

**Supplementary Table 1. WB and IF/ ICC antibodies**

| <b>Primary antibodies</b>  | <b>Catalog no.</b> | <b>Dilution</b>             | <b>Supplier</b> |
|----------------------------|--------------------|-----------------------------|-----------------|
| Rabbit anti-KIM1           | ab228973           | IF: 1 to 50                 | Abcam           |
| Mouse anti-4-HNE           | ab48506            | IF: 1 to 50                 | Abcam           |
| Rabbit anti-PPAR $\alpha$  | bs-23398R          | WB: 1 to 1000; IF: 1 to 50  | bioss           |
| Rabbit anti-CPT1           | 15184-1-AP         | WB: 1 to 1000               | Proteintech     |
| Rabbit anti-ACOX1          | AB184032           | WB: 1 to 1000;              | Abcam           |
| Rabbit anti-PGC-1          | SAB2108742         | WB: 1 to 1000; IF: 1 to 50  | Sigma           |
| Mouse anti-AMPK $\alpha$   | GTX60403           | WB: 1 to 1000               | GeneTex         |
| Rabbit anti-pAMPK $\alpha$ | 2535               | WB: 1 to 1000               | CST             |
| Rabbit anti-CDase          | DF9192             | WB: 1 to 1000               | Affinty         |
| Rabbit anti-Sphk1          | 10670-1-AP         | WB: 1 to 1000; IF: 1 to 50  | Proteintech     |
| Rabbit anti-Spns2          | AB82629            | WB: 1 to 1000               | Abcam           |
| Rabbit anti-S1pr1          | AB11424            | WB: 1 to 1000               | Abcam           |
| Mouse anti- $\alpha$ -SMA  | BM0002             | WB: 1 to 1000               | Bosterbio       |
| Rabbit anti-E-ca           | 3195T              | WB: 1 to 1000               | CST             |
| Rabbit anti-cPLA2          | 5479               | WB: 1 to 1000; ICC: 1 to 50 | CST             |
| Rabbit anti- P-cPLA2       | 53044              | WB: 1 to 1000               | CST             |
| Rabbit anti-cPLA2f         | DF9430             | WB: 1 to 1000; IF: 1 to 50  | Affinty         |
| Mouse anti- $\beta$ -actin | BM0627             | WB: 1 to 1000               | Bosterbio       |

**Supplementary Table 2. Sequences of the realtime PCR Primers**

| <b>Genes</b>   | <b>Forward Primers (5'-3')</b> | <b>Reverse Primers (5'-3')</b> |
|----------------|--------------------------------|--------------------------------|
| <i>Cd36</i>    | CACAGCTGCCTTCTGAAATGTGTGG      | TTTCTACGTGGCCCGTTCTAATTC       |
| <i>Fabp4</i>   | GGCATGGCCAAACCTAACAT           | TGTACCAGGACACCCCCATC           |
| <i>Srebfl</i>  | GTGAGGCGGCTCTGGAACAGAC         | ATAGGGGGCGTCAAACAGGCC          |
| <i>Fasn</i>    | GGCTCTATGGATTACCCAAGC          | CCAGTGTTCTGTTCTCTCGGA          |
| <i>Acaca</i>   | CAACACTGGGCGCAGGTTTA           | CAACACTGGGCGCAGGTTTA           |
| <i>Scd1</i>    | ACCATCACAGCACCTCCTTC           | ATTTTCAGGGCGGATGTCTTC          |
| <i>Ppara</i>   | CAATGGAGATGGTGGACACA           | TTGTAGGAAGTCTGCCGAGAG          |
| <i>cpt1a</i>   | GATCTACAATTCCCCTCTGCTCT        | TAGAGCCAGACCTTGAAGTAACG        |
| <i>acox1</i>   | TATTCGGCTATGACTGGGCACA         | GATG-GATACTTTCTCGGCAGGA        |
| <i>Hkl</i>     | AAAGCGAGGGGACTATGA             | ATCAATGTGCCTCAGTTCC            |
| <i>Phkl</i>    | TGTGGTCCGAGTTGGTATCTT          | GCACTTCCAATCACTGTGCC           |
| <i>Pkm</i>     | GTGGCTCGGCTGAATTTCTCT          | GTGGCTCGGCTGAATTTCTCT          |
| <i>Acer1</i>   | TCTGAGGTGGATTGGTGTGAG          | TGAGGGGTCCAAAGATGAGGA          |
| <i>Spt</i>     | TCCTCTTGATCGCTTCCAAAGG         | GGCTTTTTGTCTAAGCTCCTCTT        |
| <i>Cers2</i>   | ATGCTCCAGACCTTGTATGACT         | CTGAGGCTTTGGCATAGACAC          |
| <i>Sgpl1</i>   | CTGAAGGACTTCGAGCCTTATTT        | CTGAAGGACTTCGAGCCTTATTT        |
| <i>SphK1</i> * | GCTCTGGTGGTCATGTCTGG           | GCTCTGGTGGTCATGTCTGG           |
| <i>cPla2</i> * | GGCGGGAAACCTACCCATAC           | CCACAGTTGCACATAGCAGT           |
| <i>cPla2a</i>  | CAGCACATTATAGTGGAACACCA        | AGTGTCCAGCATATCGCCAAA          |
| <i>cPla2b</i>  | TGGCCCCCTAGCCAACTTTG           | TGGCCCCCTAGCCAACTTTG           |
| <i>cPla2c</i>  | AGGAGCTGAAACATCGGTATGA         | CTGCAAAGATGGGATAGGGC           |
| <i>cPla2d</i>  | CCATCCTTACCAGGAGGAGG           | TGGAGTTAGTGACTGTTTGGGT         |
| <i>cPla2e</i>  | ATGGTGACAGACTCCTTCGAG          | CCTCTGCGTAAAGCTGTGG            |
| <i>cPla2f</i>  | AGCCATACTGCTACGGAAGAC          | TTTGGACAACTTATCTGTGTGCT        |
| 18s            | ACACGGA CAGGATTGACAGA          | GGACATCTAAGGGCATCACAG          |

\*Human

Supplementary Table 3.

| ID                  | Metabolite                     | ratio       | t.test_p.value | t.test_p.value_BHcorrec | VIP      | regulated |
|---------------------|--------------------------------|-------------|----------------|-------------------------|----------|-----------|
| pos-0.964_260.05078 | suprofen                       | 1.345029176 | 0.049058836    | 0.999216615             | 1.778286 | up        |
| pos-1.572_189.06339 | aminodhq                       | 1.91883867  | 0.046595085    | 0.999216615             | 2.182525 | up        |
| pos-3.011_87.10479  | isoamylamine                   | 2.403145466 | 0.046579771    | 0.999216615             | 0.965273 | up        |
| neg-4.321_225.13639 | terbutaline                    | 1.251426113 | 0.042040581    | 0.995485198             | 1.790896 | up        |
| pos-3.734_232.08443 | nalidixic acid                 | 1.456722866 | 0.041888044    | 0.999216615             | 1.923989 | up        |
| pos-0.772_240.02344 | l-cystine                      | 1.302309068 | 0.041806489    | 0.999216615             | 1.432361 | up        |
| neg-3.753_232.0846  | nalidixic acid                 | 1.500196343 | 0.03531295     | 0.995485198             | 2.242636 | up        |
| neg-1.366_192.0268  | citric acid                    | 5.057683575 | 0.03226811     | 0.995485198             | 2.08456  | up        |
| neg-0.903_112.0159  | 2-furoate                      | 3.02321469  | 0.030022557    | 0.995485198             | 2.283844 | up        |
| pos-2.715_159.0683  | 3-methyl-quinolin-2-ol         | 1.693582582 | 0.027617335    | 0.999216615             | 1.704483 | up        |
| pos-3.738_129.05781 | quinoline                      | 1.486236588 | 0.027546471    | 0.999216615             | 2.180134 | up        |
| pos-0.883_244.06909 | pseudouridine                  | 1.214621851 | 0.026848482    | 0.999216615             | 1.881152 | up        |
| pos-9.804_311.12588 | imazaquin                      | 1.426737931 | 0.025872051    | 0.999216615             | 1.88121  | up        |
| neg-3.126_86.03667  | crotonic acid                  | 41.89435072 | 0.025000503    | 0.995485198             | 2.058501 | up        |
| neg-3.291_177.04577 | n-formyl-l-methionine          | 1.881885885 | 0.023666756    | 0.995485198             | 1.446308 | up        |
| pos-3.318_205.0376  | xanthurenic acid               | 1.569062009 | 0.019532163    | 0.999216615             | 1.022362 | up        |
| neg-3.418_145.05264 | 1(2h)-isoquinolinone           | 1.611893372 | 0.018585595    | 0.995485198             | 2.473893 | up        |
| neg-0.742_226.10647 | carnosine                      | 1.662403392 | 0.016805154    | 0.995485198             | 1.419471 | up        |
| neg-0.84_158.04364  | (r)(-)-allantoin               | 1.583720325 | 0.01556653     | 0.995485198             | 1.907263 | up        |
| pos-3.638_285.10329 | probenecid                     | 2.620980812 | 0.013941072    | 0.999216615             | 2.218814 | up        |
| pos-3.521_146.03668 | coumarin                       | 2.070601659 | 0.047058777    | 0.999216615             | 1.386331 | up        |
| pos-1.342_188.11575 | 6-acetamido-3-aminohexanoate   | 1.68860826  | 0.046444273    | 0.999216615             | 2.285881 | up        |
| pos-0.881_254.12615 | midodrine                      | 1.491980867 | 0.046088752    | 0.999216615             | 1.418811 | up        |
| pos-3.739_304.10289 | vicine                         | 2.450435261 | 0.045964138    | 0.999216615             | 2.092452 | up        |
| pos-3.308_297.08976 | 5'-s-methyl-5'-thioadenosine   | 1.366392772 | 0.039538598    | 0.999216615             | 2.211922 | up        |
| neg-3.837_342.13147 | coniferin                      | 3.876808225 | 0.033483079    | 0.995485198             | 2.13873  | up        |
| neg-3.337_205.03737 | xanthurenic acid               | 1.705330387 | 0.030321183    | 0.995485198             | 1.221983 | up        |
| neg-0.902_174.01618 | trans-aconitic acid            | 1.445849225 | 0.03008955     | 0.995485198             | 2.709393 | up        |
| neg-3.517_176.06826 | 2-isopropylmalic acid          | 1.676147123 | 0.028732288    | 0.995485198             | 1.6486   | up        |
| pos-3.474_180.05345 | nicotinuric acid               | 2.932233781 | 0.021031368    | 0.999216615             | 2.809489 | up        |
| pos-1.38_250.06201  | gamma-glutamylcysteine         | 1.453525102 | 0.018158003    | 0.999216615             | 2.181422 | up        |
| pos-0.885_216.07431 | 8-hydroxyalanylclavam          | 1.355554475 | 0.016459101    | 0.999216615             | 2.493403 | up        |
| pos-3.403_196.12128 | fasoracetam                    | 1.905480492 | 0.014942857    | 0.999216615             | 2.563992 | up        |
| pos-4.728_299.28183 | d-sphingosine                  | 1.989727494 | 0.014811645    | 0.999216615             | 2.652118 | up        |
| pos-4.567_285.26612 | c17 sphingosine                | 2.195959587 | 0.013682936    | 0.995485198             | 1.530609 | up        |
| neg-3.474_444.1746  | difenacoum                     | 2.736027548 | 0.011254393    | 0.995485198             | 2.951155 | up        |
| neg-0.842_156.05338 | 4-imidazolone-5-propanoate     | 2.02366249  | 0.010805049    | 0.995485198             | 3.411759 | up        |
| pos-0.809_165.04566 | l-methionine sulfoxide         | 1.667202354 | 0.007146735    | 0.999216615             | 1.678909 | up        |
| pos-3.343_269.10829 | fenothiocarb sulfoxide         | 4.277163592 | 0.003110912    | 0.952872474             | 2.639896 | up        |
| pos-3.388_285.10348 | probenecid                     | 6.211689667 | 0.001420755    | 0.621681935             | 3.283284 | up        |
| pos-4.756_224.14073 | (+/-)-6-hydroxy-3-oxo-alpha-io | 0.852675962 | 0.049548706    | 0.999216615             | 1.315322 | down      |
| pos-3.233_503.27477 | mycalamide a                   | 0.705828732 | 0.049450927    | 0.999216615             | 1.461809 | down      |
| pos-3.447_300.11205 | desmedipham                    | 0.719960085 | 0.045508164    | 0.999216615             | 1.209003 | down      |
| pos-6.149_120.05751 | phenylacetaldehyde             | 0.199159987 | 0.043835625    | 0.999216615             | 1.875731 | down      |
| neg-3.516_217.1311  | o-propanoylcarnitine           | 0.720445684 | 0.042265456    | 0.995485198             | 1.12677  | down      |
| pos-0.813_117.07879 | betaine                        | 0.802382752 | 0.041786837    | 0.999216615             | 2.022711 | down      |
| pos-0.802_254.05674 | 5-l-glutamyl-taurine           | 0.723645591 | 0.037904748    | 0.999216615             | 1.820923 | down      |
| pos-0.888_211.0967  | zalcitabine                    | 0.2490287   | 0.037027003    | 0.999216615             | 2.111219 | down      |
| neg-3.124_203.07925 | n2-acetyl-l-aminoadipate       | 0.595685257 | 0.033555506    | 0.995485198             | 0.695216 | down      |
| neg-3.333_172.01933 | p-toluenesulfonic acid         | 0.080793444 | 0.033076764    | 0.995485198             | 2.152947 | down      |
| neg-1.408_337.06755 | 5-hydroxymethyldeoxycytidylate | 0.397303249 | 0.032063258    | 0.995485198             | 2.491772 | down      |
| pos-1.613_179.09449 | phenacetin                     | 0.409167333 | 0.030003539    | 0.999216615             | 2.258032 | down      |
| pos-4.166_164.08348 | 4-phenylbutyric acid           | 0.511272771 | 0.029789437    | 0.999216615             | 1.232304 | down      |
| neg-0.915_177.94297 | pyrophosphate                  | 0.823058526 | 0.026651953    | 0.995485198             | 1.570991 | down      |
| neg-0.796_254.05714 | 5-l-glutamyl-taurine           | 0.704028798 | 0.015733276    | 0.995485198             | 2.473922 | down      |
| neg-4.137_139.02677 | 6-hydroxynicotinic acid        | 0.827518136 | 0.013967259    | 0.995485198             | 1.875475 | down      |
| pos-4.074_515.29088 | taurocholate                   | 0.341261451 | 0.010069186    | 0.999216615             | 1.43204  | down      |
| pos-3.547_475.29891 | netilmicin                     | 0.714908156 | 0.006551238    | 0.999216615             | 1.25114  | down      |
| pos-0.881_167.05794 | 3-hydroxy-4-methylanthranilate | 0.780188901 | 0.002627847    | 0.999216615             | 1.677679 | down      |
| neg-4.088_515.29168 | taurocholate                   | 0.321610207 | 0.001760639    | 0.995485198             | 1.672785 | down      |
| neg-0.809_246.05043 | glycerophosphoglycerol         | 0.723324609 | 0.000109267    | 0.995485198             | 1.892328 | down      |
| pos-4.104_179.0943  | phenacetin                     | 0.233687877 | 0.049257162    | 0.999216615             | 2.558988 | down      |
| neg-0.801_74.03647  | (r)-lactaldehyde               | 0.599765984 | 0.047986016    | 0.995485198             | 2.467496 | down      |
| neg-1.501_384.1216  | s-adenosylhomocysteine         | 0.777253731 | 0.043945565    | 0.995485198             | 1.886084 | down      |
| pos-0.922_111.99242 | hydroxymethylphosphonate       | 0.611346681 | 0.041207833    | 0.999216615             | 1.971634 | down      |
| pos-3.188_75.03197  | glycine                        | 0.502861701 | 0.030307685    | 0.999216615             | 1.284167 | down      |
| neg-0.923_111.99234 | hydroxymethylphosphonate       | 0.696133726 | 0.019528007    | 0.995485198             | 2.982042 | down      |
| neg-3.174_75.03191  | glycine                        | 0.529215619 | 0.01844057     | 0.995485198             | 1.36575  | down      |
| pos-3.688_333.16069 | ipconazole                     | 0.646346876 | 0.015218876    | 0.999216615             | 2.831941 | down      |
| neg-3.185_146.0578  | (r)-4-dehydropantoate          | 0.705700024 | 0.009987056    | 0.995485198             | 1.300061 | down      |
| pos-0.849_125.01449 | taurine                        | 0.742653027 | 0.008914399    | 0.999216615             | 1.688694 | down      |