Knock Down of Plakophilin 2 Dysregulates Adhesion Pathway through Upregulation of miR200b and Alters the Mechanical Properties in Cardiac Cells

Puzzi L.§, Borin D.§, Gurha P., Lombardi R., Martinelli V., Weiss M., Andolfi L., Lazzarino M., Mestroni L., Marian A.J. and Sbaizero O*.

§ = share first authorship

* Corresponding Author

Orfeo Sbaizero, PhD.; Engineering and Architecture Department; University of Trieste; Via Valerio 10; 34127 Trieste (Italy). Phone (+39)040-5583770; fax: (+39)040572044; Email: sbaizero@units.it

Lentiviral vector production, cell culture and immunofluorescence analysis: The lentiviruses were produced by transfecting the plasmids into 293T cells using X-tremeGENE9 DNA transfection reagent (Roche Life Science) and the viral particles were harvested at 48 and 72 hrs post-transfection, cleared by precipitation and finally filtered through 0.45 µm-pore cellulose acetate filters (WWR International). 70-90% confluent HL-1PKP2 cells were subjected to 48 hrs of virus infection and then cultured in virus-free medium for another 24 hrs; GFP signal was used to assess transduction efficiency by both fluorescence microscopy and FACS. GFP positive cells were isolated by flow cytometry. Asynchronous growing HL-1 cells were seeded in Petri dishes pre-coated with 0.005% fibronectin and 0.02% gelatin and cultured in Claycomb medium supplemented by 2 mM L-glutamine, 10% of fetal bovine serum, 100U/ml penicillin, 100 µg/ml streptomycin and 10 mM Norepinephrine and incubated at 37° C and 5% CO2. All chemicals for cell culture were purchased from Sigma-Aldrich.

Immunostaining of HL_1 cells was performed by first washing the cells twice with PBS and fixing with 4% PFA at room temperature for 20 minutes; thereafter aldehydes were quenched with 0.1 M glycine for 20 minutes at room temperature. Cells were made permeable with 0.5% Triton X-
100 for 10 minutes, blocked with 1:5 goat serum in PBS for 1 h at room temperature and incubated with an anti α-tubulin (mouse monoclonal Sigma Aldrich T5168, dilution 1:4000) or an anti Vinculin (mouse monoclonal Sigma Aldrich V9131, dilution 1:400) primary antibody diluted in blocking solution overnight at 4°C. Then, cells were washed 3 times with 0.5% Triton X-100 and finally incubated with an Alexa-Fluor 594 conjugated anti mouse or anti rabbit secondary antibody (Thermo Fisher Scientific) diluted 1:1000 in blocking solution for 60 min at room temperature. F-Actin filaments were counterstained with Alexa Fluor 594 Phalloidin (1:500 Life Technologies A12381) in PBS for 45 min at room temperature. Each slide was then mounted in Vectashield with DAPI (Vector Labs) to counterstain nuclei. For image acquisition, a Nikon C2 Confocal Microscope System equipped with a Plan-Apochromat λ 60X/ 1.40 oil objective was used.

**mRNA, microRNA targets analysis and quantitative PCR**

Genes of interest were analysed by real time PCR using specific primers, as follows: Rap2c FW 5’-ATGAGGGAATACAAGGTAGTGGT-3’ and REV 5’-ACTTCGATCTCTTTGCGGTAAG-3’; Src FW 5’-CAATGCCAAGGGCCTAAATGT-3’ and REV 5’-TGTGTTGGAGTAGTAAGCCACGA-3’; Itgal FW 5’-CCTTCCCTCGGATGTGAGTCA-3’ and REV 5’-AAGTCTCCGATGGTAAG-3’; Col4a4 FW 5’-CGGGCTAACAGCATTTA-3’ and REV 5’-CCAGAAAGGGGACTGGAGT-3’; Col4a5 FW 5’-GAAAAAGGCGAACAGGTCTTC-3’ and REV 5’-CAGGGAGCCCTCTATCACCA-3’; Pik3cb FW CTATGGCAGACACCTTGTGACAT-3’ and REV 5’-CTTCCCGAGGTACTTCAA-3’; Arhgef3 FW 5’-TCAAACCCTTTCCAGAGTCA-3’ and REV 5’-TCTCCGTTTTGTGCTTGAAG-3’; RPL37 FW 5’-CGCAAGGAAAGTATAACTGGAG-3’ and REV 5’-TCTGAATCTGGGTAGACAATCT-3’. Annealing temperature was set at 60°C for all samples.

**Single cell spectroscopy experiments using atomic force microscopy (AFM)**
Biomechanical experiments were carried out through a Solver Pro-M AFM from NT-MDT (Moscow Russia), as previously reported(1,2). For these measurements, sQube CP-PNPL-Au-C cantilevers were used, with a nominal spring constant of 0.08 N/m, which was checked prior each experiment by Sader method. A spherical gold probe of about 5 μm-diameter was glued at the cantilever’s apex.

Measurements on single living cells were performed in physiological conditions of medium and temperature, within one hour. Since the nuclear elasticity is correlated with the stages of cell division(3), cells with nuclei optically showing mitosis were excluded. For each investigated area, a preliminary scan was made to assess the cell morphology and the nuclear position, which corresponds to the highest portion of the cell. In order to avoid possible artefacts due to substrate stiffness and/or due to hydrodynamic forces, indentations were performed above the nucleus, at the constant speed of 1 μm/s for approach and withdrawal of the cantilever.

Cell elasticity was calculated from the first portion of the indentation curve (10% of cell deformation).

Here, the experimental data were fitted with the model proposed by Sneddon for spherical probes (4):

\[
F = \frac{E}{(1-\nu^2)} \left( \frac{R^2 + a^2}{2} \cdot \log \frac{R + a}{R - a} - aR \right) \tag{1}
\]

\[
\delta = \frac{a}{2} \cdot \log \frac{R + a}{R - a} \tag{2}
\]

Where \( F \) is the loading force, \( E \) is the Young’s modulus, \( \nu \) the Poisson’s ratio, \( R \) the radius of the probe, \( a \) is the contact radius (function of the tip penetration) and \( \delta \) is the probe penetration into the cell. Approximating the cell to an incompressible body (i.e. a flexible object filled with liquid), the Poisson’s ratio was assumed as \( \nu = 0.5 \) (5). All the curves analysis was performed using AtomicJ software (6).

The model used for estimating the Young’s modulus value is conventionally used to yield a general idea of cell elasticity (7). Other models could be used for this task. One fairly new and accurate is the “Brush Model” developed by Sokolov et al. (8,9). In the present study, it has been decided to use a model which does not consider the brush since (i) this model is the one most commonly used, (ii) the
cell line was the same throughout the all research and (iii) the same protocol/methodology and the same model has been used for all cells and indentations. Therefore, it has been considered that the calculated Young's modulus values might be compared for all specimens within the presented experiments. Furthermore, resulting Young's modulus data are reasonably similar to others reported by another group for the same cell line (10).

To describe the cell viscoelastic behaviour towards an external applied force, we used a parameter introduced by Klymenko et al. (11) and indicated as “plasticity index” $\eta$ (even though “plastic” stands for non-recoverable deformation). This was assessed from the hysteresis between the approach and withdrawal curves as:

$$\eta=1-\left(\frac{A_2}{A_1}\right)$$  \hspace{1cm} (3)

where $A_1$ and $A_2$ are the areas under the loading and unloading curves (green box in Figure S1), respectively. Intermediate values between a fully elastic ($\eta=0$) and a fully plastic behaviour ($\eta=1$), indicate mixed viscoelastic properties.

For both the Young’s modulus and the plasticity index assessment, each cell was subjected to three consecutive indentations at the same position and the mean of the results was considered as a single cell value ($n=1$).

Cell-to-ECM protein interaction was assessed through a JPK NanoWizard II AFM equipped with a CellHesion module, using tipless V-shaped silicon nitride gold covered cantilevers having nominal spring constant value of 0.32 N/m (NanoWorld, Innovative Technologies). O$_2$ plasma treated cantilevers were functionalized with fibronectin (Thermo Fisher Scientific) at the final concentration of 20 µg/ml for 15 hrs at 4° C, and stored in PBS (12). Before each experiment, the cantilever spring constant was calibrated using the thermal noise method. Measurements were performed according to published protocols(13-15) (Figure S2). Briefly, HL-1 cell suspension was overlaid on a BSA coated glass coverslip inserted into a petri dish previously coated with type I collagen or fibronectin (both from Thermo Fisher Scientific) at the final concentration of 50 and 20 µg/ml, respectively. A single
cell from the suspension was captured by pressing it with the fibronectin-functionalized cantilever against the glass for 30 sec with a contact force of 0.5 nN. Next, the cell was lifted up from the surface and allowed establishing a firm adhesion to the cantilever for about 20 minutes. Afterwards, the cantilever with the cell was moved far away reaching a coated plastic surface and the adhesion measurements were performed at a constant force of 0.5 nN for 20 seconds. After each force measurement, the cell was retracted to recover for 60 seconds before repeating the measure on the same spot or adhering to a different spot on the surface. During contact, the force exerted was kept constant using the AFM closed loop feedback mode. The cantilever was withdrawn at constant speed of 5 μm/s over pulling ranges of 80 μm to ensure complete detachment of the cell from substrate.

During this step, the cantilever deflection, which is proportional to the vertical force that exists between the cell and substrate, is recorded in a force-distance curve. This curve provides information regarding the cell adhesion. The work that is required to detach the cell can be used to describe the adhesion strength of the cell. It is calculated from the area that is enclosed by the retraction-force-distance curve. This curve also carries other information: after the cell starts to detach from the substrate, individual force steps can be observed. During this phase, the receptors either detaches from the substrate surface or are pulled away from the cell cortex as a membrane tether. While cell membrane is still in contact with the substrate, either of these processes can occur. During the final phase of detachment, the cell body is no longer in contact with the substrate and, thus, attachment is due only to the tethers. Since the receptors are anchored in the cell cortex they unbind as the force increases (in the AFM curve they are denoted as jumps or ruptures). The second type of unbinding event occurs when membrane tethers are pulled out of the cell. In this case, long plateaus of constant force characterize tethers. Our withdrawn (unloading) curves were analyzed classifying receptors detachment events as “rupture” or “tether” based on the slope of the curve preceding the force step. Withdrawn curves were analysed using the JPK Data Processing software. Positive steps at the right of the minimum force were automatically identified (using default fit parameters values: “Smoothing” = 5; “Significance” = 0.001). Detachment events were classified as “rupture” or “tether” based on the
slope of the curve preceding the force step as follows: values $\leq -0.15$ mN/m, corresponding to the 15% derivation were associated to ruptures, while slopes between -0.15 and 0.15 mN/m were classified as tethers(14). Intervals between steps lower than 12.5 nm were discarded, as fit was made only on two experimental points. For these experiments, each cell was subjected to 4-6 consecutive indentations at the same collagen or fibronectin spot and the mean of the results was considered as a single cell-ECM interaction ($n=1$).

**Actin aggregates**

A quantification of the actin aggregates amount has been done using imageJ software. The calculations were performed for every cell line on 20 cells from 4 independent experiment. The results are shown in the figure below and presented as the amount of actin aggregates on the total cytoskeleton area. They are: (median: NT = 1.08%, WT = 0.97%, PKP2 = 2.90%, PKP2/antimiR= 2.59%) ($p$ value calculated using unpaired Wilcoxon-Mann-Whitney test (confidence level 95%), NT vs WT: $p$-value = 0.4652, NT vs PKP2: $p$-value = 1.466e-07, NT vs antimiR: $p$-value = 1.466e-07, WT vs PKP2: $p$-value = 1.475e-07, WT vs antimiR: $p$-value = 1.475e-07, PKP2 vs antimiR: $p$-value = 0.04873).
Supplementary Figure S1. A quantification of the actin aggregates amount found in the cells cytoskeleton
SUPPLEMENTARY REFERENCES

1. Puzzi L, Borin D, Martinelli V, Mestroni L, Kellsell DP, Sbaizer O. Cellular biomechanics impairment in keratinocytes is associated with a C-terminal truncated desmoplakin: An atomic force microscopy investigation. Micron. 2018;106:27-33.

2. Borin D, Puzzi L, Martinelli V, Cibinel M, Lapasin R, Sbaizer O. An engineering insight into the relationship of selective cytoskeletal impairment and biomechanics of HeLa cells. Micron. 2017;102:88-96.

3. Matzke R, Jacobson K, Radmacher M. Direct, high-resolution measurement of furrow stiffening during division of adherent cells. Nature cell biology. 2001;3(6):607-10.

4. Sneddon IN. The relation between load and penetration in the axisymmetric boussinesq problem for a punch of arbitrary profile. Int J Eng Sci. 1964;3:47-57.

5. Radmacher M. Measuring the elastic properties of living cells by the atomic force microscope. Methods in cell biology. 2002;68:67-90.

6. Hermanowicz P, Sarna M, Burda K, Gabrys H. AtomicJ: an open source software for analysis of force curves. The Review of scientific instruments. 2014;85(6):063703.

7. Carl P, Schillers H. Elasticity measurement of living cells with an atomic force microscope: data acquisition and processing. Pflugers Archiv : European journal of physiology. 2008;457(2):551-9.

8. Guz N, Dokukin M, Kalaparthi V, Sokolov I. If cell mechanics can be described by elastic modulus: study of different models and probes used in indentation experiments. Biophysical journal. 2014;107(3):564-75.

9. Dokukin M, Ablaeva Y, Kalaparthi V, Seluanov A, Gorbunova V, Sokolov I. Pericellular Brush and Mechanics of Guinea Pig Fibroblast Cells Studied with AFM. Biophysical journal. 2016;111(1):236-46.

10. Kossivas F, Michaelides M, Hadjisavvas A, Kyprianou A, Kyriacou K, Constantinides C. Elasticity Measurements from Left Ventricular Murine HL-1 Cardiomyocytes using Atomic Force Microscopy. The FASEB Journal. 2015;29(1_supplement):799.8.
11. Klymenko OW-Z, J.; Lekka, M; Kwiatek, W.M. Energy Dissipation in the AFM Elasticity Measurements. Acta Physica Polonica A. 2009;115:4.

12. Bharadwaj M, Strohmeyer N, Colo GP, Helenius J, Beerenwinkel N, Schiller HB, et al. alphaV-class integrins exert dual roles on alpha5beta1 integrins to strengthen adhesion to fibronectin. Nature communications. 2017;8:14348.

13. Andolfi L, Bourkoula E, Migliorini E, Palma A, Pucer A, Skrap M, et al. Investigation of adhesion and mechanical properties of human glioma cells by single cell force spectroscopy and atomic force microscopy. PloS one. 2014;9(11):e112582.

14. Chu C, Celik E, Rico F, Moy VT. Elongated membrane tethers, individually anchored by high affinity alpha4beta1/VCAM-1 complexes, are the quantal units of monocyte arrests. PloS one. 2013;8(5):e64187.

15. Friedrichs J, Helenius J, Muller DJ. Quantifying cellular adhesion to extracellular matrix components by single-cell force spectroscopy. Nature protocols. 2010;5(7):1353-61.
Supplementary Table 1. Summary of the genes altered by PKP2 downregulation. Overlap between miR-200 targets genes and dysregulated genes in HL-1PKP2 detected in RNA-seq analysis revealed that out of 816 differential expressed potential targets, 560 genes were suppressed (p<0.001).

| Gene-ID   | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value   | FC     |
|-----------|-------------|---------|---------|---------|---------|-----------|--------|
| Krt80     | Krt80       | 0.02    | 0.03    | 0.93    | 0.6     | 0.022243  | 30.5425|
| Mgat3     | Mgat3       | 0.02    | 0       | 0.39    | 0.4     | 1.66E-05  | 21.89637|
| 4932418E24Rik | 4932418E24Rik | 0.08    | 0.04    | 1.16    | 1.16    | 0.040599  | 17.88034|
| Nptx1     | Nptx1       | 0.04    | 0.05    | 0.51    | 0.53    | 6.95E-08  | 12.47215|
| RGS3      | Rgs3        | 1.23    | 0.89    | 10.78   | 10.88   | 0         | 8.426225|
| Hivep3    | Hivep3      | 1.3     | 1.68    | 2.76    | 2.54    | 0.000128  | 7.672605|
| Hivep3    | Hivep3      | 0.14    | 0.06    | 0.07    | 0.12    | 0.000128  | 7.672605|
| Zcchc24   | Zcchc24     | 0.81    | 0.82    | 6.55    | 6.17    | 0         | 7.519725|
| TIMP3     | Timp3       | 0.24    | 0.3     | 2.14    | 1.82    | 0         | 6.783645|
| PODXL     | Podxl       | 0.72    | 0.74    | 5.21    | 4.5     | 0         | 6.390263|
| NOTCH1    | Notch1      | 0.2     | 0.16    | 1.11    | 0.9     | 0         | 5.037838|
| THBD      | Thbd        | 2.78    | 2.3     | 13.38   | 12.28   | 0         | 4.944279|
| ETS1      | Ets1        | 0.16    | 0.09    | 0.59    | 0.55    | 7.29E-08  | 4.908215|
| ZCCHC3    | Zcchc3      | 0.17    | 0.11    | 0.86    | 0.57    | 7.02E-06  | 4.790255|
| Hif       | Hif         | 0.2     | 0.11    | 0.83    | 0.8     | 1.27E-08  | 4.680739|
| Fstl4     | Fstl4       | 0.05    | 0.03    | 0.35    | 0.29    | 0.011022  | 3.371436|
| E130309F12Rik | E130309F12Rik | 0.7     | 0.87    | 2.63    | 2.56    | 3.47E-10  | 3.250179|
| Rps6ka2   | Rps6ka2     | 5.52    | 5.19    | 17.25   | 15.95   | 0         | 3.023525|
| DUSP5     | Dusp5       | 1.56    | 1.05    | 4.31    | 3.6     | 9.97E-15  | 2.965387|
| MAP3K6    | Map3k6      | 0.53    | 0.42    | 1.4     | 1.08    | 9.38E-07  | 2.921686|
| Dact1     | Dact1       | 0.59    | 0.53    | 1.78    | 1.67    | 0.00013   | 2.918841|
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC  |
|---------|-------------|---------|---------|---------|---------|---------|-----|
| PTPRM   | Ptprm       | 0.27    | 0.46    | 0.99    | 1       | 8.75E-10| 2.879424|
| PLAU    | Plau        | 0.52    | 0.59    | 1.77    | 1.35    | 1.17E-05| 2.840903|
| Napb    | Napb        | 1.76    | 2       | 5.43    | 5.2     | 8.86E-09| 2.65058 |
| PHF15   | Phf15       | 0.46    | 0.37    | 1.15    | 0.98    | 2.57E-05| 2.576895|
| Frem1   | Frem1       | 2.53    | 2.96    | 6.88    | 7.25    |         | 2.465527|
| Jag2    | Jag2        | 0.82    | 0.95    | 2.44    | 2.14    | 3.05E-08| 2.458426|
| Fhl1    | Fhl1        | 23.75   | 23.13   | 60.26   | 58.78   |         | 2.446972|
| SLC2A3  | Slc2a3      | 2.58    | 2.22    | 5.37    | 4.82    | 1.18E-05| 2.383514|
| ACOT7   | Acot7       | 19.57   | 17.59   | 47.11   | 42.26   |         | 2.336728|
| NACC2   | Nacc2       | 1.76    | 1.45    | 3.9     | 3.66    | 1.9E-11 | 2.313103|
| ASAP2   | Asap2       | 0.2     | 0.21    | 0.48    | 0.42    | 0.048604| 2.29226 |
| Cacna1c | Cacna1c     | 3.06    | 3.32    | 7.46    | 6.67    |         | 2.286936|
| WNK1    | Wnk1        | 12.74   | 11.93   | 30.67   | 27.05   |         | 2.274337|
| Phactr2 | Phactr2     | 10.65   | 10.91   | 24.67   | 24.02   |         | 2.273698|
| ZBED4   | Zbed4       | 3.01    | 2.77    | 7.39    | 6.59    |         | 2.265985|
| GNB4    | Gnb4        | 1.84    | 2.05    | 4.51    | 4       | 0.005311| 2.200025|
| Rfx3    | Rfx3        | 1.07    | 1.06    | 2.17    | 2       | 4.23E-06| 2.072599|
| SLC35F2 | Slc35f2     | 1.59    | 1.42    | 3.46    | 3.18    | 1.59E-05| 2.072078|
| REEP5   | Reep5       | 19.26   | 18.47   | 42.54   | 39.59   |         | 2.063445|
| Taf4a   | Taf4a       | 4.51    | 4.42    | 9.49    | 8.61    | 2.51E-11| 2.034499|
| Gpr161  | Gpr161      | 0.73    | 0.68    | 1.35    | 1.37    | 0.000429| 2.029302|
| HIPK2   | Hipk2       | 2.85    | 2.85    | 6.16    | 5.53    | 1.13E-08| 2.014495|
| LRP11   | Lrp11       | 0.37    | 0.24    | 0.64    | 0.55    | 0.014825| 1.968097|
| CAP2    | Cap2        | 16.72   | 15.69   | 33.18   | 32.56   |         | 1.966595|
| Glcci1  | Glcci1      | 2.77    | 2.18    | 5.42    | 7.48    | 2.45E-10| 1.964746|
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|---------|-------------|---------|---------|---------|---------|---------|------|
| Nova1   | Nova1       | 0.32    | 0.4     | 0.83    | 0.72    | 5.06E-05 | 1.949492 |
| TNFRSF21| Tnfrsf21    | 1.2     | 1.06    | 2.35    | 2.17    | 2.24E-05 | 1.936216 |
| Slc24a4 | Slc24a4     | 1.16    | 1.1     | 2.17    | 2.44    | 0.003401 | 1.9115  |
| ELK3    | Elk3        | 0.27    | 0.48    | 0.7     | 0.63    | 0.029069 | 1.872517 |
| ADIPOR2 | Adipor2     | 24.6    | 24.5    | 48.98   | 45.78   | 0       | 1.871734 |
| INPP1   | Inpp1       | 2.13    | 1.95    | 4.35    | 3.75    | 0.001038 | 1.859247 |
| Sbf1    | Sbf1        | 6.34    | 6.02    | 12.56   | 11.25   | 5.69E-14 | 1.856658 |
| SLC38A9 | Slc38a9     | 0.59    | 0.57    | 1.01    | 1.01    | 0.002332 | 1.854167 |
| Hivep3  | Hivep3      | 1.3     | 1.68    | 2.76    | 2.54    | 0.03627 | 1.828735 |
| KLHDC10 | Klhdc10     | 29.88   | 28.64   | 55.52   | 55.67   | 0       | 1.827731 |
| WDFY1   | Wdfy1       | 4.69    | 4.36    | 9.06    | 8.2     | 0.007871 | 1.827057 |
| MAP3K1  | Map3k1      | 2.69    | 2.06    | 4.76    | 3.86    | 5.22E-07 | 1.813242 |
| PSMF1   | Psmf1       | 14.38   | 13.95   | 30.04   | 27.98   | 0       | 1.797353 |
| Fyn     | Fyn         | 1.13    | 1.31    | 2.15    | 2.02    | 0.005718 | 1.777707 |
| DNAJC5  | Dnajc5      | 27.09   | 25.77   | 50.23   | 46.31   | 9.97E-15 | 1.753041 |
| PDE4A   | Pde4a       | 3.76    | 2.66    | 5.77    | 5.34    | 3.67E-05 | 1.752007 |
| Tln2    | Tln2        | 1.86    | 1.81    | 3.26    | 3.05    | 2.95E-09 | 1.735057 |
| TOMM34  | Tomm34      | 30.64   | 28.94   | 54.4    | 52.18   | 0       | 1.729104 |
| ARID2   | Arid2       | 2.63    | 2.67    | 4.81    | 5.09    | 2.24E-11 | 1.716535 |
| Tmem170 | Tmem170     | 1.5     | 1.08    | 1.4     | 1.26    | 0.025376 | 1.713441 |
| MED30   | Med30       | 22.92   | 25.61   | 40.67   | 45.31   | 1.31E-11 | 1.710977 |
| MEF2A   | Mef2a       | 21.3    | 21.73   | 39.99   | 36.74   | 6.75E-13 | 1.701665 |
| Ncoa7   | Ncoa7       | 0.62    | 0.85    | 1.55    | 1.46    | 0.010067 | 1.699557 |
| Zeb1    | Zeb1        | 3.3     | 3.07    | 6.37    | 5       | 3.34E-06 | 1.694834 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|---------|-------------|----------|----------|----------|----------|---------|-------|
| MTMR12  | Mtmr12      | 7.04     | 6.85     | 13.21    | 11.63    | 1.48E-11| 1.689288 |
| NUDCD1  | Nudcd1      | 7.22     | 7.24     | 12.53    | 13.07    | 3.07E-06| 1.668957 |
| HES1    | Hes1        | 5.16     | 4.58     | 7.47     | 8.31     | 2.68E-05| 1.668102 |
| ARHGAP1 | Arhgap1     | 34.08    | 30.49    | 57.43    | 52.22    | 2.04E-13| 1.667268 |
| NECAP2  | Necap2      | 20.53    | 19.93    | 37.25    | 35.1     | 1.7E-12 | 1.665595 |
| PTPN1   | Ptpn1       | 9.5      | 8.63     | 19.47    | 16.77    | 2.48E-12| 1.657331 |
| Dennd1b | Dennd1b     | 8.74     | 9.19     | 18.78    | 18.11    | 1.13E-11| 1.643506 |
| CDKN1B  | Cdkn1b      | 28.94    | 28.96    | 49.49    | 49.65    | 2.59E-10| 1.63941  |
| CAST    | Cast        | 18.66    | 18.24    | 31.19    | 30.64    | 1.33E-08| 1.636178 |
| ELMO2   | Elmo2       | 11.06    | 10.07    | 19.07    | 18.07    | 1.13E-08| 1.6325  |
| LIMS1   | Lims1       | 19.61    | 20.01    | 39.75    | 38       | 1.91E-13| 1.631916 |
| Eil2    | Eil2        | 4.19     | 4.35     | 7.2      | 7.09     | 3.1E-08 | 1.630162 |
| HDAC4   | Hdac4       | 2.8      | 2.91     | 4.96     | 4.36     | 2.44E-06| 1.620895 |
| HDAC4   | Hdac4       | 4.3      | 3.86     | 7.18     | 6.06     | 2.44E-06| 1.620895 |
| Sox12   | Sox12       | 3.2      | 2.92     | 5.41     | 4.68     | 2.35E-07| 1.609669 |
| RALGAPB | Ralgapb     | 9.23     | 10.74    | 17.99    | 15.96    | 5.02E-11| 1.608122 |
| JAZF1   | Jazf1       | 1.63     | 1.42     | 2.59     | 2.49     | 0.002097| 1.60726 |
| ENC1    | Enc1        | 0.99     | 0.98     | 1.77     | 1.57     | 0.000576| 1.603919 |
| Snrpb2  | Snrpb2      | 20.52    | 24.5     | 40.42    | 40.04    | 1.67E-10| 1.591182 |
| ASXL1   | Asxl1       | 9.44     | 9.29     | 15.98    | 14.88    | 2.4E-10 | 1.59111  |
| Dgka    | Dgka        | 2.24     | 2.43     | 3.57     | 4.28     | 0.002759| 1.58848 |
| Aim1    | Aim1        | 0.71     | 0.55     | 0.89     | 0.97     | 0.038293| 1.588385 |
| LGR4    | Lgr4        | 5.04     | 5.71     | 9        | 8.77     | 3.15E-06| 1.573989 |
| PARD6B  | Pard6b      | 1.64     | 1.38     | 2.35     | 2.53     | 0.00077 | 1.568525 |
| DCP1A   | Dcp1a       | 4.8      | 4.8      | 7.92     | 7.59     | 5.1E-07 | 1.557783 |
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC   |
|----------|-------------|---------|---------|---------|---------|---------|------|
| PLAGL2   | Plagl2      | 1.46    | 1.14    | 2.13    | 1.72    | 0.000611 | 1.557011 |
| ITM2C    | Itm2c       | 46.56   | 44.6    | 73.42   | 70.75   | 2.13E-12 | 1.54581  |
| Ipo8     | Ipo8        | 8.7     | 8.9     | 14.82   | 14.43   | 6.6E-08  | 1.532839 |
| KLF10    | Klf10       | 10.5    | 10.72   | 16.48   | 17.13   | 8.98E-09 | 1.532376 |
| MANBAL   | Manbal      | 12.8    | 13.13   | 21.53   | 21.17   | 2.68E-06 | 1.530318 |
| Prdm16   | Prdm16      | 2.29    | 1.6     | 2.83    | 3.13    | 0.027582 | 1.525588 |
| FN1      | Fn1         | 3.22    | 2.94    | 5.13    | 4.36    | 3.62E-05 | 1.525467 |
| Clasp1   | Clasp1      | 27.48   | 26.79   | 42.72   | 39.72   | 2.53E-10 | 1.520238 |
| GPX8     | Gpx8        | 6.71    | 8.58    | 12.17   | 10.05   | 0.003036 | 1.515593 |
| ADNP     | Adnp        | 1.56    | 1.54    | 2.77    | 2.2     | 0.004371 | 1.514231 |
| MRE11A   | Mre11a      | 12.17   | 11.3    | 17.65   | 15.63   | 0.000061 | 1.510015 |
| Rnf5     | Rnf5        | 6.75    | 6.53    | 10.46   | 10.2    | 0.000705 | 1.49724  |
| BSG      | Bsg         | 402.35  | 377.61  | 611.85  | 584.55  | 8.29E-10 | 1.495822 |
| GCLC     | Gclc        | 8.02    | 7.92    | 12.1    | 12.62   | 2.56E-05 | 1.492475 |
| NOL12    | Nol12       | 8.47    | 8.13    | 11.34   | 12.83   | 0.004173 | 1.482285 |
| VPS13B   | Vps13b      | 4.29    | 4.59    | 7.17    | 6.51    | 4.14E-07 | 1.474251 |
| TSGA14   | Tsga14      | 2.74    | 2.73    | 4.74    | 4.07    | 0.02658  | 1.472676 |
| IFRD2    | Ifrd2       | 14.99   | 13.38   | 23.3    | 20.87   | 6.51E-07 | 1.472085 |
| AES      | Aes         | 105.3   | 90.82   | 151.1   | 142.66  | 3.7E-10  | 1.471443 |
| SMARCAD1 | Smarcad1    | 4.24    | 4.75    | 6.56    | 7.09    | 0.010732 | 1.471292 |
| Ppm1b    | Ppm1b       | 23.52   | 22.2    | 36.08   | 34.84   | 8.83E-06 | 1.467686 |
| Immp2l   | Immp2l      | 3.64    | 3.57    | 5.54    | 6.57    | 0.049354 | 1.467317 |
| SERPINB9 | Serpinb9    | 2.49    | 2.05    | 3.37    | 3.58    | 0.00372  | 1.466848 |
| RAB22A   | Rab22a      | 11.32   | 10.16   | 15.55   | 15.01   | 1.03E-05 | 1.466622 |
| Pbx3     | Pbx3        | 12.37   | 12.9    | 19.39   | 17.86   | 0.000271 | 1.456454 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC   |
|---------|-------------|---------|---------|---------|---------|---------|------|
| POFUT1  | Pofut1      | 7.76    | 7.49    | 12.29   | 10.94   | 3.34E-06| 1.454448 |
| HYLS1   | Hyls1       | 7.41    | 8.69    | 11.76   | 12.34   | 0.007821| 1.447862 |
| TMEM65  | Tmem65      | 9.25    | 8.97    | 14.11   | 13.8    | 4.74E-06| 1.43896 |
| Pkia    | Pkia        | 19.44   | 21.07   | 30.5    | 31.38   | 2.31E-08| 1.435706 |
| SCRN1   | Scrn1       | 1.81    | 1.79    | 2.75    | 2.53    | 0.038541| 1.431997 |
| Jmy     | Jmy         | 3.92    | 3.82    | 6.21    | 5.4     | 0.000379| 1.43144 |
| GOLT1B  | Golt1b      | 19.02   | 20.46   | 30.29   | 29.47   | 1.95E-07| 1.42988 |
| Fam57a  | Fam57a      | 8.96    | 8.23    | 13.11   | 11.69   | 3.04183 | 1.419681 |
| Six1    | Six1        | 2.32    | 1.39    | 2.94    | 2.21    | 0.005392| 1.418853 |
| ADAR    | Adar        | 6.19    | 5.98    | 8.59    | 9.6     | 0.0006  | 1.418582 |
| Zfp217  | Zfp217      | 2.65    | 2.39    | 3.96    | 3.38    | 0.014816| 1.417933 |
| YTHDF1  | Ythdf1      | 15.48   | 16.82   | 24.52   | 23.09   | 3.03E-07| 1.415641 |
| QSOX2   | Qsox2       | 5.8     | 5.66    | 8.85    | 8.01    | 0.00042 | 1.415608 |
| SPATA2  | Spata2      | 5.51    | 5.53    | 8.47    | 7.9     | 0.033395| 1.414062 |
| Chd2    | Chd2        | 7.35    | 7.77    | 11.04   | 10.08   | 8.66E-05| 1.413159 |
| St13    | St13        | 65.58   | 71.61   | 101.68  | 98.81   | 7.27E-06| 1.412346 |
| Ppp2r3a | Ppp2r3a     | 7.86    | 8.31    | 11.27   | 12.09   | 0.000106| 1.411153 |
| DNA2    | Dna2        | 8.41    | 9.07    | 12.79   | 12.9    | 7.77E-06| 1.410956 |
| SLC25A30| Slc25a30    | 10.22   | 10.58   | 15.57   | 14.29   | 0.000736| 1.409991 |
| Rps6ka6 | Rps6ka6     | 5.82    | 5.64    | 8.43    | 7.16    | 0.00107 | 1.40845 |
| DDAH1   | Ddah1       | 0.88    | 0.94    | 1.85    | 1.36    | 0.047534| 1.407905 |
| Kras    | Kras        | 5.78    | 7.17    | 10.7    | 9.83    | 0.000837| 1.406761 |
| MTDH    | Mtdh        | 31.15   | 34.5    | 47.3    | 50.05   | 1.17E-06| 1.4043  |
| Bcl2    | Bcl2        | 1.61    | 1.5     | 2.39    | 1.99    | 0.025099| 1.400664 |
| CBFA2T2 | Cbfa2t2     | 6.18    | 5.93    | 9.69    | 9.55    | 0.001042| 1.398412 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|---------|-------------|---------|---------|---------|---------|---------|-------|
| AMPD3   | Ampd3       | 9.89    | 8.85    | 14.07   | 12.22   | 0.001873| 1.397122|
| NCOA3   | Ncoa3       | 8.55    | 7.88    | 12.61   | 11.05   | 0.002881| 1.39062 |
| CDYL    | Cdyl        | 4.71    | 4.24    | 6.54    | 5.97    | 0.001061| 1.390548|
| Zfr     | Zfr         | 65.34   | 68.76   | 98.31   | 91.72   | 1.88E-07| 1.387079|
| Siah1a  | Siah1a      | 5.26    | 6.24    | 8.7     | 8.56    | 0.00155 | 1.38564 |
| RERE    | Rere        | 7.78    | 7.97    | 12.22   | 9.44    | 0.018576| 1.383272|
| GHITM   | Ghitm       | 59.22   | 62.79   | 87.11   | 88.89   | 1.59E-07| 1.383206|
| ACVR2A  | Acvr2a      | 3.86    | 3.95    | 5.39    | 5       | 0.006433| 1.382212|
| Mapk7   | Mapk7       | 3.89    | 3.48    | 5.52    | 4.89    | 0.03634 | 1.382098|
| Trp53inp2 | Trp53inp2   | 62.64   | 64.08   | 95.33   | 86.05   | 4.71E-06| 1.380824|
| TNRC6B  | Tnrc6b      | 3.5     | 3.68    | 5.52    | 4.83    | 1.13E-05| 1.380356|
| TBC1D4  | Tbc1d4      | 10.91   | 11.63   | 17.3    | 15.2    | 8.37E-06| 1.379721|
| Lpl     | Lpl         | 104.29  | 110.98  | 154.14  | 145.88  | 6.93E-07| 1.379716|
| EIF2S2  | Eif2s2      | 78.72   | 88.59   | 128.05  | 120.98  | 4.23E-07| 1.373171|
| GATA6   | Gata6       | 11.47   | 11.2    | 16.4    | 15.9    | 0.000611| 1.372337|
| HEXIM1  | Hexim1      | 3.36    | 3.29    | 5.28    | 4.25    | 0.002684| 1.371303|
| PDRG1   | Pdrg1       | 45.8    | 44.73   | 68.42   | 63.68   | 0.000013| 1.369745|
| ROCK2   | Rock2       | 15.72   | 18.25   | 24.94   | 23.66   | 8.27E-07| 1.369699|
| Rad21   | Rad21       | 23.24   | 23.19   | 35.13   | 32.55   | 1.79E-06| 1.368987|
| Rbm26   | Rbm26       | 7.12    | 7.89    | 10.97   | 10.3    | 0.00458 | 1.36703 |
| LPCAT1  | Lpcat1      | 4.85    | 4.63    | 7.28    | 5.58    | 0.016958| 1.366197|
| PLEKHB2 | Plekhb2     | 18.16   | 17.33   | 26.45   | 24.7    | 5.83E-06| 1.36556 |
| Qk      | Qk          | 35.99   | 35.37   | 52.66   | 48.51   | 9.26E-05| 1.364261|
| Qk      | Qk          | 0.8     | 0.65    | 1.7     | 1.21    | 9.26E-05| 1.364261|
| PIP4K2A | Pip4k2a     | 3.42    | 2.99    | 4.39    | 4.14    | 0.005905| 1.360864|
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|----------|-------------|---------|---------|---------|---------|---------|-------|
| YWHAB    | Ywhab       | 45.47   | 44.79   | 68.06   | 61.49   | 9.15E-07 | 1.360272 |
| NFYA     | Nfya        | 10.22   | 11.26   | 16.34   | 14.52   | 0.007204 | 1.358941 |
| PDGFA    | Pdgfa       | 13.82   | 12.83   | 20.18   | 19.61   | 0.014361 | 1.358684 |
| LPIN2     | Lpin2       | 5.5     | 4.68    | 6.86    | 7.13    | 0.002166 | 1.356379 |
| PDLIM1    | Pdlim1      | 23.1    | 20.77   | 37.4    | 29.95   | 0.000273 | 1.352694 |
| Sik1      | Sik1        | 9.67    | 8.57    | 13.18   | 12.42   | 0.000129 | 1.346371 |
| DERL1     | Derl1       | 29.91   | 30.5    | 42.73   | 42.69   | 1.23E-05 | 1.344818 |
| PIP5K1B   | Pip5k1b     | 5.06    | 5.03    | 6.87    | 6.72    | 0.006247 | 1.343383 |
| CRLF3     | Crlf3       | 11.91   | 12.39   | 17.74   | 15.95   | 0.000995 | 1.339905 |
| Trim44    | Trim44      | 9.67    | 10.11   | 14.5    | 13.69   | 3.11E-05 | 1.334779 |
| Ccdc47    | Ccdc47      | 26.54   | 31.85   | 38.88   | 38.3    | 5.87E-05 | 1.334071 |
| HNRNPF    | Hnrnpf      | 212     | 230.91  | 308.47  | 306.93  | 2.27E-05 | 1.333284 |
| OSBPL8    | Osbpl8      | 4.39    | 4.93    | 6.72    | 6.49    | 0.000895 | 1.330613 |
| DLAT      | Dlat        | 43.59   | 45.34   | 61.99   | 57.17   | 1.33E-05 | 1.329959 |
| COMMD7    | Commd7      | 23.61   | 22.89   | 33.37   | 31.91   | 0.002596 | 1.328677 |
| CDC42EP1  | Cdc42ep1    | 4.46    | 3.89    | 6.02    | 5.33    | 0.033298 | 1.325599 |
| EIF5      | Eif5        | 35.43   | 36.68   | 52.49   | 51.06   | 1.29E-05 | 1.325425 |
| RASA1     | Rasa1       | 7.03    | 8.6     | 10.69   | 10.63   | 0.001257 | 1.324873 |
| ANKRD28   | Ankrd28     | 5.11    | 4.94    | 6.93    | 7.17    | 0.008186 | 1.322578 |
| Prkar1a   | Prkar1a     | 59.17   | 60.32   | 85.92   | 82.17   | 3.89E-05 | 1.320025 |
| MAPRE1    | Mapre1      | 49.24   | 50      | 69.91   | 74.11   | 1.19E-05 | 1.317138 |
| CPEB4     | Cpeb4       | 6.18    | 6.85    | 9.11    | 8.54    | 0.017815 | 1.314845 |
| PPP1R12A  | Ppp1r12a    | 38.09   | 41.28   | 51.44   | 52.16   | 0.000327 | 1.309776 |
| Secisbp2l | Secisbp2l   | 3.9     | 4.15    | 5.91    | 5.25    | 0.001426 | 1.307054 |
| RFK       | Rfk         | 10.57   | 11.93   | 15.08   | 14.94   | 0.005091 | 1.300948 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC  |
|---------|-------------|---------|---------|---------|---------|---------|-----|
| Rfx7    | Rfx7        | 3.08    | 3.31    | 4.73    | 4.21    | 0.025563| 1.293671|
| BCL2L2  | Bcl2l2      | 6.27    | 6.89    | 8.95    | 9.03    | 0.00879 | 1.287121|
| Prkar2a | Prkar2a     | 6.91    | 7.16    | 10.35   | 8.77    | 0.003928| 1.285457|
| LPGAT1  | Lpgat1      | 14.23   | 15.95   | 22.77   | 20.58   | 0.000206| 1.285206|
| COL4A1  | Col4a1      | 31.34   | 28.2    | 41.85   | 36.55   | 0.000111| 1.280141|
| NHLRC2  | Nhlr2c      | 10.3    | 10.2    | 14.11   | 13.25   | 0.012976| 1.276292|
| PUM2    | Pum2        | 54.35   | 59.79   | 78.34   | 76.67   | 0.000614| 1.275763|
| Tex2    | Tex2        | 15.51   | 14.81   | 20.2    | 18.81   | 0.000712| 1.275253|
| UBE2E3  | Ube2e3      | 21.86   | 21.74   | 28.49   | 26.52   | 0.014353| 1.274552|
| ESPL1   | Espl1       | 7.99    | 7.2     | 10.82   | 9.29    | 0.002664| 1.273741|
| Trio    | Trio        | 3.44    | 3.41    | 4.73    | 4.31    | 0.016401| 1.272414|
| Ppp2r5c | Ppp2r5c     | 21.97   | 22.48   | 32.08   | 29.85   | 0.005096| 1.271995|
| JUND    | Jund        | 10.13   | 8.94    | 12.2    | 12.51   | 0.003693| 1.271845|
| MBOAT7  | Mboat7      | 11.57   | 11.84   | 15.91   | 13.61   | 0.005543| 1.268972|
| PRPF40A | Prpf40a     | 36.32   | 37.8    | 47.78   | 46.55   | 0.001665| 1.265245|
| HDGFRP3 | Hdgfrp3     | 10.13   | 10.99   | 14.23   | 13.84   | 0.001959| 1.264476|
| CDC25B  | Cdc25b      | 10.08   | 9.72    | 14.22   | 11.96   | 0.023384| 1.263837|
| Acyp1   | Acyp1       | 18.47   | 19.92   | 25.79   | 25.62   | 0.037419| 1.261974|
| MIB1    | Mib1        | 19.21   | 20.33   | 27.54   | 25.73   | 0.005824| 1.25864|
| NEDD4   | Nedd4       | 116.39  | 115.31  | 157.43  | 147.04  | 0.001558| 1.256904|
| RIT1    | Rit1        | 26.28   | 24.01   | 33.15   | 31.78   | 0.015084| 1.255991|
| ARL6IP1 | Arl6ip1     | 94.27   | 97.09   | 126.62  | 126.99  | 0.00045 | 1.254665|
| ZCCHC2  | Zcchc2      | 4.9     | 4.99    | 6.71    | 5.94    | 0.040483| 1.249729|
| DDX24   | Ddx24       | 26.17   | 25.48   | 34.41   | 32.29   | 0.001739| 1.2492|
| Fam3c   | Fam3c       | 18.72   | 17.84   | 24.15   | 24.31   | 0.005624| 1.247964|
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC  |
|---------|-------------|---------|---------|---------|---------|---------|-----|
| SESN2   | Sesn2       | 7.34    | 6.17    | 8.6     | 8.2     | 0.035519| 1.247867 |
| VPS13C  | Vps13c      | 5.33    | 5.7     | 7.31    | 7.03    | 0.00454 | 1.247833 |
| WAPAL   | Wapal       | 18.87   | 23.27   | 27.71   | 26.98   | 0.004368| 1.247131 |
| RMNDS5A | Rmnd5a      | 16.04   | 17.68   | 24.03   | 21.69   | 0.002566| 1.246106 |
| BLCAP   | Blcap       | 14.99   | 15.94   | 19.95   | 19.9    | 0.031309| 1.244427 |
| YAP1    | Yap1        | 17.7    | 17.22   | 24.05   | 23.96   | 0.007612| 1.24396  |
| Nbr1    | Nbr1        | 24.63   | 26.27   | 32.39   | 32.38   | 0.002116| 1.243403 |
| DENND5B | Dennd5b     | 5.42    | 5.55    | 8.18    | 7.4     | 0.009152| 1.240311 |
| CTSC    | Ctsc        | 13.89   | 13.73   | 17.27   | 15.16   | 0.016239| 1.239215 |
| Aplp2   | Aplp2       | 57.89   | 54.05   | 75.8    | 70.11   | 0.002876| 1.230864 |
| HMOX1   | Hmox1       | 18.84   | 17.28   | 24.2    | 20.99   | 0.016205| 1.228884 |
| VEGFA   | Vegfa       | 20.37   | 19.55   | 25.21   | 25.39   | 0.039137| 1.227264 |
| USP4    | Usp4        | 17.95   | 16.76   | 22.75   | 21.62   | 0.007121| 1.22262  |
| Tbc1d2b | Tbc1d2b     | 5.3     | 4.94    | 7.09    | 6.06    | 0.018093| 1.22252  |
| Myo9a   | Myo9a       | 5.81    | 5.96    | 7.49    | 7.49    | 0.021506| 1.219239 |
| Fam60a  | Fam60a      | 12.72   | 13.43   | 16.36   | 16.8    | 0.021772| 1.217956 |
| PHIP    | Phip        | 7.43    | 8.09    | 10.29   | 9.57    | 0.01139 | 1.213597 |
| RND3    | Rnd3        | 26.26   | 27.12   | 33.79   | 34.36   | 0.0083  | 1.206129 |
| KIF13A  | Kif13a      | 9.04    | 8.58    | 11.55   | 10.37   | 0.041871| 1.205663 |
| Fxr2    | Fxr2        | 30.95   | 29.11   | 37.72   | 37.49   | 0.007404| 1.205155 |
| ZFP106  | Zfp106      | 16.28   | 14.65   | 20.89   | 20.06   | 0.015302| 1.203638 |
| CALM1   | Calm1       | 115.87  | 98.23   | 152.94  | 135.14  | 0.010239| 1.2011  |
| PPP1R11 | Ppp1r11     | 45.42   | 41.22   | 58.65   | 49.63   | 0.026819| 1.200068 |
| ATP5G3  | Atp5g3      | 464.59  | 446.23  | 578.86  | 573.04  | 0.008199| 1.20004  |
| KBTBD2  | Kbtbd2      | 15.22   | 15.57   | 19.61   | 19.04   | 0.034227| 1.196404 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC  |
|---------|-------------|---------|---------|---------|---------|---------|-----|
| IDI1    | Idi1        | 27.35   | 29.35   | 38.5    | 34.65   | 0.011444 | 1.193936 |
| Zc3hav1 | Zc3hav1     | 25.01   | 25.96   | 31.58   | 30.75   | 0.040241 | 1.191238 |
| PRNP    | Prnp        | 32.57   | 31.06   | 39.94   | 38      | 0.018343 | 1.187896 |
| Sdc2    | Sdc2        | 19.39   | 20.33   | 25.27   | 23.77   | 0.019589 | 1.187068 |
| Slc38a2 | Slc38a2     | 21.71   | 21.96   | 28.81   | 26.14   | 0.02516  | 1.187054 |
| BC005537| BC005537    | 13.49   | 14.42   | 18.68   | 16.57   | 0.046808 | 1.183772 |
| MRPS35  | Mrps35      | 39.47   | 41.61   | 51.07   | 49.02   | 0.041739 | 1.179813 |
| OAZ1    | Oaz1        | 351.07  | 314.32  | 414.43  | 401.67  | 0.017999 | 1.176567 |
| IPO5    | Ipo5        | 96.46   | 98.05   | 123.03  | 115.06  | 0.047865 | 1.155842 |
| FKB9    | Fkb9        | 76.91   | 74.13   | 71.4    | 66.82   | 0.043604 | -1.15186 |
| ADAM19  | Adam19      | 16.92   | 16.17   | 15.56   | 13.52   | 0.038945 | -1.16135 |
| Ptbp2   | Ptbp2       | 33.13   | 35.71   | 32.21   | 30.56   | 0.045393 | -1.16263 |
| DYNC1LI2| Dync1li2    | 44.92   | 47.43   | 42.83   | 40.69   | 0.023627 | -1.16876 |
| PCNP    | Pcnp        | 47.12   | 52.41   | 46.89   | 46.81   | 0.033753 | -1.16951 |
| Prmt7   | Prmt7       | 66.04   | 60.75   | 57.15   | 54.45   | 0.020486 | -1.17796 |
| FBXW11  | Fbxw11      | 19.59   | 18.38   | 18.47   | 16.66   | 0.049596 | -1.17809 |
| PTP4A2  | Ptp4a2      | 112.67  | 119.22  | 99.86   | 103.98  | 0.018603 | -1.17874 |
| PJA2    | Pja2        | 17.99   | 18.34   | 16.7    | 15.76   | 0.036692 | -1.17924 |
| Eri1    | Eri1        | 15.63   | 16.6    | 14.3    | 14.24   | 0.023167 | -1.17937 |
| TAX1BP1 | Tax1bp1     | 66.47   | 72.15   | 61.03   | 61.05   | 0.01324 | -1.1837 |
| Crk     | Crk         | 27.52   | 27.63   | 25.34   | 23.81   | 0.021635 | -1.18719 |
| DNAJC13 | Dnajc13     | 9.28    | 10.05   | 8.89    | 8.25    | 0.023656 | -1.18732 |
| Arhgef17| Arhgef17    | 15.32   | 13.07   | 13.37   | 11.25   | 0.012101 | -1.18782 |
| ATP11B  | Atp11b      | 8.32    | 9.12    | 7.76    | 7.51    | 0.040945 | -1.18835 |
| CFL2    | Cfl2        | 84.78   | 89.63   | 80.13   | 77.24   | 0.012023 | -1.1897 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|---------|-------------|---------|---------|---------|---------|---------|-------|
| MED13   | Med13       | 7.01    | 7.17    | 6.57    | 6.4     | 0.019528 | -1.19173 |
| BUB3    | Bub3        | 92.34   | 83.43   | 80.66   | 74.83   | 0.009184 | -1.19313 |
| Pten    | Pten        | 30.55   | 33.17   | 28.71   | 28.24   | 0.008697 | -1.19404 |
| SDPR    | Sdpr        | 97.22   | 92.04   | 83.53   | 80.33   | 0.008601 | -1.19595 |
| NAE1    | Nae1        | 58.76   | 68.65   | 56.5    | 56.22   | 0.009588 | -1.1979  |
| LARP4B  | Larp4b      | 16.48   | 17.86   | 15.48   | 14.88   | 0.014993 | -1.199   |
| CHSY1   | Chsy1       | 7.84    | 7.87    | 7.23    | 6.53    | 0.030751 | -1.2001  |
| IQGAP1  | Iqgap1      | 46.98   | 44.31   | 40.92   | 37.64   | 0.007753 | -1.20057 |
| HSPA5   | Hspa5       | 482.06  | 488.1   | 427.57  | 416.02  | 0.036181 | -1.20164 |
| SFPQ    | Sfpq        | 84.24   | 85      | 74.57   | 72.39   | 0.032389 | -1.20272 |
| PARP1   | Parp1       | 66.29   | 66.9    | 59.67   | 54.01   | 0.008709 | -1.20301 |
| NHP2L1  | Nhp2l1      | 120.53  | 117.67  | 107.69  | 100.84  | 0.00527  | -1.20779 |
| UHRF1BP1| Uhrf1bp1    | 5.66    | 5.87    | 5.46    | 4.54    | 0.015242 | -1.21087 |
| FAM178A | Fam178a     | 13.99   | 15.06   | 12.61   | 12.29   | 0.009797 | -1.21356 |
| MAZ     | Maz         | 42.28   | 36.84   | 35.36   | 30.75   | 0.011051 | -1.21515 |
| H6PD    | H6pd        | 5.71    | 5.3     | 4.82    | 4.58    | 0.036328 | -1.21524 |
| KLF6    | Klf6        | 5.32    | 5.15    | 4.71    | 4.35    | 0.042641 | -1.21686 |
| Rap1b   | Rap1b       | 16.38   | 16.51   | 15.32   | 13.4    | 0.023905 | -1.2175  |
| Gdi2    | Gdi2        | 80.7    | 84.19   | 73.59   | 68.64   | 0.012761 | -1.21806 |
| Pip4k2b | Pip4k2b     | 5.06    | 4.5     | 4.24    | 3.6     | 0.041651 | -1.21915 |
| CRKL    | Crkl        | 12.98   | 12.52   | 11.45   | 10.14   | 0.013131 | -1.21975 |
| DPY19L1 | Dpy19l1     | 17.44   | 17.02   | 15.11   | 14.64   | 0.026387 | -1.2201  |
| CLSPN   | Clspn       | 15.62   | 16.39   | 14.09   | 13.65   | 0.020316 | -1.22108 |
| GNG12   | Gng12       | 18.56   | 18.1    | 16.26   | 17.81   | 0.032172 | -1.22286 |
| MCL1    | Mcl1        | 36.64   | 37.45   | 33.59   | 32.19   | 0.002867 | -1.22364 |
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC   |
|----------|-------------|---------|---------|---------|---------|---------|------|
| HDLBP    | Hdlbp       | 93.56   | 92.57   | 80.85   | 76.74   | 0.007967 | -1.22406 |
| EZR      | Ezr         | 83.58   | 80.77   | 70.67   | 63.65   | 0.004895 | -1.22412 |
| IGF1R    | Igf1r       | 9.22    | 8.12    | 8.22    | 7.27    | 0.016178 | -1.22473 |
| SLBP     | Slbp        | 48.32   | 50.46   | 44.56   | 45.76   | 0.005125 | -1.22502 |
| Zranb2   | Zranb2      | 44.83   | 50.84   | 40.98   | 41.95   | 0.008972 | -1.22722 |
| UBXN4    | Ubxn4       | 42.48   | 45.29   | 37.73   | 35.85   | 0.002153 | -1.22725 |
| Cnot8    | Cnot8       | 29.26   | 29.99   | 26.42   | 24.93   | 0.008049 | -1.22905 |
| AFF4     | Aff4        | 23.25   | 26.8    | 21.93   | 20.18   | 0.005788 | -1.22908 |
| Pin1     | Pin1        | 33.92   | 31.73   | 27.92   | 26.66   | 0.002129 | -1.23083 |
| LEPROT1  | Leprotl1    | 12.24   | 12.19   | 9.99    | 10.09   | 0.011898 | -1.2327 |
| TMEM30A  | Tmem30a     | 26.88   | 28.74   | 26.69   | 24.98   | 0.002509 | -1.23321 |
| DCK      | Dck         | 10.92   | 11.43   | 9.44    | 9.77    | 0.013327 | -1.23354 |
| SLC7A6   | Slc7a6      | 22.84   | 21.66   | 20.31   | 17.29   | 0.021428 | -1.23428 |
| GORASP2  | Gorasp2     | 29.61   | 27.84   | 25.25   | 22.82   | 0.009766 | -1.2346 |
| RABEP1   | Rabep1      | 24.07   | 27.23   | 21.64   | 20.61   | 0.035058 | -1.23561 |
| Ddx1     | Ddx1        | 167.8   | 170.72  | 147.37  | 141.35  | 0.001933 | -1.23672 |
| CCDC6    | Ccdc6       | 11.13   | 10.16   | 9.13    | 8.8     | 0.018619 | -1.23789 |
| Tra2b    | Tra2b       | 82.91   | 80.21   | 71.11   | 69.08   | 0.001221 | -1.23886 |
| Rnf11    | Rnf11       | 43.21   | 41.96   | 37.42   | 34.94   | 0.009038 | -1.24006 |
| CD164    | Cd164       | 22.8    | 23.92   | 20.42   | 19.81   | 0.004302 | -1.24027 |
| 1810013L24Rik | 1810013L24Rik | 10.49   | 10.65   | 9.4     | 8.68    | 0.041342 | -1.24082 |
| FAM126A  | Fam126a     | 17.05   | 17.33   | 15.68   | 13.71   | 0.005748 | -1.24085 |
| FRMD6    | Frmd6       | 6.52    | 6.05    | 5.22    | 5.42    | 0.035613 | -1.24105 |
| C78339   | C78339      | 20.08   | 20.41   | 16.09   | 16.24   | 0.020869 | -1.24293 |
| PCBP1    | Pcbp1       | 32.52   | 28.35   | 26.32   | 23.8    | 0.005304 | -1.24674 |
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value  | FC    |
|----------|-------------|---------|---------|---------|---------|----------|-------|
| CHRAC1   | Chrac1      | 58.37   | 59.22   | 48.57   | 48.07   | 0.004319 | -1.24774 |
| Dnajb9   | Dnajb9      | 7.92    | 7.44    | 6.86    | 6.17    | 0.045802 | -1.24991 |
| MCFD2    | Mcfd2       | 64.98   | 63.9    | 58.6    | 52.65   | 0.00185  | -1.25029 |
| HEXA     | Hexa        | 62.36   | 66.45   | 52.79   | 51.98   | 0.001072 | -1.25144 |
| PUM1     | Pum1        | 14.41   | 12.99   | 11.53   | 10.05   | 0.017499 | -1.2518  |
| UBE2i    | Ube2i       | 234.87  | 230.07  | 210.6   | 201.98  | 0.006719 | -1.2519  |
| Bptf     | Bptf        | 8.1     | 8.8     | 6.97    | 6.22    | 0.00887  | -1.25253 |
| Sephs1   | Sephs1      | 15.79   | 15.68   | 13.84   | 13.18   | 0.012081 | -1.25473 |
| LSM14A   | Lsm14a      | 17.55   | 17.95   | 16.56   | 14.67   | 0.008396 | -1.25626 |
| PANK3    | Pank3       | 14.5    | 15.95   | 12.99   | 12.77   | 0.000656 | -1.25743 |
| STAM2    | Stam2       | 9.81    | 9.32    | 9       | 7.29    | 0.007842 | -1.25744 |
| NR2C2    | Nr2c2       | 11.81   | 12.51   | 9.44    | 10.11   | 0.019591 | -1.25801 |
| BNIP3L   | Bnip3l      | 37.81   | 40.23   | 45.13   | 37.45   | 0.001069 | -1.25843 |
| FAM168A  | Fam168a     | 5.53    | 5.06    | 4.54    | 4.1     | 0.019162 | -1.25942 |
| IRAK2    | Irak2       | 7.75    | 7.66    | 6.63    | 6.36    | 0.032575 | -1.26018 |
| GIGYF2   | Gigyf2      | 15.86   | 17.02   | 13.85   | 13.05   | 0.007765 | -1.26233 |
| ORMDL3   | Ormdl3      | 12.77   | 12.84   | 11.14   | 10.16   | 0.008827 | -1.26448 |
| Abcb7    | Abcb7       | 14.24   | 15.19   | 12.18   | 12.12   | 0.000717 | -1.26484 |
| SEC23A   | Sec23a      | 25.61   | 26.39   | 22.2    | 21.31   | 0.001708 | -1.26503 |
| DENND5A  | Dennd5a     | 51.96   | 51.56   | 42.8    | 41.95   | 0.000307 | -1.26651 |
| Otud4    | Otud4       | 30.82   | 31.37   | 27.41   | 26.13   | 0.000352 | -1.26686 |
| Rnf169   | Rnf169      | 7.03    | 7.29    | 5.85    | 5.84    | 0.01381  | -1.26787 |
| PIK3R1   | Pik3r1      | 7.03    | 7.23    | 6.07    | 5.79    | 0.002776 | -1.26883 |
| CCNG2    | Ccng2       | 11.57   | 11.68   | 9.57    | 9.42    | 0.006407 | -1.27001 |
| PRKD3    | Prkd3       | 34.82   | 37.22   | 29.76   | 30.27   | 0.000519 | -1.27007 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|---------|-------------|---------|---------|---------|---------|---------|-------|
| SNIP1   | Snip1       | 15.17   | 14.67   | 13.15   | 11.52   | 0.004525 | -1.27143 |
| TEAD1   | Tead1       | 15.11   | 15.59   | 14.32   | 12.93   | 0.006315 | -1.27281 |
| CCNL1   | Ccnl1       | 22.39   | 24.8    | 21.21   | 19.54   | 0.023094 | -1.27307 |
| VEZF1   | Vezf1       | 9.4     | 8.84    | 7.88    | 7.5     | 0.013131 | -1.27446 |
| REST    | Rest        | 8.6     | 9.02    | 7.43    | 7.04    | 0.004246 | -1.27469 |
| RHEB    | Rheb        | 47.75   | 54.89   | 43.39   | 43.91   | 0.001694 | -1.27567 |
| IFNGR2  | Ifngr2      | 70.93   | 68.64   | 56.33   | 57.07   | 0.000165 | -1.27647 |
| Rhot1   | Rhot1       | 21.79   | 23.49   | 18.95   | 19.34   | 0.00354  | -1.27904 |
| Ptpn11  | Ptpn11      | 23.63   | 23.77   | 20.27   | 18.12   | 0.002558 | -1.27951 |
| Rps6kb1 | Rps6kb1     | 11.72   | 13.28   | 9.83    | 11.29   | 0.030984 | -1.2797 |
| ZFAND5  | Zfand5      | 31.03   | 30.6    | 27.11   | 24.39   | 0.00091  | -1.28161 |
| SRPK2   | Srpk2       | 9.85    | 10.51   | 8.68    | 8.14    | 0.002314 | -1.28243 |
| Ppp4r2  | Ppp4r2      | 24.13   | 26.53   | 21.42   | 20.35   | 0.000955 | -1.28316 |
| PRKAG2  | Prkag2      | 33.77   | 29.7    | 25.26   | 25.89   | 0.008025 | -1.28402 |
| SMC4    | Smc4        | 86.7    | 101.67  | 76.57   | 76.89   | 0.000193 | -1.28436 |
| Spast   | Spast       | 10.85   | 11.6    | 9.73    | 8.91    | 0.006495 | -1.28442 |
| Ulk2    | Ulk2        | 11.98   | 12.5    | 10.24   | 9.6     | 0.003053 | -1.28589 |
| Nudt4   | Nudt4       | 10.09   | 10.47   | 9.04    | 8.03    | 0.01381  | -1.28596 |
| MDFIC   | Mdfic       | 18.68   | 19.06   | 15.64   | 14.91   | 0.005806 | -1.28756 |
| PPP1CC  | Ppp1cc      | 210.75  | 215.91  | 191.39  | 187.56  | 0.000108 | -1.28772 |
| Piga    | Piga        | 5.8     | 5.78    | 5.21    | 4.51    | 0.009989 | -1.28787 |
| ATP13A3 | Atp13a3     | 19.19   | 19.1    | 16.43   | 15.42   | 0.001199 | -1.28832 |
| Asap1   | Asap1       | 11.76   | 11.1    | 9.84    | 8.28    | 0.006313 | -1.2891 |
| Mybl1   | Mybl1       | 18.6    | 21.05   | 15.27   | 15.44   | 0.004047 | -1.29031 |
| ADD1    | Add1        | 36.79   | 34.99   | 30.59   | 28.65   | 0.000555 | -1.29097 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC  |
|---------|-------------|---------|---------|---------|---------|---------|-----|
| ILDR2   | Ildr2       | 11.6    | 10.33   | 9.11    | 8.66    | 0.000603 | -1.29178 |
| DNMBP   | Dnmbp       | 2.42    | 2.05    | 1.75    | 1.74    | 0.024789 | -1.29296 |
| Fez2    | Fez2        | 15.98   | 14.95   | 12.44   | 12.81   | 0.002775 | -1.29482 |
| Pmpcb   | Pmpcb       | 104.01  | 105.43  | 87.64   | 82.84   | 6.27E-05 | -1.29518 |
| ARHGAP5 | Arhgap5     | 28.5    | 32.72   | 25.43   | 24.6    | 0.000378 | -1.29523 |
| TTF2    | Ttf2        | 14.86   | 14.47   | 12.09   | 11.2    | 0.000284 | -1.29787 |
| TCF12   | Tcf12       | 10.46   | 10.26   | 8.59    | 7.86    | 0.001732 | -1.29918 |
| YTHDC1  | Ythdc1      | 15.74   | 16.84   | 13.7    | 13.21   | 0.008044 | -1.2998 |
| KPNA1   | Kpna1       | 20.27   | 20.95   | 16.95   | 17.14   | 0.001323 | -1.29981 |
| Mpp5    | Mpp5        | 5.48    | 6.3     | 4.93    | 4.65    | 0.0045   | -1.29998 |
| Osbpl11 | Osbpl11     | 9.3     | 9.42    | 7.54    | 7.56    | 0.002175 | -1.30205 |
| TTC3    | Ttc3        | 51.2    | 57.56   | 45.78   | 43.33   | 0.000346 | -1.30244 |
| Kif26b  | Kif26b      | 12.96   | 12.17   | 10.27   | 9.14    | 0.001464 | -1.30338 |
| Slc6a6  | Slc6a6      | 17.62   | 15.96   | 14.31   | 12.41   | 7.91E-05 | -1.3051 |
| MIER1   | Mier1       | 16.27   | 17.52   | 13.07   | 12.78   | 0.006283 | -1.30519 |
| Rab8b   | Rab8b       | 6.95    | 6.78    | 5.78    | 5.33    | 0.00119  | -1.30853 |
| GATAD2B | Gatad2b     | 6.55    | 5.49    | 5.15    | 4.39    | 0.002959 | -1.30893 |
| CAPN2   | Capn2       | 41.49   | 40      | 33.47   | 30.68   | 3.67E-05 | -1.30955 |
| Ythdf2  | Ythdf2      | 34.07   | 35.17   | 28.14   | 27.21   | 0.000108 | -1.31019 |
| SNX27   | Snx27       | 10.46   | 9.05    | 8.22    | 7.09    | 0.003575 | -1.31023 |
| SPRED1  | Spred1      | 8.8     | 8.08    | 7.66    | 7.3     | 0.007223 | -1.31112 |
| STK17B  | Stk17b      | 14.52   | 14.99   | 11.86   | 11.77   | 0.000299 | -1.31349 |
| ACBD3   | Acbd3       | 16.56   | 16.76   | 13.83   | 12.76   | 0.000422 | -1.31444 |
| BET1L   | Bet1L       | 12.11   | 11.67   | 8.98    | 9.71    | 0.013182 | -1.31581 |
| AGFG1   | Agfg1       | 29.83   | 29.48   | 24.47   | 23.1    | 0.000837 | -1.31604 |
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|----------|-------------|---------|---------|---------|---------|---------|-------|
| ATPAF1   | Atpaf1      | 12.58   | 13.11   | 11.36   | 10.64   | 0.012786| -1.3172 |
| FOSL2    | Fosl2       | 4.75    | 4.43    | 3.81    | 3.34    | 0.001557| -1.32153|
| S100pbp  | S100pbp     | 11.95   | 12.12   | 10.63   | 9.98    | 0.018762| -1.322  |
| FAM160B1 | Fam160b1    | 6.61    | 6.27    | 5.36    | 4.5     | 0.0066  | -1.32254|
| Ubxn7    | Ubxn7       | 7.28    | 7.91    | 6.37    | 5.77    | 0.000156| -1.32268|
| Rnf38    | Rnf38       | 10.17   | 10      | 7.26    | 7.02    | 0.011698| -1.32314|
| SACS     | Sacs        | 5.97    | 6.61    | 5.07    | 5.09    | 0.000621| -1.32329|
| MESDC1   | Mesdc1      | 7.04    | 6.71    | 5.47    | 5.24    | 0.001407| -1.32579|
| PTPN12   | Ptpn12      | 4.74    | 4.84    | 4.29    | 3.83    | 0.01843 | -1.32949|
| Agap1    | Agap1       | 6.51    | 5.95    | 5.21    | 4.59    | 0.005685| -1.33005|
| Ankrd44  | Ankrd44     | 3.82    | 4.14    | 3.19    | 2.96    | 0.033318| -1.33032|
| LARP1    | Larp1       | 20.86   | 18.82   | 15.79   | 15.03   | 8.06E-05| -1.33136|
| IPO7     | Ipo7        | 93.44   | 100.37  | 78.02   | 75.82   | 0.000251| -1.33203|
| Dock9    | Dock9       | 2.6     | 2.78    | 2.13    | 2       | 0.036976| -1.33205|
| BNIP3    | Bnip3       | 54.62   | 53.1    | 42.63   | 41.92   | 0.000121| -1.33259|
| Yipf5    | Yipf5       | 15.96   | 15.25   | 12.79   | 12.19   | 0.000331| -1.33544|
| NOTCH2   | Notch2      | 7.62    | 6.71    | 5.99    | 5.17    | 2.87E-05| -1.33596|
| FOXJ3    | Foxj3       | 7.67    | 7.16    | 6.77    | 5.38    | 0.004748| -1.34301|
| MAP3K7   | Map3k7      | 20.61   | 20.63   | 13.67   | 14.33   | 4.32E-05| -1.34394|
| ABHD10   | Abhd10      | 8.35    | 9.7     | 7.36    | 6.71    | 0.028375| -1.34543|
| LGALS8   | Lgals8      | 14.13   | 14.1    | 10.58   | 10.36   | 0.005441| -1.34622|
| Lrig1    | Lrig1       | 6.5     | 6.59    | 5.77    | 5.25    | 0.003309| -1.34674|
| Rprd1a   | Rprd1a      | 14.96   | 15.68   | 12.51   | 11.42   | 0.000889| -1.34844|
| LRRRC40  | Lrrc40      | 23.37   | 21.34   | 18.8    | 16.42   | 0.000052| -1.34971|
| Ddx3x    | Ddx3x       | 134.19  | 149.95  | 115.28  | 110.37  | 1.57E-05| -1.35122|
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value  | FC     |
|----------|-------------|---------|---------|---------|---------|----------|--------|
| Pdk1l    | Pdk1l       | 11.86   | 12.45   | 9.69    | 9.12    | 0.001611 | -1.35208 |
| FRS2     | Frs2        | 3.4     | 3.78    | 2.82    | 2.71    | 0.008208 | -1.35241 |
| Mnk1     | Mnk1        | 16.92   | 16.78   | 14.81   | 12.05   | 0.006823 | -1.35549 |
| AP1S3    | Ap1s3       | 10.16   | 9.93    | 7.68    | 7.31    | 0.003654 | -1.35625 |
| ARL6IP6  | Arl6ip6     | 12.98   | 14.27   | 10.66   | 9.01    | 0.002093 | -1.35652 |
| PKD2     | Pkd2        | 7.26    | 7.2     | 5.93    | 5.52    | 0.000247 | -1.35784 |
| CTDSP2   | Ctdsp2      | 15.92   | 14.63   | 12.04   | 11.24   | 0.000041 | -1.35799 |
| Hsph1    | Hsph1       | 21.27   | 20.7    | 16.24   | 15.4    | 1.55E-05 | -1.35803 |
| UBE2K    | Ube2k       | 29.73   | 29.48   | 23.14   | 23.68   | 5.35E-05 | -1.35808 |
| Pkd1     | Pkd1        | 5.43    | 4.76    | 4.11    | 3.53    | 0.0001   | -1.35901 |
| Lrrc8a   | Lrrc8a      | 9.82    | 8.8     | 7.12    | 6.8     | 0.00035  | -1.35994 |
| Hook3    | Hook3       | 8.05    | 8.2     | 5.97    | 6.17    | 8.13E-05 | -1.36022 |
| Senp5    | Senp5       | 9.34    | 9.6     | 7.9     | 6.89    | 0.000336 | -1.36182 |
| Stard13  | Stard13     | 12.49   | 11.64   | 9.33    | 8.5     | 6.13E-05 | -1.36513 |
| Mboat2   | Mboat2      | 10.36   | 11.19   | 8.58    | 7.99    | 0.004173 | -1.36561 |
| MFHAS1   | Mfhas1      | 11.24   | 10.43   | 8.49    | 7.67    | 5.71E-05 | -1.36585 |
| BAG2     | Bag2        | 37.43   | 36.87   | 29.81   | 26.85   | 7.4E-06  | -1.36905 |
| SEL1L    | Sel1l       | 16.76   | 16.98   | 15.36   | 14.23   | 0.00013  | -1.36946 |
| Cdh20    | Cdh20       | 4.82    | 4.88    | 3.72    | 3.63    | 0.003347 | -1.37015 |
| CTTN     | Cttn        | 55.13   | 54.66   | 44.5    | 41.76   | 6.84E-07 | -1.37044 |
| SIKE1    | Sike1       | 13.81   | 17.15   | 12.57   | 11.24   | 0.00093  | -1.37075 |
| Mtfr1    | Mtfr1       | 22.48   | 21.45   | 16.08   | 16.88   | 0.000608 | -1.37122 |
| USP25    | Usp25       | 24.04   | 25.66   | 19.38   | 18.17   | 9.27E-06 | -1.37136 |
| BHLHE40  | Bhlhe40     | 24.42   | 23.16   | 18.63   | 16.71   | 4.85E-06 | -1.37231 |
| CDC42SE1 | Cdc42se1    | 20.52   | 19.76   | 14.46   | 15.56   | 0.016672 | -1.37278 |
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC   |
|---------|-------------|---------|---------|---------|---------|---------|------|
| LMO4    | Lmo4        | 11.19   | 10.9    | 8.71    | 8       | 0.008267| -1.37314|
| CHMP5   | Chmp5       | 38.23   | 41.35   | 29.82   | 30.99   | 2.86E-05| -1.37583|
| SETX    | Setx        | 16.76   | 19.19   | 15.47   | 12.66   | 7.61E-06| -1.37631|
| Sec24a  | Sec24a      | 9.01    | 8.89    | 9.62    | 8.08    | 0.017896| -1.37688|
| Hmgb3   | Hmgb3       | 24.23   | 28.09   | 21.22   | 19.72   | 3.02E-05| -1.37872|
| FAT1    | Fat1        | 19.1    | 18.62   | 15.09   | 12.99   | 4.09E-06| -1.37994|
| TMEM185B| Tmem185b    | 24.92   | 24.02   | 19.47   | 18.25   | 6.14E-06| -1.38012|
| Fmr1    | Fmr1        | 27.56   | 29.97   | 23.1    | 22.75   | 2.15E-05| -1.38076|
| EDEM1   | Edem1       | 17.52   | 17.85   | 13.86   | 13.37   | 3.2E-06 | -1.38106|
| Btf3l4  | Btf3l4      | 49.83   | 58.97   | 47.83   | 44.27   | 1.05E-05| -1.38345|
| GSK3B   | Gsk3b       | 12.04   | 13.11   | 10.43   | 8.74    | 2.37E-06| -1.38375|
| SMAD7   | Smad7       | 2.74    | 2.51    | 2.3     | 1.87    | 0.008095| -1.38487|
| Baz2b   | Baz2b       | 10.48   | 10.23   | 7.93    | 9.8     | 0.005273| -1.38514|
| TRIM33  | Trim33      | 5.4     | 5.85    | 4.38    | 4.29    | 7.46E-05| -1.38527|
| MAP4K4  | Map4k4      | 32.27   | 33.3    | 25.35   | 23.82   | 1.77E-06| -1.38735|
| Bbx     | Bbx         | 19.96   | 22.45   | 16.38   | 15.18   | 5.47E-06| -1.38753|
| Lphn2   | Lphn2       | 9.55    | 9.59    | 6.9     | 6.63    | 0.000446| -1.39042|
| FNDC3B  | Fndc3b      | 8.39    | 7.61    | 6.47    | 5.52    | 0.000061| -1.3929|
| USP32   | Usp32       | 7.46    | 8.15    | 6.01    | 5.79    | 3.52E-05| -1.3944|
| Tmem170b| Tmem170b    | 2.84    | 3.16    | 2.3     | 2.21    | 0.000987| -1.39523|
| RAB5B   | Rab5b       | 14.97   | 16.08   | 11.83   | 11.14   | 2.57E-05| -1.39746|
| SLAIN2  | Slain2      | 20.5    | 20.5    | 15.66   | 14.9    | 3.48E-05| -1.39812|
| SGK1    | Sgk1        | 5.82    | 5.66    | 3.27    | 4.54    | 0.005372| -1.39817|
| Ptbp1   | Ptbp1       | 108.41  | 100.59  | 83.29   | 71.9    | 4.3E-07 | -1.39892|
| YWHAQ   | Ywhaq       | 170.83  | 179.3   | 131.09  | 132.25  | 2.38E-06| -1.39895|
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC   |
|---------|-------------|---------|---------|---------|---------|---------|------|
| Fermt2  | Fermt2      | 22.47   | 22.22   | 17.93   | 17.24   | 8.54E-06 | -1.40217 |
| ZC4H2   | Zc4h2       | 2.83    | 3.42    | 2.3     | 2.25    | 0.020316 | -1.40265 |
| TACC1   | Tacc1       | 7.42    | 7.33    | 5.68    | 5.2     | 0.000185 | -1.4035 |
| CD2AP   | Cd2ap       | 17.25   | 19.65   | 14.61   | 12.64   | 1.99E-05 | -1.40552 |
| Gosr2   | Gosr2       | 46.23   | 45.52   | 31.46   | 33.27   | 2.03E-07 | -1.40587 |
| MRFAP1  | Mrfap1      | 236.55  | 255.57  | 186.9   | 181.51  | 1.25E-07 | -1.40657 |
| Socs5   | Socs5       | 3.3     | 3.18    | 2.32    | 2.31    | 0.005291 | -1.40658 |
| CLCN3   | Clcn3       | 12.03   | 13.42   | 9.73    | 9.62    | 6.64E-05 | -1.4074 |
| GNAI3   | Gna13       | 30.14   | 33.01   | 23.58   | 23.92   | 1.71E-07 | -1.40813 |
| NRP1    | Nrp1        | 81.76   | 82.29   | 58.07   | 57.03   | 2.82E-06 | -1.40824 |
| Atp6v0e | Atp6v0e     | 220.15  | 215.89  | 165.05  | 161.23  | 5.54E-08 | -1.40875 |
| Zfp148  | Zfp148      | 13.04   | 14.85   | 9.95    | 9.59    | 3.73E-07 | -1.40951 |
| C030046E11Rik | C030046E11Rik | 21.27 | 20.37 | 16.66 | 15.35 | 5.06E-06 | -1.41189 |
| UBA6    | Uba6        | 9.44    | 10.19   | 7.23    | 7.21    | 0.000118 | -1.41753 |
| FAM168B | Fam168b     | 44.72   | 42.46   | 33.57   | 30.78   | 8.54E-07 | -1.41879 |
| TMOD3   | Tmod3       | 11.74   | 11.42   | 8.66    | 8.59    | 4.98E-06 | -1.41968 |
| PSD3    | Psd3        | 8.72    | 9.77    | 7.73    | 6.86    | 1.13E-05 | -1.42059 |
| DCAF7   | Dcaf7       | 19.16   | 18.53   | 14.35   | 12.76   | 6.98E-06 | -1.42082 |
| CTDSPL  | Ctdsp1      | 3.15    | 3.08    | 2.28    | 2.06    | 0.008261 | -1.42148 |
| Golga7  | Golga7      | 37.61   | 36.87   | 28.92   | 27.89   | 4.56E-06 | -1.42172 |
| Ube2b   | Ube2b       | 35.38   | 36.11   | 28.31   | 26.29   | 9.12E-05 | -1.4236 |
| CCNG1   | Ccng1       | 127.02  | 136.4   | 97.58   | 97.68   | 6.23E-08 | -1.42456 |
| Rab13   | Rab13       | 17.99   | 20.99   | 14.94   | 12.68   | 0.000225 | -1.4264 |
| MMD     | Mmd         | 38.68   | 36.74   | 29.85   | 28.47   | 0.000141 | -1.42734 |
| Dnajb5  | Dnajb5      | 5.05    | 4.62    | 3.45    | 3.57    | 0.025743 | -1.42834 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value   | FC       |
|---------|-------------|---------|---------|---------|---------|-----------|---------|
| RAP2B   | Rap2b       | 3.13    | 3.16    | 2.64    | 2.13    | 0.000895  | -1.43084|
| FUS     | Fus         | 20.92   | 22.41   | 15.14   | 15.44   | 0.000217  | -1.43213|
| PPFIA1  | Ppfla1      | 15.69   | 15.9    | 13.21   | 11.18   | 2.53E-05  | -1.43227|
| TAF5L   | Taf5l       | 31.58   | 30.44   | 23.66   | 21.25   | 2.51E-06  | -1.43389|
| Acaca   | Acaca       | 25.14   | 24.99   | 20.07   | 18.6    | 1.2E-08   | -1.43481|
| Ppm1f   | Ppm1f       | 16.84   | 15.58   | 12.43   | 11.09   | 6.67E-07  | -1.43562|
| MBNL1   | Mbnl1       | 40.27   | 40.97   | 30.47   | 29.56   | 7.23E-07  | -1.43594|
| DYSPL2  | Dyps1l2     | 45.56   | 40.57   | 34.07   | 28.66   | 7.66E-09  | -1.43686|
| TOMM70A | Tomm70a     | 51.62   | 55.17   | 40.37   | 38.12   | 3.5E-07   | -1.43965|
| DUSP3   | Dusp3       | 14.69   | 15.49   | 10.17   | 8.96    | 0.002024  | -1.43994|
| Acap2   | Acap2       | 8.91    | 9.17    | 6.51    | 6.62    | 2.77E-07  | -1.44009|
| Phf6    | Phf6        | 15.69   | 16.69   | 11.92   | 11.34   | 9.52E-08  | -1.4478 |
| SEC31A  | Sec31a      | 61.08   | 56.13   | 43.04   | 39.22   | 4.85E-08  | -1.4486 |
| CAV2    | Cav2        | 9.19    | 9.19    | 7.09    | 6.96    | 5.25E-05  | -1.44974|
| VT11A   | Vt11a       | 6.2     | 6.14    | 4.82    | 4.11    | 0.010138  | -1.44991|
| Mpdz    | Mpdz        | 34.77   | 34.98   | 24.1    | 22.96   | 6.02E-08  | -1.45086|
| NAV3    | Nav3        | 1.61    | 1.56    | 1       | 0.71    | 0.029423  | -1.45113|
| DAG1    | Dag1        | 42.57   | 40.49   | 31.62   | 26.76   | 2.42E-08  | -1.45321|
| BRMS1L  | Brms1l      | 11.54   | 13.14   | 9.45    | 8.47    | 5.1E-06   | -1.45371|
| Tmem164 | Tmem164     | 11.98   | 11.31   | 8.73    | 8.04    | 1.26E-05  | -1.45698|
| UBE2Q1  | Ube2q1      | 25.68   | 25.62   | 18.26   | 18.16   | 2.23E-08  | -1.45817|
| SSFA2   | Ssfa2       | 11.56   | 10.81   | 8.17    | 7.49    | 1.86E-07  | -1.45855|
| PRDX1   | Prdx1       | 455.19  | 486.15  | 341.27  | 348.52  | 2.78E-08  | -1.46153|
| DKC1    | Dkc1        | 51.08   | 48.21   | 36.62   | 34.59   | 9.38E-07  | -1.46335|
| AP1S2   | Ap1s2       | 9.52    | 9.96    | 7.55    | 7.59    | 0.000292  | -1.46561|
| Gene-ID  | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC       |
|----------|-------------|---------|---------|---------|---------|---------|----------|
| Ranbp10  | Ranbp10     | 7.77    | 7.64    | 5.65    | 5.32    | 4.87E-05| -1.46603 |
| ARPC5    | Arpc5       | 50.08   | 52.04   | 38.66   | 38.7    | 9.64E-09| -1.46775 |
| Scd2     | Scd2        | 264.6   | 253.65  | 201.68  | 169.61  | 2.05E-06| -1.46781 |
| RAD23B   | Rad23b      | 102.11  | 96.54   | 70.84   | 67.25   | 8.56E-10| -1.47109 |
| SNX19    | Snx19       | 18.45   | 17.59   | 12.93   | 12.28   | 7.21E-07| -1.47473 |
| DSP      | Dsp         | 31.76   | 32.35   | 23.78   | 21.39   | 2.66E-08| -1.47772 |
| DNAJA1   | Dnaja1      | 134.99  | 155.82  | 106.81  | 100.52  | 9.22E-07| -1.4788  |
| ACO1     | Aco1        | 27.23   | 25.96   | 19.66   | 17.79   | 1.8E-09 | -1.47942 |
| Ank3     | Ank3        | 15.76   | 13.87   | 11.29   | 10.43   | 4.8E-06 | -1.48139 |
| Golim4   | Golim4      | 10.38   | 10.1    | 7.5     | 6.59    | 5.47E-06| -1.48342 |
| Tmem120b | Tmem120b    | 4.52    | 4.55    | 3.07    | 3.51    | 0.011172| -1.48653 |
| HIPK1    | Hipk1       | 12.26   | 11.86   | 8.87    | 8.24    | 3.55E-09| -1.48802 |
| ZFX      | Zfx         | 18.16   | 17.74   | 13.24   | 15.02   | 9.64E-07| -1.48833 |
| Zeb2     | Zeb2        | 20.41   | 21.14   | 12.98   | 11.9    | 4E-07   | -1.49063 |
| GOLPH3   | Golph3      | 55.92   | 52.92   | 39.26   | 37.79   | 2.13E-10| -1.49182 |
| Sfxn1    | Sfxn1       | 26.15   | 27.38   | 19.13   | 18.41   | 2.76E-09| -1.49586 |
| ELMOD2   | Elmod2      | 13.4    | 14.48   | 12.32   | 11.69   | 8.09E-07| -1.49678 |
| lgsf3    | lgsf3       | 5.73    | 5.83    | 4.19    | 3.86    | 7.56E-06| -1.49695 |
| STX2     | Stx2        | 10.35   | 9.94    | 7.71    | 6.47    | 8.37E-05| -1.49742 |
| Bnc2     | Bnc2        | 4.29    | 4.4     | 3.04    | 2.81    | 0.006741| -1.49817 |
| PGK1     | Pgk1        | 645.92  | 626.42  | 452.03  | 446.24  | 9E-08   | -1.49838 |
| N4bp2    | N4bp2       | 5.52    | 6.38    | 4.03    | 3.5     | 6.05E-05| -1.49931 |
| SLC25A23 | Slc25a23    | 12.11   | 11.38   | 7.85    | 7.08    | 2.51E-06| -1.50316 |
| CBX1     | Cbx1        | 33      | 35.8    | 25.33   | 22.46   | 1.01E-06| -1.50532 |
| Vps33a   | Vps33a      | 18.8    | 17.59   | 12.84   | 12.11   | 2.65E-08| -1.50873 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC    |
|---------|-------------|---------|---------|---------|---------|---------|-------|
| Phc3    | Phc3        | 5.05    | 4.6     | 3.95    | 3.09    | 0.000006| -1.50928|
| CREBBP  | Crebbp      | 4.74    | 4.7     | 3.49    | 2.88    | 0.00001 | -1.51067|
| ZMYM1   | Zmym1       | 10.03   | 9.53    | 8.41    | 6.47    | 0.046068| -1.52363|
| CLDN12  | Cldn12      | 21.29   | 23.21   | 15.71   | 15.29   | 3.24E-08| -1.52401|
| IDS     | Ids         | 3.82    | 3.5     | 2.25    | 2.68    | 5.63E-05| -1.52622|
| KDELRE2 | Kdelr2      | 64.75   | 65.4    | 45.48   | 43.76   | 3.48E-11| -1.52668|
| LZTR1   | Lztr1       | 82.72   | 77.2    | 98.76   | 80.31   | 7.67E-07| -1.5273 |
| RAB12   | Rab12       | 26.43   | 28.14   | 19.69   | 17.97   | 4.39E-09| -1.52783|
| Mxd4    | Mxd4        | 18.1    | 18.44   | 11.7    | 11.23   | 9.47E-06| -1.52951|
| Eif4A2  | Eif4a2      | 89.6    | 104.93  | 69.19   | 71.57   | 2.14E-07| -1.53 |
| RCHY1   | Rchy1       | 18.9    | 17.89   | 12.74   | 11.66   | 6.2E-07 | -1.53033|
| LHFP    | Lhfp        | 50.46   | 50.09   | 34.01   | 34.63   | 3.74E-11| -1.53098|
| Gjc1    | Gjc1        | 18.18   | 20.33   | 13.15   | 12.16   | 1.99E-05| -1.53132|
| CPD     | Cpd         | 25.39   | 25.74   | 18.23   | 16.95   | 5.96E-12| -1.53201|
| Tmem41b | Tmem41b     | 66.74   | 76.59   | 50.51   | 51.98   | 2.24E-10| -1.5325 |
| Gucy1a3 | Gucy1a3     | 102.99  | 111.5   | 75.01   | 70.41   | 5.29E-11| -1.53287|
| SSH1    | Ssh1        | 1.68    | 1.35    | 1.06    | 0.8     | 0.041712| -1.53321|
| Atrx    | Atrx        | 47.38   | 56.08   | 33.91   | 37.59   | 3.32E-08| -1.53672|
| Ednra   | Ednra       | 6.53    | 6.98    | 4.56    | 4.42    | 1.69E-06| -1.53749|
| ARNT    | Arnt        | 11.15   | 11.41   | 9.24    | 8.19    | 0.000274| -1.53763|
| SHCBP1  | Shcbp1      | 24.7    | 28.15   | 19.06   | 17.7    | 1.72E-09| -1.53828|
| Amotl2  | Amotl2      | 18.91   | 15.15   | 11.52   | 10.25   | 3.03E-09| -1.54011|
| Rif     | Rif         | 11.38   | 12.75   | 8.22    | 7.88    | 5.89E-09| -1.54488|
| Plaa    | Plaa        | 52.82   | 58.28   | 38.96   | 37.61   | 6.54E-11| -1.54619|
| IRAK1   | Irak1       | 14.14   | 12.83   | 10.9    | 9.36    | 1.07E-05| -1.54935|
| Gene-ID     | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value   | FC        |
|------------|-------------|---------|---------|---------|---------|-----------|-----------|
| GCLM       | Gclm        | 21.05   | 20.78   | 13.71   | 12.16   | 0.03359   | -1.55043  |
| SLC6A9     | Slc6a9      | 6.75    | 4.78    | 5.22    | 3.47    | 0.000544  | -1.55151  |
| Cggbp1     | Cggbp1      | 42.14   | 40.7    | 28.87   | 28.74   | 1.41E-10  | -1.55248  |
| Glis2      | Glis2       | 6.78    | 6.57    | 4.73    | 4.28    | 0.002359  | -1.55286  |
| SLC30A7    | Slc30a7     | 5.75    | 5.75    | 4.05    | 3.65    | 4.23E-08  | -1.5532   |
| Hccs       | Hccs        | 33.45   | 33.6    | 24.01   | 22.21   | 1.98E-07  | -1.5542   |
| Klf9       | Klf9        | 16.28   | 17.56   | 11.1    | 11.4    | 2.49E-07  | -1.55551  |
| Plk2       | Plk2        | 14.37   | 14.33   | 9.49    | 9.54    | 9.79E-09  | -1.55582  |
| EVI5       | Evi5        | 23.71   | 25.44   | 16.85   | 17.34   | 5E-10     | -1.55764  |
| PALLD      | Palld       | 4.47    | 4.93    | 3.42    | 3.1     | 0.00028   | -1.55879  |
| Zfp292     | Zfp292      | 12.02   | 15.12   | 9.11    | 9       | 7.83E-12  | -1.56228  |
| DCTN3      | Dctn3       | 70.1    | 63.5    | 47.12   | 43.32   | 5.48E-10  | -1.56362  |
| PPP6C      | Ppp6c       | 18.47   | 20.3    | 12.12   | 11.1    | 2.33E-07  | -1.56861  |
| KLHL15     | Klhl15      | 5.33    | 4.48    | 3.94    | 3.19    | 0.004461  | -1.57161  |
| Mecp2      | Mecp2       | 11.43   | 11.05   | 7.89    | 7.38    | 7.47E-10  | -1.5729   |
| NFIX       | Nfix        | 8.34    | 7.36    | 5.07    | 4.23    | 0.000885  | -1.57421  |
| CMPK1      | Cmpk1       | 32.77   | 36.81   | 24.4    | 22.88   | 5.31E-12  | -1.57545  |
| PIK3C2A    | Plk3c2a     | 16.42   | 19.09   | 11.59   | 12.01   | 1.07E-11  | -1.57875  |
| 4931406P16Rik | 4931406P16Rik | 33.74 | 31.06   | 21.13   | 19.32   | 2.74E-10  | -1.58103  |
| LPP        | Lpp         | 9.71    | 10.3    | 6.88    | 6.2     | 1.52E-05  | -1.58565  |
| UBE2E1     | Ube2e1      | 7.91    | 6.98    | 4.99    | 5.23    | 0.016212  | -1.58698  |
| Ripk2      | Ripk2       | 12.39   | 12.95   | 8.44    | 7.89    | 9.73E-07  | -1.58755  |
| Crybg3     | Crybg3      | 16.36   | 17.34   | 11.21   | 11.42   | 1.97E-12  | -1.58786  |
| EIF4EBP2   | Eif4ebp2    | 6.47    | 5.53    | 4.48    | 3.61    | 2.08E-08  | -1.58925  |
| 2700081O15Rik | 2700081O15Rik | 8.13   | 9.19    | 6.39    | 5.64    | 0.000673  | -1.58947  |
| Gene-ID     | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC     |
|------------|-------------|---------|---------|---------|---------|---------|--------|
| TOMM20     | Tomm20      | 110.82  | 108.75  | 69.45   | 67.5    | 7.59E-11 | -1.59041 |
| SRP72      | Srp72       | 33.01   | 32.66   | 22.86   | 21.7    | 8.33E-13 | -1.59054 |
| SLC7A5     | Slc7a5      | 70.04   | 59.14   | 45.53   | 38.34   | 6.13E-14 | -1.59237 |
| UBE2A      | Ube2a       | 9.89    | 10.89   | 7.52    | 6.57    | 2.44E-06 | -1.59456 |
| Zmym4      | Zmym4       | 12.23   | 13.63   | 8.4     | 8.24    | 3.42E-06 | -1.59559 |
| Pi4kb      | Pi4kb       | 18.16   | 15.59   | 11.91   | 10.18   | 5.5E-08  | -1.59945 |
| Slc35a2    | Slc35a2     | 13.62   | 11.88   | 8.46    | 7.82    | 0.000473 | -1.60064 |
| AMMECR1L   | Ammecr1l    | 6.05    | 5.49    | 4       | 3.64    | 2.59E-05 | -1.60141 |
| ATP6V1A    | Atp6v1a     | 47.32   | 47.26   | 32.61   | 29.7    | 4.14E-13 | -1.60218 |
| GALNT2     | Galnt2      | 98.45   | 99.94   | 68.39   | 62.24   | 2.39E-13 | -1.60273 |
| EGLN1      | Egln1       | 42.02   | 37.03   | 27.32   | 24.24   | 3.07E-06 | -1.60433 |
| BACH1      | Bach1       | 6.08    | 6.4     | 4.29    | 3.78    | 3.91E-07 | -1.60483 |
| Trim2      | Trim2       | 20.83   | 21.83   | 13.7    | 13.54   | 4.85E-09 | -1.60619 |
| Arl8b      | Arl8b       | 38.71   | 41.91   | 26.35   | 26.23   | 8.39E-14 | -1.60826 |
| GCA        | Gca         | 7.6     | 11.1    | 7.07    | 5.27    | 4.79E-06 | -1.61074 |
| Irs1       | Irs1        | 3.98    | 3.52    | 2.74    | 2.48    | 8.44E-08 | -1.61435 |
| A830080D01Rik | A830080D01Rik | 6.55   | 6.85    | 5.25    | 3.75    | 0.000132 | -1.61547 |
| Mmgt1      | Mmgt1       | 25.62   | 28.08   | 17.22   | 17.92   | 5.22E-14 | -1.6161 |
| TFG        | Tfg         | 40.2    | 38.78   | 25.43   | 25.15   | 1.56E-11 | -1.61817 |
| XIAP       | Xiap        | 7.43    | 8.47    | 5.55    | 5.29    | 9.73E-09 | -1.6186 |
| Twistnb    | Twistnb     | 38.83   | 43.53   | 27.58   | 26.08   | 4.93E-11 | -1.6193 |
| Sh3pxd2a   | Sh3pxd2a    | 7.33    | 6.89    | 4.63    | 4.38    | 2.51E-09 | -1.61991 |
| RAB31      | Rab31       | 35.73   | 35.24   | 23.37   | 22.86   | 1.96E-14 | -1.62097 |
| TMEM9      | Tmem9       | 39.84   | 37.12   | 24.88   | 24.21   | 2.69E-10 | -1.62282 |
| RAP2C      | Rap2c       | 7.64    | 7.92    | 5.33    | 4.98    | 3.89E-06 | -1.6231 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC     |
|---------|-------------|---------|---------|---------|---------|---------|-------|
| GALC    | Galc        | 5.01    | 4.56    | 3.41    | 3.04    | 5.88E-07 | -1.62367 |
| IMPAD1  | Impad1      | 31.65   | 33.67   | 22.66   | 20.94   | 4.81E-11 | -1.62448 |
| SCHIP1  | Schip1      | 26.25   | 25.75   | 16.49   | 16.6    | 6.22E-10 | -1.6253  |
| TOMM5   | Tomm5       | 141.74  | 151.53  | 96.69   | 92.81   | 1.5E-11  | -1.63273 |
| FNIP1   | Fnip1       | 14.33   | 17.15   | 10.3    | 10.16   | 5.33E-13 | -1.63562 |
| Plekhm3 | Plekhm3     | 2.39    | 2.63    | 1.49    | 1.89    | 0.005431 | -1.6357  |
| ERRFI1  | Errfi1      | 3.94    | 3.49    | 2.55    | 2.17    | 3.41E-05 | -1.63597 |
| Mex3a   | Mex3a       | 3.6     | 3.57    | 2.34    | 2.11    | 7.18E-05 | -1.63658 |
| PAICS   | Paics       | 117.49  | 118.88  | 76.48   | 73.25   | 5.24E-11 | -1.64039 |
| SLC19A2 | Slc19a2     | 21.57   | 21.29   | 14.93   | 13.32   | 2.54E-12 | -1.64701 |
| Prkacb  | Prkacb      | 17.79   | 16.58   | 11.9    | 10.44   | 2.43E-13 | -1.64979 |
| Csrp2   | Csrp2       | 167.97  | 177.96  | 109.23  | 110.02  | 0       | -1.65002 |
| SPRED2  | Spred2      | 2.13    | 1.71    | 1.34    | 1.21    | 0.042252 | -1.65251 |
| Nr2f2   | Nr2f2       | 9.74    | 9.19    | 5.54    | 5.08    | 1.06E-05 | -1.65301 |
| TRAPPC2 | Trappc2     | 12.5    | 12.4    | 7.82    | 8.42    | 1.31E-05 | -1.65854 |
| Plxna4  | Plxna4      | 1.68    | 1.62    | 1.57    | 1.46    | 0.000223 | -1.66056 |
| RAB35   | Rab35       | 25.26   | 22.67   | 15.88   | 13.71   | 1.2E-12  | -1.66082 |
| ERI3    | Eri3        | 37.47   | 35.56   | 22.12   | 21.64   | 4.5E-09  | -1.67369 |
| LDLR    | Ldlr        | 40.2    | 35.42   | 25.02   | 22.04   | 0       | -1.67446 |
| JUN     | Jun         | 2.03    | 1.34    | 1.01    | 1.01    | 0.005807 | -1.67589 |
| RUFY2   | Rufy2       | 5.66    | 6.13    | 4.08    | 3.85    | 0.000618 | -1.6764 |
| LAMP2   | Lamp2       | 103.98  | 108.62  | 66.13   | 66.29   | 1.02E-11 | -1.67751 |
| CYTH3   | Cyth3       | 19.8    | 19.03   | 12.07   | 11.61   | 2.73E-13 | -1.67915 |
| Ikrf2   | Ikrf2       | 1.1     | 1.2     | 0.69    | 0.72    | 0.001823 | -1.68979 |
| Cdk16   | Cdk16       | 35.29   | 33.88   | 23.01   | 21.72   | 3.84E-14 | -1.69075 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value   | FC       |
|---------|-------------|---------|---------|---------|---------|-----------|----------|
| Mkl2    | Mkl2        | 6.06    | 6.01    | 3.86    | 3.62    | 5.48E-07  | -1.69218 |
| Naa50   | Naa50       | 33.33   | 33.99   | 21.61   | 20.84   | 4.6E-13   | -1.69494 |
| Frmd4a  | Frmd4a      | 4.51    | 4.72    | 2.62    | 2.18    | 2.74E-05  | -1.6966  |
| IKBIP   | Ikbip       | 21.45   | 22.52   | 12.85   | 14.54   | 2.97E-07  | -1.69899 |
| CDR2    | Cdr2        | 15.65   | 15.82   | 9.77    | 9.32    | 5.38E-12  | -1.70075 |
| STAG2   | Stag2       | 46.3    | 54.01   | 31.89   | 31.82   | 5.11E-15  | -1.70334 |
| Dmd     | Dmd         | 7.78    | 9.14    | 4.81    | 4.19    | 3.64E-05  | -1.70396 |
| Hspa13  | Hspa13      | 11.5    | 12.05   | 7.49    | 7.69    | 8.53E-11  | -1.70417 |
| GSPT1   | Gspt1       | 41.69   | 42.6    | 27.61   | 25.77   | 1.61E-13  | -1.7067  |
| STAT5B  | Stat5b      | 11.09   | 10.45   | 6.5     | 6.5     | 5.52E-11  | -1.70987 |
| Psip1   | Psip1       | 87.53   | 96.23   | 55.42   | 55.32   | 7.25E-12  | -1.7109  |
| Itpr1   | Itpr1       | 28.67   | 28.79   | 18.38   | 16.61   | 0         | -1.71192 |
| Rab21   | Rab21       | 35.76   | 34.02   | 17.19   | 15.04   | 0.000493  | -1.71228 |
| Acp1    | Acp1        | 95.3    | 100.97  | 59.48   | 59.12   | 3.84E-14  | -1.71339 |
| Apoo    | Apoo        | 76.49   | 84.97   | 53.07   | 53.84   | 9.77E-14  | -1.71469 |
| Ndst1   | Ndst1       | 23.36   | 21.15   | 14.5    | 12.3    | 5.86E-08  | -1.71634 |
| POLA1   | Pola1       | 41.46   | 45.01   | 32.43   | 30.51   | 0         | -1.71639 |
| DLG1    | Dlg1        | 32.41   | 33.37   | 23.17   | 25.73   | 1.29E-13  | -1.71747 |
| ZBTB33  | Zbtb33      | 8.39    | 9.24    | 5.42    | 5.05    | 7.72E-09  | -1.7286  |
| KDM5B   | Kdm5b       | 6.55    | 6.41    | 4.21    | 3.98    | 2.86E-11  | -1.72932 |
| Lats2   | Lats2       | 6.67    | 5.83    | 3.78    | 3.28    | 1.97E-07  | -1.73043 |
| ZMIZ1   | Zmiz1       | 10.76   | 9.77    | 6.62    | 5.83    | 1.86E-11  | -1.73058 |
| Vbp1    | Vbp1        | 67.95   | 75.95   | 43.8    | 45.05   | 0         | -1.73124 |
| Zfp532  | Zfp532      | 7.66    | 6.29    | 4.24    | 3.67    | 1.12E-05  | -1.73171 |
| VCL     | Vcl         | 126.18  | 123.17  | 78.02   | 71.58   | 1.66E-11  | -1.74043 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value  | FC    |
|---------|-------------|---------|---------|---------|---------|----------|-------|
| IFIT2   | Ifit2       | 11.51   | 14.09   | 7.05    | 7.64    | 1.64E-11 | -1.75064 |
| Setd7   | Setd7       | 19.95   | 21.89   | 12.93   | 11.91   | 0        | -1.7511 |
| Ckap4   | Ckap4       | 33.09   | 31.33   | 19.45   | 17.94   | 0        | -1.75975 |
| Hear5a  | Hear5a      | 10.61   | 11.03   | 6.66    | 6.16    | 5.22E-14 | -1.76253 |
| Trim62  | Trim62      | 0.94    | 0.69    | 0.54    | 0.39    | 0.03871  | -1.76904 |
| AGPAT9  | Agpat9      | 11.77   | 12.28   | 7.43    | 7.09    | 5.67E-09 | -1.77136 |
| WDR1    | Wdr1        | 154.09  | 147.22  | 89.39   | 85.21   | 0        | -1.77585 |
| INPP5B  | Inpp5b      | 12.02   | 11.85   | 7.75    | 7.04    | 9.61E-10 | -1.77643 |
| CAV1    | Cav1        | 60.28   | 58.51   | 34.47   | 33.86   | 0        | -1.79023 |
| BC030336| BC030336    | 9.09    | 9.23    | 6.4     | 6.46    | 1.92E-05 | -1.79306 |
| INSIG1  | Insig1      | 166.65  | 179.17  | 104.57  | 98.63   | 0        | -1.79329 |
| SPIN4   | Spin4       | 2.32    | 2.45    | 1.49    | 1.36    | 1.41E-06 | -1.79965 |
| SMC1A   | Smc1a       | 63.69   | 71.73   | 37.26   | 39.48   | 0        | -1.8184 |
| SLC36A1 | Slc36a1     | 4.49    | 4.77    | 2.78    | 2.39    | 3.9E-08  | -1.82 |
| SORT1   | Sort1       | 49.88   | 51.69   | 29.61   | 27.84   | 0        | -1.82339 |
| Arcn1   | Arcn1       | 112.53  | 118.83  | 70.52   | 64.3    | 0        | -1.82662 |
| Tln1    | Tln1        | 39.34   | 35.31   | 22.84   | 21.15   | 0        | -1.84005 |
| OAT     | Oat         | 179.93  | 173.72  | 101.65  | 98.84   | 0        | -1.84154 |
| Ppp1r12b| Ppp1r12b    | 32.21   | 30.99   | 18.82   | 17.08   | 0        | -1.84404 |
| SPG20   | Spg20       | 27.73   | 29.99   | 16.59   | 16.08   | 0        | -1.84598 |
| Tsc22d1 | Tsc22d1     | 118.64  | 112.45  | 65.37   | 63.94   | 0        | -1.85556 |
| MORC4   | Morc4       | 12.05   | 12.14   | 7.47    | 6.92    | 6.42E-13 | -1.85675 |
| HSP90AB1| Hsp90ab1    | 257.88  | 246.79  | 145.76  | 131.05  | 0        | -1.87936 |
| COL4A5  | Col4a5      | 61.15   | 60.3    | 33.78   | 32.46   | 0        | -1.88061 |
| DENND4C | Dennd4c     | 13.43   | 14.22   | 8.75    | 8.28    | 0        | -1.88198 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC |
|---------|-------------|---------|---------|---------|---------|---------|-----|
| PITPNA  | Pitpna      | 55.09   | 57.68   | 32.67   | 30.91   | 0       | -1.90704 |
| Snx30   | Snx30       | 9.07    | 9.01    | 5       | 4.9     | 0       | -1.90797 |
| CCDC112 | Ccdc112     | 2.01    | 2.36    | 1.26    | 1.12    | 2.48E-05 | -1.9158 |
| ZYG11B  | Zyg11b      | 14.42   | 15.63   | 8.24    | 8.24    | 0       | -1.91817 |
| ANKRD52 | Ankrd52     | 5.94    | 5.36    | 3.33    | 3.18    | 3.41E-13 | -1.9197 |
| CCDC50  | Ccdc50      | 24.36   | 27.48   | 16.06   | 16.46   | 0       | -1.92339 |
| SLC44A1 | Scl44a1     | 12.53   | 13.64   | 7.36    | 6.85    | 1.4E-12  | -1.95433 |
| Mospd2  | Mospd2      | 16.18   | 17.92   | 9.53    | 9.4     | 6.83E-13 | -1.95638 |
| Tmeff2  | Tmeff2      | 3.16    | 2.93    | 1.29    | 1.68    | 6.66E-07 | -1.95828 |
| NDRG1   | Ndrg1       | 8.32    | 7.23    | 4.03    | 3.96    | 1.04E-12 | -1.9659 |
| KLHL29  | Klhl29      | 4.25    | 3.83    | 2.31    | 1.92    | 4.72E-13 | -1.96929 |
| MGST3   | Mgst3       | 35      | 32.01   | 18.06   | 16.83   | 0       | -1.9713 |
| Snx13   | Snx13       | 38.87   | 44.87   | 22.39   | 21.49   | 0       | -2.00464 |
| TMEM64  | Tmem64      | 15.34   | 14.72   | 8.23    | 7.86    | 0       | -2.00562 |
| ANKIB1  | Ankib1      | 27.42   | 27.76   | 14.73   | 14.08   | 0       | -2.01475 |
| Pard3b  | Pard3b      | 10.97   | 12.01   | 6.08    | 6.25    | 0       | -2.02054 |
| TRAM2   | Tram2       | 2.99    | 2.79    | 1.16    | 0.99    | 0.00041 | -2.02362 |
| RUSC2   | Rusc2       | 7.51    | 6.68    | 3.55    | 3.59    | 1.86E-11 | -2.03535 |
| Dcun1d4 | Dcun1d4     | 6.95    | 6.58    | 3.55    | 3.75    | 4.09E-12 | -2.04128 |
| SCARB2  | Scarb2      | 207.52  | 220.65  | 109.97  | 103.41  | 0       | -2.07525 |
| RHOB    | Rhob        | 75.82   | 64.36   | 35.96   | 33.73   | 0       | -2.08137 |
| TUFT1   | Tuft1       | 5.19    | 5.25    | 2.62    | 2.93    | 1.95E-08 | -2.08159 |
| PRELID2 | Prelid2     | 6.29    | 6.75    | 3.39    | 3.06    | 0.003366 | -2.08293 |
| NCEH1   | Nceh1       | 68.8    | 77.29   | 37.15   | 35.86   | 0       | -2.08947 |
| Gpr173  | Gpr173      | 3.38    | 3.05    | 2.15    | 1.89    | 0.000193 | -2.09985 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value   | FC    |
|---------|-------------|---------|---------|---------|---------|-----------|-------|
| Pik3cb  | Pik3cb      | 6.91    | 7.05    | 3.64    | 3.36    | 5.11E-15  | -2.11808 |
| MARCKSL1| Marcksl1    | 73.68   | 67.11   | 34.39   | 33.05   | 0         | -2.11902 |
| GNPNAT1 | Gnpnat1     | 5.82    | 6.94    | 3.52    | 3.1     | 0.000205  | -2.15141 |
| Atp11c  | Atp11c      | 10.91   | 13.17   | 6.13    | 5.91    | 3.83E-10  | -2.15405 |
| HYOU1   | Hyou1       | 240.27  | 217.74  | 114.26  | 100.75  | 0         | -2.15651 |
| ARHGEF3 | Arhgef3     | 2.59    | 2.78    | 1.32    | 1.15    | 8.23E-07  | -2.16115 |
| CDC16   | Cdc16       | 38.45   | 38.82   | 18.98   | 18.24   | 0         | -2.18035 |
| PLOD2   | Plod2       | 62.71   | 64.59   | 30.71   | 32.23   | 0         | -2.18216 |
| Kctd10  | Kctd10      | 67.33   | 62.02   | 31.36   | 30.15   | 0         | -2.19595 |
| Arhgap6 | Arhgap6     | 4.59    | 4.6     | 2.19    | 2.2     | 2.19E-10  | -2.21123 |
| CREB3L2 | Creb3l2     | 11.32   | 9.88    | 5.04    | 4.34    | 0         | -2.21712 |
| Prkca   | Prkca       | 14.53   | 13.29   | 6.74    | 6.24    | 0         | -2.22281 |
| Brwd3   | Brwd3       | 2.72    | 3.17    | 1.51    | 1.31    | 2.51E-11  | -2.23024 |
| NFI1B   | Nfib        | 42.19   | 44.53   | 22.02   | 19.28   | 0         | -2.25203 |
| CUL4B   | Cul4b       | 39.96   | 43.25   | 20.29   | 19.48   | 0         | -2.26224 |
| Rab21   | Rab21       | 35.76   | 34.02   | 17.19   | 15.04   | 0         | -2.27635 |
| PRMT6   | Prmt6       | 7.85    | 7.87    | 3.53    | 3.6     | 4.47E-13  | -2.29214 |
| SWAP70  | Swap70      | 23.33   | 21.95   | 10.71   | 9.86    | 0         | -2.31066 |
| Prkg1   | Prkg1       | 14.86   | 14.53   | 11.86   | 10.12   | 1.74E-11  | -2.31209 |
| SPATS2L | Spats2l     | 9.5     | 9.92    | 3.59    | 4.36    | 3.47E-11  | -2.34991 |
| FOXC1   | Foxc1       | 1.3     | 1.07    | 0.62    | 0.47    | 0.00021   | -2.35297 |
| DCBLD2  | Dcbld2      | 47.45   | 48.7    | 23.79   | 22.85   | 0         | -2.3683  |
| Pak3    | Pak3        | 6.16    | 6.13    | 2.48    | 2.11    | 2.05E-07  | -2.36897 |
| ZFHX3   | Zfhx3       | 4.08    | 3.99    | 1.82    | 1.65    | 0         | -2.37265 |
| ADCY9   | Adcy9       | 2.01    | 1.84    | 0.96    | 0.95    | 4.01E-06  | -2.38993 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC  |
|---------|-------------|---------|---------|---------|---------|---------|------|
| POLE3   | Pole3       | 27.77   | 28.99   | 10.65   | 10.04   | 1.78E-12 | -2.41257 |
| STX17   | Stx17      | 8.94    | 9.91    | 4.31    | 3.99    | 5.69E-14 | -2.41619 |
| Slc30a4 | Slc30a4    | 17.34   | 18.84   | 8.25    | 7.59    | 3.84E-14 | -2.41631 |
| Fhod1   | Fhod1      | 6.27    | 5.87    | 3.58    | 2.59    | 0       | -2.46414 |
| Nuak1   | Nuak1      | 5.11    | 4.55    | 1.98    | 1.79    | 3.84E-14 | -2.49591 |
| Rgl1    | Rgl1       | 14.4    | 13.83   | 6.23    | 5.58    | 0       | -2.49685 |
| UBASH3B | Ubash3b    | 3.21    | 2.49    | 1.44    | 0.99    | 1.73E-08 | -2.52443 |
| Akt3    | Akt3       | 8.69    | 10.55   | 3.55    | 3.53    | 0       | -2.53254 |
| Fam120c | Fam120c    | 3.42    | 3.41    | 1.58    | 1.44    | 0       | -2.53544 |
| Cadm1   | Cadm1      | 11.88   | 10.99   | 5.75    | 4.4     | 0       | -2.55293 |
| Fgd1    | Fgd1       | 10.5    | 8.82    | 4.32    | 3.79    | 0       | -2.55359 |
| Nrip1   | Nrip1      | 3.14    | 3.62    | 1.52    | 1.3     | 7.85E-12 | -2.5689 |
| RAB11FIP1 | Rab11fip1 | 11.43   | 10.32   | 4.43    | 4.1     | 0       | -2.64192 |
| CNN3    | Cnn3       | 124.81  | 118     | 48.86   | 45.21   | 0       | -2.66303 |
| Pfn2    | Pfn2       | 37.29   | 36.47   | 14.83   | 14.85   | 0       | -2.66453 |
| EIF5A2  | EIF5A2     | 18.22   | 20.32   | 8.09    | 7.44    | 0       | -2.67225 |
| Klf3    | Klf3       | 3.95    | 3.37    | 1.51    | 1.4     | 8.26E-13 | -2.68352 |
| Rps6ka3 | Rps6ka3    | 11.29   | 11.46   | 4.91    | 4.5     | 0       | -2.71827 |
| LRRC58  | Lrrc58     | 14.7    | 14.27   | 6.33    | 5.42    | 0       | -2.72137 |
| Zfp704  | Zfp704     | 2.76    | 2.88    | 1.16    | 0.95    | 0       | -2.73114 |
| Mtss1l  | Mtss1l     | 4.01    | 3.7     | 1.69    | 1.25    | 1.16E-10 | -2.75063 |
| LIMA1   | Lima1      | 11.24   | 11.2    | 4.38    | 3.94    | 0       | -2.75722 |
| Gem     | Gem        | 8.82    | 9.48    | 2.92    | 3.69    | 0       | -2.84983 |
| DUSP6   | Dusp6      | 7.74    | 6.84    | 3.06    | 2.4     | 0       | -2.877 |
| Efna1   | Efna1      | 14.96   | 15.39   | 5.59    | 5.07    | 0       | -2.88808 |
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC       |
|---------|-------------|---------|---------|---------|---------|---------|---------|
| TM4SF1  | Tm4sf1      | 13.66   | 12.6    | 4.53    | 5.05    | 0       | -2.94195|
| Nrp2    | Nrp2        | 49.35   | 49.03   | 17.63   | 16.25   | 0       | -3.03079|
| Xkr4    | Xkr4        | 0.48    | 0.61    | 0.24    | 0.19    | 0.002415| -3.09353|
| SRPX    | Srpx        | 11.51   | 10.13   | 3.33    | 3.76    | 0       | -3.18586|
| Frmd4b  | Frmd4b      | 2.4     | 2.1     | 1.01    | 1.75    | 1.05E-06| -3.19252|
| Slc4a4  | Slc4a4      | 16.48   | 15.76   | 5.54    | 4.65    | 0       | -3.27047|
| PLS3    | Pls3        | 26.38   | 27.43   | 8.17    | 8.01    | 0       | -3.44485|
| PSD3    | Psd3        | 8.72    | 9.77    | 7.73    | 6.86    | 0.023699| -3.45772|
| ABCA1   | Abca1       | 36.71   | 35.49   | 11.15   | 10.21   | 0       | -3.63669|
| Plcl1   | Plcl1       | 1.46    | 1.4     | 0.42    | 0.43    | 2.27E-11| -3.64586|
| MAMLD1  | Mamld1      | 2.48    | 2.23    | 0.78    | 0.53    | 1.91E-09| -3.7578 |
| FSTL1   | Fstl1       | 257.3   | 257.88  | 72.93   | 72.18   | 0       | -3.79234|
| SERPINE1| Serpine1    | 7.24    | 6.13    | 2       | 1.59    | 0       | -3.92088|
| DLG5    | Dlg5        | 6.77    | 6.38    | 1.85    | 1.02    | 0       | -4.0172 |
| Prkar2b | Prkar2b     | 5.41    | 6.05    | 1.44    | 1.45    | 0       | -4.05181|
| LPAR1   | Lpar1       | 4.77    | 4.45    | 1.25    | 0.98    | 0       | -4.12137|
| ETV5    | Etv5        | 8.18    | 7.12    | 1.99    | 1.81    | 0       | -4.1448 |
| Col4a3  | Col4a3      | 22.91   | 23.71   | 6       | 5.02    | 0       | -4.33234|
| Fam107b | Fam107b     | 12.99   | 14.14   | 3.13    | 3.35    | 0       | -4.37158|
| CLTA    | Clta        | 221.41  | 208.5   | 52.57   | 48.56   | 0       | -4.40659|
| HS3ST3B1| Hs3st3b1    | 3.84    | 3.4     | 0.94    | 0.81    | 0       | -4.44233|
| Nxph1   | Nxph1       | 2.25    | 2.5     | 0.64    | 0.51    | 4.04E-07| -4.60035|
| RUNX1   | Runx1       | 5.33    | 5.11    | 1.24    | 1.01    | 0       | -4.89122|
| Mras    | Mras        | 7.55    | 8.11    | 1.61    | 1.87    | 0       | -4.98725|
| Cyp1b1  | Cyp1b1      | 1.03    | 1.2     | 0.21    | 0.18    | 2.38E-10| -5.18351|
| Gene-ID | Gene Symbol | MG33304 | MG33303 | MG33306 | MG33305 | q_value | FC   |
|--------|-------------|---------|---------|---------|---------|---------|------|
| KDR    | Kdr         | 2.67    | 2.57    | 0.53    | 0.53    | 0       | -5.20678 |
| Hs3st1 | Hs3st1      | 3.23    | 2.87    | 0.29    | 0.37    | 0       | -5.50743 |
| SMARCA1| Smarca1     | 7.53    | 8.33    | 1.14    | 1.6     | 0       | -5.68076 |
| Ppap2b | Ppap2b      | 22.11   | 20.83   | 4.17    | 3.57    | 0       | -5.79803 |
| CDK5R1 | Cdk5r1      | 10.35   | 8.94    | 1.75    | 1.74    | 0       | -5.80345 |
| Rasgef1b| Rasgef1b  | 11.89   | 12.37   | 2.42    | 2       | 0       | -5.99168 |
| ADM    | Adm         | 142.69  | 133.88  | 22.8    | 21.43   | 0       | -6.421 |
| IGFBP4 | Igfbp4      | 53.38   | 48.95   | 10.1    | 9.4     | 0       | -7.78608 |
| Reck   | Reck        | 6.19    | 5.09    | 0.78    | 0.71    | 0       | -8.12236 |
| Inhba  | Inhba       | 8.38    | 7.82    | 0.9     | 1.08    | 0       | -8.91328 |
| ANXA1  | Anxa1       | 0.67    | 0.73    | 0.3     | 0.11    | 0.000566 | -9.22248 |
| Kank1  | Kank1       | 2.87    | 2.73    | 0.32    | 0.37    | 0       | -10.5403 |
| MYOF   | Myof        | 5.7     | 5.39    | 0.58    | 0.5     | 0       | -10.6167 |
| Rims3  | Rims3       | 1.01    | 0.83    | 0.09    | 0.08    | 1.02E-13 | -10.6999 |
| PEG10  | Peg10       | 11.18   | 9.84    | 1.15    | 1.08    | 0       | -10.9477 |
| THBS1  | Thbs1       | 0.64    | 0.56    | 0.06    | 0.05    | 2.99E-10 | -17.8662 |
| Adamts8| Adamts8     | 13.8    | 11.29   | 0.61    | 0.33    | 0       | -28.3337 |
| Fat3   | Fat3        | 3.46    | 3.48    | 0.11    | 0.13    | 0       | -29.2762 |
| PMEPA1 | Pmepa1      | 4.79    | 4.95    | 0.13    | 0.06    | 3.03E-08 | -388.792 |
**Supplementary Table 2. miR-200 family highly influence focal adhesion pathway.** Pathways analysis of miR-200 family targets genes showed a remarkable influence of miR-200 family to the focal adhesion pathway.

| p-value  | q-value   | pathway                      | source | external_id   | members_input_overlap | members_input_overlap_geneids | size | effective_size |
|----------|-----------|------------------------------|--------|---------------|-----------------------|-------------------------------|------|----------------|
| 2,51E-10 | 8,42E-09  | Membrane Trafficking         | Reactome | R-HSA-199991  | CTTN; PUM1; DENND5A;   | 23011; 130340; 5286; 5869;     |      |                |
|          |           |                              |        |               | PRKAG2; CPD; KIF26B;   | 10092; 9698; 90411; 288; 51762;|      |                |
|          |           |                              |        |               | AKT3; CLTA; AP1S2;     | 950; 1362; 10000; 9265; 6399;  |      |                |
|          |           |                              |        |               | AP1S3; DCTN3; CHMP5;   | 9135; 6272; 5537; 10254; 2590; |      |                |
|          |           |                              |        |               | RAB8B; RAB35; SEC23A;  | 5872; 10971; 51422; 55014;     |      |                |
|          |           |                              |        |               | RAB31; STAM2;          | YWHAQ; PPP6C;                  |      |                |
|          |           |                              |        |               | SEC31A; RABEP1;        | 8905; 3267; 11021; 10342;      |      |                |
|          |           |                              |        |               | RAB13; RAB12;          | 201475; 51272; 1783; 55667;    |      |                |
|          |           |                              |        |               | DENND4C; RAB5B;        | 10484; 2017; 2665; 10802; 372; |      |                |
|          |           |                              |        |               | ARPC5; KDELR2;         | 27333; 11014; 51510; 64746;    |      |                |
|          |           |                              |        |               | PIK3C2A; SEC24A;       | 55083; 143187; 9570; 23258;    |      |                |
|          |           |                              |        |               | DYNC1LI2; GDI2;        | 3949; 1211; 22872; 11031; 11258|      |                |
| Vesicle-mediated transport | Reactome | R-HSA-5653656 |
|---------------------------|----------|----------------|
| 2.55E-10                  | 8.42E-09 |                |

| Genes                                | 23011; 5286; 5869; 10092; 9698; 201475; 90411; 288; 10802; 950; 10000; 9265; 6399; 9135; 6272; 5537; 10254; 1362; 2590; 10971; 130340; 51422; 55014; 8905; 3267; 11021; 10342; 3949; 10808; 51272; 55667; 1783; 10484; 2017; 2665; 51762; 372; 27333; 11014; 51510; 64746; 55083; 143187; 9570; 23258; | 619 | 618 |
| Focal adhesion | KEGG | Gene ID | Pathway ID |
|---------------|------|---------|------------|
| Homo sapiens (human) | path:hsa04510 | PIK3C2A; SEC24A; DYNC1LI2; GDI2; MCFD2; CYTH3; GOSR2; GALNT2; SEC23A; RAB21; BET1L; SCARB2; TFG; TRAPPC2; LDLR; ARCN1; ACBD3; ANK3; VTI1A; STX17; SORT1; AGFG1 | 5872; 1211; 22872; 10525; 11031; 11258 |
| 4.18E-09 | 9.20E-08 | 201 | 200 |
| ID     | P-value | Pathway/Database | Details                                                                 | Gene IDs | 121 | 121 |
|--------|---------|------------------|------------------------------------------------------------------------|----------|-----|-----|
| 1,27E-06 | 2,09E-05 | Neurotrophin signaling pathway - Homo sapiens (human) | KEGG path:hsa04722 | GSK3B; PTEN; PAK3, ITGA1 | 6197; 8767; 10818; 3654; 3656; 3667; 6272; 3725; 5781; 5291; 5295; 10000; 5908; 2932; 1398; 1399 | 121 | 121 |
| 2,02E-06 | 2,33E-05 | Signaling by PDGF | Reactome R-HSA-186797 | CRKL; RAP1B; SPRED2; FRS2; PRKAR2B; CRK; THBS1; IQGAP1; IRS1; PIK3CB; TLN1; PIK3R1; DUSP6; PIP4K2B; PTEN; PRKCA; VCL; SPRED1; COL4A5; COL4A3; ITPR1; PTPN12; PTPN11 | 3667; 5567; 5578; 5577; 115; 1848; 10818; 200734; 7057; 1398; 5295; 5782; 5781; 8396; 5908; 5728; 5291; 7414; 1399; 8826; 6777; 7094; 2932; 161742; 1287; 10000; 3708; 1285 | 331 | 330 |
| p-value   | q-value   | pathway                                      | source   | external_id   | members_input_overlap                                                                 | members_input_overlap_geneids                                                                 | size | effective_size |
|----------|-----------|----------------------------------------------|----------|---------------|----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|------|----------------|
| 2,12E-06 | 2,33E-05  | Proteoglycans in cancer - Homo sapiens (human) | KEGG     | path:hsa05205 | IGF1R; CTTN; PIK3R1; ANK3; PIK3CB; THBS1; PTPN11; PPP1CC; RPS6KB1; MRAS; E2R; FRS2; PRKCA; AKT3; PPP1R12B; PRKACB; ITPR1; CAV2; IQGAP1; KDR; CAV1 | 7430; 4660; 6198; 10818; 10000; 8826; 3708; 5781; 5291; 5295; 3791; 5567; 22808; 288; 857; 858; 5501; 7057; 3480; 5578; 2017 | 205  | 205            |
| 1,57E-05 | 0,000148  | Signalling by NGF                            | Reactome | R-HSA-166520  | CRKL; SPRED1; SPRED2; FRS2; AKT3; CLTA; CRK; IQGAP1; PIK3CB; ARHGEF3; TLN1; ADCY9; PIK3R1; IRAK1; DUSP3 | 5578; 1848; 9828; 200734; 5291; 8826; 8767; 7094; 10000; 3708; 3667; 5567; 5577; 1398; 5728; 6197; 2245; 7414; 8396; 10818; 161742; 3654; 1399; 1845; | 433  | 429            |
|   |   |   |   |   |
|---|---|---|---|---|
| 2,14E-05 | 0,000169 | ER to Golgi Anterograde Transport | Reactome | R-HSA-199977 |
|   |   |   |   |   |
| 2,69E-05 | 0,000169 | mTOR signaling pathway - Homo sapiens (human) | KEGG | path:hsa04150 |

**ER to Golgi Anterograde Transport**

| Gene Symbols | P-Values |
|--------------|----------|
| PIP4K2B; FGD1; ARHGEF17; PRKCA; VCL; RAP1B; PRKAR2B; ITPR1; RPS6KA3; DUSP6; PTPN11; IRS1; GSK3B; PTEN; RIPK2; PRKACB | 50650; 5295; 5781; 5908; 1211; 2932; 115 |

**mTOR signaling pathway - Homo sapiens (human)**

| Gene Symbols | P-Values |
|--------------|----------|
| ULK2; FNIP1; IGF1R; RPS6KA3; ATP6V1A; SGK1; PRKCA; PIK3CB; SLC7A5; RPS6KB1; IRS1; | 523; 6197; 6198; 3667; 5728; 5291; 96459; 10000; 6446; 5295; 2932; 6009; 3480; 5578; 8140; 9706 |
| p-value  | q-value  | pathway     | source      | external_id   | members_input_overlap                      | members_input_overlap_geneids                                                                 | size | effective_size |
|---------|----------|-------------|-------------|---------------|---------------------------------------------|-----------------------------------------------------------------------------------------------|------|----------------|
| 2.73E-05 | 0.000169 | Axon guidance | Reactome    | R-HSA-422475  | RAP1B; SPRED2; FRS2; CLTA; GSK3B; PITPNA; IQGAP1; DLG1; TNL1; HSP90AB1; CDK5R1; DUSP6; KDR; DPYSL2; PRKCA; VCL; EFNA1; SPRED1; COL4A5; COL4A3; ARPC5; RHOB; NRP1; NRP2; RPS6KA3; PTPN11; IRS1; EZR; PLXNA4; PFN2; ANK3; PRKACB; PAK3 | 5578; 7430; 1848; 1739; 10092; 200734; 1287; 8829; 288; 8826; 7094; 1808; 1942; 3667; 5567; 3326; 1285; 6197; 5063; 5306; 5217; 10818; 388; 8828; 3791; 91584; 8851; 5781; 5908; 7414; 1211; 2932; 161742 | 487  | 484            |
| 2,82E-05 | 0,000169 | NGF signalling via TRKA from the plasma membrane | Reactome | R-HSA-187037 | CRKL; RAP1B; SPRED2; FRS2; PRKAR2B; CLTA; CRK; GSK3B; IQGAP1; PIK3CB; TLN1; PIK3R1; DUSP6; DUSP3; PIP4K2B; PRKCA; VCL; SPRED1; ITPR1; RPS6KA3; PTPN11; IRS1; ADCY9; PTEN; AKT3; PRKACB | 3667; 5567; 5578; 8396; 1399; 5577; 1845; 5728; 1848; 10818; 200734; 115; 5781; 1398; 5295; 1211; 5908; 6197; 5291; 7414; 8826; 7094; 2932; 161742; 10000; 3708 |
| 3,60E-05 | 0,000198 | Insulin signalling pathway - Homo sapiens (human) | KEGG | path:hsa04910 | PRKAG2; ACACA; PPP1CC; CRKL; PIK3CB; MKNK1; RPS6KB1; IRS1; GSK3B; AKT3; PIK3R1; PRKACB; PRKAR2B; CRK; RHEB | 31; 6198; 3667; 5291; 5295; 8569; 51422; 10000; 2932; 1398; 1399; 6009; 5501; 5567; 5577 |

| 340 | 339 |
| 4.00E-05 | 0.000203 | Downstream signal transduction | Reactome | R-HSA-186763 | CRKL; RAP1B; SPRED2; FRS2; PRKAR2B; CRK; IQGAP1; IRS1; PIK3CB; TLN1; PIK3R1; DUSP6; PIP4K2B; PTEN; PRKCA; VCL; SPRED1; ITPR1; PTPN11; ADCY9; GSK3B; STAT5B; AKT3; PRKACB | 3667; 5567; 5578; 5577; 115; 1848; 10818; 200734; 1398; 5295; 5781; 8396; 5908; 5728; 5291; 7414; 1399; 8826; 6777; 7094; 2932; 161742; 10000; 3708 | 307 | 306 |
| 7.37E-05 | 0.000348 | Signaling by EGFR | Reactome | R-HSA-177929 | RAP1B; SPRED2; FRS2; AKT3; IQGAP1; IRS1; STAM2; TLN1; PIK3R1; DUSP6; PIP4K2B; PRKCA; VCL; SPRED1; ITPR1; LRIG1; PTPN12; PTPN11; ADCY9; GSK3B; PTEN; PRKAR2B; PRKACB; PIK3CB | 3667; 5567; 5578; 5577; 115; 5728; 10254; 1848; 10818; 200734; 5295; 5782; 5781; 8396; 5908; 5291; 7414; 8826; 7094; 2932; 161742; 10000; 3708; 26018 | 319 | 318 |
| P-value | FDR-corrected p-value | Pathway                                | Organism          | KEGG Pathway            | Genes                                                                 | Gene IDs                        |
|---------|-----------------------|----------------------------------------|-------------------|-------------------------|-----------------------------------------------------------------------|---------------------------------|
| 0.000137 | 0.000599              | Rap1 signaling pathway - Homo sapiens  | Human             | KEGG path:hsa04015     | MRAS; LPAR1; IGF1R; CRKL; PRKCA; PIK3CB; ADCY9; EFNA1; TNL1; PPFN2; AKT3; RAP1B; PIK3R1; CRK; THBS1; GNAI3; KDR; PRKD3 | 5291; 7094; 5217; 115; 23683; 5295; 3791; 10000; 5908; 22808; 2773; 7057; 1902; 1398; 1399; 3480; 1942; 5578 |
| 0.000145 | 0.000599              | Regulation of actin cytoskeleton - Homo sapiens | Human | KEGG path:hsa04810     | ARPC5; FGD1; PIK3R1; CRKL; EZR; PIK3CB; PPP1CC; VCL; MRAS; GNG12; PPFN2; CFL2; PPP1R12B; SSH1; CRK; PAK3; IQGAP1; PIP4K2B | 5217; 1073; 7430; 4660; 8826; 55970; 5291; 5295; 2245; 8396; 22808; 10092; 1398; 1399; 5501; 54434; 7414; 5063 |
| 0.000154 | 0.000599              | Pathways in cancer - Homo sapiens      | Human             | KEGG path:hsa05200     | CRKL; XIAP; AKT3; EDNRA; CRK; GNAI3; PTEN; PIK3CB; JUN; GNG12; HSP90AB1; PIK3R1; IGF1R; PRKCA; | 10342; 115; 331; 405; 6777; 55970; 2773; 54583; 861; 2932; 5291; 5295; 1285; 1287; 1387; 1398; 1399; 3480; 5567; 5578; |
| p-value    | q-value | pathway                        | source  | external_id   | members_input_overlap            | members_input_overlap_geneids                        | size | effective_size |
|-----------|---------|--------------------------------|---------|---------------|----------------------------------|----------------------------------------------------|------|----------------|
| 0.000226  | 0.000752 | Endocytosis - Homo sapiens (human) | KEGG    | path:hsa04144 | RAB35; IGF1R; RAB31; SPG20; ACAP2; STAM2; RAB5B; RAB11FIP1; ARPC5; PSD3; AGAP1; LDLR; CLTA; CHMP5; RABEP1; CYTH3; CAV2; ASAP1; KDR; CAV1 | 10254; 857; 9265; 23111; 50807; 1211; 3791; 5869; 11021; 11031; 23362; 51510; 858; 80223; 10092; 3949; 3480; 9135; 116987; 23527 | 260  | 260            |
| 0.000233  | 0.000752 | Transport to the Golgi and     | Reactome | R-HSA-948021  | SEC23A; TFG; TRAPPC2; ARCN1; SEC24A; GOSR2; ANK3; PPP6C; STX17; | 5537; 11014; 10484; 51272; 1783; 90411; 9570; 288; 55014; | 165  | 165            |
| Score | Gene | Protein | KEGG Pathway | Reactome Pathway | P-value | FDR |
|-------|------|---------|--------------|-----------------|---------|-----|
| 0.000233 | DYNC1LI2, DCTN3, KDEL2, MCFD2, BET1L, SEC31A | Protein processing in endoplasmic reticulum - Homo sapiens (human) | KEGG path: hsa04141 | RECK, UBE2B, RAD23B, CLSPN, SMAD7, MAP3K7, RIPK2, RHOT1, DCTN3, USP25, SEC31A, RAB8B, RAB35, SEC23A, RAB31, STM2, ADAMTS8, THBS1, PPP6C, PHC3, PTP4A2 | 22872; 10802; 372; 10342; 6399; 11258 | 0.000233 |
| 0.000239 | BAG2, SEL1L, DNAJA1, RAD23B, HSPH1, HSPA5, HYOU1, SEC31A, HSP90AB1, SEC24A, CAPN2, EDEM1, PLAA, CKAP4, SEC23A | Post-translational protein modification | Reactome R-HSA-597592 | RECK, UBE2B, RAD23B, CLSPN, SMAD7, MAP3K7, RIPK2, RHOT1, DCTN3, USP25, SEC31A, RAB8B, RAB35, SEC23A, RAB31, STM2, ADAMTS8, THBS1, PPP6C, PHC3, PTP4A2 | 23011; 1605; 4092; 5277; 5869; 11095; 10735; 29761; 90411; 288; 5872; 6885; 51762; 8767; 5537; 10484; 10254; 2590; 7057; 80012; 55288; 5728; 55014; 51272; 1783; 7324; 56648; 6400; 1026 | 0.000239 |
| 0.000345 | 0.001036 | Signaling by VEGF | Reactome | R-HSA-194138 | IQGAP1; ITPR1; PRKCA; PIK3CB; VCL; IRS1; SPRED2; FRS2; PAK3; AKT3; RAP1B; TLN1; PIK3R1; PRKACB; NRP2; | 10000; 8828; 5063 | 290 | 289 |
| CRK; DUSP6; SPRED1; NRP1; KDR; CAV1 |
|-----------------------------------|
| IQGAP1; ITPR1; PRKCA; VCL; PTPN11; GSK3B; FRS2; ADCY9; SPRED2; IRS1; AKT3; PTEN; PRKAR2B; RAP1B; TLN1; PIK3R1; PRKACB; DUSP6; SPRED1; PIK3CB; PIP4K2B |
| 3667; 5567; 5578; 5577; 115; 1848; 10818; 200734; 5295; 5781; 8396; 5908; 5728; 5291; 7414; 8826; 7094; 2932; 161742; 10000; 3708 |

| 0.000865 | 0.002482 | DAP12 signaling | Reactome | R-HSA-2424491 |
|----------|----------|-----------------|----------|----------------|

| 0.001197 | 0.003292 | PI3K-Akt signaling pathway - Homo sapiens (human) | KEGG | path:hsa04151 |
|----------|----------|--------------------------------------------------|------|--------------|

| AKT3; MCL1; PIK3CB; YWHAQ; RPS6KB1; GNG12; THBS1; HSP90AB1; PIK3R1; KDR; IGF1R; PRKCA; EFNA1; COL4A5; COL4A3; RHEB; |
|--------------------------------------------------|------|--------------|

| 1285; 3326; 6198; 5728; 4170; 3667; 55970; 2932; 3791; 6009; 1287; 10000; 6446; 10971; 7057; 1902; 64764; 1942; 3480; 5578; 5291; 5295 |

| 311 | 310 |

| 341 | 340 |
| 0.001318 | Developmental Biology | Reactome | R-HSA-1266738 |
|----------|-----------------------|----------|----------------|
|          |                       |          | SGK1; IRS1; GSK3B; CREB3L2; PTEN; LPAR1 |
|          |                       |          | RAP1B; SPRED2; FRS2; AKT3; CLTA; GSK3B; PITPNA; IQGAP1; DLG1; TLN1; HSP90AB1; TSC22D1; MED13; CDK5R1; DUSP6; KDR; DPYSL2; PRKCA; TCF12; VCL; EFNA1; SPRED1; COL4A5; COL4A3; ARPC5; RHOB; NRP1; NRP2; RPS6KA3; PTPN11; IRS1; EZR; PLXNA4; DSP; PFN2; ANK3; PRKACB; CREBBP; PAK3 |
|          |                       |          | 5578; 1848; 1739; 10092; 200734; 8829; 288; 8826; 1808; 7094; 7430; 1942; 6938; 3667; 5567; 8848; 10000; 3326; 1285; 6197; 5908; 1287; 5063; 5306; 5217; 10818; 388; 1387; 8828; 9969; 3791; 91584; 8851; 1832; 5781; 7414; 1211; 2932; 161742 |
| 0.00336  |                       |          | 748 | 745 |
| Metabolism of proteins | Reactome | R-HSA-392499 |
|-----------------------|----------|--------------|
| RECK; UBE2B; RAD23B;  |          |              |
| VBP1; HSPA5; CLSPN;   |          |              |
| SMAD7; SEL1L;         |          |              |
| ADAMTS8; RIPK2;       |          |              |
| RHOT1; DCTN3; USP25;  |          |              |
| THBS1; SLC30A7;       |          |              |
| SEC31A; RAB8B; RAB35; |          |              |
| TOMM5; PMPCB;         |          |              |
| RAB31; STAM2; FKBPs9; |          |              |
| MAP3K7; GNG12;        |          |              |
| GNAI3; INHBA;         |          |              |
| DYNC1LI2; PPP6C; PHC3;|          |              |
| PTP4A2; RAB13; BET1L; |          |              |
| SMC1A; PIGA; GSPT1;   |          |              |
| GNPAT1; RAB5B;        |          |              |
| STAG2; RAB12; SENPs;  |          |              |
| UBE2E1; PARP1; UBA6;  |          |              |

|                  |          |              |
| 23011; 29761; 64841; 6885; |          |              |
| 401505; 6399; 10254; 3093; |          |              |
| 51272; 56648; 1974; 8434; 3309; |          |              |
| 142; 22872; 5887; 9512; 5869; |          |              |
| 11095; 55970; 5537; 63967; |          |              |
| 11021; 7411; 3624; 7319; 9570; |          |              |
| 10970; 148867; 11031; 10802; |          |              |
| 10484; 2590; 5728; 6731; 8073; |          |              |
| 10342; 2773; 201475; 372; |          |              |
| 55288; 3487; 11014; 288; 8243; |          |              |
| 7320; 9804; 1605; 4092; 5277; |          |              |
| 10735; 90411; 10238; 8767; |          |              |
| 5872; 7057; 80012; 55014; |          |              |
| 55236; 2935; 1783; 7324; 11328; |          |              |
| 6400; 51762; 7329; 205564; |          |              |
| 11258 |          |              |
| p-value | q-value | pathway | source | external_id | members_input_overlap | members_input_overlap_geneids | size | effective_size |
|---------|---------|---------|--------|-------------|-----------------------|-------------------------------|------|----------------|
| 0.00143 | 0.003496 | HTLV-I infection - Homo sapiens (human) | KEGG | path:hsa05166 | DLG1; CDC16; BUB3; PIK3CB; JUN; ADCY9; MRAS; STAT5B; XIAP; AKT3; POLE3; TLN1; PIK3R1; PRKACB; | 5295; 1739; 10000; 115; 6777; 8829; 3725; 5291; 8881; 1387; 22808; 54107; 2932; 7094; 5567; 331; 9184; 4603 | 258 | 258 |
| PMID | FDR | Pathway/Interactions | Reactome ID | Genes in Pathway | Pathway Score |
|------|-----|-----------------------|-------------|-----------------|---------------|
| 0.001536 | 0.003557 | VEGFA-VEGFR2 Pathway | R-HSA-4420097 | MYBL1; GSK3B; NRP1; CREBBP | 282 |
|      |      |                       |             | ITPR1; PRKCA; PIK3CB; VCL; IRS1; SPRED2; FRS2; PAK3; AKT3; RAP1B; TTN1; PIK3R1; PRKACB; CRK; DUSP6; SPRED1; IQGAP1; KDR; CAV1 | 281 |
| 0.001563 | 0.003557 | DAP12 interactions | R-HSA-2172127 | IQGAP1; ITPR1; PRKCA; VCL; PTPN11; GSK3B; FRS2; ADCY9; SPRED2; IRS1; AKT3; PTEN; PRKAR2B; RAP1B; TTN1; PIK3R1; PRKACB; DUSP6; SPRED1; PIK3CB; PIP4K2B | 326 |
|      |      |                       |             | 3667; 5567; 5578; 3791; 1848; 10818; 200734; 1398; 5295; 857; 5908; 5291; 7414; 8826; 7094; 161742; 10000; 3708; 5063 | 325 |
| Pathway                                                                 | Gene ID Range                                                                 | HSA          | Reactome          | Significance |
|------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------|-------------------|--------------|
| Asparagine N-linked glycosylation                                       | SEL1; GNPAT1; SEC23A; TFG; TRAPPC2; RAD23B; ARCN1; SEC24A; KDEL2; ANK3; PPP6C; STX17; DYNC1LI2; DCTN3; GOSR2; MCFD2; BET1L; SEC31A | R-HSA-446203 | 0.003897          | 0.008298      | 283          | 283 |
| Platelet activation, signaling and aggregation                          | ITPR1; GNAI3; WDR1; HSPA5; PRKCA; PTPN11; VCL; RAP1B; GNG12; THBS1; AKT3; PIK3CB; LAMP2; PIK3R1; CRK; RHOB; TLN1; SERPINE1 | R-HSA-76002  | 0.003897          | 0.008298      | 283          | 283 |
| Signaling by SCF-KIT                                                   | IQGAP1; STAT5B; PRKCA; PIK3CB; GSK3B; VCL; IRS1; SPRED2;                     | R-HSA-1433557| 0.0052            | 0.010573      | 292          | 291 |
| ID     | p-value   | Gene Set                                                                 | Signaling Pathway                                                                 | KEGG Path ID | Path ID | Gene Name                                                                 | Score 1 | Score 2 |
|--------|-----------|--------------------------------------------------------------------------|----------------------------------------------------------------------------------|--------------|---------|----------------------------------------------------------------------------|---------|---------|
| 0.005286 | 0.010573  | Interleukin-3, 5 and GM-CSF signaling                                      | Reactome (HSA-512988)                                                           |              |         | FRS2; PTEN; AKT3; RAP1B; TNL1; PIK3R1; DUSP6; SPRED1; PTPN11; PIP4K2B     | 7414; 5781; 8826; 6777; 7094; 2932; 161742; 10000 |         |
| 0.00596  | 0.01157   | Ras signaling pathway - Homo sapiens (human)                              | KEGG (path:hsa04014)                                                            |              |         | CRKL; IQGAP1; PIK3CB; VCL; IRS1; SPRED2; FRS2; STAT5B; RAP1B; TNL1; PIK3R1; CRK; DUSP6; SPRED1; PTPN11 | 3667; 1399; 1848; 10818; 200734; 1398; 5295; 5908; 5291; 7414; 5781; 8826; 6777; 7094; 161742 |         |
| 0.006422 | 0.011774  | IRS-related events                                                        | Reactome (HSA-2428928)                                                          |              |         | IGF1R; RAB5B; RGL1; PIK3CB; RAP1B; GNG12; MRAS; PRKCA; AKT3; EFNA1; PIK3R1; PRKACB; PTPN11; KDR; PAK3 | 10000; 5908; 23179; 5781; 55970; 5291; 3791; 22808; 5295; 5869; 1942; 3480; 5567; 5063; 5578 |         |
| p-value    | q-value | pathway                              | source | external_id  | members_input_overlap                  | members_input_overlap_geneids                  | size | effective_size |
|------------|---------|--------------------------------------|--------|--------------|----------------------------------------|-----------------------------------------------|------|----------------|
| 0.006422   | 0.011774| IGF1R signaling cascade              | Reactome| R-HSA-2428924| IGF1R; RHEB; IQGAP1; VCL; PTPN11; PRKAG2; RPS6KB1; IRS1; SPRED2; FRS2; RAP1B; TLN1; PIK3R1; DUSP6; SPRED1; PIK3CB | 3667; 1848; 10818; 6009; 200734; 51422; 5781; 6198; 5908; 5291; 7414; 5295; 8826; 7094; 161742; 3480 | 254  | 252           |
| 0.006664   | 0.011886| Signaling by Type 1 Insulin-like Growth Factor 1 Receptor (IGF1R) | Reactome| R-HSA-2404192| IGF1R; RHEB; IQGAP1; VCL; PTPN11; PRKAG2; RPS6KB1; IRS1; SPRED2; FRS2; RAP1B; TLN1; PIK3R1; DUSP6; SPRED1; PIK3CB | 3667; 1848; 10818; 6009; 200734; 51422; 5781; 6198; 5908; 5291; 7414; 5295; 8826; 7094; 161742; 3480 | 255  | 253           |
| Pathway | Signaling by Interleukins | Reactome | R-HSA-449147 | SOCS5; IRAK1; FBXW11; CRKL; IRS1; IQGAP1; VCL; PIK3CB; FRS2; MAP3K7; SPRED2; TLN1; STAT5B; RIPK2; RAP1B; PIK3R1; IRAK2; CRK; DUSP6; SPRED1; PTPN11 | 1848; 200734; 6885; 5291; 8767; 7094; 3667; 3656; 1398; 6777; 10818; 7414; 3654; 1399; 23291; 5295; 9655; 5781; 5908; 8826; 161742 | 373 | 372 |
Supplementary Figure S2.

(A) Cartoon representative of single cell force spectroscopy by AFM. A single living cell is approached by the AFM cantilever (A), recording a force-distance curve (red curve) until the maximum cell compression is reached (B). Thereafter, the cantilever is pulled-off from the cell (C) and a withdraw curve is recorded (black curve). Hysteresis between the curves along y-axis defines the plasticity index (green dashed box).
Supplementary Figure S3

(A) Representative cartoon of a typical cell-to-ECM interaction measurement by AFM. In the approaching phase (red curve), a cell is captured, attached and let adhere to a fibronectin functionalized cantilever (A); next, cell is pressed with a constant force, over a surface coated with the ECM protein of interest, to establish a firm interaction between the cell and the substrate (B). Thereafter, the cell is pulled-off (withdraw phase – black curve) and the interactions between ECM and the cell membrane adhesion receptors linked (ruptures – C) or not linked (tethers – D) to the cytoskeleton are recorded (E). The energy required to detach each cell from the specific substrate (work of detachment – grey area) is also recorded.