

## Supplemental Materials

# Integrative Metabolomic and Transcriptomic Analysis for the Study of Bladder Cancer

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### Supplemental methods

**Tissue preparation for  $^1\text{H}$  HRMAS NMR spectroscopy:** Tissue were prepared for measurements according to already published data [1]. Briefly, each sample was weighted. The amount of tumor tissue analyzed for each patient ranged from 8.7 to 37.8 mg. Each sample was introduced into a disposable Kelf insert with an external diameter of 3 mm and an internal diameter of 2.6 mm (Bruker, Billerica, MA, USA). The total internal volume of the insert was about 30  $\mu\text{L}$ . 10  $\mu\text{L}$  of  $\text{D}_2\text{O}$  was added to each insert and it was sealed with a small screw cap.

**Tissue spectra acquisition by  $^1\text{H}$  HRMAS NMR spectroscopy:** The insert containing the bladder tissue was put in a standard 4mm  $\text{ZrO}_2$  rotor, and this was transferred to the NMR probe, which was precooled at 0  $^\circ\text{C}$ . Experiments were acquired at a real temperature of 277  $^\circ\text{K}$ . Tissue spectra were acquired using a Bruker Avance DRX 600 spectrometer (Bruker GmbH, Rheinstetten, Germany) operating at a  $^1\text{H}$  frequency of 600.13 MHz. The instrument was equipped with a 4 mm triple resonance  $^1\text{H}/^{13}\text{C}/^{15}\text{N}$  HRMAS probe with magnetic field gradients aligned with the magic angle axis. A Bruker cooling unit was used to control the temperature by cooling down the bearing air flowing into the probe. For all NMR experiments, samples were spun at 5 kHz in order to keep the rotation sidebands out of the acquisition window. For each tissue sample, one-dimensional (1D)  $^1\text{H}$  NOESY spectrum with water presaturation was acquired in 5 min using a 1.14 s acquisition time, 128 transients, a 12 ppm (7211 Hz) spectral width, a mixing time of 100 ms and a relaxation delay of 1 s. In addition, two-dimensional (2D)  $^1\text{H}$ - $^1\text{H}$  TOCSY using a DIPSI2 sequence for mixing were acquired with a 142 ms acquisition time, 50 ms spin lock duration, 7211 Hz spectral width, and a 1.5 s relaxation delay. Sixteen transients were averaged for each of the 256 increments during  $t_1$ , corresponding to a total acquisition time of 2 h 33 min.

**Urine sample preparation for  $^1\text{H}$  NMR spectroscopy:** Urine samples were thawed at room temperature and were prepared following the established procedures for urine samples [2]. Phosphate buffer (pH 7.4) was prepared by weighing  $\text{Na}_2\text{HPO}_4$  (28.85 g),  $\text{NaH}_2\text{PO}_4$  (5.25 g),  $\text{NaN}_3$  (0.195 g) and DSS (0.218 g) into a 1 L volumetric flask. 200 mL of  $\text{D}_2\text{O}$  were added and the flask was filled to 1 l with water. 500  $\mu\text{L}$  of urine were added 200  $\mu\text{L}$  of phosphate buffer. This mix was centrifuged at 10,000 rpm for 5 min at 5  $^\circ\text{C}$ . After this, 550  $\mu\text{L}$  of the supernatant were transferred to a 5 mm NMR tube for analysis.

**Urine spectra acquisition by  $^1\text{H}$  NMR spectrometry:** The experiments were recorded at 298  $^\circ\text{K}$ . Spectra were acquired using a Bruker Avance DRX 600 spectrometer (Bruker GmbH, Rheinstetten, Germany) operating at a  $^1\text{H}$  frequency of 600.13 MHz. The instrument was equipped with a 5mm triple resonance  $^1\text{H}/^{13}\text{C}/^{31}\text{P}$  probe. For each urine sample, 1D  $^1\text{H}$  NOESY spectra using water presaturation were acquired in 3 min using a 3.91 s acquisition time, 32 transients, a 14 ppm (8370 Hz) spectral width, a mixing time of 100 ms and a relaxation delay of 1 s. Moreover, 2D  $^1\text{H}$ - $^{13}\text{C}$  HSQC spectra were acquired, to assess the assignments of the overlapped signals in 1D  $^1\text{H}$  spectra.

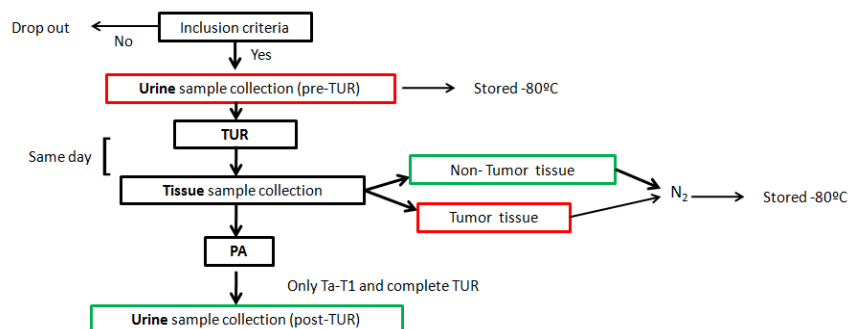
**Data pre-processing and statistical analysis:** After spectra acquisition, the free induction decay (FID)'s was Fourier transformed, phase and baseline corrected and chemical shift referenced with MestReNova version 6.0.2 (Mestrelab Research SL, Santiago de Compostela, Spain).

In tissue samples, chemical shift was referenced to creatine ( $\text{CH}_3$ ) singlet 3.03 ppm and to alanine ( $\text{CH}_3$ ) doublet 1.48 ppm and peak alignment was performed after chemical shift referencing

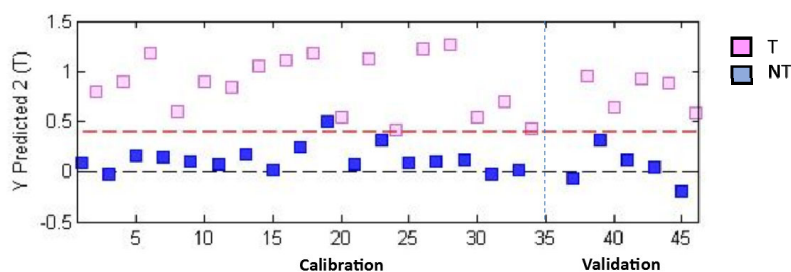
using Icoshift algorithm [3]. Entire spectrum was divided into 178 segments and each segment was aligned separately. For chemometrics analysis the chemical shift spectral region of 0.5–9.5 ppm was considered. Spectral region of water (4.79–5.2 ppm) was excluded. Tissue spectra were normalized to their weight (mg).

PCA and PLS-DA were performed using the software PLS\_Toolbox Solo 8.0 (Eigenvector Research, Inc., Manson, WA, USA). Before PCA and PLS-DA analysis, data were autoscaled. This pre-processing method uses mean-centering followed by division of each column (variable) by the standard deviation of that column. The number of LVs was selected according to the minimum root mean square error for cross-validation (RMSECV). The selection of the VIP threshold values was based on the analysis of the evolution of CV-figures of merit ( $dQ_2$  and mean classification error of CV) as a function of the threshold value. Features election during model optimization aimed at improving the predictive model performance and facilitating its interpretation.

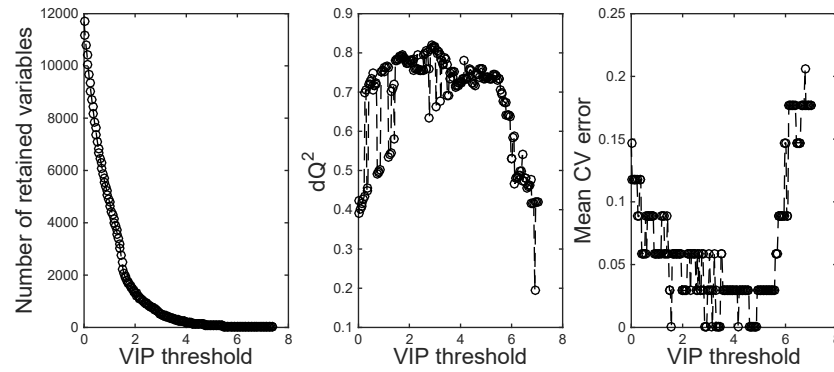
In urine samples, the chemical shift was referenced to 4,4-dimethyl-4-silapentane-1-sulfonic acid (DSS at known concentration) at 0.0 ppm and 1D  $^1\text{H}$  NOESY spectra were binned into 0.003 ppm buckets using MestReNova. The chemical shift spectral region (0.8–4.5 6.5–9.0 ppm) were considered for the statistical analysis. Water (4.5–5.1 ppm), urea (5.5–6.1 ppm) and regions lower 0.8 ppm and greater 9.00 ppm were excluded from the analysis to avoid interferences arising from differences in water suppression and variability from urea and DSS signals. The number of LVs was selected according to the RMSECV. PCA and PLS-DA were performed using PLS\_Toolbox Solo 8.0 before PCA and PLS-DA analysis data were normalized to the sum of all data and were autoscaled.



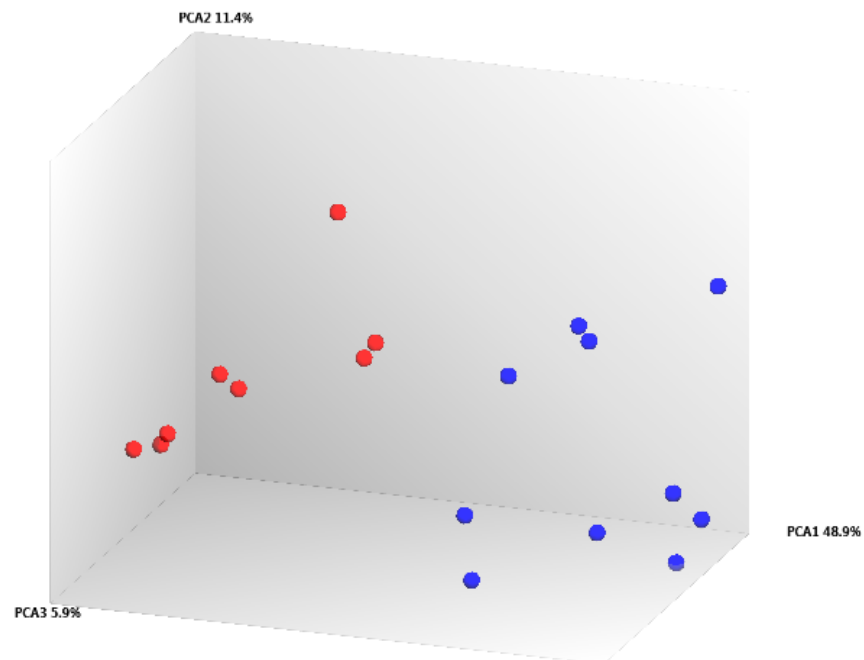
**Figure S1.** Sample collection scheme. NOTE: PA: Pathological Anatomy; TUR: transurethral resection.



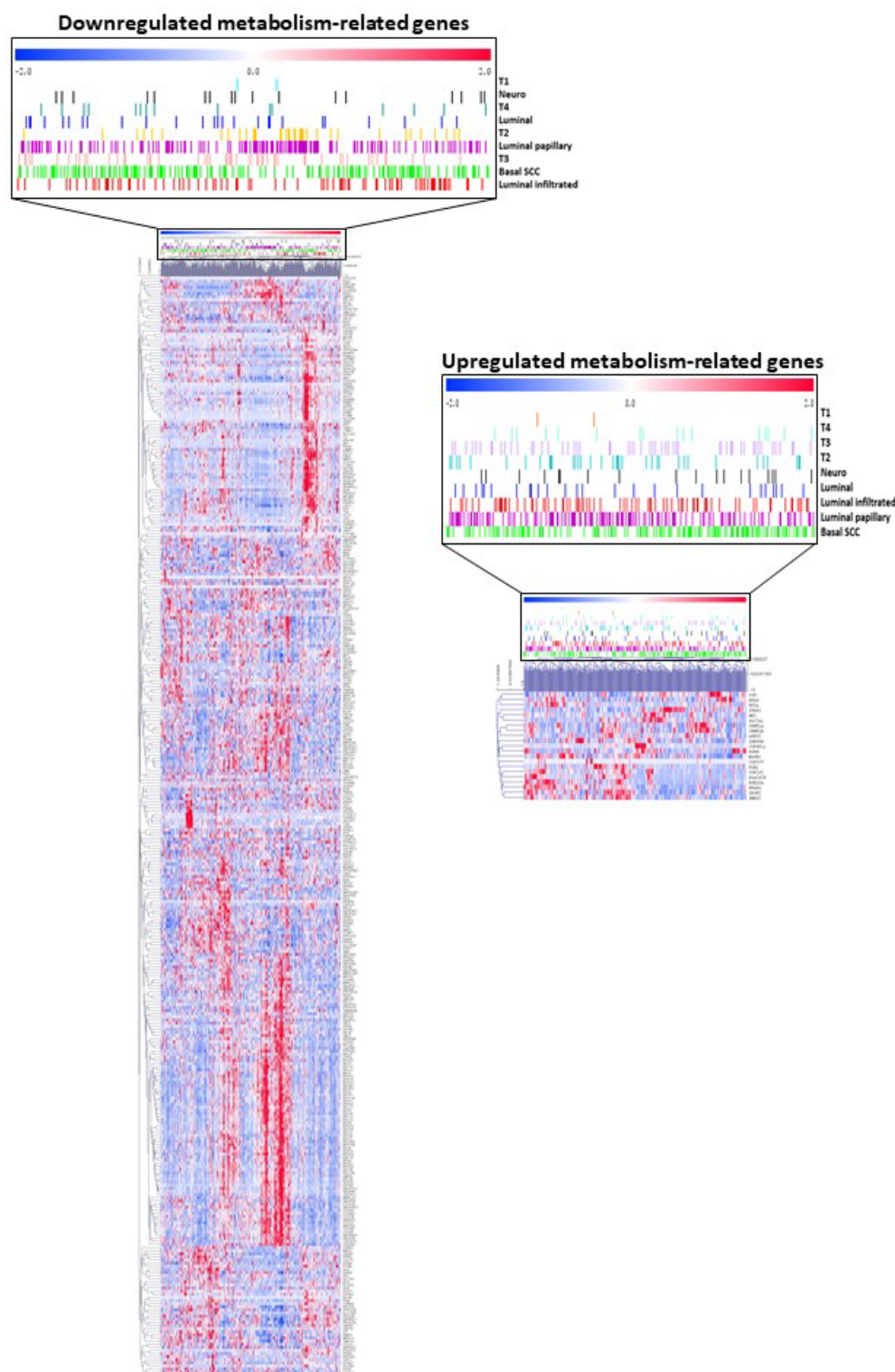
**Figure S2.** Predicted y values for calibration and validation subsets considering the PLS-DA model performed in bladder tissues after an initial feature selection (VIP>1).



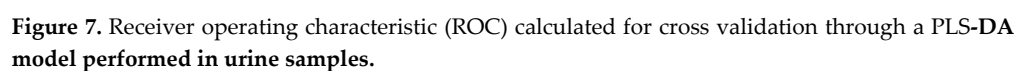
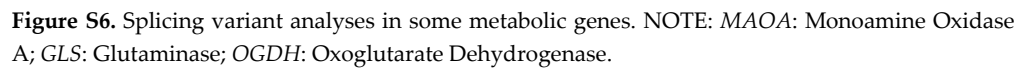
**Figure S3.** Evolution of three indicators (number of features, discriminant  $Q^2$  and mean CV-classification error) of the discriminant performance of the PLS-DA model as a function of the VIP cutoff value used for the elimination of features in an initial PLS-DA model.

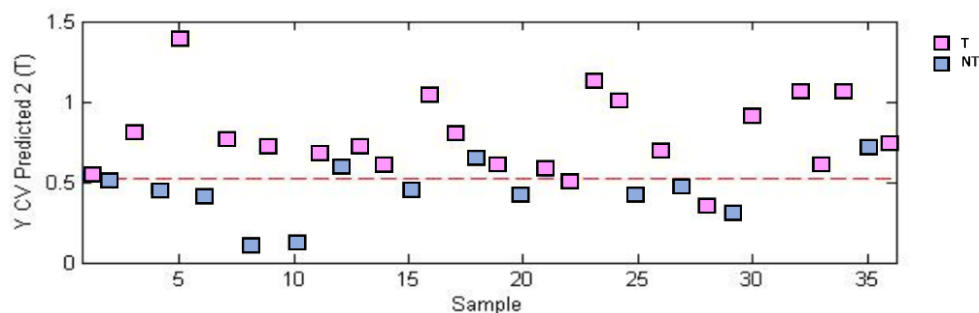


**Figure S4.** Principal Component Analysis (PCA) using the overall transcriptome. NOTE: Tumors are shown in red and non-tumors in blue.



**Figure S5.** Comparison between upregulated and downregulated metabolism-related genes with gene expression of tumor samples present in the TCGA cohort.





**Figure S8.** Predicted  $y$  values for CV considering the PLS-DA model performed in bladder urines.

**Table S1.** Assignment of the main metabolites identified in NMR tissue spectra.

| N. Assignment | Metabolite                                               | Group            | Chemical shift (ppm) |
|---------------|----------------------------------------------------------|------------------|----------------------|
| 1.1           | Lipid fragment $-(n)CH_2-CH_2-CH_2-CH_3$ (a)             | $CH_3$           | 0.90                 |
| 2             | Leucine                                                  | $\delta CH_3$    | 0.93                 |
| 3             | Valine                                                   | $\gamma CH_3$    | 0.98                 |
| 3             | Valine                                                   | $\gamma CH_3$    | 1.04                 |
| 1.1           | Lipid fragment $-(n)CH_2-CH_2-CH_2-CH_3$ (a)             | (n) $CH_2$       | 1.29                 |
| 1.1           | Lipid fragment $-(n)CH_2-CH_2-CH_2-CH_3$ (a)             | (2) $CH_2$       | 1.29                 |
| 1.2           | Lipid fragment $-CH=CH-CH_2-CH=CH-CH_2-CH_2-(n)CH_2$ (b) | (n) $CH_2$       | 1.29                 |
| 1.3           | Lipid fragment $-(n)CH_2-CH_2-CH_2-COOH$ (c)             | (n) $CH_2$       | 1.29                 |
| 1.1           | Lipid fragment $-(n)CH_2-CH_2-CH_2-CH_3$ (a)             | (1) $CH_2$       | 1.33                 |
| 1.2           | Lipid fragment $-CH=CH-CH_2-CH=CH-CH_2-CH_2-(n)CH_2$ (b) | (1) $CH_2$       | 1.33                 |
| 4             | Lactate                                                  | $CH_3$           | 1.33                 |
| 5             | Threonine                                                | $\gamma CH_3$    | 1.33                 |
| 6             | Alanine                                                  | $\beta CH_3$     | 1.46                 |
| 1.3           | Lipid fragment $-(n)CH_2-CH_2-CH_2-COOH$ (c)             | (2) $CH_2$       | 1.59                 |
| 8             | Arginine                                                 | $\gamma CH_2$    | 1.68                 |
| 2             | Leucine                                                  | $\beta CH_2$     | 1.70                 |
| 2             | Leucine                                                  | $\gamma CH$      | 1.70                 |
| 7             | Lysine                                                   | $\beta CH_2$     | 1.71                 |
| 8             | Arginine                                                 | $\beta CH_2$     | 1.90                 |
| 1.2           | Lipid fragment $-CH=CH-CH_2-CH=CH-CH_2-CH_2-(n)CH_2$ (b) | (2) $CH_2$       | 2.03                 |
| 9             | Glutamate                                                | $\beta CH_2$     | 2.05                 |
| 11            | Proline                                                  | $\beta CH_2$     | 2.06                 |
| 12            | Glutamine                                                | $\beta CH_2$     | 2.13                 |
| 10            | Glutathione                                              | $CH_2$           | 2.15                 |
| 1.3           | Lipid fragment $-(n)CH_2-CH_2-CH_2-COOH$ (c)             | (1) $CH_2$       | 2.26                 |
| 9             | Glutamate                                                | $\gamma CH_2$    | 2.33                 |
| 11            | Proline                                                  | $\beta CH_2$     | 2.34                 |
| 12            | Glutamine                                                | $\gamma CH_2$    | 2.44                 |
| 10            | Glutathione                                              | $CH_2$           | 2.54                 |
| 13            | Creatine                                                 | $CH_3$           | 3.03                 |
| 14            | Choline                                                  | $-N^+- (CH_3)_3$ | 3.18                 |
| 15            | Phosphocholine                                           | $-N^+- (CH_3)_3$ | 3.20                 |
| 16            | Glycerophosphocholine                                    | $-CH_2- NH_3^+$  | 3.21                 |
| 17            | Taurine                                                  | $-CH_2- NH_3^+$  | 3.25                 |
| 18            | Methanol                                                 | $CH_3$           | 3.34                 |



|     |                                                                                                       |                                                |      |
|-----|-------------------------------------------------------------------------------------------------------|------------------------------------------------|------|
| 17  | Taurine                                                                                               | -CH <sub>2</sub> -SO <sub>3</sub> <sup>-</sup> | 3.42 |
| 19  | Myo-inositol                                                                                          | C <sub>1',3'</sub> - H                         | 3.52 |
| 20  | Glycine                                                                                               | αCH                                            | 3.55 |
| 19  | Myo-inositol                                                                                          | C <sub>4',6'</sub> - H                         | 3.62 |
| 7   | Lysine                                                                                                | αCH                                            | 3.74 |
| 21  | Glycerol                                                                                              | -CH-(OH)-                                      | 3.78 |
| 13  | Creatine                                                                                              | CH <sub>2</sub>                                | 3.92 |
| 4   | Lactate                                                                                               | CH                                             | 4.10 |
| 1.2 | Lipid fragment -CH=CH-CH <sub>2</sub> -CH=CH-CH <sub>2</sub> -CH <sub>2</sub> -(n)CH <sub>2</sub> (b) | =CH-                                           | 5.30 |
| 22  | UDP-sugars                                                                                            | —                                              | 5.99 |
| 23  | Tyrosine                                                                                              | C <sub>3',5'</sub> - H                         | 6.89 |
| 23  | Tyrosine                                                                                              | C <sub>2',6'</sub> - H                         | 7.17 |
| 24  | Phenylalanine                                                                                         | C <sub>2',6'</sub> - H                         | 7.32 |
| 24  | Phenylalanine                                                                                         | C <sub>3',5'</sub> - H                         | 7.42 |
| 25  | Cytidine diphosphate                                                                                  | CH                                             | 7.97 |
| 10  | Glutathione                                                                                           | NH                                             | 8.15 |

**Table S2.** Significant metabolites in bladder tissues using U-Mann-Whitney test between tumor and non-tumor tissues (Table S2-A); ANOVA test among NMIBC, MIBC and CTRL tissues (Table S2-B); and ANOVA test among Ta, T1, T2 and CTRL tissues (Table S2-C).

| Table S2-A                                                                   |                      |           |         |      |
|------------------------------------------------------------------------------|----------------------|-----------|---------|------|
| Mol. Fmla.                                                                   | Metabolites          | HMDB      | p-value | T/NT |
| --                                                                           | UDP-sugars           | --        | <0.05   | >1   |
| C <sub>9</sub> H <sub>15</sub> N <sub>3</sub> O <sub>11</sub> P <sub>2</sub> | Cytidine diphosphate | HMDB01546 | <0.05   | >1   |
| C <sub>10</sub> H <sub>17</sub> N <sub>3</sub> O <sub>6</sub> S              | Glutathione          | HMDB00125 | <0.05   | >1   |
| C <sub>5</sub> H <sub>14</sub> NO                                            | Choline              | HMDB00097 | <0.05   | >1   |
| C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>                                | Myo-inositol         | HMDB00211 | <0.05   | >1   |
| -(n)CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -COOH                  | Lipid ( c )          | --        | <0.05   | <1   |

| Table S2-B                                                                   |                      |           |         |                        |
|------------------------------------------------------------------------------|----------------------|-----------|---------|------------------------|
| Mol. Fmla.                                                                   | Metabolites          | HMDB      | p-value | Tukey's Post-hoc tests |
| --                                                                           | UDP-sugars           | --        | <0.05   | MIBC:CTRL NMIBC:CTRL   |
| C <sub>9</sub> H <sub>15</sub> N <sub>3</sub> O <sub>11</sub> P <sub>2</sub> | Cytidine diphosphate | HMDB01546 | <0.05   | MIBC:CTRL NMIBC:CTRL   |
| C <sub>10</sub> H <sub>17</sub> N <sub>3</sub> O <sub>6</sub> S              | Glutathione          | HMDB00125 | <0.05   | MIBC:CTRL NMIBC:CTRL   |
| C <sub>5</sub> H <sub>14</sub> NO                                            | Choline              | HMDB00097 | <0.05   | MIBC:CTRL NMIBC:CTRL   |
| C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>                                | Myo-inositol         | HMDB00211 | <0.05   | NMIBC:CTRL             |

| Table S2-C                                                             |              |             |         |                                              |
|------------------------------------------------------------------------|--------------|-------------|---------|----------------------------------------------|
| Mol. Fmla.                                                             | Metabolites  | HMDB        | p-value | Tukey's Post-hoc tests                       |
| C <sub>5</sub> H <sub>14</sub> NO                                      | Choline      | HMDB00097   | <0.05   | T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL |
| C <sub>9</sub> H <sub>11</sub> NO <sub>3</sub>                         | L-Tyrosine   | HMDB0000158 | <0.05   | T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL |
| C <sub>6</sub> H <sub>12</sub> O <sub>6</sub>                          | Myo-inositol | HMDB00211   | <0.05   | T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL |
| C <sub>10</sub> H <sub>17</sub> N <sub>3</sub> O <sub>6</sub> S        | Glutathione  | HMDB00125   | <0.05   | T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL |
| -(n)CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>2</sub> -CH <sub>3</sub> | Lipid (a)    | --          | <0.05   | T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL |
| ---                                                                    | UDP-sugars   | --          | <0.05   | T2:T1 T2:Ta T1:Ta T2:CTRL                    |

|                                                    |                      |           |       |                                                                 |
|----------------------------------------------------|----------------------|-----------|-------|-----------------------------------------------------------------|
| $C_9H_{15}N_3O_{11}P_2$                            | Cytidine diphosphate | HMDB01546 | <0.05 | T1:CTRL Ta:CTRL<br>T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL |
| $-CH=CH-CH_2-$<br>$CH=CH$<br>$-CH_2-CH_2-(n)CH_2-$ | Lipid (b)            | --        | <0.05 | T2:T1 T2:Ta T1:Ta T2:CTRL<br>T1:CTRL Ta:CTRL                    |

NOTE: HMDB: Human Metabolome Database; Mol.Fmla: Molecular formula; T/NT: ratio mean value in tumor over non-tumor samples.

**Table 3.** Indices of test validity estimated for the evaluation of predictive performance of PLS-DA models between tumor and non-tumor tissue samples with LVs = 2. PLS-DA model using all features = 11698.

| PLS-DA model                    | CV                | Validation       |
|---------------------------------|-------------------|------------------|
| <b>Sensitivity</b>              | 82.4 (62.3–97.9)% | 100 (46.3–98.1)% |
| <b>Specificity</b>              | 88.2 (55.8–95.3)% | 100 (46.3–98.1)% |
| <b>PPV<sup>a</sup></b>          | 87.5 (60.4–97.8)% | 100 (46.3–98.1)% |
| <b>NPV<sup>b</sup></b>          | 83.3 (57.7–95.6)% | 100 (46.3–98.1)% |
| <b>ACC<sup>c</sup></b>          | 85.3%             | 100%             |
| <b>MCC<sup>d</sup></b>          | 0.707             | 1                |
| <b>PT<sup>e</sup> (p-value)</b> | --                | 0.015            |
| <b>AUROC</b>                    | --                | 1                |

NOTE: CV: Cross validation; <sup>a</sup> Positive predictive value; <sup>b</sup> Negative predictive value; <sup>c</sup> Diagnostic accuracy; <sup>d</sup> Matthew's correlation coefficient; <sup>e</sup> Permutation test).

**Table S4.** Metabolic genes significantly altered in bladder tumors.

| Gene   | Description                                           | Regulation | FC     | p-value  | FDR p-val |
|--------|-------------------------------------------------------|------------|--------|----------|-----------|
| AASS   | aminoadipate-semialdehydesynthase                     | DOWN       | −2.55  | 2.00E-03 | 8.90E-03  |
| ABL1   | ABL proto-oncogene 1, non-receptor tyrosinekinase     | DOWN       | −5.80  | 6.63E-06 | 2.00E-04  |
| ACAA2  | acetyl-CoAacyltransferase 2                           | DOWN       | −5.13  | 2.10E-06 | 6.80E-05  |
| ACACB  | acetyl-CoAcarboxylase beta                            | DOWN       | −8.43  | 5.27E-07 | 2.36E-05  |
| ACADM  | acyl-CoAdehydrogenase, C-4 to C-12 straightchain      | DOWN       | −2.31  | 1.95E-07 | 1.12E-05  |
| ACAT1  | acetyl-CoAacetyltransferase 1                         | DOWN       | −2.60  | 4.68E-06 | 1.00E-04  |
| ACO1   | aconitase 1, soluble                                  | DOWN       | −4.27  | 1.38E-08 | 1.54E-06  |
| ACSL3  | acyl-CoAsynthetase long-chainfamilymember 3           | DOWN       | −2.09  | 8.00E-04 | 4.70E-03  |
| ADARB1 | adenosine deaminase, RNA-specific, B1                 | DOWN       | −14.27 | 1.67E-07 | 9.90E-06  |
| ADH1B  | alcohol dehydrogenase 1B (class I), beta polypeptide  | DOWN       | −97.23 | 4.94E-06 | 1.00E-04  |
| ADH1C  | alcohol dehydrogenase 1C (class I), gamma polypeptide | DOWN       | −3.84  | 7.78E-06 | 2.00E-04  |
| ADH5   | alcohol dehydrogenase 5 (class III), chi polypeptide  | DOWN       | −3.58  | 1.65E-10 | 9.70E-08  |



|         |                                                                                                     |      |        |          |          |
|---------|-----------------------------------------------------------------------------------------------------|------|--------|----------|----------|
| AK2     | adenylate kinase 2                                                                                  | DOWN | −2.40  | 1.00E-04 | 1.30E-03 |
| AK4     | adenylate kinase 4                                                                                  | DOWN | −12.83 | 1.25E-06 | 4.61E-05 |
| ALDH1B1 | aldehyde dehydrogenase 1 family, member B1                                                          | DOWN | −7.33  | 3.33E-08 | 2.85E-06 |
| ALDH2   | aldehyde dehydrogenase 2 family (mitochondrial)                                                     | DOWN | −5.62  | 1.19E-07 | 7.65E-06 |
| ALDH6A1 | aldehyde dehydrogenase 6 family, member A1                                                          | DOWN | −2.39  | 2.47E-07 | 1.32E-05 |
| ALDH9A1 | aldehyde dehydrogenase 9 family, member A1                                                          | DOWN | −2.04  | 1.31E-09 | 3.21E-07 |
| AMD1    | adenosylmethionine decarboxylase 1                                                                  | DOWN | −2.13  | 4.00E-04 | 3.10E-03 |
| AOC3    | amineoxidase, copper containing 3                                                                   | DOWN | −6.48  | 7.01E-07 | 2.98E-05 |
| APLP2   | amyloid beta (A4) precursor-like protein 2                                                          | DOWN | −5.67  | 9.07E-05 | 1.10E-03 |
| APP     | amyloid beta (A4) precursor protein                                                                 | DOWN | −4.43  | 7.61E-07 | 3.15E-05 |
| ASS1    | argininosuccinate synthase 1                                                                        | DOWN | −2.07  | 2.23E-05 | 4.00E-04 |
| ATIC    | 5-aminoimidazole-4-carboxamide ribonucleotide formyl transferase/IMP cyclohydrolase                 | DOWN | −2.48  | 4.57E-06 | 1.00E-04 |
| ATP5A1  | ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, alphasubunit 1, cardiac muscle | DOWN | −2.18  | 1.84E-05 | 3.00E-04 |
| ATP5B   | ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, beta polypeptide               | DOWN | −9.72  | 4.72E-09 | 7.48E-07 |
| ATP5C1  | ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, gamma polypeptide 1            | DOWN | −3.83  | 2.29E-07 | 1.26E-05 |
| ATP5D   | ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, delta subunit                  | DOWN | −2.95  | 2.39E-09 | 4.62E-07 |
| ATP5E   | ATP synthase, H <sup>+</sup> transporting, mitochondrial F1 complex, epsilon subunit                | DOWN | −4.53  | 1.55E-06 | 5.43E-05 |
| ATP5F1  | ATP synthase, H <sup>+</sup> transporting, mitochondrial Fo complex subunit B1                      | DOWN | −2.05  | 3.19E-08 | 2.77E-06 |
| ATP5G2  | ATP synthase, H <sup>+</sup> transporting, mitochondrial Fo complex subunit C2 (subunit 9)          | DOWN | −41.60 | 4.29E-10 | 1.63E-07 |
| ATP5G3  | ATP synthase, H <sup>+</sup> transporting, mitochondrial Fo complex subunit C3 (subunit 9)          | DOWN | −19.75 | 1.29E-08 | 1.48E-06 |
| ATP5H   | ATP synthase, H <sup>+</sup> transporting, mitochondrial Fo complex subunit D                       | DOWN | −4.29  | 7.01E-06 | 2.00E-04 |
| ATP5I   | ATP synthase, H <sup>+</sup> transporting, mitochondrial Fo complex subunit E                       | DOWN | −10.48 | 3.33E-08 | 2.85E-06 |
| ATP5J   | ATP synthase, H <sup>+</sup> transporting, mitochondrial Fo complex subunit F6                      | DOWN | −2.06  | 1.20E-08 | 1.40E-06 |
| ATP5L   | ATP synthase, H <sup>+</sup> transporting,                                                          | DOWN | −2.31  | 1.00E-04 | 1.30E-   |

|                   |                                                                                                                         |      |        |          |                |
|-------------------|-------------------------------------------------------------------------------------------------------------------------|------|--------|----------|----------------|
| ATP5O             | mitochondrial Fo complex subunit G<br>ATP synthase, H <sup>+</sup> transporting,<br>mitochondrial F1 complex, O subunit | DOWN | -17.06 | 2.97E-08 | 03<br>2.62E-06 |
| ATP6AP1           | ATPase, H <sup>+</sup> transporting,<br>lysosomal accessory protein 1                                                   | DOWN | -6.97  | 6.39E-05 | 8.00E-04       |
| ATP6V0A1          | ATPase, H <sup>+</sup> transporting, lysosomal V0<br>subunit a1                                                         | DOWN | -2.78  | 2.80E-05 | 5.00E-04       |
| ATP6V0E1          | ATPase, H <sup>+</sup> transporting, lysosomal 9kDa, V0<br>subunit e1                                                   | DOWN | -6.95  | 4.73E-08 | 3.71E-06       |
| ATP6V1E1          | ATPase, H <sup>+</sup> transporting, lysosomal 31kDa,<br>V1 subunit E1                                                  | DOWN | -2.32  | 1.82E-07 | 1.06E-05       |
| ATP6V1F           | ATPase, H <sup>+</sup> transporting, lysosomal 14kDa,<br>V1 subunit F                                                   | DOWN | -3.98  | 3.16E-06 | 9.25E-05       |
| ATP8B2            | ATPase, aminophospholipid transporter, class<br>I, type 8B, member 2                                                    | DOWN | -2.10  | 5.04E-05 | 7.00E-04       |
| AUH               | AU RNA binding protein/enoyl-<br>CoA hydratase                                                                          | DOWN | -2.39  | 7.82E-05 | 1.00E-03       |
| B2M               | beta-2-microglobulin                                                                                                    | DOWN | -2.36  | 3.30E-02 | 6.82E-02       |
| BACE1             | beta-site APP-cleaving enzyme 1                                                                                         | DOWN | -2.58  | 5.00E-04 | 3.30E-03       |
| BCHE              | butyrylcholinesterase                                                                                                   | DOWN | -3.66  | 7.93E-06 | 2.00E-04       |
| C3                | complement component 3                                                                                                  | DOWN | -2.35  | 6.20E-03 | 1.94E-02       |
| C4A               | complement component 4A<br>(Rodgers blood group)                                                                        | DOWN | -4.18  | 1.30E-03 | 6.50E-03       |
| CALM2             | calmodulin 2 (phosphorylase kinase, delta)                                                                              | DOWN | -9.27  | 1.25E-10 | 8.38E-08       |
| CALM3,2,1         | calmodulin 3 ); calmodulin 1 ); calmodulin 2                                                                            | DOWN | -7.15  | 2.87E-09 | 5.23E-07       |
| CALU              | calumenin                                                                                                               | DOWN | -5.32  | 2.83E-07 | 1.47E-05       |
| CAT               | catalase                                                                                                                | DOWN | -3.44  | 1.88E-05 | 4.00E-04       |
| CDC42BPA          | CDC42 binding protein kinase alpha (DMPK-<br>like)                                                                      | DOWN | -5.89  | 3.74E-09 | 6.25E-07       |
| CHPT1             | choline phosphotransferase 1                                                                                            | DOWN | -22.00 | 7.78E-11 | 6.49E-08       |
| CHRD1             | chordin-like 1                                                                                                          | DOWN | -3.73  | 1.00E-04 | 1.40E-03       |
| CHRM2             | cholinergic receptor, muscarinic 2                                                                                      | DOWN | -4.70  | 3.00E-06 | 8.90E-05       |
| CHRM3             | cholinergic receptor, muscarinic 3                                                                                      | DOWN | -12.79 | 1.47E-06 | 5.21E-05       |
| CIT;<br>MIR1178   | citron rho-interacting serine/threonine kinase;<br>microRNA 1178                                                        | UP   | 2.45   | 2.70E-05 | 5.00E-04       |
| CKB               | creatine kinase, brain                                                                                                  | DOWN | -2.95  | 4.32E-06 | 1.00E-04       |
| CKMT1A;<br>CKMT1B | creatine kinase, mitochondrial 1A; creatine<br>kinase, mitochondrial 1B                                                 | UP   | 2.77   | 8.00E-04 | 4.60E-03       |
| COA5              | cytochrome c oxidase assembly factor 5                                                                                  | DOWN | -2.09  | 6.00E-04 | 4.00E-         |

|                   |                                                                           |      |        |          |          |
|-------------------|---------------------------------------------------------------------------|------|--------|----------|----------|
|                   |                                                                           |      |        |          | 03       |
| COX10             | COX10 heme A:farnesyl transferase<br>cytochrome c oxidase assembly factor | DOWN | -2.57  | 5.22E-07 | 2.35E-05 |
| COX11             | COX11 cytochrome c oxidase copper<br>chaperone                            | DOWN | -5.49  | 6.72E-09 | 9.62E-07 |
| COX15             | cytochrome c oxidase assembly homolog 15<br>(yeast)                       | DOWN | -2.67  | 3.25E-08 | 2.81E-06 |
| COX20             | COX20 cytochrome c oxidase assembly factor                                | DOWN | -4.40  | 1.45E-08 | 1.58E-06 |
| COX4I1            | cytochrome c oxidase subunit IV isoform 1                                 | DOWN | -4.84  | 3.14E-11 | 5.04E-08 |
| COX5A             | cytochrome c oxidase subunit Va                                           | DOWN | -3.13  | 1.50E-07 | 9.14E-06 |
| COX5B             | cytochrome c oxidase subunitVb                                            | DOWN | -5.14  | 1.28E-07 | 8.10E-06 |
| COX6A1            | cytochrome c oxidase subunit VI<br>apolyptide 1                           | DOWN | -4.01  | 2.00E-04 | 2.00E-03 |
| COX6C             | cytochrome c oxidase subunit VIc                                          | DOWN | -2.31  | 1.51E-08 | 1.63E-06 |
| COX7A1            | cytochrome c oxidase subunit VII<br>apolyptide 1 (muscle)                 | DOWN | -8.45  | 3.59E-10 | 1.52E-07 |
| COX7A2            | cytochrome c oxidase subunit VII<br>apolyptide 2 (liver)                  | DOWN | -5.00  | 2.93E-08 | 2.61E-06 |
| COX7B             | cytochrome c oxidase subunitVIIb                                          | DOWN | -4.85  | 1.94E-07 | 1.12E-05 |
| COX7C;<br>MIR3607 | cytochrome c oxidase subunitVIIc;<br>microRNA 3607                        | DOWN | -3.74  | 9.68E-10 | 2.71E-07 |
| COX8A             | cytochrome c oxidase subunit VIIIA<br>(ubiquitous)                        | DOWN | -82.96 | 5.73E-11 | 5.92E-08 |
| CRYM              | crystallinmu                                                              | DOWN | -2.56  | 8.16E-07 | 3.33E-05 |
| CSRP2             | cysteine and glycine-richprotein 2                                        | DOWN | -8.27  | 4.03E-08 | 3.32E-06 |
| CST3              | cystatin C                                                                | DOWN | -2.44  | 2.07E-07 | 1.16E-05 |
| CYCS              | cytochrome c, somatic                                                     | DOWN | -2.44  | 1.20E-03 | 6.10E-03 |
| CYP1B1            | cytochrome P450, family 1, subfamily B,<br>polypeptide 1                  | DOWN | -2.10  | 4.10E-03 | 1.45E-02 |
| CYP2C9            | cytochrome P450, family 2, subfamily C,<br>polypeptide 9                  | UP   | 2.18   | 2.00E-04 | 1.60E-03 |
| CYP2J2            | cytochrome P450, family 2, subfamily J,<br>polypeptide 2                  | UP   | 7.98   | 1.59E-02 | 3.85E-02 |
| CYP4F11           | cytochrome P450, family 4, subfamily F,<br>polypeptide 11                 | UP   | 2.03   | 2.52E-02 | 5.44E-02 |
| CYP4V2            | cytochrome P450, family 4, subfamily V,<br>polypeptide 2                  | DOWN | -2.68  | 4.61E-08 | 3.65E-06 |
| CYR61             | cysteine-rich, angiogenic inducer, 61                                     | DOWN | -4.12  | 1.27E-02 | 3.25E-02 |
| DARS              | aspartyl-tRNA synthetase                                                  | DOWN | -2.27  | 1.18E-05 | 3.00E-04 |
| DGKB              | diacylglycerol kinase, beta 90kDa                                         | DOWN | -2.95  | 3.00E-04 | 2.30E-   |

|          |                                                                      |      |        |          |          |    |
|----------|----------------------------------------------------------------------|------|--------|----------|----------|----|
|          |                                                                      |      |        |          |          | 03 |
| DGKG     | diacylglycerol kinase gamma                                          | DOWN | -3.82  | 1.65E-06 | 5.69E-05 |    |
| DGKH     | diacylglycerol kinase, eta                                           | UP   | -2.12  | 3.14E-02 | 6.45E-02 |    |
| DLAT     | dihydrolipoamide S-acetyltransferase                                 | DOWN | -2.03  | 1.01E-06 | 3.92E-05 |    |
| DLD      | dihydrolipoamide dehydrogenase                                       | DOWN | -3.22  | 1.31E-05 | 3.00E-04 |    |
| DNAJC3   | DnaJ (Hsp40) homolog, subfamily C, member 3                          | DOWN | -11.87 | 1.51E-07 | 9.20E-06 |    |
| DPYD     | dihydropyrimidine dehydrogenase                                      | DOWN | -2.67  | 2.00E-04 | 1.90E-03 |    |
| ECH1     | enoyl-CoA hydratase 1, peroxisomal                                   | DOWN | -5.42  | 6.34E-07 | 2.74E-05 |    |
| ECI2     | enoyl-CoA delta isomerase 2                                          | DOWN | -3.14  | 1.12E-08 | 1.34E-06 |    |
| EEF1A1   | eukaryotic translation elongation factor 1 alpha 1                   | DOWN | -4.04  | 4.33E-07 | 2.03E-05 |    |
| EEF1G    | eukaryotic translation elongation factor 1 gamma; microRNA 3654      | DOWN | -4.68  | 1.95E-05 | 4.00E-04 |    |
| EIF4EBP2 | eukaryotic translation initiation factor 4E bindingprotein 2         | DOWN | -2.19  | 8.25E-05 | 1.00E-03 |    |
| ENTPD1   | Ectonucleoside triphosphate diphosphohydrolase 1                     | DOWN | -9.40  | 6.96E-09 | 9.80E-07 |    |
| ESD      | esterase D                                                           | DOWN | -8.14  | 4.76E-10 | 1.73E-07 |    |
| FARSB    | phenylalanyl-tRNA synthetase beta subunit                            | DOWN | -2.91  | 5.27E-07 | 2.36E-05 |    |
| FAXDC2   | fatty acid hydroxylase domain containing 2                           | DOWN | -5.15  | 3.24E-12 | 1.37E-08 |    |
| FBN1     | fibrillin 1                                                          | DOWN | -3.44  | 1.00E-04 | 1.40E-03 |    |
| FH       | fumarate hydratase                                                   | DOWN | -2.79  | 4.34E-09 | 7.01E-07 |    |
| FN1      | fibronectin 1                                                        | DOWN | -55.97 | 7.47E-08 | 5.30E-06 |    |
| FNBP1    | formin bindingprotein 1                                              | DOWN | -11.83 | 1.62E-09 | 3.68E-07 |    |
| FSTL1    | Follistatin like 1; microRNA 198                                     | DOWN | -3.21  | 3.89E-06 | 1.00E-04 |    |
| GAPDH    | glyceraldehyde-3-phosphate dehydrogenase                             | DOWN | -3.10  | 1.32E-05 | 3.00E-04 |    |
| GAS6     | growth arrest-specific 6                                             | DOWN | -2.80  | 7.92E-08 | 5.56E-06 |    |
| GATA6    | GATA bindingprotein 6                                                | DOWN | -3.50  | 1.20E-05 | 3.00E-04 |    |
| GATM     | glycine amidino transferase (L-arginine:glycine amidino transferase) | DOWN | -6.37  | 1.00E-04 | 1.30E-03 |    |
| GLRX3    | glutaredoxin 3                                                       | DOWN | -2.09  | 9.45E-05 | 1.10E-03 |    |
| GLS      | glutaminase                                                          | DOWN | -2.08  | 1.03E-06 | 3.94E-   |    |

|        |                                                                                          |      |        |          |          |    |
|--------|------------------------------------------------------------------------------------------|------|--------|----------|----------|----|
|        |                                                                                          |      |        |          |          | 05 |
| GMPS   | guanine monophosphate synthase                                                           | DOWN | -2.67  | 2.48E-05 | 4.00E-04 |    |
| GNPDA2 | glucosamine-6-phosphate deaminase 2                                                      | DOWN | -2.41  | 9.93E-07 | 3.86E-05 |    |
| GOT2   | glutamic-oxaloacetic transaminase 2, mitochondrial                                       | DOWN | -3.15  | 5.58E-06 | 1.00E-04 |    |
| GPX3   | glutathione peroxidase 3                                                                 | DOWN | -2.77  | 7.20E-07 | 3.03E-05 |    |
| GPX4   | glutathione peroxidase 4                                                                 | DOWN | -2.83  | 2.77E-08 | 2.50E-06 |    |
| GSN    | gelsolin                                                                                 | DOWN | -3.52  | 2.88E-07 | 1.49E-05 |    |
| GSTA4  | glutathione S-transferase alpha 4                                                        | DOWN | -2.60  | 8.28E-07 | 3.37E-05 |    |
| GSTO1  | glutathione S-transferase omega 1                                                        | DOWN | -2.20  | 2.32E-08 | 2.19E-06 |    |
| GSTO2  | glutathione S-transferase omega 2                                                        | UP   | 2.38   | 5.20E-03 | 1.71E-02 |    |
| GSTT1  | glutathione S-transferase theta 1                                                        | DOWN | -3.00  | 2.20E-03 | 9.50E-03 |    |
| H3F3A  | H3 histone, family 3A                                                                    | DOWN | -3.60  | 1.00E-04 | 1.20E-03 |    |
| HADHA  | hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase, alpha subunit | DOWN | -2.46  | 1.78E-05 | 3.00E-04 |    |
| HADHB  | hydroxyacyl-CoA dehydrogenase/3-ketoacyl-CoA thiolase/enoyl-CoA hydratase, beta subunit  | DOWN | -2.49  | 3.00E-04 | 2.60E-03 |    |
| HIBADH | 3-hydroxyisobutyrate dehydrogenase                                                       | DOWN | -2.89  | 1.52E-07 | 9.23E-06 |    |
| HK2    | hexokinase 2                                                                             | UP   | 2.25   | 2.57E-05 | 4.00E-04 |    |
| IDH2   | isocitrate dehydrogenase 2 (NADP+), mitochondrial                                        | DOWN | -2.26  | 5.00E-04 | 3.50E-03 |    |
| IDH3A  | isocitrate dehydrogenase 3 (NAD+) alpha                                                  | DOWN | -2.20  | 3.44E-06 | 9.89E-05 |    |
| IDH3B  | isocitrate dehydrogenase 3 (NAD+) beta                                                   | DOWN | -2.53  | 6.93E-05 | 9.00E-04 |    |
| IGF1   | insulin-like growth factor 1 receptor                                                    | DOWN | -2.20  | 3.20E-03 | 1.22E-02 |    |
| IGFBP5 | insulin like growth factor binding protein 5                                             | DOWN | -12.84 | 2.06E-06 | 6.70E-05 |    |
| IGFBP6 | insulin like growth factor binding protein 6                                             | DOWN | -2.28  | 5.61E-07 | 2.48E-05 |    |
| IGFBP7 | insulin like growth factor binding protein 7                                             | DOWN | -20.02 | 2.26E-10 | 1.14E-07 |    |
| IMPA2  | inositol(myo)-1(or 4)-monophosphatase 2                                                  | DOWN | -2.62  | 5.41E-06 | 1.00E-04 |    |
| INPP4B | inositol polyphosphate-4-phosphatase type II B                                           | UP   | 2.11   | 6.00E-03 | 1.90E-02 |    |
| IP6K2  | inositol hexakisphosphate kinase 2                                                       | UP   | 2.37   | 2.33E-02 | 5.14E-   |    |

|          |                                                                  |      |        |          |  |          |
|----------|------------------------------------------------------------------|------|--------|----------|--|----------|
|          |                                                                  |      |        |          |  | 02       |
| ITM2B    | integral membrane protein 2B                                     | DOWN | -7.06  | 6.36E-07 |  | 2.74E-05 |
| ITPK1    | inositol-tetrakisphosphate 1-kinase                              | DOWN | -2.49  | 1.74E-06 |  | 5.93E-05 |
| ITPKB    | inositol-trisphosphate 3-kinase B                                | DOWN | -5.52  | 1.79E-06 |  | 6.05E-05 |
| ITPR1    | inositol 1,4,5-trisphosphate receptor, type 1                    | DOWN | -5.27  | 4.35E-05 |  | 6.00E-04 |
| ITPR3    | inositol 1,4,5-trisphosphate receptor, type 3                    | UP   | 2.31   | 3.00E-04 |  | 2.60E-03 |
| ITPRIPL2 | inositol 1,4,5-trisphosphate receptor interacting protein-like 2 | DOWN | -2.01  | 1.30E-03 |  | 6.50E-03 |
| KDSR     | 3-ketodihydrosphingosine reductase                               | DOWN | -13.58 | 7.27E-09 |  | 1.00E-06 |
| LAMB2    | laminin, beta 2 (laminin S)                                      | DOWN | -2.83  | 1.22E-06 |  | 4.54E-05 |
| LAMC1    | laminin, gamma 1 (formerly LAMB2)                                | DOWN | -2.39  | 1.15E-05 |  | 2.00E-04 |
| LGALS1   | lectin, galactoside-binding, soluble, 1                          | DOWN | -20.98 | 1.03E-07 |  | 6.85E-06 |
| LMCD1    | LIM and cysteine-rich domains 1                                  | DOWN | -3.98  | 1.50E-08 |  | 1.62E-06 |
| LTBP1    | latent transforming growth factor beta binding protein 1         | DOWN | -8.63  | 1.89E-09 |  | 4.02E-07 |
| MAOA     | monoamine oxidase A                                              | DOWN | -3.26  | 2.94E-06 |  | 8.79E-05 |
| MAOB     | monoamine oxidase B                                              | DOWN | -9.60  | 4.75E-10 |  | 1.73E-07 |
| MDH1     | malate dehydrogenase 1                                           | DOWN | -2.44  | 1.11E-07 |  | 7.24E-06 |
| MDH2     | malate dehydrogenase 2                                           | DOWN | -2.42  | 2.12E-07 |  | 1.18E-05 |
| MFGE8    | milk fat globule-EGF factor 8 protein                            | DOWN | -2.07  | 2.68E-05 |  | 5.00E-04 |
| MGST1    | microsomal glutathione S-transferase 1                           | UP   | 5.90   | 2.50E-03 |  | 1.01E-02 |
| MGST3    | microsomal glutathione S-transferase 3                           | DOWN | -2.46  | 1.78E-06 |  | 6.03E-05 |
| MIA3     | melanoma inhibitory activity family, member 3                    | DOWN | -2.29  | 3.87E-07 |  | 1.86E-05 |
| MMP2     | matrix metalloproteinase 2                                       | DOWN | -3.14  | 2.00E-04 |  | 1.50E-03 |
| MPC1     | mitochondrial pyruvate carrier 1                                 | DOWN | -3.19  | 4.94E-11 |  | 5.64E-08 |
| MPC2     | mitochondrial pyruvate carrier 2                                 | DOWN | -2.08  | 5.12E-07 |  | 2.31E-05 |
| MRPL11   | mitochondrial ribosomal protein L11                              | DOWN | -5.02  | 2.31E-05 |  | 4.00E-04 |
| MRPL24   | mitochondrial ribosomal protein L24                              | DOWN | -2.52  | 9.58E-09 |  | 1.21E-06 |
| MRPL3    | mitochondrial ribosomal protein L3                               | DOWN | -2.60  | 8.28E-05 |  | 1.00E-   |

|         |                                                                   |      |        |          |          |    |
|---------|-------------------------------------------------------------------|------|--------|----------|----------|----|
|         |                                                                   |      |        |          |          | 03 |
| MRPL35  | mitochondrial ribosomal protein L35                               | DOWN | -3.08  | 2.85E-05 | 5.00E-04 | 04 |
| MRPL42  | mitochondrial ribosomal protein L42                               | DOWN | -2.56  | 4.97E-05 | 7.00E-04 | 04 |
| MRPS14  | mitochondrial ribosomal protein S14                               | DOWN | -6.50  | 4.00E-10 | 1.59E-07 | 07 |
| MRPS18A | mitochondrial ribosomal protein S18A                              | DOWN | -2.40  | 2.00E-04 | 2.00E-03 | 03 |
| MRPS18C | mitochondrial ribosomal protein S18C                              | DOWN | -2.20  | 6.90E-06 | 2.00E-04 | 04 |
| MRPS21  | mitochondrial ribosomal protein S21                               | DOWN | -3.18  | 1.95E-05 | 4.00E-04 | 04 |
| MRPS36  | mitochondrial ribosomal protein S36                               | DOWN | -2.07  | 2.81E-05 | 5.00E-04 | 04 |
| MRPS7   | mitochondrial ribosomal protein S7                                | DOWN | -3.55  | 5.58E-06 | 1.00E-04 | 04 |
| MSRB1   | methioninesulfoxide reductase B1                                  | DOWN | -2.42  | 1.34E-07 | 8.40E-06 | 06 |
| MSRB2   | methioninesulfoxide reductase B2                                  | DOWN | -4.80  | 3.39E-10 | 1.50E-07 | 07 |
| MSRB3   | methioninesulfoxide reductase B3                                  | DOWN | -5.39  | 6.34E-08 | 4.69E-06 | 06 |
| MTR     | 5-methyltetrahydrofolate-homocysteine methyltransferase           | DOWN | -2.39  | 3.00E-04 | 2.70E-03 | 03 |
| MUT     | methylmalonyl-CoA mutase                                          | DOWN | -2.30  | 4.24E-06 | 1.00E-04 | 04 |
| NDUFA1  | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 1, 7.5kDa     | DOWN | 2.38   | 2.69E-02 | 5.73E-02 | 02 |
| NDUFA11 | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 11, 14.7kDa   | DOWN | -6.23  | 1.32E-10 | 8.68E-08 | 08 |
| NDUFA12 | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 12            | DOWN | -5.33  | 3.40E-09 | 5.85E-07 | 07 |
| NDUFA2  | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 2, 8kDa       | DOWN | -5.29  | 6.40E-06 | 2.00E-04 | 04 |
| NDUFA4  | NDUFA4, mitochondrial complex associated                          | DOWN | -18.25 | 1.07E-08 | 1.30E-06 | 06 |
| NDUFA6  | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6, 14kDa      | DOWN | -7.61  | 7.74E-11 | 6.49E-08 | 08 |
| NDUFA9  | NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 9, 39kDa      | DOWN | -2.03  | 2.00E-04 | 1.80E-03 | 03 |
| NDUFAB1 | NADH dehydrogenase (ubiquinone) 1, alpha/beta subcomplex, 1, 8kDa | DOWN | -9.44  | 1.48E-07 | 9.05E-06 | 06 |
| NDUFAF1 | NADH dehydrogenase (ubiquinone) complex I, assembly factor 1      | DOWN | -2.07  | 4.11E-07 | 1.95E-05 | 05 |
| NDUFAF2 | NADH dehydrogenase (ubiquinone) complex I, assembly factor 2      | DOWN | -10.19 | 6.06E-11 | 5.92E-08 | 08 |
| NDUFAF2 | NADH dehydrogenase (ubiquinone) complex I, assembly factor 2      | DOWN | -4.36  | 1.39E-08 | 1.55E-06 | 06 |
| NDUFAF4 | NADH dehydrogenase (ubiquinone) complex I, assembly factor 4      | DOWN | -2.40  | 1.47E-05 | 3.00E-04 | 04 |
| NDUFB10 | NADH dehydrogenase (ubiquinone) 1 beta                            | DOWN | -3.46  | 2.16E-08 | 2.08E-   |    |



|        |                                                                                   |      |        |          |          |
|--------|-----------------------------------------------------------------------------------|------|--------|----------|----------|
|        | subcomplex, 10, 22kDa                                                             |      |        |          | 06       |
| NDUFB3 | NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 3, 12kDa                       | DOWN | -2.81  | 2.93E-06 | 8.77E-05 |
| NDUFB5 | NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 5, 16kDa                       | DOWN | -3.40  | 2.38E-06 | 7.47E-05 |
| NDUFB6 | NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 6, 17kDa                       | DOWN | -5.17  | 4.87E-07 | 2.22E-05 |
| NDUFB7 | NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 7, 18kDa                       | DOWN | -4.61  | 2.20E-06 | 7.03E-05 |
| NDUFB9 | NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 9, 22kDa                       | DOWN | -2.73  | 1.98E-06 | 6.53E-05 |
| NDUFS3 | NADH dehydrogenase (ubiquinone) Fe-S protein 3, 30kDa (NADH-coenzyme Q reductase) | DOWN | -2.35  | 5.04E-07 | 2.28E-05 |
| NDUFS4 | NADH dehydrogenase (ubiquinone) Fe-S protein 4, 18kDa (NADH-coenzyme Q reductase) | DOWN | -3.95  | 8.79E-08 | 6.03E-06 |
| NDUFS5 | NADH dehydrogenase (ubiquinone) Fe-S protein 5, 15kDa (NADH-coenzyme Q reductase) | DOWN | -12.64 | 4.16E-09 | 6.78E-07 |
| NDUFV2 | NADH dehydrogenase (ubiquinone) flavoprotein 2, 24kDa                             | DOWN | -2.15  | 2.13E-06 | 6.88E-05 |
| NEDD8  | neural precursor cell expressed, developmentally down-regulated 8                 | DOWN | -2.05  | 2.71E-06 | 8.26E-05 |
| NME4   | NME/NM23 nucleosidediphosphate kinase 4                                           | DOWN | -2.09  | 5.97E-09 | 8.79E-07 |
| OAT    | ornithineaminotransferase                                                         | DOWN | -2.47  | 2.92E-05 | 5.00E-04 |
| OAZ1   | ornithinedecarboxylase antizyme 1                                                 | DOWN | -3.37  | 2.05E-06 | 6.68E-05 |
| ODC1   | ornithinedecarboxylase 1                                                          | DOWN | -2.21  | 1.50E-03 | 7.20E-03 |
| OGDH   | oxoglutarate (alpha-ketoglutarate) dehydrogenase (lipoamide)                      | DOWN | -2.97  | 1.99E-07 | 1.13E-05 |
| OXCT1  | 3-oxoacid CoA-transferase 1                                                       | DOWN | -2.22  | 8.00E-04 | 4.90E-03 |
| PAM    | peptidylglycine alpha-amidatingmonooxygenase                                      | DOWN | -4.59  | 1.22E-06 | 4.54E-05 |
| PCMT1  | protein-L-isoaspartate (D-aspartate) O-methyltransferase                          | DOWN | -2.51  | 2.46E-07 | 1.32E-05 |
| PDE10A | phosphodiesterase 10A                                                             | UP   | 2.38   | 1.86E-02 | 4.34E-02 |
| PDE1C  | phosphodiesterase 1C, calmodulin-dependent 70kDa                                  | DOWN | -5.91  | 1.24E-06 | 4.58E-05 |
| PDGFC  | platelet derived growth factor C                                                  | DOWN | -2.13  | 1.64E-05 | 3.00E-04 |
| PDHA1  | pyruvate dehydrogenase (lipoamide) alpha 1                                        | DOWN | -2.52  | 2.47E-08 | 2.27E-06 |
| PDHB   | pyruvate dehydrogenase (lipoamide) beta                                           | DOWN | -3.46  | 4.74E-08 | 3.71E-06 |
| PDHX   | pyruvate dehydrogenase complex, component X                                       | DOWN | -2.13  | 4.69E-08 | 3.70E-06 |

|             |                                                                                   |      |        |          |          |
|-------------|-----------------------------------------------------------------------------------|------|--------|----------|----------|
| PDK4        | pyruvate dehydrogenase kinase, isozyme 4                                          | DOWN | -11.76 | 9.57E-07 | 3.75E-05 |
| PELO        | pelotahomolog (Drosophila); integrin alpha 1                                      | DOWN | -2.50  | 2.41E-07 | 1.30E-05 |
| PFAS        | phosphoribosylformylglycinamidine synthase                                        | UP   | 2.09   | 1.01E-05 | 2.00E-04 |
| PGAM1       | phosphoglyceratemuase 1 (brain)                                                   | DOWN | -3.62  | 1.53E-06 | 5.36E-05 |
| PGM2L1      | phosphoglucomutase 2-like 1                                                       | DOWN | -2.73  | 4.74E-05 | 7.00E-04 |
| PGM5        | phosphoglucomutase 5                                                              | DOWN | -28.42 | 1.63E-09 | 3.69E-07 |
| PHKB        | Phosphorylase kinase, beta                                                        | DOWN | -2.77  | 1.63E-06 | 5.65E-05 |
| PICALM      | phosphatidylinositol binding clathrin assembly protein                            | DOWN | -2.63  | 5.67E-07 | 2.50E-05 |
| PIGP        | phosphatidylinositolglycananchorbio synthesis class P                             | DOWN | -4.09  | 3.61E-07 | 1.76E-05 |
| PIGT        | phosphatidylinositolglycananchorbio synthesisclass T                              | DOWN | -2.26  | 8.46E-05 | 1.00E-03 |
| PIGY; PYURF | phosphatidylinositolglycananchorbio synthesisclass Y; PIGY upstream reading frame | DOWN | -2.10  | 4.06E-06 | 1.00E-04 |
| PIK3C2A     | phosphatidylinositol-4-phosphate 3-kinase, catalyticsubunittype 2 alpha           | DOWN | -2.32  | 3.07E-06 | 9.07E-05 |
| PIK3CA      | phosphatidylinositol-4,5-bisphosphate 3-kinase, catalytic subunit alpha           | DOWN | -4.42  | 1.35E-08 | 1.51E-06 |
| PIP4K2A     | phosphatidylinositol-5-phosphate 4-kinase, type II, alpha                         | DOWN | -4.14  | 2.12E-11 | 4.33E-08 |
| PITPNC1     | Phosphatidylinositol transfer protein, cytoplasmic 1                              | DOWN | -2.44  | 8.00E-03 | 2.33E-02 |
| PLA2G12A    | phospholipase A2, group XIIA                                                      | DOWN | -2.08  | 2.21E-05 | 4.00E-04 |
| PLA2G16     | phospholipase A2, group XVI                                                       | DOWN | -2.08  | 7.30E-03 | 2.18E-02 |
| PLA2G2F     | phospholipase A2, group IIF                                                       | UP   | 2.18   | 1.47E-02 | 3.62E-02 |
| PLA2G4A     | phospholipase A2, group IVA (cytosolic, calcium-dependent)                        | DOWN | -3.23  | 2.11E-07 | 1.17E-05 |
| PLB1        | phospholipase B1                                                                  | UP   | 2.29   | 8.10E-03 | 2.34E-02 |
| PLCB4       | phospholipase C, beta 4                                                           | DOWN | -7.50  | 7.80E-09 | 1.06E-06 |
| PLCD4       | phospholipase C, delta 4                                                          | DOWN | -2.42  | 8.40E-05 | 1.00E-03 |
| PLCL1       | phospholipase C-like 1                                                            | DOWN | -2.23  | 6.32E-06 | 2.00E-04 |
| PLOD2       | procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2                                | DOWN | -2.11  | 2.64E-02 | 5.65E-02 |
| PLPP1       | phospholipidphosphatase 1                                                         | DOWN | -3.81  | 5.14E-05 | 7.00E-04 |
| PLPP3       | phospholipidphosphatase 3                                                         | DOWN | -4.09  | 4.72E-07 | 2.17E-   |

|         |                                                          |      |        |          |          |          |
|---------|----------------------------------------------------------|------|--------|----------|----------|----------|
|         |                                                          |      |        |          |          | 05       |
| PLSCR4  | phospholipidscramblase 4                                 | DOWN | -4.43  | 1.00E-08 | 1.24E-06 | 1.24E-06 |
| PMPCB   | peptidase (mitochondrial processing) beta                | DOWN | -3.52  | 1.18E-08 | 1.39E-06 | 1.39E-06 |
| PPA1    | pyrophosphatase (inorganic) 1                            | DOWN | -2.77  | 3.00E-04 | 2.40E-03 | 2.40E-03 |
| PPARG   | peroxisome proliferator-activated receptor gamma         | UP   | 6.47   | 6.72E+00 | 4.50E-03 | 4.50E-03 |
| PPM1K   | protein phosphatase, Mg2+/Mn2+ dependent, 1K             | DOWN | -8.62  | 2.92E-09 | 5.26E-07 | 5.26E-07 |
| PPM1L   | protein phosphatase, Mg2+/Mn2+ dependent, 1L             | DOWN | -17.00 | 2.36E-09 | 4.60E-07 | 4.60E-07 |
| PPP2CA  | protein phosphatase 2, catalytic subunit, alphasozyme    | DOWN | -2.27  | 2.95E-06 | 8.81E-05 | 8.81E-05 |
| PPP2CB  | protein phosphatase 2, catalytic subunit, beta isozyme   | DOWN | -3.28  | 6.33E-09 | 9.17E-07 | 9.17E-07 |
| PPP2R1A | proteinphosphatase 2, regulatory subunit A, alpha        | DOWN | -3.06  | 5.00E-04 | 3.50E-03 | 3.50E-03 |
| PRKAA2  | protein kinase, AMP-activated, alpha 2 catalytic subunit | DOWN | -19.76 | 3.28E-07 | 1.64E-05 | 1.64E-05 |
| PRKACB  | protein kinase, cAMP-dependent, catalytic, beta          | DOWN | -2.08  | 5.23E-07 | 2.35E-05 | 2.35E-05 |
| PRKCA   | protein kinase C, alpha                                  | DOWN | -5.10  | 2.00E-03 | 8.60E-03 | 8.60E-03 |
| PRKCB   | protein kinase C, beta                                   | DOWN | -2.31  | 8.20E-06 | 2.00E-04 | 2.00E-04 |
| PRPS1   | phosphoribosylpyrophosphate synthetase 1                 | DOWN | -2.59  | 3.84E-08 | 3.21E-06 | 3.21E-06 |
| PRSS23  | protease, serine, 23                                     | DOWN | -2.46  | 2.00E-04 | 1.60E-03 | 1.60E-03 |
| PTEN    | phosphatase and tensin homolog                           | DOWN | -2.12  | 7.24E-06 | 2.00E-04 | 2.00E-04 |
| PWP1    | PWP1 homolog, endonuclein                                | DOWN | -2.09  | 2.73E-07 | 1.43E-05 | 1.43E-05 |
| PYGB    | phosphorylase, glycogen; brain                           | DOWN | -33.99 | 1.55E-08 | 1.65E-06 | 1.65E-06 |
| PYGM    | phosphorylase, glycogen, muscle                          | DOWN | -8.47  | 1.42E-07 | 8.78E-06 | 8.78E-06 |
| RARS    | arginyl-tRNA synthetase                                  | DOWN | -2.00  | 1.00E-04 | 1.40E-03 | 1.40E-03 |
| RPIA    | ribose 5-phosphate isomerase A                           | UP   | 2.95   | 3.00E-04 | 2.20E-03 | 2.20E-03 |
| RPL12   | ribosomal protein L12                                    | DOWN | -3.44  | 1.71E-09 | 3.82E-07 | 3.82E-07 |
| RPL13   | ribosomal protein L13                                    | DOWN | -6.57  | 2.22E-10 | 1.14E-07 | 1.14E-07 |
| RPL13A  | ribosomal protein L13a                                   | DOWN | -22.61 | 1.62E-08 | 1.71E-06 | 1.71E-06 |
| RPL14   | ribosomal protein L14                                    | DOWN | -3.07  | 1.52E-07 | 9.20E-06 | 9.20E-06 |
| RPL15   | ribosomal protein L15                                    | DOWN | -2.05  | 5.24E-06 | 1.00E-   | 1.00E-   |

|        |                             |      |        |          |        |    |
|--------|-----------------------------|------|--------|----------|--------|----|
|        |                             |      |        |          |        | 04 |
| RPL17  | ribosomal protein L17       | DOWN | -2.03  | 7.29E-06 | 2.00E- | 04 |
| RPL18  | ribosomal protein L18       | DOWN | -4.18  | 9.53E-08 | 6.41E- | 06 |
| RPL18A | ribosomal protein L18a      | DOWN | -10.32 | 1.38E-08 | 1.54E- | 06 |
| RPL19  | ribosomal protein L19       | DOWN | -2.53  | 1.25E-07 | 7.94E- | 06 |
| RPL21  | ribosomal protein L21       | DOWN | -23.51 | 4.55E-08 | 3.61E- | 06 |
| RPL24  | ribosomal protein L24       | DOWN | -4.48  | 1.13E-06 | 4.24E- | 05 |
| RPL26  | ribosomal protein L26       | DOWN | -4.31  | 2.30E-07 | 1.26E- | 05 |
| RPL27  | ribosomal protein L27       | DOWN | -6.93  | 3.60E-06 | 1.00E- | 04 |
| RPL30  | ribosomal protein L30       | DOWN | -2.60  | 8.22E-07 | 3.35E- | 05 |
| RPL35  | ribosomal protein L35       | DOWN | -2.36  | 1.63E-06 | 5.65E- | 05 |
| RPL35A | ribosomal protein L35a      | DOWN | -2.11  | 1.23E-08 | 1.42E- | 06 |
| RPL36  | ribosomal protein L36       | DOWN | -2.06  | 2.41E-06 | 7.54E- | 05 |
| RPL37  | ribosomal protein L37       | DOWN | -5.54  | 1.35E-05 | 3.00E- | 04 |
| RPL38  | ribosomal protein L38       | DOWN | -2.40  | 3.78E-08 | 3.17E- | 06 |
| RPL4   | ribosomal protein L4        | DOWN | -8.15  | 9.61E-07 | 3.76E- | 05 |
| RPL41  | ribosomal protein L41       | DOWN | -2.38  | 2.73E-07 | 1.43E- | 05 |
| RPL5   | ribosomal protein L5        | DOWN | -3.09  | 4.50E-11 | 5.43E- | 08 |
| RPL6   | ribosomal protein L6        | DOWN | -9.13  | 4.72E-09 | 7.48E- | 07 |
| RPL8   | ribosomal protein L8        | DOWN | -6.80  | 4.51E-09 | 7.24E- | 07 |
| RPL9   | ribosomal protein L9        | DOWN | -2.40  | 4.17E-08 | 3.40E- | 06 |
| RPLP0  | ribosomalprotein, large, P0 | DOWN | -2.76  | 2.02E-06 | 6.62E- | 05 |
| RPLP1  | ribosomalprotein, large, P1 | DOWN | -3.80  | 5.20E-12 | 1.95E- | 08 |
| RPS10  | ribosomal protein S10       | DOWN | -2.08  | 1.25E-06 | 4.61E- | 05 |
| RPS11  | ribosomal protein S11       | DOWN | -10.30 | 6.91E-07 | 2.94E- | 05 |
| RPS13  | ribosomal protein S13       | DOWN | -51.68 | 7.28E-11 | 6.49E- | 08 |
| RPS14  | ribosomal protein S14       | DOWN | -2.41  | 1.36E-07 | 8.50E- |    |

|         |                                                             |      |        |          |        |    |
|---------|-------------------------------------------------------------|------|--------|----------|--------|----|
|         |                                                             |      |        |          |        | 06 |
| RPS15   | ribosomal protein S15                                       | DOWN | -10.26 | 1.68E-08 | 1.76E- | 06 |
| RPS15A  | ribosomal protein S15a                                      | DOWN | -5.23  | 8.35E-10 | 2.49E- | 07 |
| RPS16   | ribosomal protein S16                                       | DOWN | -25.84 | 3.33E-08 | 2.85E- | 06 |
| RPS18   | ribosomal protein S18                                       | DOWN | -3.28  | 1.34E-05 | 3.00E- | 04 |
| RPS19   | ribosomal protein S19                                       | DOWN | -7.24  | 6.01E-09 | 8.82E- | 07 |
| RPS2    | ribosomal protein S2                                        | DOWN | -4.29  | 1.08E-10 | 7.95E- | 08 |
| RPS20   | ribosomal protein S20                                       | DOWN | -2.58  | 2.99E-07 | 1.53E- | 05 |
| RPS21   | ribosomal protein S21                                       | DOWN | -3.32  | 1.08E-06 | 4.10E- | 05 |
| RPS23   | ribosomal protein S23                                       | DOWN | -2.94  | 4.00E-10 | 1.59E- | 07 |
| RPS25   | ribosomal protein S25                                       | DOWN | -5.52  | 1.95E-07 | 1.12E- | 05 |
| RPS26   | ribosomal protein S26                                       | DOWN | -2.48  | 2.35E-05 | 4.00E- | 04 |
| RPS27   | ribosomal protein S27                                       | DOWN | -2.14  | 9.87E-09 | 1.23E- | 06 |
| RPS28   | ribosomal protein S28                                       | DOWN | -2.14  | 7.60E-08 | 5.37E- | 06 |
| RPS29   | ribosomal protein S29                                       | DOWN | -2.50  | 2.43E-07 | 1.31E- | 05 |
| RPS3    | ribosomal protein S3                                        | DOWN | -3.68  | 9.09E-09 | 1.16E- | 06 |
| RPS3A   | ribosomal protein S3a                                       | DOWN | -4.37  | 6.14E-10 | 2.02E- | 07 |
| RPS4X   | ribosomal protein S4, X-linked                              | DOWN | -3.90  | 2.04E-08 | 2.00E- | 06 |
| RPS5    | ribosomal protein S5                                        | DOWN | -12.72 | 5.37E-09 | 8.21E- | 07 |
| RPS9    | ribosomal protein S9                                        | DOWN | -34.45 | 1.10E-09 | 2.91E- | 07 |
| RSL1D1  | ribosomal L1 domain containing 1                            | DOWN | -2.35  | 3.91E-07 | 1.87E- | 05 |
| RSL24D1 | ribosomal L24 domain containing 1                           | DOWN | -4.60  | 2.77E-08 | 2.50E- | 06 |
| S1PR3   | sphingosine-1-phosphate receptor 3                          | DOWN | -2.73  | 9.14E-07 | 3.64E- | 05 |
| SARS    | seryl-tRNA synthetase                                       | DOWN | -3.05  | 8.97E-08 | 6.12E- | 06 |
| SAT2    | spermidine/spermine N1-acetyltransferase<br>family member 2 | DOWN | -2.43  | 2.68E-07 | 1.41E- | 05 |
| SDC2    | syndecan 2                                                  | DOWN | -3.34  | 1.70E-09 | 3.82E- | 07 |
| SDHC    | succinate dehydrogenase complex, subunit C,                 | DOWN | -2.31  | 2.10E-03 | 9.00E- |    |

|         |                                                                                            |      |         |          |          |
|---------|--------------------------------------------------------------------------------------------|------|---------|----------|----------|
|         | integral membrane protein, 15kDa                                                           |      |         |          | 03       |
| SDHD    | succinate dehydrogenase complex subunit D, integral membrane protein                       | DOWN | -5.21   | 7.62E-08 | 5.38E-06 |
| SDPR    | serum deprivation response                                                                 | DOWN | -13.78  | 7.14E-09 | 9.94E-07 |
| SERINC1 | serine incorporator 1                                                                      | DOWN | -3.61   | 2.78E-09 | 5.18E-07 |
| SIAH1   | siah E3 ubiquitin protein ligase 1                                                         | DOWN | -3.23   | 2.00E-04 | 2.00E-03 |
| SLC16A7 | solute carrier family 16 (monocarboxylate transporter), member 7                           | DOWN | -2.01   | 1.93E-05 | 4.00E-04 |
| SLC25A5 | solute carrier family 25 (mitochondrial carrier; adeninenucleotide translocator), member 5 | DOWN | -2.62   | 2.67E-06 | 8.16E-05 |
| SLC25A6 | solute carrier family 25 (mitochondrial carrier; adeninenucleotide translocator), member 6 | DOWN | -2.08   | 3.76E-06 | 1.00E-04 |
| SLC2A1  | solute carrier family 2 (facilitated glucose transporter), member 1                        | UP   | 2.66    | 4.30E-03 | 1.49E-02 |
| SLC2A12 | solute carrier family 2 (facilitated glucose transporter), member 12                       | DOWN | -2.96   | 1.42E-05 | 3.00E-04 |
| SLC2A3  | solute carrier family 2 (facilitated glucose transporter), member 3                        | DOWN | -3.22   | 1.21E-06 | 4.51E-05 |
| SLC2A4  | solute carrier family 2 (facilitated glucose transporter), member 4                        | DOWN | -2.13   | 9.12E-06 | 2.00E-04 |
| SLC35A1 | solute carrier family 35 (CMP-sialicacid transporter), member A1                           | DOWN | -3.55   | 5.55E-07 | 2.46E-05 |
| SMPD2   | sphingomyelinphosphodiesterase 2, neutral membrane (neutral sphingomyelinase)              | UP   | 2.29    | 7.68E-05 | 1.00E-03 |
| SMS     | spermine synthase                                                                          | DOWN | -2.57   | 1.04E-05 | 2.00E-04 |
| SOD1    | superoxide dismutase 1, soluble                                                            | DOWN | -40.66  | 8.52E-11 | 6.77E-08 |
| SPARCL1 | SPARC like 1                                                                               | DOWN | -127.65 | 1.30E-08 | 1.48E-06 |
| SPCS2   | signalpeptidase complex subunit 2                                                          | DOWN | -3.68   | 1.85E-05 | 3.00E-04 |
| SPCS3   | signalpeptidase complex subunit 3                                                          | DOWN | -2.32   | 1.00E-04 | 1.20E-03 |
| SPPL2A  | signal peptidepeptidase like 2A                                                            | DOWN | -3.20   | 3.97E-05 | 6.00E-04 |
| SUCLG1  | succinate-CoAligase, alpha subunit                                                         | DOWN | -3.09   | 2.42E-08 | 2.24E-06 |
| TALDO1  | transaldolase 1                                                                            | DOWN | -5.41   | 2.09E-08 | 2.04E-06 |
| TMEM208 | transmembrane protein 208                                                                  | DOWN | -3.65   | 6.90E-07 | 2.94E-05 |
| TNC     | tenascin C                                                                                 | DOWN | -2.33   | 3.10E-02 | 6.39E-02 |
| TXN     | thioredoxin                                                                                | DOWN | -13.15  | 1.96E-07 | 1.12E-05 |
| TXNRD1  | thioredoxin reductase 1                                                                    | DOWN | -2.77   | 1.88E-06 | 6.29E-   |

|         |                                                                                |      |       |          |          |
|---------|--------------------------------------------------------------------------------|------|-------|----------|----------|
| UBA52   | ubiquitin A-52 residue ribosomal prot. fusion product 1                        | DOWN | -5.37 | 2.23E-07 | 1.23E-05 |
| UBB     | ubiquitin B                                                                    | DOWN | -2.68 | 5.99E-11 | 5.92E-08 |
| UBE2L3  | ubiquitin conjugating enzyme E2L 3                                             | DOWN | -2.48 | 1.26E-05 | 3.00E-04 |
| UBE2M   | ubiquitin-conjugating enzyme E2M                                               | DOWN | -3.21 | 2.00E-04 | 1.60E-03 |
| UBL5    | ubiquitin-like 5                                                               | DOWN | -7.60 | 1.46E-08 | 1.59E-06 |
| UGDH    | UDP-glucose 6-dehydrogenase                                                    | DOWN | -2.14 | 5.94E-07 | 2.60E-05 |
| UGP2    | UDP-glucosepyrophosphorylase 2                                                 | DOWN | -2.57 | 2.23E-09 | 4.45E-07 |
| UQCR10  | ubiquinol-cytochrome c reductase, complex III subunit X                        | DOWN | -2.30 | 1.17E-02 | 3.06E-02 |
| UQCR11  | ubiquinol-cytochrome c reductase, complex III subunit XI                       | DOWN | -2.85 | 8.56E-07 | 3.46E-05 |
| UQCRB   | ubiquinol-cytochrome c reductase binding protein                               | DOWN | -2.80 | 3.01E-10 | 1.38E-07 |
| UQCRC2  | ubiquinol-cytochrome c reductase coreprotein II                                | DOWN | -2.82 | 9.14E-07 | 3.64E-05 |
| UQCRFS1 | ubiquinol-cytochrome c reductase, Rieskeiron-sulfur polypeptide 1              | DOWN | -3.45 | 6.00E-07 | 2.62E-05 |
| UQCRH   | ubiquinol-cytochrome c reductase hinge protein                                 | DOWN | -2.48 | 1.54E-05 | 3.00E-04 |
| UQCRHL  | ubiquinol-cytochrome c reductase hinge protein like                            | DOWN | -3.20 | 2.00E-04 | 2.00E-03 |
| USP25   | ubiquitin specific peptidase 25                                                | DOWN | -2.18 | 3.07E-05 | 5.00E-04 |
| USP9X   | ubiquitin specific peptidase 9, X-linked                                       | DOWN | -2.42 | 7.18E-08 | 5.13E-06 |
| WFS1    | Wolfram syndrome 1 (wolframin)                                                 | DOWN | -3.02 | 7.59E-07 | 3.15E-05 |
| YME1L1  | YME1-like 1 ATPase                                                             | DOWN | -2.56 | 1.64E-07 | 9.76E-06 |
| YWHAB   | tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta   | DOWN | -2.58 | 1.00E-04 | 1.20E-03 |
| YWHAE   | tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activationprotein, epsilon | DOWN | -3.71 | 8.10E-06 | 2.00E-04 |

NOTE: FC= Fold Change; FDR p-val= FDR p-value.

**Table S5.** Putative binding motif enrichment analysis using the Enrich webtool and showing the relative relevance of various transcription factors in the deregulated transcripts.

| Term        | p-value | Adj. p-value | Genes                                                                                                                                                                                                                                                                                  |
|-------------|---------|--------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>E2F1</b> | 6.3E-22 | 4.0E-19      | RPL4,RPL30,ACAA2,NDUFA12,ATP5C1,ADARB1,RPL8,PWP1,RPL6,UBE2L3,RPS15,RPS14,RPS16,RPL18A,RPS18,PP2R1A,PMPCB,RPL35,RPL37,RPS11,ATP6V1E1,RPS10,PELO,B2M,PDHX,RPS9,RPL21,FNBP1,RPS5,APLP2,SARS,M RPS18A,SDHC,EEF1A1,SMS,RPL24,RPL27,SUCLG1,RPL26 ,UQCRC2,UQCRB,NDUFB10,COX15,MAOA,GMPS,AK2,I |

|              |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|--------------|---------|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              |         |         | TPR1, COX7A2, ATP5O, OAZ1, UQCRH, MRPL11, ATP5L, ATP5B, ATP5E, ATP5D, COX11, IGFBP7, NDUFV2, ATP6V1F, DARS, RPL41, PDHA1, IDH2, GOT2, H3F3A, FN1, MRPL24, RPS28, RPS27, CALU, OGDH, RPS20, SERINC1, CALM1, RPS21, CALM2, ITM2B, RPS23, FARSB, PICALM, YWHAE, COX7B, MRPS14, RPLP1, PIGP, PTEN, SLC2A1, MTR, SLC2A3, LAMC1, ATP5G3, ATP5G2, COX7C, MRPL35, PITPNC1, CYR61, HK2, PIGY, MRPL3, ATIC, CSRP2, ALDH2, RARS, ACADM, DLAT, IDH3A, COX8A, ATP6AP1, ITPK1, RPL13A, RPS3A, NME4, ATP5F1, EEF1G, HADHB, PLCB4, CAT, NDUFS3, SLC25A5, ALDH9A1, PRPS1, OAT, NDUFB7, MRPS36, RPL12, ATP5A1, ODC1, NDUFB3, COX5B, COX5A, FSTL1, PPP2CA, CST3, PPP2CB, RPS15A, RPS3, CKB, RPL15, RPS2, RPL18, RPL17, RPL19, BCHE, NDUFA6, MDH1, MDH2, USP9X, NDUFA4, NDUFA2, NDUFA1, COX6C, ASS1, SOD1, SPCS3, RSL1D1, SPCS2, MSRB2 |
| <b>EKLF</b>  | 2.9E-20 | 9.3E-18 | RPL4, HIBADH, MRPS14, NDUFA12, RPLP1, SLC2A1, SLC2A4, ATP5G2, PFAS, PWP1, RPL6, RPS4X, MRPL3, RPS14, ATIC, LGALS1, RPS16, ALDH2, RPS18, IDH3B, PMPCB, RPL35, RPS11, COX8A, RPS9, GSTO1, ECH1, SARS, RPL13A, SDHC, NME4, EEF1A1, EEF1G, CAT, RPL24, RPL27, SUCLG1, SLC25A5, ALDH9A1, OAT, UQCRB, NDUFB10, MGST3, NDUFB3, GMPs, ATP5J, NEDD8, ATP5O, MRPL11, ACAT1, PPP2CA, CST3, OXCT1, RPS3, EIF4EBP2, RPL15, RPL19, MDH1, MDH2, NDUFA4, TXNRD1, GOT2, H3F3A, IDH2, RPIA, RPS26, RPS25, RSL1D1, RPS28, SPCS2, NDUFAB1, CALM3, ITM2B, UBE2M, RPS23                                                                                                                                                                                                                                                                  |
| <b>MYC</b>   | 7.8E-20 | 1.7E-17 | YWHAE, RPL4, RPL5, COX7B, RPL30, RPLP1, ATP5C1, RPL8, ATP5G2, COX7C, PWP1, PIGY, RPL6, GLS, RPS15, MRPL3, RPS14, ATIC, RPS19, RPL18A, RPS18, RARS, RPL36, RPL35, RPL38, RPL37, RPS13, COX8A, RPS9, RPL21, RPS5, SARS, NME4, RPS3A, ATP5F1, EEF1A1, EEF1G, NDUFS4, NDUFS3, YME1L1, RPL27, RPL26, NDUFB5, RPL12, ATP5A1, ODC1, MRPL11, ATP5B, RPS15A, ATP5E, RPS3, EIF4EBP2, RPL13, RPL15, RPS2, RPL18, RPL17, COX10, ATP6V1F, DARS, NDUFA4, GOT2, H3F3A, MRPL24, SOD1, RPS25, RSL1D1, RPS27, RPS29, RPS20, RPS21, FARSB, RPS23                                                                                                                                                                                                                                                                                      |
| <b>ESRRB</b> | 2.5E-18 | 3.1E-16 | HIBADH, YWHAB, NDUFA12, COX4I1, ATP5C1, PYGM, ATP5G3, COX6A1, ATP5G2, COX7C, PIGY, GLS, RPS15, CSRP2, AUH, IDH3B, UQCRFS1, DLAT, AASS, IDH3A, COX8A, PLA2G12A, GPX4, PGAM1, APLP2, SDHC, SDHD, NDUFS5, NDUFS4, NDUFS3, SUCLG1, UQCRC2, GAS6, DLD, NDUFB9, PRKAA2, UQCRB, NDUFB10, NDUFB5, MRPS36, MGST3, ATP5A1, ODC1, GMPs, AK2, COX7A2, PPM1K, PDHB, ATP5O, COX5B, COX5A, COX7A1, LTBP1, UQCRH, ACAT1, ATP5B, OXCT1, ATP5E, PDGFC, ATP5D, COX11, CKB, NDUFV2, COX10, NDUFA9, NDUFA6, MDH1, MDH2, NDUFA2, COX6C, NDUFAB1, OGDH, ACO1, CALM3, CHPT1, CALM2, ITM2B, UBE2M                                                                                                                                                                                                                                           |
| <b>XRN2</b>  | 8.1E-18 | 8.5E-16 | YWHAE, RPL4, RPL5, NDUFA11, MRPS14, RPLP0, AMD1, RPL8, MRPL35, RPL9, RPL6, UBE2L3, RPS4X, RPS14, RPS19, RPS18, RPL36, IDH3B, RPL35, RPL38, RPL37, B2M, RPS10, RPS9, RPS5, SARS, MRPS21, RPL13A, SDHC, MRPS7, EEF1A1, NDUFS5, NDUFS3, RPL24, RPL27, RPL26, GAPDH, FH, OAT, NDUFB                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |



|       |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|-------|---------|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|       |         |         | 6,RPL12,ITPR1,ATP5J,TXN,OAZ1,ACAT1,ATP5B,UGP2,RPS15A,UBB,RPL14,COX11,RPL13,RPL15,CKB,RPS2,RPL18,RPL17,IP6K2,RPL19,RPL41,MDH1,NDUFA2,RPL35A,MRPL24,SOD1,RPS26,RPS28,RPS27,GSTA4,RPS29,CYCS,CALM3,SERINC1,RPS20,CALM1,CALM2,RPS21,UBE2M,FARSB                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| NELFA | 3.5E-13 | 2.5E-11 | YWHAE,PYGB,ACAA2,HIBADH,NDUFA12,AMD1,PTEN,SLC2A1,ATP5C1,MTR,SLC2A3,ATP5G3,PIK3C2A,RPL8,RPL6,GLS,RPS15,PCMT1,CSRP2,ALDH2,RPS18,IMPA2,ACADM,RPL37,DLAT,RPS11,RPS13,PDHX,RPS9,RPL21,GPX4,FNBP1,APLP2,RPL13A,SDHC,NME4,SDHD,CIT,EEF1A1,ITPKB,UGDH,PPA1,CAT,UQCRC2,RPL26,GAPDH,UQCRB,NDUFB6,RPL12,ATP5A1,GMPS,ITPR1,ACACB,ADH5,PPP2CA,ATP5B,UGP2,UBB,RPS3,EIF4EBP2,RPL13,CKB,RPS2,ATP6V0A1,RPL19,SLC35A1,DARS,RPL41,NDUFA6,NDUFA4,H3F3A,FN1,SOD1,RPS26,RSL1D1,RPS28,SPCS2,RPS27,CALU,OGDH,RPS20,CALM1,RPS21,CALM2                                                                                                                                                                 |
| TTF2  | 5.8E-13 | 3.7E-11 | YWHAE,RPL4,RPL5,MRPS14,RPLP1,RPLP0,AMD1,COX7C,RPL9,RPL6,RPS15,RPS4X,MRPL3,RPS14,RPS18,RPL36,RPL35,RPL38,RPL37,RPS11,PRKACB,RPS13,RPS9,RPS3A,ACSL3,MRPS7,EEF1A1,EEF1G,NDUFS4,NDUFS3,RPL24,UQCRC2,RPL26,GAPDH,UQCRB,NDUFB10,RPL12,MGST3,ITPR1,COX7A2,PDHB,RPS15A,UBB,RPL14,RPS3,RPL13,RPL15,RPS2,RPL18,RPL17,RPL19,RPL41,NDUFA4,H3F3A,MRPL24,SOD1,RSL1D1,RPS28,RPS27,NDUFAF4,CYCS,CALM3,CHPT1,SERINC1,RPS20,CALM1,CALM2,PAM,UBE2M,RPS23                                                                                                                                                                                                                                        |
| ETS1  | 1.2E-12 | 7.1E-11 | RPL5,COX7B,COX4I1,RPLP0,MTR,RPL8,COX7C,RPL9,RPL6,RPS15,UBL5,RPS14,MRPL42,MRPL3,RPS16,RPS19,RARS,IDH3B,RPL36,UQCRFS1,RPL38,RPL37,ATP6V1E1,RPS11,RPS13,RPS9,RPL21,RPS5,RPL13A,RPS3A,SDHD,PGM2L1,MRPS18C,RPL24,YME1L1,SUCLG1,RPL27,UQCRC2,RPL26,UBA52,NDUFB7,NDUFB10,RPL12,MGST3,NDUFB3,ITPR1,COX7A2,ATP5O,MRPL11,RPS15A,ATP5D,RPL14,RPS3,TMEM208,RPL13,ATP6V1F,NDUFA9,SLC35A1,NDUFA4,PHKB,MRPL24,RPS26,RPIA,RPS25,RPS27,NDUFAB1,CYCS,RPS20,CALM1,RPS21,FARSB,RPS23                                                                                                                                                                                                             |
| ZFX   | 8.6E-11 | 4.6E-09 | RPL30,NDUFA12,ATP5C1,ADARB1,RPL8,PWP1,RPL6,UBE2L3,RPS14,PCMT1,RPS16,RPS19,RPL18A,RPS18,PPP2R1A,RPL36,RPL37,RPS11,PDHX,FNBP1,RPS5,MRPS18A,SDHD,EEF1A1,RPL24,RPL27,RPL26,UQCRC2,UBA52,NDUFB10,GMPS,AK2,OAZ1,LTBP1,COX7A1,ADH5,ACAT1,MRPL11,ATP5L,ATP5B,UBB,ATP5E,ESD,ATP5D,ABL1,NDUFV2,DARS,RPS27,RPS29,OGDH,RPS20,ACO1,CALM1,RPS21,ITM2B,RPS23,UBE2M,HIBADH,YWHAB,RPLP1,PIGP,PTEN,MTR,ATP5G2,COX7C,MRPL3,ATIC,AUH,IMPA2,RARS,UQCRFS1,DLAT,IDH3A,COX8A,GSTO1,ITPK1,NME4,UGDH,NDUFS3,SLC25A5,DLD,RPL12,ATP5A1,PDHB,COX5B,COX5A,PPP2CA,PPP2CB,RPS15A,RPL14,RPS3,RPL13,RPL15,RPS2,RPL18,SLC35A1,NDUFA6,MDH1,LAMB2,USP9X,NDUFA4,TXNRD1,COX6C,SOD1,RPIA,RSL1D1,GNPDA2,NDUFAB1,MSRB2 |
| VDR   | 1.5E-09 | 7.1E-08 | YWHAE,RPL5,COX7B,NDUFA11,MRPS14,NDUFA12,AM                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

|              |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
|--------------|---------|---------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              |         |         | D1,RPLP0,PTEN,SLC2A3,MRPL35,PFAS,UBE2L3,RPS15,RPS14,MRPL3,RPS19,AUH,RPL36,PMPCB,RPL38,RPL37,RPS11,RPS9,GSTO2,RPS5,ECH1,MRPS21,RPL13A,RPS3A,MRPS18C,HADHB,RPL24,YME1L1,SUCLG1,RPL27,UQCRC2,RPL26,UBA52,NDUFB7,NDUFB6,NDUFB5,ODC1,NDUFB3,ATP5I,NEDD8,COX7A2,PPM1K,COX5B,ACAT1,ATP5L,PPP2CA,UBB,OXCT1,ATP5E,TMEM208,RPL13,RPL19,ATP6V1F,NDUFA9,RPL41,NDUFA6,MDH1,RPL35A,COX6C,MRPL24,RPS26,RPIA,SPCS3,RPS27,NDUFAB1,CALU,CYCS,RPS20,CALM3,NDUFAF1,RSL24D1,RPS21,CALM2,FARSB,RPS23 |
| <b>HOXC9</b> | 2.3E-09 | 1.1E-07 | COX7B,RPL30,PIGT,HIBADH,MRPS14,NDUFA12,RPLP1,SLC2A3,ATP5G3,COX7C,MRPL35,PIGY,RPS15,UBL5,MRPL3,ATIC,LGALS1,RPS16,RPS19,IDH3B,RPL38,RPL37,ATP6V1E1,B2M,RPS9,APLP2,MRPS21,MRPS18A,RPS3A,SDHD,ACSL3,MUT,COX6B1,HADHA,CAT,NDUFS4,RPL24,YME1L1,UQCRC2,RPL26,MFGE8,DLD,OAT,NDUFB7,MRPS36,NDUFB5,ITPR1,ATP5I,PPM1K,COX5B,UQCRH,RPS15A,UBB,ATP5E,ATP5D,ESD,TMEM208,RPL15,RPS2,RPL17,IP6K2,NDUFA9,NDUFA6,MDH2,COX6C,RPS26,RPS25,RSL1D1,RPS28,RPS29,NDUFAF4,NDUFAB1,NDUFAF2,CALU,NDUFAF1  |
| <b>SPI1</b>  | 1.1E-07 | 4.7E-06 | YWHAE,RPL30,PIGT,ACAA2,MRPS14,YWHAB,ATP5C1,SLC2A3,ATP5G3,COX6A1,RPL8,PITPNC1,RPL6,GLS,RPS15,RPS14,ATIC,RPS16,RPS19,RPL18A,IMPA2,RARS,IDH3B,RPL35,RPL38,RPS11,IDH3A,GSTO2,RPL21,PGAM1,RPL13A,PLA2G4A,MRPS18A,RPS3A,EEF1G,ITPKB,NDUFS4,SUCLG1,RPL27,GAPDH,NDUFB9,NDUFB5,AK2,ITPR1,NEDD8,PDHB,COX5B,COX7A1,ACAT1,PPP2CA,CST3,ITPRIPL2,RPL14,RPS3,EIF4EBP2,RPL13,RPL17,COX10,NDUFA9,DARS,ATP8B2,GOT2,RPS26,RPS27,SERINC1,RSL24D1,RPS21,CALM2,UBE2M                                 |
| <b>YY1</b>   | 3.7E-07 | 1.5E-05 | YWHAE,RPL4,APP,COX7B,RPL30,MRPS14,AMD1,LAMC1,ATP5G2,MRPL35,COX7C,UBE2L3,MRPL42,RPL36,IDH3B,RPS11,COX8A,PDHX,ECH1,RPL13A,MRPS18A,SDHC,MRPS7,MRPS18C,EEF1A1,INPP4B,DYPD,NDUFS4,YME1L1,UBA52,DGKH,UQCRB,RPL12,ATP5A1,PDHB,OAZ1,LTBP1,UQCRH,MRPL11,ATP5L,UBB,RPS3,RPL18,COX10,ATP6V0A1,NDUFA9,NDUFA2,RPL35A,MRPL24,RPS26,RPS28,SPCS2,RPS27,OGDH,ITM2B                                                                                                                              |
| <b>CEBPB</b> | 1.0E-06 | 3.9E-05 | COX7B,NDUFA11,PIGP,SAT2,ATP5G3,PIK3C2A,CYR61,RPL6,RPS15,RPS4X,UBL5,RPS14,LGALS1,CSR2,RPS19,UQCRFS1,RPL38,ATP6V1E1,RPS10,PELO,COX8A,PDHX,RPS9,GSTO2,FNBP1,ECH1,MRPS21,SDHD,DNAJC3,SUCLG1,RPL27,SLC25A5,UQCRB,ATP5A1,ODC1,ITPR1,ATP5H,UQCR10,COX5B,ATP5O,COX7A1,MRPL11,ITPRIPL2,PPP2CB,UBB,RPL14,RPL15,COX10,IP6K2,RPL19,USP25,ATP8B2,NDUFA4,WFS1,NDUFA2,H3F3A,NDUFA1,PHKB,RPS26,RPIA,RPS25,RPS27,RPS29,NDUFAF4,CYCS,RPS20,PICALM                                                |
| <b>GABP</b>  | 1.6E-06 | 5.5E-05 | RPL30,PIGT,NDUFB7,NDUFB5,NDUFB3,COX5B,COX6A1,COX7C,UQCRH,RPL6,MRPL3,UBL5,RPS14,RPS18,RARS,I                                                                                                                                                                                                                                                                                                                                                                                    |

|              |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|--------------|---------|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              |         |         | DH3B,PMPCB,ATP6V1E1,COX10,COX8A,RPL41,MDH1,RPS5,MRPS21,RPL35A,MRPS18A,SDHC,RPS3A,SDHD,MRPL24,MRPS18C,RPS25,RPS27,CALU,NDUFS3,YME1L1,RPL27,SERINC1,RPS20,RPL26,UBE2M                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <b>CREM</b>  | 2.0E-06 | 6.8E-05 | RPL5,RPL30,ACAA2,ATP5C1,COX6A1,RPL8,PWP1,RPL6,GLS,RPS14,PCMT1,RPS16,RPS19,RPL18A,RPS18,PPP2R1A,RPL36,SLC16A7,CYP1B1,RPL38,RPS11,PRKACB,PELO,RPS13,RPS9,RPL21,IGFBP5,RPS5,APLP2,SDHC,ACSL3,EEF1A1,RPL24,RPL27,SUCLG1,RPL26,UBA52,NDUFB10,MAOA,GMPS,AK2,ATP5J,COX7A2,ATP5O,OAZ1,ADH5,ACAT1,ATP5B,UBB,ATP5D,ABL1,COX11,EIF4EBP2,NDUFV2,ATP6V1F,ATP6V0A1,DARS,RPL41,H3F3A,FN1,RPS26,RPS27,RPS29,NDUFAF4,NDUFAF2,CALU,OGDH,RPS20,CALM3,SERINC1,CALM1,CALM2,UBE2M,FARSB,PICALM,YWHAE,COX4I1,RPLP0,AMD1,PTEN,MTR,LAMC1,PIK3C2A,ATP5G2,PFAS,PRSS23,CYR61,AUH,IMPA2,RARS,IDH3B,UQCRFS1,DLAT,IDH3A,COX8A,PLA2G12A,GSTO2,GPX4,PGAM1,RPL13A,RPS3A,PGM2L1,CIT,EEF1G,DNAJC3,HADHB,ITPKB,HADHA,UGDH,NDUFS3,PPARG,GAPDH,DLD,OAT,NDUFB6,PPM1L,MRPS36,ATP5A1,ODC1,PDHB,COX5B,COX5A,PPP2CA,PPP2CB,UGP2,RPL14,RPS3,RPL13,TMEM208,CKB,RPL18,SLC35A1,USP25,NDUFA6,MDH1,MDH2,USP9X,TXNRD1,RPL35A,COX6C,CDC42BPA,SOD1,SPCS3,RSL1D1,SPCS2,PDE10A,MSRB3,CHPT1               |
| <b>PPARG</b> | 3.4E-06 | 1.0E-04 | ACAA2,COX15,YWHAB,ECH1,MGST1,AK2,SDHC,ATP5G3,COX5A,SOD1,C3,HADHB,RPS19,SDPR,CYCS,PPARG,CHPT1,ACADM                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| <b>FLI1</b>  | 3.7E-06 | 1.1E-04 | RPL4,CHRM3,RPL30,NDUFA12,TNC,ATP5C1,COX6A1,PWP1,PLB1,RPL6,UBE2L3,RPS15,RPS14,PCMT1,LGALS1,RPS16,RPS19,RPL18A,RPL36,RPL38,RPL37,RPS11,ATP6V1E1,RPL21,IGFBP5,FNBP1,PRKCB,RPS5,APLP2,SARS,SDHC,PRKCA,SDHD,COX6B1,MRPS18C,PLA2G16,INPP4B,SDPR,RPL24,SPARCL1,YME1L1,RPL27,RPL26,UBA52,ITPR1,ATP5J,ATP5I,ITPR3,ATP5H,ATP5O,LTBP1,UQCRH,ADH5,ATP5L,C3,EIF4EBP2,IGFBP7,NDUFV2,COX10,DARS,RPL41,GOT2,H3F3A,PHKB,IGF1,MRPL24,RPS26,RPS25,RPS27,RPS29,CALU,OGDH,CALM3,SERINC1,NDUFAF1,CALM1,RPS21,RSL24D1,RPS23,UBE2M,PICALM,YWHAE,PIGT,MRPS14,YWHAB,RPLP1,COX4I1,AMD1,PIGP,SLC2A1,MI A3,SLC2A3,ATP5G2,COX7C,UBL5,MRPL3,ATIC,IMPA2,RARS,CYP4V2,IDH3B,UQCRFS1,COX8A,GSTO2,GLRX3,GPX4,GSTO1,MRPS21,RPS3A,MUT,EEF1G,ITPKB,HADHA,UGDH,PIK3CA,NDUFS5,NDUFS3,MFGE8,GAPDH,DLD,ALDH9A1,SLC25A6,NDUFB9,NDUFB6,NDUFB5,RPL12,NDUFB3,COX5B,PPP2CA,CST3,RPS3,TMEM208,RPL15,RPL19,GSN,NDUFA6,MDH1,MDH2,PLCL1,TXNRD1,NDUFA2,CDC42BPA,ASS1,RPIA,RSL1D1,PDE10A,GNPDA2,NDUFAB1 |
| <b>SOX2</b>  | 7.4E-06 | 2.1E-04 | YWHAE,COX7B,COX4I1,AMD1,PTEN,SLC2A3,ATP5G2,COX7C,PITPNC1,CYR61,HK2,UBL5,RPS14,RPS19,ALDH2,R                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |

|              |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                      |
|--------------|---------|---------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|              |         |         | PS18,PMPCB,RPS11,IDH3A,COX8A,ENTPD1,RPL21,FNBP1,RPS5,RPL13A,SARS,SDHC,RPS3A,PGM2L1,CIT,EEF1A1,EEF1G,BACE1,UGDH,SMS,RPL27,GAPDH,PRPS1,ITPR1,P DHB,ATP5H,COX5A,OAZ1,FSTL1,COX7A1,CST3,UBB,PD GFC,ATP5D,CKB,NDUFV2,RPL18,ATP8B2,FN1,IGF1,COX 6C,MRPL24,RPS26,RPIA,GSTA4,CALM1,RPS21,PLCD4,RP S23                                                                                                                        |
| <b>OCT4</b>  | 7.5E-06 | 2.1E-04 | RPL5,SLC2A1,SLC2A3,RPL8,RPL9,CYR61,HK2,GLS,RPS4 X,RPS14,RPS16,RPS19,ALDH2,RPS18,RPS11,PRKACB,EN TPD1,RPL21,FNBP1,RPS5,RPL13A,SARS,RPS3A,CIT,EEF1 A1,BACE1,UGDH,PLCB4,SMS,SPARCL1,RPL27,GAPDH, PRPS1,ITPR1,NEDD8,COX7A2,COX5B,COX5A,OAZ1,CO X7A1,CST3,ATP5B,UBB,PDGFC,RPS3,ABL1,CKB,RPS2,RP L18,ATP6V1F,AOC3,ATP8B2,GOT2,FN1,COX6C,ASS1,RP S26,RPIA,GSTA4,RPS20, CALM1,RPS21,UBE2M,FARSB                              |
| <b>CHD1</b>  | 8.5E-06 | 2.5E-04 | YWHAE,RPL5,APP,MRPS14,SPPL2A,SLC2A1,ATP5C1,MI A3,LAMC1,ATP5G2,COX7C,MRPL35,CYR61,GLS,UBL5,C SRP2,IMPA2,CKMT1B,ACADM,RPS13,COX8A,GSTO2,GL RX3,PGAM1,SARS,MRPS18A,RPS3A,ACSL3,ITPKB,PPA1, UQCRC2,ALDH9A1,PPM1L,COX15,SDC2,MGST3,AK2,U QCR11,UQCRH,ATP5L,UBB,CKB,NDUFV2,IP6K2,USP25, ATP8B2,USP9X,LAMB2,CKMT1A,TXNRD1,GOT2,CDC42 BPA,RPS26,RPS25,RPS28, RPS27,RPS29,OGDH,MSRB2,CHPT1,CALM1,RPS21,CAL M2,PICALM          |
| <b>BCL3</b>  | 1.0E-05 | 2.6E-04 | YWHAE,RPL5,NDUFB10,NDUFB5,ATP5A1,PIGP,AMD1, ATP5J,PYGM,UQCR11,LAMC1,RPL8,COX5A,CYR61,HK2, MRPL11,ATP5B,PCMT1,UGP2,RPL18A,UBB,ATP5D,IDH3 B,PELO,RPL17,PDHX,RPL41,RPS5,ECH1,MRPS18A,SOD1, SPCS2,CYCS,RPS21, ITM2B                                                                                                                                                                                                      |
| <b>TAL1</b>  | 1.3E-05 | 3.1E-04 | RPL4,NDUFA11,MRPS14,COX4I1,RPLP0,PTEN,SLC2A1,A TP5G3,RPL8,RPL6,RPS15,RPS14,ATIC,RPS19,PPP2R1A,RP S18,RPL36,RPS10,B2M,RPS9,GLRX3,GPX4,RPS5,MRPS7,E EF1A1,RPL27,RPL26,UBA52,ALDH9A1,NDUFB9,NDUFB1 0,NDUFB6,RPL12,ATP5A1,ODC1,NDUFB3,ITPR1,UQCR1 1,COX5A,PPP2CA,ATP5B,UBB,RPL14,RPS3,COX11,RPL13 ,RPL18,RPL17,RPL19,DARS,RPL41,NDUFA6,MDH2,TXN RD1,RPL35A,PHKB, RPS26,RPS25,RPS27,PDE10A,RPS20,CALM1,RPS21,UBE2 M,RPS23 |
| <b>RUNX2</b> | 1.7E-05 | 3.9E-04 | PIGT,TNC,ATP5C1,PITPNC1,CYR61,HK2,GLS,LGALS1,R PS19,RPL18A,ALDH2,CYP1B1,DLAT,RPS10,PELO,LMCD 1,IGFBP5,FNBP1,GSTO1,PGAM1,MMP2,APLP2,ITPK1,MR PS18A,NME4,MRPS7,CIT,EEF1A1,EEF1G,BACE1,UGDH,P LA2G16,PLCB4,RPL26,GAS6,PRKAA2,OAT,COX15,AK2, ATP5H,UQCR10,ACACB,LTBP1,ADH5,MRPL11,UGP2,P DGFC,ATP6V0A1,RPL19,SLC35A1,DARS,GSN,MDH1,AT P8B2,LAMB2,TXNRD1,GOT2,FN1,CDC42BPA,RS1D1,RP S28,RPS20,CALM1                       |
| <b>ASH2L</b> | 1.7E-05 | 3.9E-04 | RPL5,COX7B,HIBADH,MRPS14,NDUFA12,PTEN,LAMC1, COX6A1,RPL8,MRPL35,RPL9,PITPNC1,RPL6,RPS15,RPS4 X,UBL5,RPS14,SMPD2,RPS16,CSRP2,RPS18,RPL36,IDH3B,                                                                                                                                                                                                                                                                       |

|       |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|-------|---------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|       |         |         | UQCRCF1,RPL38,DLAT,RPS10,LMCD1,RPS13,FNBP1,RPS5,ITPK1,TALDO1,SDHC,RPS3A,SDHD,PGM2L1,DNAJC3,EEF1A1,HADHA,PLCB4,NDUFS4,RPL24,SPARCL1,SUCLG1,GAS6,PRPS1,OAT,NDUFB7,UQCRB,NDUFB6,ATP5A1,COX7A2,PDHB,ATP5H,ATP5O,UQCRH,ADH5,ATP5L,RPS15A,ALDH1B1,PDGFC,ABL1,COX10,ATP6V1F,ATP6V0A1,NDUFA9,BCHE,DARS,RPL41,MDH1,NDUFA4,IDH2,NDUFA2,H3F3A,RPL35A,COX6C,MRPL24,SOD1,RPS26,RPS25,RSL1D1,GSTA4,MSRB2,CALU,RPS20,CHPT1,SERINC1,NDUFAF1,CALM1,CALM2,ITM2B,FARSB |
| EST1  | 2.1E-05 | 4.7E-04 | NDUFB5,NDUFB3,ITPR1,NEDD8,MTR,ATP5O,COX7C,RPL9,UQCRH,RPL6,MRPL11,ATP5L,MRPL42,RPS14,RPS18,LDH3B,COX10,RPL41,RPS9,MDH1,RPS5,ECH1,MRPS21,RPL35A,COX6C,MRPL24,PGM2L1,RPIA,RPS26,RPS25,SPCS2,RPS27,RPS29,NDUFS5,YME1L1,RPL27,SERINC1,UQCRC2                                                                                                                                                                                                             |
| NR0B1 | 2.6E-05 | 5.3E-04 | NDUFA12,ATP5C1,PYGM,SLC2A3,ATP5G3,CYR61,RPS14,IMPA2,RPL36,ACADM,RPS10,PGAM1,ITPK1,SARS,SDHC,SDHD,HADHB,HADHA,SMS,SLC25A5,GAPDH,PRPS1,OAT,NDUFB6,MGST3,ATP5A1,GATA6,ATP5J,PDHB,PPM1K,COX5B,ATP5O,COX5A,ATP5L,CST3,ATP5B,ALDH1B1,ATP5E,PDGFC,CKB,NDUFV2,RPL17,COX10,RPL19,GOT2,FN1,COX6C,ASS1,RPS26,GSTA4,CALU,OGDH,MSRB2,ACO1,CHPT1                                                                                                                  |
| ELK1  | 4.0E-05 | 8.0E-04 | RPL30,MRPS14,NDUFB3,MGST1,COX7A2,UQCRH,CYR61,GLS,RPS14,CSR2,RPS19,PPP2R1A,RPS18,RPL38,PRKACB,RPL19,COX8A,PDHX,DARS,RPL41,NDUFA4,ECH1,SI AH1,MRPS21,RPL35A,HADHB,DNAJC3,RPS27,NDUFS5,RPL24,MSRB3,PPARG, SUCLG1,RPS20,NDUFAF1                                                                                                                                                                                                                         |
| CTCF  | 5.3E-05 | 9.9E-04 | RPL5,APP,HIBADH,MRPS14,SLC2A1,SLC2A3,SLC2A4,ATP5G2,RPS15,RPS14,RPS19,RPL18A,RARS,RPL36,PMPCB,CYP1B1,RPL35,RPL38,RPL37,FNBP1,RPS5,ITPK1,RPL13A,MRPS18A,RPS3A,ATP5F1,RPL27,RPL26,NDUFB7,UQCRB,NDUFB10,PDE1C,COX15,MGST3,GATA6,COX5A,LTBP1,UQCRH,MRPL11,PPP2CB,OXCT1,ATP5D,NDUFV2,NDUFA6,USP9X,GOT2,ASS1,RPS26,RPS29,NDUFAB1,RPS20                                                                                                                     |
| SOX17 | 5.1E-05 | 9.9E-04 | APP,COX7B,MRPS14,COX4I1,SLC2A1,LAMC1,SLC2A4,PIK3C2A,ATP5G2,MRPL35,CYR61,HK2,UBL5,RPS16,RARS,PMPCB,RPL38,ACADM,RPL37,RPS11,COX8A,GSTO1,GPX3,RPS5,APLP2,ECH1,RPL13A,PLA2G4A,SDHC,MRPS18C,EEF1A1,DYPD,NDUFS4,PRPS1,PPM1L,ODC1,GATA6,ITPR3,COX7A2,PDHB,PPM1K,ATP5O,UQCRH,MRPL11,CST3,UBB,RPS3,ATP6V1F,RPL41,NDUFA6,USP9X,IGF1,SO D1,RPS26,RPS25,RPS27, GSTA4,MSRB3,RPS20,CALM1                                                                          |
| FOXO3 | 5.9E-05 | 1.1E-03 | PIGT,YWHAB,ATP5G3,LAMC1,PIK3C2A,RPL9,RPL6,RPL18A,AUH,ALDH2,UQCRCF1,RPL37,COA5,RPS9,GSTO2,GSTO1,MRPS18A,SDHC,SDHD,EEF1A1,YME1L1,UQCRC2,RPL26,OAT,NDUFB7,NDUFB6,MRPS36,COX15,NDUFB5,COX5B,ADH5,MRPL11,ACAT1,ATP5L,RPL14,TMEM208,RPL15,RPS2,NDUFV2,COX10,ATP6V1F,NDUFA9,USP25,                                                                                                                                                                         |

|                |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|----------------|---------|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                |         |         | NDUFA6,MDH2,NDUFA4,IDH2,RPL35A,GATM,SPCS2,RP<br>PS27,GNPDA2,CYCS,<br>ACO1,CALM3,SERINC1,RPS21,CALM2,ITM2B,FARSB,RP<br>S23                                                                                                                                                                                                                                                                                                                                     |
| <b>TAF7L</b>   | 8.4E-05 | 1.5E-03 | ACAA2,NDUFB10,COX15,PTEN,MGST1,ATP5J,PDHB,AT<br>P5G3,COX5A,CST3,SMPD2,LGALS1,RPS19,UBB,PKD4,RP<br>L38,ACADM,DLAT,LMCD1,AOC3,GSTO1,NDUFA2,ECH<br>1,RPS3A,MRPS7,ALDH6A1,SDPR,CAT,CALU,CYCS,RPL2<br>7,CALM1,CALM2,ALDH9A1                                                                                                                                                                                                                                        |
| <b>CREB1</b>   | 9.6E-05 | 1.7E-03 | PRPS1,RPL5,UQCRB,NDUFB6,MRPS14,RPL12,AK2,MTR,<br>PWP1,ATP5B,RPS14,RPS19,RPL18A,RPS18,RPL37,RPL18,<br>AASS,RPS13,NDUFA6,PDHA1,MDH1,RPS5,MRPS21,SDH<br>C,MRPL24,MUT,MRPS18C,RPS28,RPS29,CALU,OGDH,RP<br>S20,DLD,CALM2,RPS21                                                                                                                                                                                                                                     |
| <b>HOXB4</b>   | 1.0E-04 | 1.7E-03 | COX7B,RPLP1,AMD1,PTEN,COX6A1,PITPNC1,UBE2L3,U<br>BL5,MRPL3,PCMT1,RPS19,RPL18A,PPP2R1A,RPS18,RPL3<br>8,PRKACB,ECH1,MRPS21,RPL13A,PLA2G4A,ACSL3,EEF<br>1G,HADHB,NDUFS3,RPL24,SUCLG1,MFGE8,NDUFB9,U<br>QCRB,PPM1L,NDUFB3,COX7A2,PDHB,PPM1K,COX5B,O<br>AZ1,COX7A1,UQCRH,ATP5L,PPP2CA,ATP5B,UBB,EIF4E<br>BP2,RPL13,ATP6V0A1,NDUFA9,NDUFA4,GOT2,PHKB,M<br>RPL24,RPS26,RPIA,CALU,MSRB2,RPS21,PICALM                                                                  |
| <b>JARID1A</b> | 1.0E-04 | 1.7E-03 | RPL4,PIGT,COX4I1,RPLP0,ATP5C1,MRPL35,RPL9,PWP1,<br>UBL5,MRPL3,RPS16,RPL18A,AUH,RPS18,IDH3B,UQCRF<br>S1,DLAT,PRKACB,COX8A,RPS5,MRPS21,MRPS18A,SDH<br>C,SDHD,COX6B1,MRPS18C,NDUFS4,NDUFS3,YME1L1,R<br>PL27,DLD,NDUFB9,NDUFB10,NDUFB6,COX15,NDUFB5,<br>MGST3,NDUFB3,NEDD8,COX7A2,ATP5H,COX5B,ATP5D<br>,RPL14,TMEM208,RPS2,RPL18,COX10,ATP6V0A1,RPL19,<br>NDUFA9,LAMB2,NDUFA2,NDUFA1,COX6C,RSL1D1,AL<br>DH6A1,RPS28,SPCS2,NDUFAF2,SERINC1,<br>NDUFAF1,RPS21,FARSB |
| <b>FOX P3</b>  | 1.0E-04 | 1.7E-03 | NDUFB6,MRPS36,RPL12,MGST3,RPLP0,NDUFB3,PTEN,A<br>TP5J,MIA3,SLC2A3,ATP5G3,UQCRH,MRPL11,MRPL3,RP<br>S14,RPS15A,RPS19,UBB,RARS,TMEM208,RPL38,RPL15,RP<br>L37,RPS2,RPL18,NDUFA9,MDH1,RPL21,NDUFA4,ECH1,<br>COX6C,MRPL24,MRPS18C,EEF1A1,RPIA,ITPKB,RPS26,N<br>DUFS4,NDUFS3,RPL24,SUCLG1,RPS20,UQCRC2,<br>NDUFAF1,RPL26,FARSB                                                                                                                                       |
| <b>KLF4</b>    | 1.4E-04 | 2.1E-03 | RPL4,RPL5,COX7B,NDUFB7,RPL12,GATA6,PTEN,ITPR3,<br>SLC2A3,RPL8,ADH5,RPS15A,RPL18A,UBB,PPP2R1A,RPS<br>18,ATP5E,PDGFC,ABL1,RPL38,ACADM,RPL15,RPL37,RP<br>S11,RPL17,RPL19,RPL41,RPS9,RPL21,IGFBP5,RPS5,ECH1,I<br>TPK1,FN1,RPL13A,MUT,ITPKB,RPS25,SPCS2,PDE10A,ND<br>UFS4,SMS,RPL27,RPS20,GAPDH,UBA52,PICALM,RPS23                                                                                                                                                 |
| <b>GATA4</b>   | 1.8E-04 | 2.7E-03 | ACAA2,MRPS14,NDUFA12,COX4I1,COX6A1,MRPL35,PR<br>SS23,PITPNC1,HK2,RPS14,CSR2,PKD4,PELO,IGFBP5,GP<br>X4,FNBP1,RPS5,ITPK1,RPL13A,PGM2L1,COX6B1,HADH<br>B,HADHA,PLCB4,SDPR,PLSCR4,UQCRC2,GAS6,ALDH9<br>A1,OAT,ODC1,GMPS,PPM1K,COX7A1,LTBP1,UQCRH,A<br>DH5,ACAT1,CST3,ATP5B,UBB,ATP6V0A1,ATP6V1F,ND<br>UFA9,SLC35A1,DARS,H3F3A,IGF1,ASS1,SOD1,RPIA,SPC                                                                                                             |

|                |         |         |                                                                                                                                                                                                                                                                                                                                                                                 |
|----------------|---------|---------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                |         |         | S3,RSL1D1,CYCS,<br>CALM3,CALM1,PAM,CALM2,FARSB,PICALM                                                                                                                                                                                                                                                                                                                           |
| <b>DCP1A</b>   | 1.9E-04 | 2.7E-03 | UQCRB,RPLP0,SLC2A1,RPL8,OAZ1,ATP5L,RPS16,LGALS1,CYP4V2,RPL37,RPL21,MDH1,NDUFA4,PGAM1,GOT2,RPL13A,RPL35A,MRPS7,MRPL24,RPS26,NDUFS3,CYCS,CALM3,RPS20,CALM1,MFGE8,CALM2,UBE2M,PICALM                                                                                                                                                                                               |
| <b>ZFP42</b>   | 1.9E-04 | 2.7E-03 | YWHAH,RPL4,RPL5,PIGT,UQCRB,NDUFB5,MAOA,RPL12,UQCRH,ATP5L,UBE2L3,ATP5B,RPS14,UBB,ALDH2,PPP2R1A,RPS18,RPL36,ACADM,RPL15,CKB,RPS11,PELO,NDUFA9,PDHX,RPS9,NDUFA6,GSTO2,PGAM1,NDUFA2,ECH1,MRPS21,RPL13A,RPL35A,MRPS18A,PHKB,MRPS7,MRPL24,ASS1,EEF1A1,HADHB,HADHA,GSTA4,RPL24,YME1L1,ITM2B,RPS23                                                                                      |
| <b>HCFC1</b>   | 6.0E-04 | 7.4E-03 | MRPS14,MDH2,NDUFB5,ATP5F1,UQCRH,MRPL11,RPIA,RPS28,RPS19,RPS18,COX11,RPL27,SUCLG1,RPL26,RPS23                                                                                                                                                                                                                                                                                    |
| <b>ESR1</b>    | 6.4E-04 | 7.8E-03 | PRKAA2,PDHA1,ACAA2,NDUFA4,GOT2,GATA6,MGST1,ASS1,ATP5L,SOD1,C3,PCMT1,UBB,ALDH2,PKD4,RPL15,B2M,PELO,PICALM                                                                                                                                                                                                                                                                        |
| <b>PPARD</b>   | 9.9E-04 | 1.1E-02 | ITPKB,HADHB,HADHA,CSRP2,OXCT1,ITPR1,PLA2G4A,PRKCA,SDHD,MFGE8,ALDH9A1                                                                                                                                                                                                                                                                                                            |
| <b>RARG</b>    | 1.0E-03 | 1.1E-02 | PIGT,PPM1L,NDUFB10,NDUFA4,MMP2,FN1,RPL13A,LAMC1,FSTL1,LTBP1,PIGY,PITPNC1,ESD,IDH3B,CALU,ACADM,RPL19                                                                                                                                                                                                                                                                             |
| <b>CEBPD</b>   | 1.0E-03 | 1.2E-02 | CHRM2,HIBADH,RPLP0,PTEN,PRSS23,CYR61,HK2,RPS14,LGALS1,AUH,PKD4,CYP1B1,RPS13,RPS9,GSTO2,GSTO1,MMP2,MRPS18A,RPS3A,NME4,PLCB4,CAT,NDUFS4,PPARG,GAS6,SLC25A5,UBA52,MGST3,ITPR1,MGST1,ATP5O,FSTL1,LTBP1,ATP5L,UGP2,UBB,PDGFC,ABL1,COX10,ATP6V0A1,ATP6V1F,USP25,FN1,COX6C,ASS1,RPIA,CALU,CALM2,ITM2B,FBN1                                                                             |
| <b>NFE2L2</b>  | 1.2E-03 | 1.2E-02 | RPL5,PYGB,CHRM3,OAT,MAOA,NDUFB3,TNC,LAMC1,ATP5G3,ACACB,RPS15A,PDGFC,ESD,CYP1B1,IGFBP7,S1PR3,LMCD1,FNBP1,TXNRD1,FN1,PLA2G4A,TALDO1,MRPS18A,IGF1,COX6C,CDC42BPA,SPCS3,PIK3CA,GSTA4,SDPR,DYPD,CAT,CHPT1,PAM                                                                                                                                                                        |
| <b>NRF2</b>    | 1.2E-03 | 1.2E-02 | RPL5,PYGB,CHRM3,OAT,MAOA,NDUFB3,TNC,LAMC1,ATP5G3,ACACB,RPS15A,PDGFC,ESD,CYP1B1,IGFBP7,S1PR3,LMCD1,FNBP1,TXNRD1,FN1,PLA2G4A,TALDO1,MRPS18A,IGF1,COX6C,CDC42BPA,SPCS3,PIK3CA,GSTA4,SDPR,DYPD,CAT,CHPT1,PAM                                                                                                                                                                        |
| <b>YAP1</b>    | 1.2E-03 | 1.2E-02 | YWHAH,DGKG,CHRM3,APP,TNC,SLC2A1,SLC2A3,ATP5G3,RPL8,COX7C,CHRD1,PITPNC1,RPL6,GLS,PCMT1,AUH,PKD4,PGM5,RPL38,RPL37,RPS9,GLRX3,PRKCB,RPS5,APLP2,RPL13A,PLA2G4A,PRKCA,EEF1A1,ITPKB,INPP4B,DYPD,NDUFS4,SPARCL1,PPARG,SUCLG1,DLD,PPM1L,PDE1C,COX5A,ACACB,PPP2CA,ATP5B,UGP2,UBB,RPS3,IGFBP7,S1PR3,COX10,LAMB2,IDH2,GOT2,FN1,PHKB,COX6C,SOD1,SPCS3,PDE10A,GNPDA2,NDUFAB1,OGDH,ACO1,CALM2 |
| <b>TCFAP2C</b> | 1.3E-03 | 1.4E-02 | PYGB,PIGT,YWHAB,RPLP1,COX4I1,AMD1,SLC2A1,LAM                                                                                                                                                                                                                                                                                                                                    |

|       |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|-------|---------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|       |         |         | C1, COX6A1, PIK3C2A, RPL8, PRSS23, PITPNC1, CYR61, HK2, RPL6, UBL5, PCMT1, LGALS1, RPS18, CYP1B1, RPL35, RPL38, ACADM, RPS11, LMCD1, IGFBP5, GPX4, FNBP1, APLP2, EC H1, ITPK1, SDHC, RPS3A, SDHD, EEF1G, HADHB, UGDH, MFGE8, PRPS1, OAT, PPM1L, ATP5A1, ODC1, GATA6, ITPR1, NEDD8, ITPR3, COX7A2, COX5A, ATP5L, PPP2CA, UGP2, UBB, OXCT1, ATP6V0A1, ATP6V1F, LAMB2, TXNRD1, IDH2, H3F3A, FN1, SOD1, RPIA, CALU, MSRB3, CALM1, PAM, RPS21, PICALM                                                                                              |
| NANOG | 2.0E-03 | 2.0E-02 | PRPS1, RPL30, YWHAB, SLC2A3, ATP5G2, RPL9, CYR61, HK2, MRPL11, CST3, CSRP2, RPS19, UBB, ALDH1B1, PMPCB, PIP4K2A, RPL15, RPL18, NDUFA9, PDHA1, APLP2, IDH2, PHKB, IGF1, GSTA4, SMS, CALM3, RPS23                                                                                                                                                                                                                                                                                                                                               |
| CUX1  | 2.2E-03 | 2.2E-02 | CHRM2, AMD1, SLC2A1, MTR, SLC2A3, ATP5G3, COX7C, HK2, RPS4X, C4A, UBL5, MRPL42, PCMT1, RPS16, RPS19, RPS18, RARS, PMPCB, RPL37, DLAT, RPS11, B2M, RPS13, PDHX, RPL21, MRPS21, SARS, MRPS18A, SDHC, SDHD, MUT, EEF1A1, HADHB, DNAJC3, HADHA, SDPR, PPARG, SUCLG1, RPL27, UQCRC2, PRPS1, NDUFB9, FH, OAT, UQCRB, PPM1L, MGST3, GATA6, GSTT1, TXN, LTBP1, UQCRH, MRPL11, PPP2CA, ATP5B, ESD, RPL14, RPL15, RPL18, RPL17, RPL19, ATP6V1F, USP25, GSN, MDH1, NDUFA2, H3F3A, COX6C, SOD1, RPIA, RPS28, PDE10A, GSTA4, RPS29, PAM, CALM2, UBE2M      |
| ESR2  | 2.4E-03 | 2.3E-02 | PRPS1, ATP6V0E1, WFS1, MAOA, SLC2A1, PLOD2, LAMC1, PITPNC1, BACE1, UGDH, PLA2G16, RPL13, PIP4K2A, CYP1B1, S1PR3, CHPT1, LMCD1, YWHA, RPL4, APP, PIGT, MRPS14, RPLP1, PTEN, LAMC1, SLC2A4, ATP5G2, PITPNC1, CYR61, UBL5, PCMT1, RPS16, RPS19, ALDH2, PPP2R1A, RPL36, PMPCB, ATP6V1E1, PELO, PLA2G12A, RPS9, IGFBP5, RPS5, TALDO1, SARS, MUT, PGM2L1, HADHB, HADHA, OAT, NDUFB10, NDUFB6, MGST3, AK2, ITPR1, PPM1K, ATP5O, OAZ1, ATP5L, ATP5B, UBB, ATP5D, RPL18, RPL19, ATP6V1F, WFS1, GOT2, NDUFA2, FN1, RPS25, ALDH6A1, OGDH, MSRB2, SERINC1 |
| CCND1 | 2.8E-03 | 2.4E-02 | CHRM3, APP, PIGT, PTEN, PLOD2, MTR, PRSS23, PLB1, AUH, RARS, PDK4, SLC16A7, RPL38, DLAT, PRKACB, LMCD1, COA5, PDHX, ATP6V0E1, GLRX3, SARS, PRKCA, HADHA, INPP4B, PLCB4, SDPR, NDUFS5, PLSCR4, DPYD, NDUFS4, PRPS1, PDE1C, MAOB, MAOA, GATA6, ITPR3, OXCT1, IGFBP7, DARS, USP25, NDUFA4, PLCL1, PHKB, CDC42BPA, ASS1, SOD1, RPIA, GATM, RPS27, GNPDA2, RPS29, CALU, MSRB2, PAM, PLCD4                                                                                                                                                          |
| OLIG2 | 2.7E-03 | 2.4E-02 | HIBADH, COX4I1, RPLP0, TNC, SLC2A1, PLOD2, ATP5G3, LAMC1, ATP5G2, PITPNC1, CYR61, GLS, MRPL42, ATIC, SLC16A7, PIP4K2A, CYP1B1, ACADM, COX8A, PDHX, IGFBP5, SLC2A12, PLA2G4A, ACSL3, PGM2L1, CIT, EEF1G, UGDH, INPP4B, PLCB4, SDPR, NDUFS4, SMS, SPARCL1, PPARG, SUCLG1, NDUFB9, PPM1L, PDE1C, ODC1, ITPR1, MGST1, PPM1K, COX5B, LTBP1, PPP2CA, RPS15A, UGP2, BCHE, MDH1, PLCL1, TXNRD1, CDC42BPA, CALM2                                                                                                                                       |
| FOXM1 | 2.8E-03 | 2.4E-02 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |



|              |         |         |                                                                                                                                                                                                                                                                                                                                                                 |
|--------------|---------|---------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>TBX20</b> | 2.8E-03 | 2.4E-02 | YWHAE,DGKG,PYGB,RPLP0,SLC2A1,MTR,ATP5G2,RPL8,RPL9,CYR61,HK2,ATIC,IMPA2,PKD4,LMCD1,GSTO2,GPX3,PRKCA,CIT,EEF1A1,DNAJC3,PLCB4,PIK3CA,PPARG,RPL27,GAS6,SLC25A5,PRKAA2,NDUFB7,PDE1C,SDC2,MGST3,ATP5A1,GATA6,ITPR1,PDHB,ATP5H,COX5B,ACACB,ACAT1,CST3,RPS15A,UGP2,ABL1,EIF4EBP2,IGFBP7,KDSR,IP6K2,GSN,MDH1,IDH2,GOT2,FN1,FBN1                                          |
| <b>FOXA1</b> | 2.8E-03 | 2.4E-02 | PYGB,RPL5,MRPS14,RPLP1,SPPL2A,LAMC1,PRSS23,CYR61,MRPL42,ATIC,ACADM,LMCD1,COX8A,GLRX3,GPX4,GSTO1,PGAM1,APLP2,TALDO1,MRPS21,ATP5F1,PGM2L1,UGDH,PLA2G16,PPA1,NDUFS5,DYPD,RPL26,GAPDH,ALDH9A1,PRKAA2,ADH1C,MGST3,AK2,UQCR11,PPM1K,UQCRH,ATP5L,UGP2,COX11,KDSR,IGFBP6,ATP6V0A1,CYP2J2,SLC35A1,RPL41,H3F3A,CDC42BPA,RPS26,CYP2C9,RPS27,NDUFAF1,CALM2,PICALM           |
| <b>ERG</b>   | 3.3E-03 | 2.8E-02 | YWHAE,RPL4,RPL5,PIGT,NDUFA11,RPLP0,RPS15,ATIC,RPS16,IMPA2,IDH3B,PMPCB,IDH3A,RPL21,GPX4,GSTO1,RPS5,TALDO1,PGM2L1,EEF1G,PLSCR4,RPL24,YME1L1,SUCLG1,RPL26,ALDH9A1,PRPS1,ATP5A1,ODC1,GMPS,AK2,ITPR1,ITPR3,COX5B,UBB,OXCT1,ATP5D,RPL14,COX11,TMEM208,RPL13,RPL17,ATP6V1F,MDH2,TXNRD1,RPL35A,SOD1,CALU,OGDH,MSRB2,ACO1,RPS21,RPS23                                    |
| <b>MYCN</b>  | 3.8E-03 | 3.2E-02 | YWHAE,ACAA2,HIBADH,PIGP,LAMC1,RPL9,PITPNC1,GLS,RPS4X,PCMT1,RPS16,RPL38,RPS11,PGAM1,RPL13A,MRPS18A,PGM2L1,PPA1,UBA52,PPM1L,COX15,NDUFB5,MAOA,ODC1,ITPR1,ITPR3,PDHB,COX5A,UQCRH,ADH5,ATP5L,PPP2CB,UGP2,UBB,ATP5D,RPL14,RPL19,RPL41,WFS1,TXNRD1,H3F3A,FN1,RPL35A,PHKB,ASS1,SOD1,RPS26,ALDH6A1,RPS28,RPS29,NDUFAB1,RPS20,CALM3,NDUFAF1,CALM1,PAM,RPS21,CALM2,PICALM |
| <b>PPAR</b>  | 4.1E-03 | 3.4E-02 | PYGB,FH,MAOA,MGST3,GATA6,AK2,PLOD2,ATP5O,FSMTL1,LTBP1,HK2,MRPL3,AUH,PDGFC,RPS3,PKD4,CYP1B1,BCHE,TXNRD1,ECH1,SIAH1,SARS,MRPS18A,ACSL3,UQCRHL,EEF1A1,HADHB,HADHA,INPP4B,NDUFS5,CAT,ACO1,RPL26,PICALM,FBN1                                                                                                                                                         |
| <b>SALL4</b> | 4.9E-03 | 4.0E-02 | NDUFB6,NDUFB5,MRPS14,MGST3,AMD1,PTEN,ATP5I,SLC2A3,ATP5G3,PRSS23,PCMT1,RPS15A,RPS16,UBB,ABL1,IDH3B,IGFBP7,IGFBP6,NDUFV2,RPS11,PELO,B2M,SLC35A1,ENTPD1,RPL41,RPS9,MDH1,NDUFA4,MMP2,RPS5,H3F3A,SARS,PLA2G4A,HADHA,PLSCR4,CYCS,RPL27,RPS20,RPL26,RPS23                                                                                                              |
| <b>EGR1</b>  | 5.4E-03 | 4.3E-02 | HADHB,NDUFB9,H3F3A,ITPK1,GMPS,PIP4K2A,ATP5I,KDSR,ATP5H,CYP4F11,CRYM,PRSS23                                                                                                                                                                                                                                                                                      |
| <b>FOXP2</b> | 5.5E-03 | 4.3E-02 | APP,HIBADH,YWHAB,PIGP,ADARB1,PLB1,PCMT1,UGP2,AUH,UBB,RARS,PDGFC,PKD4,EIF4EBP2,PIP4K2A,NDUFV2,USP25,ATP6V0E1,GOT2,H3F3A,PLA2G4A,MUT,RPIA,ITPKB,SPCS2,GSTA4,CYCS                                                                                                                                                                                                  |

|               |         |         |                                                                                                                                                                   |
|---------------|---------|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>THAP11</b> | 5.5E-03 | 4.4E-02 | YWHAE,NDUFB7,ITPR1,ATP5J,NEDD8,MTR,ATP5O,ATP5G2,COX7C,RPS18,ATP5E,RPL36,RPS3,RPL15,RPL18,ATP6V1F,MDH1,GOT2,PGM2L1,RPIA,BACE1,RPS26,SPCS2,SUCLG1,RPS20,RPL26,RPS23 |
| <b>FUS</b>    | 6.1E-03 | 4.7E-02 | PRKAA2,MAOA,PLA2G4A,PHKB,MTR,ATP5G3,RPL9,FSTL1,COX7C,MUT,CYR61,ACAT1,EEF1A1,RPS4X,RARS,ATP5E,RPL15,PAM,GAPDH                                                      |

NOTE: FC= Fold Change; FDR p-val= FDR p-value.

**Table S6.** Putative binding motif enrichment analysis using the Enrich webtool and showing the relative relevance of various histone marks in the deregulated transcripts.

| Term            | p-value | Adj. p-val | Genes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|-----------------|---------|------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>H3K79me2</b> | 7.2E-24 | 3.0E-21    | NDUFA11;NDUFA12;ATP5C1;COX6A1;RPL9;RPL6;RPS15;LGA<br>LS1;RPS16;RPL18A;RPS18;RPL35;PMPCB;RPL37;RPS11;RPS10;R<br>PS13;PDHX;RPS9;IGFBP5;RPL21;SDHC;SDHD;MRPS18C;COX6<br>B1;EEF1A1;RPL27;RPL26;UBA52;UQCRB;SDC2;ITPR3;ATP5O;<br>OAZ1;UQCRH;ADH5;ATP5B;UBB;ESD;NDUFV2;COX10;ATP6<br>V0A1;<br>DARS;RPL41;ATP8B2;MRPL24;RPS26;RPS25;RPS28;NDUFAF4;<br>CALU;CYCS;RPS20;ACO1;RPS21;RSL24D1;RPS23;COX20;MRPS<br>14;RPLP1;RPLP0;ATP5G3;PFAS;CYR61;RPS4X;UBL5;MRPL3;CS<br>RP2;ATIC;IDH3B;COA5;GPX4;GSTO1;MRPS21;RPS3A;ATP5F1;<br>MRPS7;CIT;EEF1G;NDUFS5;NDUFS4;DLD;NDUFB7;NDUFB6;<br>RPL12;ATP5A1;NDUFB3;UQCR10;PDHB;COX5B;FSTL1;PPP2C<br>B;RPS3;TMEM208;RPL15;RPS2;RPL18;RPL17;USP25;NDUFA6;L<br>AMB2;NDUFA2;RPL35A;RSL1D1;NDUFAB1 |
| <b>H3K36me3</b> | 6.4E-18 | 6.5E-16    | COX7B;RPL30;MRPS14;YWHAB;NDUFA12;RPLP1;COX4I1;ECI<br>2;SPPL2A;RPLP0;ATP5G3;COX7C;CYR61;RPS15;MRPL3;RPS14;<br>ATIC;RPS16;ALDH2;RPS19;RPS18;RPL36;RPL35;RPL38;ACAD<br>M;RPL37;DLAT;RPS11;PELO;RPS10;RPS13;COA5;COX8A;RPL2<br>1;GSTO2;GPX4;ATP6AP1;ECH1;MRPS21;SDHD;ATP5F1;MRPS1<br>8C;EEF1A1;EEF1G;PIK3CA;RPL24;RPL27;RPL26;UQCRC2;SLC2<br>5A5;GAPDH;UBA52;NDUFB10;COX15;RPL12;ATP5A1;MGST1;<br>ITPR1;ATP5J;PDHB;ATP5H;ATP5O;COX5B;ACACB;ADH5;C3;<br>ATP5B;ATP5E;ATP5D;RPL14;EIF4EBP2;RPL13;TMEM208;RPL1<br>5;RPL18;RPL17;RPL19;FN1;IGF1;COX6C;SOD1;RPS26;SPCS3;RP<br>S25;RPS28;RPS27;<br>RPS29;NDUFAB1;CYCS;CHPT1;RPS20;RSL24D1;COX20;RPS23                                                                              |
| <b>H3K79me3</b> | 6.4E-18 | 6.5E-16    | MRPS14;NDUFA12;RPLP1;COX4I1;ATP5C1;PLOC2;COX6A1;C<br>OX7C;RPL9;RPL6;RPS4X;RPS15;MRPL42;PCMT1;LGALS1;RPS1<br>6;RPS19;RPL18A;RPS18;RPL36;PMPCB;ATP6V1E1;RPS11;RPS10<br>;RPS13;RPS9;GPX4;GLRX3;RPS5;RPS3A;SDHC;SDHD;MRPS7;C<br>IT;COX6B1;EEF1G;EEF1A1;PPA1;NDUFS5;NDUFS4;NDUFS3;R<br>PL27;RPL26;SLC25A5;DLD;UBA52;GAPDH;OAT;NDUFB6;UQ<br>CRB;NDUFB5;NDUFB3;COX7A2;COX5B;ATP5O;OAZ1;ADH5;<br>UBB;ATP5E;ESD;RPS3;TMEM208;IGFBP7;RPL15;RPS2;NDUFV2<br>;RPL18;RPL17;RPL19;NDUFA9;RPL41;NDUFA6;MDH1;LAMB2<br>;NDUFA2;H3F3A;RPL35A;RPS25;RSL1D1;RPS28;SPCS2;RPS29;<br>NDUFAF4;NDUFAB1;NDUFAF2;CALU;CYCS;RPS20;CALM3;<br>NDUFAF1;CALM1;RSL24D1;RPS21;RPS23                                                                        |

|                 |         |         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|-----------------|---------|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>H4K20me1</b> | 4.0E-09 | 7.5E-08 | RPL4;RPL5;ACAA2;RPLP1;ECI2;RPLP0;ATP5C1;SLC2A3;ADARB1;ATP5G3;RPL8;CYR61;UBE2L3;RPS15;RPS14;RPL18A;RPL36;RPL35;SLC16A7;RPL38;RPL37;RPS11;RPS9;RPL21;FNBP1;RPS5;MMP2;RPL13A;RPS3A;PRKCA;MRPS7;EEF1A1;UGDH;PPA1;YME1L1;RPL24;SUCLG1;RPL27;UQCRC2;RPL26;UBA52;GAPDH;OAT;MAOB;PPM1L;RPL12;ATP5J;UQCR10;PPM1K;OAZ1;ADH5;ITPRIPL2;ATP5B;UGP2;UBB;ABL1;RPL13;RPS2;RPL15;NDUFV2;RPL18;RPL17;ATP6V0A1;IP6K2;RPL19;MDH2;GOT2;RPS26;RPS28;MSRB3;RPS20;CALM3;ACO1;FBN1                                                                                                                                                                                                                          |
| <b>H3K27ac</b>  | 3.0E-07 | 4.0E-06 | CHRM2;ACAA2;NDUFA11;NDUFA12;SPPL2A;COX6A1;PWP1;PCMT1;RPS19;RPL36;PDK4;ATP6V1E1;PELO;PRKACB;RPS10;RPS9;RPL21;IGFBP5;RPS5;MRPS18A;SDHC;ACSL3;SUCLG1;UQCRC2;DGKH;COX15;ITPR1;GSTT1;ITPR3;COX7A2;UQCRH;ITPRIPL2;UBB;ATP5E;ESD;COX11;IGFBP7;COX10;SIAH1;PHKB;RPS26;RPS25;RPS27;RPS29;NDUFAF4;OGDH;SERINC1;NDUFAF1;CALM1;PAM;FBN1;RPS23;FARSB;PYGB;YWHAB;RPLP1;AMD1;SLC2A1;MIA3;MRPL35;PITPNC1;SMPD2;IDH3B;PGM5;AASS;IDH3A;PLA2G12A;GSTO2;SLC2A12;PLA2G4A;MRPS21;MRPS7;CIT;HADHB;HADHA;UGDH;CAT;NDUFS3;NDUFB9;NDUFB5;NDUFB3;ODC1;UQCR10;COX5B;PPP2CB;RPS15A;OXCT1;TMEM208;RPL13;RPL15;RPS2;RPL19;NDUFA9;BCHE;NDUFA6;MDH1;USP9X;NDUFA4;TXNRD1;NDUFA2;RPL35A;RPIA;RSL1D1;SPCS2;MSRB3;PLCD4 |
| <b>H2AFZ</b>    | 1.1E-04 | 9.8E-04 | YWHAE;DGKG;PIGT;HIBADH;NDUFA12;MRPS14;PIGP;SLC2A1;MIA3;ATP5G3;ATP5G2;RPL6;RPS14;CSRP2;ATIC;ALDH2;PP2R1A;CYP4V2;RPL36;PMPCB;UQCRFS1;PGM5;RPL37;PELO;RPS10;COX8A;PLA2G12A;GPX3;SDHC;ACSL3;MRPS7;ATP5F1;CIT;INPP4B;UGDH;PPA1;SMS;SUCLG1;UBA52;PRPS1;NDUFB9;NDUFB7;NDUFB5;NDUFB3;AK2;COX7A2;PDHB;ATP5L;RPS15A;ATP5D;RPL14;EIF4EBP2;COX10;MDH2;PLCL1;NDUFA2;RSL1D1;RPS20;SERINC1;RSL24D1                                                                                                                                                                                                                                                                                                |
| <b>H3K4me3</b>  | 6.1E-04 | 4.3E-03 | CHRM2;RPL4;PYGB;SPPL2A;ECI2;SAT2;ATP5G2;CHRD1;PCMT1;MRPL3;MRPL42;ATIC;ALDH2;PDK4;UQCRFS1;ACADM;DLAT;ATP6V1E1;B2M;AASS;IDH3A;RPS9;GSTO2;ITPK1;ECH1;MRPS7;DPYD;NDUFS4;MFGE8;GAPDH;DLD;PDE1C;NDUFB6;MAOB;NDUFB10;COX15;SDC2;MGST3;ITPR1;FSTL1;ESD;TMEM208;IP6K2;PDHA1;NDUFA4;FN1;NDUFA1;RPS26;RSL1D1;ALDH6A1;RPS27;GSTA4;ACO1;NDUFAF1;PLCD4;FARSB;MSRB1                                                                                                                                                                                                                                                                                                                               |
| <b>H3K9me1</b>  | 1.0E-03 | 6.3E-03 | RPL4;RPL30;NDUFA11;RPLP1;RPLP0;ATP5C1;ATP5G3;ATP5G2;GLS;LGALS1;ATIC;RPL36;PMPCB;RPL35;RPL37;RPS11;RPL21;ATP5F1;COX6B1;PPA1;UQCRC2;RPL26;MFGE8;UBA52;SLC25A6;FH;MAOB;COX15;MAOA;RPL12;ACACB;ACAT1;ITPRIPL2;RPS15A;UGP2;ALDH1B1;ATP5E;RPL14;TMEM208;EIF4EBP2;RPL13;RPS2;RPL15;RPL18;RPL17;ATP6V0A1;GSN;ATP8B2;MDH1;MDH2;FN1;UQCRHL;RPS28;GNPDA2;CHPT1;FARSB                                                                                                                                                                                                                                                                                                                          |
| <b>H3ac</b>     | 2.8E-03 | 1.4E-02 | NDUFA11;NDUFA12;COX4I1;RPLP1;SLC2A1;ATP5C1;PLOD2;PRSS23;MRPL35;CSRP2;MPC1;IDH3B;ACADM;PRKACB;PELO;RPS10;RPS13;PLA2G12A;GSTO1;APLP2;ITPK1;RPS3A;NME4;SDHD;MRPS7;HADHB;PPA1;NDUFS5;NDUFS3;UQCRC2;PRKA2;PPM1L;NDUFB5;UQCR11;NEDD8;COX7A2;FSTL1;MRPL11;COX11;TMEM208;NDUFV2;SLC35A1;DARS;USP25;NDUFA6;N                                                                                                                                                                                                                                                                                                                                                                                |

|             |         |         |                                                                                                                                                                                                                                                                                                                                          |
|-------------|---------|---------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|             |         |         | DUFA4;RSL1D1;NDUFAF4;NDUFAF2;CYCS;MSRB3;ACO1;PIC<br>ALM;COX20                                                                                                                                                                                                                                                                            |
| H3K9me<br>3 | 1.1E-02 | 4.5E-02 | RPL5;PIGT;NDUFA12;YWHAB;RPLP1;RPLP0;ATP5C1;ATP5G2<br>;RPL6;RPS14;RPS16;AUH;RPL18A;ALDH2;RPS19;RPL35;ACAD<br>M;RPS10;RPS13;RPL21;RPL13A;RPS3A;SDHD;MRPS7;EEF1A1;<br>HADHB;HADHA;CAT;NDUFS4;RPL27;UQCRC2;UBA52;MAO<br>A;AK2;COX7A2;TXN;ATP5B;RPS3;RPL13;RPS2;RPL18;ATP6V0<br>A1;RPL41;<br>NDUFA6;COX6C;RSL1D1;MSRB2;RPS20;CALM3;RPS21;FBN1 |

NOTE: FC= Fold Change; FDR p-val= FDR p-value.

**Table S7.** Assignment of the main metabolites identified in NMR urine spectra.

| N.<br>Assignment | Metabolite                                             | Group                              | Chemical shift<br>(ppm) |
|------------------|--------------------------------------------------------|------------------------------------|-------------------------|
| 2                | Branched chain amino acids                             | --                                 | --                      |
| 3                | Valine                                                 | $\gamma\text{CH}_3$                | 0.98                    |
| 3                | Valine                                                 | $\gamma\text{CH}_3$                | 1.04                    |
| 4                | Methylsuccinic acid                                    | $\alpha\text{CH}_3$                | 1.08                    |
| 5                | Lactate                                                | $\text{CH}_3$                      | 1.33                    |
| 6                | Alanine                                                | $\beta\text{CH}_3$                 | 1.46                    |
| 7                | Lysine                                                 | $\beta\text{CH}_2$                 | 1.71                    |
| 8                | Acetic acid                                            | $\text{CH}_3$                      | 1.97                    |
| 7                | Lysine                                                 | $\beta\text{CH}_2$                 | 1.91                    |
| 9                | N-acetylneuraminic acid                                | $\text{CH}_3$                      | 2.04                    |
| 10               | Glutamine                                              | $\beta\text{CH}_2$                 | 2.13                    |
| 11               | Succinic acid                                          | 2,3 $\text{CH}_2$                  | 2.39                    |
| 10               | Glutamine                                              | $\gamma\text{CH}_2$                | 2.44                    |
| 12               | Citrate                                                | $\text{CH}_2$                      | 2.52                    |
| 12               | Citrate                                                | $\text{CH}_2$                      | 2.66                    |
| 13               | Dimethylamine                                          | $\text{CH}_3$                      | 2.71                    |
| 14               | Trimethylamine                                         | $\text{CH}_3$                      | 2.93                    |
| 15               | Dimethylglycine                                        | $\text{CH}_3$                      | 2.96                    |
| 16               | Creatinine                                             | $\text{CH}_3$                      | 3.03                    |
| 19               | Taurine                                                | $-\text{CH}_2-$<br>$\text{NH}_3^+$ | 3.25                    |
| 17               | Trimethylamine N-oxide                                 | $\text{CH}_3$                      | 3.28                    |
| 18               | Methanol                                               | $\text{CH}_3$                      | 3.34                    |
| 19               | Taurine                                                | $-\text{CH}_2-$<br>$\text{SO}_3^-$ | 3.42                    |
| 20               | Glycine                                                | $\alpha\text{CH}$                  | 3.55                    |
| 21               | Sucrose                                                | $\text{C}_6'-\text{H}_2$           | 3.82                    |
| 21               | Sucrose                                                | $\text{C}_5'-\text{H}$             | 3.87                    |
| 22               | Creatine                                               | $\text{CH}_2$                      | 3.92                    |
| 23               | Hippuric acid                                          | $\alpha\text{CH}_2$                | 3.97                    |
| 16               | Creatinine                                             | $\text{CH}_2$                      | 4.05                    |
| 5                | Lactate                                                | $\text{CH}$                        | 4.10                    |
| 24               | Trigonelline                                           | $\text{CH}_3$                      | 4.43                    |
| 25               | Urea                                                   | $-\text{NH}_2$                     | 5.80                    |
| 26               | 3-(3-hydroxyphenyl)-3-hydroxypropionic<br>acid (HPPHA) | $\text{C}_4'-\text{H}$             | 6.93                    |
| 26               | 3-(3-hydroxyphenyl)-3-hydroxypropionic<br>acid (HPPHA) | $\text{C}_6'-\text{H}$             | 6.97                    |

|    |               |                      |      |
|----|---------------|----------------------|------|
| 27 | Phenylalanine | C <sub>2,6'</sub> -H | 7.32 |
| 27 | Phenylalanine | C <sub>3,5'</sub> -H | 7.42 |
| 23 | Hippuric acid | C <sub>3,5'</sub> -H | 7.60 |
| 28 | Pseudouridine | CH                   | 7.66 |
| 23 | Hippuric acid | C <sub>2,6'</sub> -H | 7.82 |
| 29 | Hypoxanthine  | C <sub>7'</sub> -H   | 8.20 |
| 30 | Formic acid   | CH                   | 8.45 |
| 24 | Trigonelline  | C <sub>3,5'</sub> -H | 8.82 |
| 24 | Trigonelline  | C <sub>1'</sub> -H   | 9.10 |

## References

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