Transcriptome alterations of vascular smooth muscle cells in aortic wall of myocardial infarction patients

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A B S T R A C T
This article contains further data and information from our published manuscript [1]. We aim to identify significant transcriptome alterations of vascular smooth muscle cells (VSMCs) in the aortic wall of myocardial infarction (MI) patients. Microarray gene analysis was applied to evaluate VSMCs of MI and non-MI patients. Prediction Analysis of Microarray (PAM) identified genes that significantly discriminated the two groups of samples. Incorporation of gene ontology (GO) identified a VSMCs-associated classifier that...
discriminated between the two groups of samples. Mass spectrometry-based iTRAQ analysis revealed proteins significantly differentiating these two groups of samples. Ingenuity Pathway Analysis (IPA) revealed top pathways associated with hypoxia signaling in cardiovascular system. Enrichment analysis of these proteins suggested an activated pathway, and an integrated transcriptome-proteome pathway analysis revealed that it is the most implicated pathway. The intersection of the top candidate molecules from the transcriptome and proteome highlighted overexpression.

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### Specifications Table

| Subject area               | Biology                                      |
|----------------------------|----------------------------------------------|
| More specific subject area | Genomics, Proteomics, Bioinformatics, Cardiovascular |
| Type of data               | Tables, figures                              |
| How data was acquired      | Microarray (Gene Titan Instrument, Affymetrix), mass spectrometry (LC-MS/MS system comprised of a Dionex Ultimate 3000 RSLC nano-HPLC system, coupled to an online Q-Exactive hybrid quadrupole-Orbitrap mass spectrometer (Thermo Scientific, Hudson, NH, USA)), RT-qPCR (QuantStudio™ 12K Flex system (Life Technologies; Thermo Fisher Scientific Inc, USA)) |
| Data format                | Raw, analyzed                                |
| Experimental factors       | Laser capture microdissection, total RNA extraction and protein extraction from aortic tissues from surgical patients |
| Experimental features      | Data analysis with Principal Component Analysis (PCA), Prediction Analysis of Microarray (PAM), Gene Ontology (GO), Ingenuity Pathway Analysis (IPA) |
| Data source location       | Singapore                                    |
| Data accessibility         | Data is with this article.                   |

### Value of the data

- Combination of multiple technologies and bioinformatics analysis performed in this study reveals the molecular changes induced by myocardial infarction on aortic smooth cells in humans.
- The alterations of the VSMCs transcriptome are congruent with alterations at the protein levels. Both levels show notably the up-regulation of the superoxide dismutase (SOD) with the activation of superoxide radical degradation pathway.
- Differentially expressed genes and pathways identified in these comparisons may be used in future experiments investigating response in myocardial infarction.

### 1. Data

#### 1.1. Clinical analysis

The characteristics of the myocardial infarction (MI) and non-MI samples undergoing transcriptomics and proteomics studies are presented in Tables 1(A) and 1(B) respectively. The baseline demographic and clinical characteristics of samples undergoing transcriptomics study were
### Table 1A
Demographic characteristics of MI and non-MI groups undergoing transcriptomics analysis.

| Characteristics       | Transcriptomics | Transcriptomics | p-value |
|-----------------------|-----------------|-----------------|---------|
|                       | MI (n=17)       | Non-MI (n=19)   |         |
| Ethnic                |                 |                 |         |
| Chinese               | 12              | 10              | 0.557   |
| Malay                 | 2               | 6               |         |
| Indian                | 2               | 2               |         |
| Others                | 1               | 1               |         |
| Gender                |                 |                 |         |
| Male                  | 14              | 16              | 0.881   |
| Female                | 3               | 3               |         |
| Age (Mean ± SD)       | 59.53 ± 8.28    | 59.68 ± 8.85    | 0.957   |
| Ejection Fraction     |                 |                 |         |
| Good (>45%)           | 11              | 13              | 0.292   |
| Fair (30–45%)         | 4               | 6               |         |
| Poor (<30%)           | 2               | 0               |         |
| Smoking               |                 |                 |         |
| No                    | 8               | 9               | 0.985   |
| Yes                   | 9               | 10              |         |
| Renal Impairment      |                 |                 |         |
| No                    | 15              | 19              | 0.124   |
| Yes                   | 2               | 0               |         |
| Diabetes Mellitus     |                 |                 |         |
| No                    | 9               | 7               | 0.332   |
| Yes                   | 8               | 12              |         |
| Hypertension          |                 |                 |         |
| No                    | 1               | 3               | 0.345   |
| Yes                   | 16              | 16              |         |
| Hyperlipidaemia       |                 |                 |         |
| No                    | 0               | 0               | -       |
| Yes                   | 17              | 19              |         |
| Antihyperlipidemic Medication |         |                 |         |
| No                    | 0               | 0               | -       |
| Yes                   | 17              | 19              |         |
| Troponin I (µg/L) (Mean ± SD) | 12.20 ± 20.86  | 0.01 ± 0.004    | <0.05   |
|                        | (n=15)          | (n=4)           |         |

### Table 1B
Demographic characteristics of MI and non-MI proteomics groups.

| Characteristics       | Proteomics | Proteomics | p-value |
|-----------------------|------------|------------|---------|
|                       | MI n=25    | Non-MI n=25|         |
| Ethnic                |            |            |         |
| Chinese               | 11         | 13         | 0.745   |
| Malay                 | 8          | 7          |         |
| Indian                | 5          | 5          |         |
| Others                | 1          | 0          |         |
| Gender                |            |            |         |
| Male                  | 20         | 18         | 0.508   |
| Female                | 5          | 7          |         |
| Age (Mean ± SD)       | 60.88 ± 12.34 | 61.68 ± 8.26 | 0.789   |
| Ejection Fraction     |            |            |         |
| Good (>45%)           | 14         | 16         | 0.344   |
| Fair (30–45%)         | 9          | 9          |         |
| Poor (<30%)           | 2          | 0          |         |
| Smoking               |            |            |         |
| No                    | 12         | 12         | 1       |
| Yes                   | 13         | 13         |         |
| Renal Impairment      |            |            |         |
| No                    | 25         | 25         | NA      |
| Yes                   | 0          | 0          |         |
| Diabetes Mellitus     |            |            |         |
| No                    | 10         | 9          | 0.771   |
| Yes                   | 15         | 16         |         |
| Hypertension          |            |            |         |
| No                    | 3          | 1          | 0.297   |
| Yes                   | 22         | 24         |         |
| Hyperlipidaemia       |            |            |         |
| No                    | 1          | 0          | 0.312   |
| Yes                   | 24         | 25         |         |
| Antihyperlipidemic Medication |         |            |         |
| No                    | 4          | 1          | 0.157   |
| Yes                   | 21         | 24         |         |
| Troponin I (µg/L) (Mean ± SD) | 19.54 ± 19.24 | 0.015 ± 0.006 | <0.05   |
|                        | (n=22)     | (n=9)      |         |
compared with those of the samples from the proteomics study (Table 2). In addition, the characteristics of the transcriptomic MI and non-MI samples with those of the independent cohorts comprising additional MI and non-MI patients undergoing RT-qPCR were compared (Tables 3 and 4).

1.2. Gene expression data analysis and class prediction by Prediction Analysis of Microarray (PAM)

The samples were preprocessed through several steps, including quality assessment and outlier identification, normalization, batch effect correction and evaluation (Fig. 1). To interrogate differentially expressed genes between MI and non-MI we conducted gene-expression profiling using the Affymetrix U219 microarray platform. The R ‘limma’ package (https://www.bioconductor.org/help/workflows/arrays/) identified 4,357 probe sets, selected at a ‘limma’-defined p-value < 0.05. Based on this set of differentially expressed genes (DEGs), we performed principal component analysis (PCA) (Fig. 1).

To determine subgroup of genes distinguishing MI from non-MI subjects, we performed supervised PAM [2] and identified a set of differentially expressed genes (DEGs) that discriminated between the two subtypes at Wilcox FDR < 0.1 (Table 5).

Gene Ontology (GO) analysis of the DEGs was performed using DAVID Bioinformatics tools [3] (http://david.abcc.ncifcrf.gov/). The GO results for the down-regulated transcripts were not enriched for any GO terms. The GO analysis revealed biological processes (Table 6).

Clustering of genes were done by two methods, hierarchical and k-mean clustering. Hierarchical clustering with multiscale bootstrap resampling was done by Pvclust, an R statistical software package [4]. The Pvclust is an R package for assessing the uncertainty in hierarchical cluster analysis. For each cluster in hierarchical clustering, quantities called p-values are calculated via multiscale bootstrap resampling. The parameters (https://cran.r-project.org/web/packages/pvclust/pvclust.pdf)
used here were 10000 bootstrap replications, cluster method: Ward algorithm and distance method: Euclidean. For the heat maps plot, we used log2 scale.

The k-mean clustering was performed by R (https://stat.ethz.ch/R-manual/R-devel/library/stats/html/kmeans.html), showing that the selection of features gave a higher accuracy than PAM alone. The genes were discriminated between the MI and non-MI vascular smooth muscle cells (VSMCs) samples (Table 7). A clustered result is shown in Fig. 2 of Ref. [1].

1.3. Protein processing, electrostatic repulsion-hydrophilic interaction chromatography (ERLIC) and LC-MS/MS analysis using Q-Exactive mass spectrometer

Differential expressed proteins identified are shown in Table 8. Only peptides identified with strict spectral false discovery rate of less than 1% (q-value ≤ 0.01) were considered.

1.4. Hierarchical cluster analysis of RT-qPCR-based detected genes

Using six RT-qPCR-supported genes as a representative gene classifier characterizing the differences between MI and non-MI aortic samples, hierarchical clustering was performed with multiscale bootstrap resampling by Pvclust. The result is shown in Fig. 2.

1.5. Transcriptomic and proteomic pathways analysis

Systemic evaluation was performed using IPA (www.ingenuity.com) to identify transcriptomic and proteomic pathways, and significantly enriched canonical pathways are shown in Table 9. An integrated transcriptome-proteome correlation is performed to identify common enriched pathway and molecule (Table 10).

Table 3
Demographic characteristics of MI study group and MI validation group.

| Characteristics                        | MI Microarray (n=17) | MI Validation (n=20) | p-value |
|----------------------------------------|---------------------|----------------------|---------|
| Ethnic Chinese                         | 12                  | 14                   | 0.662   |
| Malay                                  | 2                   | 4                    |         |
| Indian                                 | 2                   | 2                    |         |
| Others                                 | 1                   | 0                    |         |
| Gender Male                            | 14                  | 17                   | 0.828   |
| Female                                 | 3                   | 3                    |         |
| Age (Mean ± SD)                        | 59.53 ± 8.28        | 61.40 ± 7.88         | 0.487   |
| Ejection Fraction Good (> 45%)         | 11                  | 10                   | 0.661   |
| Ejection Fraction Fair (30–45%)        | 4                   | 7                    |         |
| Ejection Fraction Poor (< 30%)         | 2                   | 3                    |         |
| Smoking No                             | 8                   | 8                    | 0.666   |
| Smoking Yes                            | 9                   | 12                   |         |
| Renal Impairment No                   | 16                  | 20                   | 0.272   |
| Renal Impairment Yes                  | 1                   | 0                    |         |
| Diabetes Mellitus No                  | 9                   | 6                    | 0.157   |
| Diabetes Mellitus Yes                  | 8                   | 14                   |         |
| Hypertension No                        | 1                   | 4                    | 0.211   |
| Hypertension Yes                       | 16                  | 16                   |         |
| Hyperlipidaemia No                    | 0                   | 1                    | 0.35    |
| Hyperlipidaemia Yes                    | 17                  | 19                   |         |
| Antihyperlipidemic Medication No      | 0                   | 1                    | 0.35    |
| Antihyperlipidemic Medication Yes     | 17                  | 19                   |         |
| Troponin I (µg/L) (Mean ± SD)          | 12.20 ± 20.86 (n=15) | 20.94 ± 27.80 (n=17) | 0.319   |
2. Experimental design, materials and methods

2.1. Sample collection

Aortic tissue samples were obtained from patients who presented with coronary artery disease undergoing coronary artery bypass graft (CABG) surgery at the National University Hospital of Singapore from 2009 to 2013. Patients underwent CABG either after a recent myocardial infarction (MI group) or as stable angina patients (non-MI group). An aortic punch tissue was collected at the time of proximal anastomosis between the aorta and saphenous vein grafts. The tissues from the aortic punch were immediately preserved on dry ice, and stored in liquid nitrogen tank. The study was approved by the National Healthcare Group Domain Specific Review Board (Tissue Bank registration: NUH/2009-0073), and written informed consent was obtained from all patients. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Sample grouping

17 MI and 19 non-MI samples were recruited for laser capture microdissection (LCM) and microarray profiling. The proteomic study included 25 MI and 25 non-MI samples. Four MI and six non-MI samples overlapped between the microarray and proteomic studies. RT-qPCR was done on an independent cohort of samples, including an additional 20 MI and 20 non-MI samples. A schematic of the design and workflow is presented in Fig. 3.

### Table 4

| Characteristics                  | Non-MI Microarray (n=19) | Non-MI Validation (n=20) | p-value |
|----------------------------------|--------------------------|--------------------------|---------|
| Ethnic                           |                          |                          |         |
| Chinese                          | 10                       | 12                       | 0.763   |
| Malay                            | 6                        | 6                        |         |
| Indian                           | 2                        | 2                        |         |
| Others                           | 1                        | 0                        |         |
| Gender                           |                          |                          |         |
| Male                             | 16                       | 17                       | 0.946   |
| Female                           | 3                        | 3                        |         |
| Age (Mean ± SD)                  | 59.68 ± 8.85             | 59.95 ± 8.34             | 0.924   |
| Ejection Fraction                |                          |                          |         |
| Good (> 45%)                     | 13                       | 13                       | 0.083   |
| Fair (30–45%)                    | 6                        | 3                        |         |
| Poor (<30%)                      | 0                        | 4                        |         |
| Smoking                          |                          |                          |         |
| No                               | 9                        | 11                       | 0.634   |
| Yes                              | 10                       |                          |         |
| Renal Impairment                 |                          |                          |         |
| No                               | 18                       | 15                       | 0.088   |
| Yes                              | 1                        | 5                        |         |
| Diabetes Mellitus                |                          |                          |         |
| No                               | 7                        | 8                        | 0.839   |
| Yes                              | 12                       | 12                       |         |
| Hypertension                     |                          |                          |         |
| No                               | 3                        | 4                        | 0.732   |
| Yes                              | 16                       | 16                       |         |
| Hyperlipidaemia                  |                          |                          |         |
| No                               | 0                        | 0                        |         |
| Yes                              | 19                       | 20                       |         |
| Antihyperlipidemic Medication    |                          |                          |         |
| No                               | 0                        | 0                        |         |
| Yes                              | 19                       | 20                       |         |
| Troponin I (µg/L) (Mean ± SD)    | 0.01 ± 0.004             | NA                       | NA      |

T. Wongsurawat et al. / Data in Brief 17 (2018) 1112–1135 1117
2.3. Sample processing

The protocols for (1) cryosectioning and staining of aortic tissue, (2) LCM of VSMCs, total RNA isolation and complementary DNA (cDNA) synthesis, and (3) protein processing, ERLIC and LC-MS/MS analysis using Q-Exactive mass spectrometer are described in our manuscript [1].

2.4. RT-qPCR on an independent cohort of MI and non-MI samples

The RT-qPCR protocol is described in our manuscript [1]. The primers for ARF6, ATP1A2, GUCY1A3, HIF-1A, KLHL1, MYOCD, SOD1, and UBB were obtained from the Primer Bank: ARF6 forward primer 5′-GGGAAGGTGCTATCCAAAATCTT-3′ and reverse primer 5′-CACATCCCATACGTTGAACTTGA-3′; ATP1A2 forward primer 5′-TCTATCCACGCGAGAACAGAC-3′ and reverse primer 5′-CCATGAGGCATTTCCGCAGGC-3′; GUCY1A3 forward primer 5′-TCAGCTCCTACTTGGTCTTACTCC-3′ and reverse primer 5′-CCAGATAGCGATGGAATACACC-3′; HIF-1A forward primer 5′-GAACGTCTGGGAAAGAGATCTTCG-3′ and reverse primer 5′-CCCTATATAGAGTCAGTGTTGAATCAAACCTACA-3′; KLHL1 forward primer 5′-TCAGGTCTGGTGGCGGAAAGG-3′ and reverse primer 5′-AAAAATAGCCACACCCTTCTC-3′; MYOCD forward primer 5′-ACGATGCTTTTGCCTTGAAGAGGAACAGC-3′ and reverse primer 5′-AACCTGTCGAAGGGGTATCTG-3′; SOD1 forward primer 5′-AAAGATGGTGTGGCCGATGTG-3′ and reverse primer 5′-CAAGCCCAAAGCTCCACACG-3′; UBB forward primer 5′-GGTCCCTGCTGCTGAGAGGT-3′ and reverse primer 5′-GGCCCTCAGATTTTCGATGCTG-3′.

Fig. 1. (A) Normalized data. (B) Pseudo three dimensional plot of PCA analysis of the 4,357 DEGs between MI (red) and non-MI (blue). The sizes of the dot represent the loading values of the Comp.3 that perpendicular on the Comp.1 and Comp.2 plane. (C) Scree plot shows the variances explained by the individual principle component. (D) Volcano plot of expression data. Green dot represents differentially expressed genes.
### Table 5
List of differentially expressed transcripts.

| Probe ID   | Gene symbol | Up/down regulated in MI | wilcox   | wilcox FDR |
|------------|-------------|-------------------------|----------|------------|
| 11760204_x_at | CKMT1B      | Upregulated in MI       | 0.00035204 | 0.00224576 |
| 11760991_a_at | CKMT1B      | Upregulated in MI       | 0.00101536 | 0.00364739 |
| 1178483_s_at   | UBE2N       | Upregulated in MI       | 0.0001261  | 0.00150508 |
| 11752082_a_at | CDH12       | Upregulated in MI       | 0.00010799 | 0.00377744 |
| 1174327_s_at   | UBB         | Upregulated in MI       | 1.4127E-06 | 0.0026136 |
| 1173320_s_at   | RBMS3       | Upregulated in MI       | 4.8014E-05 | 0.00093501 |
| 11743116_s_at  | RPNB1       | Upregulated in MI       | 4.2217E-06 | 0.003841   |
| 11766989_s_at  | PNC2        | Upregulated in MI       | 0.00053133 | 0.00252042 |
| 11761378_at    | NAALADL2    | Upregulated in MI       | 0.0006064  | 0.00276999 |
| 11754075_s_at  | KRT222      | Upregulated in MI       | 0.0053077  | 0.00250242 |
| 1178123_at     | AIMP1       | Upregulated in MI       | 0.0010799  | 0.00377744 |
| 11732126_s_at  | UBB         | Upregulated in MI       | 0.00014694 | 0.0016669 |
| 11717422_s_at  | RBM8A       | Upregulated in MI       | 0.0001261  | 0.00150508 |
| 11785158_s_at  | FOXP1       | Upregulated in MI       | 0.0078736  | 0.030992   |
| 11740398_a_at  | TARSL2      | Upregulated in MI       | 9.2259E-05 | 0.00137744 |
| 1175501_s_at   | IGFBP7      | Upregulated in MI       | 9.2259E-05 | 0.00137744 |
| 11725969_a_at  | THUMP1D1    | Upregulated in MI       | 0.0026334  | 0.0003841  |
| 11760913_at    | ASAH2       | Upregulated in MI       | 2.0029E-05 | 0.00061757 |
| 1178344_a_at   | CNOT7       | Upregulated in MI       | 0.00146865 | 0.0044541  |
| 11735389_at    | CYLC2       | Upregulated in MI       | 0.0036725  | 0.00780935 |
| 11747800_a_at  | HIF1A       | Upregulated in MI       | 0.0443046  | 0.0488685 |
| 11721215_a_at  | TMEM106B    | Upregulated in MI       | 0.00019823 | 0.0016669 |
| 11750502_s_at  | GYPE        | Upregulated in MI       | 0.00013007 | 0.00242165 |
| 11717433_a_at  | ECHDC1      | Upregulated in MI       | 4.8104E-05 | 0.00093501 |
| 11752628_a_at  | ECHDC1      | Upregulated in MI       | 0.00376444 | 0.00791387 |
| 11747485_a_at  | SR140       | Upregulated in MI       | 0.00019823 | 0.0016669 |
| 11735657_a_at  | GLB1        | Upregulated in MI       | 0.00069158 | 0.00284317 |
| 1175402_s_at   | MED13       | Upregulated in MI       | 0.0026521  | 0.0012411 |
| 11730368_at    | ZNF557      | Upregulated in MI       | 0.02104398 | 0.028626 |
| 1178577_s_at   | NET1        | Upregulated in MI       | 0.00409148 | 0.00813896 |
| 11732339_at    | BCL11A      | Upregulated in MI       | 0.02493936 | 0.0323838 |
| 11744873_a_at  | KRP1        | Upregulated in MI       | 0.00089487 | 0.00334446 |
| 11763952_at    | –           | Upregulated in MI       | 0.0030585  | 0.00205755 |
| 1176870_at     | SETBP1      | Upregulated in MI       | 0.0006064  | 0.00276999 |
| 11727433_s_at  | NUTF2       | Upregulated in MI       | 0.02423264 | 0.03248578 |
| 11726614_at    | CDH2        | Upregulated in MI       | 0.00505725 | 0.00926328 |
| 11744333_s_at  | AMY2B       | Upregulated in MI       | 3.4121E-05 | 0.00081464 |
| 11720250_a_at  | RWDD1       | Upregulated in MI       | 0.00010799 | 0.00137744 |
| 11724140_s_at  | CRIPAK      | Upregulated in MI       | 0.0053077  | 0.00250242 |
| 11754192_s_at  | SFRS1I      | Upregulated in MI       | 2.3988E-05 | 0.00682747 |
| 11759666_s_at  | LOC284861   | Upregulated in MI       | 0.0006064  | 0.00276999 |
| 11764171_s_at  | DCUN1D1     | Upregulated in MI       | 0.00687991 | 0.01183985 |
| 1175153_s_at   | TXNDC6      | Upregulated in MI       | 0.0026334  | 0.0063836 |
| 11758715_s_at  | DEFB126     | Upregulated in MI       | 0.00502731 | 0.00926328 |
| 11755681_x_at  | HMGB1       | Upregulated in MI       | 9.4442E-06 | 0.0038514 |
| 11737234_s_at  | LOC162632   | Upregulated in MI       | 0.04365745 | 0.05177326 |
| 11751041_x_at  | PCMTD2      | Upregulated in MI       | 0.00146865 | 0.0044541 |
| 11720954_s_at  | RPL30       | Upregulated in MI       | 0.0026334  | 0.0063836 |
| 11732933_s_at  | RUNX1       | Upregulated in MI       | 0.00115015 | 0.00390417 |
| 11750455_s_at  | CNOT7       | Upregulated in MI       | 0.01229819 | 0.01883032 |
| 1176615_s_at   | REEP5       | Upregulated in MI       | 0.01477913 | 0.02163607 |
| Entrez ID | Symbol | Description | Log2 Fold Change | p-Value |
|-----------|--------|-------------|-----------------|---------|
| 200037_PM_s_at | CBX3 | Upregulated in MI | 0.00561109 | 0.01012733 |
| 11749445_a_at | ARHGap15 | Upregulated in MI | 0.00053077 | 0.00252042 |
| 11719713_a_at | PPM1B | Upregulated in MI | 0.00455191 | 0.00871434 |
| 11725073_s_at | PHF17 | Upregulated in MI | 0.02104398 | 0.028626 |
| 11715490_a_at | AMY1A | Upregulated in MI | 0.0026334 | 0.00636836 |
| 11757108_a_at | GSTP1 | Upregulated in MI | 0.0036725 | 0.00780935 |
| 11758637_x_at | AMY1A | Upregulated in MI | 0.0147944 | 0.02168302 |
| 11743386_s_at | PRPF40A | Upregulated in MI | 0.00010799 | 0.00137774 |
| 11719932_x_at | KIAA0319L | Upregulated in MI | 0.01229819 | 0.01880302 |
| 11750815_s_at | DDX5 | Upregulated in MI | 0.03190866 | 0.04002103 |
| 11761866_at | NCOA7 | Upregulated in MI | 0.01229819 | 0.01880302 |
| 11762842_s_at | PLEKH8B | Upregulated in MI | 0.0036725 | 0.00780935 |
| 11758021_s_at | DDX3 | Upregulated in MI | 0.00416865 | 0.0094541 |
| 11755779_a_at | ADAMTS20 | Upregulated in MI | 0.00294638 | 0.00689976 |
| 11734919_s_at | TCEA1 | Upregulated in MI | 0.00053077 | 0.00252042 |
| 11741476_x_at | MAPK7 | Upregulated in MI | 0.00455191 | 0.00871434 |
| 11745795_s_at | DDX5 | Upregulated in MI | 0.0118421 | 0.01603471 |
| 11746794_a_at | CSorf33 | Upregulated in MI | 0.01617252 | 0.0232834 |
| 11758181_s_at | HMG21 | Upregulated in MI | 0.0119828 | 0.01740908 |
| 11758811_x_at | HRNRPA1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| 11761671_a_at | ETV7 | Upregulated in MI | 0.00186355 | 0.00526347 |
| 11758000_s_at | CKADR | Upregulated in MI | 0.0036725 | 0.00780935 |
| 11733216_s_at | USP53 | Upregulated in MI | 0.0143891 | 0.02012593 |
| 200012_PM_x_at | RPL21 | Upregulated in MI | 5.1905E-06 | 0.00038514 |
| 11722616_at | URLCP1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| 11743186_a_at | KIAA1430 | Upregulated in MI | 0.01018421 | 0.01603471 |
| 11758697_x_at | MATR3 | Upregulated in MI | 0.0062978 | 0.01284168 |
| 11739605_a_at | CDC88A | Upregulated in MI | 0.00839186 | 0.01392372 |
| 11718654_s_at | PKD2 | Upregulated in MI | 0.0119828 | 0.01740908 |
| 11740007_at | POLR3G | Upregulated in MI | 0.0036725 | 0.00780935 |
| 11723448_x_at | MALL | Upregulated in MI | 0.0026334 | 0.00636836 |
| 11725386_a_at | HOMER1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| 11721237_a_at | LHFP2 | Upregulated in MI | 0.00925052 | 0.01488126 |
| 11740255_x_at | UBE2NL | Upregulated in MI | 0.0069158 | 0.00284317 |
| 11763843_a_at | UACA | Upregulated in MI | 0.0069158 | 0.00284317 |
| 11753332_a_at | TJP1 | Upregulated in MI | 0.0019528 | 0.0016699 |
| 11731400_s_at | TMCO1 | Upregulated in MI | 0.00089487 | 0.00334446 |
| 11755203_x_at | RPL21 | Upregulated in MI | 7.6666E-05 | 0.00137774 |
| 11746807_at | PTPR8 | Upregulated in MI | 0.02710422 | 0.03543661 |
| 11751975_a_at | SGIP1 | Upregulated in MI | 0.0036725 | 0.00780935 |
| 11739563_s_at | ITPR1 | Upregulated in MI | 0.00010799 | 0.00137774 |
| 11719614_a_at | LAPR4 | Upregulated in MI | 0.00030585 | 0.00205955 |
| 11722359_x_at | EPB41L2 | Upregulated in MI | 0.00146865 | 0.0044541 |
| 11754410_s_at | APLNR | Upregulated in MI | 0.00235021 | 0.00680896 |
| 11739606_x_at | CCDC88A | Upregulated in MI | 0.00505725 | 0.00926328 |
| 11737468_at | PDC | Upregulated in MI | 0.00409148 | 0.00813896 |
| 11732569_at | SLCO1B3 | Upregulated in MI | 0.04365745 | 0.05177326 |
| 11733180_a_at | ETVI | Upregulated in MI | 0.02493936 | 0.0283831 |
| 11742053_a_at | COG5 | Upregulated in MI | 0.05746656 | 0.05859759 |
| 11733720_a_at | EREG | Upregulated in MI | 0.00376444 | 0.00791387 |
| 11722645_s_at | ZNBTF6 | Upregulated in MI | 0.02104398 | 0.028626 |
| 11727892_a_at | EPNH | Upregulated in MI | 1.145E-05 | 0.0038514 |
| 11746051_s_at | HP1BP3 | Upregulated in MI | 0.00066163 | 0.0173715 |
| 11758520_s_at | JUCY1A3 | Upregulated in MI | 0.00209437 | 0.00574011 |
| 11751517_a_at | PRKAA1 | Upregulated in MI | 0.00235021 | 0.00680896 |
| 11757817_s_at | BASP1 | Upregulated in MI | 0.00165565 | 0.00486183 |
| 11719053_s_at | CEP250 | Upregulated in MI | 0.0062173 | 0.0110067 |
| 11763534_x_at | CNTNAP3 | Upregulated in MI | 0.00235021 | 0.00680896 |
| 11715329_at | SLC6A15 | Upregulated in MI | 0.0069158 | 0.00284317 |
| 11761881_at | ZNF33A | Upregulated in MI | 0.0146865 | 0.0044541 |
| 11723314_x_at | PXMP2 | Upregulated in MI | 2.476E-07 | 9.161E-05 |
| 11758802_a_at | ENY2 | Upregulated in MI | 0.00069158 | 0.00284317 |
| ProbeID          | Description     | Expression Level | Fold Change |
|------------------|-----------------|------------------|-------------|
| 11758108_s_at    | EFEMP1          | Upregulated in MI | 0.0027968   |
| 11739011_s_at    | PAFAH1B1        | Upregulated in MI | 0.0026334   |
| 11749062_a_at    | ERG             | Upregulated in MI | 0.00103627  |
| 11761958_s_at    | TRA@            | Upregulated in MI | 0.01348981  |
| 1173646_x_at     | CFL1            | Upregulated in MI | 0.00455191  |
| 11723447_at      | MALL            | Upregulated in MI | 0.00053077  |
| 11725729_s_at    | C1orf56         | Upregulated in MI | 0.0040442   |
| 11726588_a_at    | MTFR1           | Upregulated in MI | 0.0092502   |
| 11725466_a_at    | AGPAT9          | Upregulated in MI | 0.00687991  |
| 11735325_at      | ZNF660          | Upregulated in MI | 0.00186327  |
| 11754898_s_at    | ZNF573          | Upregulated in MI | 0.00839186  |
| 11719509_a_at    | CSR2P28         | Upregulated in MI | 0.00039848  |
| 11729721_s_at    | LILRB3          | Upregulated in MI | 5.1905E-06  |
| 11728429_a_at    | LCOR            | Upregulated in MI | 4.053E-05   |
| 11750795_a_at    | KLHL1           | Upregulated in MI | 1.145E-05   |
| 11754487_x_at    | C5orf33         | Upregulated in MI | 0.01018421  |
| 11727856_s_at    | NUP50           | Upregulated in MI | 0.00069158  |
| 11732303_a_at    | CREB1           | Upregulated in MI | 0.00035204  |
| 11738720_s_at    | OR2T3           | Upregulated in MI | 0.00209437  |
| 11718993_at      | CRKL            | Upregulated in MI | 0.00409148  |
| 11727390_a_at    | STEAP2          | Upregulated in MI | 0.00121855  |
| 1175724_s_at     | TMEM14B         | Upregulated in MI | 0.00186355  |
| 11765010_x_at    | SS18            | Upregulated in MI | 0.02292193  |
| 11720574_s_at    | OR6R2           | Upregulated in MI | 0.00017084  |
| 11772747_s_at    | ARGLU1          | Upregulated in MI | 0.00035204  |
| 11729916_s_at    | ARL5B           | Upregulated in MI | 0.00224576  |
| 11722126_s_at    | TMEM106B        | Upregulated in MI | 0.0017084   |
| 11759049_at      | ACS5            | Upregulated in MI | 0.08324897  |
| 11736190_a_at    | OGN             | Upregulated in MI | 0.01929797  |
| 11734314_at      | SPTA1           | Upregulated in MI | 0.00089487  |
| 11753680_x_at    | RPL21           | Upregulated in MI | 0.00186355  |
| 11736501_x_at    | SS18            | Upregulated in MI | 0.02292193  |
| 11771574_s_at    | PFN1            | Upregulated in MI | 0.00186355  |
| 11757274_s_at    | ARGLU1          | Upregulated in MI | 0.00035204  |
| 11729916_s_at    | ARL5B           | Upregulated in MI | 0.00224576  |
| 11729216_s_at    | TMEM106B        | Upregulated in MI | 0.0017084   |
| 11759047_x_at    | ACS5            | Upregulated in MI | 0.08324897  |
| 1173995_x_at     | C5orf33         | Upregulated in MI | 0.00406184  |
| 11719660_at      | ATP1A2          | Upregulated in MI | 0.00069158  |
| 11732982_at      | OR2J2           | Upregulated in MI | 0.0026334   |
| 11720945_x_at    | SRP1A           | Upregulated in MI | 0.05534295  |
| 11759697_at      | SLITRK3         | Upregulated in MI | 0.00209437  |
| 11757257_at      | PIR2            | Upregulated in MI | 0.04365745  |
| 11722149_a_at    | YTHDC2          | Upregulated in MI | 0.05462796  |
| 11748766_a_at    | FBXW7           | Upregulated in MI | 0.0002952   |
| 11765080_s_at    | MASP1           | Upregulated in MI | 0.00235021  |
| 11733995_x_at    | C5orf33         | Upregulated in MI | 0.00046374  |
| 11759047_x_at    | ABC1            | Upregulated in MI | 0.0146865   |
| 1173995_x_at     | C5orf33         | Upregulated in MI | 0.00245118  |
| 11759047_x_at    | ABC1            | Upregulated in MI | 0.0146865   |
| 11733995_x_at    | C5orf33         | Upregulated in MI | 0.00046374  |
| 11747000_at      | ASPN            | Upregulated in MI | 0.00089487  |
| 11753282_a_at    | CMTM4           | Upregulated in MI | 0.00089487  |
| 11759361_at      | SHOX            | Upregulated in MI | 0.00089487  |
| 11742378_a_at    | AKR1B10         | Upregulated in MI | 0.00089487  |
| Gene ID   | Description | Fold Change | P-Value |
|----------|-------------|-------------|---------|
| 11757489_x_at | RPL22 | Upregulated in MI | 0.00078736 | 0.0030992 |
| 11720443_s_at | BAZ1A | Upregulated in MI | 0.03470276 | 0.04597682 |
| 11756351_x_at | SOD1 | Upregulated in MI | 0.00069158 | 0.00284317 |
| 11716368_x_at | PRR13 | Upregulated in MI | 0.0019823 | 0.0016669 |
| 11741875_x_at | AKTIP | Upregulated in MI | 0.02104398 | 0.028626 |
| 11756560_s_at | KRR1 | Upregulated in MI | 0.02493936 | 0.03283831 |
| 11720443_s_at | BAZ1A | Upregulated in MI | 0.0019823 | 0.0016669 |
| 11756351_x_at | SOD1 | Upregulated in MI | 0.00069158 | 0.00284317 |
| 11716368_x_at | PRR13 | Upregulated in MI | 0.0019823 | 0.0016669 |
| 11721520_at | ZDHHC17 | Upregulated in MI | 0.04709299 | 0.05549174 |
| 11753061_a_at | SLFN5 | Upregulated in MI | 0.0026334 | 0.00636836 |
| 11728110_at | GRIP1 | Upregulated in MI | 0.00505725 | 0.00926328 |
| 11753820_s_at | ZDHHC17 | Upregulated in MI | 0.04709299 | 0.05549174 |
| 11741875_x_at | AKTIP | Upregulated in MI | 0.02104398 | 0.028626 |
| 11756560_s_at | KRR1 | Upregulated in MI | 0.02493936 | 0.03283831 |
| 11720443_s_at | BAZ1A | Upregulated in MI | 0.0019823 | 0.0016669 |
| 11756351_x_at | SOD1 | Upregulated in MI | 0.00069158 | 0.00284317 |
| 11716368_x_at | PRR13 | Upregulated in MI | 0.0019823 | 0.0016669 |
| 11721520_at | ZDHHC17 | Upregulated in MI | 0.04709299 | 0.05549174 |
| 11753061_a_at | SLFN5 | Upregulated in MI | 0.0026334 | 0.00636836 |
| 11728110_at | GRIP1 | Upregulated in MI | 0.00505725 | 0.00926328 |
| 11738606_s_at | KCTD16 | Upregulated in MI | 0.0119828 | 0.01740908 |
| 11728882_at | KRR1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| 11737293_at | TACR3 | Upregulated in MI | 0.02104398 | 0.028626 |
| 11746047_x_at | KGFLP2 | Upregulated in MI | 0.00409148 | 0.00813896 |
| 11734530_x_at | HLA-F | Upregulated in MI | 4.4442E-06 | 0.00038514 |
| 11723507_s_at | ZNF609 | Upregulated in MI | 0.05074665 | 0.05885975 |
| 11742902_s_at | CORO2A | Upregulated in MI | 0.00839186 | 0.01392372 |
| 11724290_x_at | ZNF641 | Upregulated in MI | 0.0119828 | 0.01740908 |
| 11738606_s_at | KCTD16 | Upregulated in MI | 0.00115015 | 0.00390417 |
| 11728882_at | KRR1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| 11737293_at | TACR3 | Upregulated in MI | 0.02104398 | 0.028626 |
| 11746047_x_at | KGFLP2 | Upregulated in MI | 0.00409148 | 0.00813896 |
| 11738606_s_at | KCTD16 | Upregulated in MI | 0.00115015 | 0.00390417 |
| 11728882_at | KRR1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| 11737293_at | TACR3 | Upregulated in MI | 0.02104398 | 0.028626 |
| 11746047_x_at | KGFLP2 | Upregulated in MI | 0.00409148 | 0.00813896 |
| 11738606_s_at | KCTD16 | Upregulated in MI | 0.00115015 | 0.00390417 |
| 11728882_at | KRR1 | Upregulated in MI | 0.00329182 | 0.00729325 |
| Probe ID | Description | Fold Change (Control/MI) |
|---------|-------------|-------------------------|
| AFFX-r2-Ec-bioB-5_at | Upregulated in MI | 0.00019823/0.0016669 |
| 1175938_a_at | ITFG2 | 0.0662173/0.0110067 |
| 1175468_a_at | MAP3K2 | 0.00235021/0.00608096 |
| 11717578_a_at | VPS26A | 0.03190866/0.0402103 |
| 11744671_x_at | CTBP2 | 0.0631128/0.0718515 |
| 11751946_a_at | ARHGAP21 | 0.00130072/0.00422165 |
| 11729687_at | LYRM7 | 0.02104398/0.028626 |

... (remaining entries in the table)
| Gene ID | Symbol | Description | Fold Change (Control) | Fold Change (MI) |
|---------|--------|-------------|-----------------------|------------------|
| 11743193_at | PARD6G | Downregulated in MI | 0.00019823 | 0.0016669 |
| 11726367_at | ERICH1 | Downregulated in MI | 0.03740276 | 0.04597682 |
| 11750342_at | FRMPD1 | Downregulated in MI | 0.08324897 | 0.09305777 |
| 11744231_at | MAPK7 | Downregulated in MI | 0.00294638 | 0.00689976 |
| 11724255_at | OAS1 | Downregulated in MI | 0.0176765 | 0.02515502 |
| 11737305_at | FAM166A | Downregulated in MI | 0.00561109 | 0.01012733 |
| 11733958_at | GTPBP3 | Downregulated in MI | 0.0176765 | 0.02515502 |
| 11739429_at | ZDHHC24 | Downregulated in MI | 0.01900683 | 0.02694455 |
| 11751172_at | TRIB3 | Downregulated in MI | 0.05732237 | 0.06586732 |
| 11737677_at | BTBD18 | Downregulated in MI | 0.02104398 | 0.028626 |
| 11725393_s_at | MAK16 | Downregulated in MI | 0.0631128 | 0.0718515 |
| 11744029_at | BBS4 | Downregulated in MI | 0.04043046 | 0.0488865 |
| 11743134_x_at | FBKP8 | Downregulated in MI | 0.00022952 | 0.00176918 |
| 11745187_at | BET1L | Downregulated in MI | 0.00925052 | 0.01488126 |
| 11737856_at | OPCML | Downregulated in MI | 0.00101536 | 0.00364739 |
| 11759126_at | THRA | Downregulated in MI | 0.04365745 | 0.05177326 |
| 11722129_at | FAM102B | Downregulated in MI | 0.00165565 | 0.00486183 |
| 11762149_at | C18orf45 | Downregulated in MI | 0.00115015 | 0.00390417 |
| 11734407_at | MATN4 | Downregulated in MI | 0.00760327 | 0.0128457 |
| 11730872_x_at | RASSF5 | Downregulated in MI | 0.00409148 | 0.00813896 |
| 11753413_x_at | DLK1 | Downregulated in MI | 0.07262653 | 0.08242889 |
| Category         | Term                                                                 | Count | %       | p-value     | Genes                                                                 | List Total | Pop Hits | Pop Total | Fold Enrichmen | tBonferroni | Benjamini | FDR       |
|------------------|----------------------------------------------------------------------|-------|---------|-------------|----------------------------------------------------------------------|------------|----------|-----------|----------------|-------------|------------|-----------|
| G0007647         | protein modification by small protein conjugation or removal          | 12    | 4.109589| 4.96E-05   | ENY2, UBE2N, SUZ12, SUPT3H, ATG10, FBXW7, UBE3A, UBB, UBE2D1, TMEM189, FBXW11, LN1 | 216        | 160      | 13528     | 4.697222222 | 0.08427547 | 0.084275  | 0.084054  |
| G0003246         | protein modification by small protein conjugation                      | 10    | 3.4246575| 2.56E-04  | UBE2N, SUZ12, ATG10, FBXW7, UBE3A, UBB, UBE2D1, TMEM189, FBXW11, LN1 | 216        | 132      | 13528     | 4.744668911 | 0.365690828 | 0.203565  | 0.433849  |
| G00016567        | protein ubiquitination                                                 | 9     | 3.0821918| 6.19E-04  | UBE2N, SUZ12, FBXW7, UBE3A, UBB, UBE2D1, TMEM189, FBXW11, LN1       | 216        | 119      | 13528     | 4.736694768 | 0.666812995 | 0.30674   | 1.044247  |
| G0006940         | regulation of smooth muscle contraction                               | 5     | 1.7123288| 0.00299912| TAC3, MYOCD, GUCY1A3, ATP1A2, SOD1                                   | 216        | 38       | 13528     | 8.240740741 | 0.995162875 | 0.736278  | 4.964734  |
| G0005114         | regulation of muscle cell differentiation                              | 5     | 1.7123288| 0.00330086| TBX3, MYOCD, EREG, UBB, HDAC9                                       | 216        | 39       | 13528     | 8.029439696 | 0.99717351  | 0.690793  | 5.451184  |
| G0006414         | translational elongation                                              | 7     | 2.3972603| 0.00544585| TAC3, MYOCD, GUCY1A3, ATP1A2, SOD1                                   | 216        | 101      | 13528     | 4.3406674    | 0.999938274 | 0.801202  | 8.842269  |
| G0006937         | regulation of muscle contraction                                       | 6     | 2.0547945| 0.00571597| TAC3, MYOCD, TNNC1, GUCY1A3, ATP1A2, SOD1                           | 216        | 72       | 13528     | 5.219135802 | 0.999961887 | 0.766265  | 9.261108  |
| G0008472         | regulation of skeletal muscle fiber development                         | 4     | 1.369863 | 0.00703496| TBX3, MYOCD, UBB, HDAC9                                              | 216        | 25       | 13528     | 10.02074074 | 0.999996388 | 0.791204  | 11.28038  |
| G0007507         | heart development                                                       | 10    | 3.4246575| 0.00750053| CRKL, TBX3, MYOCD, HEXIM1, TNNC1, PKD2, HDAC9, CXADR, ITGB1, FOXP1   | 216        | 215      | 13528     | 2.913006029 | 0.999998429 | 0.773463  | 11.98298  |
| G00016202        | regulation of striated muscle tissue development                        | 5     | 1.7123288| 0.00807194| TBX3, MYOCD, UBB, HDAC9, CXADR, ITGB1                                | 216        | 50       | 13528     | 6.262962963 | 0.99999435  | 0.762736  | 12.83814  |
| G00048634        | regulation of muscle development                                        | 5     | 1.7123288| 0.00865211| TBX3, MYOCD, UBB, HDAC9, CXADR, ITGB1                                | 216        | 51       | 13528     | 6.140159768 | 0.9999998   | 0.753948  | 13.69842  |
| G00048534        | hemopoietic or lymphoid organ development                                | 11    | 3.7671233| 0.00874561| PTPRC, CRKL, RPL22, BCL11A, TCEA1, SPTA1, ITGB1, HDAC9, SOD1, RUNX1, ITGB1, FOXP1 | 216        | 260      | 13528     | 2.6497151   | 0.99999831  | 0.727281  | 18.36332  |
| G00030036        | actin cytoskeleton organization                                         | 10    | 3.4246575| 0.01017938| EPB41L2, FFN1, CALD1, CFL1, PAFH1B1, ARF6, SPTA1, PRKG1, ITGB1, KLHL1 | 216        | 226      | 13528     | 2.77122255  | 0.99999987  | 0.752662  | 15.92501  |
| G0008641         | regulation of skeletal muscle tissue development                         | 4     | 1.369863 | 0.01066911| TBX3, MYOCD, UBB, HDAC9                                              | 216        | 29       | 13528     | 8.638569604 | 0.999999995 | 0.743329  | 16.62747  |
| G0006417         | regulation of muscle development                                        | 19    | 6.5068493| 0.01072364| ENY2, BMP3, PTPRC, TBX3, GRP1, CREB1, MED13                        | 216        | 624      | 13528     | 1.906991928 | 0.99999995  | 0.720797  | 16.70534  |
| Category | Term | Count | %     | p-value | Genes                                                                 | List | Pop Hits | Pop Total | Fold Enrichmen | tBonferroni | Benjamini | FDR     |
|----------|------|-------|-------|---------|----------------------------------------------------------------------|------|----------|-----------|----------------|-------------|-----------|---------|
|          |      |       |       |         |                                                                 | 197  | 515     | 12782     | 2.393750924     | 0.246766301 | 0.246766  | 1.275853 |
| GO:0045935~positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism | DDX5, CNOT7, UBE2N, YWHAH, HIF1A, MYOCD, EREG, ZNF48, GU | | | | | | | | | | | |
| GO:0005829~ribonucleoprotein complex | KRR1, SNRP1, ERG, RPL15, SYNCRIP, HSPA1A, DDX5, HNRNP1, HNRNP3, MRPL20, RPL30, RBM8A, RPL22, PNRCT, R | | | | | | | | | | | |
| GO:0030529~ribonucleoprotein complex | NAMPT, ENAH, UBE3A, GRP1, RPL15, MAP3K7, RPL30, MAP3K2, MAP7, GSTZ1, GUCY1A3, PAFAH1B1, PPP5CA, RPL12 | | | | | | | | | | | |
| GO:0005654~nucleoplasm | CCDC88A, AIMP1, BECN1, PTRP, AP3S1, ARF6, ARFIP1, CXADR, PRKGI, GCC2, TJAP1, B2M, ARH-GAP21, PNPLA8, ZDHHC22 | | | | | | | | | | | |
| GO:0005654~nucleoplasm | ENY2, HMG1, SYNCP, ZNF655, CNOT7, ZNF330, CORO2A, DDX3, RBM8A, ZNF148, NUP50, TCEA1, UBE2D | | | | | | | | | | | |
| GO:0005794~Golgi apparatus | CDC68A, AIM1, BECN1, PTRP, AP3S1, ARF6, ARFIP1, CXADR, PRKGI, GCC2, TJAP1, B2M, ARH-GAP21, PNPLA8, ZDHHC22 | | | | | | | | | | | |
| GO:0005794~Golgi apparatus | ENY2, HMG1, SYNCP, ZNF655, CNOT7, ZNF330, CORO2A, DDX3, RBM8A, NUP50, TCEA1, UBE2D | | | | | | | | | | | |
| GO:0005654~nucleoplasm | CDC68A, AIM1, BECN1, PTRP, AP3S1, ARF6, ARFIP1, CXADR, PRKGI, GCC2, TJAP1, B2M, ARH-GAP21, PNPLA8, ZDHHC22 | | | | | | | | | | | |
| GO:0005654~nucleoplasm | ENY2, HMG1, SYNCP, ZNF655, CNOT7, ZNF330, CORO2A, DDX3, RBM8A, NUP50, TCEA1, UBE2D | | | | | | | | | | | |
| GO:0005864~cortical actin cytoskeleton | EPB41L2, CALD1, CFL1, SPTA1 | | | | | | | | | | | |
| GO:0005635~nuclear envelope | UACA, NUP50, CBX3, PAFAH1B1, TMPO, RANBP2, KPNB1, PRP40A, POLR | | | | | | | | | | | |
| GO:0005635~nuclear envelope | ENY2, HMG1, SYNCP, ZNF655, CNOT7, ZNF330, MRPL20, CORO2A, DDX3, RBM8A, ZNF148, NUP50, TCEA | | | | | | | | | | | |
| GO:0007001~intracellular organelle lumen | ENY2, HMG1, SYNCP, ZNF655, CNOT7, ZNF330, MRPL20, CORO2A, DDX3, RBM8A, ZNF148, NUP50, TCEA | | | | | | | | | | | |
| GO:0004451~nucleoplasm part | ENY2, POLR3G, SYNCP, U1A, CREB1, YY1, MED13, CNOT7, SUZ12, CORO2A, DDX3 | | | | | | | | | | | |

T. Wongsurawat et al. / Data in Brief 17 (2018) 1112–1135
| GOTERM_CC_FAT | GO:0031965--nuclear membrane | 5 | 1.7857143 | 0.02568978 | PHF17, HIF1A, DDX3x, RBM8A, HDAC9, CDX3, PAFAH1B1, TMPO, MATR3, ITPR1 | 197 | 73 | 12782 | 4.444058132 | 0.999524672 | 0.534736 | 29.29883 |
| GOTERM_CC_FAT | GO:0043233--organelle lumen | 39 | 13.928571 | 0.0276102 | ENY2, SUPT3H, HMG1B, SYNRIP, ZNF655, CN017, ZNF330, MRPL20, CORO2A, DDX3x, RBM8A, ZNF418, NUP50, TCEA, ARHGAP21, PTPRC, ENAH, CTBP2, CADPS2, GRIP1, PVR13, CD99L2, ABC81, CDH2, HOMER1, CXADR, ITGB1, RIM51, TJA RPL30, PFDN1, UACA, RPL22, RPL21, GUCY1A3, UBB | 197 | 1820 | 12782 | 1.39035533 | 0.999733881 | 0.526841 | 31.13293 |
| GOTERM_CC_FAT | GO:0030054--cell junction | 15 | 5.3571429 | 0.02853488 | PTPRC, ENAH, PVRL3, ABC81, CDH2, CXADR, ITGB1 RPL30, PFDN1, UACA, RPL22, RPL21, GUCY1A3, UBB | 197 | 518 | 12782 | 1.878858554 | 0.9999799239 | 0.508085 | 32.0679 |
| GOTERM_CC_FAT | GO:0044445--cytosolic part | 7 | 2.5 | 0.02964735 | RPL30, PFDN1, UACA, RPL22, RPL21, GUCY1A3, UBB | 197 | 152 | 12782 | 2.988044349 | 0.999856352 | 0.4937 | 33.0304 |
| GOTERM_CC_FAT | GO:0005912--adherens junction | 7 | 2.5 | 0.03218777 | PTPRC, ENAH, PVRL3, ABC81, CDH2, CXADR, ITGB1 | 197 | 155 | 12782 | 2.930211233 | 0.999933536 | 0.496948 | 35.32875 |
| GOTERM_CC_FAT | GO:0031974--membrane-enclosed lumen | 39 | 13.928571 | 0.03603007 | ENY2, SUPT3H, HMG1B, SYNRIP, ZNF655, CN017, ZNF330, MRPL20, CORO2A, DDX3x, RBM8A, ZNF418, NUP50, TCEA | 197 | 1856 | 12782 | 1.363387231 | 0.999973962 | 0.512871 | 38.6672 |
| GOTERM_MF_FAT | GO:0003723--RNA binding | 23 | 8.2142857 | 0.0016071 | KRR1, SNRPA1, AIM1P, CPE2, RPL15, SYNRIP, MBN1, IGF2BP3, DDX5, HRNRPA1, HRNRPU, MRPL20, RPL30, LARP4 | 201 | 718 | 12983 | 2.069104339 | 0.477004104 | 0.477004 | 2.220802 |
| GOTERM_MF_FAT | GO:0003702--RNA polymerase II transcription factor activity | 11 | 3.9285714 | 0.00457311 | SUPT3H, ET7V, HIF1A, TBX3, ZNF418, CREB1, TCEA1, MED13, TCEB1, LCOR, FOX1 | 201 | 244 | 12983 | 2.911936221 | 0.815507665 | 0.36985 | 6.199674 |
| GOTERM_MF_FAT | GO:0016879--ligase activity, forming carbon-nitrogen bonds | 10 | 3.5714286 | 0.00955683 | UBE2N, AKTIP, UBE3A, HERC4, UBE2NL, UBE2D1, TMEM189, FBXW11, LNX1, UBE2R2 | 201 | 231 | 12983 | 2.796192199 | 0.979140063 | 0.538828 | 12.54851 |
| GOTERM_MF_FAT | GO:003735--structural constituent of ribosome | 8 | 2.8571429 | 0.01527537 | UBE2N, AKTIP, UBE3A, HERC4, UBE2NL, UBE2D1, TMEM189, FBXW11, LNX1, UBE2R2 | 201 | 168 | 12983 | 3.075811419 | 0.997977614 | 0.644387 | 19.34096 |
| Category                        | Term                                                        | Count | p-value | Genes |
|--------------------------------|-------------------------------------------------------------|-------|---------|-------|
| GOTERM_MF_FAT                  | GO:0016566--specific transcriptional repressor activity     | 4     | 0.01770409 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
| GOTERM_MF_FAT                  | GO:0030528--transcription regulator activity                | 34    | 0.02428221 | ENY2, SUPT3H, ETV7, GRIP1, CBX3, CNOT7, MXII, MYOCD, HEXIM1, ZNF148, BCL11A, ETV1, TCEA1, ERG, ZNF33A, SSB |
| GOTERM_MF_FAT                  | GO:0003712--transcription cofactor activity                 | 12    | 0.02515659 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
| GOTERM_MF_FAT                  | GO:0004842--ubiquitin-protein ligase activity               | 7     | 0.0262357 | UBE2N, UBE3A, UBE2NL, UBE2D1, FBXW11, LNX1, UBE2R2 |
| GOTERM_MF_FAT                  | GO:0008134--transcription factor binding                    | 15    | 0.02754274 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
| GOTERM_MF_FAT                  | GO:0003779--actin binding                                   | 11    | 0.02969715 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
| GOTERM_MF_FAT                  | GO:0019899--enzyme binding                                  | 15    | 0.03171181 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
| GOTERM_MF_FAT                  | GO:0008092--cytoskeletal protein binding                    | 14    | 0.04821415 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
| GOTERM_MF_FAT                  | GO:0016564--transcription repressor activity               | 10    | 0.05535048 | RPL30, RPL22, RPL21, RPL15, UBB, RPL10A, RPL12, MRPL20, HEXIM1, YY1, HDAC9, FOXP1 |
Table 7
Contingency table of prediction results from 21 genes.

| Prediction | Reference | MI | Non-MI | Total |
|------------|-----------|----|--------|-------|
| MI         | 16        | 2  | 18     | 18    |
| Non-MI     | 1         | 18 | 20     | 37    |
| Total      | 17        | 20 | 37     |       |

| Prediction | Reference | Event | No-Event | Total |
|------------|-----------|-------|----------|-------|
| Event      | A         | B     | A+B+C+D  |       |
| No-Event   | C         | D     | C+D      |       |
| Total      | A+C       | B+D   | A+B+C+D  |       |

Sensitivity = \( \frac{A}{A+C} \) = 0.94
Specificity = \( \frac{D}{B+D} \) = 0.9
Accuracy = \( \frac{(A+D)}{(A+B+C+D)} \) = 0.92

Fig. 2. Hierarchical clustering on six RT-qPCR-based validation genes.
Table 8
Differentially expressed proteins.

| Number | Accession | Protein name | Description | MI/NMI | NMI/MI |
|--------|-----------|--------------|-------------|---------|--------|
| 1      | P35527    | KRT9         | Keratin, type I cytoskeletal 9 OS=Homo sapiens GN=KRT9 PE=1 SV=3 - [K1C9_HUMAN] | 0.608   | 1.644737 |
| 2      | P67954    | FH           | Fumarate hydratase, mitochondrial OS=Homo sapiens GN=FH PE=1 SV=3 - [FUMH_HUMAN] | 0.641   | 1.560062 |
| 3      | P36405    | ARL3         | ADP-ribosylation factor-like protein 3 OS=Homo sapiens GN=ARL3 PE=1 SV=2 - [ARL3_HUMAN] | 0.663   | 1.508296 |
| 4      | H0Y614    | UFM1         | Ubiquitin-fold modifier 1 (Fragment) OS=Homo sapiens GN=UFM1 PE=4 SV=1 - [HOY614_HUMAN] | 0.667   | 1.49925 |
| 5      | J3QLR1    | RUVBL1       | RuvB-like 1 (Fragment) OS=Homo sapiens GN=RUVBL1 PE=4 SV=1 - [J3QLR1_HUMAN] | 0.693   | 1.443001 |
| 6      | C0Y2Z2    | TTN          | Titin OS=Homo sapiens GN=TTN PE=2 SV=1 - [C0Y2Z2_HUMAN] | 0.705   | 1.41844 |
| 7      | Q9BQB4    | SOST         | Sclerostin OS=Homo sapiens GN=SOST PE=1 SV=1 - [SOST_HUMAN] | 0.708   | 1.412429 |
| 8      | E5JR3     | SKP1         | S-phase kinase-associated protein 1 OS=Homo sapiens GN=SKP1 PE=2 SV=1 - [E5JR3_HUMAN] | 0.737   | 1.356852 |
| 9      | D6RL4     | CD14         | Monocyte differentiation antigen CD14, urinary form (Fragment) OS=Homo sapiens GN=CD14 PE=2 SV=1 - [D6RL4_HUMAN] | 0.738   | 1.355014 |
| 10     | H0YN19    | MYF2         | Myelin expression factor 2 (Fragment) OS=Homo sapiens GN=MYF2 PE=4 SV=1 - [H0YN19_HUMAN] | 0.76    | 1.315789 |
| 11     | P61006    | RAB8A        | Ras-related protein Rab-8A OS=Homo sapiens GN=RAB8A PE=1 SV=1 - [RAB8A_HUMAN] | 0.768   | 1.302083 |
| 12     | Q5TG3     | LRRC1        | Leucine rich repeat containing 1 OS=Homo sapiens GN=LRRC1 PE=4 SV=1 - [Q5TG3_HUMAN] | 0.775   | 1.290323 |
| 13     | P43686    | PSMC4        | 26S protease regulatory subunit 6B OS=Homo sapiens GN=PSMC4 PE=1 SV=2 - [P43686_HUMAN] | 0.778   | 1.285347 |
| 14     | B2RN4     | TUBGCP6      | TUBGCP6 protein OS=Homo sapiens GN=TUBGCP6 PE=2 SV=1 - [B2RN4_HUMAN] | 0.778   | 1.285347 |
| 15     | O00168    | FXYD1        | Phospholemman OS=Homo sapiens GN=FXYD1 PE=1 SV=2 - [FXYD1_HUMAN] | 0.781   | 1.28041 |
| 16     | G3V220    | TCERG1       | Transcription elongation regulator 1 OS=Homo sapiens GN=TCERG1 PE=2 SV=1 - [G3V220_HUMAN] | 0.783   | 1.277139 |
| 17     | E5JR90    | C1orf198     | Uncharacterized protein C1orf198 (Fragment) OS=Homo sapiens GN=C1orf198 PE=2 SV=1 - [E5JR90_HUMAN] | 0.789   | 1.267427 |
| 18     | Q86Y22    | COL23A1      | Collagen alpha-1(XXIII) chain OS=Homo sapiens GN=COL23A1 PE=2 SV=1 - [COL23A1_HUMAN] | 0.79    | 1.265823 |
| 19     | H0YA15    | SGC6         | Beta-sarcoglycan (Fragment) OS=Homo sapiens GN=SGCB PE=4 SV=1 - [H0YA15_HUMAN] | 0.792   | 1.262626 |
| 20     | P15270    | SPR          | Septaperin reductase OS=Homo sapiens GN=SPR PE=1 SV=1 - [SPR_HUMAN] | 0.803   | 1.24533 |
| 21     | Q4G1A8    | CAMK2D       | CAMK2D protein (Fragment) OS=Homo sapiens GN=CAMK2D PE=2 SV=1 - [Q4G1A8_HUMAN] | 0.803   | 1.24533 |
| 22     | P30050    | RPL12        | 60S ribosomal protein L12 OS=Homo sapiens GN=RPL12 PE=1 SV=1 - [RPL12_HUMAN] | 0.806   | 1.246059 |
| 23     | Q53GN4    | WDR1         | WD repeat domain 1, isoform CRA_a (Fragment) OS=Homo sapiens GN=WDR1 PE=2 SV=1 - [Q53GN4_HUMAN] | 0.806   | 1.246095 |
| 24     | E5R135    | CPQ          | Carboxypeptidase Q (Fragment) OS=Homo sapiens GN=CPQ PE=2 SV=1 - [E5R135_HUMAN] | 0.81    | 1.234568 |
| 25     | K7ER23    | PLIN3        | Perilipin-3 (Fragment) OS=Homo sapiens GN=PLIN3 PE=4 SV=1 - [K7ER23_HUMAN] | 0.813   | 1.230012 |
| 26     | Q562M3    | ACT          | Actin-like protein (Fragment) OS=Homo sapiens GN=ACT PE=2 SV=1 - [Q562M3_HUMAN] | 0.815   | 1.226994 |
| 27     | Q9H4B7    | TUBB1        | Tubulin beta-1 chain OS=Homo sapiens GN=TUBB1 PE=1 SV=1 - [TUBB1_HUMAN] | 0.822   | 1.216545 |
| 28     | P82987    | ADAMTSL3     | ADAMTS-like protein 3 OS=Homo sapiens GN=ADAMTSL3 PE=2 SV=4 - [ADAMTSL3_HUMAN] | 0.823   | 1.215067 |
| 29     | Q5SW55    | ITLN1        | Intelectin 1 OS=Homo sapiens GN=ITLN1 PE=2 SV=1 - [Q5SW55_HUMAN] | 0.824   | 1.213592 |
| 30     | Q5T1H1    | EYS          | Protein eyes shut homolog OS=Homo sapiens GN=EYS PE=1 SV=5 - [EYS_HUMAN] | 0.826   | 1.210654 |
| 31     | E5R1H4    | CCAR2        | DBIRD complex subunit KIAA1967 (Fragment) OS=Homo sapiens GN=KIAA1967 PE=2 SV=1 - [E5R1H4_HUMAN] | 0.826   | 1.210654 |
| #  | Gene       | Protein Function                                                                 | OS = Homo sapiens | NSO = Other Species |
|----|------------|----------------------------------------------------------------------------------|------------------|---------------------|
| 52 | ITBRM5     | COX5A, mitochondrial COX3 oxidase subunit 5A                                  | 0.826            | 1.216654            |
| 33 | IL2LT3     | Meteorin (Fragment) OS = Homo sapiens                                          | 0.826            | 1.216654            |
| 34 | P53396     | ACP5, citrate synthase OS = Homo sapiens                                       | 0.827            | 1.20919             |
| 35 | P53304     | BLVR, biliverdin reductase A OS = Homo sapiens                                  | 0.828            | 1.207729            |
| 36 | O94760     | DDAH1, (N,G,N) dimethylarginine dimethylaminohydrolase 1 OS = Homo sapiens       | 0.83             | 1.204819            |
| 1  | Q12860     | CTNNT1, contactin-1 OS = Homo sapiens                                          | 1.201            | 0.832639            |
| 2  | Q8TE77     | SOD3, protein-phosphatase Siphollogon homolog 3 OS = Homo sapiens                | 1.201            | 0.832639            |
| 3  | Q9Y317     | CHMP3, charged monoevolutionary body protein 3 OS = Homo sapiens                 | 1.201            | 0.832639            |
| 4  | Q53117     | ADAM23, paracrine uncharacterized protein ADAM23 (Fragment) OS = Homo sapiens    | 1.203            | 0.831255            |
| 5  | P08319     | LPA, apolipoprotein(a) OS = Homo sapiens                                         | 1.206            | 0.829187            |
| 6  | P19562     | ORM2, alpha-1-acid glycoprotein 2 OS = Homo sapiens                               | 1.208            | 0.827815            |
| 7  | P03930     | ANG, angiotensin OS = Homo sapiens                                               | 1.21             | 0.826446            |
| 8  | A1WWW4     | SOD1, superoxide dismutase 1 (Fragment) OS = Homo sapiens                        | 1.211            | 0.825764            |
| 9  | G3V4Y7     | BTN, kinesin OS = Homo sapiens                                                   | 1.212            | 0.825083            |
| 10 | Q8N105     | DSW, protein-Dos OS = Homo sapiens                                               | 1.214            | 0.823723            |
| 11 | P54040     | CAT, catalase OS = Homo sapiens                                                   | 1.217            | 0.821693            |
| 12 | H7C036     | CPA69, uncharacterized protein C7orf63 (Fragment) OS = Homo sapiens              | 1.219            | 0.820345            |
| 13 | Q5Q16      | PPA1, inorganic pyrophosphatase OS = Homo sapiens                               | 1.22             | 0.819672            |
| 14 | Q9Y333     | LSM2, U6 snRNA-associated Sm-like protein LSM2 OS = Homo sapiens                  | 1.223            | 0.817661            |
| 15 | Q5UL6B     | VIH, immunoglobulin heavy chain (Fragment) OS = Homo sapiens                     | 1.231            | 0.812348            |
| 16 | Q10888     | BST1, ADP-ribosyl cyclase OS = Homo sapiens                                       | 1.232            | 0.811688            |
| 17 | Q9Q76U     | DBNL, Drosophila-like protein OS = Homo sapiens                                  | 1.232            | 0.811688            |
| 18 | I9P9QY     | EIF3F, eukaryotic translation initiation factor 3 subunit B OS = Homo sapiens     | 1.236            | 0.809061            |
| 19 | F55J35     | NDUF9, NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 9, mitochondrial | 5.1              | 0.809061            |
| 20 | H10YA6     | GNB2L1, guanine nucleotide-binding protein subunit beta-2-like 1 (Fragment) OS = | 1.237            | 0.808407            |
| 21 | Q5TCY1     | TTBK1, tubulin kinase I OS = Homo sapiens                                        | 1.238            | 0.807754            |
| 22 | Q9UE8I     | NDUFS2, 24-KDa subunit of complex 1 (Fragment) OS = Homo sapiens                 | 1.241            | 0.805802            |
| 23 | Q8WWX9     | SELM, Selene protein OS = Homo sapiens                                           | 1.245            | 0.803213            |
| 24 | Q9R82X     | FAM213A, redox-regulatory protein FAM213A OS = Homo sapiens                      | 1.254            | 0.797448            |
| 25 | FSWDN7     | SACM1L, phosphatidylinositol phosphatase SAC1 OS = Homo sapiens                   | 1.278            | 0.782473            |
| 26 | 3QQRO      | VWA1, von Willebrand factor A domain-containing protein 1 (Fragment) OS = Homo    | 1.281            | 0.78064             |
| 27 | P08311     | CTGP, cathepsin G OS = Homo sapiens                                             | 1.295            | 0.772201            |
| 28 | K7EP6E     | EIF3G, eukaryotic translation initiation factor 3 subunit G (Fragment) OS = Homo  | 1.298            | 0.770416            |
| 29 | Q6PIK2     | SFQ, SFQ protein (Fragment) OS = Homo sapiens                                    | 1.3              | 0.769231            |
| 30 | O00231     | PSDM11, 26S proteasome non-ATPase regulatory subunit 11 OS = Homo sapiens         | 1.309            | 0.763942            |
| #  | Accession  | Description                                                                 | Organism                     | Year  | PMID  |
|----|------------|-------------------------------------------------------------------------------|------------------------------|-------|-------|
| 31 | G3V2K7     | TMED10 Transmembrane empr24 domain-containing protein 10 OS=Homo sapiens     | GN=TMED10 PE=2 SV=1 - [G3V2K7_HUMAN] | 1.311 | 0.762777 |
| 32 | G3V333     | SYNE3 Nesprin-3 OS=Homo sapiens GN=SYNE3 PE=2 SV=1 - [G3V333_HUMAN]           |                             | 1.318 | 0.758725 |
| 33 | Q5IQ44     | DKFZp547A061 Putative uncharacterized protein DKFZp547A0616 (Fragment) OS=Homo sapiens GN=DKFZp547A0616 PE=2 SV=1 - [Q5IQ44_HU] |                             | 1.321 | 0.757002 |
| 34 | Q4LE33     | TNC TNC variant protein (Fragment) OS=Homo sapiens GN=TNC variant protein PE=2 SV=1 - [Q4LE33_HUMAN] |                             | 1.322 | 0.756435 |
| 35 | F6T1Q0     | PDE12 2',5'-phosphodiesterase 12 OS=Homo sapiens GN=PDE12 PE=2 SV=1 - [F6T1Q0_HUMAN] |                             | 1.331 | 0.751315 |
| 36 | B2ZP79     | BID BID interacting domain death agonist, isoform CRA_b OS=Homo sapiens GN=BID PE=2 SV=1 - [B2ZP79_HUMAN] |                             | 1.332 | 0.750751 |
| 37 | Q9HDP7     | ACBD3 Golgi resident protein GCP60 OS=Homo sapiens GN=ACBD3 PE=1 SV=4 - [GCP60_HUMAN] |                             | 1.334 | 0.749625 |
| 38 | P36543     | ATP5V1E V-type proton ATPase subunit E 1 OS=Homo sapiens GN=ATP5V1E1 PE=1 SV=1 - [VATE1_HUMAN] |                             | 1.336 | 0.748503 |
| 39 | C936K0     | SPP2 Secreted phosphoprotein 2 (Fragment) OS=Homo sapiens GN=SPP2 PE=2 SV=1 - [C936K0_HUMAN] |                             | 1.347 | 0.74239 |
| 40 | E9PLT0     | CSDE1 Cold shock domain-containing protein 1 OS=Homo sapiens GN=CSDE1 PE=2 SV=1 - [E9PLT0_HUMAN] |                             | 1.351 | 0.740192 |
| 41 | Q9BY32     | ITPA Inosine triphosphate pyrophosphatase OS=Homo sapiens GN=ITPA PE=1 SV=2 - [ITPA_HUMAN] |                             | 1.365 | 0.752691 |
| 42 | C93F6      | TBC1D5 TBC1 domain family member 5 OS=Homo sapiens GN=TBC1D5 PE=2 SV=1 - [C93F6_HUMAN] |                             | 1.369 | 0.73046 |
| 43 | Q9UI1L     | SCOC Short coiled-coil protein OS=Homo sapiens GN=SCOC PE=1 SV=2 - [SCOC_HUMAN] |                             | 1.378 | 0.725689 |
| 44 | G3V2V6     | ATP6V1D V-type proton ATPase subunit D OS=Homo sapiens GN=ATP6V1D PE=2 SV=1 - [G3V2V6_HUMAN] |                             | 1.4   | 0.714286 |
| 45 | Q9H3K6     | BOLA2 BolA-like protein 2 OS=Homo sapiens GN=BOLA2 PE=1 SV=1 - [BOLA2_HUMAN] |                             | 1.454 | 0.678758 |
| 46 | L3L4N8     | ACTG1 Actin, cytoplasmic 2, N-terminally processed (Fragment) OS=Homo sapiens GN=ACTG1 PE=3 SV=1 - [L3L4N8_HUMAN] |                             | 1.47  | 0.680272 |
| 47 | E9PP06     | EEF1D Elongation factor 1-delta (Fragment) OS=Homo sapiens GN=EEF1D PE=2 SV=1 - [E9PP06_HUMAN] |                             | 1.486 | 0.672948 |
| 48 | P13553     | MYH6 Myosin-6 OS=Homo sapiens GN=MYH6 PE=1 SV=5 - [MYH6_HUMAN] |                             | 1.516 | 0.659631 |
| 49 | E9PPK0     | TNKS1BP1 182 kDa tankyrase-1-binding protein OS=Homo sapiens GN=TNKS1BP1 PE=2 SV=1 - [E9PPK0_HUMAN] |                             | 1.551 | 0.644745 |
| 50 | Q96RI1     | RPS4X RPS4X protein (Fragment) OS=Homo sapiens GN=RPS4X PE=2 SV=2 - [Q96RI1_HUMAN] |                             | 1.561 | 0.640615 |
| 51 | P50711     | GSTT1 Glutathione S-transferase theta-1 OS=Homo sapiens GN=GSTT1 PE=1 SV=4 - [GSTT1_HUMAN] |                             | 1.573 | 0.635728 |
| 52 | P50395     | GID2 Rab GDP dissociation inhibitor beta OS=Homo sapiens GN=GID2 PE=1 SV=2 - [GID2_HUMAN] |                             | 1.602 | 0.62422 |
| 53 | Q6PCC8     | URB2 URB2 protein (Fragment) OS=Homo sapiens GN=URB2 PE=2 SV=1 - [Q6PCC8_HUMAN] |                             | 1.609 | 0.621504 |
| 54 | F5GXW5     | C12orf57 Protein C10 OS=Homo sapiens GN=C12orf57 PE=2 SV=1 - [F5GXW5_HUMAN] |                             | 1.623 | 0.616143 |
| 55 | C9JLS9     | PSMC2 26S proteasome regulatory subunit 7 (Fragment) OS=Homo sapiens GN=PSMC2 PE=4 SV=1 - [C9JLS9_HUMAN] |                             | 1.675 | 0.597015 |
| 56 | P13645     | KRT10 Keratin, type I cytoskeletal 10 OS=Homo sapiens GN=KRT10 PE=1 SV=6 - [K1C10_HUMAN] |                             | 1.744 | 0.573394 |
| 57 | Q9BXO0     | EMILN2 EMILN-2 OS=Homo sapiens GN=EMILN2 PE=1 SV=3 - [EMIL2_HUMAN] |                             | 2.539 | 0.398856 |
| 58 | C9JNH9     | SERPINE2 Glia-derived nexin (Fragment) OS=Homo sapiens GN=SERPINE2 PE=2 SV=1 - [C9JNH9_HUMAN] |                             | 2.703 | 0.369959 |
### Table 9
Pathway mapping of 370 transcripts (highlighted in light blue) and 94 proteins (highlighted in yellow).

| Ingenuity Canonical Pathways | -log(p-value) | Ratio | Molecules |
|------------------------------|---------------|-------|-----------|
| Hypoxia Signaling in the Cardiovascular System | 3.02 | 0.0952 | UBE2N,UBE2R2,CREB1,UBE2V1,HIF1A,UBE2D1 |
| Protein Ubiquitination Pathway | 2.63 | 0.0472 | H2M,UBB,UBE2N,USP5,UBE2R2,UBE2V1,HSPA1A,HSPA1B,FBXW7,USP6,TCEB1,UBE2C3,UBE2D1 |
| Nrf2, Sirt7 Signaling in T Lymphocytes | 2.03 | 0.087 | HDAC9,MAPK7,PPP3CA,MAP3K2 |
| Sertoli Cell-Sertoli Cell Junction Signaling | 1.9 | 0.0468 | ITGB1,T1AP1,PRKGI,GUCY1A3,NECTIN3,MAPK7,SP1A1,MAP3K2 |
| Gap Junction Signaling | 1.7 | 0.0464 | PRKGI,CSNK1G1,GUCY1A3,MAPK7,ITPR1,PPP3CA,MAP3K2 |
| Dopamine-DARPP32 Feedback in cAMP Signaling | 1.62 | 0.0446 | PRKGI,CSNK1G1,GUCY1A3,PPP1R12A,CREB1,ITPR1,PPP3CA |
| ERK5 Signaling | 1.59 | 0.0645 | YWHAH,CREB1,MAPK7,MAP3K2 |
| Nrlin Signaling | 1.48 | 0.076 | PRKGI,PPP3CA,ENAH |
| β Cell Receptor Signaling | 1.48 | 0.0417 | PTPRC,CPL1,CREB1,MAPK7,RASSF5,PPP3CA,MAP3K2 |
| Neuroprotective Role of THOP1 in Alzheimer's Disease | 1.45 | 0.075 | MAP7,CREB1,J1H-A-F |
| EIF2 Signaling | 1.44 | 0.0409 | RPL15,RPL22,RPS27L1,RPL30,RPL21,RPL12,RPL10A |
| AMPK Signaling | 1.39 | 0.0398 | PP1B,CPT1B,CREB1,PRKAA1,SMARCE1,MAP3K7,PPAT |
| Lipid Antigen Presentation by CD1 | 1.34 | 0.105 | B2M,ARF6 |
| Superoxide Radicals Degradation | 3.27 | 0.4 | CAT,SOD1 |
| Acetyl-CoA Biosynthesis III (from Citrate) | 2.13 | 1 | ACLY |
| Amyotrophic Lateral Sclerosis Signaling | 2.04 | 0.0517 | CAT,BID,SOD1 |
| Mitochondrial Dysfunction | 1.9 | 0.0331 | NDUFA9,NDUFV2,AT,COX5A |
| Crosstalk between Dendritic Cells and Natural Killer Cells | 1.77 | 0.074 | CAMK2D,ACTG1 |
| Oxidative Phosphorylation | 1.66 | 0.0375 | NDUFA9,NDUFV2,COX5A |
| Tetrahydrobiopterin Biosynthesis I | 1.65 | 0.333 | SPTR |
| Tetrahydrobiopterin Biosynthesis II | 1.65 | 0.333 | SPTR |
| EIF2 Signaling | 1.64 | 0.0276 | EIF3G,EIF3F,RPL12,RPS4X |
| Mechanisms of Viral Exit from Host Cells | 1.58 | 0.0588 | ACTG1,CHMP3 |
| Rhodanese Signaling | 1.57 | 0.0345 | RACK1,GID2,ACTG1 |
| Heme Degradation | 1.53 | 0.25 | HLRV |
| GM-Csf Signaling | 1.35 | 0.0444 | CAMK2D,RACK1 |

### Table 10
Pathway mapping of combined 21 gene signature and 94 proteins.

| Ingenuity Canonical Pathways | -log(p-value) | Ratio | Molecules |
|------------------------------|---------------|-------|-----------|
| Superoxide Radicals Degradation | 3.1 | 0.4 | CAT,SOD1 |
| Rhodanese Signaling | 2.11 | 0.046 | ITGB1,RACK1,GID2,ACTG1 |
| Acetyl-CoA Biosynthesis III (from Citrate) | 2.04 | 1 | ACLY |
| Clathrin-mediated Endocytosis Signaling | 1.9 | 0.04 | ITGB1,UBB,ARF6,ACTG1 |
| Amyotrophic Lateral Sclerosis Signaling | 1.82 | 0.052 | CAT,BID,SOD1 |
| Paxillin Signaling | 1.82 | 0.052 | ITGB1,ARF6,ACTG1 |
| Regulation of eIF4 and p70S6K Signaling | 1.69 | 0.035 | ITGB1,EIF3G,EIF3F,RPS4X |
| Actin Cytoskeleton Signaling | 1.64 | 0.033 | ITGB1,PFN1,SSH3,ACTG1 |
| Mitochondrial Dysfunction | 1.63 | 0.033 | NDUFA9,NDUFV2,AT,COX5A |
| Crosstalk between Dendritic Cells and Natural Killer Cells | 1.61 | 0.074 | CAMK2D,ACTG1 |
| NRF2-mediated Oxidative Stress Response | 1.57 | 0.032 | UBB,CAT,SOD1,ACTG1 |
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Fig. 3. Work flow and study design.
Transparency document. Supplementary material

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