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

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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 1: Significantly and relevantly upregulated proteins in pgWAT at G15.5 in HFD vs SD. 53 proteins are significantly (q-value < 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               |
| A0A0R4JOF6 | Cyclin-G-associated kinase                        | Gak      | < 0.005 | 4.27        | 5                | 0               |
| Q9WTQ5     | A-kinase anchor protein 12                         | Akap12   | < 0.01  | 4.23        | 5                | 5               |
| Q920F7     | Gamma-synuclein                                   | Snscg    | < 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               |
| Q88492     | 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               |
Table 2: 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 | < 0,005  | -8,76       | 0                 | 5              |
| Q3V117     | ATP-citrate synthase | Acly | < 0,005  | -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              |
| Q99I39     | 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              |
| Gene Name | Description | Fold Change | p-value | q-value | Enrichment Score |
|-----------|-------------|-------------|---------|---------|-----------------|
| Q8BG57    | 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-polyrenyl-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 |
| B7ZM1    | Probable Xaa-Pro aminopeptidase 3 | Xpnpep3 | < 0.05 | -3.93 | 0 5 |
| G3UZ2Y    | Thioredoxin, mitochondrial | Txn2 | < 0.01 | -3.88 | 0 5 |
| Q8K027    | Translational activator of cytochrome c oxidase 1 | Tac1 | < 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 |
| Q99L7     | Sarcosine dehydrogenase, mitochondrial | Sardh | < 0.05 | -3.17 | 5 5 |
| Q08528    | 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 |
| A0A1L1SXR2 | AMP deaminase 3 | Ampd3 | < 0.05 | -2.93 | 5 5 |
| Q8JU2     | Tricarboxylate transport protein, mitochondrial | Slt25a1 | < 0.01 | -2.92 | 5 5 |
| Q8VHY0    | Chondroitin sulfate proteoglycan 4 | Csgp4 | < 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 |
| E9PX1     | 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 | Slt25a22 | < 0.001 | -2.69 | 5 5 |
| Q922B1    | O-acetyl-ADP-ribose deacetylase MACROD1 | Macrd1 | < 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 | Ndafa9 | < 0.05 | -2.59 | 5 5 |
| Q9CV5     | 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 |
| Gene ID | Description                                                                 | Protein ID | p-value | Log2FC | Count | Category |
|---------|------------------------------------------------------------------------------|------------|---------|--------|-------|----------|
| 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        |
| Q9QZ8A  | Carbonic anhydrase 5B, mitochondrial                                         | Ca5b       | <0.01   | -2.48  | 5     | 5        |
| Q8CAY6  | Acetyl-CoA acetyltransferase, cytosolic                                      | Acat2      | <0.05   | -2.47  | 5     | 5        |
| Q8R1L4  | Valacyclovir hydrolase                                                       | Bphl       | <0.05   | -2.46  | 5     | 5        |
| Q9D04I  | Syntaxin-17                                                                  | Stx17      | <0.05   | -2.44  | 5     | 5        |
| Q7OS89  | Peripheral plasma membrane protein CASK                                      | Cask       | <0.05   | -2.43  | 5     | 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        |
| E9QN1L5 | Sulfortransferase                                                            | 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        |
| Q8BW0M  | Prostaglandin E synthase 2                                                   | Ptges2     | <0.01   | -2.27  | 5     | 5        |
| G5E8R3  | Pyruvate carboxylase                                                         | Pcx        | <0.05   | -2.25  | 5     | 5        |
| F8W1U1  | UPF0687 protein C2orf27 homolog                                              | 1700037H04Rik | <0.05   | -2.25  | 5     | 5        |
| Q9CQC7  | NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 4                 | Ndufb4     | <0.01   | -2.25  | 5     | 5        |
| Q8KOC4  | Lanosterol 14-alpha demethylase                                               | Cyp51a1    | <0.05   | -2.23  | 5     | 5        |
| Q505D7  | Optic atrophy 3 protein homolog                                               | Op3        | <0.05   | -2.20  | 0     | 5        |
| Q9ET01  | Glycogen phosphorylase, liver form                                           | Pygl       | <0.01   | -2.17  | 5     | 5        |
| A0A0R4J1R7 | Pterin-4-alpha-carbolamine 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        |
| Q88696  | 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 adenyllytransferase 3             | Nmnat3     | <0.05   | -2.09  | 5     | 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        |
| Q91W0D5 | NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial        | Ndufs2     | <0.05   | -2.07  | 5     | 5        |
| Q9CQQ7  | ATP synthase F(0) complex subunit B1, mitochondrial                          | Atpf51     | <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        |
| P5613S  | ATP synthase subunit f, mitochondrial                                         | Atpf5j2    | <0.05   | -2.00  | 5     | 5        |
| Q9CQQ8  | NADH dehydrogenase [ubiquinone] 1 beta subcomplex subunit 9                 | Ndufb9     | <0.05   | -2.00  | 5     | 5        |
| Q7TM88  | 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        |
| Gene ID | Description                                                                 | Exp. | Fold Change | P-Value | Tissue | NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial |
|---------|-------------------------------------------------------------------------------|------|-------------|---------|--------|---------------------------------------------------------------|
| Q99P31  | Hsp70-binding protein 1                                                        |      | <0.05       | -1.93   | 0      | 5                                                             |
| Q91Z5J  | UTP-glucose-1-phosphate uridylyltransferase                                   |      | <0.05       | -1.91   | 5      | 5                                                             |
| Q8CHT0  | Delta-1-pyruvoly-5-carboxylate dehydrogenase, mitochondrial                   |      | <0.05       | -1.91   | 5      | 5                                                             |
| A0A0A0MQ68 | Glutaryl-CoA dehydrogenase, mitochondrial                                      |      | <0.05       | -1.91   | 5      | 5                                                             |
| Q9DBL7  | Bifunctional coenzyme A synthase                                               |      | <0.05       | -1.90   | 5      | 5                                                             |
| P35486  | Pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial|      | <0.05       | -1.88   | 5      | 5                                                             |
| Q9DCT2  | NADH dehydrogenase [ubiquinone] iron-sulfur protein 3, mitochondrial         |      | <0.05       | -1.87   | 5      | 5                                                             |
| P03911  | NADH-ubiquinone oxidoreductase chain 4                                         |      | <0.05       | -1.87   | 5      | 5                                                             |
| P52480  | Pyruvate kinase PKM                                                           |      | <0.05       | -1.86   | 5      | 5                                                             |
| Q9QZD8  | Mitochondrial dicarboxylate carrier                                            |      | <0.05       | -1.85   | 5      | 5                                                             |
| Q8BGC4  | Zinc-binding alcohol dehydrogenase domain-containing protein 2                |      | <0.05       | -1.82   | 5      | 5                                                             |
| Q91VT4  | Carbonyl reductase family member 4                                            |      | <0.05       | -1.82   | 5      | 5                                                             |
| Q8CG76  | Afatoxin B1 aldehyde reductase member 2                                       |      | <0.05       | -1.81   | 5      | 5                                                             |
| P97372  | Proteasome activator complex subunit 2                                       |      | <0.05       | -1.80   | 5      | 5                                                             |
| P03888  | NADH-ubiquinone oxidoreductase chain 1                                        |      | <0.05       | -1.80   | 5      | 5                                                             |
| Q9QYR9  | Acyl-coenzyme A thiosterase 2, mitochondrial                                   |      | <0.05       | -1.80   | 5      | 5                                                             |
| Q9DOM3  | Cytochrome c1, heme protein, mitochondrial                                    |      | <0.01       | -1.79   | 5      | 5                                                             |
| Q9DC61  | Mitochondrial-processing peptidase subunit alpha                              |      | <0.05       | -1.79   | 5      | 5                                                             |
| P14142  | Solute carrier family 2, facilitated glucose transporter member 4             |      | <0.05       | -1.79   | 5      | 5                                                             |
| P05202  | Aspartate aminotransferase, mitochondrial                                     |      | <0.05       | -1.78   | 5      | 5                                                             |
| Q9DCJ5  | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 8                 |      | <0.05       | -1.77   | 5      | 5                                                             |
| Q9DB77  | Cytochrome b-c1 complex subunit 2, mitochondrial                              |      | <0.01       | -1.77   | 5      | 5                                                             |
| Q925I1  | ATPase family AAA domain-containing protein 3                                   |      | <0.05       | -1.76   | 5      | 5                                                             |
| Q8CGK3  | Lon protease homolog, mitochondrial                                           |      | <0.05       | -1.74   | 5      | 5                                                             |
| Q8K2B3  | Succinate dehydrogenase [ubiquinone] flavoprotein subunit, mitochondrial      |      | <0.01       | -1.72   | 5      | 5                                                             |
| P06745  | Glucose-6-phosphate isomerase                                                  |      | <0.01       | -1.72   | 5      | 5                                                             |
| Q3UW66  | Sulfurtransferase                                                             |      | <0.05       | -1.72   | 5      | 5                                                             |
| P55302  | Alpha-2-macroglobulin receptor-associated protein                             |      | <0.05       | -1.70   | 5      | 5                                                             |
| P12382  | ATP-dependent 6-phosphofructokinase, liver type                               |      | <0.01       | -1.70   | 5      | 5                                                             |
| Q6PB66  | Leucine-rich PPR motif-containing protein, mitochondrial                      |      | <0.05       | -1.67   | 5      | 5                                                             |
| Q9R1J0  | Sterol-4-alpha-carboxylate 3-dehydrogenase, decarboxylating                    |      | <0.05       | -1.67   | 5      | 5                                                             |
| Q9D172  | ES1 protein homolog, mitochondrial                                            |      | <0.05       | -1.64   | 5      | 5                                                             |
| Q9DAR7  | m7GpppX diphosphatase                                                          |      | <0.01       | -1.63   | 5      | 5                                                             |
| P47738  | Aldehyde dehydrogenase, mitochondrial                                         |      | <0.05       | -1.62   | 5      | 5                                                             |
| Q8BQ47  | Protein canopy homolog 4                                                       |      | <0.001      | -1.62   | 5      | 5                                                             |
| Q9JM6H  | Thioredoxin reductase 1, cytoplasmian                                          |      | <0.01       | -1.60   | 5      | 5                                                             |
| Q9D1D4  | Transmembrane emp24 domain-containing protein 10                              |      | <0.05       | -1.60   | 5      | 5                                                             |
| Q9D6J6  | NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial                |      | <0.05       | -1.60   | 5      | 5                                                             |
| Q9D6J6  | NADH dehydrogenase [ubiquinone] flavoprotein 2, mitochondrial                |      | <0.05       | -1.60   | 5      | 5                                                             |
| P46325  | 40S ribosomal protein S10                                                     |      | <0.05       | -1.59   | 5      | 5                                                             |
| Q88GH2  | Sorting and assembly machinery component 50 homolog                           |      | <0.05       | -1.58   | 5      | 5                                                             |
| P15105  | Glutamine synthetase                                                          |      | <0.05       | -1.58   | 5      | 5                                                             |
| Q03958  | Prefoldin subunit 6                                                           |      | <0.05       | -1.56   | 5      | 5                                                             |
Table 3: 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 |
| Q920Y1     | Dynactin subunit 3 | Dctn3 | < 0,01 | 8,53 | 4 | 0 |
| Q61555     | Fibrillin-2 | Fbn2 | < 0,05 | 8,00 | 4 | 0 |
| B1A215     | Cordon-bleu protein-like 1 | Cobl1 | < 0,05 | 7,94 | 4 | 0 |
| Q9CQ84     | Acyl-coenzyme A thioesterase 13 | Acot13 | < 0,05 | 7,46 | 4 | 0 |
| Q9J139     | 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 |
| D3YQ3      | Heterogeneous nuclear ribonucleoprotein D-like | Hnrnpd1 | < 0,05 | 4,80 | 4 | 0 |
| Q9J1C1     | Ig lambda-2 chain C region | Igcl2 | < 0,05 | 4,73 | 4 | 0 |
| Q9QT0      | Ammonium transporter Rh type A | Rhag | < 0,05 | 4,69 | 4 | 0 |
| Q591W6     | 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 |
| Q6GQ7T     | Alpha-2-macroglobulin-P | A2m | < 0,05 | 4,29 | 4 | 5 |
| G3XQ2      | Guanine nucleotide-binding protein subunit gamma | Gng7 | < 0,05 | 4,29 | 4 | 0 |
| P528Z3     | 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 | Ndubf2 | < 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 |
| Q8C8C6     | Nicotinate phosphoribosyltransferase | Naprt | < 0,05 | 3,35 | 4 | 0 |
| Q9D020     | Cytosolic 5-nucleotidase 3A | NtSc3a | < 0,05 | 3,34 | 4 | 0 |
| F6RJ39     | Apoptotic chromatin condensation inducer in the nucleus | Acin1 | < 0,05 | 3,34 | 4 | 0 |
| H3B37      | 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 |
| Q9JJZ9     | Phospholipid scramblase 3 | Plscr3 | < 0,05 | 3,08 | 4 | 0 |
| Q3U422     | NADH dehydrogenase [ubiquinone] flavoprotein 3, mitochondrial | Nduv3 | < 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 |
| Q8V715     | Importin-4 | Ipo4 | < 0,05 | 2,69 | 4 | 5 |
| Q9CPU4     | Microsomal glutathione S-transferase 3 | Mgst3 | < 0,05 | 2,66 | 4 | 5 |
| Q8CS70     | mRNA export factor | Rae1 | < 0,05 | 2,40 | 4 | 0 |
Table 4: 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  | -3.30       | 0                   | 5               |
| A0AOU1RNP7 | 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 |
| Q9D0J0     | Epididymal secretory protein E1 | Npc2 | < 0.05  | -3.49 | 0 | 5 |
| Q91XL1     | Leucine-rich HEV glycoprotein | Lrg1 | < 0.05  | -3.40 | 4 | 5 |
| Q62356     | Follistatin-related protein 1 | Fst1 | < 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 |
| Q9D8X6     | Cytochrome P450 251 | 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 |
| Q9CQ58     | Protein transport protein Sec61 subunit beta | Sec61b | < 0.05  | -1.90 | 4 | 5 |
| Q9ERE7     | LDLR chaperone MESD | Mesdc2 | < 0.05  | -1.89 | 4 | 5 |
| Gene ID | Protein Name | Description | E-Value | Log2 Fold Change | q-value | Strand |
|---------|--------------|-------------|---------|-----------------|---------|--------|
| Q8R317  | Ubiquilin-1  |              | < 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 | Selbp1 | < 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      |
| Q9Z122  | 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 | Hdh2 | < 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      |
| Q35945  | 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      |
| Q70274  | Protein tyrosine phosphatase type IVA 2 | Ptp4a2 | < 0.05  | -1.58           | 4       | 5      |
| Q9DAK9  | 14 kDa phosphohistidine phosphatase | Pht1 | < 0.05  | -1.57           | 4       | 5      |
| Q91V41  | Ras-related protein Rab-14 | Rab14 | < 0.05  | -1.56           | 4       | 5      |
| Q35598  | 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      |
| Q88KE6  | Cytochrome P450 20A1 | Cyp20a1 | < 0.05  | -1.55           | 4       | 5      |
| Q8IZN1  | 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      |