5	5
Q3UW66	Sulfurtransferase	Mpst	< 0,05	-1,72	5	5
P55302	Alpha-2-macroglobulin receptor-associated protein	Lrpap1	< 0,05	-1,70	5	5
P12382	ATP-dependent 6-phosphofructokinase, liver type	Pfkl	< 0,01	-1,70	5	5
Q6PB66	Leucine-rich PPR motif-containing protein, mitochondrial	Lrprrc	< 0,05	-1,67	5	5
Q9R1J0	Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating	Nsdhl	< 0,05	-1,67	5	5
Q9D172	ES1 protein homolog, mitochondrial	D10Jhu81e	< 0,05	-1,64	5	5
Q9DAR7	m7GpppX diphosphatase	Dcps	< 0,01	-1,63	5	5
P47738	Aldehyde dehydrogenase, mitochondrial	Aldh2	< 0,05	-1,62	5	5
Q8BQ47	Protein canopy homolog 4	Cnpy4	< 0,001	-1,62	5	5
Q9JMH6	Thioredoxin reductase 1, cytoplasmic	Txnrd1	< 0,01	-1,60	5	5
Q9D1D4	Transmembrane emp24 domain-containing protein 10	Tmed10	< 0,05	-1,60	5	5
Q9D6J6	NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial	Ndufv2	< 0,05	-1,60	5	5
O08749	Dihydrolipoyl dehydrogenase, mitochondrial	Dld	< 0,05	-1,59	5	5
P63325	40S ribosomal protein S10	Rps10	< 0,05	-1,58	5	5
Q8BGH2	Sorting and assembly machinery component 50 homolog	Samm50	< 0,05	-1,58	5	5
P15105	Glutamine synthetase	Glul	< 0,05	-1,58	5	5
Q03958	Prefoldin subunit 6	Pfdn6	< 0,05	-1,56	5	5
Q8R0Y6	Cytosolic 10-formyltetrahydrofolate dehydrogenase	Aldh1l1	< 0,05	-1,55	5	5
Q9CY27	Very-long-chain enoyl-CoA reductase	Tecr	< 0,05	-1,54	5	5
P28063	Proteasome subunit beta type-8	Psmb8	< 0,05	-1,52	5	5
Q9R0X4	Acyl-coenzyme A thioesterase 9, mitochondrial	Acot9	< 0,05	-1,52	5	5

Table S4: Significantly and relevantly upregulated proteins in pgWAT at G15.5 in HFD+MF vs HFD. 58 proteins are significantly (q-value < 0.05) and relevantly (fold change > 1.5) upregulated in obese dams treated with metformin during pregnancy (HFD+MF) compared to obese dams (HFD). Protein ID, protein name, gene, q-value (p-value corrected for multiple testing), fold change and valid values of both groups (= number of samples in which a protein was detected) are shown. The table is sorted according to fold change. 4 HFD+MF samples and 5 HFD samples were analyzed.

Protein ID	Protein name	Gene	q-Value	Fold change	Valid values HFD+MF	Valid values HFD
S4R211	Serine-rich coiled-coil domain-containing protein 2	Ccser2	< 0,05	13,01	4	0
Q9Z0Y1	Dynactin subunit 3	Dctn3	< 0,01	8,53	4	0
Q61555	Fibrillin-2	Fbn2	< 0,05	8,00	4	0
B1AZ15	Cordon-bleu protein-like 1	Cobll1	< 0,05	7,94	4	0
Q9CQR4	Acyl-coenzyme A thioesterase 13	Acot13	< 0,05	7,46	4	0
Q99J39	Malonyl-CoA decarboxylase, mitochondrial	Mlycd	< 0,05	7,19	4	0
Q8K019	Bcl-2-associated transcription factor 1	Bclaf1	< 0,05	5,71	4	0
Q8K0D5	Elongation factor G, mitochondrial	Gfm1	< 0,05	4,87	4	0
D3YTQ3	Heterogeneous nuclear ribonucleoprotein D-like	Hnrnpdl	< 0,05	4,80	4	0
Q99JC1	Ig lambda-2 chain C region	Iglc2	< 0,05	4,73	4	0
Q9QUT0	Ammonium transporter Rh type A	Rhag	< 0,05	4,69	4	0
Q59IW6	ABI gene family, member 3 (NESH)-binding protein	Abi3bp	< 0,05	4,44	4	0
Q9JK42	[Pyruvate dehydrogenase (acetyl-transferring)] kinase isozyme 2, mitochondrial	Pdk2	< 0,05	4,35	4	0
Q9D0R8	Protein LSM12 homolog	Lsm12	< 0,05	4,35	4	0
Q6GQT1	Alpha-2-macroglobulin-P	A2m	< 0,05	4,29	4	5
G3X9Q2	Guanine nucleotide-binding protein subunit gamma	Gng7	< 0,05	4,29	4	0
P52623	Uridine-cytidine kinase 1	Uck1	< 0,05	3,87	4	0
A0A0R4J1Z3	Transmembrane protein 33	Tmem33	< 0,05	3,86	4	0
Q9CPU2	NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 2, mitochondrial	Ndufb2	< 0,05	3,71	4	0
Q61584	Fragile X mental retardation syndrome-related protein 1	Fxr1	< 0,05	3,57	4	0
Q569Z5	Probable ATP-dependent RNA helicase DDX46	Ddx46	< 0,05	3,55	4	0
B1AUB9	Nuclear factor 1	Nfia	< 0,05	3,48	4	0
A0A0G2JER9	DnaJ homolog subfamily B member 6	Dnajb6	< 0,05	3,36	4	0
Q8CC86	Nicotinate phosphoribosyltransferase	Naprt	< 0,05	3,35	4	0
Q9D020	Cytosolic 5-nucleotidase 3A	Nt5c3a	< 0,05	3,34	4	0
F6RJ39	Apoptotic chromatin condensation inducer in the nucleus	Acin1	< 0,05	3,34	4	0
H3BL37	Treacle protein	Tcof1	< 0,05	3,30	4	0
Q3UE37	Ubiquitin-conjugating enzyme E2 Z	Ube2z	< 0,05	3,21	4	0
A0A0R4J1W7	Cell division cycle protein 23 homolog	Cdc23	< 0,05	3,08	4	0
Q9JIZ9	Phospholipid scramblase 3	Plscr3	< 0,05	3,08	4	0
Q3U422	NADH dehydrogenase [ubiquinone] flavoprotein 3, mitochondrial	Ndufv3	< 0,05	3,04	4	5
Q9D289	Trafficking protein particle complex subunit 6B	Trappc6b	< 0,05	2,88	4	5
D3Z2Z1	CAP-Gly domain-containing linker protein 1	Clip1	< 0,05	2,69	4	0
Q8VI75	Importin-4	Ipo4	< 0,05	2,69	4	5
Q9CPU4	Microsomal glutathione S-transferase 3	Mgst3	< 0,05	2,66	4	5

Q8C570	mRNA export factor	Rae1	< 0,05	2,40	4	0
Q3UID0	SWI/SNF complex subunit SMARCC2	Smarcc2	< 0,05	2,39	4	5
Q91V35	Receptor-type tyrosine-protein phosphatase	Ptptra	< 0,05	2,38	4	0
D3Z7P3	Glutaminase kidney isoform, mitochondrial	Gls	< 0,05	2,31	4	5
A0A0R4J0X5	Alpha-1-antitrypsin 1-3	Serpina1c	< 0,05	2,25	4	5
P30355	Arachidonate 5-lipoxygenase-activating protein	Alox5ap	< 0,05	2,20	4	0
A2AEM2	Chloride channel CLIC-like protein 1	Clcc1	< 0,05	2,19	4	0
Q91VS7	Microsomal glutathione S-transferase 1	Mgst1	< 0,05	2,11	4	5
P22599	Alpha-1-antitrypsin 1-2	Serpina1b	< 0,05	2,05	4	5
P06728	Apolipoprotein A-IV	Apoa4	< 0,05	1,91	4	5
A0A0R4J170	Transcription activator BRG1	Smarca4	< 0,05	1,86	4	0
Q3UIA2	Rho GTPase-activating protein 17	Arhgap17	< 0,05	1,85	4	5
Q99LC5	Electron transfer flavoprotein subunit alpha, mitochondrial	Etfa	< 0,05	1,79	4	5
Q9Z0U1	Tight junction protein ZO-2	Tjp2	< 0,05	1,78	4	0
Q505D7	Optic atrophy 3 protein homolog	Opa3	< 0,05	1,71	4	0
Q9Z204	Heterogeneous nuclear ribonucleoproteins C1/C2	Hnrnpc	< 0,05	1,69	4	5
Q91XD7	Cysteine-rich with EGF-like domain protein 1	Creld1	< 0,05	1,64	4	5
Q9DB20	ATP synthase subunit O, mitochondrial	Atp5o	< 0,05	1,61	4	5
Q9QYJ0	DnaJ homolog subfamily A member 2	Dnaja2	< 0,05	1,61	4	5
P16858	Glyceraldehyde-3-phosphate dehydrogenase	Gapdh	< 0,05	1,58	4	5
P21619	Lamin-B2	Lmnb2	< 0,05	1,56	4	5
P54822	Adenylosuccinate lyase	Adsl	< 0,05	1,54	4	5
Q62465	Synaptic vesicle membrane protein VAT-1 homolog	Vat1	< 0,01	1,53	4	5

Table S5: Significantly and relevantly downregulated proteins in pgWAT at G15.5 in HFD+MF vs HFD. 45 proteins are significantly (q-value < 0.05) and relevantly (fold change > 1.5) downregulated in obese dams treated with metformin during pregnancy (HFD+MF) compared to obese dams (HFD). Protein ID, protein name, gene, q-value (p-value corrected for multiple testing), fold change and valid values of both groups (= number of samples in which a protein was detected) are shown. The table is sorted according to fold change. 4 HFD+MF samples and 5 HFD samples were analyzed.

Protein ID	Protein name	Gene	q-Value	Fold change	Valid values HFD+MF	Valid values HFD
P20065	Thymosin beta-4	Tmsb4x	< 0,05	-33,30	0	5
A0A0U1RNP7	Perilipin-1	Plin1	< 0,01	-15,75	0	5
Q9ERT9	Protein phosphatase 1 regulatory subunit 1A	Ppp1r1a	< 0,05	-9,09	0	5
P58044	Isopentenyl-diphosphate Delta-isomerase 1	Idi1	< 0,05	-5,57	0	5
G5E870	E3 ubiquitin-protein ligase TRIP12	Trip12	< 0,05	-3,60	0	5
Q9Z0J0	Epididymal secretory protein E1	Npc2	< 0,05	-3,49	4	5
Q91XL1	Leucine-rich HEV glycoprotein	Lrg1	< 0,05	-3,40	4	5
Q62356	Follistatin-related protein 1	Fstl1	< 0,05	-3,16	4	5
Q9QXC1	Fetuin-B	Fetub	< 0,05	-2,60	4	5
Q8QZR5	Alanine aminotransferase 1	Gpt	< 0,05	-2,39	4	5
Q9DBX6	Cytochrome P450 2S1	Cyp2s1	< 0,05	-2,33	4	5
P51855	Glutathione synthetase	Gss	< 0,05	-2,28	4	5
P67984	60S ribosomal protein L22	Rpl22	< 0,05	-2,07	4	5
Q9D1X0	Nucleolar protein 3	Nol3	< 0,05	-2,05	4	5
Q9QZ06	Toll-interacting protein	Tollip	< 0,05	-2,03	4	5
Q9CXR1	Dehydrogenase/reductase SDR family member 7	Dhrs7	< 0,05	-1,97	4	5

P62897	Cytochrome c, somatic	Cycs	< 0,05	-1,96	4	5
Q9R099	Transducin beta-like protein 2	Tbl2	< 0,05	-1,93	4	5
Q9CQS8	Protein transport protein Sec61 subunit beta	Sec61b	< 0,05	-1,90	4	5
Q9ERE7	LDLR chaperone MESD	Mesdc2	< 0,05	-1,89	4	5
Q8R317	Ubiquilin-1	Ubqln1	< 0,05	-1,77	4	5
P63330	Serine/threonine-protein phosphatase 2A catalytic subunit alpha isoform	Ppp2ca	< 0,05	-1,74	4	5
Q9CQ65	S-methyl-5-thioadenosine phosphorylase	Mtap	< 0,05	-1,72	4	5
Q922Q8	Leucine-rich repeat-containing protein 59	Lrrc59	< 0,05	-1,72	4	5
P17563	Selenium-binding protein 1	Selenbp1	< 0,05	-1,71	4	5
P70296	Phosphatidylethanolamine-binding protein 1	Pebp1	< 0,05	-1,71	4	5
A0A0B4J1E7	Importin subunit alpha-3	Kpna4	< 0,05	-1,70	4	5
Q9Z1Z2	Serine-threonine kinase receptor-associated protein	Strap	< 0,05	-1,69	4	5
Q61035	Histidine--tRNA ligase, cytoplasmic	Hars	< 0,05	-1,68	4	5
O08915	AH receptor-interacting protein	Aip	< 0,05	-1,67	4	5
Q3UGR5	Haloacid dehalogenase-like hydrolase domain-containing protein 2	Hdhd2	< 0,05	-1,67	4	5
P68037	Ubiquitin-conjugating enzyme E2 L3	Ube2l3	< 0,05	-1,66	4	5
Q91YJ2	Sorting nexin-4	Snx4	< 0,05	-1,64	4	5
O35945	Aldehyde dehydrogenase, cytosolic 1	Aldh1a7	< 0,05	-1,63	4	5
P57759	Endoplasmic reticulum resident protein 29	Erp29	< 0,05	-1,61	4	5
E9Q137	Testis-expressed gene 264	Tex264	< 0,05	-1,61	4	5
Q9QZ88	Vacuolar protein sorting-associated protein 29	Vps29	< 0,05	-1,58	4	5
O70274	Protein tyrosine phosphatase type IVA 2	Ptp4a2	< 0,05	-1,58	4	5
Q9DAK9	14 kDa phosphohistidine phosphatase	Phpt1	< 0,05	-1,57	4	5
Q91V41	Ras-related protein Rab-14	Rab14	< 0,05	-1,56	4	5
O35598	Disintegrin and metalloproteinase domain-containing protein 10	Adam10	< 0,05	-1,55	4	5
Q07797	Galectin-3-binding protein	Lgals3bp	< 0,05	-1,55	4	5
Q8BKE6	Cytochrome P450 20A1	Cyp20a1	< 0,05	-1,55	4	5
Q8JZN1	Macrophage galactose N-acetyl-galactosamine-specific lectin 2	Mgl2	< 0,05	-1,54	4	5
Q02819	Nucleobindin-1	Nucb1	< 0,05	-1,52	4	5