The Assembly of miRNA-mRNA-protein Regulatory Networks Using High-throughput Expression Data

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Supplementary Material

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Supplemental text

Additional methods

Placentas and trophoblast culture

This study was approved by the Institutional Review Board at the University of Pittsburgh. All placentas were procured from consenting healthy pregnant women who delivered a healthy newborn at term (37-40 weeks) after an uncomplicated pregnancy. Trophoblasts, the key functional cells in the placenta, were dispersed using a trypsin-deoxyribonuclease-dispase/Percoll method as described (Kliman, et al., 1986; Schaiff, et al., 2005). Trophoblasts were plated at a density of 300,000 cells/cm^2 in 6 well plates, and maintained in standard culture conditions (O_2=20%) for 4 h (defined as time 0). At that point the plates were divided to those in continued standard culture conditions, or to culture in hypoxia (O_2=0%), using a hermetically enclosed incubator (Thermo Electron, Marietta, OH) that provided the desired level of oxygen level (O_2=0%: 5% CO_2, 10% H_2, and 85% N_2). All media were pre-equilibrated to the gas mixture before addition to the culture plate, and refreshed every 24 h. Oxygen concentration was continuously monitored using a sensor connected to a data acquisition module (Scope; Data Translation, Marlboro, MA). Cells were harvested at 6 h, 12 h, 24 h, 48 h and 72 h, and processed for RNA arrays or proteomics, as described below. The experiment was repeated five times, but because of poor cell quality, trophoblasts were only analyzed from four replicates for a total of 44 time points (4 sets x 11 time points each).

Expression microarrays for mRNA and miRNA

RNA was purified from trophoblasts as we previously described (Oh, et al., 2011; Schaiff, et al., 2005) and quantified by absorbance at 260 nm using a Nanodrop UV-Vis spectrophotometer (Thermo Scientific) and by RNA 6000 Nano Assay Kit (Agilent Technologies, Santa Clara, CA) in an Agilent 2100 Bioanalyzer (Agilent). All RNA integrity number (RIN) values were in the range of 8.0 to 9.9 (minimum acceptable RIN =7). For mRNA labeling we used the Low Input Quick Amp Labeling Kit, One-Color (Agilent), and prepared the labeled RNA for hybridization on SurePrint G3 HMN GE 8x60K slides using the Gene Expression Hybridization Kit (both from Agilent). Slides were scanned using Agilent's SureScan Microarray Scanner System, and data extracted using Agilent's Feature Extraction Software (version 11.0.1.1). A similar procedure was used for miRNA arrays, but the hybridization was performed on Human miRNA V3 8x15K slides using the miRNA Complete Labeling and Hyb Kit (both from Agilent). The data are deposited in NCBI's Gene Expression Omnibus and are accessible through GEO Series accession number GSE60433 (http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE60433).

Proteomic analysis using mass-spectrometry

Proteomic analysis was performed using three million primary trophoblasts per paradigm. The cells were sonicated to disrupt cell membranes, solubilized, and protein concentrations determined by the bicinchoninic assay (Pierce, Rockford, IL, USA). Thirty mg of each sample was resolved just into the stacking portion of a 1D-SDS-PAGE gel, excised, and digested in-gel with sequencing grade porcine trypsin (Promega, Madison, WI, USA). Peptides were extracted and analyzed with five recursive injections by liquid chromatography-tandem mass spectrometry on a linear ion trap mass spectrometer (LTQ, ThermoFischer Scientific, San Jose, CA, USA) essentially as described (Bateman, et al., 2010). Tandem mass spectra were searched against a combined UniProt human protein database from the European Bioinformatics Institute (Kersey, et al., 2005) using SEQUEST (Thermo) for peptide/protein identification. Results were further filtered using software developed locally to determine unique peptides and proteins. Differences in protein abundance between the samples were derived by spectral counting and peptides whose sequence mapped to multiple protein isoforms were grouped as per the principle of parsimony (Marengo, et al., 2010).

Data processing

In the analyses of the miRNA/mRNA/protein expression data, we divided the samples into 11 exposure groups: Time 0, and either standard condition or hypoxia at 6 h, 12 h, 24 h, 48 h, and 72 h. Each exposure group contains 3 to 4 samples, except for the protein data, where no data were available for samples collected at 6 h.

The miRNA microarray data were log2 transformed, normalized, and summarized using the Robust Multi-array Average procedure (Irizarry, et al., 2003), as implemented in the AgiMicroRna R package (Lopez-Romero, 2011). Summarized miRNA data were filtered to remove miRNAs with very low expression levels across all samples. The summarized miRNA data were filtered in two steps to remove miRNAs with very low expression across all samples. In step 1), a miRNA was removed if, for none of the 11 exposure groups, the miRNA was considered detected by the Agilent feature extractor in at least 2 samples in that group. In step 2), miRNAs in each sample were clustered into two clusters using the EM algorithm, representing unexpressed and expressed miRNAs respectively. A miRNA was removed if in none of the 11 exposure groups, the miRNA belonged to the expressed cluster in at least 2 samples in that group.

We assumed that the expression of miRNAs could be represented by linear mixed effect models, with exposure to standard or hypoxic conditions at various time points as a categorical fixed effect, and the placental origin of the samples as a random effect. We used the algorithm implemented in R package maanova (Kerr and Churchill, 2001) to identify miRNAs that were differentially expressed between standard or hypoxic conditions over the time course. The maanova package employs a shrinkage method to estimate the variance of each miRNA, and performs a permutation test on the F statistics to estimate p values. The p-values were adjusted by the Benjamini and Hochberg's method to control for the false discovery rate (Benjamini and Hochberg, 1995).

The mRNA data were log2 transformed and normalized using the cyclic loess normalization algorithm, and filtered to remove mRNAs with very low expression. The mRNA data were analyzed following the same procedure as the differential expression analysis for the miRNA data.

The protein data, which are count data, were filtered to remove those proteins whose total counts over the 36 samples were less than 12, and analyzed using the generalized linear mixed effect models, with the standard or hypoxic conditions as the fixed effect, and the placenta origin as the random effect. Log likelihood ratio test was used to determine if a protein is differentially expressed, with p-values adjusted using the Benjamini and Hochberg's method.

Unsupervised machine learning algorithms were applied to the miRNA, mRNA, and protein data to explore their inherent relations. For unsupervised analysis, the protein data were smoothed by adding 1 to the count of each protein, normalized by the total count of proteins in each sample, and log2 transformed. Differentially expressed miRNAs, mRNAs, and proteins were clustered using the k-means algorithm into five groups with distinct expression patterns over the culture conditions. Classical multi-dimensional scaling and hierarchical clustering were applied to all expressed miRNAs, mRNAs, and proteins.

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Auxiliary algorithms

The *Splitting algorithm for Markov Blanket with known direct effects* (SAMB-KDE), described below, was used in the first step of the MBSmRN algorithm to identify the Markov Blanket of a target mRNA, when the number of candidate regulators of the target mRNA far exceeded the sample size. In the first step, after filtering out variables independent of the target given the direct effects of the target, the remaining variables were divided into multiple subsets, and a Markov blanket search for the target variable was performed on each subset. The variables in the resulting Markov blankets from all subsets were combined. A further Markov blanket search on the combined set of variables yielded the Markov blanket of the target variable. Lemma 1 proves the correctness of the SAMB-KDE algorithm. Lemma 2 and Corollary 1 showed that the second step of the MBSmRN algorithm was correct. The time complexity of SAMB-KDE algorithm varies based on the different model selection methods. For example, assuming the use of stepwise model selection, and a linear model for the target molecule, the time complexity of SAMB-KDE algorithms will be $O(np+ndm^3)$, where n is sample size, p the number of variables, d the number of variables dependent with the target, m the number of variables in each of the split parts. The $O(np)$ term is needed for identifying variables independent of the target, where the $O(ndm^3)$ term is the cost of the second part of step 1. The cost of step 2 can be ignored if we assume that the size of the output from step 1 is $O(m)$.

The *general splitting algorithm for Markov Blanket* (SAMB-G) was used in the first step of the MBSNIG algorithm to identify the Markov Blanket of a target protein, when the number of candidate regulators of the target protein far exceeded the sample size. Like the SAMB-KDE algorithm, in the first step, after filtering out variables independent of the target, the remaining variables were divided into multiple subsets, and a Markov blanket search for the target variable was performed on each subset. The variables in the resulting Markov blankets from all subsets were combined, and a further Markov blanket search for the target variable was performed on this combined set of variables. The resulting set of variables, in combination with variables independent of the target given those variables, were subject to a Markov blanket search to yield the Markov blanket of the target variable. Lemma 3 showed that the SAMB-G algorithm was correct. Like the SAMB-KDE algorithm, the time complexity of SAMB-G algorithm varies based on the model selection method used. For example, assuming using stepwise model selection, and a generalized linear model for the target molecule, the time complexity of SAMB-G algorithm will be $O(cnpm+cndm^2)$, where n is sample size, p the number of variables, d the number of variables dependent with the target, m the number of variables in each of the split parts, and c the average number of iterations needed to fit a generalized linear model. The $O(cnpm)$ term is the cost for step 3, assuming that the size of the output from step 2 is $O(m)$. Note that it dominates the cost of identifying variables independent of the target in step 1. The $O(cndm^2)$ term is the cost of the second part of step 1. If we assume that the size of the output from step 1 is $O(m)$, the cost of step 2 can be ignored.

The *Partial Orientation of the Markov Blanket for a non-Gaussian variable* (POMB-NG) algorithm was used in the second step of the MBSNIG algorithm to determine, among the variables in the Markov Blanket of a target protein, which of them were direct regulators of proteins. In the first two steps, a heuristic bidirectional search was performed on the Markov blanket of the target variable to obtain a set of non-descendent variables of the target that contains all direct causes of the target. From this set of non-descendent variables, a Markov blanket search produced the set of direct causes of the target variable. Assuming that the data are generated from generalized linear models, using iteratively reweighted least square with conjugate gradient descent, it takes $O(cnb)$ time to fit a model, where n is the sample size, b the number of variables in the Markov Blanket, and c the number of iterations needed. The complexity of the POMB-NG algorithm therefore is $O(cnb^4)$, as it needs to fit $O(b^2)$ model in each step of the upward or downward search. Note that in our PHT data we observed that the number b was usually modest, often less than 10, and very rarely above 20.

Splitting algorithm for Markov Blanket with known direct effects:

Let $\mathbf{V}$ be the set of measured variables that is causal sufficient, i.e., for any two variables $X_1, X_2 \in \mathbf{V}$, if X_3 is a cause of both X_1 and X_2 , then $X_3 \in \mathbf{V}$. Let $X \in \mathbf{V}$, and $Ch(X;\mathbf{V}) \subseteq \mathbf{V}$ be the set of direct effects of X (“Ch” stands for “children”). To identify $MB(X;\mathbf{V})$, the Markov blanket of X from $\mathbf{V}$, the splitting algorithms has the following two steps:

> Step 1. Let $Ind(X; \mathbf{V} \mid Ch(X;\mathbf{V}))$ be the set of variables in $\mathbf{V} \setminus (Ch(X;\mathbf{V}) \cup \{X\}$ independent of X conditional on $Ch(X;\mathbf{V})$. Divide $\mathbf{V} \setminus (Ch(X;\mathbf{V}) \cup \{X\} \cup Ind(X; \mathbf{V} \mid Ch(X;\mathbf{V})))$ into k disjoint subsets $\mathbf{V}'_1,\dots,\mathbf{V}'_k$ such that $\mathbf{V} \setminus (Ch(X;\mathbf{V}) \cup \{X\} \cup Ind(X; \mathbf{V} \mid Ch(X;\mathbf{V}))) = \cup_i \mathbf{V}'_i$.
> For $i = 1,\dots,k$, identify $MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, i.e., the Markov blanket of X from $\mathbf{V}'_i \cup Ch(X;\mathbf{V})$, by identifying the optimal set of predictors of X in $\mathbf{V}'_i \cup Ch(X;\mathbf{V})$ using model selection method.
>
> Step 2. Identify $MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$, the Markov blanket of X from the union of the k Markov blankets $\cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, by identifying the optimal set of predictors of X using model selection method. Return $MB(X;\mathbf{V}) = MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$.

Lemma 1:

Assuming Faithfulness and Causal Sufficiency, the splitting algorithm for Markov Blanket with known direct effects is correct.

Proof:

First, let us show that $MB(X,\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$. That is, the Markov blanket of X is a subset of the output from step 1 of the algorithm.

Let $Pa(X;\mathbf{V})$ be the direct causes of X in $\mathbf{V}$, and $Sp(X;\mathbf{V})$ the direct causes of $Ch(X;\mathbf{V})$ other than X itself in $\mathbf{V}$. Clearly $Pa(X;\mathbf{V}) \subseteq \mathbf{V} \setminus (\{X\} \cup Ind(X; \mathbf{V} \mid Ch(X;\mathbf{V}))) = \cup_i (\mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, and $Sp(X;\mathbf{V}) \subseteq \mathbf{V} \setminus (\{X\} \cup Ind(X; \mathbf{V} \mid Ch(X;\mathbf{V}))) = \cup_i (\mathbf{V}'_i \cup Ch(X;\mathbf{V}))$. Note that $MB(X,\mathbf{V}) = Pa(X;\mathbf{V}) \cup Ch(X;\mathbf{V}) \cup Sp(X; \mathbf{V})$.

For $i = 1,\dots,k$, it is easy to see that:

1) For each variable Z in $Pa(X;\mathbf{V}) \cap (\mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, we have: $\forall \mathbf{Y} \subseteq (\mathbf{V}'_i \cup Ch(X;\mathbf{V})) \setminus \{Z\}$, X and Z are dependent conditional on $\mathbf{Y}$. Therefore $Pa(X;\mathbf{V}) \cap (\mathbf{V}'_i \cup Ch(X;\mathbf{V})) \subseteq MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$.
2) For each variable Z in $Ch(X;\mathbf{V})$, we have: $\forall \mathbf{Y} \subseteq (\mathbf{V}'_i \cup Ch(X;\mathbf{V})) \setminus \{Z\}$, X and Z are dependent conditional on $\mathbf{Y}$. Therefore $Ch(X;\mathbf{V}) \subseteq MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$.
3) For each variable Z in $Sp(X;\mathbf{V}) \cap (\mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, we have: $\forall \mathbf{Y} \subseteq (\mathbf{V}'_i \cup Ch(X;\mathbf{V})) \setminus \{Z\}$, X and Z are dependent conditional on $\mathbf{Y} \cup Ch(X;\mathbf{V})$. Therefore $Sp(X;\mathbf{V}) \cap (\mathbf{V}'_i \cup Ch(X;\mathbf{V})) \subseteq MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$.

Therefore, we have $Pa(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, $Ch(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, and $Sp(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$, hence $MB(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$.

Second, let us show that $MB(X;\mathbf{V}) = MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$.

It is easy to see that $MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))) \subseteq MB(X;\mathbf{V})$. For each variable Z in $\cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})) \setminus MB(X;\mathbf{V})$, we have $Z \in \mathbf{V}$, hence is independent of X conditional on $MB(X;\mathbf{V})$.

To show that $MB(X;\mathbf{V}) \subseteq MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$, we notice that:

1) $Pa(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$. Moreover, for each variable Z in $Pa(X;\mathbf{V})$, we have: $\forall \mathbf{Y} \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})) \setminus \{Z\}$, X and Z are dependent conditional on $\mathbf{Y}$. Therefore $Pa(X;\mathbf{V}) \subseteq MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$.
2) $Ch(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$. Moreover, for each variable Z in $Ch(X;\mathbf{V})$, we have: $\forall \mathbf{Y} \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})) \setminus \{Z\}$, X and Z are dependent conditional on $\mathbf{Y}$. Therefore $Ch(X;\mathbf{V}) \subseteq MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$.
3) $Sp(X;\mathbf{V}) \subseteq \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V}))$. Moreover, for each variable Z in $Sp(X;\mathbf{V})$, assume $Z \notin MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$. Then given that $Ch(X;\mathbf{V}) \subseteq MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$, X and Z are dependent conditional on $MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$. Contradiction. Therefore $Sp(X;\mathbf{V}) \subseteq MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$.

Therefore, we have $MB(X,\mathbf{V}) \subseteq MB(X; \cup_i MB(X; \mathbf{V}'_i \cup Ch(X;\mathbf{V})))$.

Lemma 2:

Let $\mathbf{V}$ be the set of measured variables that is causal sufficient, $Pa(X;\mathbf{V})$ be the set of direct causes of $X \in \mathbf{V}$, and $\mathbf{N}$ a set of non-descendants of X such that $Pa(X;\mathbf{V}) \subseteq \mathbf{N}$. Then the Markov blanket of X over $\mathbf{N}$ is the set of direct causes of X, that is, $\boldsymbol{Pa(X) = MB(X; N)}$.

Proof:

It is easy to show that $Pa(X;\mathbf{V}) \subseteq MB(X; \mathbf{N})$, given that $Pa(X;\mathbf{V}) \subseteq \mathbf{N}$, and that $\forall Y \in Pa(X; \mathbf{V})$, $\forall \mathbf{Z} \subseteq \mathbf{V} \setminus \{X, Y\}$, X and Y are dependent conditional on $\mathbf{Z}$.

To show that that $MB(X; \mathbf{N}) \subseteq Pa(X; \mathbf{V})$, we notice that, given its direct causes $Pa(X; \mathbf{V})$, X is independent of all its non-descendants. Now $\forall\ Z \in MB(X; \mathbf{N}) \setminus Pa(X; \mathbf{V})$, Z is a non-descendant of X, hence X and Z are independent conditional on $Pa(X; \mathbf{V})$. This implies that $MB(X; \mathbf{N}) \subseteq Pa(X; \mathbf{V})$.

Corollary 1:

Let $\mathbf{V}$ be the set of measured variables that is causal sufficient, and $MB(X; \mathbf{V})$ is the Markov blanket for $X \in \mathbf{V}$. If X has only one direct effect C, then the Markov blanket of X over $MB(X; \mathbf{V}) \setminus \{C\}$ is the set of direct causes of X, that is, $Pa(X) = MB(X; MB(X; \mathbf{V}) \setminus \{C\})$.

Proof:

We note that the Markov blanket $MB(X; \mathbf{V})$ of X is the union of the set of all direct causes of X, the set of all direct effects of X, and, excluding X, the set of all direct causes of the direct effects of X. Because X has only one direct effect C, a direct cause of C cannot be a descendant of C, hence cannot be a descendant of X. Therefore, $MB(X; \mathbf{V}) \setminus \{C\}$ consists of only non-descendants of X. Given that $MB(X; \mathbf{V})$, hence $MB(X; \mathbf{V}) \setminus \{C\}$, include all direct causes of X, by Lemma 2, we have $Pa(X) = MB(X; MB(V; \mathbf{V}) \setminus \{C\})$.

General Splitting algorithm for Markov Blanket:

Let $\mathbf{V}$ be the set of measured variables that is causal sufficient, i.e., for any two variables $X_1, X_2 \in \mathbf{V}$, if X_3 is a cause of both X_1 and X_2 , then $X_3 \in \mathbf{V}$. Let $X \in \mathbf{V}$, and $Ch(X;\mathbf{V}) \subseteq \mathbf{V}$ be the set of direct effects of X in $\mathbf{V}$. To identify $MB(X,\mathbf{V})$, the Markov blanket of X from $\mathbf{V}$, the general splitting algorithms has the following three steps:

Step 1. Let $Ind(X; \mathbf{V})$ be the set of variables in $\mathbf{V}$ independent of X. Divide $\mathbf{V} \setminus Ind(X; \mathbf{V}_i)$ into k disjoint subsets $\mathbf{V}'_1,\ldots,\mathbf{V}'_k$ such that $\mathbf{V} \setminus Ind(X; \mathbf{V}) = \cup_i \mathbf{V}'_i$. For $i = 1,\ldots,k$, identify $MB(X; \mathbf{V}'_i)$, i.e., the Markov blanket of X from $\mathbf{V}'_i$, by identifying the optimal set of predictors of X in $\mathbf{V}'_i$ using model selection method.

Step 2. Identify $\boldsymbol{M'} = MB(X; \cup_i MB(X; \boldsymbol{V'}_i))$, the Markov blanket of X from the union of the k Markov blankets $\cup_i MB(X; \boldsymbol{V'}_i)$ by identifying the optimal set of predictors of X in $\cup_i MB(X; \boldsymbol{V'}_i)$ using model selection method.

Step 3. Let $Dep(X; \boldsymbol{V} \mid \boldsymbol{M'})$ be the set of variables in $\boldsymbol{V}$ dependent of X given $\boldsymbol{M'}$. That is, $\forall Z \in \boldsymbol{V} \setminus \boldsymbol{M'}$, X and Z are dependent given $\boldsymbol{M'}$. Identify $MB(X; \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'}))$ by identifying the optimal set of predictors of X in $\boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'})$ using model selection method. Return $MB(X,\boldsymbol{V}) = MB(X; \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'}))$.

Lemma 3:
Assuming Faithfulness and Causal Sufficiency, $MB(X,\boldsymbol{V}) = MB(X; \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'}))$. That is, the general splitting algorithm for Markov Blanket is correct.

Proof:
Let $Pa(X;\boldsymbol{V})$ be the direct causes of X in $\boldsymbol{V}$, $Ch(X;\boldsymbol{V})$ the direct effects of X in $\boldsymbol{V}$, and $Sp(X;\boldsymbol{V})$ the direct causes of $Ch(X;\boldsymbol{V})$ other than X itself in $\boldsymbol{V}$. Note that $MB(X,\boldsymbol{V}) = Pa(X;\boldsymbol{V}) \cup Ch(X;\boldsymbol{V}) \cup Sp(X; \boldsymbol{V})$.

First, following the same argument as in the first part of the proof for Lemma 1, it is easy to see that $Pa(X;\boldsymbol{V}) \subseteq \boldsymbol{V} \setminus Ind(X; \boldsymbol{V})$, hence $Pa(X;\boldsymbol{V}) \subseteq \cup_i MB(X; \boldsymbol{V}_i)$, therefore $Pa(X;\boldsymbol{V}) \subseteq MB(X; \cup_i MB(X; \boldsymbol{V}_i)) = \boldsymbol{M'}$. Similarly, we can show that $Ch(X;\boldsymbol{V}) \subseteq \boldsymbol{M'}$.

Next, we note that $\forall Z \in Sp(X;\boldsymbol{V}) \setminus \boldsymbol{M'}$, X and Z are dependent given $\boldsymbol{M'}$. Thus, $Sp(X;\boldsymbol{V}) \subseteq \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'})$. It then follows that $MB(X;\boldsymbol{V}) \subseteq \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'})$, hence $MB(X;\boldsymbol{V}) \subseteq MB(X; \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'}))$.

It is easy to see that $MB(X; \boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'})) \subseteq MB(X;\boldsymbol{V})$. For each variable Z in $(\boldsymbol{M'} \cup Dep(X; \boldsymbol{V} \mid \boldsymbol{M'})) \setminus MB(X;\boldsymbol{V})$, we have $Z \in \boldsymbol{V}$, hence is independent of X conditional on $MB(X;\boldsymbol{V})$.

Partial Orientation of the Markov Blanket for a non-Gaussian variable (POMB-NG)
First, let us introduce some notations. Let $\boldsymbol{X} = \langle X_1, \ldots, X_k \rangle$ and $\boldsymbol{Y} = \langle Y_1, \ldots, Y_m \rangle$ be ordered sets of variables (or tuples), we define the following operations on ordered sets:

$\langle \boldsymbol{X}, Y_i \rangle = \langle X_1, \ldots, X_k, Y_i \rangle$
$\langle Y_i, \boldsymbol{X} \rangle = \langle \boldsymbol{Y_i}, X_1, \ldots, X_k \rangle$
$\boldsymbol{X} \setminus \langle X_i \rangle = \langle X_1, \ldots, X_{i-1}, X_{i+1}, \ldots, X_k \rangle$
$\langle \boldsymbol{X}, \boldsymbol{Y} \rangle = \langle X_1, \ldots, X_k, Y_1, \ldots, Y_m \rangle$

Without causing confusion, we will some time use the same symbol refer to both a set and an ordered set with same set of elements.

Let $X \sim \boldsymbol{Y}$ represent a regression model where X is the dependent variable and $\boldsymbol{Y}$ the set of independent variables. Define $LL_R\ (X \sim \boldsymbol{Y})$ as the log likelihood of the (generalized) linear regression model $X \sim \boldsymbol{Y}$ fitted using maximum likelihood method. The regression model could be a Poisson regression model when X is count data. Moreover, if some independent variable $Y_i \in \boldsymbol{Y}$ is count data, it will be replaced by its smoothed logarithm $log(Y_i+1)$ in the regression model for the dependent variable X. Let $\boldsymbol{X} = \langle X_1, \ldots, X_k \rangle$ be an ordered set, $\boldsymbol{X}_0 = \emptyset$, and $\boldsymbol{X}_i = \{X_1, \ldots, X_i\}$ for $i = 1, \ldots, k$ be regular sets. Define $LL_R\ (\boldsymbol{X} \sim \boldsymbol{Y}) = \Sigma_i\ LL_R\ (X_i \sim \boldsymbol{X}_{i-1} \cup \boldsymbol{Y})$. Note that $LL_R\ (\boldsymbol{X}) = \Sigma_i\ LL_R\ (X_i \sim \boldsymbol{X}_{i-1})$ when $\boldsymbol{Y} = \emptyset$.

Now let $\boldsymbol{V}$ be the set of measured variables that is causal sufficient, $X \in \boldsymbol{V}$, and $\boldsymbol{M}_X = MB(X;\boldsymbol{V}) \subseteq \boldsymbol{V}$ be the Markov blanket of X in $\boldsymbol{V}$. Let $\boldsymbol{D}_X \subseteq \boldsymbol{M}_X$ be the set of descendent variables of X in $\boldsymbol{M}_X$, that is, variables in $\boldsymbol{D}_X$ are either direct of indirect effects of X. Let $\boldsymbol{N}_X = \boldsymbol{M}_X \setminus \boldsymbol{D}_X$ be the set of non-descendent variables of X in $\boldsymbol{M}_X$. Assume X is count data with a Poisson distribution conditional on its direct causes, $\boldsymbol{N}_X$ has a jointly multivariate normal distribution, and $\boldsymbol{D}_X$ has a jointly multivariate normal distribution conditional on $\boldsymbol{N}_X$ and X. Given X and $\boldsymbol{M}_X$, the goal of the POMB-NG algorithm is to use regression methods to identify the sets of descendent variables and the set of non-descendent variables of X in $\mathbf{M}_X$, and most importantly, the set of direct causes of X.

Step 1. Upward search:

```
1.1 Arbitrarily order the variables in $\mathbf{M}_X$. Initialize ordered sets $\mathbf{N} \leftarrow \emptyset$, $\mathbf{D} \leftarrow \mathbf{M}_X$, and score $s \leftarrow LL_R(\langle \mathbf{M}_X, X \rangle)$

1.2 While $\mathbf{D} \neq \emptyset$:
    $D' = \text{ArgMax}\,[LL_R(\langle \mathbf{D} \setminus \langle D_i \rangle, X, D_i, \mathbf{N} \rangle), D_i]$. That is, $\forall D_i \in \mathbf{D}$,
    $LL_R(\langle \mathbf{D} \setminus \langle D_i \rangle, X, D_i, \mathbf{N} \rangle) \leq LL_R(\langle \mathbf{D} \setminus \langle D' \rangle, X, D', \mathbf{N} \rangle)$.
    If $LL_R(\langle \mathbf{D} \setminus \langle D' \rangle, X, D', \mathbf{N} \rangle) > s$:
      $s \leftarrow LL_R(\langle \mathbf{D} \setminus \langle D' \rangle, X, D', \mathbf{N} \rangle)$
      $\mathbf{N} \leftarrow \langle D', \mathbf{N} \rangle$, $\mathbf{D} \leftarrow \mathbf{D} \setminus \langle D' \rangle$,

Else, stop the upward search.
```

Step 2. Downward search:

```
2.1 Initialize $\mathbf{N}$, $\mathbf{D}$, and $s$ to the values returned by the upward search

2.2 While $\mathbf{N} \neq \emptyset$:
    $N' = \text{ArgMax}\,[LL_R(\langle \mathbf{D}, N_i, X, \mathbf{N} \setminus \langle N_i \rangle \rangle), N_i]$. That is, $\forall N_i \in \mathbf{N}$,
    $LL_R(\langle \mathbf{D}, N_i, X, \mathbf{N} \setminus \langle N_i \rangle \rangle) \leq LL_R(\langle \mathbf{D}, N', X, \mathbf{N} \setminus \langle N' \rangle \rangle)$
    If $LL_R(\langle \mathbf{D}, N', X, \mathbf{N} \setminus \langle N' \rangle \rangle) > s$:
      $s \leftarrow LL_R(\langle \mathbf{D}, N', X, \mathbf{N} \setminus \langle N' \rangle \rangle)$
      $\mathbf{N} \leftarrow \mathbf{N} \setminus \langle N' \rangle$, $\mathbf{D} \leftarrow \langle \mathbf{D}, N' \rangle$

Else, stop the downward search.
```

Step 3. Identify the direct causes of X.

```
3.1 Initialize $\mathbf{N}$ to the value returned by the downward search.
3.2 $\mathbf{P} \leftarrow MB(X, \mathbf{N})$
    $\mathbf{D} \leftarrow Dep(X; \mathbf{M}_X \mid \mathbf{P})$, the set of variables in $\mathbf{M}_X$ dependent of $X$ given $\mathbf{P}$.
    $\mathbf{N} \leftarrow \mathbf{M}_X \setminus \mathbf{D}$.
3.3 Return $\mathbf{P}$ as the set of direct causes of $X$, $\mathbf{D}$ as the set of descendent variables of $X$ in $\mathbf{M}_X$, $\mathbf{N}$ as the set of
    non-descendent variables of $X$ in $\mathbf{M}_X$.
```

Comments:

Given a variable X and its Markov blanket $\mathbf{M}_X$, let $\mathbf{D}$ and $\mathbf{N}$ be any two disjoint sets of variables such that $\mathbf{M}_X = \mathbf{D} \cup \mathbf{N}$. Let variables in $\mathbf{D}$ and $\mathbf{N}$ be ordered arbitrarily as $\langle D_1, \ldots, D_p \rangle$ and $\langle N_1, \ldots. N_q \rangle$, $\mathbf{D}_0 = \emptyset$, $\mathbf{D}_i = \{D_1, \ldots, D_i\}$, $\mathbf{N}_0 = \emptyset$, and $\mathbf{N}_i = \{N_1, \ldots, N_i\}$. The joint log likelihood of $\mathbf{M}_X \cup \{X\}$ can be decomposed as:

$$\begin{aligned} LL(\mathbf{D} \cup \{X\} \cup \mathbf{N}) &= LL(\mathbf{D} \mid \{X\} \cup \mathbf{N}) + LL(X \mid \mathbf{N}) + LL(\mathbf{N}) \\ &= \Sigma_i \, LL(D_i \mid \{X\} \cup \mathbf{D}_{i-1}) + LL(X \mid \mathbf{N}) + \Sigma_j \, LL(N_j \mid \mathbf{N}_{j-1}). \end{aligned}$$

If $\mathbf{M}_X \cup \{X\}$ jointly have a multivariate normal distribution, then each component of the joint log likelihood can be estimated by maximum likelihood estimation of the corresponding linear regression model, e.g., $LL(D_i \mid \{X\} \cup \mathbf{D}_{i-1})$ estimated by $LL_R(D_i \sim \{X\} \cup \mathbf{D}_{i-1})$. However, when X is integer valued and generated according to a generalized linear model like Equation (2), unless $\mathbf{N}$ contains all the direct causes and none of the descendants of X, $LL_R(\langle \mathbf{D}, X, \mathbf{N} \rangle)$ is not longer maximum likelihood estimation of $LL(\mathbf{D} \cup \{X\} \cup \mathbf{N})$, because conditional on $\mathbf{N}$, X is not Poisson distributed with the log of mean expressed as a linear function of $\mathbf{N}$.

The first two steps of the POMB-NG algorithm search through a set of systems of regression models for variables in $\mathbf{M}_X \cup \{X\}$, where the systems all have the same number of parameters and only differ from each other on the ordering of the variables in $\boldsymbol{M}_X \cup \{X\}$. The ordered set $\boldsymbol{N}$ identified at the end of step 2 is not unique. First, the ordering of variables in $\boldsymbol{N}$ is not important, as long as $\boldsymbol{N}$ consists of only non-descendent variables of X., i.e., $\boldsymbol{N} \subseteq \boldsymbol{N}_X$, where $\boldsymbol{N}_X$ is the set of non-descendent variables of X in $\boldsymbol{M}_X$. This is because, by the assumption that $\boldsymbol{N}_X$ has a multivariate normal distribution, the score of the system of regression models is independent of the ordering of variables in $\boldsymbol{N}$. Moreover, $\boldsymbol{N}$ does not have to contain all non-descendent variables. For example, if $Y \in \boldsymbol{N}_X$ is an exogenous variable that is neither a direct nor an indirect cause of X, then the score for the system of regression models with $\boldsymbol{N} = \boldsymbol{N}_X \setminus \langle Y \rangle$ is the same as the score for the true system of regression models:

$$LL_R\,(\langle \boldsymbol{D}_X,\, Y,\, X,\, \boldsymbol{N}_X \setminus \langle Y \rangle\rangle) = LL_R\,(\langle \boldsymbol{D}_X,\, X,\, \boldsymbol{N}_X\rangle)$$

However, as discussed earlier, the ordered set $\boldsymbol{N}$ would contain all the direct causes and none of the descendants of X, therefore ensure the correctness of the step 3 of the POMG-NG algorithm. In particular, by Lemma 2, we note that $\boldsymbol{P} = MB(X, \boldsymbol{N})$ returned by step 3.2 is indeed the set of direct causes of X.

It should also be noted that the non-Gaussian assumption of X is not only sufficient but also necessary for the identification of the direct causes of X. For example, consider a DAG G_1: $Y \rightarrow X \rightarrow Z$, where the variable X has one direct cause Y and one direct effect Z. If X, Y, and Z jointly have a multivariate normal distribution, then the joint distribution of $\{X, Y, Z\}$ is consistent with not only G_1, but also other two Markov equivalent DAGs G_2: $Y \leftarrow X \rightarrow Z$, where both Y and Z are direct effects of X, and G_3: $Y \leftarrow X \leftarrow Z$, where Z is a direct cause of X, and X is a direct cause of Y.

Simulation data

Four simulated miRNA/mRNA/protein regulatory networks, each consisting of 40 miRNAs, 80 mRNAs and 80 proteins that are encoded by the mRNAs, were generated based on equations [1] and [2]. In each simulated network, there were a total of 30 exogenous miRNAs and mRNAs, which had no direct regulator in the simulated network. The protein product of an exogenous mRNA had only the mRNA as its direct regulator. Each endogenous miRNAs/mRNAs was assigned randomly 3 to 5 miRNAs and/or proteins as direct regulators. The protein product of an endogenous mRNA was also randomly assigned, in addition to its mRNA transcript, 3 to 5 miRNAs and/or proteins as direct regulators. The absolute values of the regulators coefficients in equations [1] and [2] were restricted to the interval [0.4,1). The coefficient a_i in equation [2], representing the effect of an mRNA transcript on its protein product, was always positive.

When applying the causal learning algorithms to the simulation data, we chose only mRNA/protein pair that satisfied the following two conditions: 1) the mRNA could not be exogenous; and 2) the protein must regulate at least one miRNA/mRNA/protein. This is because we believe that in real data, each miRNA or mRNA will have at least one direct regulator, and each protein will regulate at least one miRNA/mRNA/protein.

The MBSmRN and MBSNIG algorithms were implemented in R. For this simulation, we chose the stepwise (generalized) linear regression, based on AIC score corrected for finite sample size (Hurvich and Tsai, 1989), as the model selection method for the SAMB-KDE and SAMB-G routines of the MBSmRN and MBSNIG algorithms. The Lasso algorithm was based on the R package *glmnet*, and the MMHC algorithm was based on R package *bnlearn*.

When calculating the area under ROC curves (AUC) for these algorithms, we restricted the curve to a range of specificity between 0.95 and 1. This is because, in the simulated models, each target mRNA/protein has 3 to 5 direct regulators, where the number of candidate regulators is 120. Therefore, 95% specificity means 6 false positives, which in turn means a precision of 45% or lower. Lower the specificity implies that the precision will be well below 50%.

Additional reference

Hurvich, C. M. and Tsai, C.-L. (1989) Regression and time series model selection in small samples, *Biometrika* 76, 297–307.

Supplemental figures

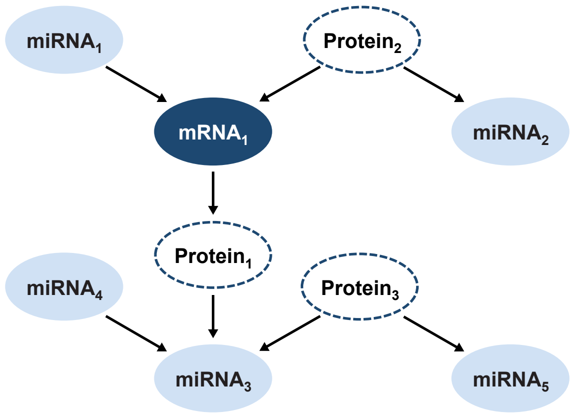
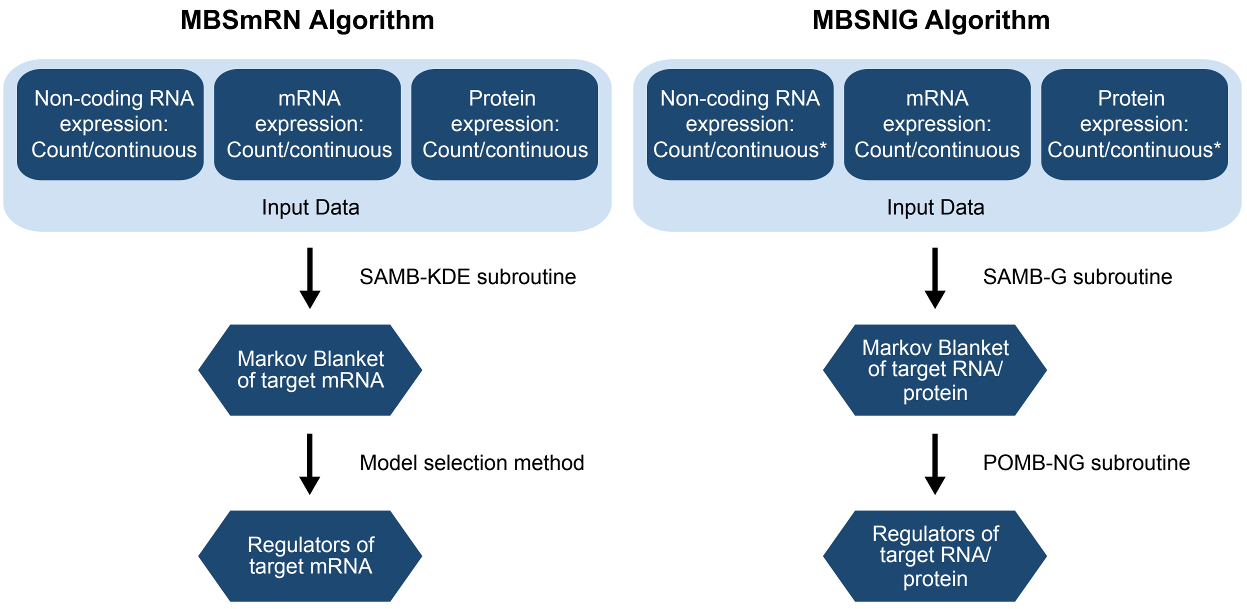


Fig. S1. A hypothetical miRNA/mRNA/protein regulatory networks. For illustration, let us consider a hypothetical miRNA/mRNA/protein regulatory network, shown in Fig. S1. This diagram represents the following regulatory relations: miRNA$_1$ and protein$_2$ regulate mRNA$_1$; mRNA$_1$ regulates protein$_1$, which it encodes; protein$_2$ also regulates miRNA$_2$; miRNA$_3$ is regulated by protein$_1$, protein$_3$, and miRNA$_4$; protein$_3$ also directly regulates miRNA$_5$. The nodes representing the proteins are circled with dashed line to indicate that the expression of the proteins is not measured. It can be shown that, except for some unlikely cases, as the sample size goes to infinity, when regressing against mRNA$_1$, all the miRNAs in Fig. S1's diagram would be identified as potentially regulating mRNA$_1$ (Pellet and Elisseeff, 2008; Spirtes, et al., 2000). In general, a regression model with a target mRNA or protein as the dependent variable and the miRNAs as independent variables may include many miRNAs that neither directly nor indirectly regulate the mRNA or protein.

References to Fig. S1

Pellet, J-P and Elisseeff, A. (2008) Using Markov blankets for causal structure learning. *JMLR*, 9, 1295-1342.
Spirtes, P*, et al.* (2000) *Causation, Prediction, and Search*. Cambridge: MIT Press.



* The expression data for the target RNA/protein of MBSNIG must be count data

Fig. S2. Flow charts for the MBSmRN and MBSNIG algorithms. Note that users can incorporate their prior knowledge about the regulator relations by filtering the input data. (See discussion at the end of the Method section).

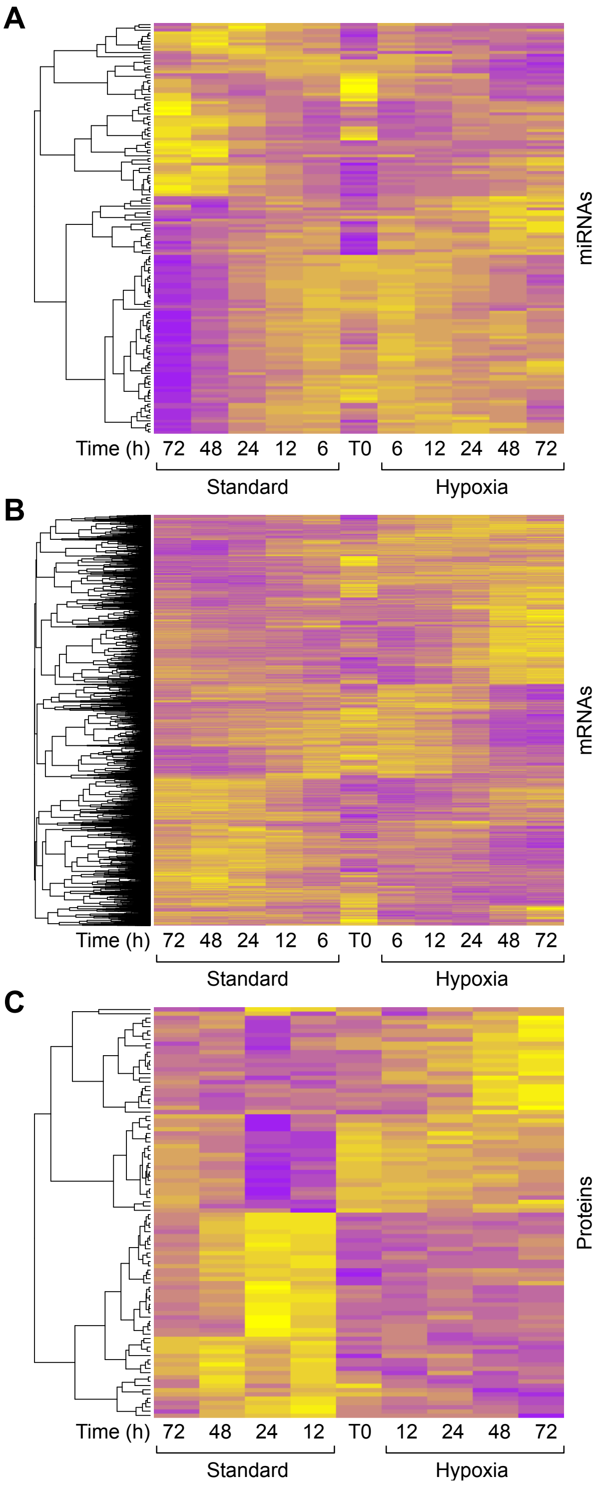


Fig. S3. Heatmaps of miRNAs/mRNAs/proteins that are differentially expressed between standard and hypoxic conditions. A miRNA/mRNA/protein is considered differentially expressed if it exhibits altered expression between the standard and the hypoxic conditions in at least one time point. Values plotted are log2 intensity for miRNAs and mRNAs, and log2 count for proteins. Yellow color represents higher expression, purple represents lower expression. The miRNAs/mRNAs/proteins are clustered using hierarchical clustering.

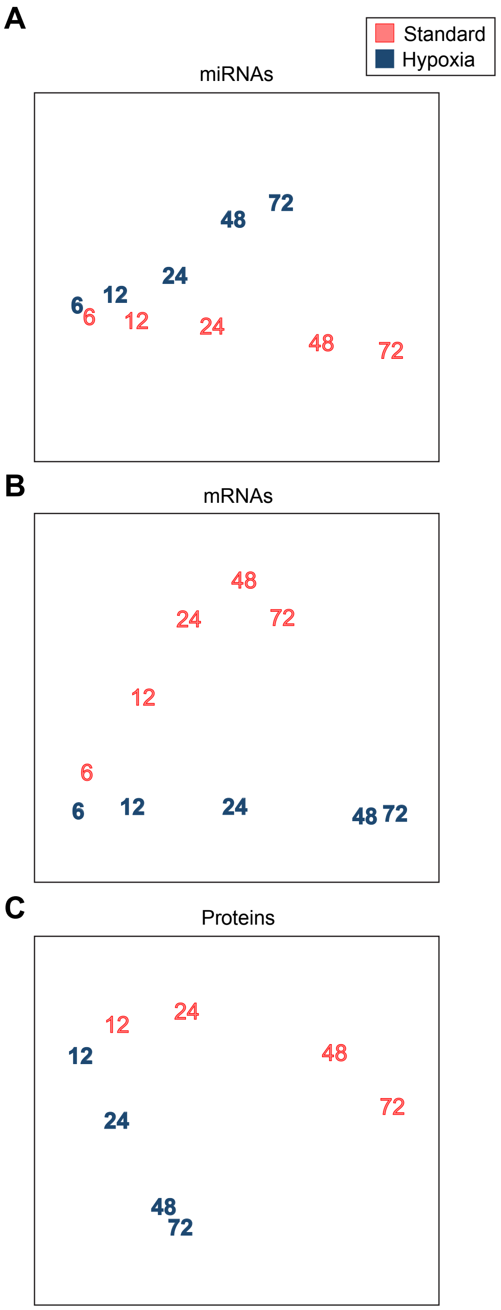


Fig. S4. Classical multidimensional scaling of all expressed miRNAs/mRNAs/proteins. Expression values are averaged over the four placentas. The numbers are the time (hours) of cell exposure to standard or hypoxic conditions. The x and y axes are the first two principal components of the expression data. Note the high similarity among the expression patterns of the miRNAs, mRNAs, and proteins, showing a divergence between the hypoxic and standard conditions over the time course.

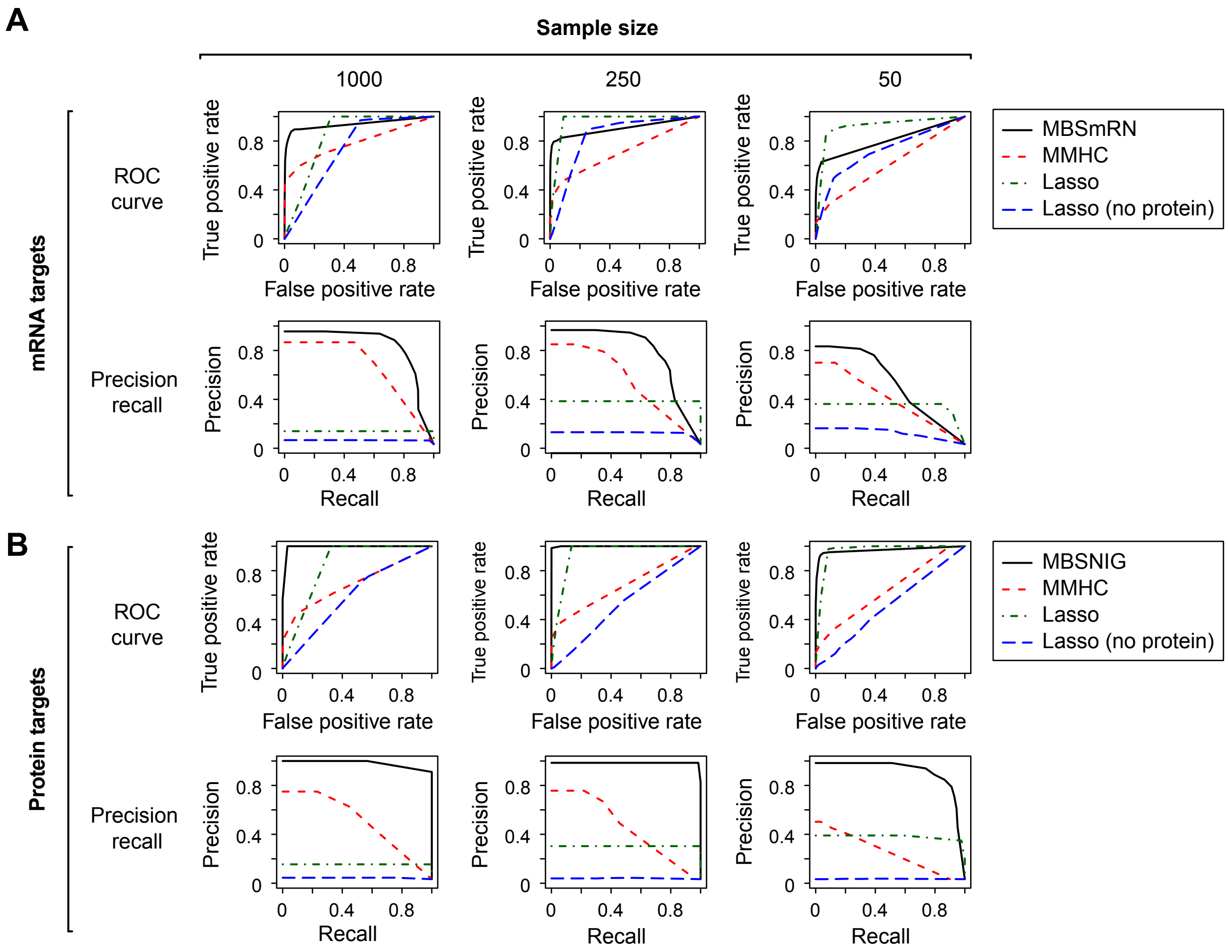


Fig. S5. The precision-recall curves and ROC curves of the competing regulatory network learning algorithms for direct regulators of (A) mRNA targets and (B) protein targets, based on the data generated using the second simulated network.

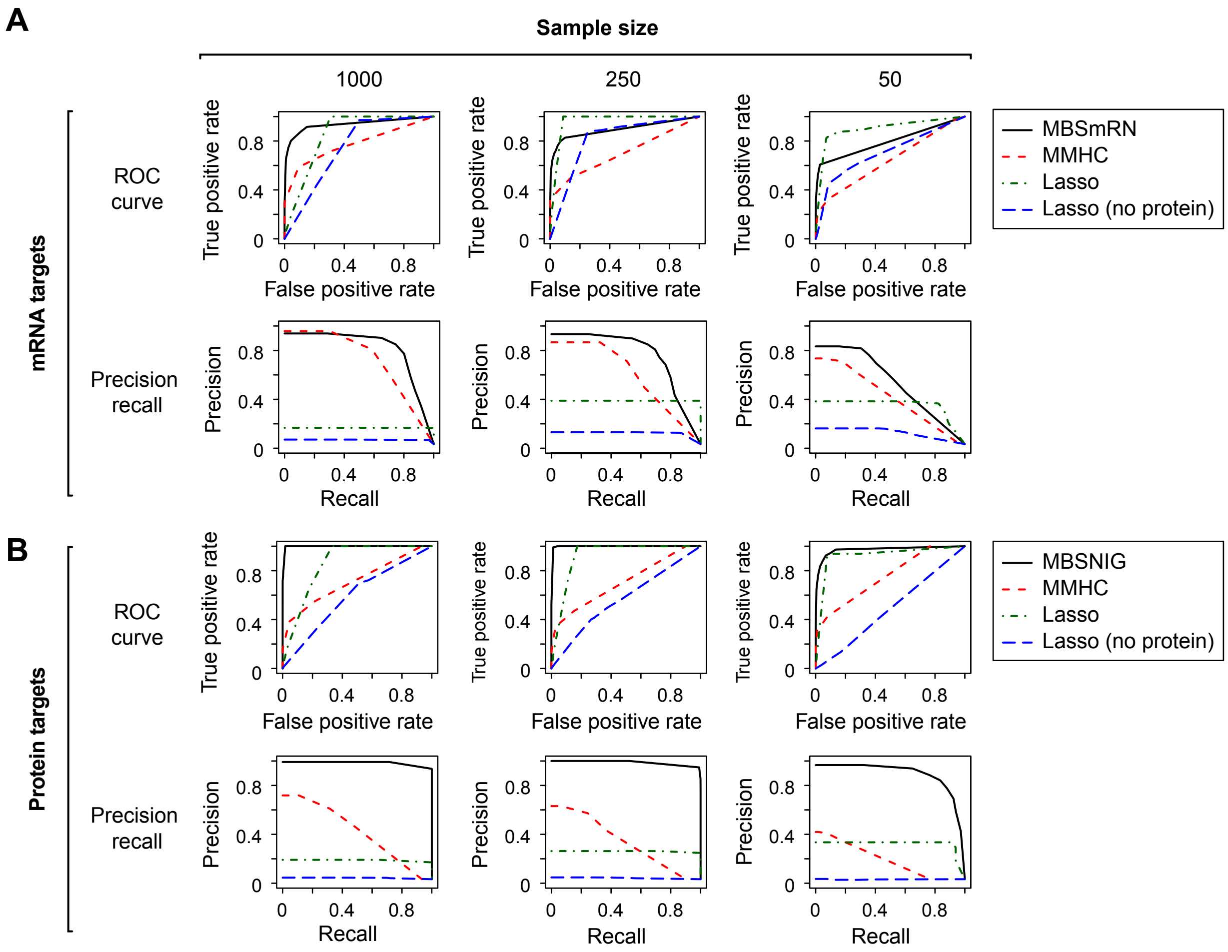


Fig. S6. The precision-recall curves and ROC curves of the competing regulatory network learning algorithms for direct regulators of (A) mRNA targets and (B) protein targets, based on the data generated using the third simulated network.

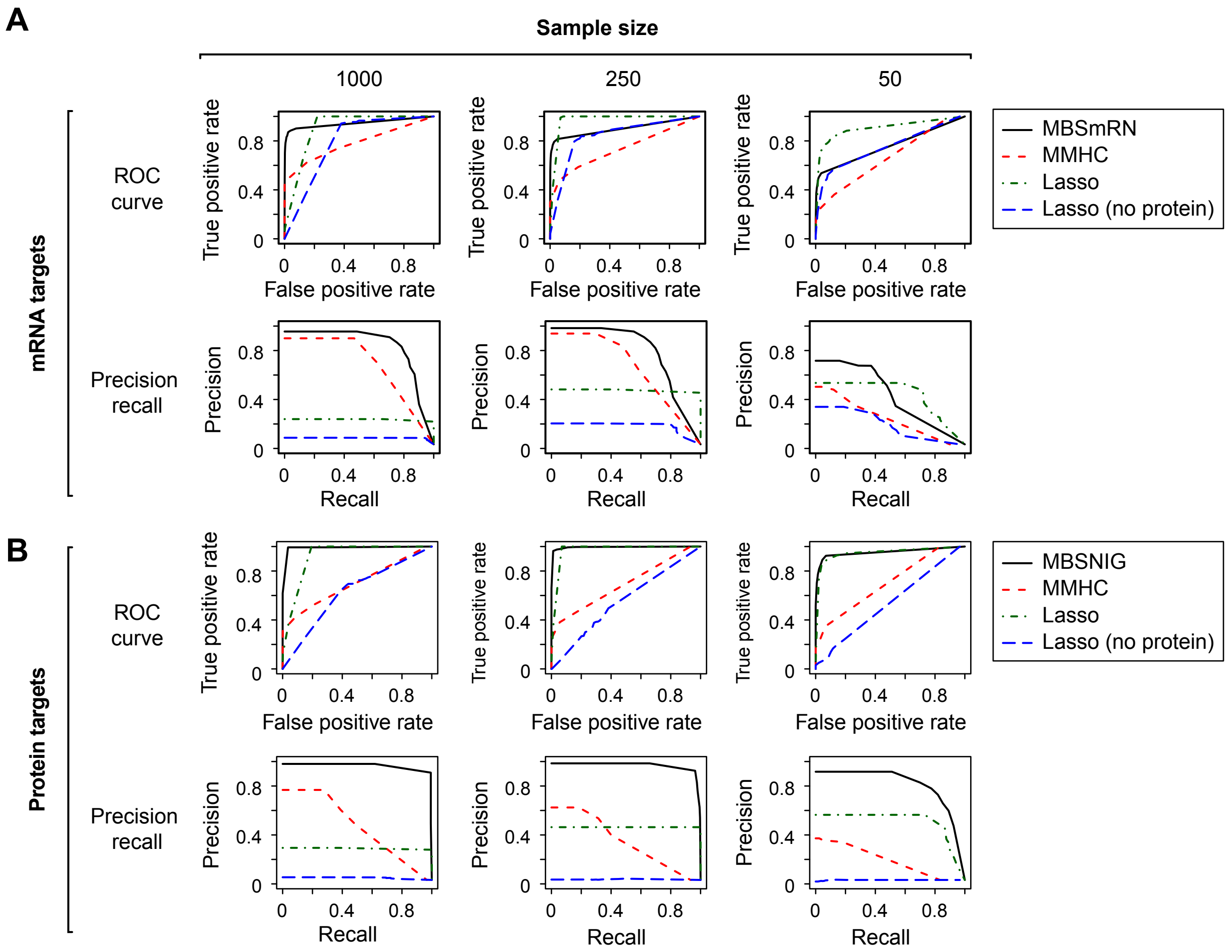


Fig. S7. The precision-recall curves and ROC curves of the competing regulatory network learning algorithms for direct regulators of (A) mRNA targets and (B) protein targets, based on the data generated using the fourth simulated network.

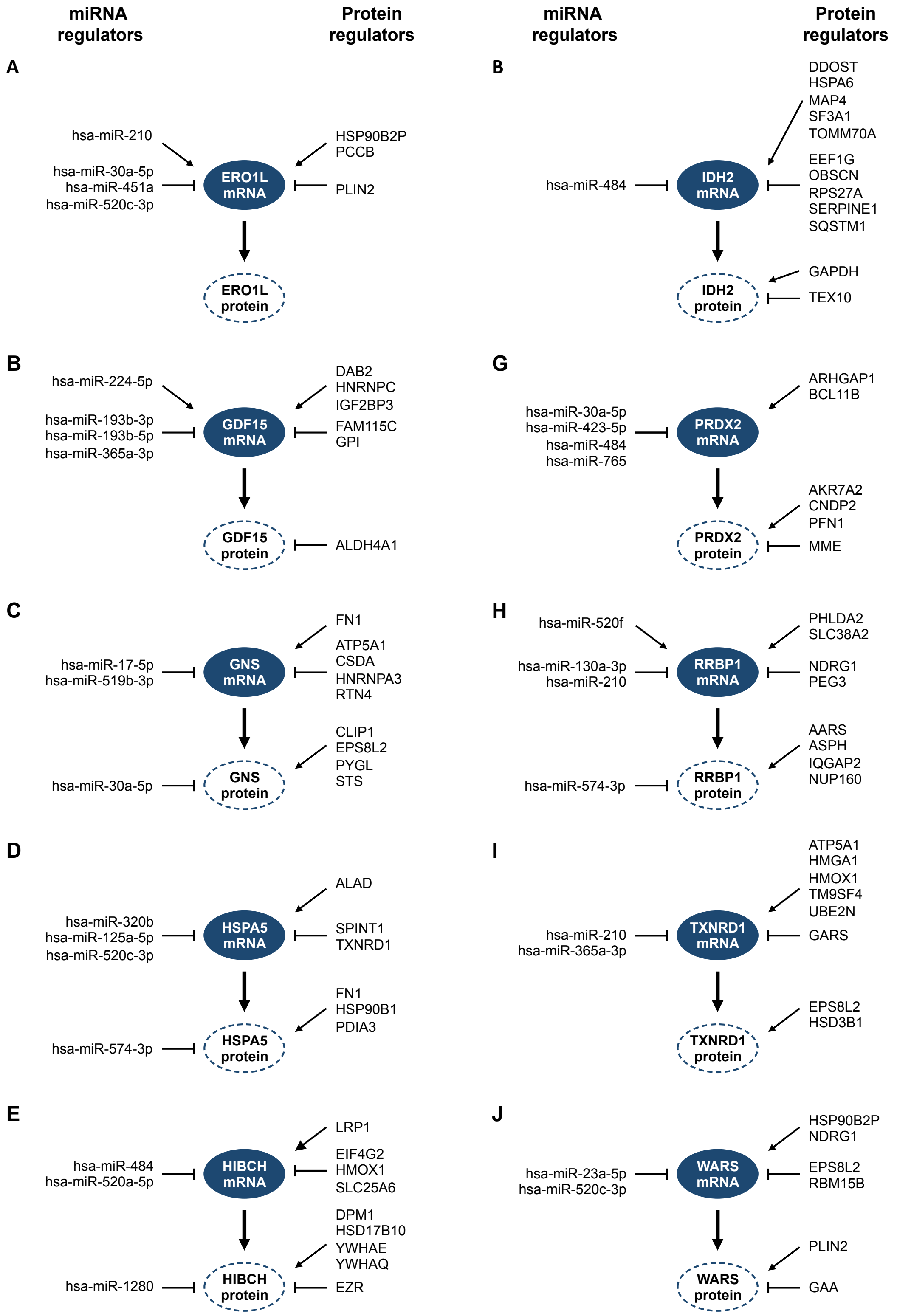
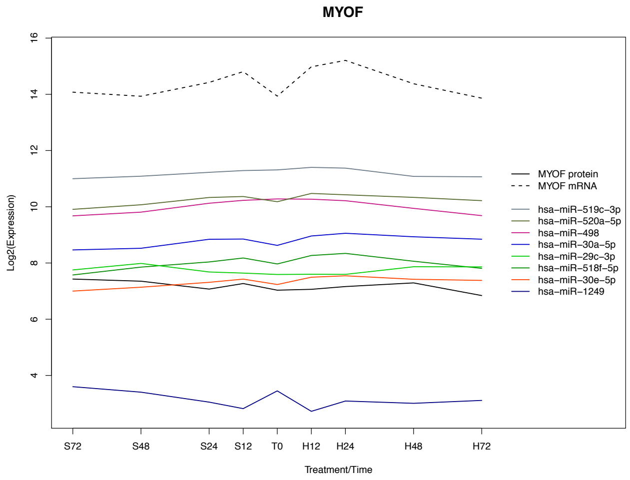
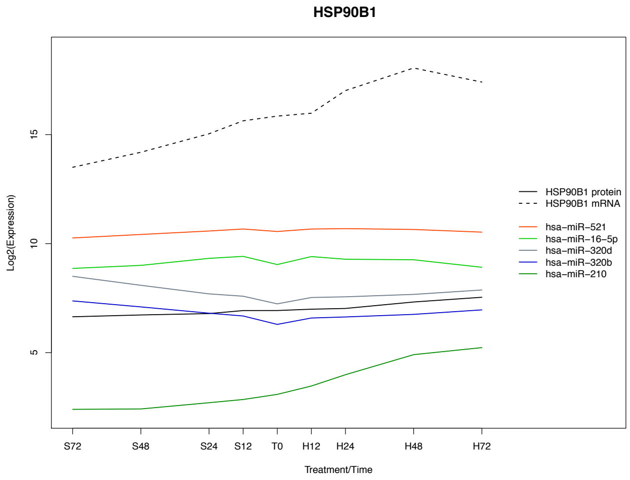
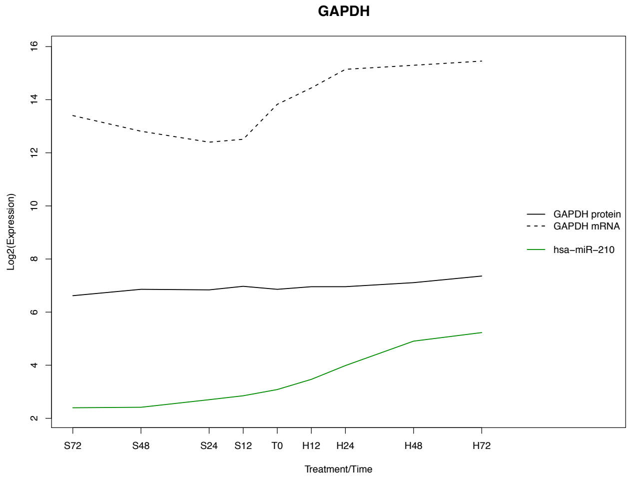


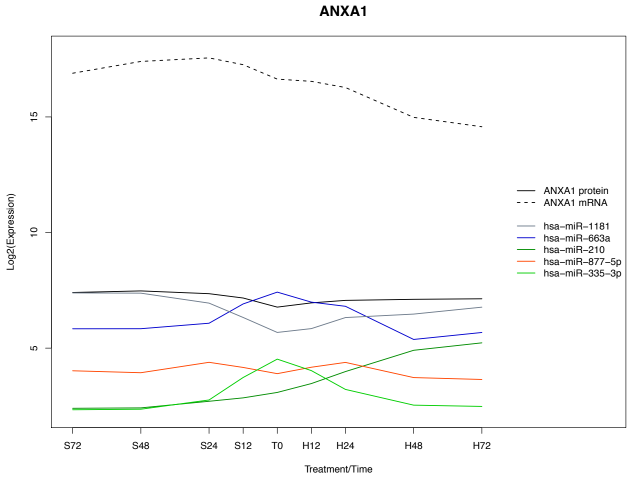
Fig. S8. miRNA/mRNA/protein regulatory network for nine proteins derived by the MBSmRN and MBSNIG algorithms.

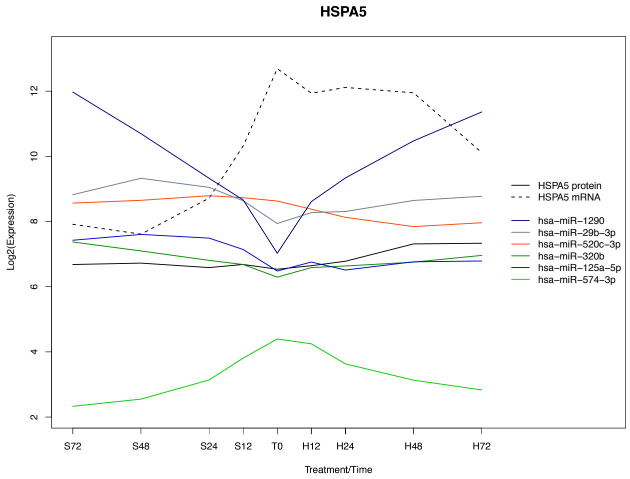
Fig. S9 (See following pages) The expression level of the 78 proteins, their mRNA transcripts, and the miRNA directly regulating the mRNA/protein pairs over the time course under standard and hypoxic conditions. Expression values are averaged over the four placentas.

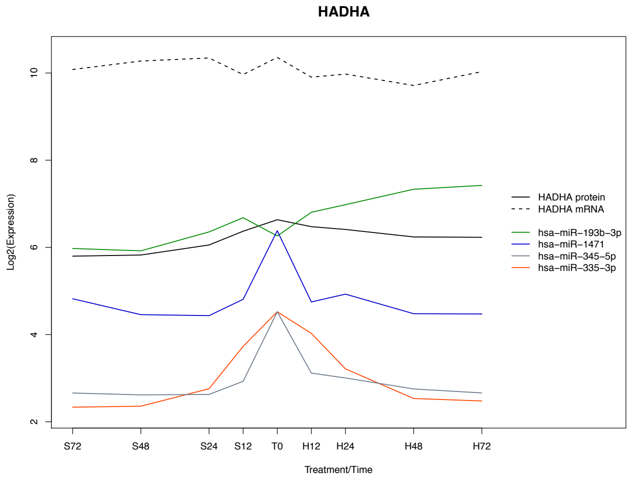

MYOF
Log2(Expression)
16
14
12
10
8
6
4
MYOF protein
MYOF mRNA
hsa−miR−519c−3p
hsa−miR−520a−5p
hsa−miR−498
hsa−miR−30a−5p
hsa−miR−29c−3p
hsa−miR−518f−5p
hsa−miR−30e−5p
hsa−miR−1249
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

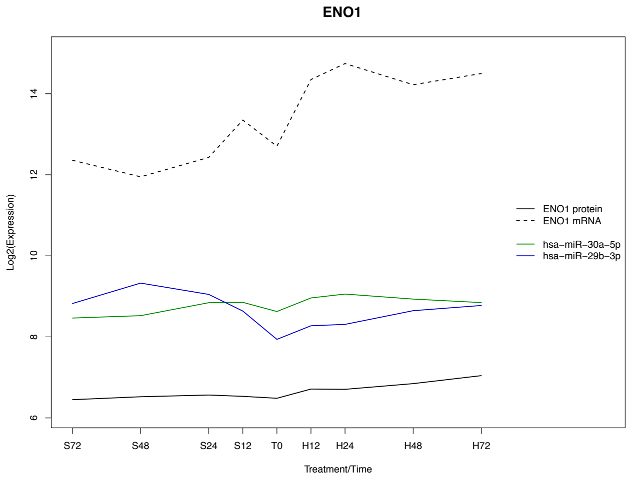

HSP90B1
Log2(Expression)
15
10
5
HSP90B1 protein
HSP90B1 mRNA
hsa−miR−521
hsa−miR−16−5p
hsa−miR−320d
hsa−miR−320b
hsa−miR−210
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

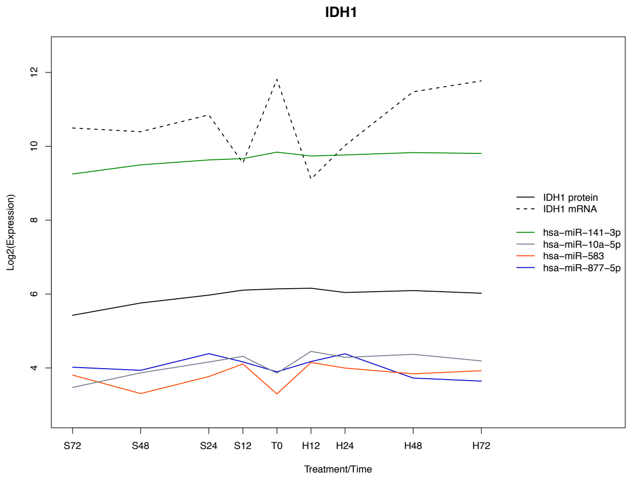

GAPDH
Log2(Expression)
16
14
12
10
8
6
4
2
GAPDH protein
GAPDH mRNA
hsa−miR−210
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

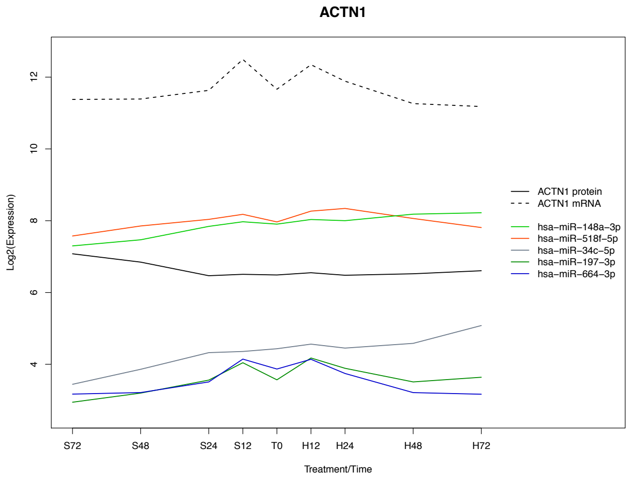

ANXA1
Log2(Expression)
15
10
5
ANXA1 protein
ANXA1 mRNA
hsa−miR−1181
hsa−miR−663a
hsa−miR−210
hsa−miR−877−5p
hsa−miR−335−3p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

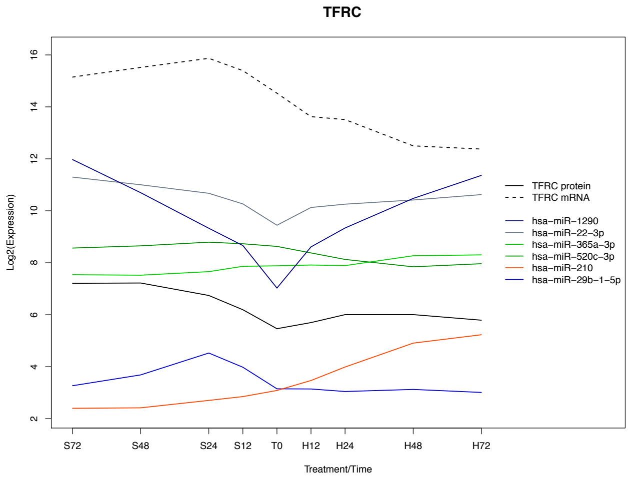

HSPA5
Log2(Expression)
12
10
8
6
4
2
HSPA5 protein
HSPA5 mRNA
hsa−miR−1290
hsa−miR−29b−3p
hsa−miR−520c−3p
hsa−miR−320b
hsa−miR−125a−5p
hsa−miR−574−3p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

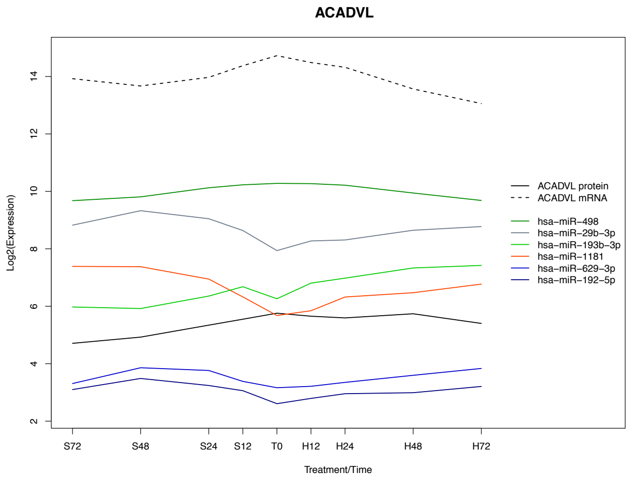

HADHA
Log2(Expression)
10
8
6
4
2
HADHA protein
HADHA mRNA
hsa−miR−193b−3p
hsa−miR−1471
hsa−miR−345−5p
hsa−miR−335−3p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

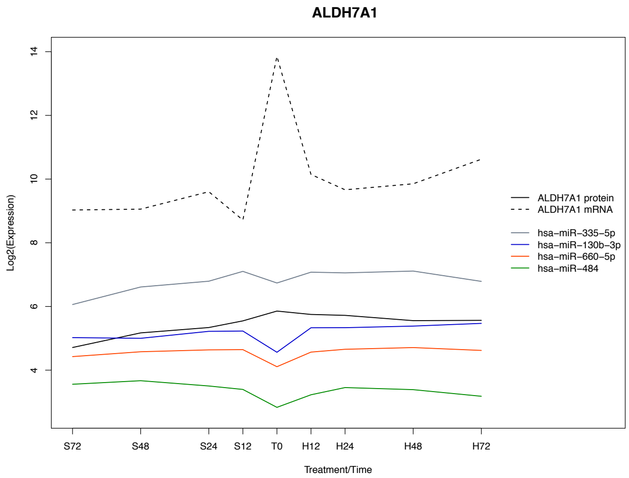

ENO1
Log2(Expression)
6
8
10
12
14
ENO1 protein
ENO1 mRNA
hsa−miR−30a−5p
hsa−miR−29b−3p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

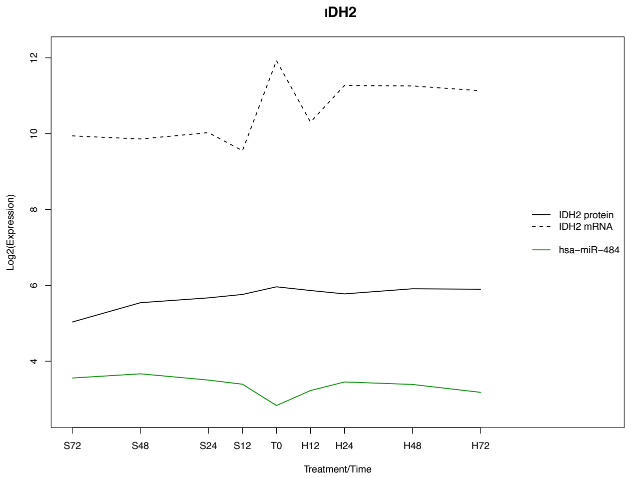

IDH1
Log2(Expression)
4
6
8
10
12
IDH1 protein
IDH1 mRNA
hsa−miR−141−3p
hsa−miR−10a−5p
hsa−miR−583
hsa−miR−877−5p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

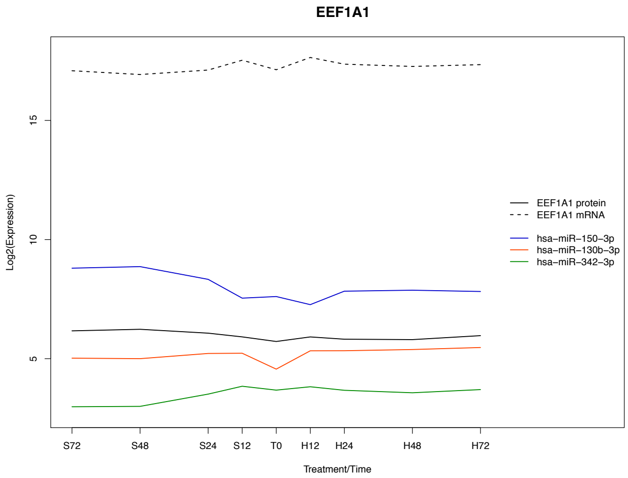

ACTN1
Log2(Expression)
4
6
8
10
12
ACTN1 protein
ACTN1 mRNA
hsa−miR−148a−3p
hsa−miR−518f−5p
hsa−miR−34c−5p
hsa−miR−197−3p
hsa−miR−664−3p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

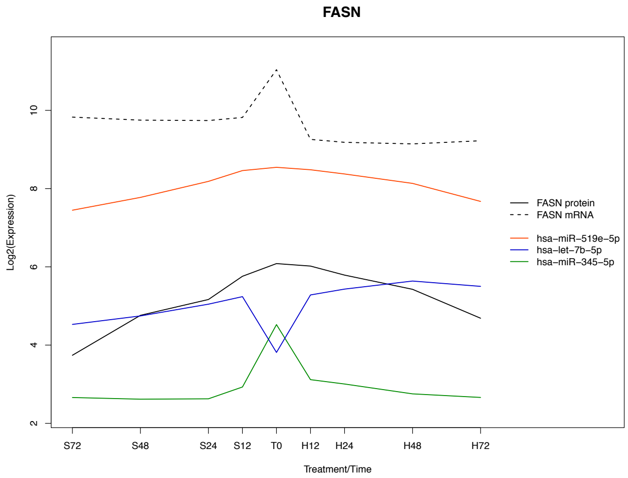

TFRC
Log2(Expression)
2
4
6
8
10
12
14
16
TFRC protein
TFRC mRNA
hsa−miR−1290
hsa−miR−22−3p
hsa−miR−365a−3p
hsa−miR−520c−3p
hsa−miR−210
hsa−miR−29b−1−5p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

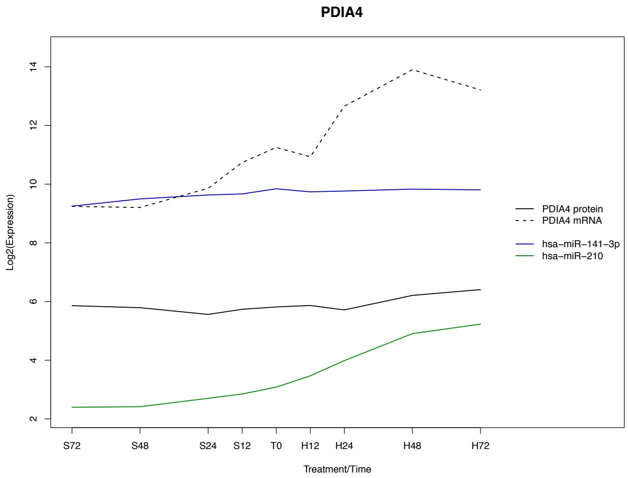

ACADVL
Log2(Expression)
2
4
6
8
10
12
14
ACADVL protein
ACADVL mRNA
hsa−miR−498
hsa−miR−29b−3p
hsa−miR−193b−3p
hsa−miR−1181
hsa−miR−629−3p
hsa−miR−192−5p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

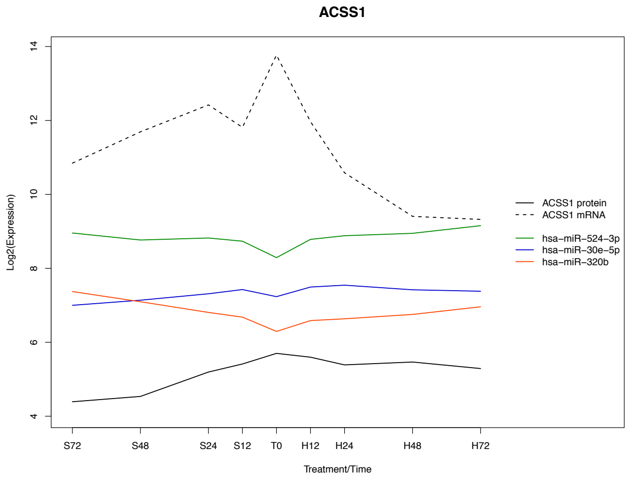

ALDH7A1
Log2(Expression)
4
6
8
10
12
14
ALDH7A1 protein
ALDH7A1 mRNA
hsa−miR−335−5p
hsa−miR−130b−3p
hsa−miR−660−5p
hsa−miR−484
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

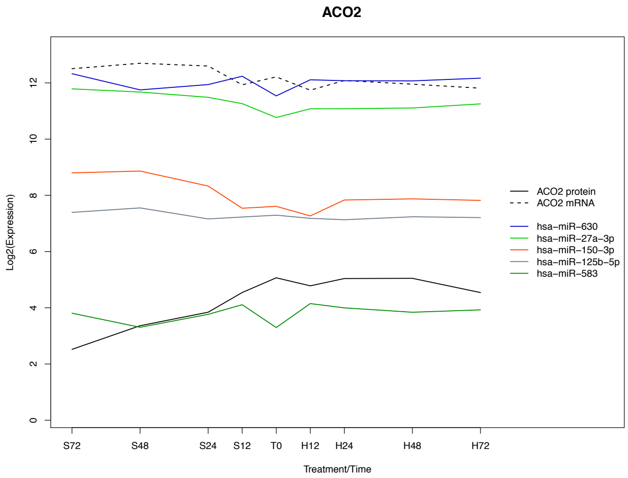

IDH2
Log2(Expression)
4
6
8
10
12
IDH2 protein
IDH2 mRNA
hsa−miR−484
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

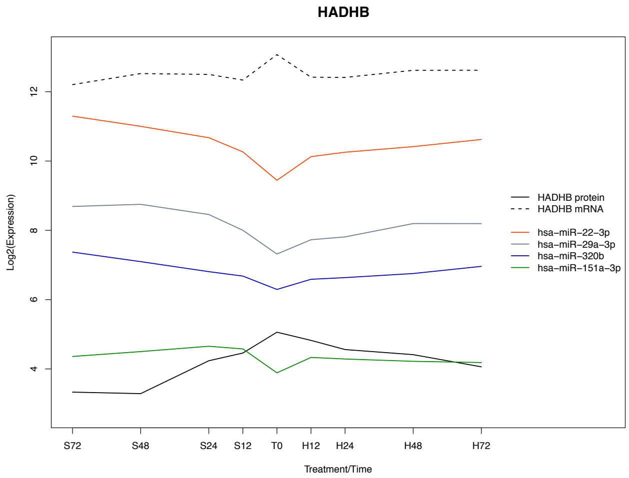

EEF1A1
Log2(Expression)
5
10
15
EEF1A1 protein
EEF1A1 mRNA
hsa−miR−150−3p
hsa−miR−130b−3p
hsa−miR−342−3p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

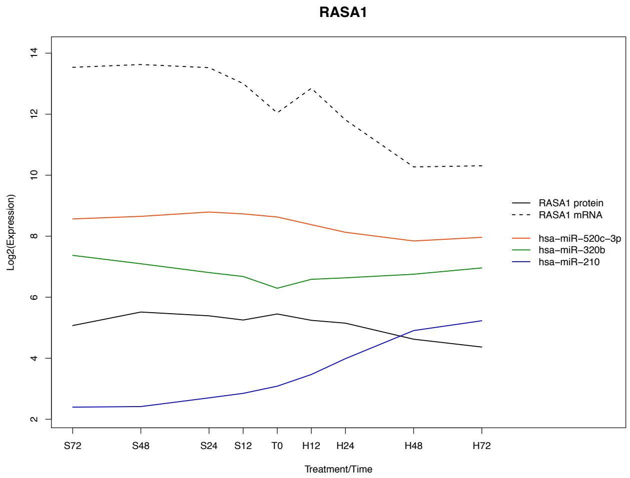

FASN
Log2(Expression)
2
4
6
8
10
FASN protein
FASN mRNA
hsa−miR−519e−5p
hsa−let−7b−5p
hsa−miR−345−5p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

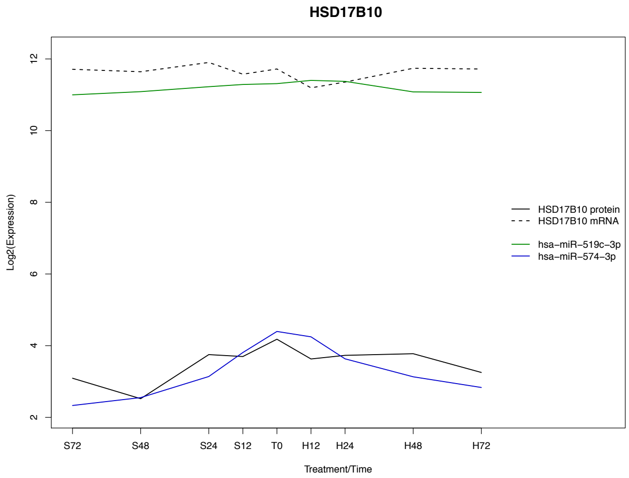

PDIA4
Log2(Expression)
2
4
6
8
10
12
14
PDIA4 protein
PDIA4 mRNA
hsa−miR−141−3p
hsa−miR−210
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

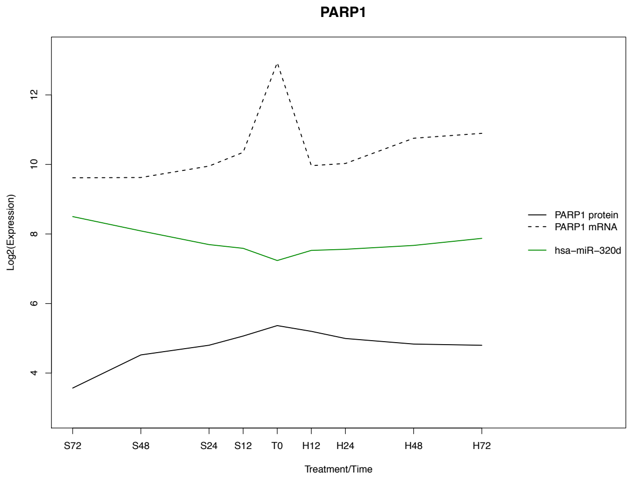

ACSS1
Log2(Expression)
4
6
8
10
12
14
ACSS1 protein
ACSS1 mRNA
hsa−miR−524−3p
hsa−miR−30e−5p
hsa−miR−320b
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

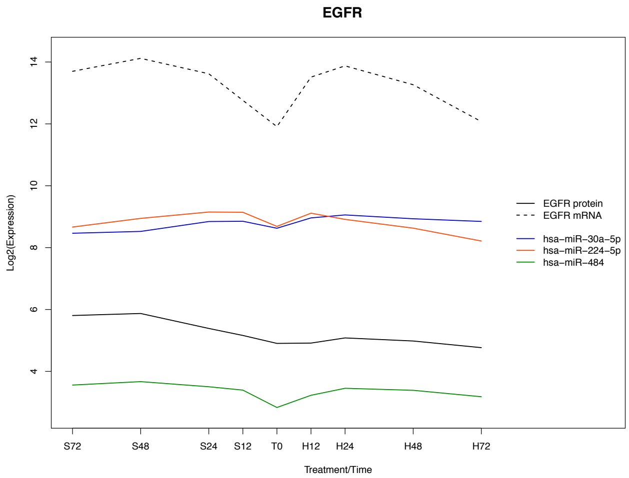

ACO2
Log2(Expression)
0
2
4
6
8
10
12
ACO2 protein
ACO2 mRNA
hsa−miR−630
hsa−miR−27a−3p
hsa−miR−150−3p
hsa−miR−125b−5p
hsa−miR−583
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

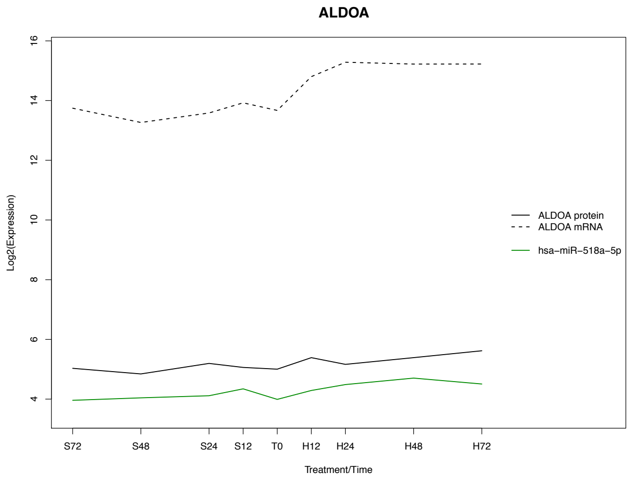

HADHB
Log2(Expression)
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
HADHB protein
HADHB mRNA
hsa−miR−22−3p
hsa−miR−29a−3p
hsa−miR−320b
hsa−miR−151a−3p

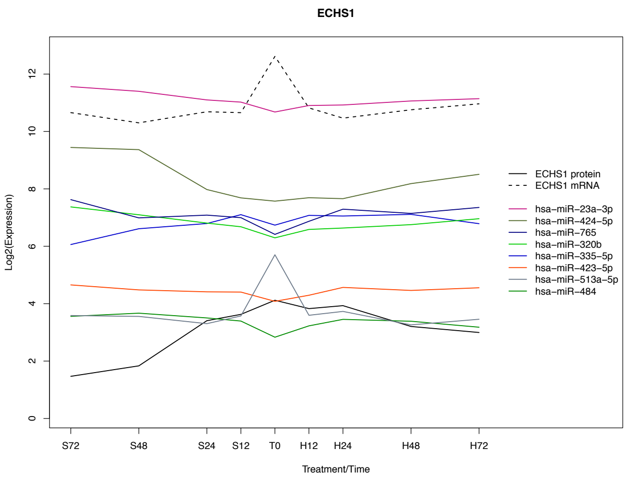

RASA1
Log2(Expression)
2
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
RASA1 protein
RASA1 mRNA
hsa−miR−520c−3p
hsa−miR−320b
hsa−miR−210

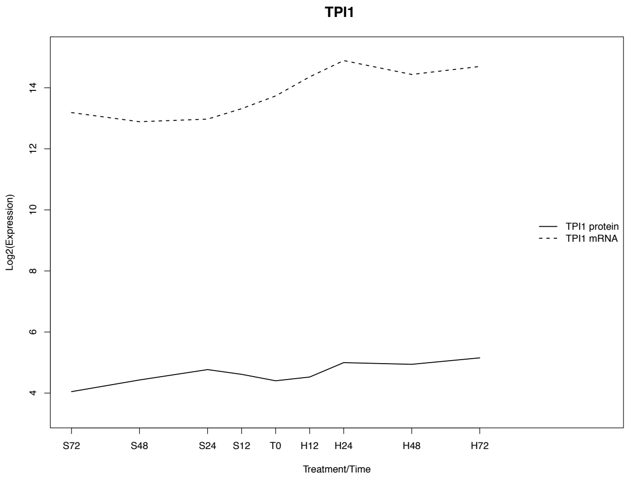

HSD17B10
Log2(Expression)
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
HSD17B10 protein
HSD17B10 mRNA
hsa−miR−519c−3p
hsa−miR−574−3p

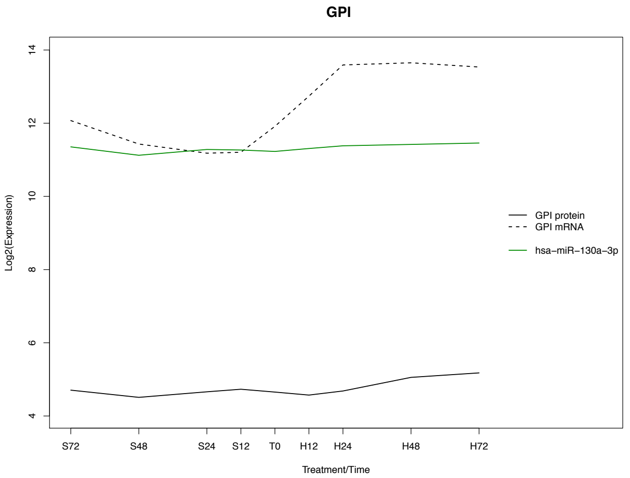

PARP1
Log2(Expression)
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
PARP1 protein
PARP1 mRNA
hsa−miR−320d

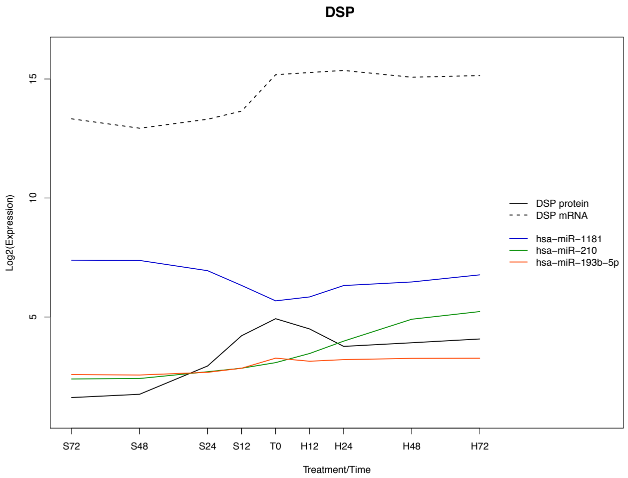

EGFR
Log2(Expression)
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
EGFR protein
EGFR mRNA
hsa−miR−30a−5p
hsa−miR−224−5p
hsa−miR−484

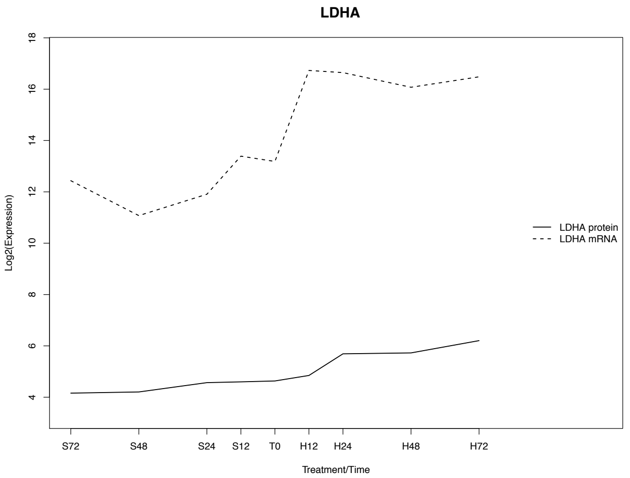

ALDOA
Log2(Expression)
4
6
8
10
12
14
16
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
ALDOA protein
ALDOA mRNA
hsa−miR−518a−5p

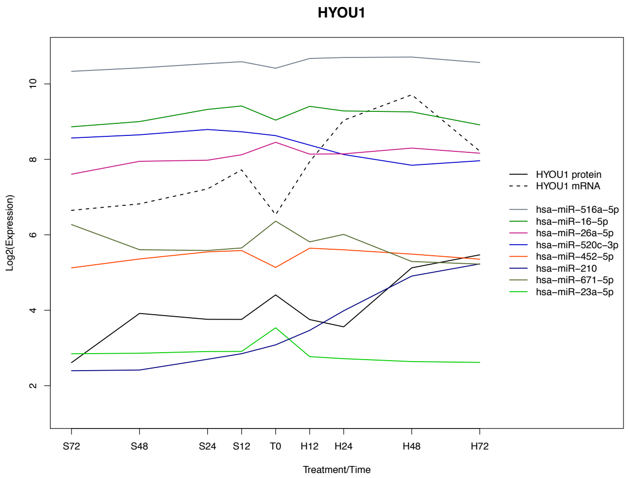

ECHS1
Log2(Expression)
0
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
ECHS1 protein
ECHS1 mRNA
hsa−miR−23a−3p
hsa−miR−424−5p
hsa−miR−765
hsa−miR−320b
hsa−miR−335−5p
hsa−miR−423−5p
hsa−miR−513a−5p
hsa−miR−484

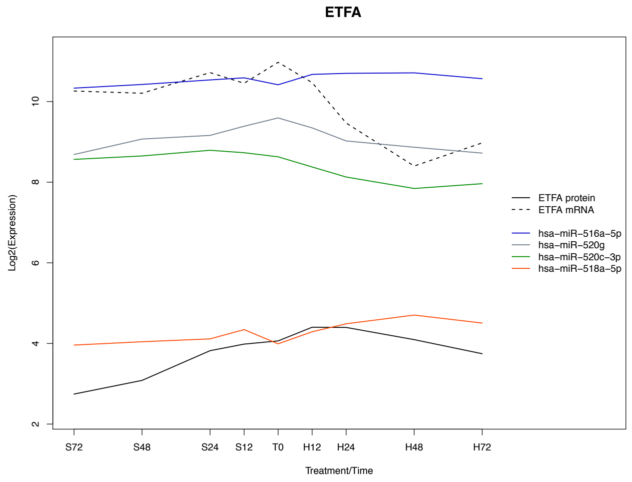

TPI1
Log2(Expression)
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
TPI1 protein
TPI1 mRNA

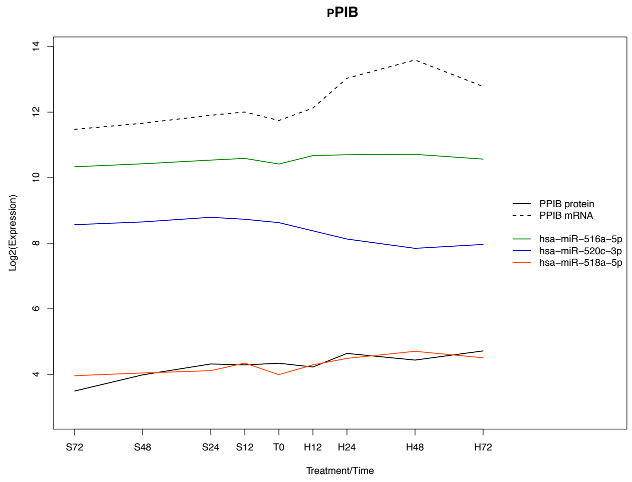

GPI
Log2(Expression)
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
GPI protein
GPI mRNA
hsa−miR−130a−3p

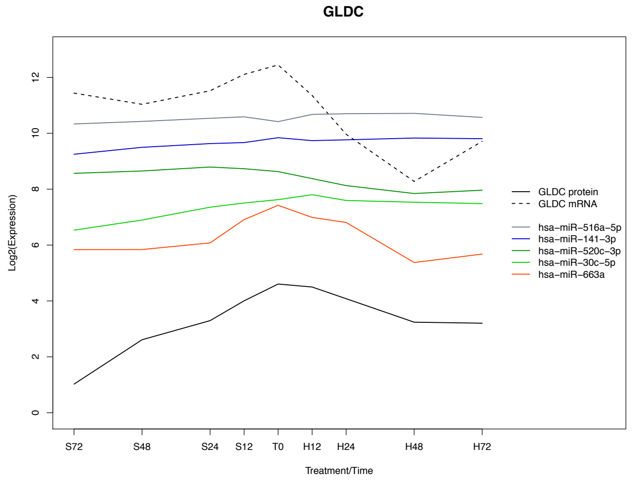

DSP
Log2(Expression)
5
10
15
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
DSP protein
DSP mRNA
hsa−miR−1181
hsa−miR−210
hsa−miR−193b−5p

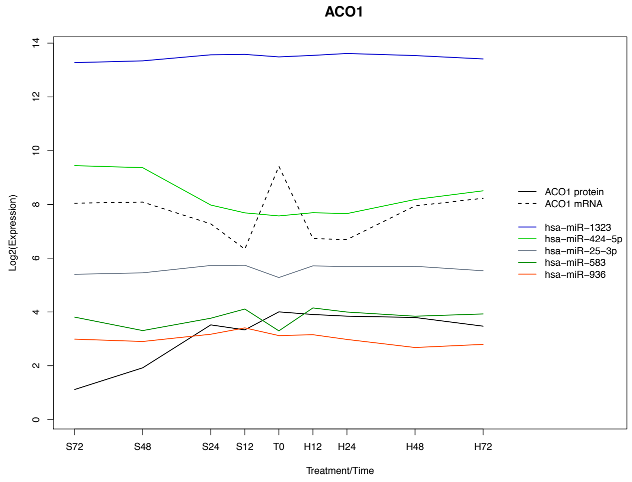

LDHA
Log2(Expression)
4
6
8
10
12
14
16
18
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
LDHA protein
LDHA mRNA

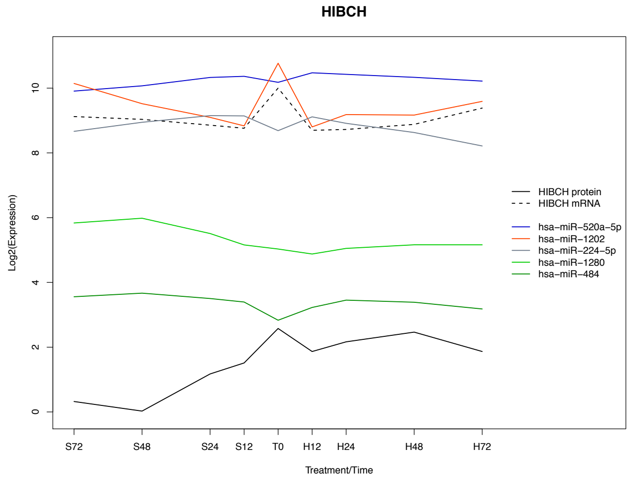

HYOU1
Log2(Expression)
2
4
6
8
10
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
HYOU1 protein
HYOU1 mRNA
hsa−miR−516a−5p
hsa−miR−16−5p
hsa−miR−26a−5p
hsa−miR−520c−3p
hsa−miR−452−5p
hsa−miR−210
hsa−miR−671−5p
hsa−miR−23a−5p

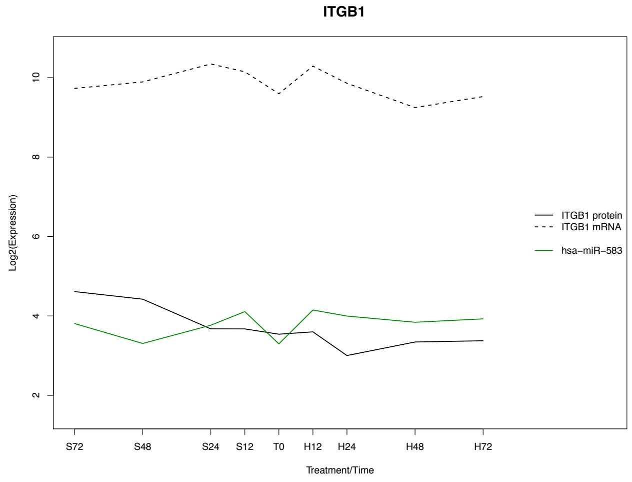

ETFA

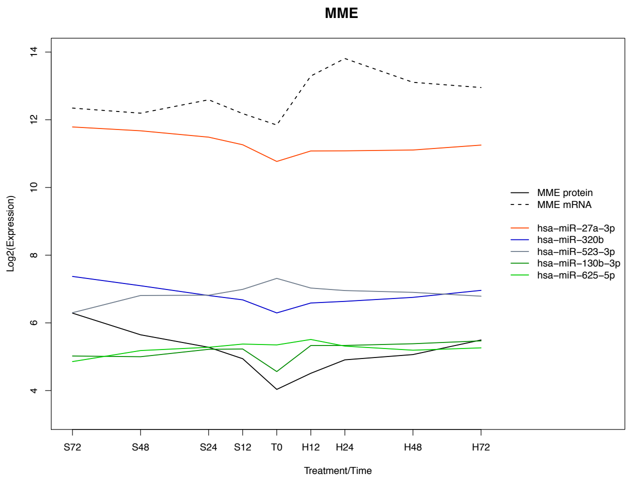

PPIB

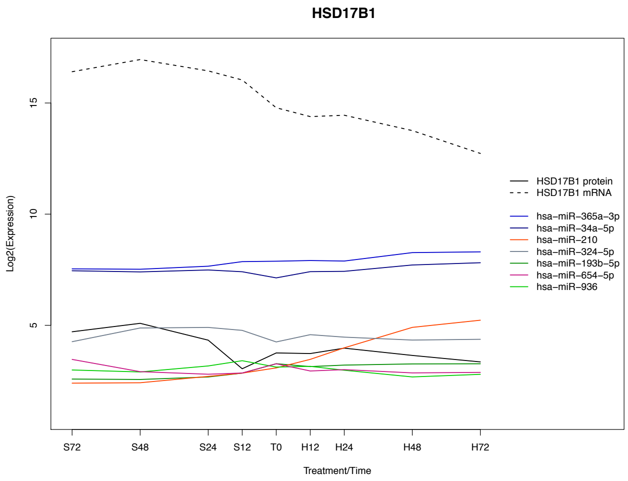

GLDC

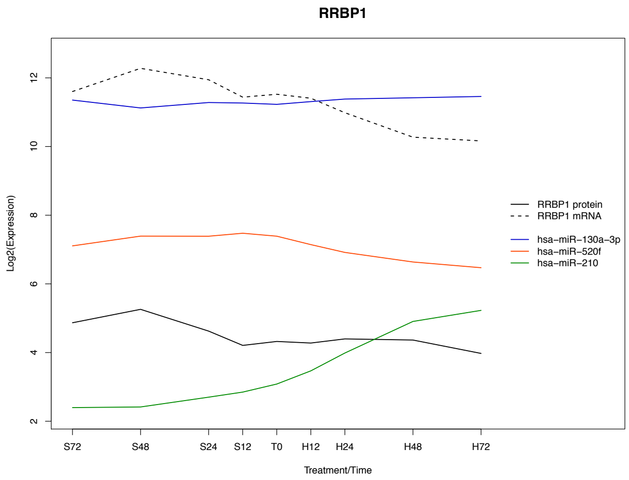

ACO1

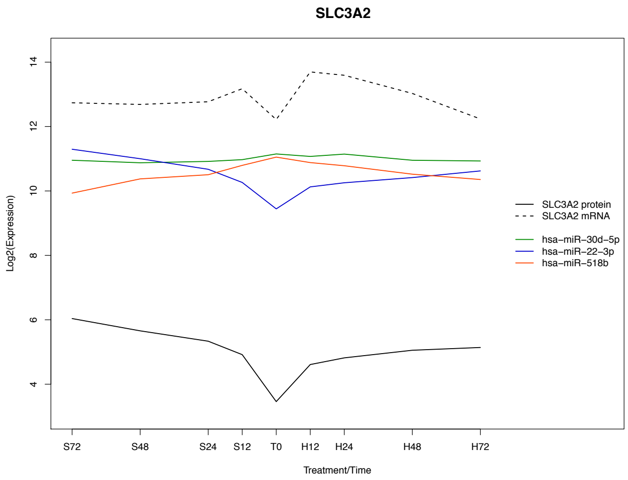

HIBCH

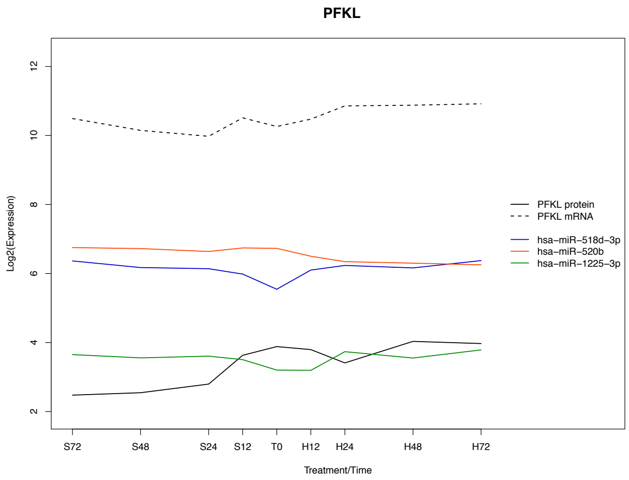

ITGB1

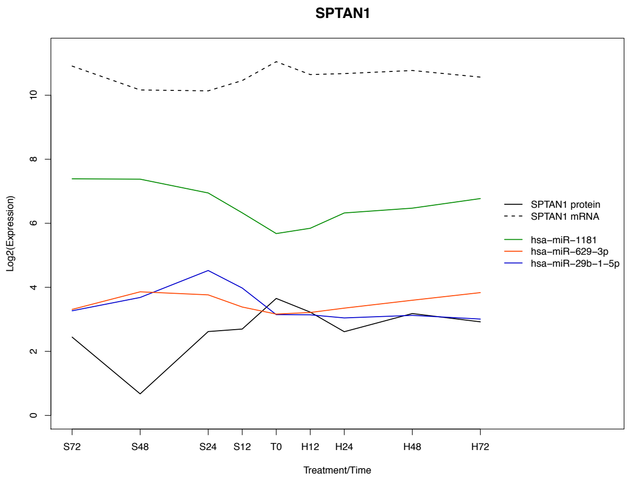

MME
Log2(Expression)
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
MME protein
MME mRNA
hsa−miR−27a−3p
hsa−miR−320b
hsa−miR−523−3p
hsa−miR−130b−3p
hsa−miR−625−5p

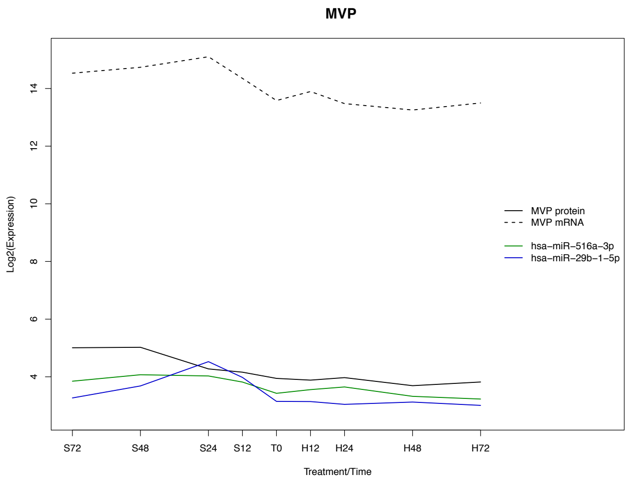

HSD17B1
Log2(Expression)
5
10
15
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
HSD17B1 protein
HSD17B1 mRNA
hsa−miR−365a−3p
hsa−miR−34a−5p
hsa−miR−210
hsa−miR−324−5p
hsa−miR−193b−5p
hsa−miR−654−5p
hsa−miR−936

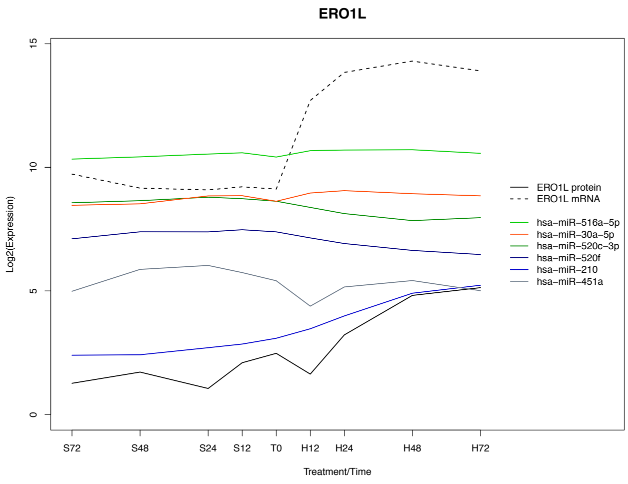

RRBP1
Log2(Expression)
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
RRBP1 protein
RRBP1 mRNA
hsa−miR−130a−3p
hsa−miR−520f
hsa−miR−210

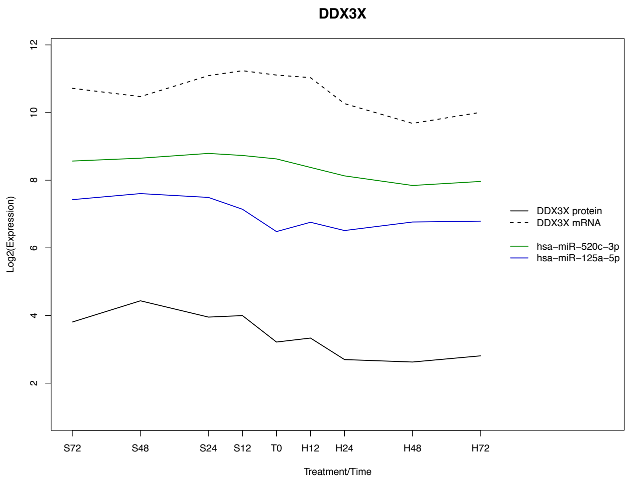

SLC3A2
Log2(Expression)
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
SLC3A2 protein
SLC3A2 mRNA
hsa−miR−30d−5p
hsa−miR−22−3p
hsa−miR−518b

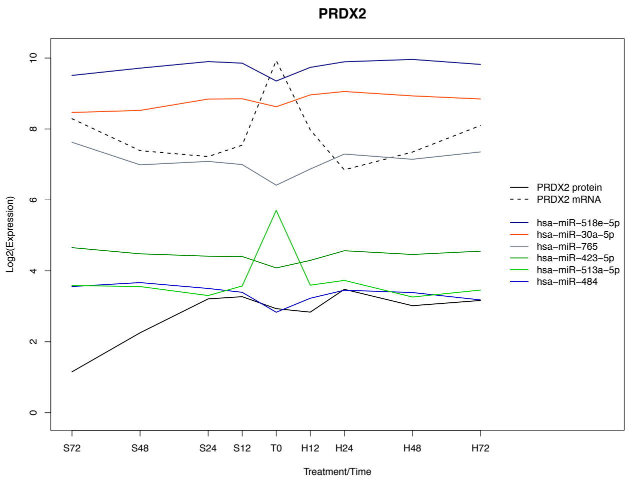

PFKL
Log2(Expression)
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
PFKL protein
PFKL mRNA
hsa−miR−518d−3p
hsa−miR−520b
hsa−miR−1225−3p

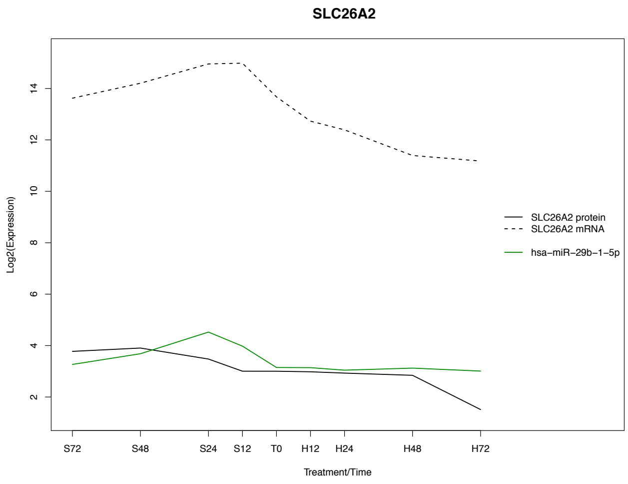

SPTAN1
Log2(Expression)
0
2
4
6
8
10
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
SPTAN1 protein
SPTAN1 mRNA
hsa−miR−1181
hsa−miR−629−3p
hsa−miR−29b−1−5p

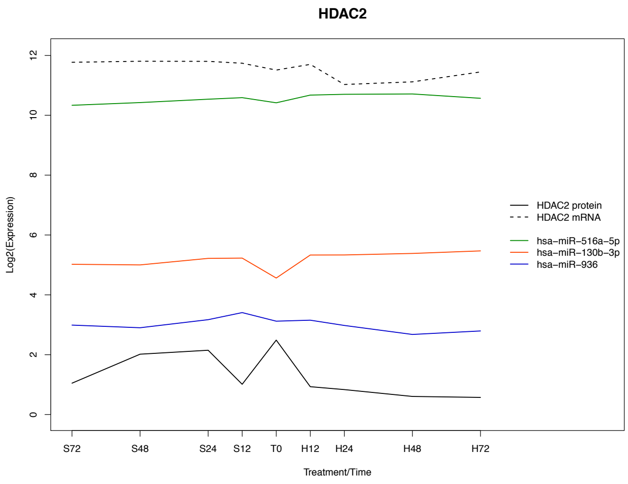

MVP
Log2(Expression)
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
MVP protein
MVP mRNA
hsa−miR−516a−3p
hsa−miR−29b−1−5p

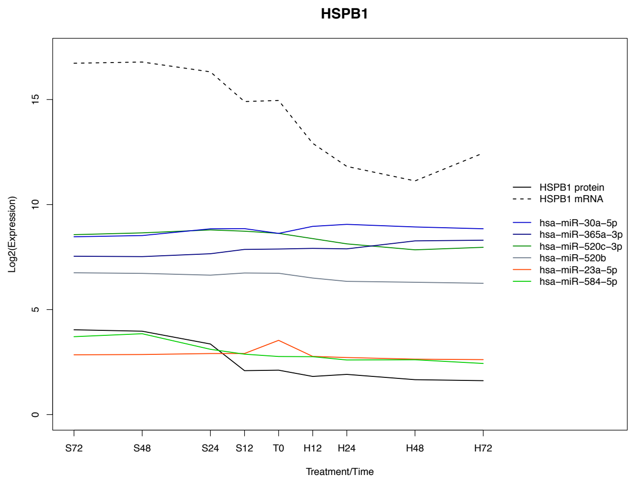

ERO1L
Log2(Expression)
0
5
10
15
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
ERO1L protein
ERO1L mRNA
hsa−miR−516a−5p
hsa−miR−30a−5p
hsa−miR−520c−3p
hsa−miR−520f
hsa−miR−210
hsa−miR−451a

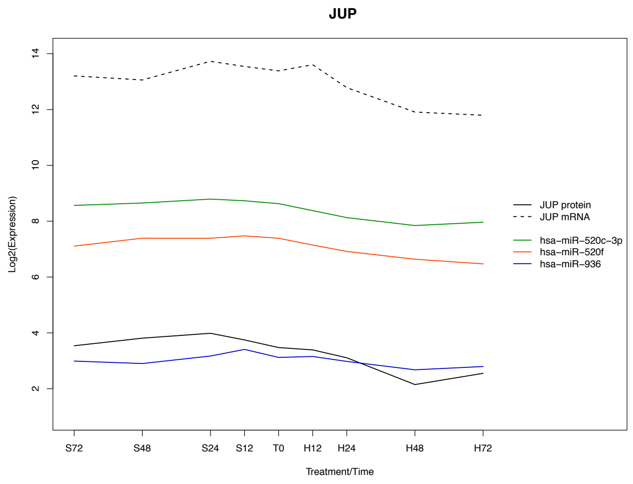

DDX3X
Log2(Expression)
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
DDX3X protein
DDX3X mRNA
hsa−miR−520c−3p
hsa−miR−125a−5p

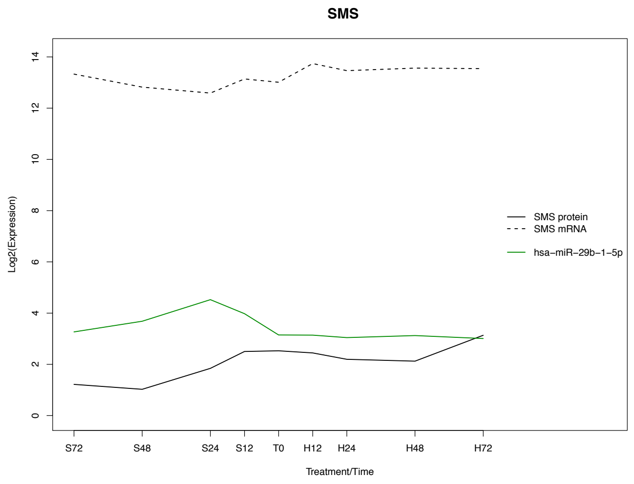

PRDX2
Log2(Expression)
0
2
4
6
8
10
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
PRDX2 protein
PRDX2 mRNA
hsa−miR−518e−5p
hsa−miR−30a−5p
hsa−miR−765
hsa−miR−423−5p
hsa−miR−513a−5p
hsa−miR−484

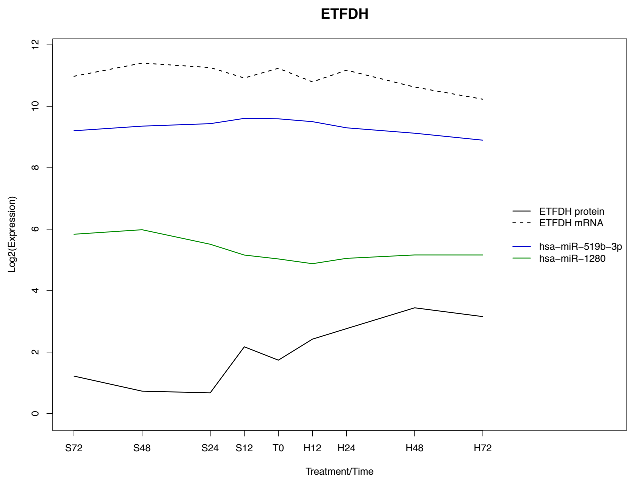

SLC26A2
Log2(Expression)
2
4
6
8
10
12
14
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
SLC26A2 protein
SLC26A2 mRNA
hsa−miR−29b−1−5p

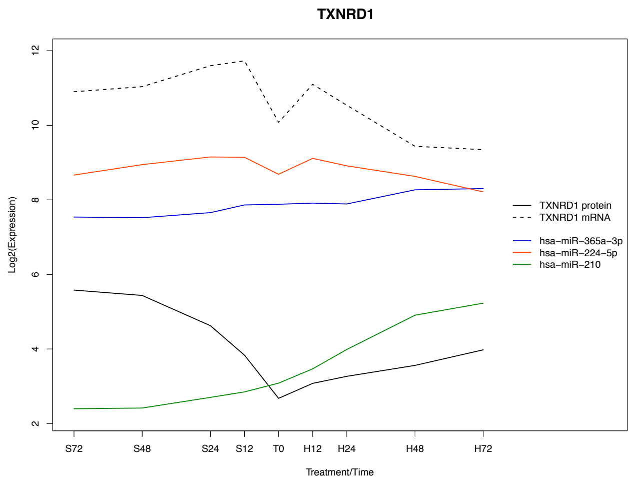

HDAC2
Log2(Expression)
0
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
HDAC2 protein
HDAC2 mRNA
hsa−miR−516a−5p
hsa−miR−130b−3p
hsa−miR−936

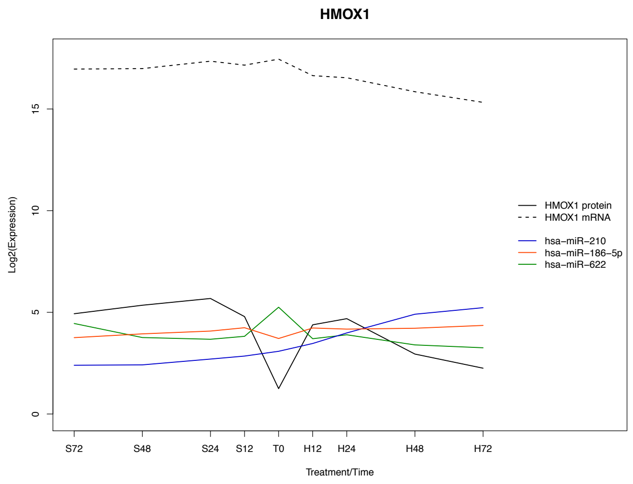

HSPB1
Log2(Expression)
0
5
10
15
HSPB1 protein
HSPB1 mRNA
hsa−miR−30a−5p
hsa−miR−365a−3p
hsa−miR−520c−3p
hsa−miR−520b
hsa−miR−23a−5p
hsa−miR−584−5p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time

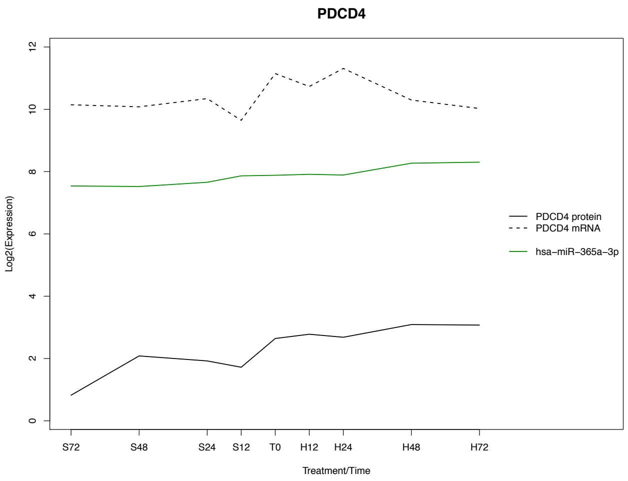

JUP
Log2(Expression)
2
4
6
8
10
12
14
JUP protein
JUP mRNA
hsa−miR−520c−3p
hsa−miR−520f
hsa−miR−936
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time


SMS
Log2(Expression)
0
2
4
6
8
10
12
14
SMS protein
SMS mRNA
hsa−miR−29b−1−5p
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time


ETFDH
Log2(Expression)
0
2
4
6
8
10
12
ETFDH protein
ETFDH mRNA
hsa−miR−519b−3p
hsa−miR−1280
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time


TXNRD1
Log2(Expression)
2
4
6
8
10
12
TXNRD1 protein
TXNRD1 mRNA
hsa−miR−365a−3p
hsa−miR−224−5p
hsa−miR−210
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time


HMOX1
Log2(Expression)
0
5
10
15
HMOX1 protein
HMOX1 mRNA
hsa−miR−210
hsa−miR−186−5p
hsa−miR−622
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time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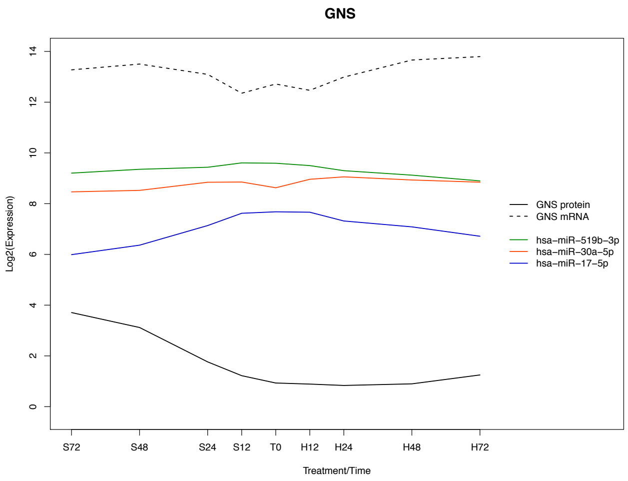
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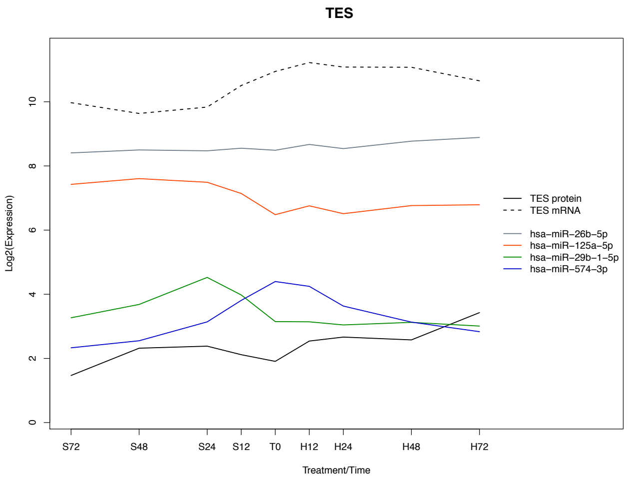
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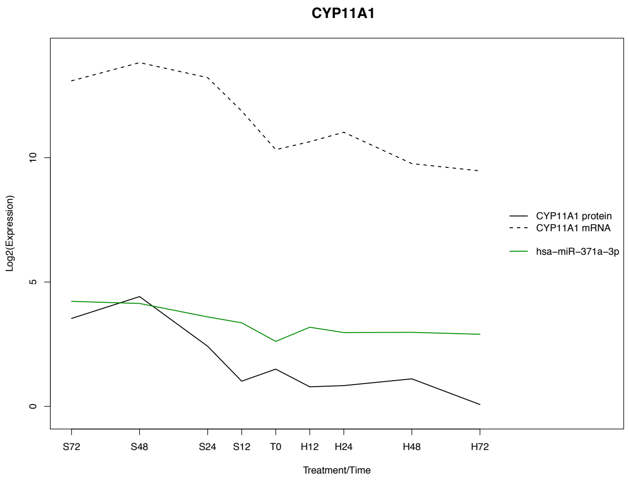
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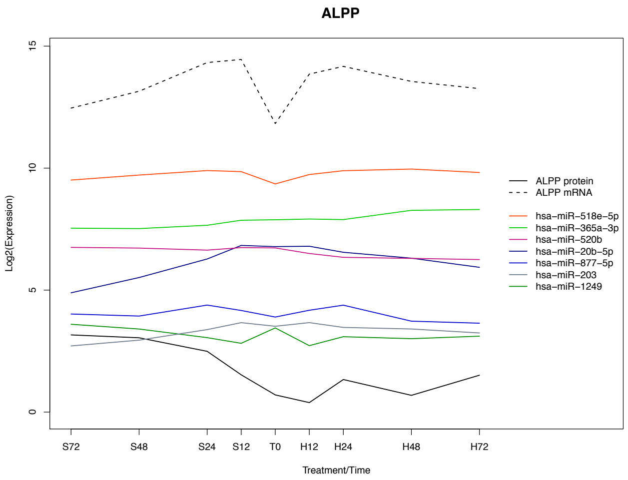
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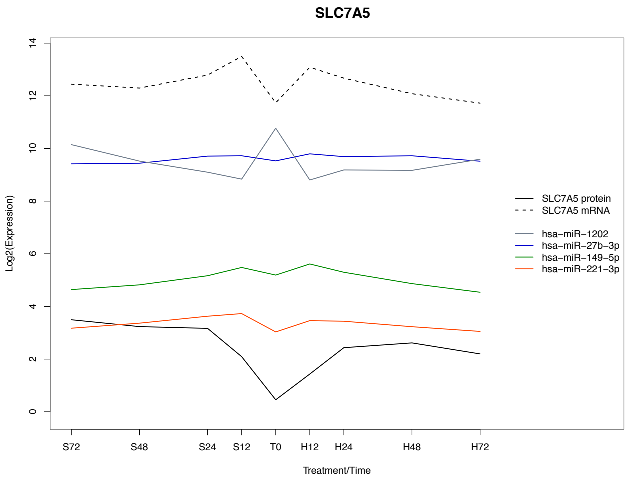
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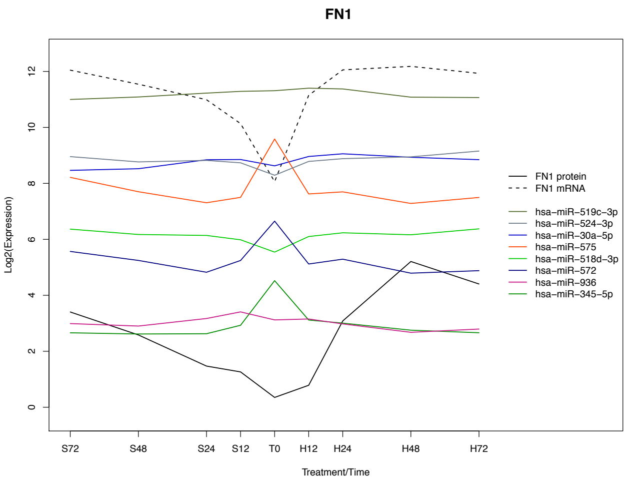
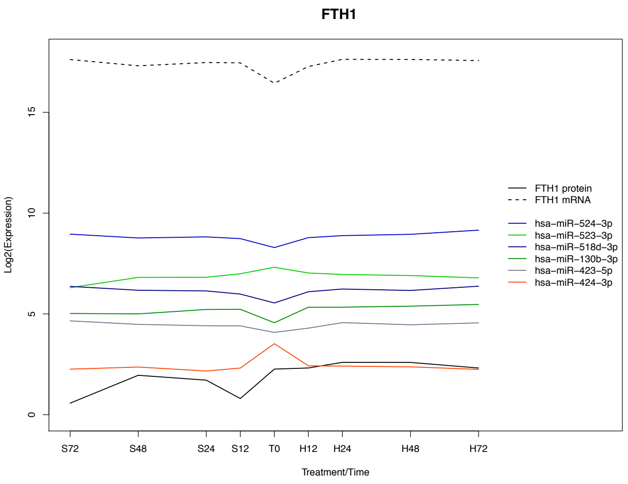

FN1
Log2(Expression)
0
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
FN1 protein
FN1 mRNA
hsa−miR−519c−3p
hsa−miR−524−3p
hsa−miR−30a−5p
hsa−miR−575
hsa−miR−518d−3p
hsa−miR−572
hsa−miR−936
hsa−miR−345−5p


FTH1
Log2(Expression)
0
5
10
15
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
FTH1 protein
FTH1 mRNA
hsa−miR−524−3p
hsa−miR−523−3p
hsa−miR−518d−3p
hsa−miR−130b−3p
hsa−miR−423−5p
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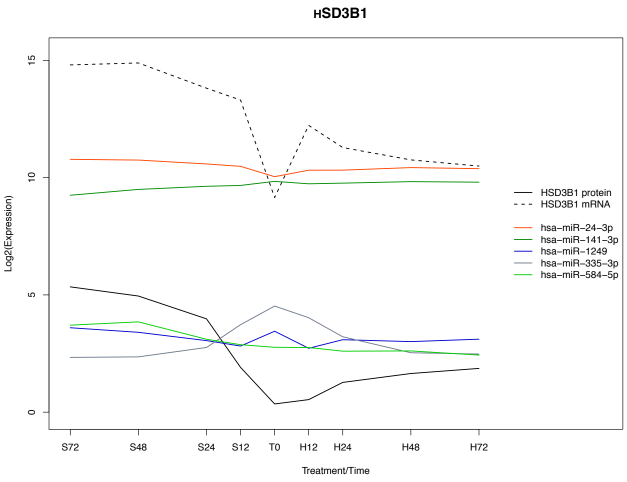
HSD3B1
Log2(Expression)
0
5
10
15
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
HSD3B1 protein
HSD3B1 mRNA
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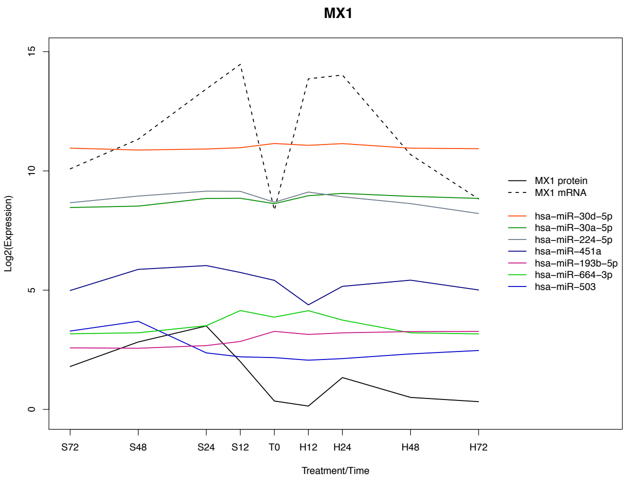
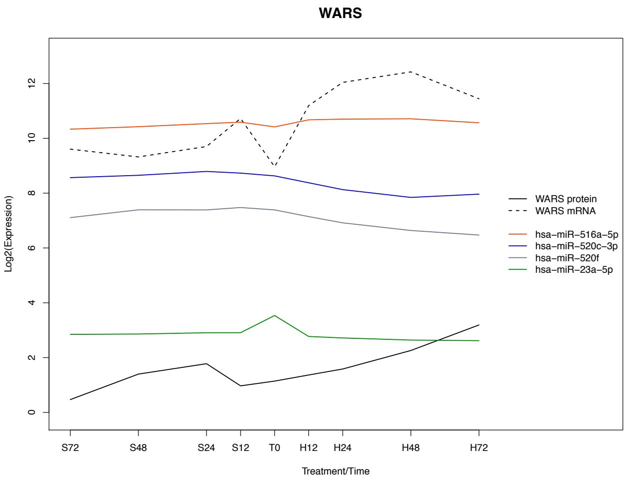
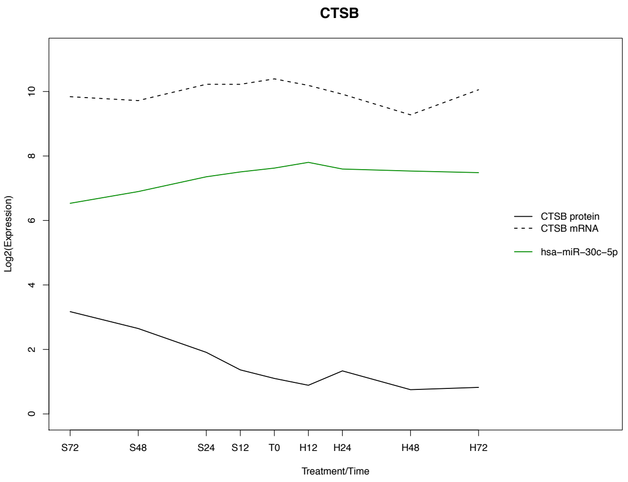
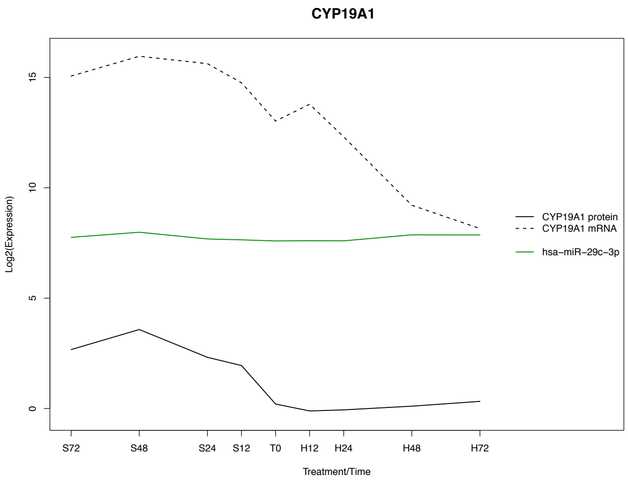
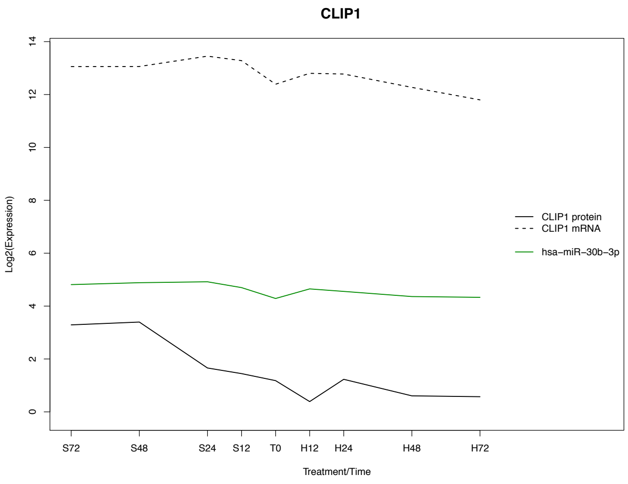
hsa−miR−141−3p
hsa−miR−1249
hsa−miR−335−3p
hsa−miR−584−5p


MX1
Log2(Expression)
0
5
10
15
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
MX1 protein
MX1 mRNA
hsa−miR−30d−5p
hsa−miR−30a−5p
hsa−miR−224−5p
hsa−miR−451a
hsa−miR−193b−5p
hsa−miR−664−3p
hsa−miR−503


WARS
Log2(Expression)
0
2
4
6
8
10
12
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
WARS protein
WARS mRNA
hsa−miR−516a−5p
hsa−miR−520c−3p
hsa−miR−520f
hsa−miR−23a−5p


CTSB
Log2(Expression)
0
2
4
6
8
10
S72
S48
S24
S12
T0
H12
H24
H48
H72
Treatment/Time
CTSB protein
CTSB mRNA
hsa−miR−30c−5p


CYP19A1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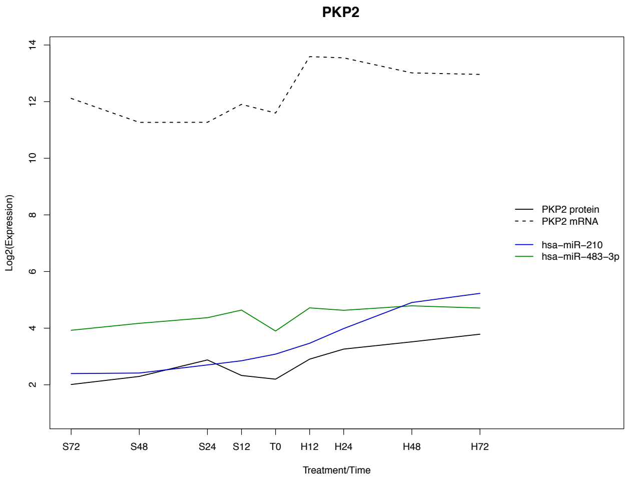
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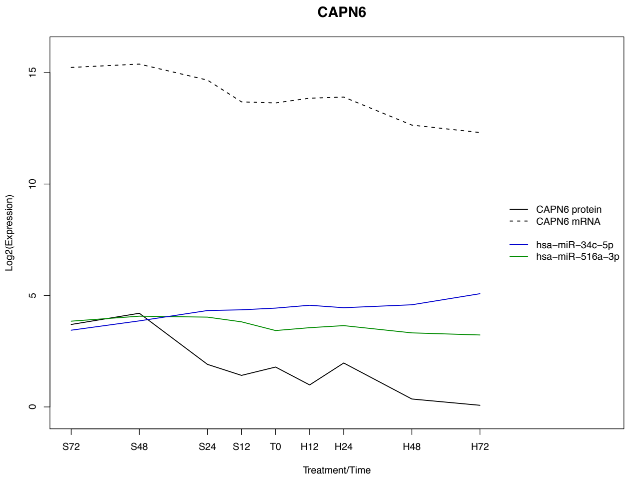
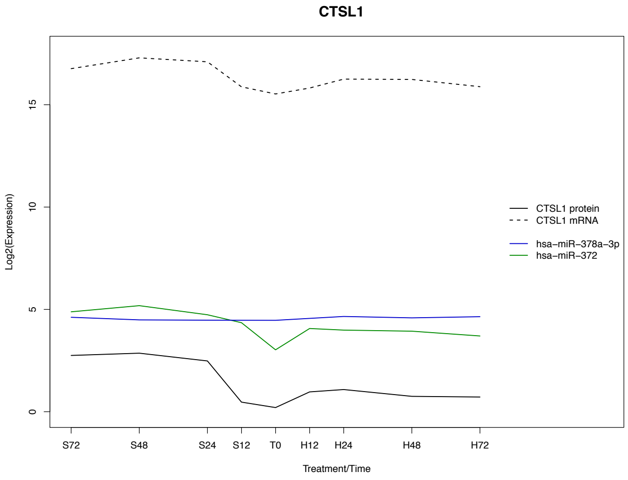
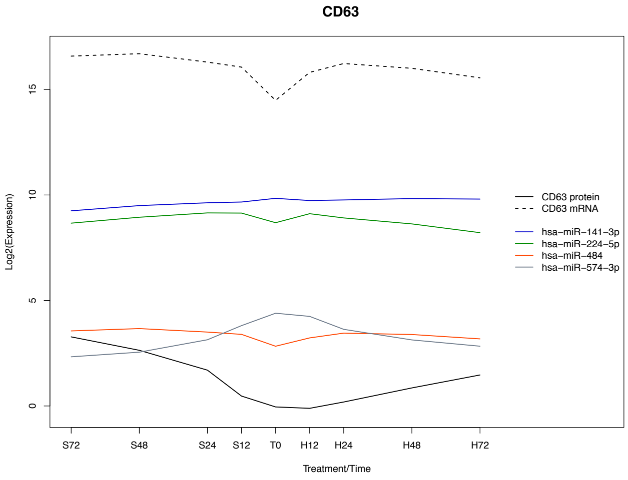
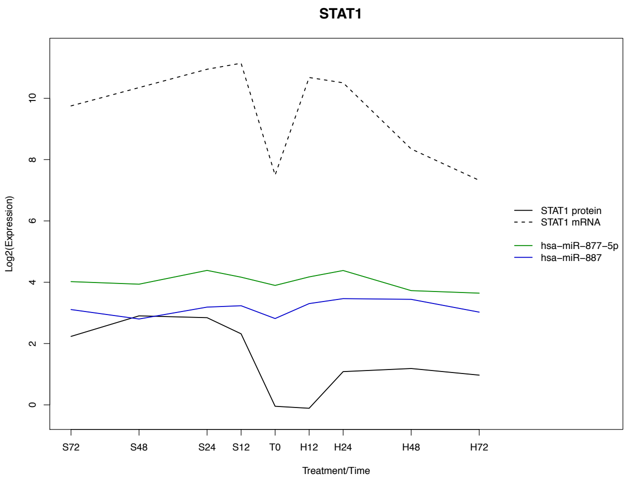
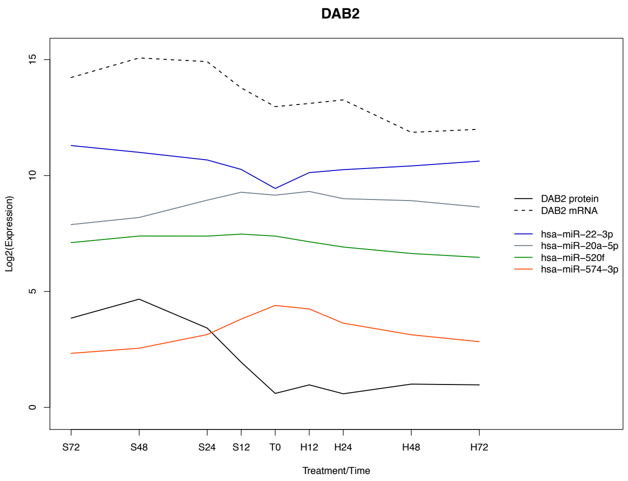
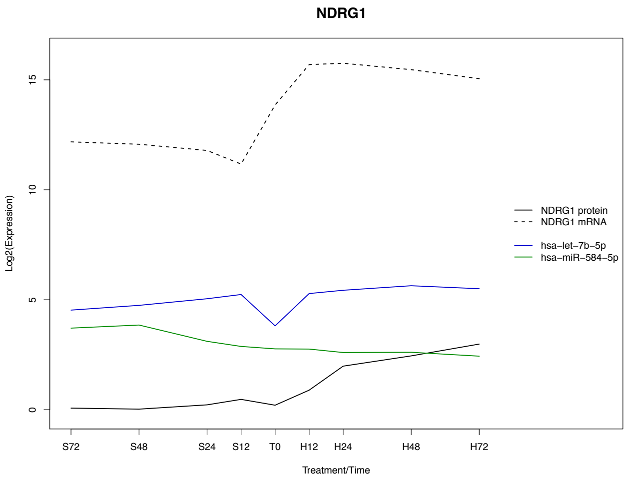

CAPN6


CTSL1


CD63


STAT1


DAB2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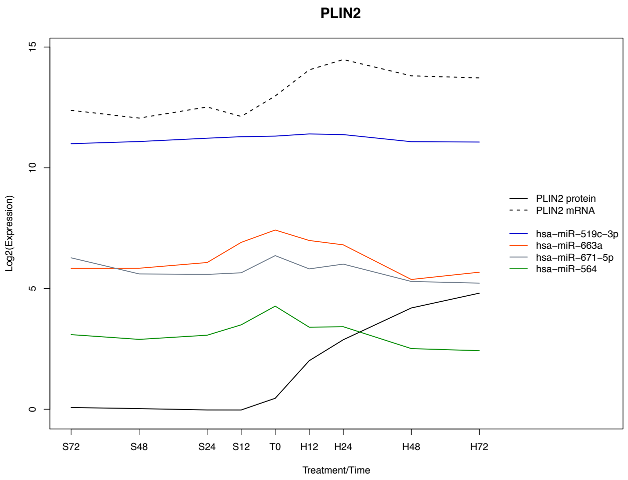
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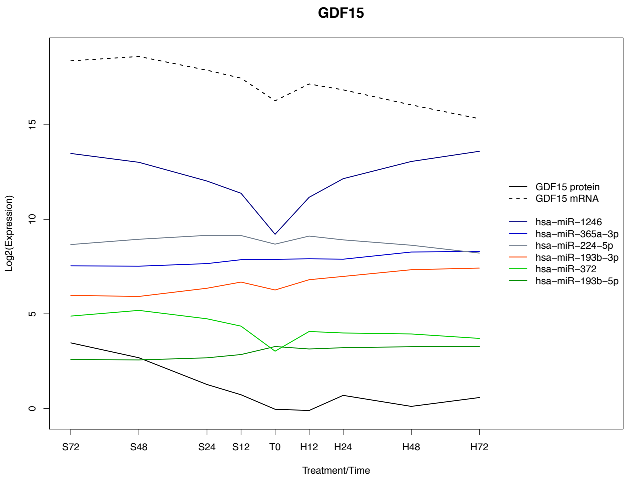
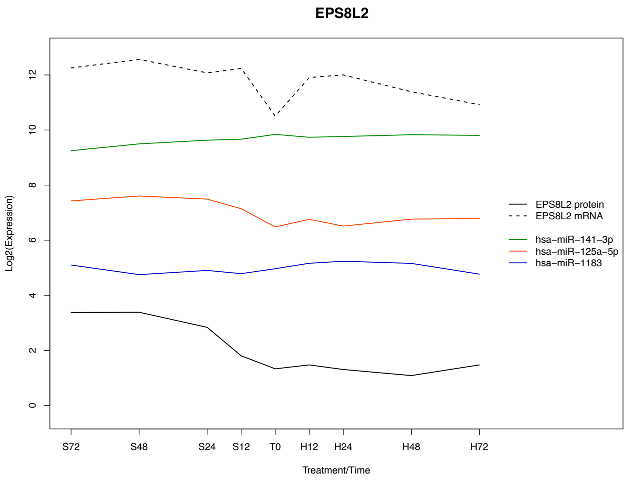

GDF15


EPS8L2

Supplementary tables

Table S1. Comparison of the area under precision-recall curve (AUPRC) of competing regulatory network learning algorithms for the first simulated network. Mean.auprc.1 and mean.auprc.2 are the average of AUPRC over 30 target mRNAs/proteins for the first and the second algorithm, respectively.

Alg1	Alg2	Sample size	Target	mean. auprc.1	mean. auprc.2	wilcox. pval
MBSmRN	MMHC	1250	mRNA	0.8665	0.8154	0.152969358
MBSmRN	Lasso	1250	mRNA	0.8665	0.1539	4.44E-11
MBSmRN	Lasso (no protein)*	1250	mRNA	0.8665	0.0771	2.97E-11
MMHC	Lasso	1250	mRNA	0.8154	0.1539	6.01E-11
MBSmRN	MMHC	250	mRNA	0.8438	0.7688	0.022792412
MBSmRN	Lasso	250	mRNA	0.8438	0.3872	8.30E-08
MBSmRN	Lasso (no protein)	250	mRNA	0.8438	0.1664	9.91E-11
MMHC	Lasso	250	mRNA	0.7688	0.3872	1.59E-07
MBSmRN	MMHC	50	mRNA	0.6566	0.5394	0.067823
MBSmRN	Lasso	50	mRNA	0.6566	0.3899	2.11E-05
MBSmRN	Lasso (no protein)	50	mRNA	0.6566	0.1743	9.30E-11
MMHC	Lasso	50	mRNA	0.5394	0.3899	0.000615181
MBSNIG	MMHC	1250	Protein	0.9861	0.5952	5.63E-11
MBSNIG	Lasso	1250	Protein	0.9861	0.1531	2.64E-12
MBSNIG	Lasso (no protein)	1250	Protein	0.9861	0.0444	2.36E-12
MMHC	Lasso	1250	Protein	0.5952	0.1531	3.32E-06
MBSNIG	MMHC	250	Protein	0.9875	0.5591	2.30E-11
MBSNIG	Lasso	250	Protein	0.9875	0.2980	3.50E-11
MBSNIG	Lasso (no protein)	250	Protein	0.9875	0.0386	6.44E-12
MMHC	Lasso	250	Protein	0.5591	0.2980	0.000690063
MBSNIG	MMHC	50	Protein	0.8757	0.3251	1.29E-08
MBSNIG	Lasso	50	Protein	0.8757	0.3446	5.39E-09
MBSNIG	Lasso (no protein)	50	Protein	0.8757	0.0530	3.94E-11
MMHC	Lasso	50	Protein	0.3251	0.3446	0.641168504

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S2A. Comparison of the area under precision-recall curve (AUPRC) of competing regulatory network learning algorithms for the second simulated network. Mean.auprc.1 and mean.auprc.2 are the average of AUPRC over 30 target mRNAs/proteins for the first and the second algorithm, respectively.

Alg1	Alg2	Sample size	Target	mean.auprc.1	mean.auprc.2	wilcox.pval
MBSmRN	MMHC	1250	mRNA	0.844367286	0.687050253	0.00185612
MBSmRN	Lasso	1250	mRNA	0.844367286	0.139583485	2.86E-10
MBSmRN	Lasso (no protein)*	1250	mRNA	0.844367286	0.066141833	4.48E-11
MMHC	Lasso	1250	mRNA	0.687050253	0.139583485	1.61E-10
MBSmRN	MMHC	250	mRNA	0.792800043	0.596652203	0.000690657
MBSmRN	Lasso	250	mRNA	0.792800043	0.384771683	5.67E-08
MBSmRN	Lasso (no protein)	250	mRNA	0.792800043	0.128665779	3.14E-10
MMHC	Lasso	250	mRNA	0.596652203	0.384771683	0.000237324
MBSmRN	MMHC	50	mRNA	0.594870473	0.481001698	0.166824911
MBSmRN	Lasso	50	mRNA	0.594870473	0.346552738	0.000553939
MBSmRN	Lasso (no protein)	50	mRNA	0.594870473	0.144111929	4.58E-09
MMHC	Lasso	50	mRNA	0.481001698	0.346552738	0.043498901
MBSNIG	MMHC	1250	Protein	1	0.576072364	4.56E-12
MBSNIG	Lasso	1250	Protein	1	0.154725404	1.21E-12
MBSNIG	Lasso (no protein)	1250	Protein	1	0.045268633	1.21E-12
MMHC	Lasso	1250	Protein	0.576072364	0.154725404	5.96E-05
MBSNIG	MMHC	250	Protein	0.983686949	0.549144412	4.62E-11
MBSNIG	Lasso	250	Protein	0.983686949	0.303488177	4.32E-12
MBSNIG	Lasso (no protein)	250	Protein	0.983686949	0.041289413	4.11E-12
MMHC	Lasso	250	Protein	0.549144412	0.303488177	0.000951139
MBSNIG	MMHC	50	Protein	0.917802322	0.312819747	4.46E-10
MBSNIG	Lasso	50	Protein	0.917802322	0.390030886	2.31E-10
MBSNIG	Lasso (no protein)	50	Protein	0.917802322	0.04166279	2.87E-11
MMHC	Lasso	50	Protein	0.312819747	0.390030886	0.386842392

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S2B. Comparison of pAUC of competing regulatory network learning algorithms for the second simulated network.

Alg1	Alg2	Sample size	Target	mean.pauc.1	mean.pauc.2	wilcox.pval
MBSmRN	MMHC	1250	mRNA	0.916043085	0.801152132	0.001068913
MBSmRN	Lasso	1250	mRNA	0.916043085	0.580066896	1.94E-10
MBSmRN	Lasso (no protein)*	1250	mRNA	0.916043085	0.521359744	1.95E-11
MMHC	Lasso	1250	mRNA	0.801152132	0.580066896	5.89E-09
MBSmRN	MMHC	250	mRNA	0.886196856	0.750093235	0.000137573
MBSmRN	Lasso	250	mRNA	0.886196856	0.796880906	0.00313111
MBSmRN	Lasso (no protein)	250	mRNA	0.886196856	0.572378832	1.28E-10
MMHC	Lasso	250	mRNA	0.750093235	0.796880906	0.102168908
MBSmRN	MMHC	50	mRNA	0.775059337	0.676538493	0.031399625
MBSmRN	Lasso	50	mRNA	0.775059337	0.8443569	0.116738874
MBSmRN	Lasso (no protein)	50	mRNA	0.775059337	0.61811706	0.000116194
MMHC	Lasso	50	mRNA	0.676538493	0.8443569	3.57E-05
MBSNIG	MMHC	1250	Protein	1	0.728173664	5.73E-11
MBSNIG	Lasso	1250	Protein	1	0.595003729	1.65E-11
MBSNIG	Lasso (no protein)	1250	Protein	1	0.505969491	1.21E-12
MMHC	Lasso	1250	Protein	0.728173664	0.595003729	0.000495308
MBSNIG	MMHC	250	Protein	0.996668333	0.693595057	1.42E-11
MBSNIG	Lasso	250	Protein	0.996668333	0.746508951	1.96E-11
MBSNIG	Lasso (no protein)	250	Protein	0.996668333	0.499793313	2.23E-12
MMHC	Lasso	250	Protein	0.693595057	0.746508951	0.286850656
MBSNIG	MMHC	50	Protein	0.959052131	0.597161467	8.54E-11
MBSNIG	Lasso	50	Protein	0.959052131	0.830898745	4.23E-06
MBSNIG	Lasso (no protein)	50	Protein	0.959052131	0.50029106	1.61E-12
MMHC	Lasso	50	Protein	0.597161467	0.830898745	2.46E-08

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S3A. Comparison of the area under precision-recall curve (AUPRC) of competing regulatory network learning algorithms for the third simulated network. Mean.auprc.1 and mean.auprc.2 are the average of AUPRC over 30 target mRNAs/proteins for the first and the second algorithm, respectively.

Alg1	Alg2	Sample size	Target	mean.auprc.1	mean.auprc.2	wilcox.pval
MBSmRN	MMHC	1250	mRNA	0.837204491	0.747209953	0.029144888
MBSmRN	Lasso	1250	mRNA	0.837204491	0.167312506	2.15E-10
MBSmRN	Lasso (no protein)*	1250	mRNA	0.837204491	0.070872442	3.01E-11
MMHC	Lasso	1250	mRNA	0.747209953	0.167312506	9.71E-10
MBSmRN	MMHC	250	mRNA	0.793194346	0.641743688	0.002748844
MBSmRN	Lasso	250	mRNA	0.793194346	0.388817302	4.52E-06
MBSmRN	Lasso (no protein)	250	mRNA	0.793194346	0.127966085	1.09E-10
MMHC	Lasso	250	mRNA	0.641743688	0.388817302	0.000103444
MBSmRN	MMHC	50	mRNA	0.580239624	0.501897648	0.198338863
MBSmRN	Lasso	50	mRNA	0.580239624	0.353748549	0.00011031
MBSmRN	Lasso (no protein)	50	mRNA	0.580239624	0.140191024	1.99E-10
MMHC	Lasso	50	mRNA	0.501897648	0.353748549	0.004846558
MBSNIG	MMHC	1250	Protein	0.991666667	0.498667785	1.20E-11
MBSNIG	Lasso	1250	Protein	0.991666667	0.191384574	7.71E-12
MBSNIG	Lasso (no protein)	1250	Protein	0.991666667	0.046505692	1.72E-12
MMHC	Lasso	1250	Protein	0.498667785	0.191384574	0.004961709
MBSNIG	MMHC	250	Protein	0.999410383	0.425016014	4.07E-12
MBSNIG	Lasso	250	Protein	0.999410383	0.262977428	4.07E-12
MBSNIG	Lasso (no protein)	250	Protein	0.999410383	0.046514062	4.11E-12
MMHC	Lasso	250	Protein	0.425016014	0.262977428	0.111847353
MBSNIG	MMHC	50	Protein	0.915541611	0.293945755	9.16E-10
MBSNIG	Lasso	50	Protein	0.915541611	0.32938974	1.25E-09
MBSNIG	Lasso (no protein)	50	Protein	0.915541611	0.039328461	3.24E-11
MMHC	Lasso	50	Protein	0.293945755	0.32938974	0.276748316

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S3B. Comparison of pAUC of competing regulatory network learning algorithms for the third simulated network.

Alg1	Alg2	Sample size	Target	mean.pauc.1	mean.pauc.2	wilcox.pval
MBSmRN	MMHC	1250	mRNA	0.909356972	0.812055509	0.003903093
MBSmRN	Lasso	1250	mRNA	0.909356972	0.595459819	6.77E-09
MBSmRN	Lasso (no protein)*	1250	mRNA	0.909356972	0.524087753	2.50E-11
MMHC	Lasso	1250	mRNA	0.812055509	0.595459819	9.45E-08
MBSmRN	MMHC	250	mRNA	0.879990771	0.74376233	0.000369427
MBSmRN	Lasso	250	mRNA	0.879990771	0.794742399	0.007528166
MBSmRN	Lasso (no protein)	250	mRNA	0.879990771	0.570701057	3.05E-10
MMHC	Lasso	250	mRNA	0.74376233	0.794742399	0.175490377
MBSmRN	MMHC	50	mRNA	0.779038967	0.676536527	0.004421149
MBSmRN	Lasso	50	mRNA	0.779038967	0.816709174	0.188089204
MBSmRN	Lasso (no protein)	50	mRNA	0.779038967	0.591866775	5.92E-07
MMHC	Lasso	50	mRNA	0.676536527	0.816709174	7.86E-05
MBSNIG	MMHC	1250	Protein	0.998526378	0.677972481	9.81E-11
MBSNIG	Lasso	1250	Protein	0.998526378	0.610856144	6.92E-12
MBSNIG	Lasso (no protein)	1250	Protein	0.998526378	0.50683179	1.71E-12
MMHC	Lasso	1250	Protein	0.677972481	0.610856144	0.060343623
MBSNIG	MMHC	250	Protein	1	0.646041773	1.64E-11
MBSNIG	Lasso	250	Protein	1	0.716196736	4.53E-12
MBSNIG	Lasso (no protein)	250	Protein	1	0.507128069	1.13E-12
MMHC	Lasso	250	Protein	0.646041773	0.716196736	0.093227023
MBSNIG	MMHC	50	Protein	0.957748939	0.594169156	2.46E-10
MBSNIG	Lasso	50	Protein	0.957748939	0.835231458	2.51E-06
MBSNIG	Lasso (no protein)	50	Protein	0.957748939	0.498304919	2.56E-12
MMHC	Lasso	50	Protein	0.594169156	0.835231458	4.16E-08

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S4A. Comparison of the area under precision-recall curve (AUPRC) of competing regulatory network learning algorithms for the fourth simulated network. Mean.auprc.1 and mean.auprc.2 are the average of AUPRC over 30 target mRNAs/proteins for the first and the second algorithm, respectively.

Alg1	Alg2	Sample size	Target	mean.auprc.1	mean.auprc.2	wilcox.pval
MBSmRN	MMHC	1250	mRNA	0.833701484	0.729567143	0.040575476
MBSmRN	Lasso	1250	mRNA	0.833701484	0.239770514	7.41E-09
MBSmRN	Lasso (no protein)*	1250	mRNA	0.833701484	0.087052624	3.02E-11
MMHC	Lasso	1250	mRNA	0.729567143	0.239770514	3.33E-08
MBSmRN	MMHC	250	mRNA	0.796255368	0.698437644	0.072441629
MBSmRN	Lasso	250	mRNA	0.796255368	0.482132786	6.04E-06
MBSmRN	Lasso (no protein)	250	mRNA	0.796255368	0.19516312	1.61E-10
MMHC	Lasso	250	mRNA	0.698437644	0.482132786	0.000376261
MBSmRN	MMHC	50	mRNA	0.515499705	0.335441548	0.020226324
MBSmRN	Lasso	50	mRNA	0.515499705	0.480570475	0.520121422
MBSmRN	Lasso (no protein)	50	mRNA	0.515499705	0.250238284	0.000144901
MMHC	Lasso	50	mRNA	0.335441548	0.480570475	0.087609064
MBSNIG	MMHC	1250	Protein	0.977121795	0.54707146	2.90E-10
MBSNIG	Lasso	1250	Protein	0.977121795	0.294424398	1.60E-10
MBSNIG	Lasso (no protein)	1250	Protein	0.977121795	0.052802736	4.11E-12
MMHC	Lasso	1250	Protein	0.54707146	0.294424398	0.009874172
MBSNIG	MMHC	250	Protein	0.971782242	0.451735429	5.05E-10
MBSNIG	Lasso	250	Protein	0.971782242	0.463484962	3.82E-09
MBSNIG	Lasso (no protein)	250	Protein	0.971782242	0.044494787	1.10E-11
MMHC	Lasso	250	Protein	0.451735429	0.463484962	0.870753838
MBSNIG	MMHC	50	Protein	0.844089842	0.25877698	1.13E-08
MBSNIG	Lasso	50	Protein	0.844089842	0.540945243	0.000241704
MBSNIG	Lasso (no protein)	50	Protein	0.844089842	0.035957453	3.11E-11
MMHC	Lasso	50	Protein	0.25877698	0.540945243	0.000521047

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S4B. Comparison of pAUC of competing regulatory network learning algorithms for the fourth simulated network.

Alg1	Alg2	Sample size	Target	mean.pauc.1	mean.pauc.2	wilcox.pval
MBSmRN	MMHC	1250	mRNA	0.912956241	0.826791542	0.015179283
MBSmRN	Lasso	1250	mRNA	0.912956241	0.613980913	1.29E-08
MBSmRN	Lasso (no protein)*	1250	mRNA	0.912956241	0.525134167	2.11E-11
MMHC	Lasso	1250	mRNA	0.826791542	0.613980913	7.79E-07
MBSmRN	MMHC	250	mRNA	0.881315776	0.788357107	0.004937004
MBSmRN	Lasso	250	mRNA	0.881315776	0.766642086	0.00262161
MBSmRN	Lasso (no protein)	250	mRNA	0.881315776	0.596813524	5.28E-09
MMHC	Lasso	250	mRNA	0.788357107	0.766642086	0.491331111
MBSmRN	MMHC	50	mRNA	0.737974895	0.613277184	0.001592329
MBSmRN	Lasso	50	mRNA	0.737974895	0.78276361	0.155649239
MBSmRN	Lasso (no protein)	50	mRNA	0.737974895	0.634520986	0.001989519
MMHC	Lasso	50	mRNA	0.613277184	0.78276361	8.85E-06
MBSNIG	MMHC	1250	Protein	0.992708414	0.706977076	3.02E-10
MBSNIG	Lasso	1250	Protein	0.992708414	0.651354833	6.69E-11
MBSNIG	Lasso (no protein)	1250	Protein	0.992708414	0.509314822	2.36E-12
MMHC	Lasso	1250	Protein	0.706977076	0.651354833	0.099130811
MBSNIG	MMHC	250	Protein	0.98809791	0.685125291	1.51E-09
MBSNIG	Lasso	250	Protein	0.98809791	0.754808053	1.63E-09
MBSNIG	Lasso (no protein)	250	Protein	0.98809791	0.501330315	2.23E-12
MMHC	Lasso	250	Protein	0.685125291	0.754808053	0.149018815
MBSNIG	MMHC	50	Protein	0.918675589	0.599782406	2.10E-09
MBSNIG	Lasso	50	Protein	0.918675589	0.822716337	0.001355217
MBSNIG	Lasso (no protein)	50	Protein	0.918675589	0.499216659	6.62E-12
MMHC	Lasso	50	Protein	0.599782406	0.822716337	4.36E-07

*Lasso algorithm is applied to simulation data with the protein data removed.

Table S5. Direct regulators of the 78 proteins, and proteins regulated by the 78 proteins. Frequency column represents, out of the 35 resampled data sets, the number of times a miRNA/mRNA/protein was identified as a directed regulator of the target protein, or regulated by the target protein.

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
MYOF	1	mRNA	0.0815572234	8.86787577E-03	35	1	MLEC	7
	2	EIF3E	-0.1879059639	2.72807071E-29	18	2	TFRC	7
	3	MAPK1	-0.1080779714	1.86441155E-09	14	3	CBR1	6
	4	PA2G4	-0.2659352065	2.65183687E-15	12	4	HNRNPH2	4
	5	KRT36	-0.0654534516	2.10694466E-04	8	5	MAPK1	4
	6	CNDP2	-0.4002374664	1.76690420E-09	7	6	CNDP2	3
	7	RPL11	-0.1139841598	1.20012661E-04	5	7	KRT36	3
	8	HMGB1	-0.0717072684	1.35506566E-03	4	8	PPP1CB	3
	9	RPL12	-0.0876555220	3.61749008E-06	3			
HSP90B1	1	mRNA	0.1144337635	2.83406231E-20	35	1	CALU	10
	2	hsa-miR-16-5p	-0.4214643505	1.76412677E-12	19	2	NAP1L1	6
	3	PDIA3	0.4483435085	4.86015251E-10	15	3	NUFIP2	3
	4	AHSA1	0.1498572686	5.08236298E-09	13	4	PCCB	3
	5	NUFIP2	-0.1004221486	1.66188966E-06	9	5	SFRS2	3
	6	CCDC109A	-0.1342064691	3.58896107E-08	7			
	7	RFC2	-0.1027720078	1.85849409E-07	6			
	8	TMEM205	0.0733018240	1.56119797E-05	5			
	9	HELZ	-0.0700825872	1.00786626E-03	3			
GAPDH	1	LDHA	0.2671780480	9.73920226E-16	35	1	KIAA1967	13
	2	mRNA	-0.0842908412	8.56309792E-06	35	2	ANO6	11
	3	SLK	-0.1036343313	3.34828308E-09	21	3	TCEB1	10
	4	ANO6	-0.0724502447	1.76733857E-03	5	4	MAN2A1	7
	5	XPNPEP1	-0.0819605783	6.84026714E-07	5	5	RPL11	6
	6	GBE1	-0.0935472162	6.24720685E-07	3	6	SLK	5
						7	CLINT1	4
						8	HSP90AA2	4
						9	PSMA6	4
ANXA1	1	mRNA	0.0837140259	4.60375103E-07	35	1	IMMT	11
	2	KRT19	0.3966387205	2.05113104E-12	13	2	SERPINC1	5
	3	EEF1A1	0.4833784697	5.57132963E-13	9	3	TRIM28	4
	4	IMMT	-0.1086729173	7.19893619E-07	9	4	DYNC1H1	3
	5	HBB	0.0626614343	1.16049138E-04	8			
	6	RPL5	0.1321089286	6.29706327E-14	6			
	7	TRIM28	-0.1362573841	5.54116051E-09	6			
	8	hsa-miR-1181	0.1956745883	2.45793188E-22	4			
	9	TUBA1B	0.1505232777	2.88711994E-35	4			
	10	ATP12A	0.0794413107	1.84528810E-04	3			
	11	GLB1	-0.0480078471	3.03804590E-03	3			
	12	hsa-miR-335-3p	-0.1208153389	5.02437824E-08	3			
HSPA5	1	mRNA	0.0681977392	5.23199323E-05	35	1	hsa-miR-1288	7
	2	treat	NA	NA	14	2	EIF5	6
	3	FN1	0.0795169477	5.31884740E-19	11	3	APOA1BP	3
	4	hsa-miR-574-3p	-0.1745664839	3.31005580E-08	7	4	SYPL1	3
	5	HSP90B1	0.2612262098	1.96831481E-08	6			
	6	PDIA3	0.3918100415	4.52465212E-08	6			
	7	hsa-miR-1290	0.1200841333	1.20296983E-15	3			
HADHA	1	mRNA	-0.0986614562	1.75051637E-01	35	1	DARS	20
	2	GLDC	0.1375431550	1.06205160E-12	16	2	DBT	8
	3	HSPB1	-0.1300581266	6.89406751E-10	9	3	INF2	4
	4	DARS	0.2146324328	8.64707300E-13	5	4	GLDC	3
	5	hsa-miR-1471	0.1354277749	5.64976467E-06	5			
	6	hsa-miR-335-3p	0.1201677155	1.26706461E-04	4			
	7	hsa-miR-345-5p	0.1635967996	1.88792261E-06	4			
	8	TIMP3	-0.0796698502	1.99820770E-04	4			
	9	APEH	0.1745968162	3.43989029E-08	3			
	10	PPAP2B	-0.1807341302	3.14868482E-09	3			

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
ENO1	1	mRNA	0.0544383793	1.57255502E-03	35	1	RPL18	13
	2	KRT19	0.3806624789	9.65525422E-14	32	2	AP1G2	12
						3	LGALS12	9
						4	PGK1	8
						5	TEX10	7
						6	PKM2	5
						7	IDH2	3
						8	RAD50	3
IDH1	1	mRNA	0.0033442229	7.11933160E-01	35	1	hsa-miR-10a-5p	18
	2	DSP	0.1115783142	1.47414634E-13	21	2	MAGEA10	18
	3	hsa-miR-10a-5p	0.3494282011	1.03882583E-13	10	3	ACADVL	3
						4	hsa-miR-17-5p	3
						5	NAV2	3
ACTN1	1	mRNA	0.0152804061	6.24350692E-01	35	1	HEXB	11
	2	ACTN4	0.4422402460	2.35469804E-10	33	2	AHCY	6
	3	hsa-miR-34c-5p	-0.0861697964	5.05825155E-03	6	3	SF3A1	5
	4	hsa-miR-148a-3p	-0.1846897298	6.59998137E-04	5	4	UBR4	5
	5	METAP2	-0.0612033680	2.62826913E-02	5	5	RPL7	4
	6	OXSR1	-0.0548639493	5.40949542E-03	3	6	hsa-miR-30a-5p	3
						7	JUP	3
TFRC	1	mRNA	0.1413550260	1.18562012E-15	35	1	STOM	8
	2	hsa-miR-22-3p	0.4318031416	1.07981286E-14	14	2	MYOF	5
	3	STOM	0.1476035770	5.69680887E-08	11	3	SLC16A1	5
	4	CBR1	-0.1268684223	1.36116943E-08	8	4	ADAM22	3
	5	SLC7A5	0.1880261722	2.09532028E-05	8	5	HSD17B1	3
	6	ADAM22	0.1293657945	2.09841461E-04	6	6	TXNRD1	3
	7	HSPA5	0.2897701089	2.18521722E-03	5			
	8	SAE1	-0.1078705965	8.66400562E-05	5			
	9	TXNRD1	0.2129057819	1.12080377E-10	5			
	10	hsa-miR-365a-3p	-0.5141975349	1.08468370E-06	4			
	11	HSD17B1	0.1668527175	4.32218468E-06	4			
	12	ENPEP	0.1261303110	3.07220053E-05	3			
	13	hsa-miR-1290	0.1580302021	2.38953839E-23	3			
	14	NDUFA10	0.0719457175	4.17408814E-03	3			
	15	PDIA6	0.5352731297	1.94776132E-06	3			
	16	PRDX5	-0.0984775484	4.04641788E-08	3			
ACADVL	1	mRNA	0.0531668077	2.27562297E-01	35	1	cDNA.FLJ61478	5
	2	ACSS1	0.5224397647	1.81543581E-13	13	2	IDH1	5
	3	MATR3	-0.1184428286	1.07979112E-03	9	3	TARS	5
	4	PFKL	0.2755952022	1.55993547E-11	8	4	TPM1	4
	5	HADHB	0.3604684709	2.26541479E-12	6	5	hsa-miR-515-5p	3
	6	YWHAG	-0.1699196544	1.22872444E-03	3	6	MAGEA10	3
ALDH7A1	1	mRNA	0.0418645367	1.20007742E-02	35	1	hsa-miR-335-5p	19
	2	hsa-miR-335-5p	0.6224739790	6.71035128E-13	12	2	PSMC4	8
	3	TRAP1	0.1792210049	5.37252027E-11	10	3	FHL2	7
	4	FHL2	-0.0943425664	9.64805018E-04	3	4	ERLIN2	3
	5	GANAB	0.4810168542	4.53077794E-09	3			
IDH2	1	mRNA	0.0609456552	3.62342921E-02	35	1	ETFA	17
	2	GAPDH	0.3756784899	5.27920416E-10	10	2	AP1G2	6
	3	TEX10	-0.1480878893	1.10359566E-06	9	3	HSPA9	6
	4	ETFA	0.2494179122	1.21571568E-11	3	4	ALDH7A1	5
	5	MME	-0.1972734130	2.27491987E-11	3	5	hsa-miR-520h	5
						6	ROS1	5
						7	CNDP2	3
EEF1A1	1	mRNA	-0.0755701352	2.42229172E-01	35	1	ANXA1	22
	2	CTNNB1	-0.4465795861	4.77289439E-13	16	2	hsa-miR-26a-5p	6
	3	GNAI1	0.1393381567	1.35451478E-14	10	3	GNAI1	4
	4	SRRT	-0.1424023238	2.41103654E-13	3			

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
FASN	1	mRNA	-0.0496958301	2.30751203E-01	35	1	GLDC	18
	2	hsa-miR-519e-5p	1.2165717915	2.34290325E-43	30	2	MYH9	5
	3	HMGB1	-0.1384698846	1.80046453E-04	7	3	cDNA.FLJ53063	3
	4	COASY	-0.0951523696	2.68412527E-03	6			
	5	DYNC1H1	0.2644201361	3.51922868E-07	5			
	6	HSD3B1	-0.0848101329	5.71147535E-05	4			
	7	MAPK3	-0.1100532348	5.90005945E-03	4			
	8	ZNF469	0.1364551462	3.20999301E-04	3			
PDIA4	1	mRNA	0.0404743676	1.64186673E-02	35	1	ITGB1	14
	2	ATP5F1	-0.1527002994	2.67635342E-16	21	2	HSP90B1	4
	3	SLC26A2	-0.1257784549	3.88659481E-04	13	3	RPL17	3
	4	COMT	-0.1581667172	8.42584393E-15	5	4	RPS18	3
	5	HSP90B1	0.3298207130	2.57915330E-05	4			
	6	ARF1	-0.1734599125	1.46416817E-13	3			
ACSS1	1	mRNA	-0.0268824032	1.48108987E-01	35	1	CAPN6	31
	2	HADHB	0.4173786187	1.30228117E-18	22	2	PIR	14
	3	ACO2	0.2926917252	1.01055734E-15	9	3	HADHB	10
						4	SEPT2	5
ACO2	1	mRNA	-0.1089475235	2.79047010E-01	35	1	DHX15	6
	2	UPP1	-0.2777041754	2.92148009E-06	29	2	HNRNPR	5
	3	ERO1L	0.1303808913	5.06158761E-06	18	3	hsa-miR-27a-3p	4
	4	KRT18	-1.0542986534	2.31924139E-06	14			
	5	hsa-miR-27a-3p	-0.6478561718	1.72335640E-05	9			
	6	TECR	0.1985343436	7.71390614E-05	7			
	7	ATP6	0.1597689212	1.55944877E-02	3			
	8	DAB2	-0.1314805261	8.13229802E-04	3			
HADHB	1	mRNA	0.2674943482	7.70136074E-02	35	1	hsa-miR-519c-3p	9
	2	ACSS1	0.9534563822	2.28809668E-17	25	2	ACSS1	8
	3	hsa-miR-22-3p	-0.8001554882	1.52682372E-17	4	3	HSP90AB3P	7
	4	hsa-miR-29a-3p	-0.8112268556	1.74762843E-18	3	4	hsa-miR-21-5p	6
						5	TPP1	6
						6	RAB1A	4
						7	hsa-miR-512-3p	3
						8	hsa-miR-622	3
						9	NANS	3
RASA1	1	mRNA	0.1430729319	8.59812767E-10	35	1	GPI	30
	2	PHB	-0.3433707530	1.68494807E-16	25	2	ALDOA	15
	3	cDNA.FLJ34775.fis	0.0970781651	3.37158608E-02	6	3	APOA1BP	3
	4	SLC25A11	-0.1912490531	6.61284343E-15	5			
	5	VTN	-0.0816510773	3.02468290E-02	3			
HSD17B10	1	mRNA	-0.0738003556	6.68477513E-01	35	1	CYB5B	12
	2	ACTN1	-1.1678869351	2.45898821E-08	31	2	KIAA0776	7
	3	IDH3B	0.2372811537	5.78429744E-04	14	3	SARS	7
	4	HIBCH	0.2956851913	1.18138915E-14	4	4	HIBCH	6
	5	HIBADH	0.2369486207	1.08428922E-03	3	5	cDNA.FLJ54153	4
	6	PCNA	0.1440946519	4.36374257E-03	3	6	ARPC1B	3
						7	EEF2	3
						8	PDXK	3
PARP1	1	mRNA	0.0460965696	2.22902900E-01	35	1	GLDC	18
	2	GLDC	0.2760016317	8.75024132E-18	17	2	hsa-miR-1260a	13
	3	MYH10	0.4348203130	4.69564768E-13	14	3	NDUFB10	7
EGFR	1	mRNA	0.1175307528	2.63026829E-03	35	1	FAM129B	11
	2	hsa-miR-30a-5p	-0.8056092306	7.77913007E-11	13	2	hsa-miR-210	9
	3	CD63	0.1560160681	2.11641443E-09	10	3	BCL11B	4
	4	GBP1	0.1010137374	1.49735859E-03	10	4	EZR	4
	5	TFRC	0.3188186996	1.20703454E-10	7	5	hsa-miR-141-3p	4
						6	hsa-miR-25-3p	3
						7	ITGB1	3
						8	MYOF	3
						9	SERPINB1	3

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
ALDOA	1	mRNA	0.1244827010	6.05590124E-04	35	1	GCN1L1	8
	2	ISYNA1	0.3004531368	1.47734191E-06	20	2	MACF1	6
	3	LETM1	-0.1105990758	6.63898524E-04	5	3	RASA1	6
	4	COL7A1	-0.1026771697	3.57474154E-03	3	4	DNM1L	5
	5	MACF1	-0.1177171934	5.99326040E-04	3	5	EHMT2	5
	6	VAMP8	0.1607317275	1.54396084E-04	3	6	DYRK4	4
						7	NNT	4
						8	ZNF469	3
ECHS1	1	mRNA	0.1459916831	4.31903610E-02	35	1	hsa-miR-1280	13
	2	ETFA	0.7699260246	2.45961484E-14	17	2	hsa-miR-320b	7
	3	hsa-miR-23a-3p	-1.8571731758	1.91304282E-07	6	3	AHNAK	3
	4	hsa-miR-320b	-1.5887239038	4.11226177E-08	5	4	hsa-miR-425-5p	3
	5	hsa-miR-424-5p	-0.7076571858	6.76572454E-13	4			
	6	KRT79	-0.6476623805	1.48080248E-04	4			
	7	GMPS	0.2364131236	1.16853661E-04	3			
	8	NCSTN	-0.2134978836	2.44722220E-03	3			
	9	PDS5A	0.1861979197	1.84330349E-02	3			
	10	RANGAP1	-0.1606432898	1.64040780E-03	3			
TPI1	1	mRNA	0.1726514038	8.09405046E-05	35	1	FAM115A	9
	2	YWHAZ	0.6664365735	7.35944648E-12	10	2	PRDX2	9
	3	DSTN	0.2264937816	3.23435217E-10	9	3	YWHAZ	6
	4	PRDX2	0.2553462354	5.78531242E-11	9	4	NCLN	4
	5	PPIB	0.4120198935	2.02797052E-09	3	5	GAPDH	3
						6	hsa-miR-29b-1-5p	3
						7	hsa-miR-638	3
						8	LDHA	3
GPI	1	mRNA	0.0814260047	1.33245863E-02	35	1	TMED1	26
	2	TMED9	0.2516021575	1.17774654E-03	14	2	ENO1	25
	3	ALDH9A1	-0.0959292493	1.12943413E-02	7	3	SAMD9	10
						4	ATP2B1	4
						5	RASA1	3
						6	TMED9	3
DSP	1	mRNA	0.8159996680	7.14133209E-09	35	1	PLEC1	8
	2	treat	NA	NA	30	2	CYTSB	7
	3	DAK	-0.3554418159	5.53977244E-11	9	3	TCP1	7
	4	DYNC1H1	0.6490588672	2.41707270E-10	9	4	ATP6V1B2	5
	5	PLEC1	0.3364747380	7.37195720E-07	5			
	6	CYTSB	0.4373342044	2.31961587E-07	3			
LDHA	1	mRNA	0.0575468864	2.26748496E-02	35	1	GAPDH	9
	2	PLIN2	0.1674816472	6.91790048E-09	18	2	TMX1	6
	3	GAPDH	0.7370113392	1.27604025E-14	14	3	hsa-miR-371a-3p	4
	4	TPI1	0.7181842586	4.17501221E-15	12	4	IGF2BP3	4
	5	H6PD	-0.2593294893	4.20134064E-07	6	5	PLIN2	4
	6	TMX1	0.3406989729	5.19207743E-12	5	6	AP2B1	3
	7	AP2B1	-0.2804601467	3.11336832E-05	4	7	BAT3	3
	8	BLVRA	-0.0870840556	1.55878763E-02	3	8	BLVRA	3
	9	IDH3B	-0.1586124954	2.48370812E-06	3			
HYOU1	1	mRNA	0.0736292402	7.84363523E-03	35	1	PNPLA8	12
	2	treat	NA	NA	26	2	PGK1	4
	3	HMOX1	-0.2020456351	1.67236571E-12	6	3	SEPT9	4
	4	SEPT9	0.4865560170	1.03967755E-04	6	4	hsa-miR-200c-3p	3
	5	RRBP1	0.5556417841	1.48628770E-15	5	5	LRRC1	3
	6	AHNAK	0.4220999808	1.00214858E-13	4	6	PDCD10	3
	7	hsa-miR-210	0.5012703881	1.59204636E-18	3	7	SPTAN1	3
	8	hsa-miR-26a-5p	0.8061152401	2.52571766E-05	3			
	9	hsa-miR-671-5p	-0.7096326381	2.01549556E-11	3			

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
ETFA	1	mRNA	-0.0740815745	1.78364323E-01	35	1	hsa-miR-424-5p	11
	2	MME	-0.5152520466	2.37143780E-18	20	2	ACSS1	6
	3	HIST1H1A	0.2155921561	3.40177594E-03	14	3	F5	4
	4	DNAJC13	-0.1809595850	4.12044993E-04	7	4	CS	3
	5	ATP5O	0.2743605489	2.45062334E-10	3	5	hsa-miR-503	3
	6	DDX3X	-0.3089425297	1.03471084E-06	3	6	MAOA	3
	7	GANAB	1.0633877435	1.26628162E-13	3			
	8	IDH2	1.1561592158	6.79947149E-11	3			
PPIB	1	mRNA	0.2365730478	1.58055751E-06	35	1	YWHAQ	12
	2	PEBP1	0.4870305627	3.67943977E-09	11	2	PEBP1	5
	3	YWHAQ	0.3952413865	3.84415147E-11	7	3	QPRT	4
	4	RAB1B	0.1723804244	1.23308013E-04	5	4	GPD2	3
	5	ENAH	0.1154190288	2.23033036E-02	3	5	ITPR3	3
	6	RPS7	0.2111455179	2.72447475E-10	3	6	PSMD14	3
						7	RAB1B	3
GLDC	1	mRNA	-0.0075258559	3.13478402E-01	35	1	PARP1	16
	2	HADHA	1.4630168050	2.30648639E-16	17	2	PDHB	9
	3	LRPPRC	0.3953276748	5.89619188E-08	10	3	hsa-miR-30c-5p	6
	4	NDUFB10	-0.1252739215	1.98432239E-02	7	4	MCM3	5
	5	PARP1	1.4444570181	4.36231945E-16	7			
	6	FASN	0.8214136306	9.35622445E-18	6			
	7	hsa-miR-30c-5p	1.1385297858	7.71319416E-06	4			
	8	MCM3	0.2787153154	3.65381114E-03	4			
	9	PTPN1	0.2990868863	2.58685954E-07	3			
ACO1	1	mRNA	0.0852564056	6.40188330E-02	35	1	GDF15	14
	2	hsa-miR-424-5p	-0.8402135276	6.55446031E-16	33	2	RPS25	9
	3	GDF15	-0.2673753659	1.64154116E-04	10	3	MVP	6
	4	NT5C2	-0.2455978903	2.18785523E-04	7	4	GDI2	5
	5	ITGA6	-0.7439250745	1.13692365E-05	6	5	NT5C2	5
	6	ALDH4A1	0.4792966204	8.58225010E-04	4	6	STXBP3	3
	7	ALDOA	0.6834697757	2.66231221E-04	4	7	TM9SF3	3
	8	NFXL1	0.1840099594	2.18214097E-02	3			
	9	OLA1	-0.3371134721	2.07288266E-03	3			
HIBCH	1	mRNA	0.4937972688	2.86488641E-02	35	1	FAM193A	5
	2	EZR	-2.8131704338	3.60229548E-09	30	2	ACO2	4
	3	hsa-miR-1280	-1.6051347575	2.40197909E-05	11			
	4	YWHAE	1.5311033976	1.05948227E-03	11			
	5	DPM1	0.6141862960	1.20264110E-04	9			
	6	HSD17B10	1.2062249922	4.89422023E-08	6			
	7	YWHAQ	1.0505652587	2.65126721E-03	5			
	8	ATP2B1	-0.4591811894	1.29240240E-03	3			
	9	PGM1	1.3215203932	3.12847010E-04	3			
	10	SLK	-0.4555643257	1.33331963E-02	3			
ITGB1	1	mRNA	0.0646018980	5.20240969E-01	35	1	hsa-miR-25-3p	4
	2	STS	0.7522465180	1.97695096E-08	25	2	TM9SF4	4
	3	HNRNPH2	0.3038904704	7.23753840E-05	14	3	YWHAE	4
	4	ENPEP	0.3083051966	3.16872367E-05	7	4	KRT23	3
	5	YWHAE	-0.4650070281	2.00851876E-05	7	5	LRP2	3
	6	PA2G4	-0.4708349942	1.22692625E-05	3	6	PA2G4	3
						7	PPA2	3
						8	UBA1	3
MME	1	mRNA	0.0810650026	5.17115335E-02	35	1	ACSL3	21
	2	SERPINH1	-0.7353403620	4.37914401E-09	11	2	MTX1	5
	3	ETFA	-0.4459024966	8.41133795E-14	10	3	MAN2A1	4
	4	DPP4	0.6545089697	2.80827131E-17	6	4	C1orf101	3
	5	HADH	-0.1746720992	1.24093258E-12	6	5	XPNPEP1	3
	6	COMT	-0.1619103364	1.58931018E-06	5			
	7	hsa-miR-320b	0.9346249200	1.02441293E-30	5			
	8	hsa-miR-27a-3p	0.5659990837	1.43213065E-06	3			
	9	hsa-miR-523-3p	-0.4892651221	7.95415041E-09	3			
	10	hsa-miR-625-5p	-0.6309636434	3.65919645E-10	3			

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
HSD17B1	1	mRNA	0.1768363949	1.10714445E-06	35	1	AP2B1	7
	2	AP2B1	0.6936874572	1.93200773E-10	27	2	ATP5B	7
	3	hsa-miR-936	-0.7303242372	1.62707981E-07	10	3	DNAJA1	5
	4	STOM	0.2320886936	3.75567352E-05	6	4	STS	4
	5	GLB1	0.2136988693	1.99629890E-07	5	5	TGM2	4
	6	IMMT	0.2346606109	8.38192666E-04	4	6	hsa-miR-34a-5p	3
	7	RER1	-0.1949523324	4.63959195E-04	4			
	8	CCDC160	-0.2812987425	2.49263196E-05	3			
	9	GPI	-0.5736815222	3.57235457E-04	3			
	10	hsa-miR-34a-5p	0.6578191147	4.05983152E-08	3			
	11	hsa-miR-654-5p	0.3610530473	1.04892162E-03	3			
	12	NEFM	-0.1693920529	1.56215545E-04	3			
	13	UQCRFSL1	0.2284100786	1.55158788E-05	3			
RRBP1	1	mRNA	0.3567608557	3.19672541E-12	35	1	IQGAP2	22
	2	AARS	0.4688643163	2.93028067E-25	24	2	EPPK1	8
	3	IQGAP2	0.5672436585	2.05378919E-25	11	3	EIF2S3L	7
	4	NUP160	0.1835548928	5.53740439E-04	9	4	ASPH	4
	5	ASPH	0.1637790771	6.14654812E-03	6	5	KRT23	3
SLC3A2	1	mRNA	0.1381840013	2.61466672E-02	35	1	hsa-miR-1181	18
	2	hsa-miR-22-3p	0.8170555473	1.08917086E-34	29	2	CASP3	13
	3	TKT	0.8110334724	1.34939882E-06	7	3	KRT23	4
	4	hsa-miR-518b	-0.7991977534	5.58559146E-09	4	4	AIFM1	3
PFKL	1	mRNA	0.1451191694	2.22120980E-02	35	1	ACADVL	14
	2	NSD1	-0.3311467944	6.42437694E-06	14	2	SMS	8
	3	SMS	0.3534565224	3.22468330E-07	7	3	NSD1	5
	4	TFRC	-0.5029109091	2.17871296E-09	4	4	CARS	3
	5	LIN28B	0.2285836005	1.82331660E-03	3	5	PDIA5	3
SPTAN1	1	mRNA	0.2021595456	3.05337262E-01	35	1	SUPT16H	11
	2	PLEC1	0.3313451639	5.85422020E-07	30	2	HMGB3	10
	3	VDAC2	-0.2961435232	7.10174200E-08	29	3	CAPN6	6
	4	NUP210	-0.2678456912	1.75571805E-03	6	4	PGAM1	4
	5	KHSRP	-0.6006329921	2.53692918E-03	5			
	6	SPTBN1	0.2458724932	7.99058858E-06	3			
MVP	1	mRNA	0.3004968546	1.15405592E-06	35	1	CAPN6	15
	2	ACO1	-0.2323945687	6.57989816E-11	14	2	TMED9	12
	3	CALD1	0.4823860262	1.63575311E-12	14	3	CAST	9
						4	HNRNPH2	6
						5	CLIP1	5
						6	NPEPPS	5
						7	PSMB1	5
						8	SLC25A5	5
ERO1L	1	mRNA	0.2135739937	1.52488327E-01	35	1	FRY	19
	2	treat	NA	NA	33	2	CFL1	14
						3	SEPT7	12
						4	SPAG17	5
						5	SASH1	3
						6	SQSTM1	3
DDX3X	1	mRNA	-0.0270457058	6.06027457E-01	35	1	PPP2R2A	10
	2	CYP19A1	0.2459846127	1.19473269E-12	30	2	LMNA	8
	3	LMNA	1.1248709853	2.60902084E-06	16	3	DDX17	7
	4	DNM2	0.2451385475	2.76583355E-03	9	4	NONO	5
	5	PKP3	0.1989345889	1.43153361E-03	4	5	LEMD2	3
	6	hsa-miR-125a-5p	0.6042315224	8.34450351E-08	3	6	LRRC1	3
						7	PSMC6	3
						8	VAMP8	3

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
PRDX2	1	mRNA	-0.1227486846	1.09443731E-01	35	1	TPI1	23
	2	AKR7A2	0.5945643276	3.07990674E-13	11	2	MDH1	12
	3	CNDP2	1.7086447412	3.23930600E-09	11	3	CNDP2	6
	4	MME	-0.5628341531	4.66244218E-09	8	4	PFN1	5
	5	PFN1	0.8081197507	7.81568716E-05	5			
	6	YWHAE	0.9482830755	4.29047710E-07	4			
	7	CDIPT	-0.1690397413	2.58631034E-02	3			
SLC26A2	1	mRNA	0.1971883711	4.86835786E-05	35	1	HSPA6	10
	2	DSP	-0.2357970128	9.44771131E-07	12	2	CYTSB	4
	3	CYP11A1	0.1867719106	2.68015838E-06	7	3	EIF3F	4
	4	HSPA6	0.2010100328	1.08565104E-02	5	4	GFPT1	4
	5	FAM179A	0.2557952326	5.92799736E-04	4	5	TPP2	4
	6	LGR6	0.3037626456	1.25279502E-04	4	6	NSF	3
	7	NSF	-0.3537444721	3.97508742E-06	4	7	PDIA4	3
	8	ZMPSTE24	0.3659193340	1.37242588E-04	4	8	STT3A	3
	9	C3	0.2087270020	5.85784974E-07	3	9	TIAM1	3
	10	GFPT1	-0.9966622792	7.79455954E-06	3	10	UBA2	3
	11	RPL12	0.2629544832	6.71631211E-03	3			
HDAC2	1	mRNA	0.8828498490	6.25238145E-02	35	1	hsa-miR-130b-3p	9
	2	LEPRE1	1.2998082940	6.31905893E-07	12	2	GM2A	4
	3	UGP2	-3.6130963734	4.48419169E-06	9	3	CPT1A	3
	4	hsa-miR-130b-3p	-1.1205304843	2.54748911E-05	7	4	HIST1H1C	3
	5	NAPA	1.0606459575	5.08740426E-06	6	5	PDXDC1	3
	6	GM2A	0.6228665207	4.94118165E-07	5	6	RPS13	3
	7	EIF2S1	1.2049380454	4.65730579E-06	4			
HSPB1	1	mRNA	0.2212484820	4.78705468E-08	35	1	RAI14	10
	2	SERPINC1	0.6380853096	6.79953792E-07	13	2	NAGK	8
	3	HADHA	-1.0473925842	6.57749472E-08	8	3	KRT23	7
	4	hsa-miR-584-5p	0.7588319158	7.67001669E-05	5	4	hsa-miR-193b-3p	6
	5	hsa-miR-365a-3p	-1.0683967831	1.15802791E-02	4	5	PKM2	4
	6	PKM2	-1.9356893743	5.93931201E-08	3	6	CCDC109A	3
JUP	1	mRNA	0.5244387276	2.48650318E-09	35	1	SAPS3	20
	2	PHC1	0.2639489984	1.53015805E-04	20	2	LMF2	8
	3	AUTS2	0.2206589021	7.81636319E-03	4	3	AHCY	6
	4	PCBP1	0.3536006092	1.24008691E-03	4	4	EEF2	6
	5	PDCD10	-0.2034779527	9.48760359E-03	3	5	AUTS2	4
						6	ERAP1	3
SMS	1	mRNA	0.4747203606	9.60630839E-03	35	1	SNTB1	15
	2	API5	0.3158614062	7.35707026E-04	9	2	ARCN1	13
	3	TCEAL4	-0.4583926165	1.16103215E-04	7	3	CYP11A1	12
	4	ARL1	0.4350086531	2.16378081E-03	4	4	BUB3	5
	5	PSMA3	0.3892210104	1.84164749E-03	4	5	CSNK2A1	4
						6	IGF2BP3	4
						7	hsa-miR-484	3
ETFDH	1	mRNA	-0.6189700185	2.52295659E-03	35	1	HNRNPR	6
	2	ND1	0.9402376874	8.93786134E-10	11	2	ACO2	5
	3	NDUFV1	0.5899885477	8.55408762E-09	11	3	hsa-miR-1280	5
	4	hsa-miR-1280	-1.9179208801	5.81615290E-10	6	4	hsa-miR-192-5p	4
	5	ACO2	0.7659311769	1.77895040E-07	5			
	6	PEG3	0.2738198438	2.17520436E-03	5			
	7	ATP5J2	0.7428574719	6.45423674E-09	4			
	8	hsa-miR-519b-3p	-1.2835768366	6.37275531E-04	4			
	9	SLC25A24	0.7410114209	3.25434937E-06	4			
	10	CAPN6	-0.3537923397	3.60077031E-05	3			
TXNRD1	1	mRNA	-0.1544089242	2.78057472E-01	35	1	SMC1A	10
	2	treat	NA	NA	21	2	MBOAT7	7
	3	HSD3B1	0.2940607321	2.28761081E-28	10	3	TFRC	6
	4	EPS8L2	0.1910418813	3.34478660E-07	9	4	ATP5B	4
						5	PCYOX1	3
						6	RPS18	3

Protein		Regulators of the protein					Proteins regulated	
		Name	Coef	p value	Frequency		Name	Frequency
HMOX1	1	mRNA	1.2348987032	2.03280647E-28	35	1	MTX1	13
	2	treat	NA	NA	35			
	3	FLAD1	-0.1727759226	1.22340663E-05	8			
	4	MTX1	-0.2549988483	1.87258879E-06	8			
	5	CDKN2AIP	-0.2068015285	1.59057123E-05	7			
PDCD4	1	mRNA	0.2582967486	4.18909243E-02	35	1	STX7	5
	2	hsa-miR-365a-3p	1.4404855975	1.14706235E-11	27	2	hsa-miR-140-5p	4
	3	SRP68	0.2902615378	1.65868037E-03	13	3	hsa-miR-365a-3p	4
	4	RPL11	-0.4004208999	8.09081947E-04	9	4	GNAQ	3
	5	HYOU1	0.4712372687	1.66397303E-08	3	5	NOMO1	3
	6	PRDX3	-0.4103561285	3.94119546E-04	3	6	RAB5A	3
GNS	1	mRNA	0.1698757277	3.21038935E-01	35	1	EPS8L2	5
	2	EPS8L2	0.5614250326	1.36041295E-07	14	2	ATP5H	3
	3	STS	1.7553665288	3.54501087E-09	9	3	DDX3X	3
	4	PYGL	0.6320253902	1.49237744E-06	7	4	GLB1	3
	5	hsa-miR-30a-5p	-2.6480790715	3.65646063E-06	6	5	PYGL	3
	6	CLIP1	0.5616189500	4.83602998E-12	5			
	7	CAPNS1	-0.8116356795	1.77077300E-05	4			
	8	GLB1	0.5907474668	7.39805638E-07	4			
	9	NDRG1	-0.5940583657	4.96722644E-08	3			
TES	1	mRNA	-0.1757979106	1.60143738E-01	35	1	hsa-miR-26b-5p	20
	2	PDCD4	0.5249467867	5.90814423E-09	22	2	hsa-miR-30e-5p	9
	3	hsa-miR-26b-5p	2.0948881109	7.38520426E-11	12	3	NSF	9
	4	SF3A1	-0.2421888629	2.63598878E-02	4	4	STT3B	6
						5	MARS	3
CYP11A1	1	mRNA	0.9766913481	1.57317050E-32	35	1	DAB2	12
	2	NAMPT	-0.9332566028	3.94326009E-09	30	2	FAM193A	4
	3	NCLN	0.3990942001	1.00493087E-04	12	3	RAI14	3
	4	LRRC16A	-0.3457139838	1.84470263E-04	7			
	5	FAM193A	-0.5923440040	1.57526881E-04	5			
	6	HMGB1L1	-0.4072287713	2.56706678E-05	5			
	7	SF3A1	0.7743421476	1.63630268E-04	5			
	8	U2AF2	0.3049191825	1.14172611E-02	5			
	9	EEA1	0.4857336921	1.37440920E-03	3			
ALPP	1	mRNA	0.6537937816	7.97751180E-04	35	1	hsa-miR-150-3p	5
	2	M6PR	1.2458097991	8.00655878E-06	16	2	M6PR	5
	3	hsa-miR-203	-2.5210333858	1.68576076E-08	6	3	hsa-miR-365a-3p	4
	4	hsa-miR-365a-3p	-2.0976155223	5.25577087E-05	6	4	hsa-miR-518f-3p	3
	5	PRSS8	0.5734783771	2.59572401E-06	6			
	6	hsa-miR-20b-5p	-1.4948639958	3.39648440E-11	5			
	7	PSMD4	-0.3229388951	2.25639091E-02	5			
	8	AKR1B1	1.6311606917	1.68707279E-06	4			
	9	CPT1A	1.0722625112	2.15524993E-04	4			
	10	hsa-miR-520b	2.4667840237	3.58200449E-07	3			
SLC7A5	1	mRNA	-0.0602427130	6.35864015E-01	35	1	hsa-miR-345-5p	28
	2	TFRC	0.8152133185	1.58038514E-11	33	2	KDELR1	11
						3	hsa-miR-335-3p	4
FN1	1	mRNA	0.6036937154	8.06373303E-10	35	1	A2M	4
	2	HSPA5	2.3627788130	7.00744902E-55	28	2	BAZ1B	4
	3	TNFAIP3	-0.4512188867	1.74021885E-10	13	3	cDNA.FLJ33617.fis	3
	4	PDXDC1	-0.3875747019	8.18674646E-04	10			
	5	UBA6	0.4478318748	2.16703621E-10	9			
	6	NUP205	0.4969227700	3.49823521E-20	6			
	7	A2M	0.6045142186	5.11395624E-05	4			
	8	hsa-miR-936	-1.2436521547	3.20932963E-04	4			
	9	ERO1L	0.4739551087	4.85357563E-28	3			
	10	hsa-miR-519c-3p	-2.5701217367	6.71484384E-06	3			
	11	REV1	-0.4806396254	5.37481303E-04	3			
	12	treat	NA	NA	3			

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
FTH1	1	mRNA	-0.3364435047	2.32412799E-01	35	1	SEC23B	7
	2	TUFM	1.2557998516	1.08821003E-06	26	2	hsa-miR-221-3p	6
	3	RPIA	0.6095804746	9.75277681E-07	24	3	TPM4	5
	4	ACSF2	0.4441389390	1.34910355E-03	7	4	AMPD1	4
	5	G3BP2	-0.6374928514	3.65663054E-06	4	5	RPIA	4
	6	GGCT	0.4193448765	1.42983225E-03	3			
	7	NDRG1	0.3508603115	4.18472467E-06	3			
	8	PSMB6	0.9016684389	2.23103346E-06	3			
HSD3B1	1	mRNA	0.4833795507	3.80524207E-18	35	1	TXNRD1	7
	2	hsa-miR-335-3p	-0.7774832289	8.70290062E-06	15	2	TGM2	5
	3	DSP	-0.4333654679	3.60557279E-07	10	3	CTNNB1	3
	4	SLC7A5	0.6747244095	1.01551739E-05	10	4	DSP	3
	5	CTNNB1	-1.3286535021	8.05384686E-09	7			
	6	TXNRD1	0.8923962027	6.88125581E-09	7			
	7	HNRNPA3	-0.3379146394	4.04688212E-10	5			
	8	FANCM	0.3603215532	6.51405288E-04	4			
	9	CRK	0.4321364220	1.09517928E-09	3			
	10	hsa-miR-584-5p	-0.9135455640	1.32018281E-03	3			
	11	SMC1A	-0.3243864730	1.16268447E-03	3			
MX1	1	mRNA	0.3120252147	1.85202239E-06	35	1	BZW2	5
	2	HSD3B1	0.6361131636	1.56128605E-13	8	2	SNX2	4
	3	BZW2	0.9409614058	3.72976349E-07	7	3	STIP1	3
	4	ALAD	-0.6517993332	1.74672825E-03	5			
	5	ALPP	0.7447161478	2.40182849E-09	5			
	6	SLC7A5	1.5422022629	2.32692853E-11	5			
	7	DDX3X	0.9656155316	1.20439949E-06	4			
	8	hsa-miR-451a	1.1308618744	1.21076155E-05	4			
	9	TGM2	-5.6047697127	8.75954287E-10	4			
	10	hsa-miR-193b-5p	-3.9791640611	1.18289675E-15	3			
WARS	1	mRNA	-0.2696746232	1.54116639E-02	35	1	AKR1A1	15
	2	PLIN2	0.3628073422	1.72525935E-07	21	2	U2AF2	11
	3	GAA	-0.6024439688	3.31470885E-04	15	3	CLIC3	5
	4	FNTA	-0.2935975353	2.20013877E-02	4	4	GAA	5
	5	hsa-miR-520f	-1.1866303534	1.49220267E-05	3	5	CYB5R1	4
CTSB	1	mRNA	0.3373276558	4.88246135E-02	35	1	hsa-miR-30c-5p	18
	2	HSPB1	0.8466367583	7.80198485E-12	29	2	EIF3I	4
	3	EIF3I	0.3575968117	1.81704365E-02	10	3	CLIC3	3
	4	hsa-miR-30c-5p	-1.6401193560	2.94606153E-12	4	4	CUX2	3
	5	NACA	0.4195978096	6.09526604E-03	4			
	6	HNRNPF	-0.5748569912	4.67301503E-04	3			
	7	SLC25A11	0.5447890262	3.30724095E-04	3			
CYP19A1	1	mRNA	0.9885078082	2.53736663E-12	35	1	TFRC	17
	2	MAN2B1	0.9855265165	4.55897924E-08	33	2	CTNND1	6
	3	DYNC2H1	0.6052897530	1.15518790E-03	21	3	TXNRD1	6
						4	GLG1	3
CLIP1	1	mRNA	0.4300477478	9.02312934E-02	35	1	DERA	9
	2	GNS	0.6936820036	2.17386895E-15	30	2	TMED10	3
	3	DERA	-0.7702794085	2.27882190E-04	18			
	4	KRT36	-0.4075497093	3.23215349E-04	11			
	5	TMED10	0.7698192238	1.87316826E-03	8			
	6	ABCA13	0.3994422243	2.77845821E-02	4			
	7	MVP	1.8909065791	2.02386323E-16	4			
	8	MYH3	-0.5446938818	3.95743856E-05	4			
	9	KIF5A	0.5049551631	1.58528801E-06	3			
	10	RPN1	-1.3794865042	6.76932746E-03	3			
	11	TES	-0.3595371559	2.01484571E-02	3			

Protein		Regulators of the protein					Proteins regulated	
		Name	Coef	p value	Frequency		Name	Frequency
PKP2	1	mRNA	0.0685486914	1.12103874E-01	35	1	NIPSNAP1	14
	2	PLIN2	0.2412468520	7.02847763E-08	13	2	GBP1	4
	3	WDR1	0.9997099554	6.18846987E-06	8			
	4	TES	0.5698339174	5.21548526E-10	7			
	5	GBP1	0.3219572561	1.10462320E-04	5			
	6	NLN	0.2855894421	1.13602698E-03	5			
	7	hsa-miR-210	0.3940744114	7.31871756E-08	4			
CAPN6	1	mRNA	1.2612380377	7.26159298E-20	35	1	hsa-miR-148a-3p	5
	2	MYH14	0.5722352073	2.02986639E-05	17	2	AP3B1	4
	3	hsa-miR-34c-5p	-0.8444344281	2.88865394E-06	13	3	HNRPDL	3
	4	HNRNPC	0.7098843644	4.46297988E-05	11	4	MYH14	3
	5	C16orf96	0.3990555765	2.75493695E-04	10			
	6	BASP1	-0.6925788236	1.09430492E-03	5			
	7	DBNL	-0.9458960696	4.20567823E-09	3			
	8	KIAA0090	0.8535384202	6.84495246E-04	3			
	9	WNT4	0.5637188069	6.90047253E-09	3			
	10	ZCCHC2	-0.4896108394	8.99988581E-03	3			
CTSL1	1	mRNA	1.8045465723	1.68690115E-17	35	1	VAMP8	3
	2	TOMM40	0.6780309748	1.76837953E-05	26			
	3	KRT36	0.3313308029	1.14046109E-03	16			
	4	HMOX1	0.3758753697	2.31140379E-02	4			
	5	FAM25A	0.6175626330	6.26555162E-03	3			
	6	hsa-miR-378a-3p	1.5191523475	3.30109752E-03	3			
	7	KIAA0090	0.9465299435	3.50451688E-05	3			
	8	LBR	-0.4166386162	8.61293428E-04	3			
CD63	1	mRNA	0.7821901609	4.98086311E-03	35	1	HSD3B1	12
	2	hsa-miR-574-3p	-1.5623215172	3.40879838E-09	15	2	TXNRD1	8
	3	AGL	-0.8606320581	3.81048887E-06	9	3	SDHB	5
	4	SDHB	-0.8549225405	1.95903960E-04	7			
	5	TXNRD1	1.3231799432	2.12458629E-09	5			
STAT1	1	mRNA	0.3328219824	6.16773063E-03	35	1	hsa-miR-451a	26
	2	DAB2	0.4911971225	5.37610568E-12	24	2	TMEM165	14
	3	NAE1	0.3902299662	7.92163689E-03	9	3	MATR3	4
	4	LAMP2	0.5478021887	1.22546768E-11	3			
	5	MATR3	-0.5565009967	3.02150577E-04	3			
DAB2	1	mRNA	0.9636539151	4.27730684E-23	35	1	ERAP1	6
	2	ERAP1	-0.7166817830	1.52241762E-08	12	2	CYP11A1	4
	3	hsa-miR-22-3p	1.2241876241	2.46837868E-10	11	3	DDX3X	3
	4	hsa-miR-574-3p	-0.6239566873	5.99946294E-05	6	4	hsa-miR-520f	3
	5	DDX3X	0.5709885857	5.65202840E-04	5	5	SRP68	3
	6	hsa-miR-20a-5p	-0.8807232713	2.31225143E-10	3			
NDRG1	1	mRNA	0.4557303618	1.55371788E-03	35	1	hsa-miR-584-5p	7
	2	GARS	1.2550848367	4.24031048E-09	8	2	PLIN2	6
	3	hsa-miR-584-5p	-2.7339532881	1.01435988E-05	6	3	MYL6B	4
	4	PLIN2	0.8279216206	2.17474773E-10	4	4	TIMP3	3
	5	TPI1	2.2879446933	6.02504012E-06	4			
	6	ERO1L	0.6572248089	1.10581576E-08	3			
	7	hsa-let-7b-5p	1.0651451417	1.59963736E-04	3			
	8	MYL6B	0.9056328164	1.26073516E-07	3			
	9	RPIA	0.7324523050	3.77504928E-07	3			
PLIN2	1	mRNA	0.3500108384	2.25803356E-01	35		None	
	2	treat	NA	NA	35			
GDF15	1	mRNA	1.4501154791	2.42421848E-12	35	1	CAST	10
	2	ALDH4A1	-1.7086221510	3.88128757E-07	19	2	CBR1	4
	3	cDNA.FLJ52712	0.5222407465	4.28682332E-05	4	3	TFRC	3
	4	MARCKS	0.8049301693	6.19204824E-06	4			
	5	hsa-miR-1246	0.9839784090	3.01750843E-05	3			
	6	MTX1	-0.5753586644	7.30133195E-03	3			
	7	TFRC	2.4041852069	1.89912873E-04	3			

Protein	Regulators of the protein					Proteins regulated		
		Name	Coef	p value	Frequency		Name	Frequency
EPS8L2	1	mRNA	0.6182556262	7.55805652E-04	35	1	ACAT1	3
	2	NDUFS8	-0.7553233534	5.82319691E-06	13	2	GAD2	3
	3	RRBP1	1.1160251815	1.81273355E-09	10	3	NDUFS8	3
	4	SMC1A	-0.5448091555	3.01393186E-04	9			
	5	TNPO1	0.6240763438	3.45148527E-08	8			
	6	TXNRD1	0.4129499435	1.58941919E-05	6			
	7	GNS	0.3450927901	2.35297929E-06	5			
	8	ATP5A1	-2.1359293754	1.92388867E-04	4			
	9	hsa-miR-1183	-0.8636615758	6.76254045E-05	4			
	10	hsa-miR-125a-5p	0.9671597486	1.77002343E-04	4			
	11	MESDC2	0.4379737904	1.11239498E-02	4			
	12	ACSL3	0.9492916409	5.00454595E-08	3			
	13	DDX6	0.2383673149	4.14689577E-03	3			

Table S6. Direct regulators of the mRNA transcripts of the 78 proteins. Frequency column represents, out of the 35 resampled data sets, the number of times a miRNA/protein was identified as a directed regulator of the target mRNA.

Transcript		Regulator	Coef	p value	Frequency
MYOF	1	treat	NA	NA	35
	2	hsa-miR-518f-5p	0.357212904	0.017824847	16
	3	hsa-miR-30a-5p	0.458472827	0.037406309	11
	4	hsa-miR-30e-5p	1.052890383	0.009789667	11
	5	TCEB1	-0.103957181	0.005476074	10
	6	hsa-miR-519c-3p	0.51664951	0.051005086	8
	7	CNDP2	0.215383639	0.042477577	7
	8	hsa-miR-29c-3p	-0.524393626	0.012359941	6
	9	hsa-miR-1249	-0.306359334	0.007743305	5
	10	hsa-miR-498	0.771266638	0.007376039	5
	11	hsa-miR-520a-5p	0.327958918	0.076218732	5
	12	PSMD13	0.13644693	0.034285278	5
	13	PSMD8	0.090064895	0.016487441	5
HSP90B1	1	hsa-miR-210	0.667772764	5.17E-06	22
	2	HSP90B2P	0.700101963	3.05E-05	21
	3	FN1	0.195245374	0.001320197	15
	4	ETFB	0.308288424	0.000707256	13
	5	HSPA5	1.521276541	6.37E-05	7
	6	hsa-miR-320b	-1.367123398	4.10E-06	6
	7	hsa-miR-521	1.99080461	3.32E-05	6
	8	hsa-miR-320d	-1.013077529	1.38E-05	5
	9	JUP	-0.301173542	0.017252318	5
GAPDH	1	treat	NA	NA	32
	2	PLIN2	0.324787357	0.021597689	14
	3	ETFDH	0.1467939	0.012021117	11
	4	hsa-miR-210	0.442218853	0.005847569	9
	5	PCCB	0.308270377	0.002736201	8
	6	ERO1L	0.198970846	0.001312896	6
	7	FUCA1	0.307104471	3.30E-06	6
	8	LDHA	-0.341191336	0.006494027	6
	9	JUP	-0.181005747	0.008339742	5
	10	SQSTM1	-0.123801081	0.053883817	5
ANXA1	1	hsa-miR-210	-0.625084558	7.96E-11	25
	2	LCP1	-0.175746282	0.022750246	15
	3	MX1	0.170141754	0.001270247	11
	4	hsa-miR-663a	0.241552428	0.003372635	7
	5	hsa-miR-877-5p	0.468833464	4.15E-05	7
	6	treat	NA	NA	7
	7	HSPA5	-0.638551763	0.012823837	6
HSPA5	1	hsa-miR-320b	-2.086003041	0.000642968	27
	2	ALAD	0.523378988	0.001425755	21
	3	TXNRD1	-0.574676285	0.002869374	10
	4	SPINT1	-0.525194747	0.002455647	9
	5	hsa-miR-125a-5p	-1.248256899	0.000378699	7
	6	hsa-miR-520c-3p	-2.001205222	1.82E-08	7
	7	ALPP	-0.424320255	0.003257186	5
	8	CD63	-0.517819025	0.004063856	5
	9	CYP19A1	-0.369654785	0.001391222	5
	10	hsa-miR-29b-3p	-1.552182321	1.98E-06	5
	11	treat	NA	NA	5

Transcript		Regulator	Coef	p value	Frequency
HADHA	1	TNFAIP3	0.088474747	0.001220454	22
	2	MYO9A	-0.087998341	0.002097755	20
	3	treat	NA	NA	14
	4	hsa-miR-193b-3p	-0.145464576	0.002337167	12
	5	SLC25A6	-0.168132909	0.005141106	12
	6	HMGB1	0.077246814	0.019436671	11
	7	IRAK4	0.108422031	0.000177523	10
	8	HDAC2	0.081641678	0.000568631	8
	9	CNOT1	-0.070440641	0.002201109	7
	10	ST13	0.047512128	0.042502913	7
	11	MGA	-0.058958645	0.012613902	6
	12	RPS3	0.22116382	0.000699188	6
	13	RHBDL1	-0.062814309	0.001222846	5
ENO1	1	treat	NA	NA	35
	2	MYO15A	-0.143620736	0.010893665	20
	3	CTNND1	-0.271091222	0.02597366	8
	4	ETFDH	0.094722693	0.009144444	7
	5	ND5	0.080941958	0.032948561	7
	6	hsa-miR-30a-5p	0.522559217	0.042336914	6
	7	hsa-miR-29b-3p	-0.448007192	0.004769895	5
	8	JUP	-0.161352539	0.006609356	5
IDH1	1	treat	NA	NA	34
	2	hsa-miR-141-3p	1.506100807	0.003454605	11
	3	ATP2A2	0.242116315	0.015316862	10
	4	SLC4A10	0.196313962	0.034133884	10
	5	HSPA5	0.926451221	0.004013429	9
	6	GNPDA1	0.243735022	0.004223295	8
	7	hsa-miR-877-5p	-0.472164443	0.002732962	8
	8	RPL22	0.292783641	0.013232951	8
	9	hsa-miR-583	-0.534462769	0.000584098	6
	10	CYCS	0.279578778	0.000473693	5
ACTN1	1	PDZD2	-0.138298982	0.01395416	25
	2	treat	NA	NA	25
	3	hsa-miR-197-3p	0.318756172	0.002522184	19
	4	PDIA6	-0.60179612	0.015029387	11
	5	ACTR2	0.248409892	0.00109124	9
	6	MAP4	-0.20467251	0.000213117	9
	7	hsa-miR-664-3p	0.394705412	0.000210616	7
	8	TRMT2B	-0.113123473	0.023236197	7
	9	HSPA5	-0.663869717	3.60E-05	6
	10	EFR3A	-0.141539337	0.012340107	5
	11	hsa-miR-518f-5p	0.657113408	0.0001824	5
	12	PDIA5	0.151820103	0.003071486	5
	13	RGS3	-0.1181292	0.018106417	5
TFRC	1	hsa-miR-520c-3p	0.827872487	0.008087131	29
	2	PLIN2	-0.47998979	2.53E-08	19
	3	treat	NA	NA	15
	4	hsa-miR-29b-1-5p	-0.440308094	0.046365841	7
	5	ELAVL1	0.146110469	0.008234784	6
	6	MX1	0.263657722	2.48E-05	6
	7	hsa-miR-210	0.394206202	0.010332213	5
ACADVL	1	treat	NA	NA	34
	2	hsa-miR-498	0.539055885	0.007125478	13
	3	hsa-miR-629-3p	-0.172625476	3.67E-05	12
	4	hsa-miR-1181	-0.193125614	0.000146969	7
	5	hsa-miR-29b-3p	-0.277650779	0.003711896	7
	6	HYOU1	-0.087476696	0.014704582	7
	7	hsa-miR-193b-3p	-0.241667887	0.006390728	6
	8	FAM115A	0.052233378	0.030174786	5
	9	hsa-miR-192-5p	-0.219467447	0.015322752	5
	10	PGK1	-0.219942674	0.024911803	5

Transcript	Regulator		Coef	p value	Frequency
ALDH7A1	1	treat	NA	NA	35
	2	EML5	-0.33841088	0.002090432	23
	3	SLC3A2	-0.604613482	0.04269625	15
	4	SLC25A12	-0.588897036	0.001177768	13
	5	GNAI3	0.278577361	0.00111993	12
	6	ARHGAP1	0.429092079	0.039021095	10
	7	VCP	-1.015819138	0.006511701	9
	8	hsa-miR-484	-1.402153583	0.005121824	7
	9	CLINT1	-0.303619812	0.007633498	6
	10	HBB	0.199433182	0.008082481	5
	11	hsa-miR-130b-3p	-0.541860034	0.012116666	5
	12	hsa-miR-660-5p	-0.806673618	0.019281252	5
IDH2	1	hsa-miR-484	-0.812071562	0.002551178	22
	2	MAP4	0.251883246	0.001310391	19
	3	TOMM70A	0.308823956	0.000637613	18
	4	SERPINE1	-0.205921853	0.00733852	17
	5	OBSCN	-0.242442481	0.006797508	16
	6	SQSTM1	-0.179912355	0.008746341	14
	7	RPS27A	-0.2880108	0.023309816	13
	8	treat	NA	NA	12
	9	EEF1G	-0.523368993	0.016948233	8
	10	DDOST	0.861108473	0.00914094	7
	11	HSPA6	0.262817068	0.001292591	7
	12	SF3A1	0.249542002	0.003507882	7
	13	HEXA	0.376741605	0.000732979	5
EEF1A1	1	APEX1	0.124383953	0.002582265	17
	2	hsa-miR-342-3p	0.380434119	0.000106803	16
	3	CAP	0.192286984	0.020830494	10
	4	hsa-miR-150-3p	-0.221270991	0.001323928	10
	5	ARID3A	-0.111361726	0.005825608	9
	6	UQCRC2	0.396516248	7.58E-05	9
	7	RPL15	0.114606862	0.00693359	8
	8	RBM47	-0.117559848	0.006348649	6
	9	hsa-miR-130b-3p	0.278701222	0.000293917	5
	10	MYO15A	-0.142781178	0.001704464	5
	11	PDLIM1	0.074934823	0.019129734	5
	12	RFPL4A	0.105973166	0.026271242	5
FASN	1	treat	NA	NA	31
	2	COX4I1	-0.134950194	0.019017571	17
	3	MTERF	-0.127749446	0.004409498	14
	4	hsa-miR-345-5p	0.355817127	0.006631843	7
	5	MCM5	0.197428777	0.000844636	6
	6	hsa-let-7b-5p	-0.17476086	0.017334342	5
PDIA4	1	HSPA5	1.951795735	4.77E-06	27
	2	treat	NA	NA	21
	3	hsa-miR-210	0.634957574	0.001675556	15
	4	FN1	0.294631393	0.00013947	10
	5	DDX3X	-0.390662475	0.005791673	8
	6	G3BP1	-0.354856372	0.002180046	6
	7	HSP90B2P	0.37862339	0.014026951	6
	8	ETFB	0.328377145	0.008754327	5
	9	hsa-miR-141-3p	1.374928839	0.004343344	5
ACSS1	1	treat	NA	NA	35
	2	hsa-miR-524-3p	-1.226927664	0.013362008	10
	3	PLIN2	-0.424838078	0.01663384	10
	4	ETF1	0.167371294	0.009316654	7
	5	hsa-miR-30e-5p	-1.209369715	0.039485415	6
	6	hsa-miR-320b	-1.144814336	2.77E-05	6
	7	JUP	0.213829391	0.016786989	6
	8	KDELC2	0.184905182	0.001719033	5

Transcript		Regulator	Coef	p value	Frequency
ACO2	1	treat	NA	NA	16
	2	hsa-miR-583	-0.184158103	0.000811354	13
	3	STX7	0.130701495	0.003332689	13
	4	MAP4	0.08981871	0.011463992	11
	5	MAP7D3	-0.109239861	0.00536634	9
	6	PHLDA2	0.110576629	0.000470774	9
	7	hsa-miR-630	-0.244797832	1.27E-05	8
	8	DAB2	0.091733395	0.001557825	6
	9	hsa-miR-150-3p	0.350298721	1.97E-07	6
	10	hsa-miR-125b-5p	0.425681835	1.04E-05	5
HADHB	1	treat	NA	NA	27
	2	EML5	-0.079639974	0.00372106	23
	3	SRP72	-0.0981266	0.000790333	23
	4	EIF3F	-0.109199496	0.0005719	13
	5	MAP4	0.101451334	0.001937337	9
	6	AIMP1	0.082066261	0.002057201	8
	7	NDUFA10	0.074878674	0.005765905	7
	8	hsa-miR-151a-3p	-0.172460295	0.016267324	6
	9	hsa-miR-320b	-0.397910249	8.82E-05	5
RASA1	1	treat	NA	NA	18
	2	RPL15	0.253149893	0.044975179	14
	3	hsa-miR-320b	1.253305232	0.005288745	10
	4	hsa-miR-210	-0.75117118	4.37E-06	9
	5	HSPA5	-1.227143766	0.005731774	8
	6	ERO1L	-0.232991846	0.006096468	6
	7	hsa-miR-520c-3p	0.897050847	0.004377236	6
	8	EIF3F	0.415864693	0.00538859	5
	9	RTN4	0.306516104	0.044143377	5
HSD17B10	1	C16orf96	-0.13402082	0.000302749	28
	2	LAMC1	0.079909245	0.000825693	22
	3	ATP5A1	-0.365962973	0.001757704	17
	4	MAPK3	0.114267635	0.002337817	11
	5	RPL13A	0.091166495	0.004018643	11
	6	WDR5B	-0.071058004	0.005322668	11
	7	hsa-miR-519c-3p	-0.668753822	2.71E-05	10
	8	DYSF	0.084641907	0.030404703	9
	9	CFL1	-0.104540277	0.007383632	5
	10	hsa-miR-574-3p	-0.097686491	0.011026363	5
	11	IDH3B	-0.069814402	0.040353649	5
	12	ODZ3	0.087306709	0.019420711	5
	13	PSMA2	-0.075754216	0.003008344	5
PARP1	1	treat	NA	NA	35
	2	HMOX1	-0.124548329	0.022720519	15
	3	hsa-miR-320d	-0.613134919	0.006105161	9
	4	GSS	0.16295211	0.025282156	8
	5	GPD2	-0.169884225	0.013273312	7
	6	EIF4G2	-0.105442324	0.086057281	6
	7	BCL11B	0.112573761	0.087467215	5
EGFR	1	treat	NA	NA	35
	2	GALNT2	0.176840404	0.02142506	25
	3	hsa-miR-484	0.804717537	0.009934432	22
	4	hsa-miR-30a-5p	0.77427001	0.03980957	7
	5	USP16	0.191185136	0.014023333	7
	6	CPSF6	0.175157383	0.014732099	5
	7	hsa-miR-224-5p	0.580629799	0.023848059	5
	8	RPS25	0.319179016	0.004343219	5
ALDOA	1	treat	NA	NA	35
	2	MYO15A	-0.124066191	0.009465428	15
	3	hsa-miR-518a-5p	0.526977815	0.000324921	12
	4	JUP	-0.186680159	0.000414183	10
	5	PLIN2	0.225782709	0.042987239	9
	6	HDAC2	-0.078135363	0.036759374	6
	7	KRT1	-0.076781179	0.004607837	5

Transcript		Regulator	Coef	p value	Frequency
ECHS1	1	treat	NA	NA	35
	2	hsa-miR-484	-0.401910399	0.010466301	12
	3	hsa-miR-335-5p	-0.589119056	0.006058375	9
	4	hsa-miR-423-5p	-0.395895505	0.004342482	9
	5	hsa-miR-513a-5p	-0.269023434	0.023071431	7
	6	STAT1	-0.136325793	0.010321019	7
	7	hsa-miR-320b	-0.685652325	0.000638422	6
	8	EIF4G2	-0.077489702	0.072409117	5
	9	hsa-miR-765	-0.205849365	0.00078842	5
TPI1	1	treat	NA	NA	35
	2	SQSTM1	-0.171616442	0.000923267	32
	3	PLIN2	0.274173567	0.053831111	19
	4	HSPB1	-0.103751092	0.027303848	9
	5	STAT1	-0.138702203	0.035747775	7
	6	NAPA	-0.084151651	0.033777122	6
	7	TECR	0.147169481	0.012664393	6
GPI	1	treat	NA	NA	35
	2	hsa-miR-130a-3p	1.320958905	0.009931766	8
	3	RPL22	-0.168576352	0.016890407	8
	4	PCBP1	-0.3057988	0.000959326	6
	5	TRMT2B	0.130533609	0.010622336	6
	6	PCCB	0.19845886	0.036284918	5
DSP	1	treat	NA	NA	35
	2	PEG3	0.22217946	0.000141096	23
	3	FAM115C	0.170137591	0.004861255	10
	4	hsa-miR-210	0.476214356	0.003513122	10
	5	CYP19A1	0.108924674	0.084175297	9
	6	hsa-miR-1181	-0.262981223	0.015260669	6
	7	hsa-miR-193b-5p	0.469434561	0.068146657	5
	8	PCBP1	-0.26457429	0.000659001	5
LDHA	1	treat	NA	NA	35
	2	CALU	-0.240666737	0.049742087	12
	3	CTNND1	-0.607942221	0.048762898	8
HYOU1	1	FN1	0.223412243	0.000137312	22
	2	hsa-miR-16-5p	2.28581693	5.65E-09	17
	3	hsa-miR-520c-3p	-1.133705372	5.17E-05	17
	4	HSP90B2P	0.424238978	0.000498782	16
	5	PICALM	-0.64484436	0.008166886	11
	6	RBM15B	-0.326793434	0.008149407	11
	7	EIF3A	-0.53159471	0.003196427	10
	8	ETFB	0.255606106	0.00837843	9
	9	UBA2	-0.231212426	0.027166268	9
	10	hsa-miR-452-5p	1.485401405	0.004315672	8
	11	FERMT2	-0.505604135	0.00050979	6
	12	HDAC1	-0.481740151	0.001589856	6
	13	hsa-miR-516a-5p	2.470131367	0.009189356	6
	14	HSPA5	1.387980722	0.000417012	6
	15	HARS	-0.32249683	0.001637514	5
	16	hsa-miR-23a-5p	-1.062425433	0.004146106	5
	17	PDXDC1	-0.326158569	0.000565949	5
ETFA	1	treat	NA	NA	34
	2	DNMT1	0.210291657	0.001654869	15
	3	hsa-miR-520c-3p	0.502976277	0.019018266	13
	4	YWHAG	0.202506432	0.043595261	9
	5	LRPAP1	0.158293495	0.011744691	8
	6	ARL1	0.152947529	0.037918188	7
	7	FKBP4	0.125428565	0.005090033	7
	8	hsa-miR-516a-5p	-1.462811508	0.010246591	7
	9	hsa-miR-518a-5p	-0.443907618	0.024305641	6
	10	hsa-miR-520g	0.8488545	0.000587385	5

Transcript		Regulator	Coef	p value	Frequency
PPIB	1	FN1	0.155401311	2.94E-05	29
	2	HSP90B2P	0.384343406	0.000265664	23
	3	hsa-miR-516a-5p	1.522448379	0.00141253	14
	4	ETFB	0.236597103	2.27E-05	11
	5	ERO1L	0.142087824	0.011819231	6
	6	hsa-miR-520c-3p	-0.309460128	0.048813727	6
	7	ACO2	0.299416488	8.50E-05	5
	8	DNAH9	0.193061106	0.011352514	5
	9	hsa-miR-518a-5p	0.738691547	5.47E-05	5
	10	HSPA5	0.568159465	0.024587734	5
GLDC	1	treat	NA	NA	28
	2	hsa-miR-520c-3p	1.086507287	0.001321572	17
	3	HSPA5	-1.208336033	0.004550254	17
	4	hsa-miR-141-3p	-1.490154724	0.002497028	12
	5	CUL3	0.356414581	0.0006392	9
	6	hsa-miR-663a	0.43131129	0.002532782	6
	7	CSDA	0.176708188	0.072076851	5
	8	EIF3A	0.580648184	0.000819592	5
	9	hsa-miR-516a-5p	-1.877263633	0.013162939	5
	10	PSMC4	0.446603808	0.000455761	5
ACO1	1	treat	NA	NA	35
	2	EML5	-0.247098116	0.006317203	19
	3	SRP68	0.242621041	0.001457234	12
	4	ARHGAP1	0.503908212	0.000964144	10
	5	hsa-miR-583	-0.366241962	0.003912146	10
	6	hsa-miR-1323	-1.377088545	0.01534051	7
	7	hsa-miR-936	-0.583485844	0.002462732	6
	8	HSP90AB2P	-0.664332763	0.001862148	6
	9	hsa-miR-25-3p	-0.892565053	0.015422009	5
HIBCH	1	treat	NA	NA	31
	2	hsa-miR-484	-0.501555375	0.006383377	21
	3	hsa-miR-520a-5p	-0.511331357	0.01345269	16
	4	SLC25A6	-0.218908367	0.029515957	13
	5	EIF4G2	-0.09773237	0.002950069	9
	6	HMOX1	-0.070098631	0.032644556	7
	7	LRP1	0.054802241	0.002473522	7
	8	CPSF6	-0.138587528	0.000440408	5
	9	hsa-miR-1202	0.149436835	0.01772464	5
	10	hsa-miR-224-5p	-0.240010991	0.025970738	5
ITGB1	1	RPL15	0.310347255	0.000230002	25
	2	HSPA5	-0.520963791	0.001136312	16
	3	PSMD13	0.251217607	0.012384563	10
	4	C1orf173	-0.13762656	0.007298649	9
	5	POTEKP	0.418635332	0.008104846	7
	6	hsa-miR-583	0.234978118	0.008016874	6
	7	SOX11	-0.152745029	0.010946228	6
MME	1	treat	NA	NA	35
	2	PLIN2	0.435355847	0.024599189	7
	3	CALU	-0.147903984	0.037207911	6
	4	hsa-miR-130b-3p	0.423551101	0.006476441	6
	5	LGALS3BP	0.160705515	0.024988122	6
	6	LMNA	-0.470524506	0.025320542	5

Transcript		Regulator	Coef	p value	Frequency
HSD17B1	1	treat	NA	NA	35
	2	hsa-miR-193b-5p	-0.728706428	0.007000038	14
	3	HK2	-0.18236399	0.013630791	12
	4	hsa-miR-365a-3p	-0.716746851	0.013866295	8
	5	LDHA	-0.354748905	0.011535802	8
	6	ALDOA	-0.412333689	0.034882084	7
	7	ITGA6	0.545049065	0.005037426	7
	8	DAB2	0.203028925	0.015522951	6
	9	EFTUD2	0.167343034	0.012342958	6
	10	PLIN2	0.419868255	0.025454915	6
	11	EIF4A1	0.461673481	0.056484576	5
	12	GPI	-0.691226557	0.007336259	5
	13	hsa-miR-210	0.381441646	0.048676991	5
	14	hsa-miR-324-5p	0.678429452	0.000618808	5
	15	LAMC1	0.18057246	0.000129695	5
RRBP1	1	hsa-miR-210	-0.369795102	1.31E-05	29
	2	hsa-miR-130a-3p	-1.594454737	1.16E-05	24
	3	PHLDA2	0.141193963	0.004783974	13
	4	SLC38A2	0.124388444	0.010897721	13
	5	PEG3	-0.087920307	0.025597167	11
	6	NDRG1	-0.168658362	0.006429283	10
	7	hsa-miR-520f	0.527967623	0.000736427	9
	8	treat	NA	NA	8
	9	EEF1G	0.288612218	0.031047977	5
	10	NUP160	-0.13840353	0.023615653	5
SLC3A2	1	treat	NA	NA	34
	2	BAT3	-0.218280907	0.000284677	14
	3	TXNRD1	-0.275132077	0.00861079	13
	4	CD180	-0.203817689	0.003600245	8
	5	HSD3B1	-0.154537433	0.020160658	6
	6	CD63	-0.132988663	0.041926462	5
	7	CTNND1	-0.26998117	0.063870071	5
	8	GNAI3	-0.120035546	0.00211391	5
	9	hsa-miR-30d-5p	0.754578871	0.006289537	5
	10	HYOU1	-0.096118492	0.107851004	5
PFKL	1	ND2	0.238247484	0.002385276	16
	2	RPS13	-0.243244903	0.002132964	16
	3	MAP7D3	0.251859468	0.002405818	15
	4	HDAC2	-0.246458961	0.000291168	14
	5	PBX1	-0.168573121	0.011141009	14
	6	RPL29	-0.312456123	0.0013049	13
	7	GM2A	-0.20913453	0.001425832	7
	8	hsa-miR-1225-3p	0.435243063	0.017427734	7
	9	SLC4A10	-0.228043537	0.003811309	7
	10	ANXA7	0.464490194	0.002022324	6
	11	CLDN3	0.181283244	0.01986302	6
	12	hsa-miR-518d-3p	0.609596957	0.008599049	6
	13	hsa-miR-520b	-0.678464433	0.002486702	6
	14	RAB2A	-0.313589877	0.000710087	5

Transcript		Regulator	Coef	p value	Frequency
SPTAN1	1	XRCC5	-0.557628974	0.00064855	17
	2	hsa-miR-1181	-0.217319337	1.73E-05	14
	3	CYFIP1	0.145441691	0.001545352	13
	4	KRT13	0.261922852	0.009433886	10
	5	hsa-miR-29b-1-5p	-0.204638943	0.001540449	9
	6	PEG3	0.122290218	0.001954624	9
	7	TMEM205	-0.13941755	0.000144995	9
	8	UBE2N	-0.224116458	0.022926565	9
	9	EVPL	-0.159136204	0.019514368	8
	10	TBK1	-0.189089965	0.000407207	8
	11	EIF4G2	-0.13208195	0.000168476	7
	12	FAM115C	0.123945358	0.01219233	7
	13	hsa-miR-629-3p	-0.2730245	1.78E-05	7
	14	LEMD2	0.148928903	0.003028354	7
	15	PHLDA2	-0.157936434	0.001089006	7
	16	RPL18	-0.129744327	0.00402896	6
	17	CAPN2	0.118445391	0.00169485	5
	18	CENPE	0.131265933	0.011008868	5
	19	INTS4	-0.158658187	0.008358259	5
	20	SSR1	0.144712628	0.005279494	5
MVP	1	treat	NA	NA	32
	2	SF1	0.128043309	0.013012698	17
	3	FN1	-0.0934299	0.001075001	15
	4	BCL11B	-0.121818892	0.005721118	12
	5	CYP19A1	0.130082715	0.003200021	10
	6	DAB2	0.165394282	0.005797928	8
	7	hsa-miR-516a-3p	0.304283162	0.006707361	8
	8	PSMC6	0.245589764	0.00095251	7
	9	hsa-miR-29b-1-5p	0.344697039	0.007839619	6
	10	HSPA5	-0.434450741	0.015932409	6
	11	PEG3	-0.052160228	0.076601748	5
	12	SNTB1	-0.11653183	0.021764986	5
ERO1L	1	treat	NA	NA	35
	2	hsa-miR-520c-3p	-0.428494172	0.015214611	21
	3	hsa-miR-210	-0.400527299	0.00535276	17
	4	PCCB	0.200887743	0.00740574	14
	5	HSP90B2P	0.258646697	0.000752682	10
	6	hsa-miR-30a-5p	0.78941181	0.009469013	9
	7	hsa-miR-451a	-0.199671304	0.003239847	9
	8	PLIN2	-0.276890651	0.063846009	9
	9	hsa-miR-516a-5p	1.18803342	0.008730779	6
	10	hsa-miR-520f	-0.670239587	0.00048786	6
	11	JUP	-0.155207249	0.025077776	5
	12	WDR87	0.114724082	0.059796524	5
DDX3X	1	NUP62	-0.214100652	0.001432532	24
	2	PLIN2	-0.152604433	1.08E-06	17
	3	RTN4	0.268533692	0.007229203	17
	4	CAP	0.414185979	0.000116926	15
	5	PCNA	0.146849149	0.000677374	14
	6	RP2	0.263826805	0.003725067	11
	7	RHBDL1	-0.190022788	0.008657437	10
	8	AK2	0.226688698	0.004772103	8
	9	cDNA.FLJ33617.fis	-0.148080058	0.035460329	8
	10	hsa-miR-520c-3p	0.535275739	0.001107214	7
	11	PDCD4	-0.175124522	0.005960906	5
	12	YWHAG	0.308948259	0.017484542	5

Transcript		Regulator	Coef	p value	Frequency
PRDX2	1	treat	NA	NA	35
	2	hsa-miR-423-5p	-0.610144465	0.000974561	22
	3	hsa-miR-484	-0.482896512	0.03079483	21
	4	BCL11B	0.112394938	0.035622828	15
	5	hsa-miR-30a-5p	-0.51454322	0.039371185	11
	6	ARHGAP1	0.323878962	0.005133937	10
	7	hsa-miR-765	-0.362546118	1.62E-05	7
	8	hsa-miR-513a-5p	-0.258202799	0.078106707	6
	9	GALNT2	-0.074122283	0.075282805	5
	10	HNRNPH1	0.655477345	0.002638396	5
	11	hsa-miR-518e-5p	-0.592270379	0.020461495	5
SLC26A2	1	treat	NA	NA	35
	2	DDX3X	0.249790798	0.012284202	9
	3	EIF4A1	0.68320612	0.016421443	9
	4	hsa-miR-29b-1-5p	0.701267497	0.007494958	5
	5	PLIN2	0.41657057	0.045403908	5
HDAC2	1	treat	NA	NA	35
	2	DNM1L	0.058735475	0.008674958	14
	3	COPE	-0.083179279	0.009995742	12
	4	hsa-miR-516a-5p	-0.612405984	0.022204252	11
	5	CCDC109A	-0.091952684	0.027020238	9
	6	cDNA.FLJ33617.fis	-0.064346558	0.03901038	8
	7	RPL15	0.105087576	0.000166247	8
	8	SERPINC1	-0.090150121	0.015500689	7
	9	AKR7A2	-0.075695912	0.00831633	6
	10	ACAD9	-0.051561724	0.076570871	5
	11	hsa-miR-936	0.164944441	0.006939736	5
	12	SPAG17	0.07579108	0.012959292	5
HSPB1	1	treat	NA	NA	35
	2	hsa-miR-520c-3p	1.19222175	0.002187348	20
	3	SPINT1	0.247832824	0.004601156	18
	4	hsa-miR-30a-5p	-1.808504632	0.001932845	10
	5	hsa-miR-23a-5p	1.129700484	0.003616775	8
	6	TXNRD1	0.840884403	0.000210944	8
	7	NDRG1	-0.293373492	0.00620769	7
	8	EGFR	0.610645502	0.045800047	6
	9	EPS8L2	0.149271726	0.030103576	6
	10	HDAC1	0.287166152	0.027243632	6
	11	LMNA	0.622295565	0.035826275	6
	12	HIBCH	-0.188574117	0.00314395	5
	13	hsa-miR-520b	1.432934745	0.008314063	5
	14	M6PR	0.241618325	0.008677556	5
	15	UBA2	0.169884517	0.03718694	5
JUP	1	HSPA5	-0.662234684	0.001341621	28
	2	TRIM28	0.296428801	2.34E-05	20
	3	ERO1L	-0.164105558	0.000411628	17
	4	hsa-miR-520c-3p	0.446676878	0.010872103	14
	5	HSP90AB3P	0.800290778	1.93E-05	10
	6	hsa-miR-936	0.270738091	0.038202412	6
	7	LDHA	-0.253025894	0.00037072	6
	8	ATP6V1B1	0.169972541	0.002090158	5
	9	AUTS2	-0.143682127	0.056788432	5
	10	G3BP1	0.17014745	0.005036805	5
	11	hsa-miR-520f	0.457827734	0.001938249	5
SMS	1	CALU	-0.199323401	0.006297874	26
	2	hsa-miR-29b-1-5p	-0.41410781	0.000398676	18
	3	LMNB1	-0.31560583	0.004140867	16
	4	CBX2	0.2088564	0.004897722	12
	5	HDAC2	-0.157520258	0.006697803	7
	6	HIST1H1B	0.205136922	0.028655419	6
	7	MYO15A	-0.196436332	0.019015553	6

Transcript		Regulator	Coef	p value	Frequency
ETFDH	1	TMEM109	0.135383428	0.002396943	26
	2	RASA1	0.390561879	5.85E-07	13
	3	treat	NA	NA	11
	4	NUP93	0.136857015	0.004009673	10
	5	ALDOA	-0.455685378	0.000187965	9
	6	CD1A	0.109047926	0.023880891	8
	7	RBM47	0.127233956	0.006759666	6
	8	AKAP13	0.132427756	0.008145965	5
	9	GMPS	0.128254702	0.011795479	5
	10	HSP90B1	-0.402878845	9.04E-06	5
	11	HYOU1	-0.16713191	0.000210343	5
TXNRD1	1	treat	NA	NA	35
	2	hsa-miR-210	-0.473617123	0.000811072	21
	3	ATP5A1	0.640864093	0.042103681	13
	4	HMGA1	0.155514555	0.000127634	9
	5	TM9SF4	0.219199586	0.001100275	8
	6	UBE2N	0.242779687	0.008586723	8
	7	GARS	-0.169412279	0.008022145	7
	8	HMOX1	0.107958653	0.004123516	7
	9	hsa-miR-365a-3p	-0.545837998	0.002077529	7
	10	HK2	-0.121425481	0.020348557	6
	11	hsa-miR-224-5p	0.525253829	0.003424663	5
	12	HSP90AB1	0.271591949	0.015331456	5
HMOX1	1	hsa-miR-622	0.446698577	0.000646128	18
	2	treat	NA	NA	13
	3	hsa-miR-210	-0.488063099	2.87E-06	11
	4	ETF1	0.259689232	0.001875449	9
	5	hsa-miR-186-5p	-0.650776839	0.00946294	9
	6	PSMD3	0.836733455	0.001729684	8
	7	FN1	-0.183100212	0.00197009	6
	8	SOD1	0.234128471	0.03167573	6
	9	MPP1	0.262052784	0.0006189	5
PDCD4	1	treat	NA	NA	34
	2	PON2	-0.24410777	0.000176441	29
	3	MYLK	0.14234965	0.031513611	18
	4	ANXA11	-0.288233725	0.00708159	8
	5	HSPA6	0.183022031	0.003666425	7
	6	VTN	-0.203887241	0.002859198	6
	7	ACSL3	-0.129454029	0.051051511	5
	8	HYOU1	-0.12402079	0.08875632	5
GNS	1	treat	NA	NA	31
	2	hsa-miR-519b-3p	-0.594391554	0.001294295	24
	3	FN1	0.082746094	0.004328338	11
	4	ATP5A1	-0.477457723	0.004400721	10
	5	CSDA	-0.122487724	0.001661029	10
	6	HNRNPA3	-0.087147267	0.015134765	10
	7	RTN4	-0.136382348	0.03072082	8
	8	hsa-miR-17-5p	-0.631226407	0.000368272	7
	9	HBB	0.132361503	0.001476269	5
TES	1	hsa-miR-29b-1-5p	-0.33203703	0.00021879	19
	2	EGFR	-0.509877069	0.00149395	16
	3	TXNRD1	-0.207089826	0.000809936	16
	4	hsa-miR-574-3p	0.193493549	0.003072657	15
	5	LMNA	-0.342987731	0.006618406	13
	6	SNX2	-0.175354254	0.025604038	11
	7	EIF3A	-0.320252228	0.00018524	9
	8	GBP1	-0.151130849	0.002281851	9
	9	HIBCH	0.117673772	0.006076335	8
	10	ALPP	-0.119686919	0.001234166	6
	11	hsa-miR-125a-5p	-0.360942839	0.00583041	5
	12	treat	NA	NA	5

Transcript		Regulator	Coef	p value	Frequency
CYP11A1	1	treat	NA	NA	35
	2	EPS8L2	0.222463627	0.001409013	23
	3	PLIN2	0.525256625	0.023515407	14
	4	SRP72	0.232351754	0.007895791	10
	5	HSPA4	0.691396894	0.000145318	8
	6	RASA1	0.474482027	0.006416773	6
	7	hsa-miR-371a-3p	0.598675522	0.003037481	5
ALPP	1	treat	NA	NA	28
	2	hsa-miR-1249	-0.666325456	0.012428561	15
	3	MAPK1	0.168026191	0.068710702	9
	4	JUNB	0.257124841	0.024509954	8
	5	ERAP1	0.417485017	0.000830132	7
	6	hsa-miR-877-5p	0.514545727	0.000565534	7
	7	hsa-miR-518e-5p	1.802731756	0.000104309	5
SLC7A5	1	treat	NA	NA	30
	2	MCM4	0.105491842	0.038889673	15
	3	CYCS	-0.149390593	0.007217993	14
	4	HBB	-0.136905583	0.007300326	14
	5	hsa-miR-149-5p	0.3777459	0.002622374	11
	6	hsa-miR-27b-3p	1.147205276	0.016693139	10
	7	hsa-miR-221-3p	0.49600699	0.001283059	8
	8	PDIA6	-0.703508778	0.002923769	7
	9	EIF4A1	0.412771656	0.011899114	6
	10	hsa-miR-1202	0.168653486	0.017442542	5
	11	LMNA	0.389043049	0.00268523	5
FN1	1	treat	NA	NA	34
	2	hsa-miR-345-5p	-0.828634157	0.00027412	21
	3	cDNA.FLJ55918	-0.198206938	0.013754116	17
	4	HSPA9	-0.802471937	0.00041362	14
	5	hsa-miR-30a-5p	0.886889813	0.017134796	12
	6	hsa-miR-575	-0.489066178	0.000128317	8
	7	EML5	0.181513115	0.040987614	6
	8	hsa-miR-524-3p	1.30392626	0.023093978	6
	9	DEK	-0.208956514	0.004634389	5
	10	hsa-miR-518d-3p	0.421356113	0.081367856	5
	11	hsa-miR-572	-0.655163361	9.45E-06	5
FTH1	1	PDXDC1	-0.128868302	0.000179016	25
	2	hsa-miR-130b-3p	0.232913429	0.001462488	22
	3	hsa-miR-524-3p	0.650940826	9.49E-05	13
	4	hsa-miR-424-3p	-0.324823899	0.00016448	11
	5	hsa-miR-423-5p	0.411060846	0.000161793	9
	6	hsa-miR-523-3p	-0.288074124	0.000214593	7
	7	RAB1B	-0.078583539	0.006432884	6
	8	hsa-miR-518d-3p	0.353097159	0.001819607	5
	9	LGALS3BP	0.100068078	0.019330671	5
	10	SYNGR2	0.102396452	0.003023531	5
HSD3B1	1	treat	NA	NA	35
	2	hsa-miR-141-3p	-1.463565808	0.006584373	16
	3	DDX3X	0.308187527	0.016780789	10
	4	hsa-miR-1249	-0.639952084	0.054267949	6
	5	hsa-miR-24-3p	2.319732363	0.012049521	5
	6	SLC25A6	0.470225209	0.053700353	5
MX1	1	treat	NA	NA	35
	2	hsa-miR-30a-5p	3.183298676	0.004111611	12
	3	hsa-miR-503	-1.06350739	0.000339466	9
	4	HNRNPC	0.417544717	0.053181932	8
	5	hsa-miR-30d-5p	3.366756959	3.64E-05	8
	6	hsa-miR-224-5p	1.147993397	0.064727179	7
	7	GNPDA1	-0.323892153	0.084058469	5
	8	hsa-miR-664-3p	1.373489876	0.00085164	5
	9	KIF5B	0.333760252	0.006892938	5

Transcript		Regulator	Coef	p value	Frequency
WARS	1	treat	NA	NA	28
	2	hsa-miR-23a-5p	-1.246769032	0.005251291	20
	3	hsa-miR-520c-3p	-0.781952957	0.009287224	18
	4	RBM15B	-0.378847964	0.001003567	14
	5	NDRG1	0.241793332	0.056115667	13
	6	EPS8L2	-0.159073305	0.024279662	10
	7	HSP90B2P	0.400833746	0.008160342	9
	8	AP2A1	-0.73455242	0.002460028	6
	9	EIF3A	-0.478778086	0.004005548	6
	10	hsa-miR-516a-5p	2.770173324	0.001040959	5
CTSB	1	CLINT1	-0.268227445	2.61E-05	29
	2	NADH4	-0.208530014	0.000236952	17
	3	MGA	-0.255729363	0.000673547	14
	4	MROH2A	-0.157003697	0.010872142	11
	5	KIAA1632	-0.136339712	0.016701308	9
	6	SLC25A3	-0.491304068	0.000967033	9
	7	AFP	-0.168006731	0.001719096	8
	8	CAPN1	0.273322119	0.012930539	8
	9	KIAA1109	-0.171876279	0.004040876	6
	10	SSB	0.300815201	0.001539627	6
	11	LAP3	-0.116771895	0.026763422	5
CYP19A1	1	treat	NA	NA	35
	2	SLC26A2	0.516194078	0.004426267	15
	3	LCP1	-0.426063353	0.002216689	12
	4	YWHAG	0.577472061	0.006149776	9
	5	ERO1L	0.282118259	0.013202949	6
	6	hsa-miR-29c-3p	-1.428515581	0.017263437	5
CLIP1	1	treat	NA	NA	33
	2	HSP90B1	-0.354592532	0.001378079	19
	3	PLIN2	0.195407561	0.009938748	14
	4	EIF4A1	0.323528119	0.012275737	13
	5	ATP5O	0.099558219	0.001632121	10
	6	SLC25A6	0.288512387	0.00139851	10
	7	DFNA5	0.129661631	0.00214938	7
	8	GNAQ	0.129199339	0.00155141	7
	9	hsa-miR-30b-3p	0.24734614	0.024705033	5
	10	LCP1	-0.08970833	0.033941056	5
PKP2	1	treat	NA	NA	35
	2	CYP19A1	-0.180164545	0.002952302	18
	3	hsa-miR-483-3p	0.519780615	0.014366428	16
	4	PCCB	0.225606062	0.013422772	14
	5	SEC23A	-0.118764813	0.068728256	9
	6	PDS5A	-0.141399505	0.025958861	6
CAPN6	1	HSPA5	-1.46072043	5.80E-06	20
	2	HSPA4	0.748717109	0.00433449	13
	3	SRP72	0.415626427	0.007369661	11
	4	hsa-miR-516a-3p	1.24789168	0.000308408	10
	5	EPS8L2	0.309643781	0.000457198	7
	6	EML2	0.378183025	0.001480636	6
	7	AP2A1	0.628860257	0.007183469	5
	8	CLIC3	0.383373358	8.49E-06	5
CTSL1	1	RPL7A	0.245374904	0.001965598	26
	2	SLC7A5	0.276294904	0.000125911	23
	3	RPS27A	-0.192522444	0.050492056	10
	4	CYP11A1	0.212878248	8.95E-09	8
	5	hsa-miR-372	0.28178393	0.000341186	7
	6	DAB2	0.192819266	1.17E-05	6
	7	TFRC	0.470686118	0.000865538	6

Transcript		Regulator	Coef	p value	Frequency
CD63	1	treat	NA	NA	35
	2	LAMB4	0.185976938	0.000313027	19
	3	EIF4G2	0.094162365	0.013658187	16
	4	GSS	-0.10700955	0.011507687	12
	5	hsa-miR-224-5p	0.352857829	0.034784404	8
	6	hsa-miR-141-3p	-0.795862438	4.42E-05	6
	7	hsa-miR-484	-0.589220929	0.006478649	6
	8	IRS2	0.065687266	0.026829338	6
STAT1	1	treat	NA	NA	35
	2	hsa-miR-877-5p	0.421084943	0.001505402	10
	3	HMOX1	0.132877582	0.046931837	8
	4	hsa-miR-887	0.739938449	0.000142511	6
	5	PCNA	0.287116037	0.007948536	6
	6	PDIA4	-0.455985983	0.014016788	6
DAB2	1	treat	NA	NA	31
	2	hsa-miR-520f	0.742632867	0.002407225	30
	3	EGFR	0.877373347	0.001512644	26
NDRG1	1	treat	NA	NA	35
	2	PCBP1	-0.205870212	0.009840714	12
	3	cDNA.FLJ54153	-0.163680137	0.024138803	11
	4	HSD3B1	-0.136727928	0.032325922	6
PLIN2	1	treat	NA	NA	34
	2	CTNND1	-0.380550788	0.017870263	27
	3	CD180	-0.170069628	0.019180942	14
	4	hsa-miR-564	0.3881301	0.003696665	14
	5	GALNT2	0.166399649	0.007816986	11
	6	TPP2	0.111465555	0.019149622	9
	7	hsa-miR-519c-3p	1.08234356	0.016016674	6
	8	hsa-miR-663a	0.207251819	0.023851959	6
	9	GPI	-0.385242471	0.036306996	5
	10	hsa-miR-671-5p	0.278289537	0.043294034	5
GDF15	1	treat	NA	NA	35
	2	hsa-miR-193b-5p	-0.717108263	0.002766301	30
	3	HNRNPC	0.18555061	0.017054156	19
	4	IGF2BP3	0.138984184	0.046527439	15
	5	hsa-miR-365a-3p	-0.506327953	0.008028915	11
	6	DAB2	0.168548348	0.00677274	8
	7	FAM115C	-0.139416536	0.010236875	8
	8	GPI	-0.554266505	0.014884484	8
	9	hsa-miR-193b-3p	-0.63940874	0.001037938	8
	10	hsa-miR-224-5p	0.638239815	0.001867444	8
	11	hsa-miR-372	0.184325959	0.036400087	6
	12	DSP	-0.196740395	0.000396466	5
	13	TM9SF2	0.117664439	0.019884929	5
EPS8L2	1	treat	NA	NA	32
	2	ARPC1B	-0.217389147	0.0024312	11
	3	RAB1B	-0.161778511	0.010082809	8
	4	hsa-miR-141-3p	-0.739413928	0.01271383	6
	5	11-Sep	-0.147845877	0.024823025	6
	6	GSS	-0.176941428	0.002819122	5
	7	SFPQ	0.630121712	0.006517264	5